THE CARB-APPROPRIATE REVIEW

A MONTHLY RESEARCH REVIEW BY

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ABOUT CLIFF

Cliff Harvey PhD(c) is an author, clinician, and researcher. He was one of the first clinical nutritionists to begin working with ketogenic and low-carb diets, way back in the 1990s and is also considered a pioneer in the area of mind-body integrative healthcare.

Cliff's early post-graduate work was in mind-body healthcare, while his master's research focussed on medium chain triglycerides, 'keto-flu' and ketogenesis, and his doctoral thesis investigated individualisation of dietary prescription and 'carbohydrate tolerance'.

He is a former world champion strength athlete, submission grappler, and author of several best-selling books.

THIS MONTH

KETO-FLU, KETOGENESIS, AND CARB-TOLERANCE... A SUMMARY OF OUR RESEARCH

Key Findings:

- Medium chain triglycerides (MCTs) resulted in fewer symptoms of Keto-flu when compared to control oil.
- The amount of carbohydrate restriction only had a trivial effect on increasing symptoms of keto-flu.
- Very-low-carbohydrate diets were typically tolerated well and resulted in a range of self-reported health benefits, but results varied considerably between individuals.
- There were greater improvements in measures of health from a greater restriction of carbohydrate
- The benefits from greater restrictions of carbohydrate appeared to be greatest for those with poorer baseline measures of cardiometabolic health
- There might be a 'tipping point' of ketones at ~1-1.4 mmol/L βOHB for improvement of mood and symptoms during keto-induction

Low-carb diets and ketogenic diets are becoming increasingly popular for both lifestyle reasons and for the improvement of health and performance. However, there is little evidence for the superiority of keto- vs less restrictive low-carb approaches in the research. Greater carbohydrate restriction does provide additional benefits for some outcome measures like glucose, triglycerides (TG), and high-density lipoprotein cholesterol (HDL-c). There are also specific benefits from keto-diets and the levels of blood ketones they produce, including reduced inflammation, inhibited tumour growth (n some cancers), reduction in neurodegeneration, and increased metabolic flexibility.

But, despite the benefits and popularity of keto, there is surprisingly little consensus in the published research on what nutritional ketosis (NK) *actually is*!

There is also a complete lack of research on the time taken to achieve the common benchmark of nutritional ketosis (≥ 0.5 mmol/L beta-hydroxybutyrate (BOHB)) and on the symptoms of carbohydrate-withdrawal commonly described in mainstream media as 'keto-flu'. Dietary supplements and methods to improve ketonaemia (blood ketone levels), time-to-NK, and symptoms of carbohydrate withdrawal and mood during keto-induction are similarly not well understood.

> Throughout my masters and doctoral research, my team and I provided, for the first time, a synthesis of research related to the time it takes for people to achieve ketosis

Throughout my masters and doctoral research, my team and I provided, for the first time, a synthesis of research related to the time it takes for people to achieve ketosis and highlighted that there were no studies that had specifically evaluated adverse effects specifically during keto-induction.

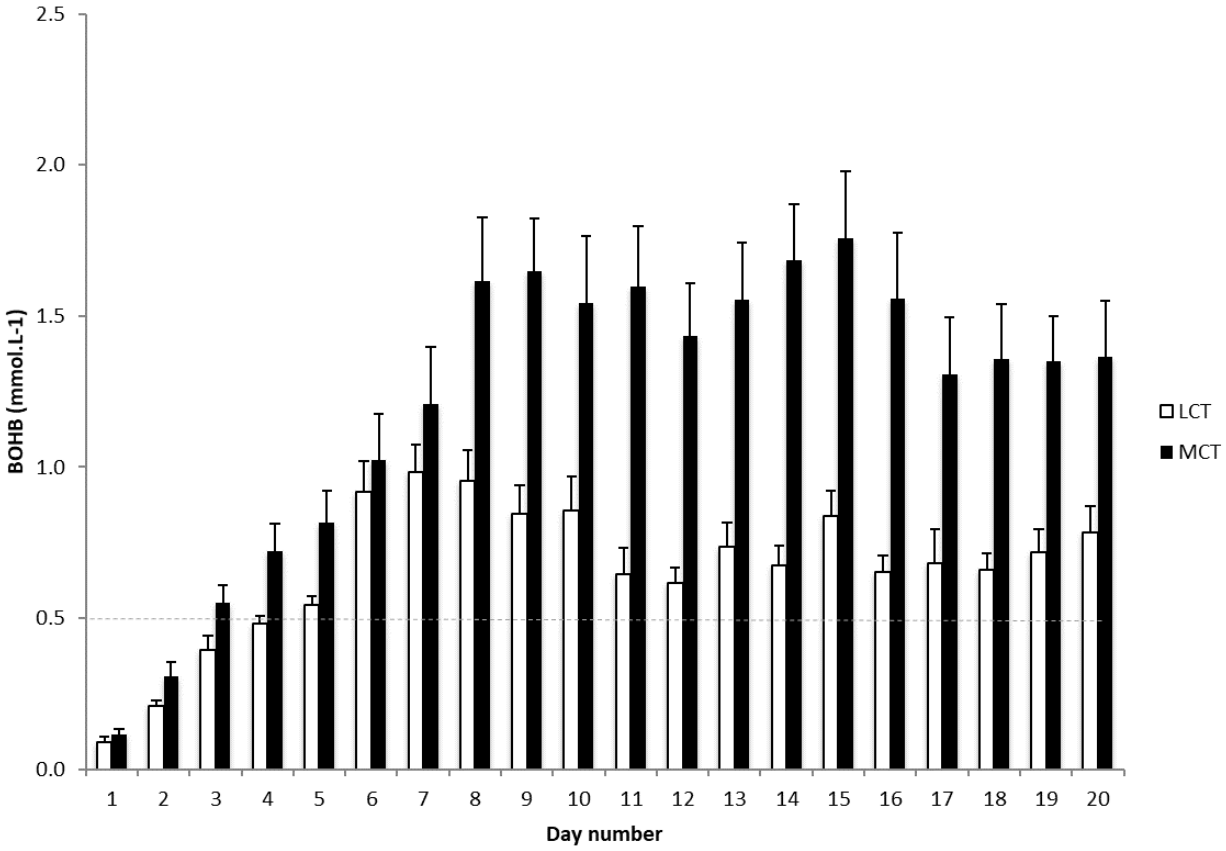
Which supplements are ketogenic?

