Why WAIT Program: A Novel Model for Diabetes Weight Management in Routine Clinical Practice

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Introduction

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The prevalence of overweight and obesity has increased rapidly among U.S. adults, and in particular, among those diagnosed with type 2 diabetes mellitus (T2DM). Data from the 1999–2002 National Health and Nutrition Examination Survey (NHANES) indicate that the prevalence of overweight and obesity among U.S. adults with diabetes now exceeds 85%. We previously demonstrated that modest weight reduction of approximately 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.[1,2]

The ongoing Look AHEAD (Action for Health in Diabetes) study is exploring the health outcomes associated with modest weight loss maintained over 10 years using an intensive lifestyle intervention (ILI) that combines decreased caloric intake, increased physical activity, and behavior modification versus standard diabetes support and education (DSE) in patients with T2DM. The Look AHEAD study group recently published their first-year results, which are encouraging.[3] They 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 to baseline, A1c improvement in the ILI group was significantly greater than that observed in the DSE group (absolute A1c reduction: −0.64% [ILI] versus −0.14% [DSE], $p < 0.001$; baseline A1c for both groups: ~7.3%). Notably, A1c lowering was

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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 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 the impressive results of such 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, and some research shows that physicians may not believe that their patients are adequately motivated to achieve weight loss. In addition, several barriers specific to the combination of diabetes and obesity make weight management for patients with diabetes even more difficult. These barriers include the weight-promoting effect of many of the currently available diabetes medications.

Over a 10-year treatment period, participants in the United Kingdom Prospective Diabetes Study gained weight, particularly patients treated with insulin. Furthermore, since insurance plans do not typically cover weight loss medications or programs, physicians often view these options as impractical and costly. Adding to these barriers in patients with diabetes is the traditional high consumption of calories from carbohydrates (currently 50%–55% of total caloric intake), the reduced capacity to exercise, and the lack of support and motivation to lose weight. Taken together, these factors may contribute to providers' inertia and skepticism about the long-term maintenance of any achievable weight loss in patients with diabetes.

The Why WAIT Program

Weight Achievement and Intensive Treatment (Why WAIT) is a 12-week multidisciplinary program for weight control and intensive diabetes management designed by the Joslin Diabetes Center for application in routine diabetes practice. The program, which is mostly covered by medical insurance, is followed by monthly support sessions aiming at long-term maintenance of weight loss.

Key aspects of the Why WAIT program include:

1. Intensive and interactive medication adjustments.
2. Structured modified dietary intervention.
3. Graded, balanced, and individualized exercise intervention.
4. Cognitive behavioral intervention.
5. Group education.

Intensive and interactive diabetes medication adjustment

From weight perspectives, antihyperglycemic medications are classified into two groups: those known to promote weight gain (Weight Fury Diabetes Medications) and those that are weight neutral or associated with weight loss or minimal weight gain (Weight Friendly Diabetes Medications; Table 1). In this program, medication regimens were adjusted to facilitate weight loss without compromising diabetes control while using more of the weight friendly diabetes medications. In patients treated with insulin and with prior good diabetes control (hemoglobin A1c < 7%), hypoglycemia is an imminent risk and an obstacle that may arise during weight loss. Such participants were advised to reduce their prandial insulin by approximately 20%–30% at the start of the program. Patterns of existing medication regimens were also adapted to maximize glycemic benefit and 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.

As appetite is frequently suppressed by pramlintide, patients usually eat much less than expected; by administering the short-acting insulin *after* the meal, the patient can calculate the dose based on what was actually consumed. This tactic minimizes both hypoglycemia risk and the consumption of unneeded calories to cover an overestimated preprandial insulin dose. However, when substituting or adjusting medications, it is essential to closely monitor glucose control. Each participant was asked to monitor blood glucose at least 4 to 6 times per day (before each meal, before and after exercise, and at bedtime) using a glucose meter with log memory. In addition, patients treated with insulin were encouraged to monitor their blood glucose 2 hours after each meal.

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 (TZDs) 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

At the beginning of each weekly session, meters were collected and downloaded. According to the weekly blood glucose pattern, medications were adjusted by a diabetes nurse practitioner and a certified diabetes educator. Close monitoring of blood glucose helped them make timely adjustments to diabetes medications as weight reduction progressed. 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 the registered dietitian (RD). 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 patients with diabetes 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.[4,5] Trans-fats were completely eliminated and saturated fat was reduced to 10% or even 7% in patients with elevated low-density lipoprotein cholesterol (> 100 mg/dL). All participants were instructed to use a nutritionally complete meal replacement for both 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 (such as 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.

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The full meal plan was consistent with Joslin guidelines and was low in glycemic index, high in fiber (approximately 30 grams) 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 asked to record food intake throughout the program.

