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The universities of Stellenbosch/Cape Town low-carbohydrate diet review: Mistake or mischief?

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A 2014 meta-analysis from the universities of Stellenbosch and Cape Town reported that diets with a lower-carbohydrate (CHO) content are no more effective for producing weight loss than are high-CHO diets, so-called isoenergetic 'balanced' diets. We have re-examined the article and found numerous errors, many material in nature. Studies were included that failed the authors' own inclusion criteria; invalid and subjective meta-analysis sub-grouping was used; and data extraction was repeatedly inaccurate. All but one error favoured the balanced diet. The article was widely publicised, highly impactful and inaccurate. This begs the question: mistake or mischief?

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In July 2014, the South African (SA) media reported that, by proving that low-carbohydrate (CHO) diets were not better than 'balanced' eating,[1] a recently published article[2] from the universities of Stellenbosch and Cape Town had effectively 'debunked the Banting diet'.[3] Other reports echoed this sentiment. The *Cape Times* personalised the message: 'Noakes's low-carb diet not healthier', while quoting the chief executive of the Heart and Stroke Foundation of SA: 'Based on the current evidence we cannot recommend a low carbohydrate diet to the public.'[4]

The claim that a low-CHO diet was no better than balanced eating does not 'debunk' the low-CHO diet. These reports could as easily have stated that eating a balanced diet is no better for producing weight loss than eating a low-CHO diet is. This media positioning is interesting and particularly important in the current context that low-CHO diets have been placed on trial in SA.[5]

More objective reporting of Naude *et al.*'s[2] systematic review should have made two important points:

First, the study could not provide any information about Banting or low-CHO diets because it failed to study either. The average carbohydrate intake for the 14 studies included in the systematic review[6] was 35% (fat 35%; protein 30%).[7-20] This is substantially different from the 5% CHO (<50 g/day), moderate protein, and high fat, which is the dietary composition of the low-CHO diet promoted for the therapeutic management of obesity and type 2 diabetes mellitus.[21-23]

Second, the objective of Naude *et al.*'s[2] article was 'To compare the effects of low (*sic*) CHO and isoenergetic balanced weight loss diets in overweight and obese adults'. As a key effect of the low-CHO diet is to reduce hunger by increasing satiety despite a reduced energy intake,[24] the caloric intake of subjects on the control diet in isoenergetic trials must be voluntarily restricted to match this effect. This effectively negates the advantage provided by the uniquely satiating effect of genuinely low-CHO diets.

Both of these points served to disadvantage the lower-CHO diets included by Naude *et al.*[2] in their systematic review.

Regarding the first point, the introduction to the Naude *et al.*[2] article confirmed the authors' understanding of what constitutes a low-CHO diet: 'Some weight loss diets widely promoted through the media … recommend a regime greatly restricting carbohydrates (CHO).' The introduction continued: 'To achieve the very low CHO intake, these diets prescribe restriction of most vegetables and fruit … .' Confirming their understanding of what constitutes a low-CHO diet, the authors proceeded to find against these diets without actually studying them. Only 1 of the 19 trials they initially reviewed was sufficiently low in CHO to qualify as a trial of the (therapeutic) low-CHO diet.[13] The other 18 trials reviewed were *lower* in CHO content than current public health dietary guidelines, but they were not *low*-CHO diets. There is a substantial difference between *lower*-(than dietary guidelines) and therapeutically *low*-CHO diets. The therapeutic low-CHO diet is prescribed specifically to lower the daily CHO intake to <50 g/day, which is the level at which optimal benefits of this dietary intervention occur.[22]

In view of the pivotal importance of this article to the conduct of the 'trial' against low-CHO diets in SA, we considered it important to submit the article to a rigorous re-analysis. In the course of our investigation we uncovered a multitude of errors that materially altered the conclusions promoted by the article.

In the context of the current debate on low-CHO diets in SA, it is important that the erroneous messages conveyed to the SA public as a result of the inaccuracies in that study[2] should be rectified expeditiously.

