

The Why WAIT Program: Improving Clinical Outcomes Through Weight Management in Type 2 Diabetes

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Targeting body weight, as an alternative model to targeting hemoglobin A_{1c}, is emerging as a viable and potentially cost-effective approach to diabetes management in clinical practice. Why WAIT (Weight Achievement and Intensive Treatment) is a 12-week multidisciplinary program for weight control and intensive diabetes management specifically designed for application in routine diabetes practice. The program, which is generally covered by insurance, is followed by continuous support aimed at long-term maintenance of weight loss and diabetes control. This model was effective in improving key metabolic abnormalities observed in diabetic patients. Eighty-two percent of participants achieved the target hemoglobin A_{1c} of less than 7% on less diabetes medications. The achieved weight reduction after 12 weeks of intervention was maintained for an additional year. Future dissemination of this intervention model in routine clinical practice may require wider endorsement by third-party payers and support of governmental health care agencies to halt the progression of the epidemic of obesity and diabetes in the United States.

Introduction

Over the past 20 years, the prevalence of type 2 diabetes mellitus (T2DM) has increased so dramatically (from 30 million cases worldwide in 1988 to 239 million cases at present) that the World Health Organization has declared it to be “the health hazard of the 21st century” [1]. A historically unique combination of two phenomena—rapid aging of the population and the dramatic increase in obesity [2]—are the major cause of this growing epidemic of diabetes in the United States. Currently, most type 2 diabetic patients are overweight, obese, or severely obese.

Data from the 1999 to 2002 National Health and Nutrition Examination Survey [3•] indicate that the prevalence of overweight and obesity among US adults with diabetes now exceeds 80%.

Several barriers specific to the combination of diabetes and obesity make weight management for diabetic patients even more difficult. These barriers include the weight-promoting effect of many of the currently available diabetes medications, including insulin, sulfonylureas, glinides, and thiazolidinediones. Although it is not systematically studied, many clinicians raise the concern that weight gain associated with diabetes medications may erode the metabolic benefits of these medications over time. Over a 10-year treatment period, participants in the United Kingdom Prospective Diabetes Study gained a significant amount of weight, particularly patients treated with insulin [4]. Similarly, type 2 diabetic patients treated with intensive insulin therapy who dropped their hemoglobin A_{1c} (HbA_{1c}) by 2.6% gained on average 8.7 kg over a 6-month period [5]. Patients may find it confusing when their treating physicians are advising them to lose weight, while providing them with medications that promote weight gain.

Further, because insurance plans do not typically cover obesity medications or weight management programs, physicians often perceive weight management as an impractical and costly approach. Adding to these paradoxes in diabetic patients is the traditional recommendation to consume a higher percentage of calories from carbohydrates (currently 50% to 55% of the total caloric intake) in a disease that is still defined as a carbohydrate intolerance problem. Taken together, these factors may contribute to providers’ inertia and skepticism about the long-term maintenance of any achievable weight loss in diabetic patients.

We previously demonstrated that modest weight reduction of about 7% over a 6-month period through caloric reduction and increased physical activity improved insulin sensitivity, endothelial function, and several markers of inflammation and coagulation in obese patients with and without diabetes [6,7]. The ongoing Look AHEAD (Action for Health in Diabetes) study is also exploring the health outcomes associated with modest

Table 1. Weight-specific effects of available classes of diabetes medications

Diabetes medications associated with weight gain (weight fury)	Diabetes medications associated with weight loss or are weight neutral (weight friendly)
Sulfonylureas Glyburide, glipizide, glimepiride: ~ 4.4 lb weight gain	Metformin Weight neutral or up to ~ 6.6 lb weight loss
Glinides Nateglinide: 0.7–2.0 lb weight gain; repaglinide: ~ 2.2–6.6 lb weight gain	Amylin analogue Pramlintide: ~ 3.3 lb weight loss
Thiazolidinediones Pioglitazone, rosiglitazone: ~ 2.2–6.6 lb weight gain	GLP-1 receptor agonist Exenatide: short-term: ~ 3.3 lb weight loss; long-term: ~ 8.8 lb weight loss
	DPP-4 inhibitor Sitagliptin: weight neutral
DPP-4—dipeptidyl peptidase IV; GLP-1—glucagon-like peptide 1.	

weight loss maintained over 10 years using an intensive lifestyle intervention (ILI) that combines decreased caloric intake, increased physical activity, and behavioral support versus the standard diabetes support and education (DSE) in patients with T2DM. The Look AHEAD study group recently published their first-year results, which are encouraging [8••]. The study found that participants randomized to ILI lost an average of 8.6% of their initial body weight compared with 0.7% in the DSE group. Although both groups experienced blood glucose reductions compared with baseline, HbA_{1c} improvement in the ILI group was significantly greater than that observed in the DSE group (absolute HbA_{1c} reduction: -0.64% [ILI] vs -0.14% [DSE]; $P < 0.001$; baseline HbA_{1c} for both groups: ~ 7.3%). Notably, HbA_{1c} lowering was observed in the context of decreased glucose-lowering medication use in the ILI group and increased medication use in the DSE group. Thus, available data indicate that short-term weight loss of 7% to 10% in patients with diabetes is metabolically beneficial. More substantial weight loss (23.4% at 2 years and 16.1% at 10 years) has recently been reported postoperatively in severely obese patients treated with bariatric surgery; this was associated with diabetes remission in 72% of patients at 2 years and 36% at 10 years.