Participants who failed to achieve 3% weight reduction by the fourth week or 5% by the eighth week were advanced to the lower caloric level. Two weeks prior to 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

Prior to 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 (EP) to construct an individualized 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 level of intensity 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 maintenance 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 the EP 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 in people with diabetes, and it does so without increasing their chances for injuries.[6] This modality of exercise has been proven to improve glucose disposal in patients with diabetes[7] and maintain bone mineral density and bone mineral content during weight loss.[8] Since 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.

Why WAIT is a 12-week multidisciplinary program for weight control and intensive diabetes management designed by Joslin Diabetes Center.

Cognitive behavioral intervention

Group behavioral support sessions were conducted weekly during the initial 12 weeks of intervention, then once monthly during follow-up. The clinical psychologist led each session. The sessions incorporated key components of cognitive-behavioral therapy for weight loss already validated in other clinical trials.[9,10] 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 by the diabetologist, EP, RD, or psychologist for the initial 12 weeks. Participants were provided with handouts for future reference. Each session covered a different topic relevant to weight management and diabetes. The sessions lasted 30 minutes.

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 the regular copayment plus a small enrollment fee to cover the additional administrative costs. Monthly support sessions were conducted at a low out-of-pocket-fee.

Why WAIT Results and Discussion

Application of this multidisciplinary intervention model in routine clinical practice resulted in a significant reduction in body weight, waist circumference, and percentage body fat. Over the first 15 months, we enrolled 5 groups of patients; a total of 62 participants (22 men/40 women) with an average age of 56.1 ± 1.4 years (mean ± standard error [SE]), diabetes duration of 7.2 ± 0.8 years, and BMI of 38.3 ± 0.69 kg/m^2. Approx-

imately 20% of participants were above the age of 70 and most of them were already receiving treatment for other comorbid chronic medical problems. After the initial 12 weeks, participants lost an average of 23.5 ± 1.2 pounds or 9.8% ± 0.4% ($p < 0.001$) of their initial body weight and 3.7 ± 0.3 inches from their waist circumference ($p < 0.001$).

Except for the first week, weight loss was steadily progressive over time and ranged from 1.2–2.5 pounds per week. Other changes in body composition are shown in Table 2. The reduction in waist circumference and waist/hip ratio suggests that fat 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 ($p < 0.001$) appears to suggest their reduction.[11,12] 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. 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.

Hemoglobin A1c decreased significantly from 7.26% ± 0.17% to 6.37% ± 0.11% ($p < 0.001$) and was found to correlate with the percentage change in BMI ($r = 0.3$, $p < 0.05$; Figure 1). Total cholesterol decreased by 12.2% ± 1.8% ($p < 0.001$), triglycerides by 21.8% ± 3.8% ($p < 0.01$), and low density lipoprotein (LDL) by 11.4% ± 3.0% ($p < 0.001$). While most clinical trials of weight loss show significant reductions in triglycerides and increases in high density lipoprotein (HDL) cholesterol, there were minimal or no changes seen in the LDL cholesterol and the non-HDL cholesterol.[1,3,13] In this intervention model, both triglycerides and LDL cholesterol decreased significantly. The significant reduction in LDL cholesterol by an additional 11.4% ± 3.0% is particularly unique to this intervention model and may be related to its distinctive dietary composition.

Reduced saturated fat and increased mono- and polyunsaturated fat and dietary fiber might also contribute to such lipid outcomes. Similar reduction in LDL was seen

Table 2. Changes in Body Composition, Metabolic Parameters, Liver, and Kidney Function after 12 Weeks of Intervention using the Why WAIT Program in Diabetes Clinical Practice

	Before	After	p
Body Composition			
Total body weight (lb)	237.5±4.8	214.3±4.5	< 0.001
BMI (Kg/m^2)	38.3±0.69	35.0±0.67	< 0.001
Percentage body fat (%)	43.23±0.91	39.95±1.04	< 0.001
Fat mass (lbs)	101.6±3.6	85.8±3.6	< 0.001
Fat free mass (lbs)	134.6±3.9	127.8±3.9	< 0.001
Lean/fat ratio	1.50±0.07	1.57±0.08	< 0.05
Waist (inches)	47.2±0.7	43.4±0.7	< 0.001
Waist/hip ratio	0.94±0.01	0.92±0.1	< 0.01
Metabolic Parameters			
HbA1c (%)	7.26±0.17	6.37±0.11	< 0.001
Systolic blood pressure (mm Hg)	128.1±1.7	122.6±1.6	< 0.001
Diastolic blood pressure (mm Hg)	75.5±0.9	72.1±1.1	< 0.001
Total cholesterol (mg/dL)	165.8±3.9	144.1±3.8	< 0.001
LDL-cholesterol (mg/dL)	100.8±3.8	86.0±3.2	< 0.001
Triglycerides (mg/dL)	138.2±8.1	99.1±5.5	< 0.001
HDL-cholesterol (mg/dL)	41.1±1.0	39.5±1.0	< 0.05
Non-HDL-cholesterol (mg/dL)	125.4±3.9	105.3±3.6	< 0.001
Total cholesterol/HDL-cholesterol ratio	4.1±0.1	3.7±0.1	< 0.001
C-reactive protein (mg/L)	6.0±0.85	4.2±0.65	< 0.01
Kidney and Liver Parameters			
Urinary albumin/creatinine ratio (µg/mg)	29.4±6.3	20.16±4.7	< 0.01
Blood urea nitrogen (mg/dL)	17.0±0.8	17.1±0.8	> 0.05
Serum creatinine (mg/dL)	0.92±0.03	0.90±0.03	> 0.05
AST (IU/L)	24.10±0.98	21.98±0.69	< 0.01
ALT (IU/L)	27.88±1.85	21.68±0.98	< 0.001

