

Weight Management: Obesity to Diabetes

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■ **IN BRIEF** Evidence supports the effectiveness of nutrition therapy across the continuum of diabetes management—obesity to prediabetes to diabetes. For people who are overweight/obese or diagnosed with prediabetes, modest weight loss is important. However, the goals of nutrition therapy for type 2 diabetes are improved glycemia, lipids, and blood pressure. To achieve these goals, a reduced energy intake is essential. For some, reducing energy intake may lead to weight loss, while for others, it may maintain weight loss or prevent weight gain. Weight loss medications and metabolic surgery have been shown to be effective weight loss therapies across the continuum.

Unfortunately, the prevalence of obesity continues to escalate, and solutions continue to be evasive. In 2015, two-thirds of the U.S. population was reported as being overweight or obese (1). Health care professionals in the diabetes field are well aware of the impact and consequences of obesity contributing to the development of prediabetes and type 2 diabetes. This article reviews the role of weight management interventions across the continuum of obesity to prediabetes to diabetes, beginning with management of obesity. Readers are reminded that weight loss is an outcome and not a weight management intervention. Interventions include reduced energy intake, regular physical activity, education and support, pharmacotherapy, and/or metabolic (bariatric) surgery.

Weight Management of Obesity

Moderate weight loss, defined as a 5–10% reduction from baseline weight, is associated with clinically meaningful improvements in obesity-related metabolic risk factors (2). A 5% weight loss has been shown to

improve pancreatic β -cell function and the sensitivity of liver and skeletal muscle to insulin, with larger relative weight losses leading to graded improvements in key adipose tissue disturbances (3).

The American College of Cardiology/American Heart Association Obesity Expert Panel recommends that patients receive high-intensity behavioral counseling, with ≥ 14 visits in 6 months (4). They report that this type of comprehensive program results in a mean weight loss of 5–8% and that ~60–65% of patients lose $\geq 5\%$ of initial weight (4). However, weight regain is common after completion of such programs, and they note that the most effective behavioral method for preventing weight regain is continued support on an every-other-week or monthly basis, whether in person or by telephone. Unfortunately, long-term counseling is not widely available. They also note that it is challenging to persuade patients to remain in counseling to maintain a weight loss that is usually smaller than they had desired (4). It is important that all health profession-

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als help educate the public regarding the benefits of moderate weight loss.

The other treatment options for overweight and obesity are weight loss medications and metabolic (bariatric) surgery. In 1-year trials, total weight losses for three monopharmacotherapies (orlistat, lorcaserin, and liraglutide), whose effects are mediated by different mechanisms, ranged from 5.8 to 8.8 kg (5.8 to 8.8% of initial body weight) (2). In 1-year trials of two combination medications (phentermine-topiramate and naltrexone-bupropion), whose effects are on neural weight loss mechanisms, weight loss ranged from 6.2 to 10.2 kg (6.4–9.8% of initial body weight) (2).

Mean weight losses of 16–32% of baseline weight are produced by metabolic surgery in patients with severe obesity and may lead to disease remission, including remission of type 2 diabetes (2). Limitations of current metabolic surgeries include high initial costs; at 1 year, risks of short- and long-term complications; and weight regain in ~5–20% of patients (2). However, Roux-en-Y gastric bypass and vertical-sleeve gastrectomy are by far the most effective long-term treatments of severe obesity. Unfortunately, only a small fraction of patients who would benefit from these three classes of treatment (lifestyle intervention, weight loss medications, and metabolic surgery) actually receive them (2).

Of interest is a recent position statement from the American Association of Clinical Endocrinologists and American College of Endocrinology, which recommends a new diagnostic term for obesity: adiposity-based chronic disease, or ABCD (5). The reason cited for the new term is to avoid the stigma and confusion related to the differential use and multiple meanings of the term “obesity.”

Weight Management of Prediabetes

Readers of this article are likely aware of the effectiveness of modest weight

loss for people with prediabetes. People with overweight or obesity who received intensive lifestyle intervention in the Diabetes Prevention Program (DPP) had a mean weight loss of 5.6 kg at 2.8 years and a 58% relative reduction in the risk of type 2 diabetes compared to a 31% risk reduction with metformin (6). Perhaps most encouraging was the finding that the incidence of type 2 diabetes remained 34% less than the incidence in the control group at 10 years’ follow-up, even though the participants in the intervention group had, on average, returned to close to their baseline weight (7).