Our review on the use of supplements to initiate ketosis showed that there is a clear ketogenic effect of supplementing with medium-chain triglycerides (MCTs) and possibly an even greater effect resulting from shorter-chain fatty acids like butyric acid, although this is by no means proven. However, the ketogenic effect of other supplements was unclear. It was also clear that although not increasing ketogenesis directly (i.e. the internal creation of ketones in the body), there was a clear and substantial effect of exogenous ketone supplements on ketone levels and that any inhibition of internal ketone production by exogenous ketones, is minimal.[1]

Do MCTs result in faster ketosis with fewer side-effects?

To understand the effect of increased ketonaemia on the time take to achieve ketosis and on symptoms of carbohydrate withdrawal, and mood, we performed a randomised controlled trial comparing the use of MCTs in a 'classic' ketogenic diet providing at least 80% calories from fat to a control diet (with the same amounts of all macronutrients) but supplemented with a long-chain dominant fat (sunflower oil) as a control.[2]

MCT supplementation resulted in higher BOHB at all time-points, and faster time-to-ketosis, but these results failed to reach statistical significance.

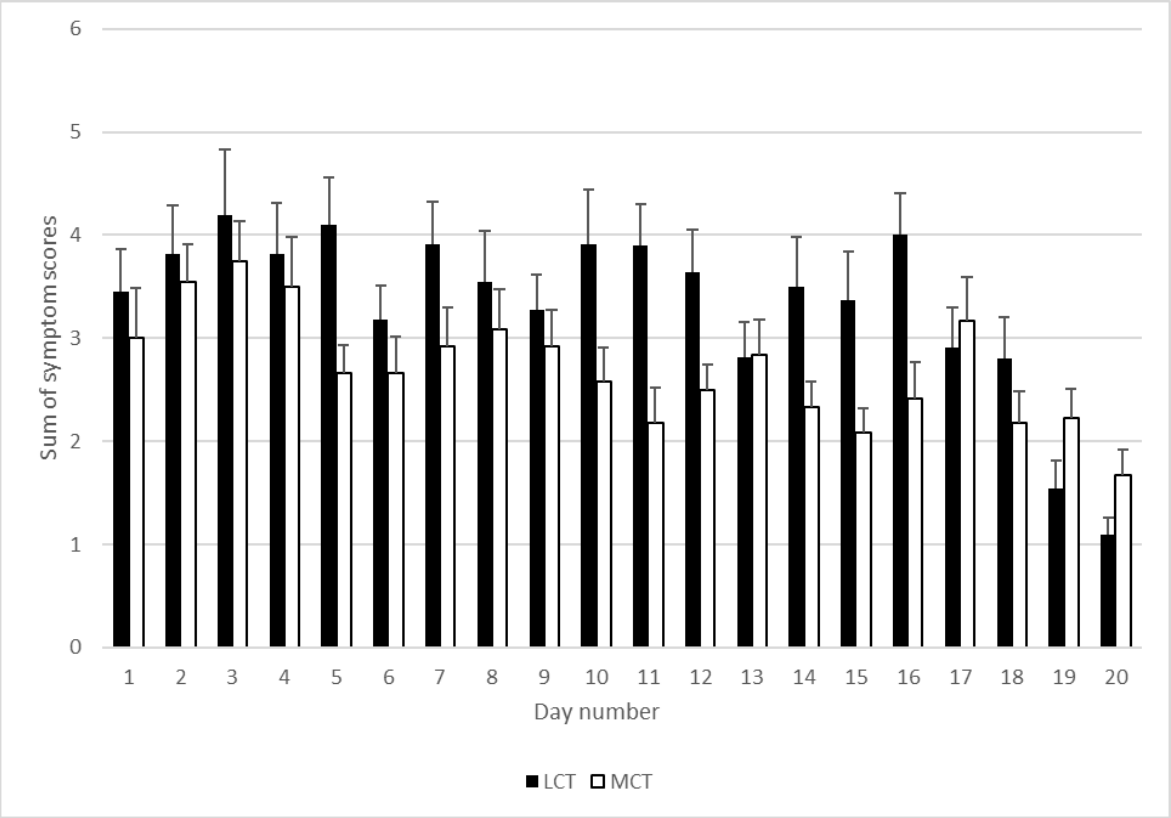


1. BOHB in a keto-diet with MCT or Sunflower Oil

Symptoms of keto-flu overall were greater in the control group, except for abdominal pain, which occurred with greater frequency and severity in the MCT-supplemented diet (a known side-effect of high-dose MCT supplementation.

Note that in this study we used 30 ml of MCT [2 x Tbsp.] three times per day!

There was also a likely benefit on symptoms of keto-flu from taking MCT but the effect on mood was *unclear.*



2. Symptoms of keto-induction (Keto-Flu) in a keto-diet using either MCT or Sunflower Oil

Based on these results, there was a clear effect of MCTs on blood ketone levels and a likely effect on symptoms of keto-flu.

How did people 'feel' on a keto-diet?

Very little research has been conducted on people's subjective experiences of diet. The study of this is incredibly important because if we are to properly understand diet and prescribe, based on holistic effects, we need to know how people feel!

We analysed this in a *qualitative* study. We identified our participants subjective mood and experiences related to the ketogenic diet from daily diary entries and focus group findings.

Despite some initial challenges with the diet, especially gastrointestinal effects (mostly related to high levels of MCTs!), the overall perception of the diet was positive.

