HHS Public Access

Author manuscript

Curr Obes Rep. Author manuscript; available in PMC 2018 June 01.

Published in final edited form as:

Curr Obes Rep. 2017 June ; 6(2): 187–194. doi:10.1007/s13679-017-0262-y.

Weight Loss and Improvement in Comorbidity: Differences at 5%, 10%, 15%, and Over

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Abstract

One begins to see improvement in glycemic measures and triglycerides with small amounts of weight loss, but with greater levels of weight loss there is even greater improvement. In fact, the relationship between weight loss and glycemia is one that is very close. This is fortunate for diabetes prevention; it takes only small amounts of weight loss to prevent progression to type 2 diabetes from impaired glucose tolerance and after the 10 kg of weight loss one cannot demonstrate much additional improvement in risk reduction. Modest weight loss (5 to 10%) is also associated with improvement in systolic and diastolic blood pressure and HDL cholesterol. With all these risk factors more weight loss produces more improvement. Further, for patients with higher BMI levels (>40 kg/m^2), the ability to lose the same proportion of weight with lifestyle intervention is equal to that of those with lower BMI levels and there is equal benefit in terms of risk factor improvement with modest weight loss. For some comorbid conditions, more weight loss is needed – 10% to 15% - to translate into clinical improvement. This is true with obstructive sleep apnea, and non-alcoholic steatotic hepatitis. There is a graded improvement in improvements in measures of quality of life, depression, mobility, sexual dysfunction, and urinary stress incontinence, whereby improvements are demonstrable with modest weight loss (5–10%) and with further weight loss there are further improvements. For polycystic ovarian syndrome and infertility, modest weight loss (beginning at 2–5%) can bring improvements in menstrual irregularities and fertility Moderate weight loss (5–10%) has been shown to be associated with reduced health care costs. Reduction in mortality may take more than 10% weight loss, although definitive studies have not been done to demonstrate that weight loss *per se* is associated with mortality reduction. Clinicians in medical weight management should bear in mind that the target should be health improvement, rather than a number on the scale. The individual patient's targeted health goal should be assessed for response, rather than a prescribed percentage weight loss.

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Compliance with Ethics Guidelines

Conflict of Interest

Donna H. Ryana and Sarah Ryan Yockey declare they have no conflict of interest.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

Keywords

obesity; obesity comorbidity; weight loss; weight management; type 2 diabetes; dysglycemia; hypertension; dyslipidemia; obstructive sleep apnea; non-alcoholic fatty liver disease; weight loss and comorbidity improvement; polycystic ovarian syndrome; infertility

INTRODUCTION and BACKGROUND

A 5% for weight loss from baseline is generally accepted as a "clinically meaningful" amount.[1] Certainly, the 2013 Obesity Guidelines recommended weight loss of 5–10% as the goal for medically supervised weight loss.[2] Further, the US Food and Drug Administration Draft Guidance for medications for management of obesity has as one of the criteria for approval, that the medication achieve an average weight loss of 5% or greater than a placebo.[3] But is it true that weight loss of 5% or 10% can bring health improvement for all obesity comorbidities? If not, how much weight is needed to produce clinically meaningful improvement in the various risk factors, comorbid diseases and mortality that are associated with obesity? This discussion will examine the link between excess body weight and comorbidity development and its counterpart weight loss and comorbidity improvement. The mechanisms by which excess body weight drives comorbid disease risk and by which weight loss improves pathology will also be explored. Finally, we will attempt to recommend a strategy for individual patients in selecting a target for body weight loss.

