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What We Know, Think We Know, or Are Starting to Know

One of the few things we can say with relative certainty: the way we're working doesn't appear to be working. From the public health level down to the individual, our current approaches to lowering chronic lifestyle disease risk via weight reduction have become subject to serious scrutiny, based on the apparent inability to maintain lost weight over the long-term [1]. What we also know with relative certainty is that weight reduction *per se* is not the issue: any multiplicity of dietary interventions can all lead to short-term reductions in weight: the issue, clear across the entire body of literature, is the paucity of evidence for longer-term maintenance of weight loss after any short-term intervention [2,3].

One historic core belief was that weight loss should be gradual and slow, and that rapid weight loss was associated with rapid weight regain [4]. This has been revealed to be more myth than fact, and rapid weight loss has not been associated with any greater weight regain than gradual weight loss [4-6]. In fact, a number of studies have suggested that greater initial weight loss may in fact have a positive impact on weight maintenance, or at least result in less weight regained over the long-term [5,7]. However, these studies are generally *post-hoc*, secondary analyses of weight loss trials, and consequently are not directly experimental in nature, but correlation [5,7]. As a result, it is unclear from these studies whether more rapid initial weight loss is the cause of improved weight loss maintenance, or whether other factors influence the results [2,3,5,7].

One study which did directly test the effect of rate of weight loss on long-term maintenance was a 1997 randomised trial by Toubro and Astrup, in which 43 obese adults either consumed a very-low calorie diet ['VLCD'] for 8-weeks, compared to a conventional gradual weight loss diet for 17-weeks [6]. At the end of the weight loss phase, both groups had lost the same amount of weight [13.6kg]; the rate of weight loss in the VLCD group was double [1.6kg/week] that of the conventional diet group [0.8kg]. At 2-years follow-up, the VLCD group had maintained 3kg greater weight loss than the conventional diet group, although this was not statistically significant. However, the interesting feature – and significant finding – from this trial was that after the weight reduction phase, subjects were re-randomised to a maintenance phase involving dietary manipulation [an *ad libitum** low-fat, high carbohydrate diet vs. a fixed energy restricted diet] and intensive support. At 2-years, mean weight regain in the *ad lib* group was only 5.4kg [from 13.6kg lost] compared to 11.3kg in the fixed diet group. What this study demonstrated was that while rate of initial weight loss did not influence long-term maintenance, a combination of dietary manipulation coupled with behaviour therapy did have significant positive benefit.

As the majority of studies assessing rapid vs. gradual weight loss are secondary analyses, the direct research question of whether rate of initial weight loss has a causative influence on long-term maintenance remains unclear, and there is a lack of trials which directly test this relationship experimentally. The study under scrutiny here did exactly that.

*Geek Box: Ad Libitum Diets

What does 'ad libitum' mean in research? The Latin for "at one's pleasure", the formal meaning of it is as much as desired or as much as you want. In nutrition research, what this means is that there are no restrictions being placed on the subjects in terms of either total calories, specified macronutrients, or specific food groups. This can be a good 'field-test' for a dietary intervention, given that the majority of people don't track calories in real life. It is a good test for the impact of dietary composition and food types on energy balance, health markers, or whatever the outcome of interest is, in a more real-world context. Researchers might use an 'ad lib' diet to look at the impacts of a diet low in one macronutrient on energy balance. Thus, an 'ad lib' low-fat diet would place restrictions on the amount of fat a subject could have (usually 20-25% energy, with subjects counselled to use certain foods/oils), but with no restrictions on the remainder of their food choices or total energy. Similarly, an 'ad lib' low-carb diet would place restrictions on carb intake (usually 10-25% energy, with no starchy carbs, fruit, refined sugar) but no restrictions on the amount of fat or total energy. With popular recent focus on low-carb diets, the research on ad-lib low-fat diets has been largely brushed aside – or just forgotten, given that it was a more popular intervention in the 1990's. What is certainly forgotten amongst carb-hysteria was how successful they were as interventions. Bottom line: macronutrient restricted ad lib diets can be effective whether it is carbohydrate or fat that is restricted, and depend on the characteristics of the diet adopted, in addition to personal preference.