There were appreciable benefits for wellbeing, mood, sleep, and sugar cravings reported, with negative experiences decreasing as participants adapted to the keto-diet.[3]

> These findings suggested that the overall experience of a VLCKD is positive but varies markedly between individuals.

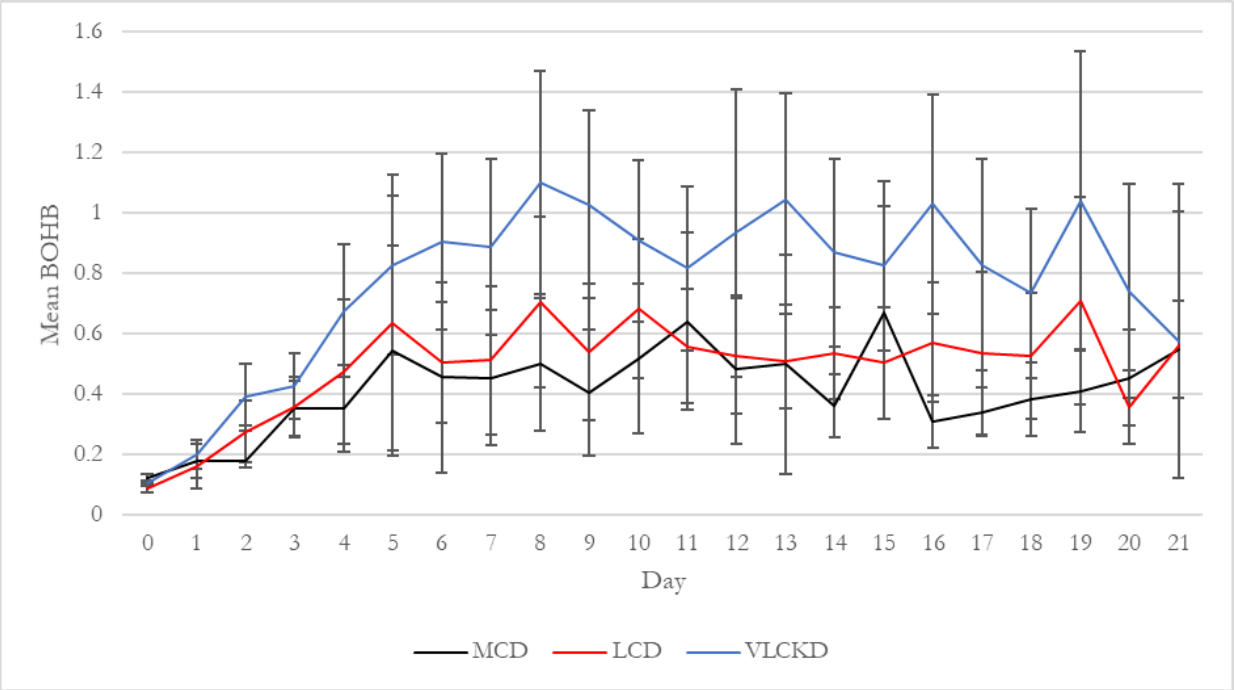
The preceding studies suggested that increased ketonaemia might positively affect symptoms of carbohydrate withdrawal during keto-induction, and mood, but it is unclear whether diets differing in carbohydrate content and resulting in differing levels of ketonaemia would elicit similar effects.

Ketosis and keto-flu in non-keto low-carb diets

The final study of this collective body of work was a randomised clinical trial comparing a ketogenic diet, a low-carb diet and moderate-low-carb diet consisting of 5%, 15%, and 25% of total energy (TE) from carbohydrate respectively, over 12 weeks.[4] The first three weeks of this study was used to compare blood ketones, symptoms of carbohydrate withdrawal (keto-flu), and mood between the dietary intervention groups.

Average blood levels of ketones (BOHB) were increased by 0.27 ± 0.32, 0.41 ± 0.38, and 0.62 ± 0.49 mmol/L for the moderate, low, and very-low-carb groups respectively ($p = 0.013$).

Ketosis was achieved consistently for both the keto-, and low-carb groups and sporadically for people in the moderate-low carb group.

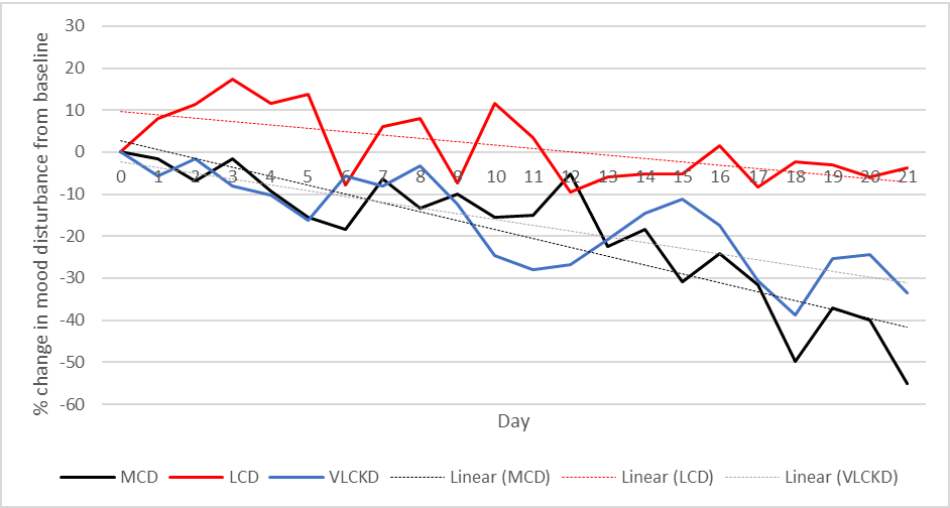


3. Average ketone levels by day between groups. Note: 'ketosis' is > 0.5 mmol/L

Overall, symptoms of 'keto-flu' between the groups were trivial, and while symptoms were increased most in the keto-diet group the differences between all groups were small and non-significant. Only halitosis (p = 0.039) and muscle weakness (p = 0.005) differed significantly between the groups with the largest effects seen in the keto-diet group.