Despite these impressive results in clinical trials, physicians remain skeptical about the feasibility of applying similar intervention protocols in routine clinical practice. Surveys indicate that one third to one half of physicians do not recommend weight management to their overweight and obese patients, with some research indicating that physicians may not believe their patients are adequately motivated to achieve weight loss [9,10].

The Why WAIT Program

Why WAIT (Weight Achievement and Intensive Treatment) is a 12-week multidisciplinary program for weight control and intensive diabetes management specifically

designed by Joslin Diabetes Center for application in routine diabetes practice. The program, which is generally covered by insurance, is followed by continuous support aimed at long-term maintenance of weight loss.

Key components of the Why WAIT program

Key components of the Why WAIT program include the following: 1) intensive and interactive medication adjustments; 2) structured modified dietary intervention; 3) graded, balanced, and individualized exercise intervention; 4) cognitive behavioral support; and 5) adult group education.

Intensive and interactive diabetes medication adjustment

For the Why WAIT intervention, antihyperglycemic medications were classified into two groups: those known to promote weight gain (weight fury diabetes medications) and those associated with weight loss or are weight neutral or associated with minimal weight gain (weight friendly diabetes medications) (Table 1). Without compromising diabetes control, medication regimens were adjusted to facilitate weight loss by using more of the weight friendly diabetes medications, if covered by the participant's medical insurance, and reducing or eliminating those that promote weight gain. In patients treated with insulin and with prior good diabetes control (HbA_{1c} < 7%), hypoglycemia is an imminent risk that may aggravate hunger and consequently slows weight reduction. Such participants were advised to reduce their prandial insulin by about 20% to 30% at the start of the program. Patterns and timing of existing insulin regimens were also adapted to maximize glycemic benefit and to enhance weight loss. For example, in patients treated with pramlintide and prandial insulin, injecting the pramlintide before meals and the short-acting insulin immediately after meals was preferred. Because appetite is frequently suppressed by pramlintide, patients usually eat much less than expected; by administering the short-acting insulin after meals, patients had the opportunity to calculate the short-acting insulin dose based on the

food that was actually consumed and not on what they presume to eat. This tactic minimized hypoglycemic risk and the consumption of unneeded extra calories to cover preplanned prandial insulin. When postprandial short-acting insulin was preferred, we used glulisine insulin for its quicker onset of action [11•]. Despite controversy, glargine insulin and neutral protamine Hagedorn (NPH) insulin were frequently changed to detemir insulin for its weight advantage [12,13•].

Regarding oral medications, metformin and sitagliptin were preferred for their weight neutrality. Metformin dose was frequently increased. Conversely, sulfonylureas, glinides, and thiazolidinediones were reduced or eliminated. Exenatide was frequently added to oral medications for its weight benefit, and pramlintide was frequently added to meal time insulin for the same reason.

Substituting or adjusting medications requires close monitoring of glucose control. Each participant was asked to monitor blood glucose at least four to six times per day (before each meal, before and after exercise, and at bedtime) using a glucose meter with a log memory. In addition, patients treated with insulin and pramlintide were encouraged to monitor their blood glucose 2 hours after each meal.

At the beginning of each weekly session, meters were downloaded. According to the weekly blood glucose pattern, diabetes medications were adjusted by a diabetes nurse practitioner and a certified diabetes educator. As weight reduction progressed, interactive and progressive adjustment of diabetes medications were frequently needed as guided by close monitoring of blood glucose. This tactic reduced the risk of hypoglycemia that might stem further weight loss. Patients were also medically evaluated for 30 minutes at weeks 4 and 8 by a nurse practitioner and at week 12 by a diabetologist.

Structured modified dietary intervention

All participants received dietary evaluation by a registered dietitian. The evaluation included a review of dietary history and 24-hour recall of typical daily intake, review of adherence to dietary instructions during previous weight management attempts, and evaluation of possible concerns or barriers to following the program's structured meal plan. Based on the typical caloric intake from the 24-hour dietary recall, each participant received a meal plan with a 500-calorie reduction rounded to the nearest 1200-, 1500-, or 1800-calorie level. With few exceptions, most men started on an 1800-calorie diet plan and most women on a 1500-calorie diet plan.