EXCESS WEIGHT AND HEALTH RISK

BMI above 25 kg/m^2 is associated with increased risk for mortality and cardiometabolic diseases and the relationship demonstrates increasing risk with increasing BMI. This has been well established since the 1970's supported by many studies of actuarial data from life insurance companies and observational studies of populations. Indeed, the recent Obesity Guidelines[2] devoted a critical question and a systematic evidence review evaluating the cut point of 25 kg/m^2 and 30 kg/m^2 as markers of "overweight" and "obesity." That review[2] confirmed the current cut points as being valid, compared to normal weight status (BMI 18.5 <25kg/m2), for identifying increased risk for diabetes, stroke and coronary heart disease. Further, when BMI is treated as a continuous variable, the greater the BMI, the greater the risk for these conditions. As for all-cause mortality, the greater the BMI the greater the risk, but the relationship between overweight (BMI 25 <30 kg/m2) was not increased compared to normal weight.[2]

MECHANISMS BY WHICH EXCESS BODY FAT INCREASES HEALTH RISK

Current thinking about how excess adiposity drives health risk is through several mechanistic pathways. The excess physical burden of body weight can play a role, especially in lower extremity arthritis and pain and in sleep apnea. For example, in knee osteoarthritis, every pound of excess weight exerts a four-fold burden on the knee per step in daily activities.[4] Another mechanistic pathway is through biochemical products of fat tissue.[5] Fat tissue itself is an active endocrine organ, secreting a number of adverse cytokines, including pro-inflammatory and pro-thrombotic molecules, among others. The "portal hypothesis"

also maintains that free fatty acids released from visceral fat stores directly into the portal vein bathing the liver and contributing to the abnormal lipid profile and insulin resistance characteristic of metabolic syndrome. Circulating free fatty acids can also affect muscle insulin sensitivity. Finally, fatty infiltration of liver and muscle can contribute to pathology.[6]

MECHANISMS BY WHICH WEIGHT LOSS CAN IMPROVE HEALTH AND HEALTH RISK

A recent paper[7] from Washington University in St Louis describes an experiment in which different levels of weight loss were assessed for their impact on metabolic function and adipose tissue biology. This experiment explored the mechanisms by which different degrees of weight loss impact a variety of advanced clinical endpoints. In the study, 40 volunteers with obesity and insulin resistance were randomly assigned to weight maintenance or to a dietary weight loss intervention which aimed for 5% weight loss, subsequently 10% weight loss and subsequently 15% weight loss. The actual mean weight losses achieved were 5.1% ± 0.9% (n = 19), 10.8% ± 1.3% (n = 9), and 16.4% ± 2.1% (n = 9). In the weight maintenance condition, 14 completed the study. Interestingly, body weight loss was associated with disproportionate loss of body fat across multiple compartments. The 5%, 11% and 16% weight loss was associated with 10%, 18% and 27% reduction in total kg fat mass, respectively and 9%, 23% and 30% reduction in intra-abdominal adipose tissue (cm^3). Even more disproportionate is the reduction in intra-hepatic triglyceride, measured as percentage on Magnetic Resonance Imaging, a 13%, 52% and 65% reduction for each weight loss level, respectively. Thus, it appears that with total body fat loss, the stores of intra-abdominal and intra-hepatic fat are preferentially lost. This preferential loss of adverse fat storage sites may account for the metabolic benefits observed with 5–16% weight loss in the study.[7]

In addition, Magkos et al[7] showed that the body composition changes were associated with a variety of improvements in clinical endpoints, but that different tissues responded to different degrees of weight loss. 5% weight loss significantly decreased the plasma concentrations of some risk factors for cardiometabolic disease (glucose, insulin, triglyceride, alanine transaminase, and leptin). but did not affect others (free fatty acids, low- and high-density lipoprotein [LDL and HDL, respectively] cholesterol, and adiponectin). Only after 16% weight loss did plasma free fatty acid and CRP concentrations decrease and plasma adiponectin concentration increase significantly. Thus, for some endpoints, greater degrees of weight loss are needed. This study[7] performed sophisticated tests of multi-organ insulin sensitivity (a two-stage hyperinsulinemic euglycemic clamp with infusion of stable isotopically-labeled tracers) and demonstrated that liver and adipose tissue insulin sensitivity improved at 5% weight loss and plateaued, but that muscle insulin sensitivity continued to improve with 11% and 16% weight loss. Beta cell function also improves in a step-wise fashion with progressive weight loss. The study examined adipose tissue expression of genes involved in cholesterol flux, lipid synthesis, extracellular matrix remodeling, and oxidative stress, again with step-wise improvement in function with progressive weight loss.

