



## Weight Loss Interventions and Outcomes: Type 2 Diabetes

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### Abstract

**Background:** Benefits of moderate weight loss for the prevention of prediabetes and diabetes are well documented; however, the benefits of weight loss interventions in overt type 2 diabetes are controversial.

**Objective:** To summarize the role of weight loss interventions for the prevention of prediabetes and diabetes and to report the association between weight loss interventions in adults with type 2 diabetes resulting in weight loss greater or less than 5% on metabolic outcomes.

**Results:** Weight loss interventions of 5% to 10% decrease risk factors for prediabetes and diabetes. However, in a systematic review and meta-analysis of weight loss interventions in persons with type 2 diabetes, the majority of the weight loss interventions resulted in weight losses less than 5% and had nonsignificant beneficial effects on A1C and other metabolic outcomes. In another systematic review, reduced-energy eating plans implemented by registered dietitian/nutritionists in persons with type 2 diabetes, regardless of weight loss, resulted in improved A1C levels.

**Conclusion:** Nutrition therapy for persons with type 2 diabetes should encourage a reduced-energy healthful eating plan, regular physical activity, education, and continued support as primary treatment strategies.

**Keywords:** Weight loss; Interventions; Type 2 Diabetes

### Introduction

The association of overweight and obesity with increased risk for prediabetes and type 2 diabetes is well documented and known [1]. Strong evidence exists for the benefits of moderate weight loss for the prevention of diabetes [2]. The question is, however, are there benefits on metabolic outcomes from weight loss interventions as prediabetes progresses to overt type 2 diabetes?

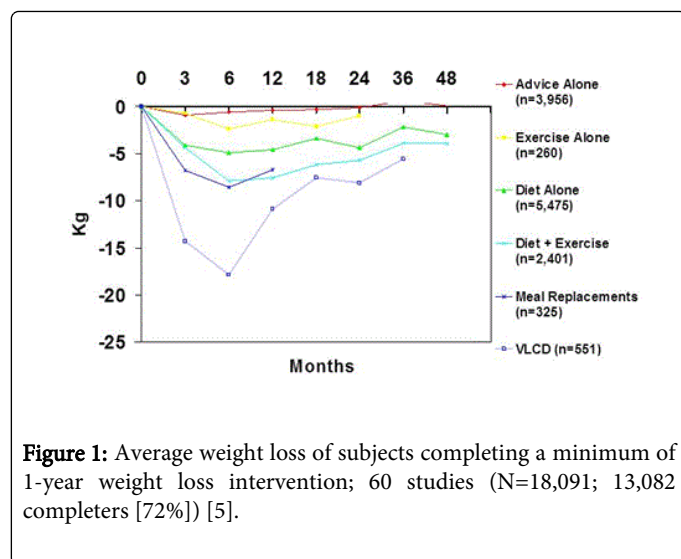
To answer this question, it is helpful to first review the benefits and effectiveness of weight loss interventions in overweight and/or obese individuals and in individuals with prediabetes and then to examine how this differs in persons with type 2 diabetes.

### Weight Loss Interventions for Overweight/Obese Persons

Addressing overweight and obesity is an important strategy in the primary and second prevention of disease including type 2 diabetes, hypertension, dyslipidemia, and cardiovascular disease [3]. A sustained modest weight loss (approximately 5% to 10%) is associated with decreased risk of prediabetes, reductions in blood pressure, and improved lipids profiles [4]. Thus, the questions of what are effective weight loss interventions, and what are realistic long-term outcomes, take on added importance for all health professionals counseling patients who are overweight/obese, as well as for the general public.

To answer these questions, we conducted a systematic review and meta-analysis of weight-loss intervention outcomes in studies with a

minimum follow-up for 12 months [5]. A total of 80 studies (n=26,355 with 18,199 completers (69%)) were reviewed. Weight-loss studies were categorized into eight types of interventions: advice alone, diet alone, diet and exercise, exercise alone, meal replacements, very-low-energy diets, and weight -loss medications (orlistat and sibutramine). A mean weight loss of 7.9 kg (8.5%) was observed during the first six months from diet and exercise, meal replacements, and/or weight-loss medications with weight plateaus at approximately six months. In studies extending to 48 months, a mean 3.9 kg (4%) of weight loss was maintained with none of the groups experiencing weight regain to baseline. Participants who received diet alone experienced a mean weight loss at six months of 4.9 kg (5%), maintaining a mean weight loss of 4.6 to 4.4 to 3.0 kg (4.2%, 3.0%, 3.0%) at 12, 24, and 48 months, respectively. Very -low-energy diet use resulted in a major mean weight loss of 17.9 kg (16%) at six months followed by a rapid regain so that at 12 months the mean weight loss was 10.9 kg (10%) and by 36 months 5.6 kg (5%). Exercise alone, without a focus on food intake, was not very effective, resulting in a mean 2.4 kg (2.7%) weight loss at six months and a mean of 1.0 kg (1.0%) at 24 months. It should, of course, be remembered the results are a bell-shaped curve, with some participants experiencing greater weight loss (the ones remembered by health professionals and reported in ads and television shows) and some participants experiencing very minimal, if any, weight loss (the ones "forgotten" by health professionals!). Figure 1 illustrates mean weight loss per subject in the lifestyle weight loss intervention groups (diet alone, diet + exercise, meal replacements, very-low calorie diets, exercise alone) and the advice alone group.