The Study

200 subjects [BMI 30] were randomly assigned to either a gradual weight loss group [n=103] or a rapid weight loss group [n=97], with a target weight loss of 15% bodyweight in both groups; the gradual group aimed to achieve this in 36-weeks while the rapid group aimed to achieve this in 12-weeks. For the divergent rates of weight loss, the rapid weight loss group consumed a liquid diet of up to 800kcal aiming for a rate of weight loss of 1.5kg/week; the gradual weight loss group consumed a diet in line with the Australian Guide to Healthy Eating with a 400-500kcal/d energy deficit. Both diets ultimately contained the same overall energy deficit, differing only in the timeframe of dieting. During the dieting phase subjects were given nutrition education materials, and attended appointments with the same dietitian every 2-weeks.

Following the weight reduction phase, those subjects who achieved a minimum of 12.5% weight loss were entered into the maintenance phase of the period for 144-weeks. During the maintenance period, subjects followed an individualised diet based on the Australian Guide to Healthy Eating while attending individual dietitian consultations, initially at 4-weeks and 12-weeks into the maintenance period, then every 12-weeks for the 144-week remainder of study duration. Food-intake during this period was self-reported. Subjects were also instructed to take 30mins of mild-moderate activity every day for the duration of the study.

The primary outcome of the study was mean weight loss maintained at 144-weeks. Secondary outcomes included appetite hormones leptin and ghrelin, and subjective appetite. The study also analysed changes in physical activity levels between groups. Measures were taken at baseline, at the end of the weight loss phase, and at weeks 48 and 144 of the maintenance phase.

Results: 179 out of 200 [89.5%] subjects completed the weight loss phase and achieved 12.5% bodyweight loss [14.6kg and 14.3kg in the rapid and gradual weight loss groups, respectively]. There were significantly more drop-outs from the gradual weight loss group [n=18] than the rapid weight loss group [n=3]. In intention-to-treat* analysis, 76 out of 97 [76%] subjects in the rapid weight loss group achieved the target weight loss, compared to 53 out of 103 [51%] in the gradual group. There were no significant differences in changes of fat mass or fat-free mass between groups. In total, 127 subjects entered the maintenance phase; 76 from the rapid group and 51 from the gradual group.

During the maintenance phase, practically all subjects who entered– 116/127 – started to regain weight, and were thus prescribed a 400-500kcal/d energy deficit. Notwithstanding this prescription, the maintenance phase was characterised by linear increases in weight regain such that by the end of the study period at week 144 average weight regain in was 10.3kg in the rapid group [71% of total weight lost in phase 1] and 10.4kg in the gradual group [70% of total weight lost in phase 1]. By week 48 both groups had regained a similar amount of weight, and there were no differences in rate of regain over the course of the study between diet groups.

Leptin decreased in both groups during the weight loss phase, with a greater reduction in the rapid group; leptin levels rose over the course of the maintenance phase – by week 48 leptin levels in both groups were similar to baseline levels – but by week 144 leptin levels were elevated significantly above baseline levels by 43% in the rapid group and 23% in the gradual group [no significant difference between groups]. Ghrelin levels increased following weight loss in both groups: 40% increase above baseline in the rapid group and 29% in the gradual group. Ghrelin levels remained elevated above baseline to the end of the study: at week 144 ghrelin was 15.5% and 10% higher the in the rapid and gradual groups, respectively. Subjective hunger was also significantly elevated after, but not during, the weight loss phase.

*Geek Box: Intention to Treat Analysis

In a randomised controlled trial, you want to match both arms of the trial to ensure that one side doesn't influence (i.e., bias) the results more than the other. This can be a problem if there is, for example, a high drop-out rate in one arm of the trial; the other arm will then have more statistical power, and it may overinflate the effect of that arm vs. the comparative arm (or the control, if it is a control arm). Intention to treat [ITT] is where the researchers will conduct analysis as if all subjects randomised in the trial completed it, irrespective of whether they dropped out, or didn't comply with the protocol. Drop-out and noncompliance are two issues which face many trials, in particular nutrition and weight loss interventions. True intention to treat analysis requires complete data to be available for all subjects who didn't complete the trial according to protocol. However, that is not always available, and so often researchers will make assumptions based on, for example, a last data point or a baseline measurement (for example, in this study for dropouts in the maintenance phase the researchers assumed that subjects returned to their baseline weight for ITT analysis – not unreasonable given the weight regain in subjects who completed the trial). Intention to treat is a positive because it maintains the sample size, and it assumes a real-world practicality – because in the real world, not everyone is compliant with a protocol (as any practitioner knows!).

The Critical Breakdown

Pros: The study had a strong design and did not have the high attrition rate of many weight loss interventions; this makes the findings more reliable than other studies. Randomisation was computer-generated and block randomisation* was employed to account for age, sex, and BMI. Intention to treat analysis incorporated baseline weight into the statistical analysis for subjects who dropped out. The study also provided data on energy balance/appetite/hunger regulatory hormones, ghrelin and leptin, providing data on a critical variable too often overlooked in weight loss trials.