Mood improved significantly from baseline

Mood improved significantly overall, with no significant difference between groups.



4. Change in mood disturbance by diet group. Note: a downward trend indicates less mood disturbance and better mood.

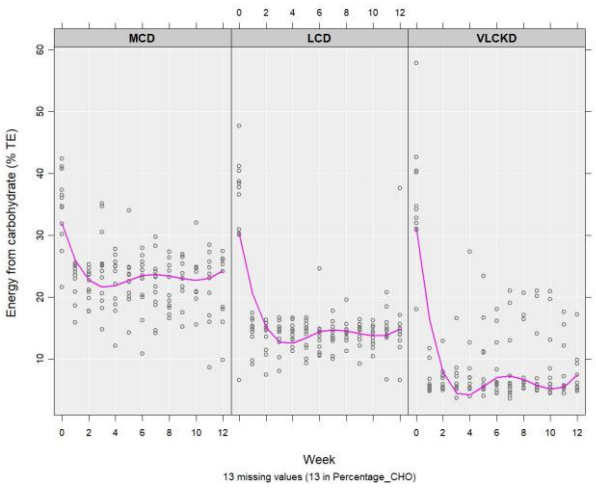
In perhaps the most interesting finding, although participants were instructed to maintain their habitual energy (calorie) intake, some people did restrict their eating. When calorie restriction DID occur, it was strongly associated with keto-flu. So, this suggests that any restriction of carbohydrate, not just 'keto' diets, if calorie-restricted can result in what was previously thought to be the 'keto-flu'. I.e. it might have more to do with energy restriction, rather than just being from drastic carb-restriction.

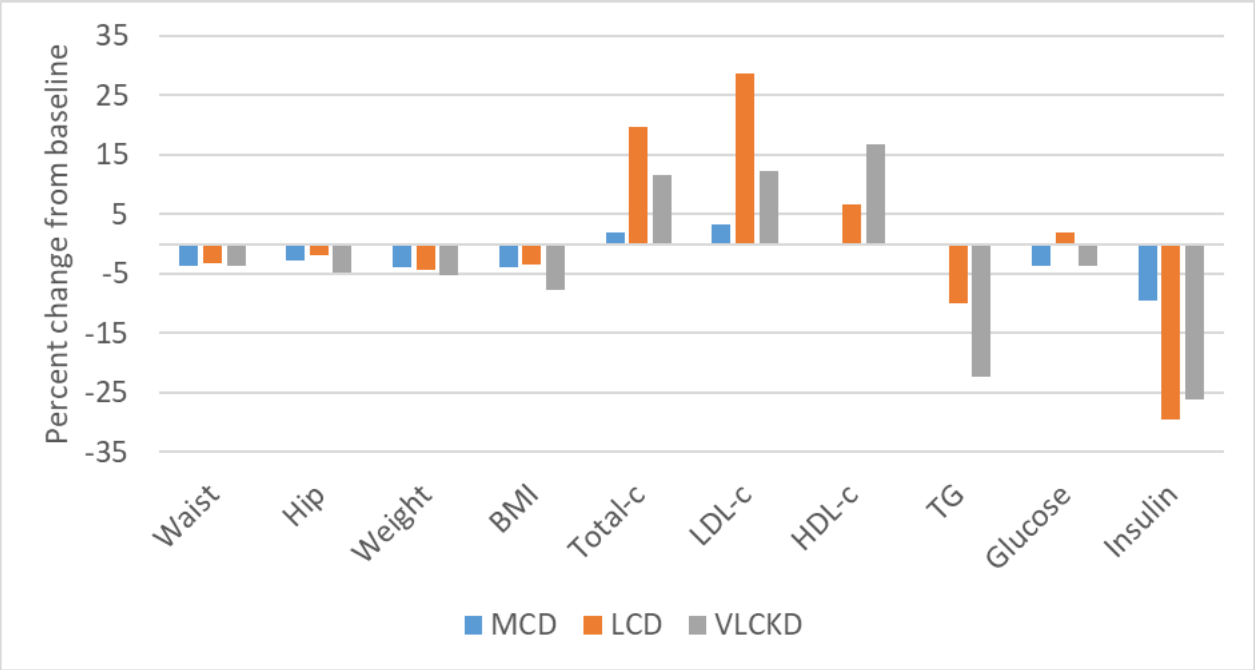
There were only small differences observed between symptoms of carbohydrate withdrawal and mood between the diets ranging from 5-25% TE from carbohydrate

Which diet performed best overall?

In completers of our 12-week study, there were significant reductions in triglycerides ('fat in the blood'), weight, and body mass index and increases in HDL, LDL, and total cholesterol.

It was more difficult for those in the VLCKD group to achieve the carbohydrate allocation of 5% calories from carbs, whereas those in the moderate-, and low-carb groups achieved their allocations more easily. Despite this, the positive effect on markers of health trended towards greater improvement from greater carbohydrate restriction with the largest improvements in HDL-c and triglycerides (perhaps THE most important of the health markers that we measured).





5. Percent change in health markers from very-low (keto), low-, and moderate-low carb diets.

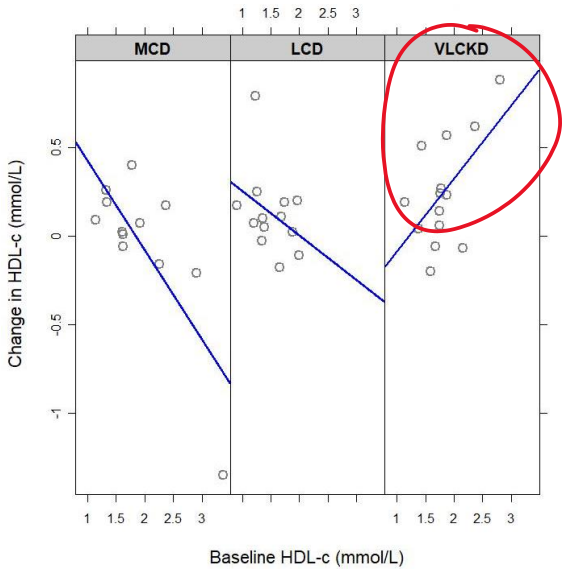
What was the effect of baseline metabolic health?

