# THE CARB-APPROPRIATE REVIEW

A MONTHLY RESEARCH REVIEW BY

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Volume 1 | Issue 2 | July 2019

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# ABOUT CLIFF

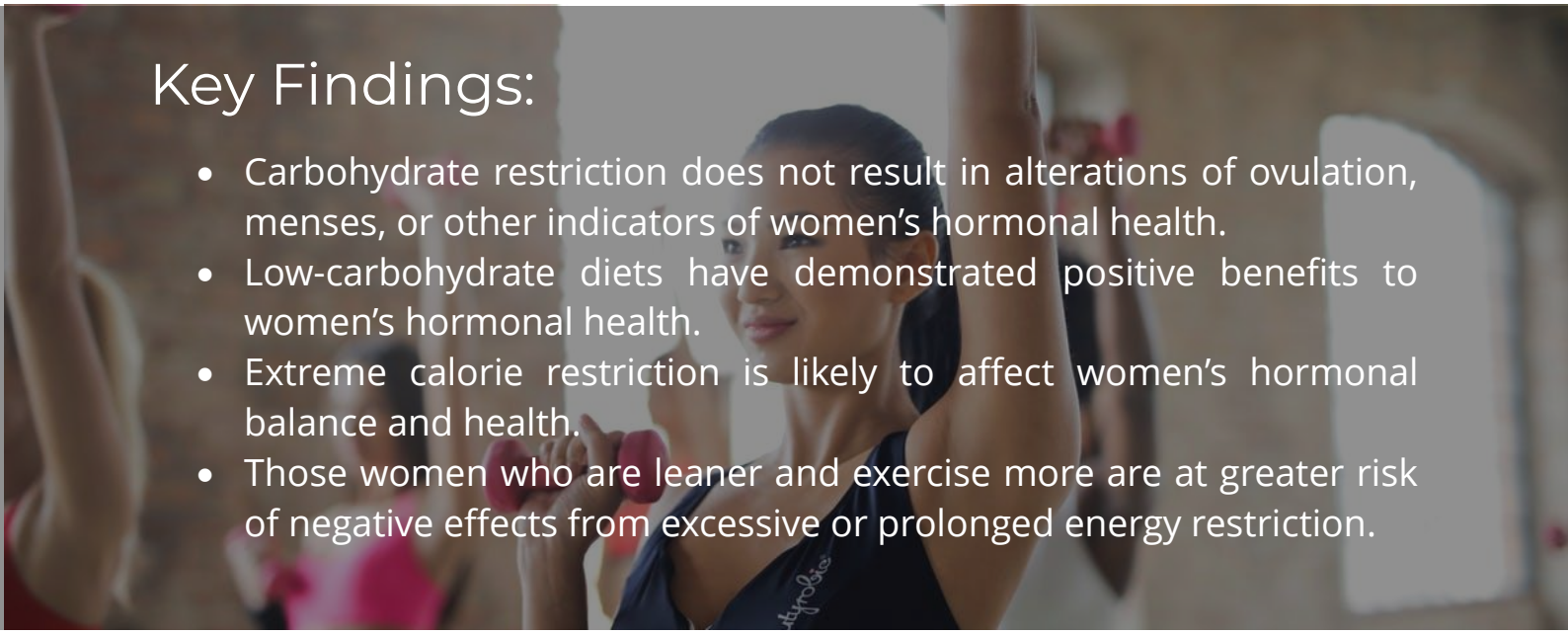
Cliff Harvey PhD (c) is an author, clinician, and researcher. He was one of the first clinical nutritionists to begin working with ketogenic and low-carb diets, way back in the 1990s and is also considered a pioneer in the area of mind-body integrative healthcare.

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

# DO LOW-CARBOHYDRATE DIETS NEGATIVELY AFFECT FEMALE HORMONE BALANCE, OVULATION, AND MENSES?



## Key Findings:

- Carbohydrate restriction does not result in alterations of ovulation, menses, or other indicators of women's hormonal health.
- Low-carbohydrate diets have demonstrated positive benefits to women's hormonal health.
- Extreme calorie restriction is likely to affect women's hormonal balance and health.
- Those women who are leaner and exercise more are at greater risk of negative effects from excessive or prolonged energy restriction.

A common claim currently doing the rounds is that a low-carb or keto-diet will negatively affect either 'female hormone balance', menstrual cycles, or ovulation.

It is claimed that there is a minimum amount of carbohydrate (i.e. 200 g per day) required to preserve hormone status and ovulation, along with other indicators of hormonal health.

## Does this claim stack up?

There is no evidence that 200 g per day is required to preserve markers of female hormone balance. In fact, the most commonly cited study to support the idea that there is a minimum requirement for carbohydrate showed no such thing.

## Luteinizing Hormone Pulsatility Is Disrupted at a Threshold of Energy Availability in Regularly Menstruating Women

Anna Loucks, Jean Thuma

*The Journal of Clinical Endocrinology & Metabolism*, Volume 88, Issue 1, 1 January 2003, Pages 297–311, https://doi.org/10.1210/jc.2002-020369


# Abstract

To investigate the dependence of LH pulsatility on energy availability (dietary energy intake minus exercise energy expenditure), we measured LH pulsatility after manipulating the energy availability of 29 regularly menstruating, habitually sedentary, young women of normal body composition for 5 days in the early follicular phase. Subjects expended 15 kcal/kg of lean body mass (LBM) per day in supervised exercise at 70% of aerobic capacity while consuming a clinical dietary product to set energy availability at 45 and either 10, 20, or 30 kcal/kg LBM per day in two randomized trials separated by at least 2 months. Blood was sampled daily during treatments and at 10-min intervals for the next 24 hours. Samples were assayed for LH, FSH, oestradiol ($E_2$), glucose, β-hydroxybutyrate, insulin, cortisol, GH, IGF-I, IGF-I binding protein (IGFBP)-1, IGFBP-3, leptin, and $T_3$. LH pulsatility was unaffected by an energy availability of 30 kcal/kg LBM per day ($p > 0.3$), but below this threshold LH pulse frequency decreased, whereas LH pulse amplitude increased (all $p < 0.04$). This disruption was more extreme in women with short luteal phases ($p < 0.01$). These incremental effects most closely resembled the effects of energy availability on plasma glucose, β-hydroxybutyrate, GH, and cortisol and contrasted with the dependencies displayed by the other metabolic hormones (simultaneously $p < 0.05$). These results demonstrate that LH pulsatility is disrupted only below a threshold of energy availability deep into negative energy balance and suggest priorities for future investigations into the mechanism that mediates the nonlinear dependence of LH pulsatility on energy availability.[1]


# Comment

The paper itself makes for some difficult reading because what at first could be inferred to be a low-carbohydrate diet intervention, is, in fact, one that has both low energy availability and low carbohydrate availability *because of adjustment for energy expenditure.*

> There is no evidence that 200 g of carbohydrate per day is required to preserve female hormone balance.