The American Diabetes Association (ADA) recommends that people with prediabetes be referred to an intensive behavioral lifestyle intervention modeled after the DPP (8). The goal is to achieve and maintain a 7% loss of initial weight and to increase moderate-intensity physical activity to at least 150 min/week. They also state that technology-assisted tools, including Internet-based social networks, distance learning, DVD-based content, and mobile applications may be useful elements of effective lifestyle modification to prevent diabetes.

Combining lifestyle interventions to prevent type 2 diabetes is reported to be helpful. Of interest is a population-based cohort study that examined lifestyle factors and the risk of new-onset diabetes (9). For all individuals, a healthy eating pattern, participation in regular physical activity, maintenance of normal weight, and moderate alcohol intake were reported to lower the risk of developing type 2 diabetes. However, adherence to a combination of these factors in this study was reported to reduce that risk by as much as 84% in women and 72% in men. Although weight was one of the most important factors, the researchers noted that even overweight individuals could lower their risk of type 2 diabetes by adopting other healthy lifestyle habits.

Medications such as metformin, α -glucosidase inhibitors, orlistat,

glucagon-like peptide receptor agonists, and thiazolidinediones can also prevent progression from prediabetes to diabetes (8). The ADA now recommends that metformin should be considered for prevention of diabetes in those with prediabetes and especially for individuals with a BMI ≥ 35 kg/m², those <60 years of age, women with prior gestational diabetes, and those with a rising A1C despite lifestyle intervention (8). They note that metformin has the strongest evidence base and has demonstrated long-term safety for diabetes prevention. For other medications, cost, side effects, and durable efficacy require consideration.

The Swedish Obese Subjects (SOS) trial reported the strongest evidence that metabolic surgery can reduce the incidence of type 2 diabetes in obese individuals (10). Ten-year data from the SOS trial, which included 407 morbidly obese people who underwent metabolic surgery and matched control subjects, showed that the incidence of diabetes was 7% in the metabolic surgery group and 24% in the control group (10). Similar results were reported from another study in Sweden, in which 1,658 obese people underwent metabolic surgery and 1,771 obese people received usual care (11). At 15 years, the incidence of type 2 diabetes was 7% in the metabolic surgery group and 22% in the control group.

Weight Management of Type 2 Diabetes

Although one of the goals for prevention of diabetes, as noted above, is weight loss, for treatment of type 2 diabetes, the goals of nutrition therapy shift to glucose, lipid, and blood pressure management (12). To determine the effectiveness of weight loss interventions (WLIs) implemented in overweight and obese adults with type 2 diabetes, a systematic review and meta-analysis was conducted of randomized clinical trials with a minimum of 12 months’ duration and an 80% completion rate (13). In

11 trials (8 comparing two WLIs and 3 comparing a WLI to a usual care control group, $n = 6,754$), weight loss plateaued at 6 months. At 12 months, 17 WLIs ($n = 1,365$) reported weight losses of $<5\%$ of initial weight (~ 3.2 kg) resulting in nonsignificant beneficial effects of A1C, lipids, or blood pressure. Only two trials ($n = 2,676$) reported weight losses $\geq 5\%$ at 12 months: a Mediterranean-style diet implemented in newly diagnosed adults and an intensive WLI implemented in the Look AHEAD trial. Both included regular physical activity and frequent contact with health professionals and reported significant beneficial effects on A1C, lipids, and blood pressure.

Additionally, compared to people without diabetes, it appears more difficult for those with diabetes to lose weight. In another systematic review of WLIs in people primarily without diabetes, weight loss also plateaued at 6 months, and the mean weight loss at 12 months was 4.5–7.5 kg (5–8%) (14), whereas in 17 of the 19 WLI groups in people with diabetes, mean weight loss was 1.9–4.8 kg (3.2%). Weight loss of $>5\%$ appears necessary for beneficial effects on A1C, lipids, and blood pressure. Achieving this level of weight loss appears to be difficult because it requires intense interventions, including energy restriction, regular physical activity, and very frequent contact with health professionals.