A re-examination of the Naude *et al.*[2] article

The main conclusion

The main conclusion presented in the abstract of the Naude *et al.*[2] article was: 'In non-diabetic participants, our analysis showed little or no difference in mean weight loss in the two groups at 3 - 6 months.' This conclusion was based on a study of 14 trials that were deemed moderate-quality evidence.[7-20]

The studies selected

The inclusion criteria set for the selection of these 14 studies by Naude *et al.*[2] were: randomised controlled trials (RCTs); published in English; >10 participants randomised in each group; diet was the only intervention; control and intervention diets were isocaloric (isoenergetic); complete macronutrient profile of intervention diet

was available; control diet was deemed balanced (defined as 45 - 65%, 25 - 35% and 10 - 20% of total energy from CHO, fat and protein, respectively); and the follow-up period was ≥12 weeks.

We started with the assumption that the 14 studies had been chosen in good faith. It transpired that the following four studies should not have been included:

- Luscombe *et al.*,[16] as it was a duplication of Farnsworth *et al.*'s[15] article.
- Keogh *et al.*[17] and Sacks *et al.*,[14] as they failed the inclusion criteria set by Naude *et al.*[2] that fat should provide 25 - 35% of the energy in a balanced diet. Instead, fat provided only 20% of the target calories in the control diets in both those studies.
- De Luis *et al.*,[9] as the data are not conducive to meta-analysis. The two De Luis *et al.*[8,9] studies are visibly incongruent in Fig. 3 of the Naude *et al.*[6] article (Supplemental material 1: Table 4*). Fig. 3 reported weight data from the end of the trial (but without data on weight at the start of the trial), when weight loss during the trial was the target outcome. The error of including these data is inexplicable. The study of De Luis *et al.*[9] cannot be used in meta-analysis, as the study did not report standard deviation (SD) data for the weight losses in the diet and control groups. However, the data of De Luis *et al.*[8] can be used in meta-analysis. We extracted the weight loss and SD data from De Luis *et al.*,[8] as Naude *et al.*[2] should have done for consistency with their other methods of data extraction (Supplemental material 1: Table 6*).

The meta-analysis sub-grouping

Naude *et al.*[6] split the 14 studies into so-called 'high fat variants' and 'high protein variants'. Neither achieved a significant result. However, this split was not justified. Sub-grouping may be undertaken in meta-analysis when two different interventions are being compared, e.g. the comparison of the effects of two different drugs v. no drug control. The sub-grouping of studies into those deemed 'high fat' or 'high protein' was not justified, as Naude *et al.*'s[2] original objective was not to compare high-fat or high-protein diets with balanced diets. Their objective was ostensibly to study the effects of 'low'-CHO diets by comparing *lower*-CHO diets v. balanced diets.

Furthermore, the classification of diets as either high fat or high protein by Naude *et al.*[2] was entirely subjective. To clarify, the studies of Frisch *et al.*[10] and Klemsdal *et al.*[11] complicated calculations of the average macronutrient compositions of all the diets, as these authors reported only the ranges of macronutrient intakes. Frisch *et al.*[10] reported CHO/fat/protein percentage proportions as <40/>35/25 and >55/<30/15 for the diet and control groups, respectively. Klemsdal *et al.*[11] reported CHO/fat/protein percentage proportions as 30 - 35/35 - 40/25 - 30 and 55 - 60/<30/15 for diet and control groups, respectively.

We used CHO/fat/protein in percentage proportions of 40/35/25 and 55/30/15 for the diet and control groups, respectively, in the study by Frisch *et al.*,[10] and 33/38/28 (mid-points rounded up) and 55/30/15 for the respective groups in the study of Klemsdal *et al.*,[11] to calculate average macronutrient intakes for the 14 studies included in the Naude *et al.*[2] meta-analysis as 35/35/30 for the diet groups and 56/27/17 for the control groups. Protein intake in the diet groups of their so-called low-CHO high-protein (LCHP) and low-CHO high-fat (LCHF) studies averaged 31.5 - 32.5% and 28.4%, respectively, probably a biologically insignificant difference. (The variation in the protein proportion for the LCHP group results from macronutrient proportions differing in the abstract and narrative of two studies[15-16] (Supplemental material 1: Table 2*)). In the studies by Lim *et al.*[13] and Aude *et al.*[7] there were higher percentage protein intakes than in four of the six studies placed in their high-protein group.[15,16,18,19] Additionally, if the four studies were excluded that should have been excluded,[9,14,16,17] the protein differential narrows even further to 31.3% and 29.3% for so-called LCHP and LCHF, respectively. The sub-grouping was therefore not necessary, not justified and not robust.