These meal plans were developed according to the Joslin Nutrition Guidelines for obese diabetic patients to provide approximately 40% of daily caloric intake from carbohydrate, with a total daily intake of no less than 130 g/d, 30% from protein (to minimize lean-mass loss during weight reduction), and the remaining 30% from fat [14••,15••]. Trans fats were entirely eliminated and satu-

rated fat was reduced to 10%, in general, and to 7% in patients with elevated low-density lipoprotein (LDL) cholesterol (> 100 mg/dL). All participants were instructed to use a nutritionally complete meal replacement for breakfast and lunch. The meal replacement selected for the Why WAIT program was BOOST Glucose Control (Nestlé HealthCare Nutrition, Inc., Minneapolis, MN). Participants were encouraged to eat two snacks between meals. A list of six choices of 100-calorie and 200-calorie snacks (eg, fruits and nuts) was provided. For dinner, participants were instructed to select from 14 different menus. Each dinner menu included meal ingredients, nutrition facts, and cooking instructions. Three menu books were designed for the 1200-, 1500-, and 1800-calorie meal plans. The full meal plan was consistent with Joslin Nutrition Guidelines and was low in glycemic index, high in fiber (~ 30 g), particularly from fresh fruits and vegetables, and low in sodium (< 800 mg). Each participant was provided with a written description of the meal plan and a dietary logbook and was instructed to record daily food intake throughout the program.

Participants who failed to achieve 3% weight reduction by the 4th week or 5% by the 8th week were advanced to the lower caloric level (eg, 1800 to 1500, or 1500 to 1200). This approach was rarely used because most patients achieved targets in that time frame. Two weeks before program completion, participants were provided with alternative menus for breakfast and lunch that contained similar choices designed to be equivalent in caloric content and dietary composition to the meal replacements. They were given the option to use the breakfast and lunch menus, to continue the meal replacements, or to use them interchangeably. Underlying all of these steps was the goal of designing individualized plans that could be maintained over the long term. Many patients found it helpful to have a structured dietary intervention that included specific suggestions for daily meals. This approach increased adherence and was easier to follow than a list of general guidelines.

Individualized balanced and graded exercise plan

Before starting the exercise plan, an evaluation of exercise capacity, ophthalmologic examination, electrocardiogram, and in most cases, exercise stress test were conducted. Participants met individually with an exercise physiologist to construct an individualized exercise plan responsive to their lifestyles. The exercise plan was based on each participant's health status and exercise capacity. Because obese individuals frequently have difficulty exercising, this process required careful attention.

In general, the intensity level of exercise was set above the minimum required to improve the participant's current exercise capacity, but below a level that might evoke abnormal clinical signs or symptoms. The exercise plan included a balanced mix of aerobic exercise (cross and interval training) to promote the development and mainte-

nance of cardiovascular health; resistance exercise (circuit and superset training) to enhance muscular strength and improve performance of daily living; and flexibility exercise (stretching) to enhance functional capabilities and reduce the risk of injury.

The exercise plan included a weekly 60-minute exercise session under the supervision of an exercise physiologist at the clinic gymnasium. In addition, each participant received an individualized exercise plan to conduct independently at home throughout the week. Participants were instructed to progress gradually during the initial 12 weeks of intervention, from 20 minutes (continuous or intermittent) 4 days per week to 60 minutes 6 days per week. Upon completion of the initial 12 weeks, they were instructed to continue to exercise independently for 60 minutes per day, 6 days per week, if possible. Emphasis was placed on moderate-intensity exercise, such as walking 20-minute miles, rather than strenuous exercise, and on strength training to maintain lean muscle mass during weight loss.

Strength training not only improves muscle strength, but also offers an alternative to aerobic exercise for improving glucose control without increasing possible chances for injuries [16]. This exercise modality has been proven to improve glucose disposal in diabetic patients [17] and maintain bone mineral density and bone mineral content during weight loss [18]. Because patients who are not used to exercising find it difficult to incorporate physical activity into daily practice, a variety of exercises were offered to avoid boredom.

Cognitive behavioral support

Group behavioral support sessions led by a clinical psychologist were conducted weekly during the initial 12 weeks of intervention, then once monthly during follow-up. The sessions incorporated key components of cognitive-behavioral therapy for weight loss already validated in other clinical trials [19,20]. These components included self-monitoring of eating and exercise, behavioral goal setting, stimulus control techniques, cognitive restructuring, assertive communication skills, stress management, and relapse-prevention. The monthly support group discussion was focused on active problem solving for relapse prevention and weight loss maintenance.

Group education

Group didactic sessions were conducted each week for 30 minutes by a diabetologist, an exercise physiologist, a registered dietitian, or psychologist during the initial 12 weeks. Participants were provided with handouts for future reference. Each session covered a different topic relevant to weight management and diabetes.