For clinicians, the take-away message from the above referenced study[7] is that modest weight loss (5%) has multiple metabolic and cardiovascular risk factor benefits and more weight loss (11% and 16%) has even more benefits for metabolism and cardiovascular risk factors. However, for some clinical endpoints, especially if one is seeking improvement in inflammatory markers, it may be necessary to achieve 16% weight loss or more. This may help to explain why clinically it requires more weight loss to see improvement in NASH activity scores for Non-Alcoholic Steatotic Hepatitis, and for improvement in symptoms of obstructive sleeppnea and for knee pain with osteoarthritis. This is discussed below.

EVIDENCE OF HEALTH BENEFITS OF DIFFERENT DEGREES OF WEIGHT LOSS

1. Modest and moderate weight loss and diabetes prevention

The health benefit of modest weight loss is best exemplified clinically in the relationship between weight loss and diabetes prevention. While an average weight loss of 6.7% reduced the incidence of diabetes by 58% in the group participating in the American Diabetes Prevention Program[8] and similarly in the Finnish Diabetes Prevention Trial,[9] it's important to distinguish group benefits versus individual benefits. An analysis by Hamman, et al[10] from the American Diabetes Prevention Program showed that in individuals with impaired glucose tolerance, for every kilogram of weight lost there was a 16% reduction in risk for progression to diabetes. Furthermore, after about 10 kg weight loss, there was negligible benefit, in terms of diabetes risk reduction, from further weight loss. This is illustrated in Figure 1. Clearly, even one or two kg of weight loss in persons at risk for developing type 2 diabetes (i.e. those with prediabetes) can have health benefits. In addition, this analysis of the Diabetes Prevention Program weight loss showed reduced diabetes incidence similarly across all race and ethnicity groups for both sexes, for all ages and for several levels of physical activity and regardless of the level of the initial obesity.

2. Modest and moderate weight loss in established type 2 diabetes

The relationship between modest weight loss and improvement in glycemia is powerful and it is not limited to diabetes prevention. This is illustrated with analyses from the Look AHEAD study of >5000 individuals with type 2 diabetes. In one analysis,[11] categories of weight loss were defined (stable weight, ≥2%<5%, ≥5%<10 %, ≥10%<15% and ≥15%). This analysis demonstrated that improvement in fasting glucose and hemoglobin A1c is observed beginning at only ≥2<5% weight loss. Of course, greater weight loss was associated with greater benefit to glycemic outcomes in a direct and linear fashion. It must be noted that these benefits to glycemic measures were achieved alongside *reductions* in antidiabetic medications.[11]

3. Modest and moderate weight loss and improvement in cardiovascular disease risk factors

Data from the Look AHEAD Study also showed that health benefits of modest weight loss are not limited to glycemic measures. The analysis cited above[11] also evaluated the impact of progressive categories of weight loss on other risk factors and showed that improvement

in triglycerides and systolic blood pressure begins with ≥2<5% weight loss.[j] For diastolic blood pressure and HDL cholesterol, improvement begins at ≥5<10% weight loss.[j] All of these risk factors improved in a direct and linear fashion with greater weight loss being associated with greater risk factor benefit. However, for LDL cholesterol, the relationship is less strong and in the Look AHEAD study, where baseline LDL was 100 mg/dl, there was no reduction in LDL.[j] However, there was a reduction in use of lipid lowering medications in the modest weight loss group (average −8.7% at year 1) in this study.[11]