Errors in data extraction

The primary claim emanating from the Naude *et al.*[2] article was that there was little or no difference in mean weight loss between a lower-CHO diet and a so-called balanced diet. This was the only part of the article that we re-examined. We found tens of errors in this re-examination. These are fully detailed in the Supplemental material 1: Tables 1 - 6.* The material errors that we detected are summarised as follows:

- The findings in the studies by Frisch *et al.*,[10] Layman *et al.*,[19] Lim *et al.*[13] and Wycherley *et al.*[20] all favoured the lower-CHO intervention. For all of these studies, Naude *et al.*[2] reported the number of completers in the study at a time later than that at which the weight loss data they included had been recorded. This resulted in lower weighting being assigned to these studies in meta-analysis, as these studies would appear to include fewer participants than was the case. This would have disadvantaged the overall pooled effect for lower-CHO diets.
- The study of Wycherley *et al.*[20] included weight loss data for 52 weeks of the trial. Naude *et al.*[2] reported that they had used those data, but they did not. Instead, they used data from 12 weeks of the study. Use of the 52-week data would have favoured the lower-CHO intervention.
- Krauss *et al.*[12] illustrated the macronutrient compositions of four different diets. Three diets differed in macronutrient composition, but not in saturated fatty acids (SFAs) and were marked as planned (a priori) comparisons. The CHO content of these three were 54%, 39% and 26%, respectively. The fourth diet also contained 26% CHO, but was reported as high in SFA and marked as intended to be compared with the 26% CHO/low-SFA diet alone. Naude *et al.*[2] compared the 26% high-SFA diet with the balanced low-SFA diet, which unnecessarily introduced a second variable and was to the disadvantage of the direct comparison between the lower-CHO and the balanced diet.
- The studies by Farnsworth *et al.*[15] and Luscombe *et al.*[16] were a duplication of the same study. Both studies favoured the control balanced dietary intervention. Furthermore, the weight loss in the control diet intervention was reported by Naude *et al.*[2] as 7.95 kg, rather than the 7.9 kg actually reported by Farnsworth *et al.*[15]
- The use of end-value data for body weight, not weight loss, in the De Luis *et al.*[8,9] studies was absurd and favoured the control balanced dietary intervention.
- The weight loss data for the study by Krauss *et al.*[12] as reported by Naude *et al.*[2] recorded equal weight losses for the diet and control groups. Those specific data could not be found in the original publication. Instead, the actual data reported by Krauss *et al.*[12] slightly favoured the lower-CHO diet intervention.
- The study by Sacks *et al.*[14] should not have been included, as it did not meet Naude *et al.*'s[2] criteria for inclusion. Having been included, the data for weight loss appear to have been reported the wrong way round so that the slightly higher weight loss occurring in the lower-CHO diet was incorrectly assigned to the control diet.
- The study by Keogh *et al.*[17] similarly failed Naude *et al.*'s[2] inclusion criteria, but the data for weight loss in that study slightly favoured the lower-CHO diet intervention. However, the data for the number of completers were taken at the end of the study, whereas the data for weight loss were from an earlier part of the trial. This mitigated some of any advantage afforded to the lower-CHO diet intervention.

All errors made, except for part of the last one listed,[17] favoured the control group.

Study limitations

A number of the studies were not designed to evaluate weight loss as their primary objective. The study of De Luis *et al.*[9] was designed to study two different hypocaloric diets on the secretion of glucagon-like peptide 1. Another study by De Luis *et al.*[8] evaluated weight loss and blood adipocytokine concentrations in obese subjects with a genetic variant. Keogh *et al.*[17] studied flow-mediated dilatation, adhesion molecules and adiponectin after weight loss. The primary aim of the Klemsdal *et al.*[11] study was to evaluate the impact of low glycaemic load v. low-fat diets in people with and without the metabolic syndrome. Krauss *et al.*[12] sought to study the effects of reduced CHO intake and weight loss on atherogenic dyslipidaemia. Lasker *et al.*[18] studied the metabolic effects of two different weight loss diets on dyslipidaemia and post-prandial insulin responses to a meal.