The primary weight-loss intervention implemented in the intervention arms was a reduced energy, lower-fat eating plan. Several studies used some combination of low-carbohydrate, high-protein diets. However, at 12 months there were no differences in weight loss based on the macronutrient content of the eating plan implemented. Specific goals for physical activity were also implemented. Continuous or intermittent moderate intensity exercise of 30 to 40 minutes three to five days per week or 150 minutes per week of moderate intensity physical activity/exercise was recommended. In addition, basic weight-loss behavioral strategies were used in nearly all of the studies, which include self-monitoring, goal setting, stimulus control, reinforcement, and cognitive change. Study participants in the clinical trials also benefitted from the continued professional support they received.

Because weight loss plateaus at approximately six months, the emphasis of a weight-management program must evolve from a focus on reduced energy intake and regular physical activity for weight loss to a focus on reduced energy intake and regular physical activity for continued weight-loss maintenance [6]. Health care professionals and participants often express frustration believing that if a reduced energy intake is maintained (or decreased even further as was done in some studies), weight loss should continue. There is no evidence that this occurs, even when weight-loss interventions are continued. However, if the weight loss interventions are discontinued, weight regain is likely to occur.

Individuals with obesity struggling to achieve and maintain weight loss are often not adequately aware of the biological adaptations that occur when they lose weight [7]. Irrespective of starting weight, caloric restriction triggers several biological adaptations designed to prevent starvation [8]. Weight is tightly regulated by neural, hormonal, and metabolic factors. Hormonal adaptations (decreased leptin, peptide YY, cholecystokinin, insulin and increased ghrelin, gastric inhibitory polypeptide, pancreatic polypeptide) that stimulate appetite and weight gain after diet-induced weight loss remain for at least one-year after the initial weight reduction [9]. Weight loss also results in adaptive thermogenesis (decrease in resting metabolic rate) that has also been shown to be maintained for up to one year [10]. Further evidence indicates that biological pressure to restore bodyweight to the highest-sustained lifetime levels gets stronger as weight loss increases [11]. Therefore, weight maintenance strategies must be ongoing and

take into account the fact that weight-loss maintenance is more difficult than weight loss.

It is, however, important to remind individuals struggling with weight that weight losses of 5% to 10% of initial bodyweight result in clinically meaningful risk reductions-prevention or delay of type 2 diabetes, decreases in blood pressure and circulating inflammatory markers (C-reactive protein and cytokines), and potential improvements in lipid levels, despite the fact that these weight loss goals might be disappointing to the individual [4].

## Weight Loss Interventions for Prediabetes

Goals of nutrition therapy for prediabetes emphasize the importance of lifestyle interventions in decreasing the risk of type 2 diabetes by promoting an eating plan that facilitates moderate weight loss (5% to 7% of body weight) and by increasing physical activity (equivalent to 30 minutes brisk walking on most days of the week). Follow-up counseling and continued support is also necessary to accomplish these objectives. In both the Finnish Diabetes Prevention Study [12] and the Diabetes Prevention Program [13] the lifestyle interventions reduced the incidence of diabetes by 58%. Of importance are the studies of lifestyle intervention showing persistent reduction in the rate of conversion to type 2 diabetes at three [14], ten [15], and 14 years [16] post-intervention follow-up. Cost data has also confirmed that lifestyle interventions for the prevention of diabetes are highly cost-effective [17].

## The Dilemma of Weight Loss in Diabetes

Although strong evidence exists for the benefits of moderate weight loss for the prevention of type 2 diabetes, the question becomes, what are the benefits from weight loss interventions as glycemic impairments progress from prediabetes to type 2 diabetes. In 2013 the American Diabetes Association (ADA) recommended weight loss for all overweight or obese individuals who have or are at risk for diabetes and graded it A [18]. However, in 2014 they note that not all weight-loss interventions lead to 1-year A1C improvements and they stated “for overweight or obese adults with diabetes or at risk for diabetes, reducing energy intake while maintaining a healthful eating pattern is recommended to promote weight loss. Modest weight loss may provide clinical benefits with diabetes, especially those early in the disease process.” The recommendation is still graded A [19]. The 2013 AHA/ACC/TOB Guideline for the Management of Overweight and Obesity reported that in overweight and obese adults with type 2 diabetes, a 2% to 5% weight loss from lifestyle interventions result in a lowering of A1C of 0.2% to 0.3%, and that weight loss of 5% to 10% is associated with A1C reductions of 0.6% to 1.0% [3]. However, the statistical significance of the changes is not reported.

