Body Weight Issues in Preventing and Treating Type 2 Diabetes

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The health topic of greatest concern for health care professionals and community leaders alike is the alarming rise in the prevalence of overweight and obesity. Based on the most recent National Health and Nutrition Examination Survey data (1999–2000), the estimated age-adjusted prevalence of overweight (BMI 25.0–29.9 kg/m^2) is 64.5% and obesity (BMI ≥ 30 kg/m^2) is 30.5% in adults in the United States.[1] The increase in overweight and obesity is evident in both men and women, across all age groups, and across all ethnic groups, although rates are highest among African-American women (77.3%) and Mexican-American men (74.7%) and women (71.9%). The prevalence of overweight is ~15% in children ages 6–19, with an additional 15% at risk for overweight (BMI for age between 85th and 95th percentile).[2]

A BMI > 25 kg/m^2, particularly when body fat is distributed in the abdominal or visceral fat region, is associated with several metabolic abnormalities and diseases, including type 2 diabetes, which in turn are associated with high mortality and morbidity rates. Even an 11-kg weight gain during midlife increases the risk of developing diabetes by 21 times when compared to a weight gain of < 5 kg after the age of 21.[3]

Body weight plays a central role in the pathway for both the development and treatment of type 2 diabetes (Figure 1). Based on population studies, obesity, particularly visceral obesity, is by far the most common risk factor associated with the prediabetic state.[4] This implies that preventing obesity in adults and children could reduce the incidence of type 2 diabetes in the future.

A population-based approach to preventing obesity suggests that strategies need to be put in place to influence both the environmental and physiological causes of obesity.[5] Public policies and social changes that encourage more physical activity and consumption of healthier foods while reducing the availability of energy-dense foods and drinks must accompany individual educational and behavioral interventions to address obesity prevention.

Although not every overweight individual develops type 2 diabetes, insulin resistance exacerbated by obesity is an early metabolic defect in nearly all individuals with type 2 diabetes. The metabolic syndrome, of which insulin resistance is a central component, is thought to be present in more than 25% of the U.S. population and is considered a component of prediabetes.[6] Studies have shown that effective weight loss interventions in already obese individuals with glucose intolerance can prevent or delay the progression to type 2 diabetes.[7,8] The challenge for health professionals is to identify high-risk individuals early and to implement effective weight loss interventions before diabetes develops.

The impact of body weight and obesity on insulin resistance and insulin requirements makes weight reduction a major therapeutic objective following the diagnosis of type 2 diabetes for many patients. The U.K. Prospective Diabetes Study (UKPDS) illustrated that individuals newly diagnosed with type 2 diabetes experienced a 2% reduction in hemoglobin A_{1c} (A1C) results—the largest reduction observed in the study—through diet therapy and weight loss.[9] However, UKPDS investigators also concluded that the improvements in glycemic control with diet therapy may have been related more to caloric restriction than to weight loss or actual body weight.

The concept that caloric or nutrient restriction may be more important than weight loss per se to glycemic control in the management of type 2 diabetes is provocative. Given the role of obesity in insulin resistance, weight loss may prove most effective in preventing diabetes before it develops or halting it early in its course when insulin resistance is the predominant metabolic defect and β-cell function is still intact. In contrast, nutrition therapy and physical activity independent of weight loss may be more important in maintaining glycemic and metabolic control as type 2 diabetes progresses.

The issue of body weight and weight gain becomes even more complicated as we move along the path of managing type 2 diabetes and introduce pharmacological therapies to achieve intensive metabolic control of blood glucose, blood pressure, and serum lipids. The natural progression of type 2 diabetes leading to loss of β-cell function requires many patients to eventually use more than one medication to address the multiple metabolic defects present. Weight gain often accompanies, although is not an inevitable result of, pharmacological therapy in type 2 diabetes. This presents an additional challenge to diabetes care teams: to help patients achieve desired medical outcomes, providers must at times appear to contradict their own weight maintenance advice by accepting some weight gain in exchange for better overall diabetes control.