Cons: Data on food intake during the maintenance phase was self-reported; with such a long follow-up, some periodic dietary collection methods could have been employed. Clearly subjects were unable to comply with the prescription of a 400-500kcal/d energy deficit in the maintenance phase, as the cohort uniformly regained the weight [i.e., they were in positive energy balance]. In effect this study was not a test of "maintenance" in a true sense, as subjects were being prescribed dieting to offset weight regain. It was, at best, a test in futile mitigation, highlighted by the fact that with the exception of a generic physical activity prescription there was zero focus on health-promoting behaviours in the study. An example of this futility can be seen in the discrepancy in practitioner contact during the weight loss period; subjects met a dietitian every two weeks, which amounted to 6 meetings for rapid group subjects and 18 for gradual group subjects. Although this could have been a bias, it clearly had no effect: the gradual group had a higher attrition rate during the weight loss phase, and only 51% achieved the target. The major limitation is the lack of implementing any behaviour modification during the maintenance phase to test what behaviours may contribute to long-term maintenance. Given what we know to date about behaviours influencing outcomes in this respect, this is a fairly critical omission.

*Geek Box: Block Randomisation

The most basic form of randomising subjects is simple randomization, which involves dividing subjects at random to allocation of either treatment group or control, preferable by using a computer-generated sequence or numbered tables. The essential characteristic of simple randomisation is that all subjects have an equal chance of allocation to either group. However, subjects may still have differing characteristics that could influence the outcome of interest, like age or sex. To address this, block randomisation divides subjects into multiple, smaller groups of equal subjects based on a predetermined group size. The advantage of block randomisation is controlling for balance across similar-sized groups, and by stratifying subjects according to similar characteristics to achieve a balance of characteristics between block groups. This allows for particular baseline characteristics, for example age, to be balanced by grouping together particular characteristics which could influence the dependent variable.

Key Characteristic

The study duration. A major limitation of much of the literature is that "long-term" is often considered anything over 6-months in duration, often only up to 12-months. The total study duration for subjects in the rapid weight loss group was 3-years, and 3.5-years in the gradual weight loss group. This allowed for important findings, not simply the time-course of weight regain and whether either diet group influenced this variable over the long-term, but in particular the persistent adaptive effects of the weight loss period on leptin and ghrelin.

Within the study duration, the other critical characteristic [and flaw] was the failure to focus on positive health-promoting behaviours to maintain weight loss. Subjects who began regaining weight were re-prescribed a 400-500kcal/d energy deficit. The failure of this is consistent with previous analysis indicating that attempting to control weight was a factor in weight regain [3]. Further, evidence of long-term maintenance from the Look AHEAD [Action for Health in Diabetes] Study demonstrated that the 42% of subjects who maintained >10% weight loss at 4-years follow-up were those who engaged most with behaviour modification, in particular successful maintainers in the Look AHEAD trial were those with the most practitioner contacts over the follow-up period [8]. It appears the researchers in the present study did not give adequate consideration to the methodology to be employed in achieving maintenance, which is clearly evident in the literature: behaviour modification.

Interesting Finding

The findings in relation to leptin and ghrelin.. A very interesting finding was that in 15 subjects who regained less than 25% of their weight loss, leptin levels remained below their baseline levels at week 144. In the subjects who regained 75% of lost weight, leptin was elevated significantly above baseline by week 144.

The decrease in leptin during energy restriction and fat mass loss is predictable, as is the gradual increase in the second phase of the study up as weight was regained, given experimental research consistently shows a compensatory response following weight loss – specifically reductions in adipose tissue [9]. This is because leptin is secreted from adipocytes [fat cells], and decreases with loss of fat mass and energy restriction, while elevating with increases in fat mass. Generally, the expected effect of leptin during weight maintenance is to remain lower, predisposing an individual to increased appetite, energy intake, and weight regain (9). Yet, in this study those who successfully maintained lost weight retained leptin levels lower than baseline. This may lend more support to the recent challenge to the traditional view of leptin as a single direct signal to the brain controlling body fat [10]. More research is certainly needed in relation to this finding.

The finding in relation to ghrelin is somewhat more straightforward: elevated ghrelin = elevated hunger. There was a persistent elevation in ghrelin levels above baseline, which indicates another adaptive response to dieting that predisposes an individual to weight regain. Sumithran et al. found persistent elevations in appetite and hunger hormones 1-year after weight reduction in 50 subjects whom had undergone a VLCD [13.5kg lost] [11].