Because Registered dietitian/nutritionists and medical care professionals routinely provide weight-loss advice to overweight and obese adults with diabetes and because of the uncertainties regarding benefits on glycemic control and other metabolic outcomes, we conducted a systematic review and meta-analysis to determine the role of nutrition therapy lifestyle weight-loss interventions for type 2 diabetes [20]. Articles were reviewed from January 1, 2000 to March 1, 2014. The primary question was: In overweight or obese adults with type 2 diabetes, what are the outcomes on A1C from lifestyle weight-loss intervention resulting in weight losses greater or less than 5% at 12 months? Secondary questions were: What are the lipid (total cholesterol, LDL-cholesterol [LDL-C], HDL-cholesterol [HDL-C], and

triglycerides [TG] and blood pressure (systolic [SBP] and diastolic [DBP]) outcomes from weight-loss intervention resulting in weight losses greater than or less than 5% at 12 months? And, what are the weight and metabolic outcomes from differing amounts of macronutrients in lifestyle weight-loss interventions in individuals with type 2 diabetes?

Eleven studies (eight compared two weight-loss interventions and three compared a weight-loss intervention with a usual care/control groups) with 6,754 participants met study criteria (randomized clinical trial, minimum 12-month duration, and a 70% completion rate). At 12 months, 17 study groups (8 categories of weight-loss intervention) reported weight loss <5% (-3.2 kg [95% CI: -5.9, -0.6]). A decrease in A1C at 12-months of 0.2% (95% CI: -0.6, 0.2) was not significant compared to baseline. Lipid and blood pressure changes from baseline were also non significant.

Only two study groups reported a weight loss  $\geq$ 5%: a low-calorie Mediterranean-style (MED-style) diet implemented in newly diagnosed adults with type 2 diabetes and an Intensive Lifestyle Intervention (ILI) implemented in the Look AHEAD (Action for Health in Diabetes) study. Both reported regular physical activity and frequent contact with health professionals. The MED-style group reported a decrease in A1C of 1.2% (95% CI: -1.4, -1.1) at 12 months from a baseline of 7.8% ( $P < 0.0001$ ). The ILI reported a decrease in A1C of 0.6% (95% CI: -0.7, 0.6) at 12 months from a baseline of 7.3% ( $P < 0.0001$ ). Both also reported significant beneficial effects on lipids and blood pressure.

Five studies compared lifestyle weight-loss intervention with differing macronutrient compositions (low-carbohydrate vs. low-fat, high-protein vs. high-carbohydrate, and high-monounsaturated fat vs. high-carbohydrate). In all five studies 12-month weight changes were less than 5% of baseline weight and did not differ statistically between study groups; changes in A1C, lipids, and blood pressure from baseline to 12 months were also all non significant.

Compared with individuals without diabetes, it is generally more difficult for individuals with diabetes to lose and/or maintain weight loss. For overweight or obese individuals with type 2 diabetes, a weight loss of at least 5% appears necessary to consistently improve glucose, lipids, and blood pressure. This amount of weight loss may not be a realistic goal for the majority of persons seen in many health care settings today. However, strong evidence reports that a reduced energy intake, with or without weight loss, improves glycemic control [21].

### Focus: Reduced Energy Intake Versus Weight Loss?

The Academy of Nutrition and Dietetics conducted a systematic review of the question: In adults with type 2 diabetes, how effective is Medical Nutrition Therapy (MNT) provided by a Registered Dietitian/Nutritionist (RD/N) on glycemia (A1C), cardiovascular risk factors, weight, medications and quality of life? Twenty one study groups from 18 studies reported that MNT provided by an RD/N significantly lowered A1C levels at three months by 0.3% to 1.8% and with ongoing support decreases in A1C were maintained or improved for >12 months [21]. The magnitude of lowering was dependent on the A1C level at the time of the intervention and the duration of diabetes. Although nutrition therapy interventions were effective throughout disease duration, the decrease in A1C was the largest in studies in which participants were newly diagnosed and/or had higher baseline A1C levels. Of importance, RD/Ns implemented a variety of nutrition therapy interventions all resulting in a reduced energy intake.

However, weight outcomes from MNT were mixed. Eleven study arms reported significantly decreased baseline weight by 2.4 to 6.2 kg; whereas, six study arms reported nonsignificant weight changes at study end.

In adults with normal to mildly elevated cholesterol, LDL-C, TG, and normal to mildly low HDL level decreases in lipid levels were mixed. In adults with near-normal blood pressure levels decreases in blood pressure were also mixed. Decreases in doses and/or number of glucose-lowering medication were reported as well as improvements in quality of life.

It can be concluded that the emphasis of nutrition therapy for overweight or obese persons with type 2 diabetes for glycemic control is a reduced energy intake. In some it may lead to weight loss, in some it may maintain weight loss, and in some (often dependent on medications used), it may prevent weight gain. But it is very clear that a reduced energy intake is of primary importance. Therefore, nutrition therapy should encourage an energy-appropriate healthy eating pattern, appropriate portion sizes, regular physical activity, education, and continued support [19,21].

### Summary

Strong evidence exists for the benefits of modest weight loss for the prevention of prediabetes and type 2 diabetes. However, nutrition therapy once type 2 diabetes develops should focus on 1) a reduced energy intake shown to improve metabolic outcomes, especially glycemia, 2) negotiating lifestyle changes individuals are willing and able to make, and 3) assisting individuals in choosing appropriate portion sizes of foods shown to have health benefits.

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