### What did the study involve?

29 regularly menstruating, sedentary young women were measured for luteinising hormone (LH) pulsatility over a 5-day period (along with other blood outcome measures). They were randomised to

receive an energy-sufficient diet matched to daily calorie expenditure (~ 2700 Kcal per day) or one of three calorie-restricted diets (~ 2000, 1500, 1100 Kcal per day respectively). (Figure 1.)

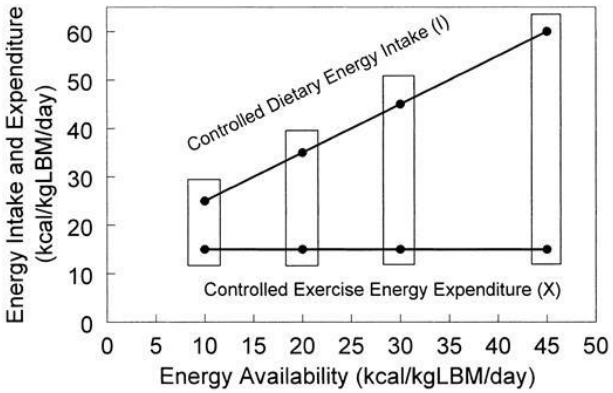



Figure 1. Energy availability: Energy intake and expenditure by groups.

The diets were standardised by using a diet supplement drink (*Ensure*) which contains 28% fat, 15% protein, and 57% carbohydrate...

Yes, you read that right... 57% carbohydrate. Definitely not a low-carbohydrate modifier!

### What did they find?

At energy availability under 30 Kcal/kg of lean body mass per day, there were significant alterations in LH pulse frequency and amplitude (Figure 2). In this case, the participants were eating 2000 Kcal per day or more than 700 Kcal per day under maintenance calories.

Therefore, based on these results, it is reasonable to conclude *in this study,* **a calorie restriction** to ~26% less than your daily energy requirement (a combination of energy intake from food and what you expend over a day) is likely to impair LH pulsatility. As you can see in Figure 2, there

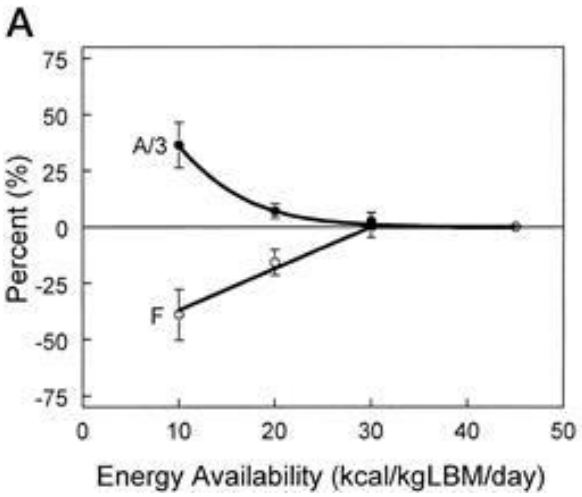



Figure 2. Luteinising hormone (LH) pulsatility amplitude (a) and frequency (F) in relation to energy availability.

was no effect above 30 Kcal per kilogram of bodyweight. There *might* be an effect of relative carbohydrate availability, but it appears to be mostly related to fuel availability, not whether a diet is 'low-carb' simply because these diets were not.

*Calorie restriction* to ~26% less than your daily energy requirement is likely to impair LH pulsatility.

## What does the research say about low-carb and hormone balance?

There are relatively few studies on low-carbohydrate (or other diets) and female hormone balance. In fact, female health has been typically underserved in research. There are, however, a few studies that are very informative for whether low-carbohydrate diets are arbitrarily 'bad' for

women and they were reviewed in 2017 by Melanie McGrice and Judi Porter.[2]

## The Effect of Low Carbohydrate Diets on Fertility Hormones and Outcomes in Overweight and Obese Women: A Systematic Review

Melanie McGrice, Judi Porter

*Nutrients* **2017**, *9*(3), 04; https://doi.org/10.3390/nu9030204


# Abstract

**Background**

Medical interventions including assisted reproductive technologies have improved fertility outcomes for many sub-fertile couples. Increasing research interest has investigated the effect of low carbohydrate diets, with or without energy restriction. We aimed to systematically review the published literature to determine the extent to which low carbohydrate diets can affect fertility outcomes.

**Methods**

The review protocol was registered prospectively with Prospective Register for Systematic Reviews (registration number CRD42016042669) and followed *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* guidelines. Infertile women were the population of interest, the intervention was low carbohydrate diets (less than 45% total energy from carbohydrates), compared to usual diet (with or without co-treatment). Four databases were searched from date of commencement until April 2016; a supplementary Google scholar search was also undertaken. Title and abstract, then full-text review, were undertaken independently and in duplicate. Reference lists of included studies and relevant systematic reviews were checked to ensure that all relevant studies were identified for inclusion. Quality assessment was undertaken independently by both authors using the Quality Criteria Checklist for Primary Research. Outcome measures were improved fertility outcomes defined by an improvement in reproductive hormones, ovulation rates and/or pregnancy rates.

**Results**

Seven studies fulfilled the inclusion criteria and were included in the evidence synthesis. Interventions were diverse and included a combination of low carbohydrate diets with energy deficit or other co-treatments. Study quality was rated as positive for six studies, suggesting a low risk of bias, with one study rated as neutral. Of the six studies which reported changes in reproductive hormones, five reported significant improvements post-intervention.

**Conclusion**

The findings of these studies suggest that low carbohydrate diets warrant further research to determine their effect. These randomised controlled trials should consider the effect of carbohydrates (with or without energy deficit) on hormonal and fertility outcomes.

## Comment

In this review, six of seven studies assessed changes in reproductive hormones, with all but one reporting *significant improvements* and one showing no meaningful difference between groups.

Four of the seven studies reported on menstrual cycles; frequency of menses and/or ovulation rates. All studies showed significant improvements in menstrual cyclicity (normalisation of menstrual cycles) and/or improvements in ovulation rates with a low-carbohydrate diet.

It should be noted that Palomba et al. demonstrated an improvement in menses frequency and ovulation rates compared to the start of the intervention, but the results were not as significant as the usual diet plus structured exercise training.[3]

> All studies showed significant improvements in menstrual cyclicity and/or improvements in ovulation rates with a low-carbohydrate diet.

Also observed by Moran et al. was that two amenorrhoeic (not menstruating) participants had a resumption of menses or improvement in ovulation after commencing a low-carbohydrate diet.[4]

Four studies also reported pregnancy outcomes. Three out of four studies showed improved pregnancy rates in low-carbohydrate intervention groups. This would not be an expected result if hormonal dysfunction was a natural consequence of a low carbohydrate diet.

It should also be noted that all of these studies were energy restricted, ranging from around 600 (followed by habitual calories) to 1400 calories per day, and with the intervention group (low carb) in the Palombo studies eating 800-1000 calories less than requirement per day. The comparison groups all consumed their usual diets.

