The fundamental flaw in obesity research

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Summary

The basic problem with comparative diet trials is our inability to measure what people eat. All conventional instruments depend on subjects’ reports. Most trials lack independent biochemical, physiological or genetic measures of intake. So, we do not know if subjects actually follow the diets being tested and compared. We can assess weight gain/loss, but we fail in a fundamental scientific requirement, accurately measuring the independent variable in a causal experiment. Worse, we know most subjects under-report their energy intake and its components, the obese especially. The problem is compounded by attempts to show diets’ effects on other risk factors, like triglycerides. Researchers seek to correlate two variables, without having accurately measured one of them, producing misleading associations. The consequence is we do not know if the results of any current diet trials are valid or reliable. Developing rigorous measures of food intake is the highest priority in obesity research. That involves improvements in technology as well as science. We need: (1) biomarkers of intake for energy, macro- and micro-nutrients and other food components relevant to weight gain/loss; (2) field measuring instruments that are cheap, rapid, painless, non-intrusive and self-administerable; and (3) electronic data transmission systems that preclude subjects’ ability to misreport.

Keywords: Biomarkers, diet trials, intake measures, under-reporting.

The silver lining inside the black cloud of the international obesity epidemic is that, at long last, weight management has become a major public health issue. One positive consequence of this new priority is the increased interest in and funding for comparative trials of weight loss diets. But the silver will soon tarnish unless we can solve the fundamental problem in dieting research – our inability to measure what people actually eat. As a result, we cannot tell whether subjects are really following the diets that are being tested and compared. Without this basic information, we will never have an evidence-based science of dieting; we will never know what works or why.

Inadequate measuring instruments

Most trials of free-living populations involve assigning subjects to alternative diets. Their food intake is measured, if at all, by one of the conventional instruments – food frequency questionnaires, diaries, recalls, diet histories, weighed records. All these methods share the same weakness; they all depend on subjects honestly telling researchers what they consumed. Most trials lack measures of food intake that are independent of subjects’ reports. ‘Independent’, in this context, means biochemical, physiological or genetic indicators of the energy, nutrients and other food components consumed. Research on such ‘biomarkers of exposure’ is expanding, but still incomplete (1). So, in most diet research, there are no objective measures, only subjective accounts.

Yet, it is universally recognized that most subjects misreport what and how much they eat. Lacking adequate measures, the process is imperfectly understood, but appears to be broadly normative. That is, people claim to
eat more than they actually do of some foods, especially those conventionally seen at the time as ‘healthy’, and less of others, especially those popularly thought to be ‘unhealthy’ or ‘fattening’.

The consequence is a complex pattern of partly inaccurate information. Some foods are overreported, others underreported, but we do not know which ones or how much. The net result, however, is that most people substantially underreport their total energy intakes (2). And the overweight underreport most, sometimes by more than 40%. All existing ‘dietary assessment methods have a strong bias towards underestimation of habitual energy intake’ (3).

Faced with these difficulties, some researchers do not even attempt to measure food intakes, because they could not trust whatever information they obtained. This is a hard-headed but rational decision, given current methods. But it is also the most basic criticism of those methods – they are not worth using.

Either way, whether we employ the conventional measures or forswear them, we remain equally ignorant. We are failing in a fundamental task of science, accurately measuring the independent variable in a causal experiment.

The independent measures that do exist have limited applicability. Experiments in sealed metabolic wards have total control over how much food subjects are given. But these are small sample, short-term studies in artificial conditions, important for some purposes, but not for studying the variegated real world or the long-term consequences of dietary restriction.

The ‘shop system’, in which subjects obtain all their food from a single monitored outlet, attempts to attain similar control over intakes with a free-living population in a dietary intervention. But extensions of the technique would still ‘require a reliable and documented method of validating an apparently strictly controlled food intake’ (4).

For unconstrained free-living subjects, double-labelled water is an acceptable surrogate measure of total energy intake (5). But normally it depends on subjects maintaining a stable weight, so in studies intentionally designed to produce weight loss, it requires additional assumptions about the composition of that loss. In any case, it is too expensive to be used in the large and lengthy trials that are needed.

Measuring what? Energy and beyond

In addition, for current research purposes, we need to measure more than total energy consumption. While the energy balance theory of weight gain/loss is almost universally accepted, one of the current controversies in the field is whether different sources of energy exert an independent effect on the process. So we also need to know, at the very least, the macronutrient composition of subjects’ intakes.

This is essential, for example, to resolve the debate over ‘low-fat’ and ‘low-carb’ diets. But we lack independent measures of both fat and carbohydrate intake, capable of being used in trials (6–8).

The inadequacies of our measures for the independent variables in diet trials contrast sharply with the precision of measures for the dependent variables. Weight is, of course, easily determined. But these days, serious trials always also attempt to measure the effects of alternative diets on other important biochemical indicators of metabolic risk, like serum cholesterol, triglycerides or body fat composition.

With sophistication, researchers commonly try to assess whether alternative diets show significant differences in their effects on these other substances. And sometimes they even draw conclusions that one diet is better for the heart (or some other organ) than the other. Yet, they do not know whether their subjects were actually eating different diets.

Researchers are trying to correlate two variables, without having adequately measured one of them. As a result, they generate spurious associations (9) or miss genuine ones (10) and often form conclusions that are ‘doubtful or actually misleading’ (11).