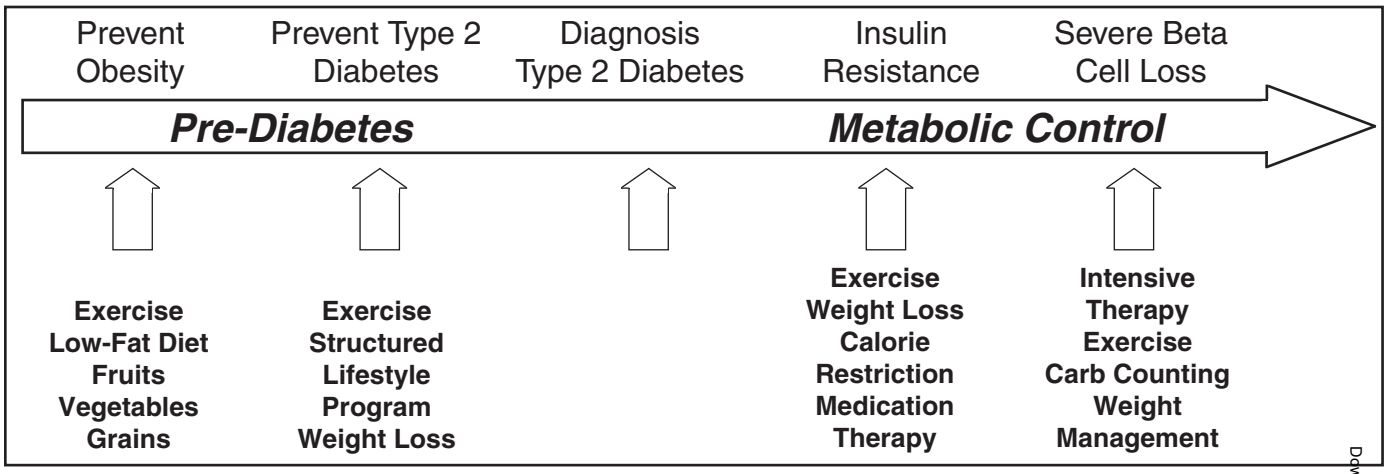

Figure 1. Managing Obesity in Type 2 Diabetes.

Physical Activity: The Foundation of Weight Control

It is generally well accepted that regular physical activity is crucial to maintaining a healthy body weight. Exercise increases energy expenditure by stimulating lipolysis of stored fat and creates a negative caloric balance as long as food intake remains constant. Because of our tremendously sedentary lifestyles, physical activity needs to be programmed into our lives at a level equal to or exceeding 30 minutes daily to achieve and maintain weight loss. The Diabetes Prevention Program (DPP) clearly supported the fact that individuals could perform at least 150 minutes of physical activity weekly to achieve a 7% weight loss.[5] Information from the National Weight Control Registry (NWCR) and other studies, however, indicates that more than 250 minutes per week of exercise may be required to maintain larger weight losses.[10,11] Because physical activity has many benefits, including enhanced insulin sensitivity and improved glycemic control, that are independent of weight loss, exercise performed regularly can be useful in both preventing and treating type 2 diabetes in adults and hopefully in children as well.

Diet and the Prevention of Obesity

Dietary fat intake has been most closely associated with likelihood of developing obesity.[12,13] Fat contains 9 kcal/g, compared to 4 kcal/g for carbohydrate and protein, and dietary fat has been reported to have a low satiety value.

Indeed, ecological studies have offered some support for this theory, finding that as the percentage of energy from fat increases from 15 to 40% in a population, the percentage of the population with a BMI > 25 kg/m^2 increases linearly.[13] Furthermore, the populations of poorer countries have the lowest average BMI and generally get the lowest proportions of calories from dietary fat. Problems inherent to these types of studies, however, make such data questionable because we do not know if the obese individuals are truly eating the high-fat diet or how other factors, such as physical activity level and caloric restriction, may influence average BMI for a given population.

Efforts to find an association between dietary fat intake and BMI in a free-living population have yielded mixed results. A Finnish study found that risk for a BMI > 30 kg/m^2 increased with increased sausage intake and decreased with moderate alcohol consumption and increased intake of fruits and vegetables.[14] A high-fat eating pattern (42% of calories) was not associated with a greater risk of obesity and did not yield a greater caloric intake compared to either a heart-healthy, light, or wine-and-moderate-eating dietary pattern in a 10-year study of women in the Framingham Heart Study.[15] However, an empty-calorie eating pattern (38% fat) consisting of sweets rich in fat, sweetened beverages, and snack foods was associated with obesity. A pattern of low fruit and vegetable consumption also predicted overweight.

