

## Is 5% Weight Loss a Satisfactory Criterion to Define Clinically Significant Weight Loss?

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The idea of quantitative measurement came to obesity in stages. Quetelet (1) introduced the body mass index (BMI) which was applied nearly a century later to the evaluation of degree of overweight in studies of familial inheritance of obesity. Publication of average weight tables in the 1850s was expanded to “ideal” weight tables by the life insurance industry in the mid-20th century. The relation of increasing weight to risk for many diseases was extended by the Framingham Study from which Gordon and Kannel (2) concluded that if everyone were at optimal weight, the incidence of coronary heart disease would be reduced by 25% and congestive failure and brain infarctions would be reduced by 35%. By 1975 there had been many observations about the association of obesity and a variety of health problems. Yet at this time, there were no generally agreed upon metrics for evaluating health effects of weight loss. In 1973, Dr. Thaddeus Prout (3) authored a final report to the Food and Drug Administration (FDA) Director of Anorectic Drugs which interpreted the statistically significant differences between placebo and anorectic drugs in the short-term clinical trials reviewed by the FDA as being “clinically trivial” (p 501). Bray (4) at the 1973 Fogarty International Center Conference noted: “Little uniformity exists in the criteria which are used for evaluating weight loss or in the uniformity of follow-up between various clinical trials” (p 60). The Fogarty Conference report suggests several criteria, including percent achieving 20- and 40-pound weight loss and a weight reduction index. Clearly, in the mid-1970s the obvious question was “What defines clinically significant weight loss?” Up to this point in the story, few, if any, had suggested that modest weight losses might have important health benefits.

In the 1980s, one approach to this question of clinical significance was based on defining clinically significant overweight as a body weight with a BMI >30. Thus, clinically significant weight loss would be reduction below BMI = 30 (5). In 1991, Rossner (6) interpreted outcomes of treatment by percent weight loss. He concluded that <5% weight loss may reduce risk but was unsatisfactory, whereas a weight loss of 5-10% was considered a “fair” response. In 1992, Goldstein (7) recommended ~10% weight loss or less to define clinically meaningful weight loss. Blackburn (8) in 1995 suggested that 5% might be a valid “single” criterion to assess significant weight loss. Two landmark studies of diabetes prevention supported this recommendation. An average weight loss of 5.5% reduced the incidence of diabetes by 58% in the American Diabetes

Prevention Program (9) trial. A systematic analysis of clinical trials with outcome data observed for at least 2 years by Douketis et al. (10) provided convincing evidence that 5% weight loss produced important improvements in risk factors or incidence of disease in populations “at risk” from their obesity. A statistical model of the weight loss data from the American Diabetes Prevention Program trial by Hamman et al. (11) showed that for every kilogram of weight lost there was a 16% reduction in risk for progression to diabetes and that 5% weight loss would produce about 50% reduction in the incidence of type 2 diabetes. A categorical analysis of weight loss (12) from the Look AHEAD trial demonstrated a strong relationship between glycemic measures and weight loss, with improvement beginning at 2.5% to 5% weight loss. For systolic and diastolic blood pressure, HDL cholesterol, and triglycerides, improvement began at ≥5% weight loss.

In 2013, an expert panel formed by the NIH conducted an evidence-based review of the literature (13) around five critical questions. Critical Question 1 addressed the health benefits of weight loss: What amount (shown as percent lost, pounds lost, etc.) of weight loss is necessary to achieve benefit with respect to CVD risk factors, morbidity, and mortality? The graded evidence statements that resulted from this effort provide the strongest support for weight loss beginning at 3% (for glycemic measures and triglycerides) and 5% (for blood pressure and HDL and LDL cholesterol) to be considered clinically meaningful. The committee went on to conclude that increased amounts of weight loss provided even greater benefits. Thus, by 2015 the consensus and evidence for 5% weight loss as a marker for clinical significance was strong, with lesser weight loss also demonstrating benefits in certain risk factors. We agree with the recommendation of the expert panel (13) that the critical time frame for defining a clinically meaningful weight loss (at least 5%) is after 1 year of treatment.

Is 5% weight loss a reasonable criterion to define clinically meaningful weight loss? The answer is yes and no. From the perspective of establishing a validated criterion for evaluating effectiveness of weight loss interventions across investigations and programs, the 5% criterion appears to be well justified. In accepting this criterion, however, several caveats must be considered. First, greater weight loss is better because more weight loss produces better health benefits (12,13). Second, initial weight loss is a strong predictor of long-

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term weight loss and if patients are to sustain health benefits when challenged by weight regain, it makes sense to implement treatment strategies that are likely to produce weight loss that is greater than 5%, e.g., by using meal replacements or procedures to induce greater weight loss during the first few months of treatment (13). And last, even lesser weight losses (2.5-5%) may bring benefit in some risk factors and for some patients (13). Our conclusion is that 5% as a meaningful marker of weight loss success for medical treatment is here to stay. It provides a benchmark for evaluating whether the patient's response to treatment is "successful." But where individual patients are concerned, we must not lose sight of the fact that greater weight loss is likely to achieve even better health outcomes, and even less weight loss may bring benefit (13). Our focus must be on targeted health measures, not just amount of weight lost. **O**

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