Improvement in glycemia from weight loss is most likely to be effective in the early stage of diabetes, when individuals still have a relatively preserved insulin secretion capacity (15). However, for many, it may be too late to improve hyperglycemia through weight loss alone (16), and not all individuals with type 2 diabetes are overweight or obese. Furthermore, any beneficial effects on blood glucose levels begin to occur early, before much weight is lost (15), suggesting that the benefits are from the reduced energy intake rather than from the weight loss.

Focusing on a reduced energy intake for people with type 2 diabetes, rather than on the scale (weight loss), is supported by a review of the effectiveness of medical nutrition therapy (MNT) provided by registered dietitian nutritionists (RDNs) (17,18). In adults with type 2 diabetes, 21 study arms from 18 studies ($n = 4,181$) reported that, at 3 months, A1C levels decreased from baseline by 0.3–2.0%, and at >12 months, with continued support, decreases ranged from 0.6 to 1.8%. Although MNT interventions were effective throughout the disease process, the decreases in A1C were largest in studies in which participants were newly diagnosed and/or had baseline A1C levels $>8.0\%$, for whom decreases ranged from 0.5 to 2.0%. A variety of MNT interventions, including individualized nutrition therapy, energy restriction, portion control, sample menus, carbohydrate counting, exchange lists, simple meal plans, and a low-fat vegan diet, were implemented and effective. However, all MNT interventions resulted in reduced energy intake.

Of importance, eating plans for people with type 2 diabetes must be based on their current food intake and on the changes the individual is willing and able to make to improve blood glucose control and other metabolic outcomes. Blood glucose monitoring must then be used to evaluate outcomes of lifestyle changes on pre- and postmeal glucose levels. It can then be determined whether food/eating and activity changes have achieved the target goals or whether pharmacotherapeutic additions or adjustments are needed. Because medications—including insulin—need to be combined with nutrition therapy, weight gain often occurs; thus, preventing this weight gain becomes important. However, glycemic control must still take precedence over concerns about weight.

Nutrition therapy for overweight and obese individuals with type 2 diabetes therefore should focus pri-

marily on encouraging a healthy eating pattern, with careful attention to portion sizes and energy intake; participation in regular physical activity; and education and support to improve metabolic outcomes. For some, this may lead to weight loss, while for others, it may maintain weight loss or prevent weight gain.

Weight loss studies using the five approved weight loss medications have been conducted in people with type 2 diabetes. Table 1 summarizes the trials comparing weight loss medication therapy to a placebo and their 52- to 56-week weight loss and A1C outcomes (19). When used as an adjunct to lifestyle intervention, these agents may help individuals sustain weight loss for a longer period of time. The weight loss resulting from the use of the medications resulted in better glycemic control, while reducing the number and doses of glucose-lowering medications and often lowering blood pressure and improving lipids. The ADA states that weight loss medications may be effective adjuncts to an energy-reduced eating plan, physical activity, and behavioral counseling for selected individuals with type 2 diabetes and a BMI ≥ 27 kg/m² (20). It further recommends that, if an individual's response to weight loss medications is $<5\%$ after 3 months or if there are any safety or tolerability issues at any time, the medication should be discontinued and alternative medications should be considered (20).

The ADA also states that a substantial body of evidence has now accumulated, including data from numerous randomized controlled clinical trials, demonstrating that metabolic surgery achieves superior glycemic control and reduction of cardiovascular risk factors in obese people with type 2 diabetes (20). The ADA's 2017 recommendations state that metabolic surgery should be recommended to treat type 2 diabetes in appropriate surgical candidates with a BMI ≥ 40 kg/m² (BMI ≥ 37.5 kg/m² in Asian Americans), regard-

TABLE 1. Weight Loss Medications in People With Type 2 Diabetes: Weight Loss and Glucose Outcomes (19)