Service coding and reimbursement

The Why WAIT program was designed to offer multidisciplinary, complementary services with appropriate reimbursement in compliance with insurance regulations.

All interventions described were affordable in routine clinical practice, especially those implemented in a group format. All services were recognized as reimbursable, but levels of payment differed based on third-party payer requirements for authorizations and copayments. Out-of-pocket expenses were limited to a \$100 enrollment fee to cover the additional administrative costs, plus the regular copayment at each of the initial 12 visits.

Support session

Upon completion of the program, participants were advised to come each month for a 1-hour group support session. Because attendance was unexpectedly poor in the first year, we switched the support program to one-on-one. Participants were advised to continue their follow-up with one provider of the intervention team on a monthly basis. In this support model, participants who needed ongoing support in one particular component of this multidisciplinary approach were advised to partner with the corresponding provider.

Why WAIT Results

The Why WAIT program started in September 2005. To date, 10 groups have completed the program. Each group included 10 to 15 participants. Application of this multidisciplinary intervention model in routine clinical practice resulted in a significant reduction in body weight and waist circumference. Eighty-five participants with a mean age of 54.2 ± 1.2 years (mean \pm SE, approximately 20% above age 70), diabetes duration of 9.8 ± 1.1 years, weight of 237.7 ± 4.6 , body mass index (BMI) of 38.4 ± 0.6 kg/m², HbA_{1c} of $7.5\% \pm 0.14\%$, and waist of 46.7 ± 0.6 inches were followed up for an average duration of 357 days.

After 12 weeks, they were able to reduce their initial weight by an average of 24.6 ± 1.2 lb (-10.3%, $P < 0.001$), and their waist by 3.6 ± 0.24 inches ($P < 0.001$). Except for the first week, weight loss was steadily progressive over time and ranged from 1.2 to 2.5 lb/wk. The reduction in waist circumference was associated with significant reduction in the waist/hip ratio (0.932 ± 0.01 to 0.916 ± 0.01 , $P < 0.001$), indicating that weight loss was predominantly from the central area. Although we did not quantify visceral or intrahepatic fat in this cohort, the significant reduction in liver transaminases at 12 weeks ($P < 0.001$) appears to suggest their reduction [21,22]. After approximately 1 year, weight remained lower by 18.2 ± 2.2 lb (-7.6 \pm 0.9%, $P < 0.001$) from baseline. Fifty-five percent of participants continued to lose weight or gained less than 5 lb from the end of the initial 12 weeks. Their average weight loss from baseline reached -11.9% after 1 year. The remaining 45% regained back more than 5 lb, but their 1-year weight remained lower than baseline by -2%. Because of the relatively higher percentage of protein intake and incorporation of strength exercise, the average reduction in the fat-free mass was relatively small, and consequently, the lean/fat

ratio significantly increased ($P < 0.001$). Maintenance of fat-free mass during weight reduction may have helped participants maintain a reasonable amount of energy expenditure by the end of the program, and possibly helped them to maintain the achieved weight loss.

HbA_{1c} decreased significantly, from $7.5\% \pm 0.14\%$ to $6.6\% \pm 0.12\%$ ($P < 0.001$). At 12 weeks, 82.3% achieved the target HbA_{1c} of less than 7% and 69.4% were able to reduce their HbA_{1c} to less than 6.5%. Reduction in HbA_{1c} correlated significantly with the percentage reduction in BMI ($P < 0.05$). Participants who maintained weight loss for a year also maintained the significant reduction in HbA_{1c}. Systolic blood pressure was reduced significantly at 12 weeks and 1 year from a baseline of 128.1 ± 1.7 mm Hg (-5.5 ± 1.7 mm Hg [$P < 0.01$] and -5.5 ± 1.8 mm Hg [$P < 0.01$], respectively). Similarly, diastolic blood pressure was reduced significantly from a baseline of 75.5 ± 0.8 mm Hg (-3.3 ± 1.0 mm Hg [$P < 0.01$] and -3.4 ± 0.9 mm Hg [$P < 0.001$], respectively).