### What does this all mean?

We already know from previous research that a relative energy deficiency syndrome (REDS) is detrimental to the creation and release of many hormones and is especially concerning for women for menstruation and ovulation, and other aspects of female hormone balance.

But the study by Louks and Thuma does not show that low-carb diets are the culprit. In this case, even the low-calorie diets that have been suggested as 'low-carb' were relatively rich in carbohydrate (ranging from ~156 g of carbohydrate per day, up to 385 g per day). The results may have been misread by some commentators due to the authors listing in a table the *'24-hr Carbohydrate availability'* (40-230 g per day from lowest to highest group). However, this figure was derived from a calculation of the daily carbohydrate intake *minus* carbohydrate usage during the prescribed

exercise regime. We would expect in a high energy expenditure situation, with relatively high calorie-restriction, that carbohydrate availability would be low. However, I must restate, the diets were not low carbohydrate (except as a function of severe energy restriction overall) by any accepted measure.

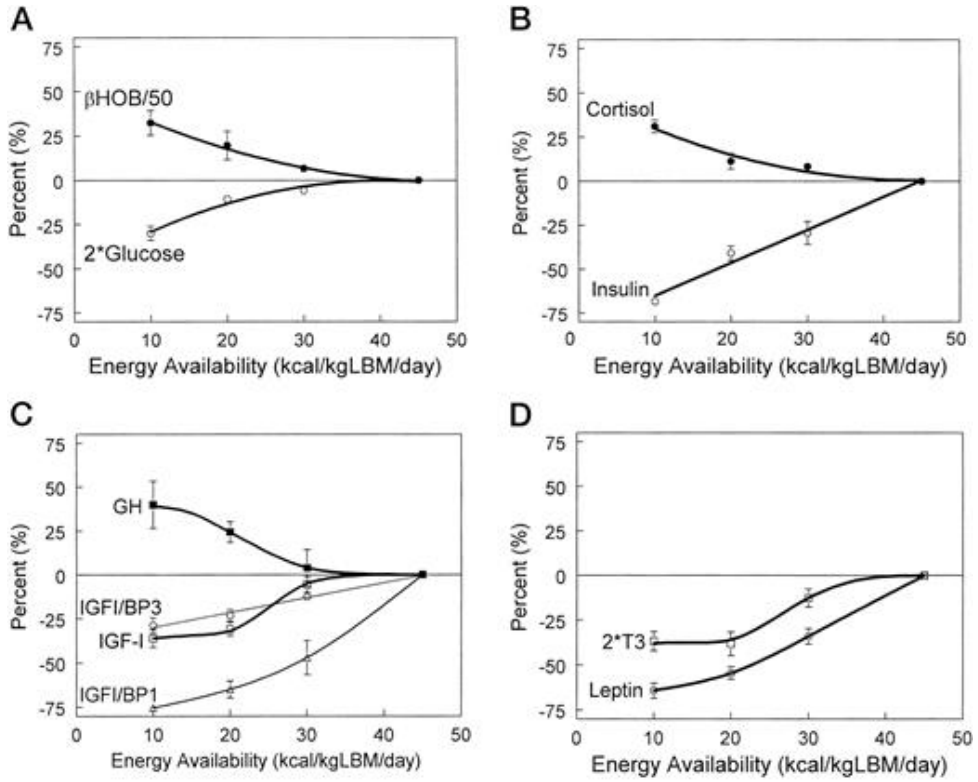
In this study, there was a negative effect on luteinising hormone pulsatility and frequency at a calorie restriction of more than 700 calories less than maintenance (< 30 calories per kilogram of bodyweight).

There are several points to consider when evaluating these results.

1. The participants in the Loucks and Thuma study were of normal body composition, so they may have had less energy availability (from stored bodyfat) than the overweight and obese participants in the studies reviewed by McGrice and Porter.

2. The participants in the Loucks and Thuma study were exercised to expend on average 896 calories per day, which would have significant effects on recovery and stress, apart from the calorie deficit created.

3. Overweight and obese people are more likely to benefit from low-carbohydrate interventions.



## How can we apply these findings?

Relative energy availability, or conversely, energy deficiency, is becoming a major talking-point in nutrition. It is clear from research on athletes that a relative energy deficiency syndrome (REDS) is a major risk for over-reaching, overtraining, and hormonal dysregulation and this is becoming more widely accepted as a causative factor in over-stress and fatigue in non-athletes.

> relative energy deficiency syndrome (REDS) is a major risk for over-reaching, overtraining, and hormonal dysregulation

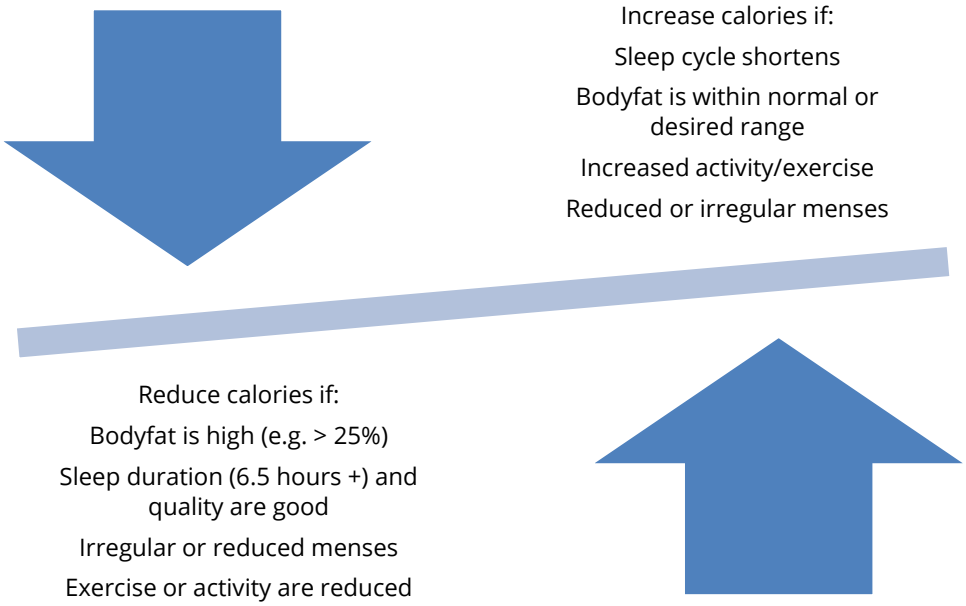
Much of our 'framing' in health and nutrition is geared towards methods to help people reduce calories, due to the epidemics of obesity and metabolic syndrome. But the growing awareness of the importance of energy sufficiency to thrive, and the clinical observation that there are a significant minority of people who are habitual under-eaters, shows the importance for clinicians and practitioners to recognise the importance of sufficient energy intake for long term health.

This is especially true when other demands (like exercise and career workload, or other stressor) are also providing for an increase in both energy expenditure AND resulting in other stress-related effects; such as increased catecholamines, increased tissue breakdown, reduced availability of substrate for hormone production, and effects on sleep, essential micronutrient intake, and mind-state. (Figure 3.)