A number of the studies lacked generalisability to whole populations. Wycherley *et al.*[20] and Krauss *et al.*[12] studied males only. Farnsworth *et al.*[15] and Luscombe *et al.*[16] (noting that these are duplicate studies) studied men and women with insulin resistance and hyperinsulinaemia. De Luis *et al.*[8] included only obese subjects with the rs9939609 genetic variant.

A number of the authors did not consider their interventions to be low-CHO diets. Lasker *et al.*[18] and Layman *et al.*[19] described their interventions as moderate-protein diets. The diet in Lasker *et al.*'s[18] study was additionally reported as 'moderate carbohydrate', whereas Farnsworth *et al.*[15] and Luscombe *et al.*[16] (duplicate studies) considered their interventions to be high-protein diets. The studies by De Luis *et al.*[8,9] were described as hypocaloric. Frisch *et al.*[10] reported that their study contrasted the effects of CHO-reduced-intake and fat-reduced-intake diets. Wycherley *et al.*[20] considered their study to be a 52-week comparison of either high-protein or high-CHO diets.

In addition, the four studies[25-28] reviewed by Naude *et al.*[2] to compare *lower*-CHO diets with balanced diets in overweight and obese adults with type 2 diabetes were of concern. We ask ourselves how interventions recommending a 40% CHO intake to participants who cannot metabolise carbohydrate effectively because they have diabetes mellitus type 2 were granted ethical approval.

A revised meta-analysis

Notwithstanding that the Naude *et al.*[2] article: (*i*) did not review genuinely low-CHO diets; and (*ii*) introduced an isocaloric inclusion criterion, which negated the natural advantage of low-CHO diets, to be robust in our re-examination we re-conducted the meta-analysis without the errors made by Naude *et al.*[2]

The meta-analysis was repeated for the 10 studies that could be included in this analysis according to the authors' own selection criteria (Supplemental material 2: Meta-analysis, Fig. 1*). Heterogeneity was evaluated using the Q-value, I^2 and T^2 calculations. Analyses were performed using Comprehensive Meta-Analysis version 2 (Biostat, USA). The overall pooled effect was calculated using random effects meta-analysis. The standard difference in means was significant at −0.272 (95% confidence interval −0.506, −0.039).

In conclusion, when meta-analysis was performed on the 10 studies that qualified for inclusion in the study of Naude *et al.*[2] using their own criteria, the data confirmed that the lower-CHO diet produced significantly greater weight loss than did the balanced diet.

Discussion

The findings of the Naude *et al.*[2] meta-analysis were widely reported in the SA media as disproof of the overall value of the LCHF diet. Indeed, some reports misused this messaging to warn about the 'dangerous' nature of low-CHO diets.

The objective of our re-examination was to test whether or not the findings of the Naude *et al.*[2] article were robust. We have demonstrated that they were not. The main limitation of our article is that we re-examined only one part of Naude *et al.*'s[2] article. We found their analysis of the weight loss data to have many errors and those errors to have made a material difference to the conclusions. Given the number of errors we detected in that single section of the article, it is inconceivable that the remainder of the article is robust. Therefore, without the need to examine all sections of the article, we have shown that in its published form, it is not robust and cannot be relied on.

We additionally showed that, notwithstanding two features of the study, which by design or by chance disadvantaged low-CHO diets, had the Naude *et al.*[2] meta-analysis been properly performed, it would have concluded that the *lower*-CHO diet produced greater weight loss than the balanced diet. This would have radically altered the nature of the message heard across SA after its publication and might have influenced the eagerness of SA medical authorities to put the LCHF/Banting diet on public 'trial'.

A reasonable question to ask is: how could the published meta-analysis have included so many errors and have come to the incorrect conclusion despite peer review? Another reasonable question to ask is: what is the chance that essentially all these errors favoured the so-called balanced diet and disadvantaged the lower-CHO diet, especially when many of the authors of this article are on public record as being vigorously opposed to lower- or low-CHO diets and to those who promote such eating plans?

*__Supplemental material.__ Supplemental material 1: Tables 1 - 6, and Supplemental material 2: Meta-analysis, are available from the corresponding author on request.

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