Lipid profile improved significantly at 12 weeks (total cholesterol by $-10.8 \pm 1.5\%$ from a baseline of 166.9 ± 3.4 mg/dL, $P < 0.001$; triglycerides by $-18.2 \pm 3.8\%$ from a baseline of 130.1 ± 7.1 mg/dL, $P < 0.001$; LDL by $-9.6 \pm 2.4\%$ from a baseline of 101.2 ± 3.3 mg/dL, $P < 0.001$), but were mostly back to baseline at 1 year except high-density lipoprotein (HDL), which was significantly higher from a baseline of 42.8 ± 1.0 mg/dL ($+9.5 \pm 3.4\%$, $P < 0.01$). Although most clinical trials of weight loss showed significant reductions in triglycerides and increases in HDL cholesterol, changes were minimal or nonexistent in LDL cholesterol and non-HDL cholesterol [6,8•,23]. In this intervention model, triglycerides and LDL cholesterol decreased significantly. The significant reduction in LDL cholesterol is particularly unique to this intervention model and may be related to its distinctive dietary composition and/or use of meal replacement with controlled fat content. Reduced saturated fat and increased mono- and polyunsaturated fat and dietary fiber might also contribute to such lipid outcomes. A similar LDL reduction was seen in one trial that used a comparable dietary composition [24]. Although HDL cholesterol showed minimal but significant reduction at 12 weeks ($-3.6 \pm 1.5\%$, $P < 0.01$), non-HDL cholesterol and the total cholesterol/HDL cholesterol ratio decreased significantly, indicating that this resultant lipid profile is possibly less atherogenic. The changes in lipid profile with this intervention are attributed solely to weight loss, as hypolipidemic medications did not change during the intervention period. C-reactive protein decreased significantly at 12 weeks, from an average of 6.0 ± 0.85 to 4.2 ± 0.65 mg/L ($P < 0.01$), and was found to correlate with percentage weight loss ($r = 0.3$, $P < 0.05$). Such change in C-reactive protein serum level may indicate a possible reduction in cardiovascular risk.

Because of the higher percentage of calories from protein in the Why WAIT meal plan, we excluded patients with renal impairment (serum creatinine > 1.5 mg/dL

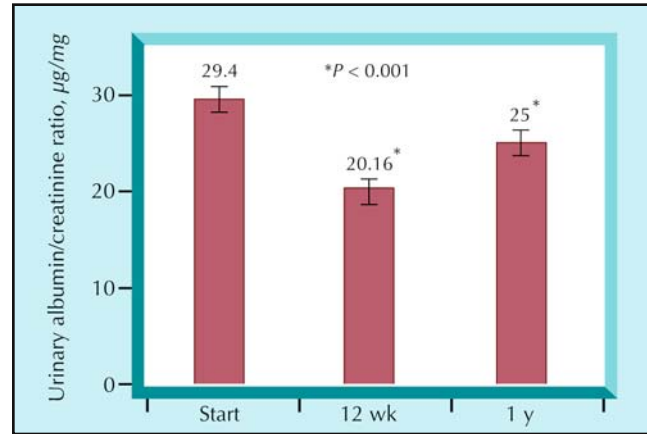


Figure 1. Change in urinary albumin/creatinine ratio after 12 weeks and 1 year of the Why WAIT program in diabetic patients.

and/or severe microalbuminuria). Blood urea nitrogen and serum creatinine did not change with this intervention, whereas significant improvement in urinary albumin/creatinine ratio was noticed at 12 weeks ($P < 0.01$). This significant improvement was maintained after 1 year of follow-up (Fig. 1). Such improvement may be explained by reduction of the mean blood pressure. However, one recent study showed that the long-term improvement in renal function after weight loss may not be related to the improvement in glomerular filtration rate but rather is attributable to the decrease in BMI and to the improvement of other weight-related metabolic factors [25•]. The use of a formula diet has also been shown to improve kidney function in patients with diabetic nephropathy [26].

Although the percentage of calories from protein was increased from an average of 15% to 30%, the total amount of protein per day did not change considerably due to the overall reduction in the daily caloric intake. It has been shown that moderate changes in dietary protein intake cause adaptive alterations in renal size and function without adverse effects [27]. Meanwhile, increasing the percentage of calories from protein to 30% was associated with a significant decrease in the 24-hour integrated glucose area and percent HbA_{1c}, irrespective of weight loss or the carbohydrate to fat ratio [28]. In a 1-year randomized, clinical trial, a high-protein weight-reduction diet was found to have a more favorable cardiovascular risk profile than a low-protein diet with similar weight reduction in people with T2DM [29].

Significant changes in diabetes medications were also seen in response to weight reduction in the Why WAIT program. Twenty-one percent of the Why WAIT patients on short-acting insulin were able to stop it completely by the program's end. In remaining patients on insulin therapy, the daily dose of long-acting analogue insulins was reduced by an average of 55% and the short-acting analogue insulins by 54%. Almost two thirds of the patients on sulfonylureas and thiazolidinediones were able to stop them, whereas the remaining participants reduced their

sulfonylurea dose by 35% to 41% and thiazolidinedione dose by 33% to 47%. The number of patients on metformin did not change, but the dose was slightly increased. In 17 patients on oral medications, exenatide was added, and in another nine patients on prandial insulin, pramlintide was added. The average cost saving on diabetes medications during the 12 weeks was \$140.34 per patient, which is projected to be \$561.37 per patient per year.