Energy restriction should, therefore, be limited in time, in order to accomplish results, and the magnitude of energy restriction should be modified based on other factors.

Carbohydrate allotment in the diet should be based on the needs of the individual, not on an arbitrary idea that carbohydrates are required in a certain amount to preserve hormonal status.

# Energy intake modification



Increase calories if:

Sleep cycle shortens

Bodyfat is within normal or desired range

Increased activity/exercise

Reduced or irregular menses

Reduce calories if:

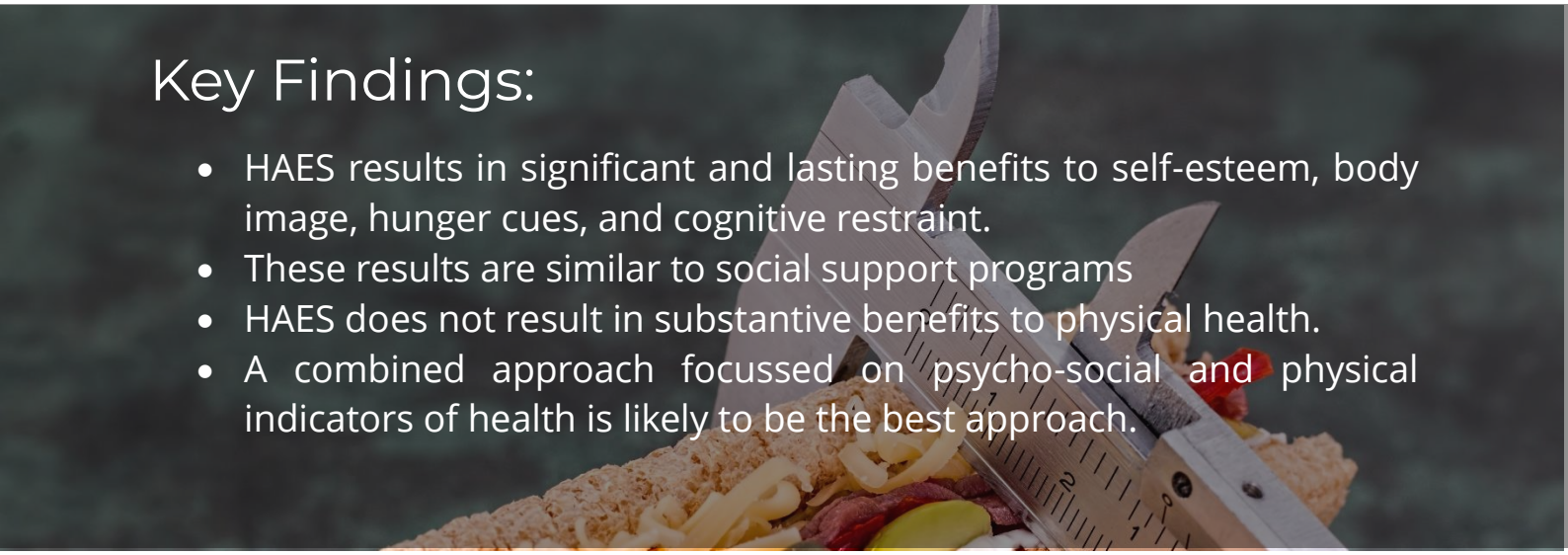
Bodyfat is high (e.g. > 25%)

Sleep duration (6.5 hours +) and quality are good

Irregular or reduced menses

Exercise or activity are reduced

# CAN YOU BE 'HEALTHY AT EVERY SIZE'?



## Key Findings:

- HAES results in significant and lasting benefits to self-esteem, body image, hunger cues, and cognitive restraint.
- These results are similar to social support programs
- HAES does not result in substantive benefits to physical health.
- A combined approach focussed on psycho-social and physical indicators of health is likely to be the best approach.

Traditional weight loss methods are based primarily on a medical model which treats obesity as a disease requiring diet, exercise, or pharmaceutical intervention. Conversely, the increasingly popular 'Health At Every Size' (HAES) movement believes that "individuals who are overweight and obese want to exercise and eat healthy foods, and they are capable of doing so when barriers are removed".[5]

The Health At Every Size® Principles are:

1. Weight Inclusivity: Accept and respect the inherent diversity of body shapes and sizes and reject the idealizing or pathologizing of specific weights.
2. Health Enhancement: Support health policies that improve and equalize access to information and services, and personal practices that improve human well-being, including attention to individual physical, economic, social, spiritual, emotional, and other needs.
3. Respectful Care: Acknowledge our biases, and work to end weight discrimination, weight stigma, and weight bias. Provide information and services from an understanding that socio-economic status, race, gender, sexual orientation, age, and other identities impact weight stigma and support environments that address these inequities.
4. Eating for Well-being: Promote flexible, individualized eating based on hunger, satiety, nutritional needs,

and pleasure, rather than any externally regulated eating plan focused on weight control.

5. Life-Enhancing Movement: Support physical activities that allow people of all sizes, abilities, and interests to engage in enjoyable movement, to the degree that they choose.

While many academics, researchers, and practitioners applaud the overall aims of the HAES movement, in particular articles 1 and 4 have drawn criticism,[6] due to the a) demonstrable harm of adverse adiposity and b) the focus on inherent cues without external regulation that is at odds with our biology (i.e. the desire to seek and find pleasure in calorie-dense, sugar and fat-rich foods).

## Are overweight and obesity a risk factor for early death and disease?

One of the key considerations in any debate about whether we can have *health at every size* is whether being overweight or obese are risk factors for poorer health outcomes, including earlier death and disease. In other words, can we, *in actuality*, be healthy irrespective of body size or adiposity?

The research is clear that increased body mass index (a proxy measure for increased adiposity or 'fatness') is associated with disease and death.

- Higher waist circumference and waist-to-hip ratio increase the risk of all-cause mortality among men and women and are associated with increased risk of cardiovascular disease, cancer and all-cause mortality.[7, 8]
- Obesity is related to a higher risk of influenza infection and mortality.[9]
- Children with obesity have a higher risk of adult obesity and greater length of hospital stays.[10]
- Obesity increases the risk of complications and mortality after liver transplants.[11]
- Obesity increases the risk of fatality from a motor vehicle accident (but might reduce the severity of head injuries).[12]
- Childhood obesity significantly increases the risk of later cardiometabolic mortality (diabetes, cardiovascular diseases).[13]
- Moderate increases in overweight, are mildly protective for the elderly due to problems associated with weight-loss (this is also reverse causation) but obesity is still a risk factor for older people.[14]
- Obesity is a significant risk factor for prostate cancer mortality.[15, 16]
- There is an increased risk of mortality in western (but not Asian or Pacific) pancreatic cancer patients with obesity.[17]

The research is clear that increased body mass index (a proxy measure for increased adiposity or 'fatness') is associated with disease and death

## Can being overweight *protect* against disease and early death?

In an oft-cited study, Flegal and colleagues found that being overweight resulted in a small yet significant *lower* mortality risk than being normal weight (0.94; 95% CI, 0.91-0.96). However, obesity was still associated with increased risk of mortality*.