Experienced diet researchers, like experienced dieters, know that most people do not keep exactly to prescribed weight loss regimes. Most deviate in some way, in some degree. But we do not know in which ways and to what degree. In reality, what subjects eat is an imperfect realization of assigned diets, not fully a ‘low-fat’ or a ‘low-carb’ diet, for example – at least not one that Ornish or Atkins would recognize.

In analyzing their data, researchers sometimes exclude reports of implausibly extreme intakes, based on a comparison of reported consumption with basal metabolic rate, most commonly using the ‘Goldberg cut-offs’ (12). But their ‘sensitivity for identifying under-reporters at the individual level is limited’ (13).

Others make various ‘energy adjustments’, but these ‘cannot eliminate differential biases in the reporting of macronutrient intake and under some conditions may even exacerbate the problem’ (5).

These are attempts to cope with the problem, rather than to correct it at source. And in their final articles on diet trials, most researchers assume, claim, or at least act as if, their subjects kept to the alternative diets to which they were assigned.

The consequences of mis-measurement

This has two perverse and contradictory consequences – their conclusions may be either too strong or too weak. On the one hand, some researchers assume that all effects they record are solely the results of radically different diets, and
hence reach firmer judgements about them than they would if they had accurate measures of actual consumption. On the other hand, some researchers report that the differences in the effects of the alternative diets were small or diminished over time – reflecting perhaps that their subjects’ real intakes were not so different as the research protocol prescribed, or at least did not remain so over the full length of the trial.

Recognizing the weakness of food intake measures leads to a daunting conclusion. If we are rigorous, none of the diet trials on free-living populations so far can be relied upon.

This is not the same as saying that their results are wrong. The conclusions may be correct – in the round or even on specifics, for all practical purposes or even clinical ones – but we cannot be certain. As we know from the histories of many sciences, meeting prevailing standards of ‘proof’ does not guarantee validity (14). Conversely, a lack of conventional proof does not mean that conclusions are false. But we just do not know.

We live in an era with increasing demands for evidence-based medicine. Until we develop independent measures of food intake, both in total and for its constituents, all weight loss studies in free-living populations will remain, literally, incredible – that is, we will not know whether the results are valid and/or reliable.

Given that developed and developing countries alike are in the midst of an obesity epidemic, when millions need practical advice on weight loss, that is a sad conclusion to draw. But it is the first step to engage with the fundamental flaw in obesity research.

Overcoming underreporting

In recent years, there has been increasing willingness to disclose and discuss underreporting, regarding it as a straightforward technical issue (15). Such candour is a great improvement on the earlier silence, which treated faulty consumption data as the skeleton in the cupboard of nutritional science, which dare not be exposed to public view.

But acknowledging a problem does not solve it, exonerate researchers, redeem results, validate conclusions, or improve applications in the real world. Developing rigorous measures of food intake in free-living populations is the highest priority in obesity research. In practice, that means discovering biomarkers for total energy intake, for energy-providing macronutrients and their principal subdivisions, for all those established micronutrients which influence metabolic processes relevant to weight gain/loss, and eventually also for the increasing number of other food components, the ‘functional ingredients’, which may prove relevant (16).

Developing a comprehensive set of validated biomarkers of intake, including new genetic indicators (17), will also help resolve a related problem which has long fuzzied nutritional research – the limitations of food composition tables.

Determining the nutritional composition of people’s diets at present is a two-stage process: first measuring the intakes of foods, then converting those foods into nutrients by using food composition tables. Although such tables are practically very useful, they all have weakness, most importantly, incompleteness and inaccuracy. They add a second source of imprecision in the assessment of intakes.

Biomarkers have their own technical problems, but they employ a radically different approach to these issues. The nutritional composition of the diet is measured inside the eater, instead of inside the food (4).

Not all biomarkers will be relevant in every trial, on cost–benefit grounds as well as theoretical applicability. But the full range will eventually be necessary for a comprehensive understanding of weight gain and loss.

Technology as well as science

However, even developing accurate and reliable laboratory measures is not sufficient. Biomarkers must be usable in trials on large numbers of free-living subjects over long periods. So, the measuring instruments and testing procedures must be cheap, rapid, painless, non-intrusive, and self-administrable. If not, researchers will be unable to afford them and subjects will use them only irregularly, or not at all.

Further, the results must be captured directly into an unalterable record or, better yet, be capable of electronic data transmission from the field to researchers, without any intermediate recording by subjects. If the outcomes of new self-administered tests have to be transcribed by subjects themselves, they become vulnerable to the same misreporting that undermines all existing instruments. It is no use developing sophisticated independent measures of food intake, if the process of reporting their results is not simultaneously transformed.

In sum, a research and development programme for the rigorous measurement of food consumption involves three components: new analytical techniques, new measuring instruments, and new reporting systems. We need improvements in technology as well as in basic science.

These are prerequisites for progress. Diet trials are already complex, but are about to become immeasurably more complicated as, for example, our understanding of genetic and hormonal influences on obesity increases (18). There will be pressure to focus attention, effort, and funding on these new fields. But research in these areas will be compromised, and of limited practical value, if we still cannot measure food intake without massive underreporting. This is the fundamental problem that must be solved first.

Only when we can accurately measure total food intake and its component parts, will we be able to determine
which diets yield sustainable weight loss. Only then will we be able to give people effective guidance on how to lose weight. Accurate measurement of food intake is the foundation stone for a science of dieting.

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References