A systematic review of 11 long-term studies with a follow-up of more than 2 years showed that mortality risk was reduced by 25% in patients with diabetes who intentionally lost a significant amount of weight [30]. It is important to observe this cohort for a much longer duration before drawing such conclusions, and to try to determine what factors are specifically associated with long-term positive results.

Compliance with the Why WAIT program was high. Patients' attendance throughout the 12 weeks was excellent. Although it was expected that participants might miss an average of 20% of the intervention sessions, only 7% of the sessions were missed. Conducting this program during the evening hours (5–7 PM) might have improved compliance as it did not conflict with the participants' working schedules. It also seems that the improved glucose control, as clearly observed through frequent blood glucose monitoring, was another important motivational tool. Acceptance of the meal replacement and the structured dinner menus was high. Most participants were able to tolerate meal replacement throughout the entire intervention period. Meanwhile, more than half of participants voluntarily elected to continue them after the initial 12 weeks.

Considering that diabetes is a costly chronic disease, a direct cost saving on diabetes medications is encouraging, especially when taken together with potential indirect cost savings that may result from improved metabolic control and quality of life. Additional studies are needed to evaluate the long-term cost effectiveness of this intervention model in relation to the improved quality of life. According to a previous cost model, the 1-year total health care cost saving after a 1% weight loss in type 2 diabetic patients was \$213, and the diabetes-related health care cost saving was \$131 [31]. These numbers project to an annual decrease of total health care cost of about \$1619, with the diabetes-related cost of about \$996 with implementation of the Why WAIT program. HbA_{1c} decreased by an average 1%. Previous reports showed that about a 1% drop of HbA_{1c} leads to cost savings of \$776 per patient per year. These figures taken together suggest that implementation of the Why WAIT program may be cost effective.

Although the results of the Why WAIT program were much better than many other intervention models, we have to be cautious in over-promoting this model for universal intervention because most institutions don't have similar resources. Until this model is replicated in other

diabetes clinical practices, we should limit our interpretation of these good results to the current intervention center. However, in our opinion, many reasons could explain these exceptional short- and long-term results, which include the following:

- Comprehensive patient evaluation by an experienced team for inclusion in and exclusion from the program
- Change in diabetes medications, specifically the reduction or elimination of weight-promoting medications
- Continuous monitoring of blood glucose and frequent adjustment of diabetes medications on a weekly basis
- Change in diet composition by reducing percentage carbohydrates to 40% and increasing percentage protein to 30%
- Use of meal replacement with controlled diet composition
- Increase percentage of resistance exercise and gradual increase of exercise duration
- Availability of gymnasium in the intervention facility
- Use of several motivational tools throughout the process of weight loss
- Structured design of intervention with limited options
- Conducting the program in group sessions and in the evening hours (5–7 PM)

It remains a challenge to simplify the Why WAIT intervention model to be applied in primary care practice, in which time and resources are traditionally limited. Development of useful written or recorded material that can be handed to patients plus the use of the Internet as an interactive educational tool are good options. Referral to community-based behavior modification support groups and partnerships with athletic centers or community exercise facilities may also be another option. The collaborative effort of academic institutions, governmental agencies, insurance companies, and pharmaceutical industry is needed to stem the progression of the obesity and diabetes epidemics in the United States.

Based on the Why WAIT program results and the early results of the Look AHEAD study, we propose that targeting body weight as the prime tool to control diabetes may evolve in the future as a valid alternative model to targeting HbA_{1c} in today's diabetes practice. A comparison of the classic model of targeting HbA_{1c} versus the alternative model of targeting body weight is summarized in Table 2. In this suggested model, providers will focus on helping their diabetic patients to lose weight in many ways. This

Table 2. Comparison between two models of diabetes managements: targeting HbA_{1c} versus targeting high body weight

	Classic model (targeting HbA _{1c})	Alternative model (targeting body weight)
Medications	Increase over time	Possible reduction or stoppage
Cost	Increases over the long term	Decreases over the long term
Weight	Mostly increases	Decreases or stationary
HbA _{1c}	May temporally decrease; target may be achieved	Frequently decreases; more patients on target
Cardiovascular risk	May decrease (currently questionable?)	Possibly decreases (improved lipids, lowered BP, decreased CRP, increased adiponectin)
Quality of life	Less than optimal	Improves

BP—blood pressure; CRP—C-reactive protein; HbA_{1c}—hemoglobin A_{1c}.

may be achieved through changing diabetes medications to enhance weight loss as described in the Why WAIT model, providing patients with a structured diet and an exercise plan, and enrolling them in individual or group behavioral support. If the patient does not achieve the target weight reduction as planned over time, providers may tighten these measures, add antiobesity medications, or even refer some patients for bariatric surgeries. Considering that obesity is a major root of T2DM, any weight loss achievement may improve diabetes control more effectively than the current method of increasing medication dosing or adding more medications over time.