However, analysis by Hu and colleagues of over 10.6 million participants has demonstrated that when reverse causation bias was corrected for (for example, when BMI was reduced as a result of smoking, or pre-existing illness) the participants with a 'normal' BMI (22-25) had the lowest risk of mortality, with risk increased significantly in the overweight and obese ranges, and every 5 BMI unit increase associated with a 31% greater risk of death overall.[18]

## Can those with obesity be 'metabolically healthy'?

It has also been suggested that those with obesity can still be metabolically healthy. While it is likely that there are some few people who can retain robust good health, despite a high BMI, increased adiposity of the body results in a milieu of biochemical, behavioural, and psychoneurophysiological factors that reduce optimal health.

While some people will be healthy in ranges outside what is considered 'optimal' body mass index (BMI), whether 'under' or 'over' weight, there is a greater risk, for most people, most of the time as adiposity increases. Those who are heavier due to increased muscle and have a higher BMI (i.e. athletes) should similarly not be included as metabolically healthy people with overweight or obesity, as they are not excessively adipose.

increased adiposity of the body results in a milieu of biochemical factors that reduce optimal health

The risks associated with obesity in those who are otherwise 'metabolically healthy', has been studied and those healthy individuals with obesity have a significantly greater risk of adverse health events

(relative risk [RR], 1.24; 95% CI, 1.02 to 1.55) over the long-term (i.e. in studies with follow-ups > 10 years),[19] and are at significantly greater risk of cardiovascular mortality.[20] The combination of factors associated with excess adiposity such as increased inflammation, non-muscular load, and the predisposing factors to obesity such as more energy-dense, nutrient-sparse foods, reduced activity, poor sleep and other contributing factors to adiposity, result in damage that has significant health consequences.[21]

## What does the evidence say about HAES?

The results from research on HAES is somewhat equivocal. Typically, people tend to feel better after being educated in a HAES approach with an improved appreciation of cognitive dietary restraint, hunger cues, and increased self-worth and body image appreciation. There are few substantive benefits to physical health outcomes though.

- In a study of 25 sedentary, overweight women, physical activity was better adhered to in an exercise + HAES intervention versus exercise only (60% vs 36%).[22]

- In a 12-month quasi-experimental trial, women following a HAES approach lost an average of 3.5 Kg (from 96.9 +/- 16.4) (4.8% bodyfat loss) and participants reported being more physically active and having a better perception of their bodies, along with hunger and satiety cues. Participants also reported that they could identify feelings with eating choices and refrain from the restrained behaviour. Interestingly, in this study dropout rates were over 50%.[23]

- In another study, no meaningful reductions in weight were noted for a HAES intervention, a social support intervention, and control over 16 months and no significant between group effects for lipid profiles or other cardiometabolic indices. Both the social support and HAES groups noted improved responses to hunger and cognitive dietary restraint.[24]

- In the previous intervention, it was also reported that energy intake and snack frequency decreased similarly over all groups (no benefit from HAES).[25]

- A three-year follow-up of participants of the previously mentioned trial showed continued improvements in perceptions of self-worth, health, and body image, for both the social support and HAES groups, however, despite some (trivial) weight-loss achieved early in the intervention, three years later, weight had increased significantly.[26]

- A trial comparing an 'enhanced' HAES program with a physical activity program and nutritional counselling to a standard HAES protocol resulted in no significant loss of weight, BMI, or waist or hip measure although the

participants self-perception of health was improved.[27]

- In a comparison of 49 non-diabetic adults, weight loss was over 3 times higher on a weight-loss diet intervention vs HAES, *despite the weight loss group eating more…*
- A trial comparing a usual diet control to 4-month HAES intervention (*n*=49 per group) found no difference in weight-loss, energy intake, or energy from snacking between groups.[28]

## What does all this mean?

The HAES movement is a positive one in that it has focused on empowerment.

Culturally we have been entrained to glorify the body beautiful and to vilify those that are larger. The typical 'fix' for obesity has been to focus solely on willpower and a person's ability to restrict food intake and increase exercise to create a calorie deficit.

> The typical 'fix' for obesity has been to focus solely on willpower and a person's ability to restrict food intake and increase exercise to create a calorie deficit

While energy balance is critical to weight- and fat-loss, the approach has been counterproductive because it has not recognised the physiological drivers of hunger (metabolic dysfunction, lack of satiety from modern foods), the modern food environment, and the psychosocial aspects of food and life-food-social enjoyment.

There is a strong implicit bias against those who are overweight and there is also a naive assumption that those with obesity are lazy and that they should simply 'exercise and eat better'. This thinking does not help us, nor further our understanding because the reality is that many people who are obese are no less proactive than those who aren't, they simply drew the 'metabolic short straw'.

HAES provides benefits to self-worth, body image, and might have some interesting benefits for shifting someone's food relationship. However, the program has proven ultimately unsuccessful for improving quantifiable measures of health and appears to have similar attrition rates to 'diets' which have greater demonstrable benefits to health such as low-carbohydrate interventions which have better adherence with greater results for those with metabolic syndrome and obesity, than standard low-fat, high-carbohydrate regimens.[29]

The similarity in results between social support interventions and HAES shows that support, empathy, and consideration for the individual are the key. If this can be married to some degree of quantification in diet which also achieves substantive benefits to health, in an empowered way, appropriate to the individual, we can achieve the best of

both worlds, both for the psycho-emotional/psycho-social state of the individual, along with the greatest improvements in cardiometabolic markers of future health risk, of which adiposity is one.

One cannot be, according to the evidence, 'Healthy at Every Size' but a caring and empowered approach to nutrition practice can, and should, take into consideration more than the quantified markers of physical health. A holistic model of nutrition practice should strive to improve mental, psychoemotional, and physical health, through empowered and effective diet and lifestyle advice.

Additional notes:

- Possibly no association between obesity and oesophageal cancer [30] and sepsis mortality. [31]
- There might be some protective effect of being overweight on mortality in chronic kidney disease. [32]

**1.18 (95% CI, 1.12-1.25) for obesity (all grades combined), 0.95 (95% CI, 0.88-1.01) for grade 1 obesity, and 1.29 (95% CI, 1.18-1.41) for grades 2 and 3 obesity. These findings persisted when limited to studies with measured weight and height that were considered to be adequately adjusted. The HRs tended to be higher when weight and height were self-reported rather than measured.*

One cannot be, according to the evidence, 'Healthy at Every Size' but a caring and empowered approach to nutrition practice can, and should, take into consideration more than the quantified markers of physical health.

# IN THE LITERATURE

## How reliable is the statistical evidence for limiting saturated fat intake? A fresh look at the influential Hooper meta-analysis

Simon Thornley, Grant Schofield, Caryn Zinn, George Henderson

https://doi.org/10.1111/imj.14325


## Abstract

**Introduction**

Evidence from meta-analyses has been influential in deciding whether or not limiting saturated fat intake reduces the incidence of cardiovascular disease. Recently, random effects analyses have been criticised for exaggerating the influence of publication bias, and an alternative proposed which obviates this issue: "inverse-variance heterogeneity". We re-analysed the influential Hooper meta-analysis which supports limiting saturated fat intake to decide whether or not the results of the study were sensitive to the method used.

