Reviewer’s report

Title: Addressing overweight and obesity: a review of the biological models underpinning recent public health interventions

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Reviewer: Richard Feinman

Reviewer’s report:

The authors have added some valuable modifications but I think the revised version of this MS does not fully answer the comments that I raised in my original review. I may have been at fault for not making my position more explicit. The paper has the great virtue of being willing to confront the failure of current nutritional thinking and recommendations. However, I think that because current recommendations have failed does not mean that we are at the starting line. In essence, the authors have to be stronger on what we do know and that rests with dietary carbohydrate restriction. To put it in perspective, there is already some tendency in this direction. I would cite Walter Willett’s opinion as recorded in the LA Times http://articles.latimes.com/2010/dec/20/health/la-he-carbs-20101220.

My POV is that there are fundamentally two approaches to treating obesity: the energy balance strategy and its associated reliance on low fat (because of the caloric density of fat), and the alternative: strategies based on carbohydrate restriction which derive from the anabolic effects of glucose, insulin and other hormones. (Although offered as alternatives, low-GI and low fructose are subsets of, and are based on the same principles, as carbohydrate restriction).

The scientific evidence shows that the first approach, energy balance model is of very limited value and the MS correctly points out that “public health interventions and dietary guidelines largely neglect this evidence, instead persisting with interventions and recommendations based on an unmodified view of the energy balance model.”

Carbohydrate restriction, however, which relies on “the effect of diet composition including nutrient profile and interaction between nutrients and hormones regulating energy balance,” as the authors put it, has demonstrated its effectiveness and, in fact, in the addition to the MS, the authors have done a good job summarizing the benefits.

Yet the authors seem to find it acceptable that “carbohydrate restricted diets remain on the fringes of public health intervention research and are noticeably absent from dietary guidelines” Refusal to accept the value of reduction in dietary carbohydrate is the flip-side of holding to the energy balance model in the face of contradictory evidence. Cases of minority opinions that can be ignored by political power has many precedents in history of science.
The authors need to recognize that carbohydrate restriction is the strategy that derives from “translation between advances in understanding of the basic science” and should sensibly take the place of the energy balance model as the recommended diet for obesity. Alternatively, they should provide evidence to indicate why this should not be the one to replace current advice. There are, of course, many practical considerations and individual responses that apply to this (as much as they did in the energy balance model, although they were rarely acknowledged there). But workers in the field only consider it “the default diet,” the one to try first.

It is not true that there is “insufficient research at this stage to conclude which of these proposals are most effective, or for whom they are most effective.” There is extensive evidence including the references that the authors have added to the MS. Much of this work provides exactly the evidence against the energy balance model. The authors offer a good summary:

“the carbohydrate restricted diets which have been linked with favorable metabolic outcomes for weight loss, weight maintenance and health [44-46]. Carbohydrate restriction may achieve, for example, improved glycemic and insulin control, increased mobilization and utilization of lipid substrates, inhibition of lipogenesis, favorable changes in circulating fatty acids and improvements in atherogenic dyslipidemia, lipoprotein markers and inflammation.

I think “have demonstrated” is more appropriate than “have been linked with” but if this were the outcome of the current guidelines, of the public health policy and of the recommendations of the nutritional establishment, they would have claimed absolute success and we would not have the progression of critics to which the current MS is a useful addition.

It’s not exactly that, as the authors suggest, that “I support the low carbohydrate approach” but rather that whatever expertise I have, is in physiology and metabolism. I am one of the people who teach metabolism to students using low-carbohydrate diets because of the unifying principles of the role of insulin (Feinman & Makowske: Metabolic Syndrome and Related Disorders 2003, 1:189-198; Pogozelski, et al Biochemistry Molecular Biology Education 2005, 33:91-100. This is of increasing importance even in cancer which is discussed in a recent editorial (Myers AP, Cantley LC: Sugar free, cancer free? Nutrition 2012, 28(10):1036).

In summary, I think the paper should be published but the authors have to go beyond the failure of energy balance and bring out the value of the alternative or say what the limitations are to accepting carbohydrate restriction as the default recommended diet.

There are also two specific points that I think need correction:

The problem with thermodynamics as invoked is not the “assumption is that energy intake and energy expenditure can be independently modified...energy input and expenditure are interdependent and regulated at several levels.” The
idea, as I pointed out in my first review is confusing thermodynamics with behavior. In this, I may qualify as a multidisciplinary input in that I actually know something about thermodynamics. In essence, as I and my colleagues explained in the new reference 45 and in my blogpost at http://wp.me/p16vK0-5S, the subject is not really about the first law but rather the second law which is an efficiency law. Intake and expenditure can be independently modified -- everybody knows that you don't have to eat more if your exercising. The efficiency with which intake and output are coupled, the extent to which intake is coupled to storage vs expenditure is determined by the free energy changes which are controlled by both laws.

Whereas homeostatic mechanisms are important as the authors describe, the rationale of low-carbohydrate diets, as a weight-loss strategy, is that hormonal effects can over-ride the hemostatic mechanisms. In other words, behavior and energetics are different things.

The second point, is that the paragraph starting on page 15 with “Recently…” is way off the mark and should be removed. Lustig and his colleagues have not, in any way, renounced energy balance nor do they demonstrate real expertise at physiology and metabolism. Just the title of the cited article Public health: the toxic truth about sugar indicates the lack of care.” It is not the truth that is toxic. In addition, sugar is very much part of the establishment energy balance program and trying to separate sugar or fructose from carbohydrate, is part of the continued attempt to stonewall carbohydrate-restriction. The authors of the current MS very precisely described the problem (p. 15): “The reliance on dietary guidelines to inform the scientific basis of interventions may be a significant factor in holding back progress as there are very few public health interventions that appear to be testing alternative models.” Targeting sugar is very much a part of guidelines and Lustig, et al was presumably accepted by Nature because of this. The article does not indicate expertise in metabolism and physiology and the comments on the Nature website provide appropriate ridicule:
http://www.nature.com/nature/journal/v482/n7383/full/482027a.html Also, the last sentence of the paragraph, is not correct. While the interventions are surely untested, the example illustrates most of all how a rush to judgement can persist in the face of lapses in fundamental biochemistry.

Finally, surely there is a better reference than [1] whose title is not quite accurate. It is not really about “low carbohydrate diets” and “realities” is something of a stretch as well.

I understand this is a tough problem and I am grateful for the open dialogue on BMC Medicine and would be glad to communicate directly with the author in the spirit of a “a multidisciplinary approach.”

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:

I declare that I have no competing interest