4. Benefits of modest and moderate weight loss on cardiometabolic risk factors across all levels of obesity

Of importance is the demonstration from another analysis[11] from the large Look AHEAD data set (n>5000) that baseline BMI category (Obese stage I, II or III) does not alter the benefit of modest weight loss.[12] Each of the BMI categories demonstrate the same amount of mean weight loss, when expressed as a percentage from baseline, with the same lifestyle intervention. Of course, those with higher BMI category would lose more weight when expressed in kilograms; but when expressed proportionally there is no significant difference across BMI categories in weight loss. Thus, for patients with BMI 40 kg/m^2 or more there was no difference in mean percentage weight loss when compared to those with BMI 35<40 or BMI 30<35. Further, the same held true for improvement in most risk factors. Except for HDL cholesterol, weight loss had the same impact across the three BMI categories with significant improvement in hemoglobin A1c, triglycerides, systolic blood pressure, and LDL cholesterol.[12]

5. Benefits of moderate weight loss on symptoms of obstructive sleep apnea

The Look AHEAD Study incorporated a substudy of sleep apnea, called Sleep AHEAD. More than 80% of the participants with type 2 diabetes in four sites of Look AHEAD had at least mild obstructive sleep apnea.[13] With the intensive lifestyle intervention (ILI), mean weight loss at one year at these four sites was 10.8 kg vs. 0.6 kg in the diabetes support and education (DSE) group. At 1 year, remission of OSA (apnea hypopnea index, AHI, <5 events per hour) was 3 times more common in the ILI participants (13.6%) than in the DSE participants (3.5%). Further, the prevalence of severe obstructive sleep apnea among ILI participants (18.4%) was half that of the DSE group (37.9%). Participants with a weight loss of 10 kg or more had the greatest improvements. In fact, weight loss of 10 kg or more was required for significant association with AHI change. At 4 years, improvements persisted, despite some weight regain to 5.2 kg below baseline in the ILI group.[14] Remission of OSA at 4 years was 5 times more common with intensive lifestyle intervention (20.7%) than diabetes support and education (3.6%).[14] For clinicians, weight loss can be a major modifier of symptoms of obstructive sleep apnea as measured by the apnea hypopnea index, but 10% or more should be the goal to impact clinical symptoms. This larger amount of weight loss required for improvement may relate to the physical impingement on airway by excess body fat and it may take more proportional weight loss to impact symptoms.

6. Benefits of modest and moderate weight loss on osteoarthritis of the knee

Osteoarthritis of the knee is closely linked to obesity as a risk factor and is quite common. Nearly half of Americans are projected to experience osteoarthritis of at least one knee in

their lifetime.[15] A diet and exercise intervention which achieved 5.7% weight loss on average, and compared to a control condition produced significant improvements in WOMAC (Western Ontario MacMaster University score, which measures self-reported function), the 6 minute walk distance ($p<0.05$), stair climb time ($p<0.05$) and knee pain.[16] Knee joint loads were also assessed in those patients and the investigators found that each pound of weight lost resulted in a 4-fold reduction in the load exerted on the knee per step during daily activities.[17] Accumulated over thousands of steps per day, a reduction of this magnitude would appear to be clinically meaningful. A subsequent study achieved average weight loss of 10.6% with diet and exercise, and compared to a control condition of exercise alone produced significant improvement in pain, function, IL-6 levels and a quality of life measure.[18] However, radiographic and Magnetic Resonance Imaging outcomes did not fare as well. Despite the positive effects of weight loss in this study on symptoms as well as mechanistic outcomes (such as joint compressive force and markers of inflammation), there was no statistically significant improvement on the rate of structural progression either on X-ray or MRI over 18-months.[19] Thus, if a real impact on osteoarthritis of the knee is to be achieved, one must treat before established pathology in the knee, at the stage of knee pain alone. In the Look AHEAD study of men and women with type 2 diabetes, there was 15% less incidence of knee pain at year one in lifestyle intervention group (−8.7% weight loss) than support group (−0.9% weight loss) at one year.[20] However, at year 4 this difference in incidence decreased to 5% and was no longer statistically significant.[20] Therefore the best strategy would be to treat early and to treat more aggressively to produce greater weight loss, thus preventing the onset of structural damage to the joint.