**Methods**

Inverse-variance heterogeneity analysis of this summary study was carried out and the results contrasted with standard methods. Publication bias was also considered.

**Results**

Inverse variance heterogeneity analysis of the Hooper combined-CVD endpoint results returned a pooled relative risk of 0.93 (95% confidence interval: 0.74 to 1.16). This finding contrasts with the traditional random effects analysis with the corresponding statistic of 0.93 (95% confidence interval: 0.88 to 0.98). Egger tests, funnel and Doi plots along with recently published suppressed trial results suggest that publication bias is present.

**Conclusions**

This study questions the use of the Hooper study as evidence to support limiting saturated fat intake. Our re-analysis, together with concordant results from other meta-analyses of trials indicate that routine advice to reduce saturated fat intake in people with (or at risk for) cardiovascular disease be reconsidered.[33]


## Comment

There are a number of meta-analyses that do not support the idea that saturated fat is a cause of heart disease. Whereas the 2015 meta-analysis by Hooper and colleagues suggested that there was a positive effect on cardiovascular mortality from reducing saturated fat intake.[34]

### Did the Hooper study *actually* show benefit from reducing saturated fat?

While there was a small, yet potentially important effect on cardiovascular *events* associated with reduced saturated fat diets (by approximately 17%; risk ratio (RR) 0.83; 95% confidence interval (CI) 0.72 to 0.96), there was *no effect on cardiovascular mortality or on stroke incidence.* The only effect seen was when saturated fat was replaced with polyunsaturated fats, and not when saturated fat was replaced with carbohydrate or monounsaturated fats.

### Was the effect observed in the replacement analysis larger because of the statistical methods they used?

In the paper by Thornley et al., the authors explain that the 'random effects models' used by Hooper and colleagues to pool their data, has the effect of biasing the results in favour of smaller trials where those disagree with larger. This seems counter-intuitive to the idea that larger numbers are more likely to have greater relevance to populations ('the law of large numbers').

In their paper, Thornley and colleagues suggest that "inverse-variance heterogeneity' analysis is more suitable because it widens confidence intervals, "*yet retain[s] the favourable weights of the fixed effect method*". Using this method of statistical analysis, a pooled relative risk of 0.93, with a 95% confidence interval of 0.74 to 1.16 is produced. This means (because the 95% CI overlaps '1') that there is no definitive effect of saturated fat on cardiovascular disease using this analysis.

## What does this all mean?

The one analysis from the Hooper study which showed benefit from reduced saturated fat was for cardiovascular events, however, there are several considerations as to why this may not be a meaningful finding:

1. Greater weighting given to small studies

When smaller studies with a higher risk of publication bias are given a smaller weighting, the effects are no longer significant.

2. No effect when carbs substituted for saturated fat

When carbohydrate is consumed in greater amounts, with a lower intake of saturated fat, there is no reduction in CVD incidence or mortality. This suggests that it's not the saturated fat that is the problem!

3. Positive benefits are only seen when polyunsaturated fats substituted for saturated fat

There *was* an effect shown when more polyunsaturated fats were consumed and less saturated fats. But because the same effect wasn't seen with carbs, or with monounsaturated fats, it doesn't make sense to label saturated fats as 'bad' but instead to look deeper into why polyunsaturated fats might be 'good' (i.e. greater intake of omega-3 fats, and/or greater intake of vegetables.)

4. No effect on cardiovascular or all-cause mortality

The most important outcome is death. And the most important 'death' outcome is overall rate, not necessarily grouped into different diseases. Put it this way, if we want to see what type of diet is 'best' overall, we need to see how many people get diseases, or die, from *all causes*, not from a particular illness. We don't see a risk for all-cause or even CVD mortality from saturated fat in the diet.

5. No substantive analysis of food 'quality'

While 'quality' is vague, it is becoming clearer by the day, that more important than macro split in the diet, is how much of the diet is made up by refined and ultra-processed foods. In most observational data we can see a clear trend towards there being greater impact of processed food and our modern food environment on mortality when compared to the amounts of macros, or sub-groups of macros that are eaten.

## Association of changes in red meat consumption with total and cause specific mortality among US women and men: two prospective cohort studies

Yan Zheng, Yanping Li, Ambika Satija, An Pan, Mercedes Sotos-Prieto, Eric Rimm, Walter C Willett, Frank B Hu

https://doi.org/10.1136/bmj.l2110

### Abstract

**Objective**

To evaluate the association of changes in red meat consumption with total and cause specific mortality in women and men.

**Design**

Two prospective cohort studies with repeated measures of diet and lifestyle factors.

**Setting**

Nurses' Health Study and the Health Professionals Follow-up Study, United States.

**Participants**

53 553 women and 27 916 men without cardiovascular disease or cancer at baseline.

**Main outcome measure**

Death confirmed by state vital statistics records, the national death index, or reported by families and the postal system.

**Results**

14 019 deaths occurred during 1.2 million person-years of follow-up. Increases in red meat consumption over eight years were associated with higher mortality risk in the subsequent eight years among women and men (both P for trend<0.05, P for heterogeneity=0.97). An increase in total red meat consumption of at least half a serving per day was associated with a 10% higher mortality risk (pooled hazard ratio 1.10, 95% confidence interval 1.04 to 1.17). For processed and unprocessed red meat consumption, an increase of at least half a serving per day was associated with a 13%

higher mortality risk (1.13, 1.04 to 1.23) and a 9% higher mortality risk (1.09, 1.02 to 1.17), respectively. A decrease in consumption of processed or unprocessed red meat of at least half a serving per day was not associated with mortality risk. The association between increased red meat consumption and mortality risk was consistent across subgroups defined by age, physical activity, dietary quality, smoking status, or alcohol consumption.

**Conclusion**

Increases in red meat consumption, especially processed meat, were associated with higher overall mortality rates.[35]

## Comment

The association shown between increased red meat intake of ½ serving per day and the risk of early death is actually quite low. A hazard ratio of 1.1 is equivalent to a 10% greater risk of death over the 8-year study period. This might seem compelling but is actually very low when we consider the 95% confidence intervals (1.04-1.17) and that small hazard ratios are inaccurate for showing causation because of the large array of other factors that could affect the outcome. For example, in this study attempts were made to adjust for baseline and change in factors such as smoking, alcohol use, diabetes, heart disease, cholesterol, total energy intake, consumption of food groups (sugar, fruit, vegetables, whole grains) and exercise. However, it is extremely difficult to effectively model for all of these and when the hazard ratio is low, the result is typically considered to be statistical noise.

This 'noise' is further exacerbated when lifestyle factors that could affect the outcome accumulate.

### What factors could have affected this outcome?

In this cohort, the group that reduced red meat intake the most over the 8-years (and had the lowest risk of mortality) also reduced alcohol, and increased activity the most, with the smallest increase in weight. (Figure 1.)