Conclusions

Multidisciplinary weight management approaches are emerging as viable and potentially cost-effective solutions to overweight and obesity management in T2DM. Applying weight loss as a T2DM treatment can delay or reduce the need for medications, reduce cardiovascular risk, and improve quality of life. When resources are limited, key aspects of the program can still be implemented (eg, diabetes medications can be adjusted and patients can be referred to community-based behavior modification support groups). It is particularly important that physicians consider medication modification strategies for all patients with T2DM; any weight loss achieved may contribute to long-term health outcomes and reduced costs.

The Why WAIT model was effective in improving key metabolic abnormalities observed in diabetic patients. The achieved weight reduction after 12 weeks of intervention was maintained for an additional year. Future dissemination of this model in routine diabetes practice may be valuable; however, longer-term metabolic and vascular benefits are yet to be determined. Dissemination of this intervention model in routine clinical practice may require wider endorsement by third-party payers and a unified effort between academic institutions, governmental agencies, insurance, and pharmaceutical industries to halt the progression of the epidemic of obesity and diabetes problems in the United States.

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References and Recommended Reading

Papers of particular interest, published recently, have been highlighted as:

- Of importance
 - Of major importance
1. King H, Aubert RE, Herman WH: **Global burden of diabetes, 1995-2025: prevalence, numerical estimates, and projections.** *Diabetes Care* 1998, **21**:1414-1431.
 2. Flegal KM, Carroll MD, Ogden CL, Johnson CL: **Prevalence and trends in obesity among US adults, 1999-2000.** *JAMA* 2002, **288**:1723-1727.
 3. Lin SX, Pi-Sunyer EX: **Prevalence of the metabolic syndrome among US middle-aged and older adults with and without diabetes—a preliminary analysis of the NHANES 1999-2002 data.** *Ethn Dis* 2007, **17**:35-39.

This is an epidemiologic study to demonstrate the high prevalence of the cardiometabolic risk factors among US adults with and without diabetes.