7. Benefits of weight loss on hepatic steatosis and non-alcoholic steatotic hepatitis (NASH)

As discussed above, in the experiment conducted by Magkos et al,[7] weight loss disproportionately reduces fat from liver. In that study, 5% weight loss reduces intrahepatic triglyceride by 13%; 11% weight loss reduced it by 52% and 16% by 65%. As part of a substudy, 96 participants in Look AHEAD underwent proton magnetic resonance spectroscopy (MRS) to quantify fatty infiltration of the liver, with hepatic steatosis defined as 5.5% or higher being non-alcoholic fatty liver disease.[21] In that study, the greater the weight loss the greater the reduction in hepatic steatosis. However, while there were group differences in steatosis, with the lifestyle intervention group reducing steatosis on average 50.8% (versus 22.8% in the support group; $P>0.04$), there were no group differences in mean ALT and ASP.[21] It appears that it may take 10% or more weight loss to have an impact on NASH Activity Scores as assessed by liver biopsy.[22]

8. Benefits of lifestyle intervention on improvement in feeling and function (Quality of Life, Depression, Mobility, Sexual Dysfunction, and Urinary Stress Incontinence)

While reducing risks for other diseases is important, equally important is improving how patients feel and function. There is a known graded response to weight loss achieved through lifestyle intervention and improvement in **quality of life** as measured by the Impact of Weight – Quality of Life Assessment Tool.[23] Indeed, in Look AHEAD, at year one, quality of life improved more in the group undertaking lifestyle intervention than those in the support condition.[24]

Also, in Look AHEAD, there were fewer patients who developed potentially significant symptoms of **depression** (defined as Beck Depression Inventory[25] score >10) in the lifestyle intervention group as compared to the support condition.[26] At 1 year, the incidence of BDI ≥10 was significantly lower in the ILI than DSE group (6.3% vs. 9.6%; P < 0.001) indicating that weight loss does not precipitate depression and may protect from it. Furthermore participants in the lifestyle intervention with and without symptoms of depression at baseline lost 7.8 ± 6.7% and 8.7 ± 6.9% of total body weight, respectively, a difference not considered clinically meaningful.

Look AHEAD also assessed functionality. For participants in the lifestyle intervention, compared to the support condition, there was attenuation in the decline in **mobility** that occurs with aging.[27]

In overweight and obese women with type 2 diabetes participating in Look AHEAD, **urinary stress incontinence** improved in those who were randomized to the lifestyle intervention as compared to the control condition.[28] Look AHEAD demonstrated the same finding in men.[29] **Sexual dysfunction** was also studied in Look AHEAD and there was improvement in measures of sexual function for participants in the lifestyle intervention compared to the support condition. There was improvement in erectile function for men[30] and sexual dysfunction in women.[31]

9. Benefits of weight loss in Polycystic Ovarian Syndrome and infertility in women

A hallmark of women with PCOS is menstrual irregularities and its resulting infertility in addition to androgen excess and metabolic dysfunction. Most of the evidence points to improvement in ovulatory cycles and subsequent pregnancy with weight loss in obese women with PCOS. Furthermore, even a minimal weight loss of only 2–5% of total body weight improves ovulatory function and is more likely to result in spontaneous pregnancy.[32] There is more robust evidence to support improved outcomes from ovulatory cycles and pregnancy at higher rates of 5 and 10% of total body weight loss.[33] The return of normal menstrual function and decreased hirsutism are thought to be due to improved insulin sensitivity, decreased Luteinizing Hormone levels, and lower androgenemia.[33,34] Not only is pregnancy easier to achieve after modest weight loss it is also more likely to result in a successful live birth-miscarriage rates are lower at lower BMIs.[35]