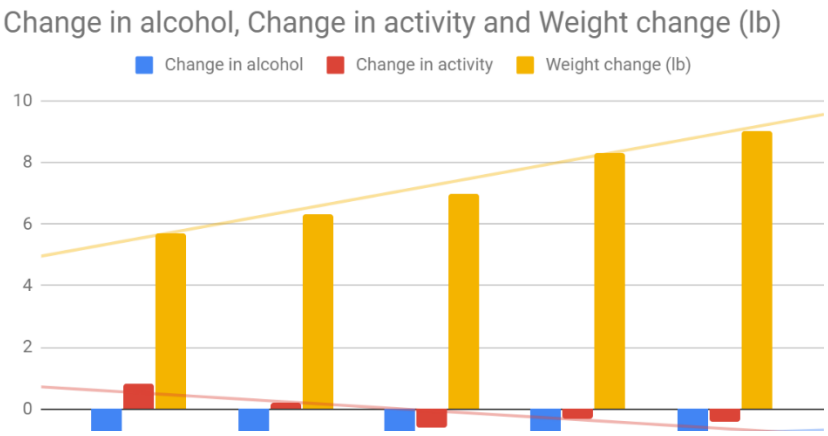



Figure 1. Change in alcohol, weight, and activity across meat reduced or increased groups.

The groups also had a linear association between energy intake (calories consumed per day) and red meat decrease/increase and, given that energy intake is one of the key factors for obesity, metabolic syndrome and future health risk (see Can You Be Healthy at Every Size) this is a major flaw in this study. (Figure 4.)

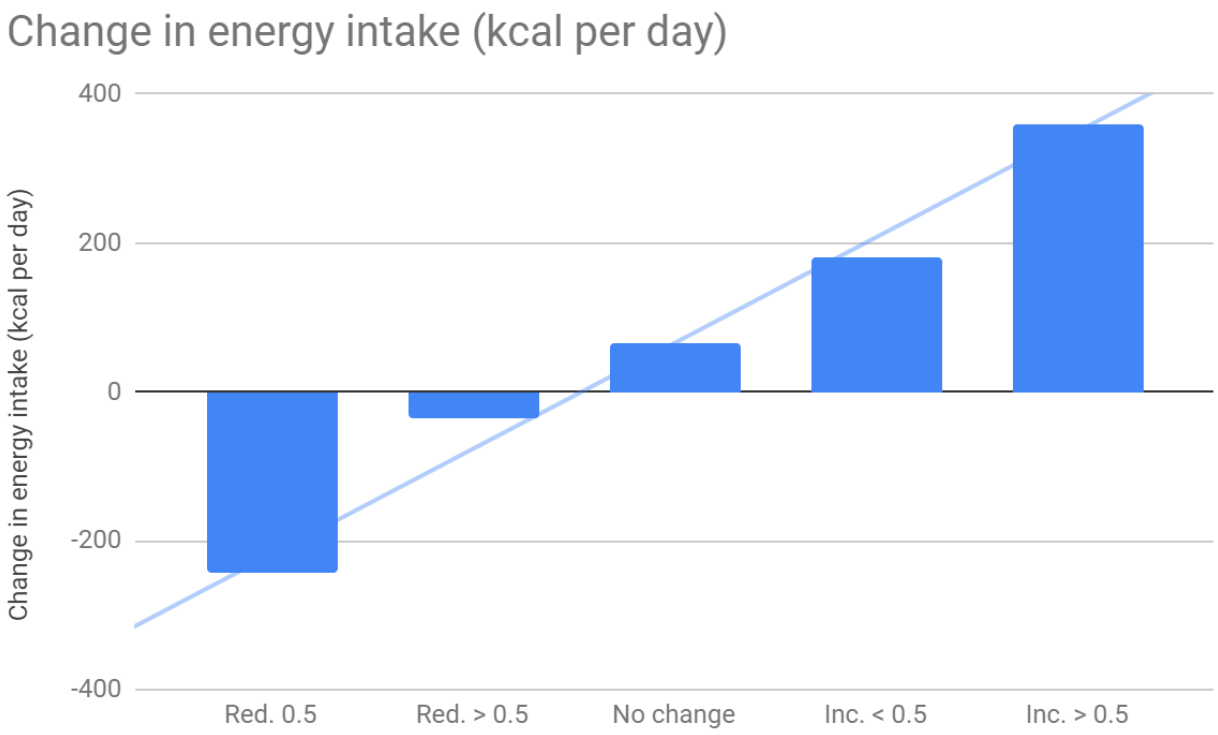



Figure 2. Change in energy intake (by group) of reduced or increased red meat consumption and linear trend.

## What does this all mean?

There are a number of factors to 'unpick' here. There are a large number of other lifestyle factors, as shown above, that might have affected the outcome. Perhaps more importantly, the lifestyle factors above suggest that those with baseline markers like high cholesterol were advised to reduce red meat...AND alcohol, and to exercise, and reduce portions.

the group that reduced red meat intake the most also reduced alcohol, and increased activity the most, with the smallest increase in weight

This is consistent with what is shown above and that those with high cholesterol at baseline tended to reduce meat intake. This is consistent with the advice provided at the time (in the low-fat crazed 1980s from which this data was drawn). Those who *did* reduce meat intake also reduced those factors indicated above and this also suggests that they were more active in their health.

Notwithstanding that we would now say that a reduction in fat and animal products does not positively impact health, an increase in natural unprocessed foods, reduced red-meat containing convenience foods (such as hamburgers and pizza which are typically found with high prevalence in these types of cohorts), reduced alcohol, and better energy balance and reduced weight gain are all powerful impactors of health. Again, those who take positive health steps are typically more motivated, more active in their health, and achieve better results. This is a clear and undeniable fact that we have seen replicated thousands of times in the literature.

### Take home message

The small percent increase in mortality from increased red meat consumption is not robust enough to warrant concern, especially when we see the range of other factors that have a higher likelihood of being responsible (in concert) for improving outcomes. Most importantly, it is highly likely that those who took control of their health by eating 'better' overall, regulated their energy intake, drank less alcohol, and were more active, achieved better results. So, eat natural foods, move, drink little alcohol (a little is fine!) and make sure that your diet allows both freedoms to live, AND an appropriate energy balance for you.

eat natural foods, move, drink little alcohol, and make sure that your diet allows both freedoms to 'live', AND an appropriate energy balance for *you*

# IN THE MEDIA

## VA Secretary Wilkie: Keto Diet Is Dangerous for Veterans with Diabetes

The Physicians Committee for Responsible Medicine (PCRM)

https://www.pcrm.org/news/blog/va-secretary-wilkie-keto-diet-dangerous-veterans-diabetes

### Article Summary

Instead of protecting veterans' health, the Department of Veterans Affairs is considering putting it at risk by partnering with *Virta Health Corp*. to place veterans with type 2 diabetes on a low-carb, ketogenic (keto) diet, which current science suggests is a risky choice for diabetes.