Data are presented as mean ± standard error.

LDL, low density lipoprotein; HDL, high density lipoprotein; AST, Aspartate aminotransferase; ALT, alanine transaminase.

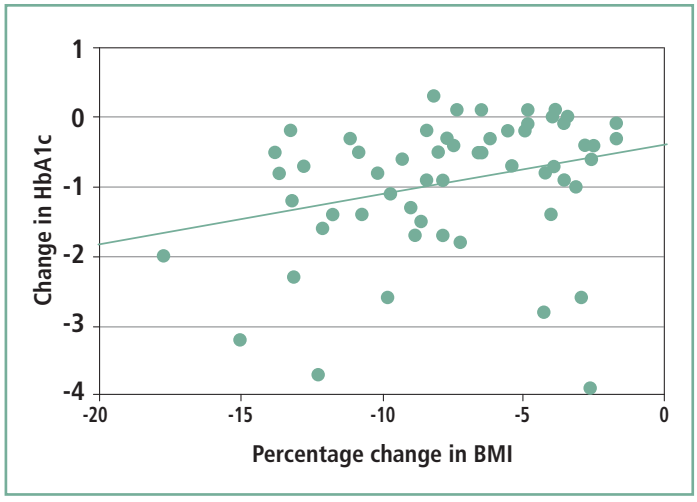

Figure 1. The relationship between the changes in HbA1c% and the percentage change in the BMI after the Why WAIT program in obese patients with type 2 diabetes.

in one trial that used a comparable dietary composition.[14] While HDL cholesterol showed minimal but significant reduction, both 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 (CRP) decreased significantly from 6.0 ± 0.85 to 4.2 ± 0.65 mg/L ($p < 0.01$) and was found to correlate with percentage weight loss ($r = 0.3$, $p < 0.05$; Figure 2). Such change in CRP serum level may indicate a possible reduction in cardiovascular risk. Other metabolic changes are shown in Table 2.

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 and/or severe microalbuminuria). Both blood-urea-nitrogen (BUN) and serum creatinine did not change with this intervention, while significant improvement in urinary albumin/creatinine ratio was noticed ($p < 0.01$; Table 2). This significant improvement was maintained after 1 year of follow-up. Such improvement may be explained by reduction of the mean blood pressure that usually accompanies weight loss. 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 (GFR), but rather, is attributable to the decrease in BMI and to the improvement of other weight-related metabolic factors.[15] The use of a formula diet has also been shown to improve kidney function in patients with diabetic nephropathy.[16]

While 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 overall reduction of 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.[17] 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 hemoglobin A1c irrespective of weight loss or the carbohydrate to fat ratio.[18] 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 type 2 diabetes.[19]

Twenty-one percent of the Why WAIT patients on short-acting insulin were able to stop it completely by the end of the program. 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 were able to stop them while the remaining participants reduced their dose by 35%–41%. Similar observations were seen with thiazolidinediones. The number of patients on metformin did not change, but the dose was slightly increased. In 13 patients who were on oral medications, exenatide was added, and in another 9 patients on prandial insulin, pramlinitide was added. The average cost saving on diabetes medications during

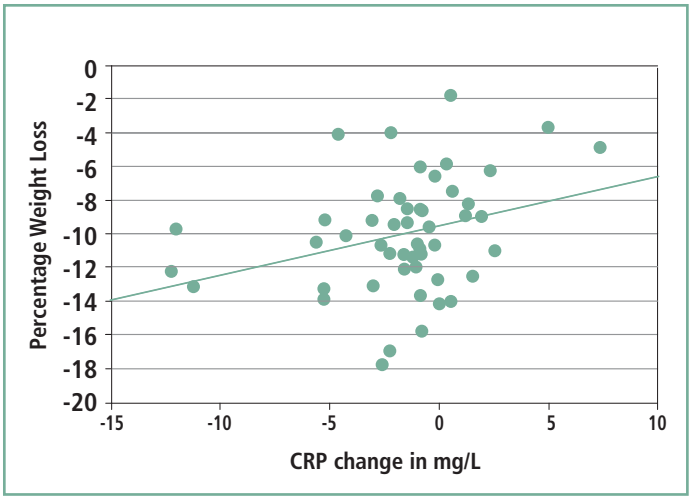

Figure 2. The relationship between the percentage weight loss and the percentage change in C-reactive protein (CRP) after the Why WAIT program in obese patients with type 2 diabetes.