Outcomes from lower- or higher-carbohydrate diets might be predicted by baseline metabolic health (i.e. how metabolically 'disordered' someone is).

Because adverse effects like keto-flu and mood differed by only a small amount between the diets, we also compared the effect of baseline cardiometabolic measures (lipid and other blood panels) on results, compared to the diet allocation.

Participants with 'poorer' baseline measures benefitted most from greater carbohydrate restriction, with 7 of 11 measures improved most by a keto-diet. If these results were purely due to chance, we would only expect 3 or 4 of the measures to be most improved by keto.

Only HDL reached significance and initially indicated that poorer baseline (lower) HDL was more likely to be improved by a moderate carb restriction. On closer examination, it was seen that HDL worsened in as many people (only two in each group) regardless of diet, and the keto group had the greatest improvements in HDL overall.



This was the first study to compare a keto-diet to a low-carb diet and a more moderate restriction.

Although the effects need to be confirmed in research with larger numbers, the findings suggest that those with poorer baseline measures of cardiometabolic health might benefit most from greater carbohydrate restriction.

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IN THE LITERATURE

Two days of calorie deprivation impairs high level cognitive processes, mood, and self-reported exertion during aerobic exercise: A randomized double-blind, placebo-controlled study

https://www.sciencedirect.com/science/article/pii/S0278262618304597

Abstract

Military personnel and emergency responders perform cognitively demanding tasks during periods of sustained physical exertion and limited caloric intake. Cognitive function is preserved during short-term caloric restriction, but it is unclear if preservation extends to combined caloric restriction and physical exertion. According to the "reticular-activating hypofrontality" model, vigorous exertion impairs prefrontal cortex activity and associated functions. This double-blind, placebo-controlled, crossover study examined cognitive function during sustained exertion while volunteers were calorically deprived. Twenty-three volunteers were calorie-depleted for two days on one occasion and fully fed on another. They completed intermittent bouts of exercise at 40–65% VO_{2peak} while prefrontal cortex-dependent tasks of cognitive control, mood, and perceived exertion were assessed. Calorie deprivation impaired accuracy on the task-switching task of set-shifting ($p < .01$) and decreased sensitivity on the go/no-go task of response inhibition ($p < .05$). Calorie deprivation did not affect risk-taking on the Rogers risk task. During exercise, calorie deprivation, particularly on day 2, increased perceived exertion ($p < .05$) and impaired mood states of tension, depression, anger, vigour, fatigue, and confusion (all $p < .01$). Physical exertion during severe calorie deprivation impairs cognitive control, mood, and self-rated exertion. Reallocation of cerebral metabolic resources from the prefrontal cortex to structures supporting movement may explain these deficits.[5]

Comment

A lot of people were freaking out about this study over the last couple of months. Fasting-haters were loving it...and fasting-devotees were floundering.

In reality, the study doesn't show a lot.

Increased perceived exertion

The only significant results were found on day two of the fast, after 60 min of exercise. The difference in perceived exertion, even though *statistically significant* ($p = 0.030$) was less than 1 on the Borg scale!

The fed group at 65 min on the day two exercise bout had an RPE of 14.23 vs the fasted group with 14.36.

So, there is practically no difference… whatsoever!

Borg's Rating of Perceived Exertion (RPE) Scale	
Perceived Exertion Rating	Description of Exertion
6	No exertion; sitting and resting
7	Extremely light
8	
9	Very light
10	
11	Light
12	
13	Somewhat hard
14	
15	Hard
16	
17	Very hard
18	
19	Extremely hard
20	Maximal exertion

Mood state

There were appreciable differences in mood-state that were most evident on day-2 of the fast and were both meaningful and significant for Tension, Depression, Anger, Vigour, Fatigue, Confusion, and for total mood disturbance.

Task-switching tests

The accuracy of results did not differ meaningfully between groups. Again, there was a *significant* effect observed (a reduction in accuracy from fasting) but the effect size was trivial. Response time was not affected by fasting. No other significant or meaningful effects of fasting were observed.

What does this all mean?

It's common sense that being calorie-restricted can affect function. This is well-known and should not surprise anyone. However, the effect of fasting on function is actually quite trivial and overall, if you are fasting for health effects, you should simply be aware that you may not function at your full capacity for the time that you are fasting, although, the difference may be so small that you don't notice it!

The main effect is on mood and emotions and this is something that people embarking on fasting should be aware of.

It also seems clear from our clinical observations that those who are habituated to fasting and are more 'fat-adapted' typically do not suffer the same negative effects that others might when embarking on a fast.

Ultra-Processed Diets Cause Excess Calorie Intake and Weight Gain: An Inpatient Randomized Controlled Trial of *Ad Libitum* Food Intake

https://www.cell.com/cell-metabolism/fulltext/S1550-4131(19)30248-7

Abstract

- 20 inpatient adults received ultra-processed and unprocessed diets for 14 days each
- Diets were matched for presented calories, sugar, fat, fibre, and macronutrients

- *Ad libitum* intake was ~500 kcal/day more on the ultra-processed versus unprocessed diet
- Body weight changes were highly correlated with diet differences in energy intake

We investigated whether ultra-processed foods affect energy intake in 20 weight-stable adults, aged (mean ± SE) 31.2 ± 1.6 years and BMI = 27 ± 1.5 kg/m^2. Subjects were admitted to the NIH Clinical Centre and randomized to receive either ultra-processed or unprocessed diets for 2 weeks immediately followed by the alternate diet for 2 weeks. Meals were designed to be matched for presented calories, energy density, macronutrients, sugar, sodium, and fibre. Subjects were instructed to consume as much or as little as desired. Energy intake was greater during the ultra-processed diet (508 ± 106 kcal/day; p = 0.0001), with increased consumption of carbohydrate (280 ± 54 kcal/day; p < 0.0001) and fat (230 ± 53 kcal/day; p = 0.0004), but not protein (−2 ± 12 kcal/day; p = 0.85). Weight changes were highly correlated with energy intake (r = 0.8, p < 0.0001), with participants gaining 0.9 ± 0.3 kg (p = 0.009) during the ultra-processed diet and losing 0.9 ± 0.3 kg (p = 0.007) during the unprocessed diet. Limiting consumption of ultra-processed foods may be an effective strategy for obesity prevention and treatment.