A keto diet also carries serious short- and long-term health risks including impaired artery function, elevated LDL cholesterol, nutrient deficiencies, increased risk of colon cancer, and increased risk of death.

Read the letter I sent to Veteran Affairs Secretary Robert Wilkie today, which describes the dangers of a keto diet and urges the VA to instead use the proven power of plant-based nutrition to help veterans fight diabetes.

### Comment

Firstly, it is important to recognise the disingenuous naming of this organisation. The 'Physicians Committee for Responsible Medicine' (PCRM) sounds like a group of evidence-based physicians upholding good standards in medicine... but this couldn't be further from the truth. The PCRM is a vegan advocacy group consisting of medical doctors and other practitioners committed to a plant-based lifestyle. While I have nothing against people wanting to be vegan for a variety of reasons, I do think that the name of this organisation is both patronising and disingenuous.

*Why not just call it what it is?*

My main 'beef' though with this group is that they cherry pick the data and deliberately misrepresent the science in order to push a vegan agenda. Now, I'm all for a vegan diet if and where it has demonstrable benefits to health but NOT when there are better alternatives to it for a particular outcome.

In this case, the Department of Veterans Affairs in the US is exploring a partnership with the *Virta Group* to use low-carbohydrate and ketogenic diets to treat type 2 diabetes in veterans. To me, this seems a sound idea.

In the letter to Secretary Wilkie, vegan advocate, Dr Neil Barnard outlines the reasons for PCRM opposition to low-carb and keto interventions. These defy the current state of knowledge for the treatment of metabolic syndrome and diabetes.

### Claim: Keto diets cause diabetes by contributing to a build-up of liver and muscle fat

This claim is patently false. It is a known fact that triglyceride levels (fats in the blood) and the *de novo* (in the body) creation of fat in the liver are both reduced most by a low-carb diet, with the greatest benefits seen with the greatest restriction of carbohydrate. (In other words, the more you reduce carbs, the more you reduce fats in the blood). This triglyceride lowering effect (when compared to low-fat diets) has been demonstrated time and time again.[29, 36-40] There are also persistent (long-term) benefits to overall fat levels in the body from keto- and low-carb vs low-fat diets over the long-term.[40]

With respect to visceral and liver-fat, animal research has strongly suggested that sugar and carbohydrate overall are the major contributors to these, with lower-carb interventions reducing liver and visceral fat levels, and a recent study has confirmed these findings in humans, with a significantly greater loss of both visceral and liver fat (and greater improvement in blood measures of cardiometabolic health) from a low-carb vs low-fat intervention over 18 months.[41]

### Claim: Keto diets reduce insulin sensitivity

This claim is actually true! But disingenuous. There IS a drop, in insulin sensitivity if you have followed a ketogenic diet for some time. But this drop is transient and is due to the low levels of dietary glucose that have been present in the diet. Overall, outside of an oral glucose tolerance test administered in a ketogenic diet, there is actually lower insulin levels and general improvement in glucose and insulin control resulting from a low-carbohydrate diet.

### Claim: Keto diets result in 'massive' increases in LDL cholesterol

Again, this claim is true yet inconsequential. Low-density lipoprotein is a carrier for cholesterol. Think of it as the 'bus' that carries cholesterol out to tissue to do its valuable job of patching up tissue and providing substrates for the creation of hormones. LDL is not in and of itself bad! For most people, a small rise in LDL and total cholesterol from a keto diet is not dangerous at all. When we look at markers of cardiovascular risk, modest increases in LDL and cholesterol pale in comparison to triglyceride (fat) concentrations in the blood, which are most convincingly linked to the incidence of and mortality from cardiovascular disease.[42-44]

> When we look at markers of cardiovascular risk, modest increases in LDL and cholesterol pale in comparison to triglyceride (fat) concentrations

For example, every 1 mmol/L increase in triglycerides is associated with a > 12% increase in risk, for both cardiovascular

disease mortality and all-cause mortality.[44] Some people will have greater increases in both LDL and cholesterol (due to genetic factors) from a keto diet. This can typically be rectified by modifying fat intake to more polyunsaturated and monounsaturated fats and the replacement of some red meat with white, and coconut oil and butter substituted for hemp, flax, and olive oils.

### Claim: A ketogenic diet removes valuable phytochemicals and essential nutrients for plant-foods

No, it doesn't. This is a misinterpretation of what keto *actually is.* I have prescribed ketogenic diets for 21 years and never have I had some reduce vegetable intake. Almost all (with the odd exception for people who do not tolerate vegetable matter well) 'good' diets include lots of vegetables and other nutrient-dense foods. Ketogenic diets based on natural, unrefined foods, include all the essential and secondary nutrients that are necessary for optimal health. A recent study by my colleague Dr Caryn Zinn at AUT University has confirmed that a low-carb diet is replete with all micronutrients.[45]

### Claim: Low-carbohydrate diets result in early death

The 2013 systematic review by Noto and colleagues is used to support this claim.[46] The problem with using pooled results from observational studies is that there is little control over the methodology. We could summarise to say, 'garbage in = garbage out'. When looking at all-cause mortality from a diet, we need to look at the research in the order of:

1. What do we see in populations over time?
2. What does the data *actually* show us?
3. Why might this be occurring? (I.e. what is the proposed mechanism)
4. Does this match what we see in randomised controlled trials? (I.e. is the proposed mechanism plausible?)

In the case of modifying carbohydrate intake, the largest published observational study actually showed a reduced likelihood of death with lower carbohydrate intake and higher fat intake.[47] However, the following year, the *Dietary carbohydrate intake and mortality: a prospective cohort study* using data from the ARIC cohort suggested that both extremes of carbohydrate intake (low and high) were associated with risk of early death.[48] When we look at the food data (as much as is available anyway) a common theme becomes clear. Those who eat ultra-processed food are at the greatest risk.

When we look at the food data (as much as is available anyway) a common theme becomes clear. Those who eat ultra-processed food are at the greatest risk.

When we correct for that, there is little difference overall between lower- and higher-carbohydrate diets. However, there are significant differences for specific populations, and those at risk of diabetes,

or with diabetes control blood glucose better and have better outcomes from low-carb and keto diets.

## What is the best diet for metabolic syndrome and diabetes?

Low-carbohydrate diets are the best treatment option for those with metabolic syndrome (prediabetes) and diabetes.

Low-carbohydrate diets have a significant effect on blood glucose levels and glucose control[49] and they consistently improve cardiometabolic risk factors such as triglycerides and HDL cholesterol, more than standard-care, or higher-carbohydrate diets.[50] Those with metabolic syndrome are also likely to stick to low-carb diets more easily than low-fat.[51]

Overall, low-carbohydrate and ketogenic diets are more effective than other dietary interventions for the treatment and management of diabetes with an approximately 150% greater reduction in HbA1c as compared to higher-carb diets.[52]

Overall, low-carbohydrate and ketogenic diets are more effective than other dietary interventions for the treatment and management of diabetes

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