	Orlistat (Xenical, Alli*)	Lorcaserin (Belviq)	Phentermine/ Topiramate (Qsymia)	Naltrexone/ Bupropion (Contrave)	Liraglutide (Saxenda)
Weight loss (%)					
Drug	6.2	4.5	9.6	5.0	6.0
Placebo	4.3	1.5	2.6	1.8	2.0
A1C change (%)					
Drug	-0.3	-0.9	-1.6	-0.6	-1.3
Placebo	+0.2	-0.4	-1.2	-0.1	-0.3

Brand names are in parentheses; study lengths were 52–56 weeks. *Over-the-counter brand name.

less of the level of glycemic control or complexity of glucose-lowering regimens, and in adults with a BMI of 35.0–39.9 kg/m² (32.5–37.4 kg/m² in Asian Americans) when hyperglycemia is inadequately controlled despite lifestyle modification and optimal medical therapy. Metabolic surgery should be considered for adults with type 2 diabetes and a BMI of 30.0–34.9 kg/m² (27.5–32.4 kg/m² in Asian Americans) if hyperglycemia is inadequately controlled despite optimal medical treatment by either oral or injectable medications (including insulin). They note that, in patients undergoing metabolic surgery, younger age, shorter duration of diabetes (e.g., <8 years), nonuse of insulin, and better glycemic control are consistently associated with higher rates of diabetes remission and a lower risk of recidivism (21).

Summary

Weight loss interventions are important for the prevention and treatment of overweight/obesity and prediabetes. Progressive β-cell loss necessitates changes in nutrition therapy just as it requires changes in medical therapy, including changes in pharmacotherapy. As type 2 diabetes is diagnosed and progresses, nutrition therapy interventions focus on attaining and maintaining treatment goals for glycemia, lipids, and blood pressure. It is important that effective therapies lower elevated blood glucose concentrations as early as possible to slow β-cell exhaustion and prevent the deleteri-

ous effects of hyperglycemia. Over time, glucose-lowering medication(s) and eventually exogenous insulin will be needed, but nutrition therapy continues to be important for diabetes management. Both weight loss medications and metabolic surgery have recent research proving effectiveness for weight loss and other metabolic outcomes in people who are overweight/obese or have been diagnosed with prediabetes or type 2 diabetes.

Knowledge of outcomes and benefits from weight management interventions can assist individuals who are overweight/obese or who have prediabetes or type 2 diabetes, and professionals should work collaboratively with patients in making decisions regarding the role of weight management interventions in patients’ care.

Duality of Interest

No potential conflicts of interest relevant to this article were reported.

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Why Weight Loss Maintenance Is Difficult

Alison B. Evert¹ and Marion J. Franz²

■ **IN BRIEF** This article reviews studies related to biological mechanisms that make weight loss maintenance difficult. Approximately 50% of weight variance is reported to be determined by genetics and 50% by the environment (energy-dense foods and reduced physical activity). Body weight is tightly regulated by hormonal, metabolic, and neural factors. Hormonal adaptations (decreases in leptin, peptide YY, cholecystokinin, and insulin and increases in ghrelin, glucagon-like peptide 1, gastric inhibitory polypeptide, and pancreatic polypeptide) encourage weight gain after diet-induced weight loss and continue for at least 1 year after initial weight reduction. Weight loss also results in adaptive thermogenesis (decreased resting metabolic rate), which is also maintained long-term. Neural factors such as dopamine also signal the need to respond to an increased desire for fatty foods after weight loss.

Health care providers (HCPs) often find that people trying to “solve” a weight loss maintenance problem feel guilty about their weight issues. They have been told by family, friends, the public, and, yes, even HCPs that it is their fault—that they simply lack willpower—or have decided on their own that it is their fault that they are regaining the weight they have worked so hard to lose. If they would just continue to eat less and exercise more, the problem would be solved. It sounds

so simple! Yet, anyone dealing with weight loss maintenance issues realizes it is not that simple. The cycle of less weight loss than expected or wanted and subsequent weight regain continues, despite individuals' best efforts to prevent it. In fact, we would probably all agree that, if they were so simple to solve, the issues of weight loss and maintenance would not continue to be problems.

It is claimed that “many clinicians are not adequately aware of the reasons that individuals with obesity

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