Collectively what these findings support is the persistent adaptive hunger-appetite responses to loss of body mass, with loss of fat mass having a stronger influence on hunger-appetite drive [12]. Again, more research is needed to determine what factors may mitigate these effects.

Relevance

The relationship between rate of weight loss and other adjuvant interventions is an area we lack good data on. On the one hand, many of the post-hoc secondary analyses are often cited as evidence that greater initial weight loss improves longer term maintenance. On the other hand, closer scrutiny of these studies reveals that rate of initial weight loss may not necessarily be the variable influencing long-term retention of weight loss, but the fact that behavioural therapy [BT] is combined. Indeed, there is support for a combination of VLCD and BT resulting in better outcomes than a conventional diet plus BT, or BT alone [2,13]. Long-term maintenance of weight loss is a multifactorial trait, and closer scrutiny of much of the literature comparing rate of weight loss and long-term follow-up reveals that the determining factors in successful maintenance are a combination of dietary intervention, intensity of follow-up [active vs. passive in terms of participant-practitioner contact/support], and behaviour modification, combining to yield the most positive results [2,6,8].

The real relevance of this study is consistent with the wider literature comparing fast vs. slow rates of weight loss: that there may be advantages to rapid weight loss for a number of reasons, but that these are an absolutely moot point unless behaviour modification is emphasised to achieve maintenance. In this regard, issues with long-term maintenance evident in the literature should not be a barrier per se to considering the factors that may underscore an advantage to rapid weight loss. Methodology can always be improved, for both processes. The emerging data for the applicability of rapid weight loss via energy restriction as a potentially low-cost, high-reward intervention for Type-2 Diabetes management warrants further investigation of improving methodology for the application of VLCD.

One reason why VLCD may be effective is the short duration, improved compliance and the unambiguous nature of the prescription. In this study, the rapid group had less drop outs, greater success of target weight loss: 81% in rapid group vs. 62% in gradual group. In analysis predicting success in achieving target weight loss, the diet group – favouring rapid loss – was a significant factor after adjusting for factors like age, baseline weight, and sex. And the rate of loss did not influence greater weight regain, which is similar irrespective of diet group. This comes back to the failure to focus on behaviour change in the maintenance period.

There are arguably two distinct elements to consider here: efficacy of the weight loss period as an intervention, and then the issue of lack of long-term maintenance. In many of the current heated debates about adiposity and health, the latter is often stated to disqualify the former. Yet this is an over-simplistic dismissal, because it is based on a position that there is no evidence for long-term maintenance: there is, it is just highly dependent on adjuvant factors in the maintenance period, with an emphasis on behaviour change [6,8,14]. It is striking that trials remain designed to look at weight loss, when what really should be tested is the efficacy of different behaviours, and combinations thereof, in facilitating maintenance. This becomes more crucial when we consider that maintenance gets easier over time: the odds of successfully maintaining weight loss improve exponentially beyond 2-years [15].

Merging the considerations of improving efficacy of weight loss interventions with efficacy of long-term maintenance creates another issue in the potential to overlook, for a myopic focus on negative factors, what positive factors may be identified. The narrative of 'weight loss is impossible so don't even try' is as problematic as the narrative of 'your weight determines your health'. Neither are helpful.

Application to Practice

We can synopsise this: **behaviours > outcomes**. This is the most important take-home point. When an overt outcome is controlling weight, the evidence indicates this is a predictor of weight regain. What behaviours are positively associated with weight loss maintenance? What appears to be vital is intensity of follow-up, i.e., frequency of contact with practitioners: for practitioners in private practice, this is something to consider when working with individual clients. Factors including increasing physical activity [the strongest and most consistent predictor of successful maintenance], fewer intentional weight loss episodes, greater time spent in maintenance, and less dietary restraint, are all behaviour modifications associated with successful maintenance

It is important to stress that VLCD is a clinical nutrition intervention, and should only be considered in this context. It is also important that practitioners start to see weight loss for what it is: an intervention. As such, it is important to appropriately assess risk in an individual, and assess whether the intervention is suitable and appropriate for that individual. We remain in a default paradigm which assumes it is, irrespective of circumstance, with no consequence. But no intervention is risk free, and it is an entirely pointless endeavour to pursue a short-term outcome if it there is no long-term benefit. This mandates an appropriate assessment of need, risk:benefit, and if the intervention is appropriate, a behaviour-orientated approach.

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