Low dairy intake was found to be associated with the development of obesity in young adults in the Coronary Artery Risk Development in Young Adults study.[16] As dairy consumption increased, so did intake of whole grains, fruits, and vegetables while the converse was true as sugared-sweetened soft drink intake increased. Indeed, sugared drink consumption has risen at the time obesity rates have risen in the United States, although no clear association is evident.

Intervention studies in already overweight individuals lend more support for restricting fat intake to control body weight. A meta-analysis of 16 ad libitum studies of 1,910 overweight and obese individuals reported a mean weight loss of 3.2 kg in individuals who had reduced fat intake by a mean of 10.2% from 38 to nearly 28% of total calories. Daily caloric intake fell by 275 calories.[12] Reducing fat intake alone by 8–10% in a 6-month intervention trial resulted in a reduction in calories and a modest weight loss of up to 1.8 kg in otherwise healthy adults.[17] A primary objective of the study was to examine whether the substitution of either sugary or starchy carbohydrate for fat would affect body weight. Body weight was not significantly influenced by the substitution of either type of carbohydrate.

There is much still unknown about the macronutrient composition of the diet and its relationship to body weight, but dietary fat intake is not likely the only dietary culprit related to overweight. U.S. consumption figures indicate that dietary fat as a percentage of calories has decreased from 38% in 1984 to 32% in 1994.[18] However, the total grams of fat consumed has actually stayed the same during that time period, whereas total

calories (from carbohydrate) have increased by 100–200 calories/day. This has caused some experts to postulate that carbohydrate, particularly high–glycemic index carbohydrate, may be responsible for obesity.[19]

No long-term studies have been conducted to support the role of low–glycemic index foods for the prevention of obesity. As a result, current data support that caloric intake remains the primary determinant of body weight and that maintaining caloric balance to prevent obesity is best achieved with a diet high in fruits, vegetables, and whole grains and modest in empty calories from both sugary and high-fat foods.

Weight Loss to Prevent Type 2 Diabetes

The DPP clearly illustrated that lifestyle modification that includes a low-fat diet and regular physical activity can reduce mean body weight by 7% and reduce progression to type 2 diabetes.[7] The NWCR provides insight into how individuals successful at losing and maintaining at least 25 lb. for 5 years have modified their diets.[10] On average, participants report eating frequently (five times/day), preparing most foods at home, reducing their fat intake to a mean of 24%, consuming 55% of calories as carbohydrate, and consuming < 1,500 kcal/day.

Despite a fair amount of evidence suggesting that reducing fat intake improves weight loss efforts, there is considerable debate over the absoluteness of this recommendation. Indeed, in controlled experimental situations in which calories are reduced and held constant, a diet that was > 50% fat produced the same weight loss as one that was < 25% fat.[20] These results should be viewed with caution, however, because the studies were very short-term (< 6 weeks), and most of us do not live in a metabolic ward. Long-term weight loss (18 months) was considered superior in a calorie-restricted diet containing 35% fat that was high in monounsaturated fats (predominately nuts), compared to a 20%-fat diet.[21] This and other studies utilizing unsaturated fat as the primary fat source imply that weight gain is not inevitable and that weight loss can occur utilizing a modest-fat diet of ~35% fat.[22] Furthermore, these studies reinforce the concept that caloric intake is the primary determinant of body weight, and caloric reduction determines weight loss.

Much of the debate over fat versus carbohydrate has centered around the possibility that a low-fat diet, because it correspondingly requires an increase in carbohydrate, may be detrimental to individuals with insulin resistance. Elevations in blood glucose and insulin levels as well as serum triglycerides are common in insulin-resistant individuals following consumption of a large amount of carbohydrate.[23]

Although it has been shown that insulin-resistant individuals respond as well to weight loss therapy as non–insulin-resistant individuals, the composition of the diet may be important.[24] Insulin-resistant subjects consuming a low-fat (25%), high–starch carbohydrate diet for 6 months experienced modest weight loss and improved lipid levels.[25] When the same individuals crossed over and substituted carbohydrate from sugar sources for starchy foods, they did not experience weight gain, but neither did they experience weight loss or see an improvement in lipids. This suggests that substituting any type carbohydrate for fat may not always result in weight loss. More research is needed in this area.