Table 3. Changes in Diabetes Medications After versus Before the Why WAIT Program

Antidiabetic Medication	Before Number of patients (dose/day)	After Number of patients (dose/day)	% Change Number (dose)
Sulfonylureas			
Glyburide	6 (9.5 mg/d)	2 (6.2 mg/d)	-67% (-35%)
Glipizide	8 (11.25 mg/d)	3 (6.6 mg/d)	-63% (-41%)
Thiazolidinediones			
Pioglitazone	8 (28.1 mg/d)	1 (15 mg/d)	-88% (-47%)
Rosiglitazone	7 (7.4 mg/d)	2 (5 mg/d)	-71% (-33%)
Metformin	46 (1664.1 mg/d)	47 (1862 mg/d)	2 % (12%)
Exenatide	8 (15 µg/d)	25 (17.6 µg/d)	213% (17)
Insulin			
NPH	6 (47.5 U/d)	3 (41.7 U/d)	-50% (-12%)
Long acting Analog	10 (60.9 U/d)	13 (27.2 U/d)	30% (-55%)
Short acting Analog	14 (52.1 U/d)	11 (24.1 U/d)	-21% (-54%)
Pramlinitide	2 (45 U/d)	11 (47.3 U/d)	450% (5%)

the 12 weeks was $140.34 per patient, which is projected to be $561.37 per patient per year.

The clinical weight-loss literature shows that maintenance of weight loss remains an ongoing problem. Many clinical trials have shown an immediate rebound in body weight by the end of the intervention period. Although very few patients regained weight during the follow-up period, the majority maintained their weight loss or even lost more over the following 6 months (Figure 3). After 1 year, weight remained lower by 18.2 ± 10.6 pounds (−7.6%, $p < 0.001$). 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.[20] 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. While 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 (5:00–7:00 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. The majority of 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 of $561.37 per patient per year 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 following a 1% weight loss in patients with type 2 diabetes was $213,

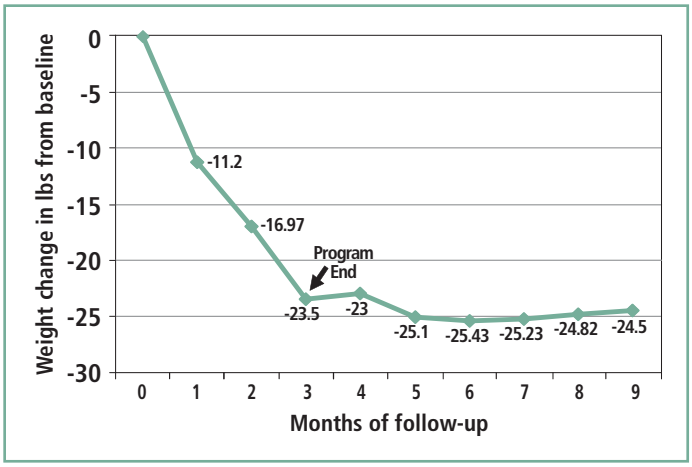

Figure 3. Follow-up of the weight loss after the end of the Why WAIT program in obese patients with type 2 diabetes.

The Why WAIT model was effective in improving key metabolic abnormalities observed in patients with diabetes.

and the diabetes-related health care cost saving was $131. These project to an annual decrease of total health care cost of approximately $1,619, with the diabetes-related cost of approximately $996 with implementation of the Why WAIT program. A1c decreased by an average 1%. Previous reports showed that approximately 1% drop of A1c leads to cost savings of $776 per patient per year. Total cholesterol decreased by 12.2% ± 1.8%, triglycerides by 21.8% ± 3.85% and LDL cholesterol by 11.4% ± 3.0%. According to the cost-effectiveness analysis of the Scandinavian Simvastatin Survival Study, this improvement in lipid profile is projected to save approximately $1,801 in direct medical cost per subject. These figures suggest that implementation of the Why WAIT program is cost effective.

Conclusion

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 (*e.g.*, 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 will contribute to both long-term health outcomes and reduced costs.

The Why WAIT model was effective in improving key metabolic abnormalities observed in patients with diabetes. The achieved weight reduction after 12 weeks of intervention was maintained for an additional 12 months. 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.

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