10. Benefits of weight loss on health care costs and mortality

In an analysis from Look AHEAD[36] the impact of the lifestyle intervention on use and costs of medical services, with the support condition as comparator, showed that in the lifestyle group, annual hospitalizations were reduced by 11% (P=0.004) and hospital days by 15% (p=0.01). The cost savings for hospitalizations were 10% less in the lifestyle group (p=0.04). Medication cost savings were 7% less in the lifestyle group compared to the support group (P<0.001). Over 10 years, the relative cost savings per person in the lifestyle group were $5280 (95% CI = $3385-$7175). However, there were no differences in outpatient costs and the savings were not observed in those with a history of cardiovascular disease. The costs of conducting the Look AHEAD intervention have not been reported so cost effectiveness cannot yet be calculated.[36]

11. Weight Loss and Mortality Reduction

The Swedish Obese Subjects Study[37] provides a relevant paradigm for assessing the impact of weight loss *per se* on mortality and cardiovascular disease mortality, because while surgery was the method of obtaining weight loss, the procedure done in >80% of participants was the vertical banded gastroplasty. This would not great physiologic changes in gut signals as the Roux-en-Y-Bypass does that might have independent effects on mortality. The results from the Swedish Obese Subjects study, showed that surgical treatment which produces on average 16% weight loss, compared with a matched but un-operated control group without weight loss, showed a 29% reduction in overall mortality after ~ 20 years.[37] In the Look AHEAD study, participants were followed for 13 years. The mean initial weight loss at 1 year was 8.7% but half of the weight was regained. At the end of the trial there was no significant difference in the incidence of a composite end-point for major cardiovascular end-points for the intensive lifestyle intervention compared to the diabetes support and education condition.[38] However, a subsequent analysis from Look AHEAD[39] where individuals who lost at least 10% of their bodyweight in either arm of the study, in the first year of the study, had a 21% lower risk of the primary outcome of major cardiovascular events (p=0·034) and a 24% reduced risk of the secondary cardiovascular disease outcome (p=0·003) compared with individuals with stable weight or weight gain. Granted, this is not a randomized comparison, but a post hoc analysis, but it suggests that more than 10% weight loss may be needed to achieve reduction in cardiovascular events and mortality.

GUIDELINE RECOMMENDATIONS FOR WEIGHT LOSS

The concept that we do not need to normalize weight or achieve major weight loss to obtain health benefits has been reinforced in recent Obesity Guidelines.[2] In 2013, an expert panel formed by the NIH conducted an evidence-based review[2] around 5 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, HDL and LDL cholesterol) to be considered clinically meaningful.[2] The Expert Panel went on to observe that increased weight loss amounts provide even greater benefits. Still, the clinical practice recommendation, based on expert opinion, was to set an initial goal of 10% weight loss. Clinical Practice Guidelines for Comprehensive Care of Patients with Obesity issued by the American Society of Clinical Endocrinologists (AACE) and the American College of Endocrinology (ACE) take a different approach.[40] That approach is more complications centric. Obesity disease stage is based on ethnic-specific BMI along with assessment cutoffs for adiposity-related complications. Stage 0 is assigned to individuals who are overweight or obese by BMI classification but have no complications, whereas Stage 1 and 2 are defined as individuals who are overweight or obese by BMI classification and having 1 or more mild-moderate complications (Stage 1) or at least 1 severe complication (Stage 2). For patients with Stage 2, 10% or more weight loss is recommended. The American College of Obstetrics and Gynecology provides an Obesity Tool Kit[41] for practitioners and relies on the

2013 Obesity Guidelines,[2] as well as other sources to inform their recommendations. The Tool Kit does not specifically address weight loss goals.[41]

CONCLUSIONS

This brief review addresses the approach to weight loss for different obesity-related comorbidities. Because different tissues respond differently to weight loss, only modest amounts of weight loss may be needed for diabetes prevention, but moderate or more weight loss may be needed, especially where the goal is to reduce inflammation (as in NASH) or to reduce fat burden (as in obstructive sleep apnea and knee pain and osteoarthritis. These concepts are broadly applicable. But where individual patients are concerned, we must judge not just success at achieving a weight loss goal, but also success in reaching targeted health outcome goals. Targeted health outcome goals may be reached by an individual with weight loss of less than 5% or more than 10%. **What is meaningful for our patients is the message that patients need not reach a BMI <25 kg/m^2 in all instances, but can be healthier at any weight, as long as it is a reduced weight**.