Comment

I think few people were surprised by these findings, well apart from a few IIFYM ('if it fits your macros') or energy-in/energy-out dogmatists.

The evidence is becoming clearer by the day that ultra-processed foods are the primary culprits for fat-gain and metabolic disorder. In fact, when we dig a little deeper into many of the cohort studies that claim to show the superiority of low-fat diets over low-carb, or that higher carb-intakes are worse than low, we actually see a different picture emerge – one of processed and refined foods being most associated with disease and early death.

For example, results from the PURE study seemed to show that high carb intakes were worse for us, and that total and saturated fat intakes were not associated with mortality outcomes,[6] on the other hand, just one year later, data from the ARIC cohort, published in the Lancet was claimed to show that low-carb diets increased the risk of early death and that a 'moderate' carbohydrate intake of around 55% calories from carbohydrate was best for health.[7]

What these studies really showed though, was that early death and disease rates were most worsened by diets that were high in processed and refined foods. In the ARIC cohort, for example, those eating both high and low-carbohydrate diets were at risk of early death. *Why was this?* 'Low-carbohydrate' diets in this observational study were not really low-carb diets. They were *lower* in carbohydrate because those people observed were choosing high-fat junk foods (think burgers, pizzas, fries etc.) that increased the relative amounts of fat and therefore lowered the proportion of

carbs from the diet, even though the diets were still relatively rich in carbs (~37%). Conversely, those eating a high-carb diet that was also associated with worse disease and mortality outcomes were more inclined to choose high-carb junk foods, relatively sparse in fat like added sugar, bakery goods, and candies, thus, they were eating higher-carb, lower-fat...but still junk...

What does this all mean?

The evidence is accumulating. Diets based on natural, unprocessed foods are superior to those based on added sugars, highly refined foods, and commercial altered fats. (Duh!)

We should strive to base our diets on a compendium of natural, unrefined foods for the vast majority of our food intake (with a little room left for treats 😉).

> At each meal, ask yourself: "Is at least 90% of my plate natural, unprocessed food?"

Meals should be based on meat, vegetables, and added healthy fats, with carbohydrate foods (also from natural, unrefined sources) added *according to your energy requirements!*

Diet and colorectal cancer in UK Biobank: a prospective study

https://academic.oup.com/ije/advance-article/doi/10.1093/ije/dyz064/5470096#133824902

Abstract

Background

Most of the previous studies on diet and colorectal cancer were based on diets consumed during the 1990s.

Methods

We used Cox-regression models to estimate adjusted hazard ratios for colorectal cancer by dietary factors in the UK Biobank study. Men and women aged 40–69 years at recruitment (2006–10) reported their diet on a short food-frequency questionnaire ($n = 475\ 581$). Dietary intakes were re-measured in a large sub-sample ($n = 175\ 402$) who completed an online 24-hour dietary assessment during follow-up. Trends in risk across the baseline categories were calculated by assigning re-measured intakes to allow for measurement error and changes in intake over time.

Results

During an average of 5.7 years of follow-up, 2609 cases of colorectal cancer occurred. Participants who reported consuming an average of 76 g/day of red and processed meat compared with 21 g/day had a 20% [95% confidence interval (CI): 4–37] higher risk of colorectal cancer. Participants in the highest fifth of intake of fibre from bread

and breakfast cereals had a 14% (95% CI: 2–24) lower risk of colorectal cancer. Alcohol was associated with an 8% (95% CI: 4–12) higher risk per 10 g/day higher intake. Fish, poultry, cheese, fruit, vegetables, tea and coffee were not associated with colorectal cancer risk.

Conclusions

Consumption of red and processed meat at an average level of 76 g/d that meets the current UK government recommendation (≤90 g/day) was associated with an increased risk of colorectal cancer. Alcohol was also associated with an increased risk of colorectal cancer, whereas fibre from bread and breakfast cereals was associated with a reduced risk.[8]

Comment

Will eating just one extra slice of bacon *really* increase my cancer risk?

The headline heard around the world was that "eating just one slice of bacon a day linked to higher risk of colorectal cancer".

This, like any other observational study, needs to be treated with some caution. While other factors like income, socio-economic factors, body mass, waist, alcohol, smoking and other factors were accounted for as potential confounders, this adjustment can never be accurate as we can never completely consider the effects on health, of a range of confounding influences—the body is simply too complex to do so.

So, *we need for there to be extremely strong evidence of harm* in these types of study to outweigh the potential of confounding and bias. This was not really seen in this study.

You can see in the hazard plot below that the effects are relatively small and most overlap '1'. This means that there is a likely positive effect for some people, negative for others, and so, we rely on the effect either being very large and/or for the 95% confidence intervals to be over 1 to indicate an effect that is more likely to be 'true'.