Protein intake has received considerable attention recently for its potential positive effect on weight loss. Most clinical trials altering the fat content of the diet contain protein levels of ~ 15% of calories. In a study comparing ad libitum food intake in normal subjects guided to consume a low-fat diet with either 12 or 25% of calories from protein, weight loss at 6 months was 5.1 kg in the low-protein/high-carbohydrate group and 8.9 kg in the high-protein group.[26] Furthermore, serum triglycerides and free fatty acid levels were only reduced in the subjects consuming the higher-protein diet, although this may have been more related to the magnitude of the weight loss in the high-protein group. More choices and freedom to consume lean meats was considered an adherence advantage for people following the higher-protein diet.

A high-protein, hypocaloric diet was also superior to a high-carbohydrate diet in a 1-month weight loss trial in hyperinsulinemic obese individuals (8.3 vs. 6.0 kg loss, respectively) although serum lipid levels did not differ.[27] The first long-term, controlled trial of the high-protein, low-carbohydrate diet plan (Atkins) illustrated that in the short term (i.e., at 3 and 6 months), weight loss was superior to a comparable low-calorie, high-carbohydrate diet in obese men and women.[28] However, at 12 months there was no difference in weight loss, although the higher fat/protein group maintained better triglyceride and HDL cholesterol levels. The authors speculated that most of their subjects were insulin resistant given their weight and that insulin sensitivity improved regardless of macronutrient composition of the diet.

Attempts to explain the effect of protein on weight loss have yielded mixed results for and against effects on appetite and energy intake. Single-meal comparisons of diets containing 32% protein versus 65% fat or 65% carbohydrate failed to show a difference in energy expenditure or substrate metabolism between the fat and carbohydrate diets but did find a slight, although not significant, increase in both on the higher-protein diet.[29] Resting energy expenditure has been shown to decrease to a lesser degree on high-protein intakes.

Because reducing calories is required to reduce weight, it follows that restricting fat intake may be the best way to reduce total calories. Yet, a moderate-fat diet (35%) offers an alternative that may enhance adherence particularly in some cultures. Lean protein choices (up to 25–30% daily intake as protein) may assist with adherence to a hypocaloric diet as well as positively influence metabolism, at least in the short term, although long-term studies of effects on renal function or cardiovascular risk factors have not taken place. More studies are supporting the concept that macronutrient composition of a weight loss diet probably takes second seat to total caloric intake.

Treating Obesity in Type 2 Diabetes

Many of the same principles that apply to overweight individuals in general also apply to those who are overweight and have type 2 diabetes. Structured lifestyle modification approaches are considered superior.

Weight reduction interventions may be most effective in improving metabolic control early in the diagnosis of type 2 diabetes because weight loss and caloric restriction enhance insulin sensitivity and reduce hepatic glucose output.[30] The UKPDS and other studies have supported the notion that a calorie-restricted diet improves glycemic control most dramatically during the first 10–30 days of caloric restriction and may not improve control significantly more despite further weight loss.[30,31] Hence, it appears that caloric restriction plays a role in improving metabolic control independent of weight loss.

Even intermittent caloric restriction utilizing a supplemented fast (either 1 day each week or 5 days every 6 weeks) has proven beneficial to weight loss in a 20-week study in type 2 diabetes.[32] Supplemental fasting products can be used as meal replacements, which in themselves have proven beneficial in promoting modest weight loss in type 2 diabetes.[33,34] Meal replacements can be used in supplemental fasting for specific populations or cultures requesting occasional fasting. Meal replacements can also be helpful by providing portion control and quick flexible meals to enhance adherence to a weight reduction plan with minimal planning and preparation.

Studies support the fact that a low-fat hypocaloric diet produces a reduction in body weight in people with type 2 diabetes.[35] Yet, there is evidence from short-term studies up to 3 months in duration that, as long as total calories are held equal, weight loss may not be compromised by a higher fat intake.[36,37] Once again, the key concept is that any increase in fat should come from unsaturated, preferably monounsaturated, fats.