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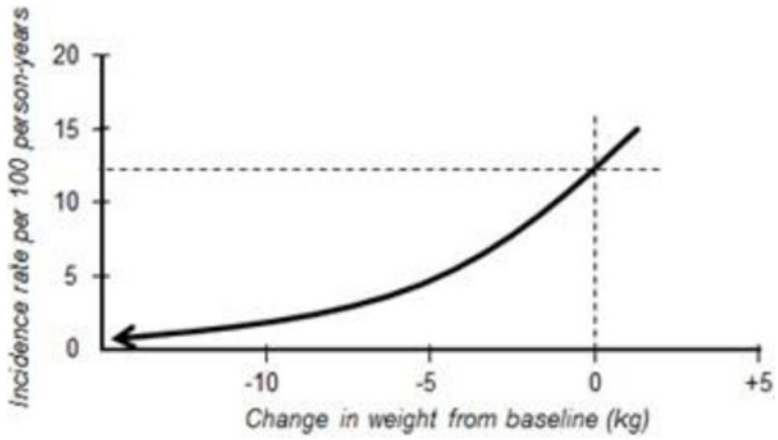

Figure 1.
The DPP experience: Every kg of weight loss was associated with 16% reduction in risk for progression to type 2 diabetes [10].

Table 1

Relationship with amount of weight loss and various comorbidities

Condition	Amount of weight loss needed to effect improvement	References
Glycemic Improvement–Diabetes prevention in impaired glucose tolerance	2.5% weight loss or more; maximal impact at 10%	2,8,9,10
Glycemic improvement–Type 2 diabetes	2.5% to >15%; greater weight loss associated with greater glycemic improvement; true for all BMI classes	11,12
Triglyceride reduction	2.5% to >15%; greater weight loss associated with greater glycemic improvement; true for all BMI classes;	11,12
HDL increase	5% to >15%; greater weight loss associated with greater glycemic improvement; not true for BMI >40 kg/m^2	11,12
Apnea Hypopnea Index Improvement in Obstructive Sleep Apnea	10%+ weight loss required for significant improvement	13,14
Knee pain and function in persons with osteoarthritis	5–10% improves knee functionality, speed, walk distance and pain; 10%+ required to improve IL-6 and CRP levels; knee MRI and X-ray findings do not change	16–19
Emergent knee pain prevalence	5–10% weight loss, with persistent maintenance required to prevent knee pain in individuals with obesity	20
Hepatic steatosis reduction	5–15%+; greater weight loss associated with greater improvement	21
Non-alcoholic steatotic hepatitis activity score	10%+ weight loss required for significant improvement	22
Impact of Weight on Quality of Life score	5%–15%+; greater weight loss associated with greater improvement	23
Depression	5–10% may reduce risk for emergent depression; individuals with depression lose as much weight as non-depressed individuals.	26
Mobility	5–10% loss attenuates mobility decline with aging	27
Urinary Incontinence	5–10% improves symptoms in men and women	28,29
Sexual Function	5–10% improves erectile function in men and sexual dysfunction in women	30,31
Polycystic Ovarian Syndrome and infertility	Improvement in ovulatory cycles and subsequent pregnancy with 2–5% weight loss, with more weight loss producing more robust effect.	32–34
Health care costs	In persons with diabetes 5–10% weight loss associated with reduction in hospitalization and medication costs, but not outpatient costs.	36
Mortality	16% weight loss (vertical banded gastrectomy) associated with reduction in all cause and cardiovascular mortality. 5–10% weight loss with lifestyle intervention had no effect on major cardiovascular outcomes, but in those with 10%+ weight loss, there was a reduction in those outcomes.	37,38,39