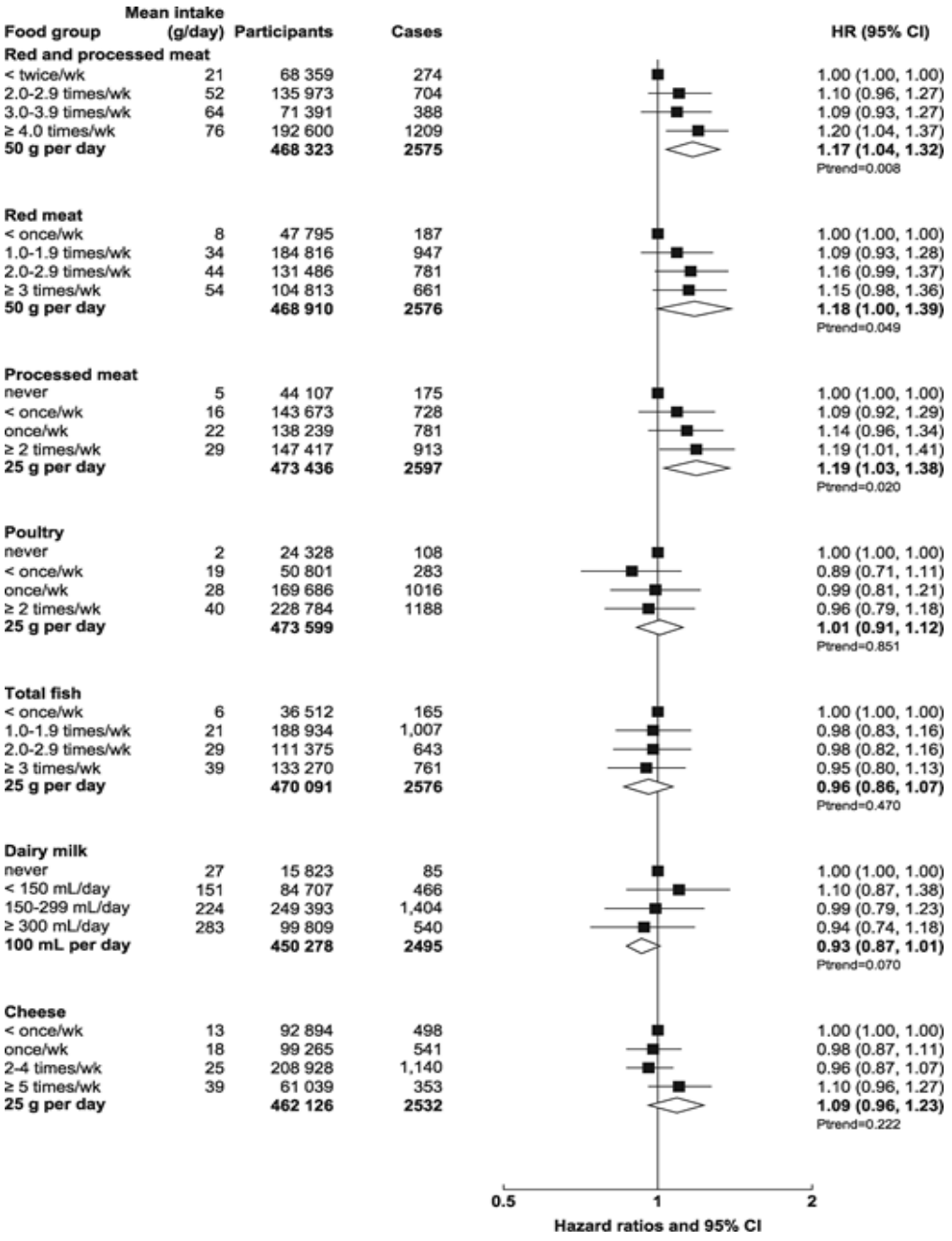
Interestingly, the authors did not publish any data on refined or processed food intake or on sugar intake, which we would suggest might have a much greater effect on outcomes than relatively small meat intakes.

In addition, if the effect were 'true' (of meat on colorectal cancer) we would expect to see it across cancer types and across demographic subsets. In this study, the effect was actually only seen in men with a trend towards reduced cancer rates in women (HR 0.94; 95% CI 0.73-1.19) at the highest levels of meat intake.

Could this be because of iron overload seen in men and not in women?

Or could it be that meat is actually protective for women?... Or simply that it is too difficult to determine much from these types of studies that rely on extremely equivocal data?

This potentially protective effect was even seen for processed meat in women!



It also does not 'pass the sniff test' when some cancers that would be expected to improve with reduced red or processed meat, do not. In this study, processed meat intake was associated with reduced risk of proximal colon cancer (HR 0.9; 95% CI 0.70-1.16) for every 25 g consumed.

It does not 'pass the sniff test' when some cancers that would be expected to improve with reduced red meat, do not.

What does all this mean?

Like most studies that have gone before on the topic of red meat, this study is extremely confounded, and the results are not strong enough to suggest that red meat is a carcinogen. Especially when we look at red meat in the context of a natural, unprocessed diet, high in vegetables and healthy fats, it is likely to be a healthy addition.

When we consider that the effect on cancer incidence and mortality was small, was not consistent across the types of colorectal cancer and that it was not consistent even across genders, we would have to say that at the very least, the study lacks veracity.

The take-home message should be that red meat in the context of an unrefined, healthy diet, is completely safe. Further, small amounts of processed meat, especially those traditionally consumed and produced in the traditional manner, also offer very little potential for harm, and I would say, none, if eaten in moderation.

Exercising with low muscle glycogen content increases fat oxidation and decreases endogenous, but not exogenous carbohydrate oxidation

https://www.sciencedirect.com/science/article/abs/pii/S0026049519300915

Abstract

- Low muscle glycogen does not impair exogenous carbohydrate oxidative capacity.
- Primary adaptation to exercise with low muscle glycogen is increased fat oxidation.
- Altered whole-body substrate oxidation result from intramuscular adaptations.

Background

Initiating aerobic exercise with low muscle glycogen content promotes greater fat and less endogenous carbohydrate oxidation during exercise. However, the extent exogenous carbohydrate oxidation increases when exercise is initiated with low muscle glycogen is unclear.