Recent studies varying the protein intake in the diet of people with type 2 diabetes suggest that these subjects have a response different from that of their counterparts without diabetes. Diets containing 1,600 calories that were 26% fat and either 28% protein or 16% protein resulted in similar weight loss after 8 weeks in obese subjects with type 2 diabetes.[38] A second study by the same investigators found similar weight loss and similar improvement in the lipid profile. Investigators observed a greater reduction in abdominal fat in women and a greater LDL cholesterol reduction in both men and women on the higher-protein diet.[39]

Because a weight loss regimen inherently involves caloric restriction, a diet plan comprising 25–30% of intake from protein would contain ~100–120 g of protein (based on 1,600 total calories). In terms of total grams, this protein intake is slightly higher than usual daily protein intake (82 g) in the United States (15% of 2,200 total calories). Therefore, consuming 100 g of protein daily constitutes a high-protein diet and seems to be the amount of protein consistently used in high-protein diets. The long-term metabolic effect of this amount of protein is unknown, and implementing such a diet requires caution. Furthermore, studies conducted on these levels of protein are generally low in total fat (< 30%) and, thus, do not support diets high in both protein and fat as interpreted by some individuals.

Modest caloric restriction and weight reduction strategies are beneficial to body weight and metabolic control, including control of glycemia, hyperlipidemia, and hypertension in overweight people with type 2 diabetes. This is particularly true early in the diagnosis of type 2 diabetes when insulin resistance is the predominant metabolic defect and β-cell function is adequate. Once β-cell function deteriorates to the point that a severe insulin deficiency exists, weight loss attempts may not be effective to improve glycemia or dyslipidemia. At this point, a shift in philosophy away from weight loss may be warranted. If desired medical outcomes are not achieved with weight loss efforts, then reducing the individual meal and snack glycemic load by distributing daily carbohydrate intake and modifying fat consumption to reduce dyslipidemia should be the focus.

Managing Body Weight During Pharmacological Therapy

The presence of multiple metabolic defects and the natural progression of type 2 diabetes suggests that many individuals with diabetes eventually will be on antidiabetic medication, either as monotherapy or combination therapy to achieve optimal metabolic control. Weight gain with monotherapy in type 2 diabetes varies with the individual and length of study. Reported weight gain varies from near none or weight loss with metformin[40] and alpha-glucosidase inhibitors[41] to a mean gain from 1.0 to 3.1 kg with the thiazolidinediones,[42] 4.0 kg with insulin secretagogues,[43] and 4.0–7.5 kg with insulin.[40,43] Combining medications produces a similar effect depending on the combination. Data from the Diabetes Control and Complications Trial, the UKPDS, and other clinical trials have identified that weight gain is correlated to improvements in glycemic control.[43,44] After 10 years of observation in the UKPDS, weight gain was 2.5 kg in the conventional group and 5.6 kg in the intensive treatment group despite a < 1% difference in mean A1C between the two groups. Individuals taking sulfonylureas gained 4.2 kg, whereas those on insulin gained 8.2 kg.

Attempts to characterize the cause of weight gain with intensive medication therapy have suggested that metabolic rate may be increased as glycemic control worsens, and, conversely, improved glycemia decreases both basal metabolic rate and glucosuria.[45,46] It appears that weight gain with insulin therapy in both type 1 and type 2 diabetes is similar to weight gain in general and is comprised of 65% fat and 35% lean tissue. Improved hydration and fluid retention may be partly responsible for some weight gain as well, particularly with some individuals on thiazolidinediones.[47] The weight loss effect of metformin has been at least partially attributed to a 200–300 calorie reduction in food intake with metformin therapy.[48]

The introduction of medication in type 2 diabetes requires close attention to total caloric intake through the use of food and blood glucose records. In this way, providers can assess usual food intake as well as increased food intake resulting from treatment of recurring hypoglycemia or inappropriate insulin dosing. Patients who do not reduce caloric intake while adopting intensive strate-

gies to improve glycemic control with medications may experience an increase in body weight. Likewise, failure to reduce some hypoglycemic medication during weight loss may negate any efforts to lose or maintain weight as individuals chase hypoglycemia with increased food intake. Fortunately, weight loss efforts are effective in people on diabetes medications, and the usual lifestyle modification techniques have proven valuable.

Summary
Effective management of body weight is difficult in a society that promotes food intake and reduces opportunities for physical activity. People who have, or are at risk for, type 2 diabetes are challenged to find a nutrition plan that best complements their exercise program and can be individualized to manage body weight without harming overall health. Health professionals must be vigilant to support patients at every step on the type 2 diabetes path, from preventing obesity to preventing diabetes and to eventually treating type 2 diabetes.

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