4. Turner RC, Cull CA, Frighi V, Holman RR: **Glycemic control with diet, sulfonylurea, metformin, or insulin in patients with type 2 diabetes mellitus: progressive requirement for multiple therapies (UKPDS 49).** UK Prospective Diabetes Study (UKPDS) Group. *JAMA* 1999, 281:2005–2012
5. Henry RR, Gumbiner B, Ditzler T, et al.: **Intensive conventional insulin therapy for type II diabetes.** Metabolic effects during a 6-mo outpatient trial. *Diabetes Care* 1993, 16:21–31
6. Hamdy O, Ledbury S, Mullooly C, et al.: **Lifestyle modification improves endothelial function in obese subjects with the insulin resistance syndrome.** *Diabetes Care* 2003, 26:2119–2125.
7. Monzillo LU, Hamdy O, Horton ES, et al.: **Effect of lifestyle modification on adipokine levels in obese subjects with insulin resistance.** *Obes Res* 2003, 11:1048–1054.
- 8.●● Pi-Sunyer X, Blackburn G, Brancati FL, et al.: **Reduction in weight and cardiovascular disease risk factors in individuals with type 2 diabetes: one-year results of the look AHEAD trial.** *Diabetes Care*. 2007, 30:1374–1383.
The first results of the Look AHEAD trial after 1 year of lifestyle interventions. It shows that weight loss resulted in reduced medications and improved diabetes control. This ongoing long-term weight-loss study aims to evaluate the health outcome of sustained weight loss compared with standard diabetes management.
9. Price JH, Desmond SM, Krol RA, et al.: **Family practice physicians' beliefs, attitudes, and practices regarding obesity.** *Am J Prev Med* 1987, 3:339–345.
10. Hill JO, Wyatt H: **Outpatient management of obesity: a primary care perspective.** *Obes Res* 2002, 10(Suppl 2):124S–130S.
- 11.● Becker RH, Frick AD: **Clinical pharmacokinetics and pharmacodynamics of insulin glulisine.** *Clin Pharmacokin* 2008, 47:7–20.
This study shows the shorter onset of action of insulin glulisine that may allow this insulin to be injected postprandial compared with the traditional preprandial injection.
12. Dornhorst A, Lüddecke HJ, Sreenan S, et al.: **Insulin detemir improves glycaemic control without weight gain in insulin-naïve patients with type 2 diabetes: subgroup analysis from the PREDICTIVE study.** *Int J Clin Pract* 2008, 62:659–665.
- 13.● Rosenstock J, Davies M, Home PD, et al.: **A randomised, 52-week, treat-to-target trial comparing insulin detemir with insulin glargine when administered as add-on to glucose-lowering drugs in insulin-naïve people with type 2 diabetes.** *Diabetologia* 2008, 51:408–416.
This study shows that detemir insulin has an additional advantage of promoting less weight gain compared with other long-acting insulin while achieving similar HbA_{1c} reduction.
- 14.●● Giusti J, Rizzotto JA: **Interpreting the Joslin Diabetes Center and Joslin Clinic Clinical Nutrition Guideline for Overweight and Obese Adults With Type 2 Diabetes.** *Curr Diab Rep* 2006, 6:405–408.
Discusses the details of the Joslin New Nutrition Guidelines for overweight and obese patients with diabetes, prediabetes, and at high risk to develop diabetes, in which percentage carbohydrates was reduced and percentage protein was increased compared with the current American Diabetes Association nutritional recommendations.
- 15.●● Campbell A: **Tackling “diabesity” head-on. Joslin Diabetes Center's new nutrition guideline.** *Diabetes Self Manag* 2005, 22:40, 42–44.
Discusses the details of the Joslin New Nutrition Guidelines for overweight and obese patients with diabetes, prediabetes, and at high risk to develop diabetes.
16. Fenicchia LM, Kanaley JA, Azevedo JL Jr, et al.: **Influence of resistance exercise training on glucose control in women with type 2 diabetes.** *Metabolism* 2004, 53:284–289.
17. Cuff DJ, Meneilly GS, Martin A, et al.: **Effective exercise modality to reduce insulin resistance in women with type 2 diabetes.** *Diabetes Care* 2003, 26:2977–2982.
18. Daly RM, Dunstan DW, Owen N, et al.: **Does high-intensity resistance training maintain bone mass during moderate weight loss in older overweight adults with type 2 diabetes?** *Osteoporos Int* 2005, 16:1703–1712.
19. Knowler WC, Barrett-Connor E, Fowler SE, et al.: **Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin.** *N Engl J Med* 2002, 346:393–403.
20. Wadden TA, Osei S: **The treatment of obesity: an overview.** In *Handbook of Obesity Treatment*. Edited by Wadden TA, Stunkard AJ. New York, NY: Guildford Press; 2002:229–248.
21. Hickman IJ, Jonsson JR, Prins JB, et al.: **Modest weight loss and physical activity in overweight patients with chronic liver disease results in sustained improvements in alanine aminotransferase, fasting insulin, and quality of life.** *Gut* 2004, 53:413–419.
- 22.● Dixon JB, Bhathal PS, O'Brien PE: **Weight loss and non-alcoholic fatty liver disease: falls in gamma-glutamyl transferase concentrations are associated with histologic improvement.** *Obes Surg* 2006, 16:1278–1286.
Shows the impact of weight loss on reducing the intrahepatic visceral fat.
23. Hsieh CJ, Wang PW: **Effectiveness of weight loss in the elderly with type 2 diabetes mellitus.** *J Endocrinol Invest* 2005, 28:973–977.
24. Parker B, Noakes M, Luscombe N, Clifton P: **Effect of a high-protein, high-monounsaturated fat weight loss diet on glycemic control and lipid levels in type 2 diabetes.** *Diabetes Care* 2002, 25:425–430.
- 25.● Navarro-Diaz M, Serra A, Romero R, et al.: **Effect of drastic weight loss after bariatric surgery on renal parameters in extremely obese patients: long-term follow-up.** *J Am Soc Nephrol* 2006, 17(12 Suppl 3):S213–S217.
Shows that significant weight loss through bariatric surgery improves renal function.
26. Saiki A, Nagayama D, Ohhira M, et al.: **Effect of weight loss using formula diet on renal function in obese patients with diabetic nephropathy.** *Int J Obes (Lond)* 2005, 29:1115–1120.
27. Skov AR, Toubro S, Bulow J, et al.: **Changes in renal function during weight loss induced by high vs low-protein low-fat diets in overweight subjects.** *Int J Obes Relat Metab Disord* 1999, 23:1170–1177.
28. Gannon MC, Nuttall FQ: **Control of blood glucose in type 2 diabetes without weight loss by modification of diet composition.** *Nutr Metab (Lond)* 2006, 3:16.
29. Brinkworth GD, Noakes M, Parker B, et al.: **Long-term effects of advice to consume a high-protein, low-fat diet, rather than a conventional weight-loss diet, in obese adults with type 2 diabetes: one-year follow-up of a randomised trial.** *Diabetologia* 2004, 47:1677–1686.
30. Aucott L, Poobalan A, Smith WC, et al.: **Weight loss in obese diabetic and non-diabetic individuals and long-term diabetes outcomes--a systematic review.** *Diabetes Obes Metab* 2004, 6:85–94.
31. Yu AP, Wu EQ, Birnbaum HG, et al.: **Short-term economic impact of body weight change among patients with type 2 diabetes treated with antidiabetic agents: analysis using claims, laboratory, and medical record data.** *Curr Med Res Opin* 2007, 23:2157–2169.