Purpose

Determine the effects of muscle glycogen content at the onset of exercise on whole-body and muscle substrate metabolism.

Methods

Using a randomized, crossover design, 12 men (mean ± SD, age: 21 ± 4 y; body mass: 83 ± 11 kg; VO2peak: 44 ± 3 mL/kg/min) completed 2 cycle ergometry glycogen depletion trials separated by 7-d, followed by a 24-h refeeding to elicit low (LOW; 1.5 g/kg carbohydrate, 3.0 g/kg fat) or adequate (AD; 6.0 g/kg carbohydrate, 1.0 g/kg fat) glycogen stores. Participants then performed 80 min of steady-state cycle ergometry (64 ± 3% VO2peak) while consuming a carbohydrate drink (95 g glucose +51 g fructose; 1.8 g/min). Substrate oxidation (g/min) was determined by

indirect calorimetry and 13C. Muscle glycogen (mmol/kg dry weight), pyruvate dehydrogenase (PDH) activity, and gene expression were assessed in muscle.

Results

Initiating steady-state exercise with LOW (217 ± 103) or AD (396 ± 70; $P < 0.05$) muscle glycogen did not alter exogenous carbohydrate oxidation (LOW: 0.84 ± 0.14, AD: 0.87 ± 0.16; $P > 0.05$) during exercise. Endogenous carbohydrate oxidation was lower and fat oxidation was higher in LOW (0.75 ± 0.29 and 0.55 ± 0.10) than AD (1.17 ± 0.29 and 0.38 ± 0.13; all $P < 0.05$). Before and after exercise PDH activity was lower ($P < 0.05$) and transcriptional regulation of fat metabolism (FAT, FABP, CPT1a, HADHA) was higher ($P < 0.05$) in LOW than AD.

Conclusion

Initiating exercise with low muscle glycogen does not impair exogenous carbohydrate oxidative capacity, rather, to compensate for lower endogenous carbohydrate oxidation acute adaptations lead to increased whole-body and skeletal muscle fat oxidation.[9]

Comment

While this study was met with a bot of 'whatever' in the academic Twittersphere, I believe this was an important study, mainly because it is a common perception (particularly among those who are anti-low-carb) that the reduction in PDH (an important 'carb-burning' enzyme) that occurs with lower glycogen levels and/or on a low-carbohydrate diet, will reduce the body's *ability* to use carbohydrate for fuel and this inhibition will be negative for performance because it will reduce the ability to provide energy for high-intensity activity.

This was not demonstrated in this study.

Instead, we saw an increased fat-utilisation in those with low glycogen. This is exactly what we would expect. Think about it; if you have low glycogen (stored carbohydrate) the body will instead up-regulate the capacity to burn fat for fuel. There is a large 'grey area' between mostly fat burning at low intensities of exercise and mostly carb-burning at higher intensities and the ability to switch well between these is what we call 'metabolic flexibility'.

AND The group with lower glycogen could use supplemental carbohydrate just as well as the group with sufficient glycogen.

What does this mean?

The FASTER study demonstrated that low-carb athletes had the same or similar glycogen levels as higher-carb athletes,[10] so low glycogen is not likely to be an impediment for low-carb athletes once they have become 'fat-adapted' anyway.

But there was still some concern that they wouldn't be able to use supplemental carbs during exercise very well (anyone, whether low-carb or high-carb, can still exhaust muscle glycogen in a long bout of exercise). This study shows that low-carb athletes can supplement with carbohydrate, during activity, and use it effectively.

References

1. Balasse EO, Neef MA. Inhibition of ketogenesis by ketone bodies in fasting humans. Metabolism. 1975;24(9):999-1007.

2. Harvey CJdC, Schofield GM, Williden M, McQuillan JA. The effect of medium chain triglycerides on time to nutritional ketosis and symptoms of keto-induction in healthy adults: a randomised controlled clinical trial. J Nutr Metab. 2018;2018:9.

3. Harvey C, Schofield G, Williden M. The lived experience of healthy adults following a ketogenic diet: A qualitative study. J Holist Perf. 2018;7782018(1):3638.

4. Harvey CJdC, Schofield GM, Zinn C, Thornley SJ, Crofts C, Merien FLR. Low-carbohydrate diets differing in carbohydrate restriction improve cardiometabolic and anthropometric markers in healthy adults: A randomised clinical trial. PeerJ. 2019;7:e6273.

5. Giles GE, Mahoney CR, Caruso C, Bukhari AS, Smith TJ, Pasiakos SM, et al. Two days of calorie deprivation impairs high level cognitive processes, mood, and self-reported exertion during aerobic exercise: A randomized double-blind, placebo-controlled study. Brain and Cognition. 2019;132:33-40.

6. Dehghan M, Mente A, Zhang X, Swaminathan S, Li W, Mohan V, et al. Associations of fats and carbohydrate intake with cardiovascular disease and mortality in 18 countries from five continents (PURE): a prospective cohort study. Lancet. 2017;390(10107):2050-62.

7. Seidelmann SB, Claggett B, Cheng S, Henglin M, Shah A, Steffen LM, et al. Dietary carbohydrate intake and mortality: a prospective cohort study and meta-analysis. The Lancet Public health. 2018;3(9):e419-e28.

8. Bradbury KE, Murphy N, Key TJ. Diet and colorectal cancer in UK Biobank: a prospective study. International journal of epidemiology. 2019.

9. Margolis LM, Wilson MA, Whitney CC, Carrigan CT, Murphy NE, Hatch AM, et al. Exercising with low muscle glycogen content increases fat oxidation and decreases endogenous, but not exogenous carbohydrate oxidation. Metabolism. 2019;97:1-8.

10. Volek JS, Freidenreich DJ, Saenz C, Kunces LJ, Creighton BC, Bartley JM, et al. Metabolic characteristics of keto-adapted ultra-endurance runners. Metabolism. 2016;65(3):100-10.