

# Diabetes Weight Management in Clinical Practice—The Why WAIT Model

a report by

**Osama Hamdy, MD, PhD**

*Medical Director, Joslin Obesity Clinical Program, and Clinical Investigator, Joslin Diabetes Center, Harvard Medical School*

DOI: 10.17925/USE.2008.04.2.49

Over the past 20 years, the prevalence of type 2 diabetes has increased dramatically from 30 million cases worldwide in 1988 to 239 million cases at present. The World Health Organization (WHO) declared diabetes to be “the health hazard of the 21st century.”<sup>1</sup> A historically unique combination of two phenomena—rapid aging of the population and the dramatic increase in obesity<sup>2</sup>—is the major cause of this growing epidemic of diabetes in the US. Currently, most patients with type 2 diabetes are overweight, obese, or severely obese. Data from the 1999–2002 National Health and Nutrition Examination Survey (NHANES)<sup>3</sup> 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 patients with diabetes even more difficult. These barriers include the weight-promoting effect of many of the currently available diabetes medications including insulin, sulfonylurea, glinides, and thiozolidenidiones. Although it has not been systematically studied, many clinicians have raised the concern that weight gain associated with diabetes medications may wipe out the metabolic benefits of these medications over time. Over a 10-year treatment period, participants in the UK Prospective Diabetes Study (UKPDS) gained a significant amount of weight, particularly those treated with insulin.<sup>4</sup> Similarly, patients with type 2 diabetes treated with intensive insulin therapy gained on average 8.7kg over a six-month period.<sup>5</sup> Patients frequently find it confusing when their treating physicians are advising them to lose weight while prescribing them medications that promote weight gain.

Furthermore, as most medical insurance companies 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, ingesting a higher percentage of calories from carbohydrates (currently 50–55% of total caloric intake) in a disease that is still defined as a carbohydrate intolerance problem is the traditional recommendation. Taken together, these factors may contribute to the inertia and skepticism of providers about the long-term maintenance of any achievable weight loss in patients with diabetes.

We previously demonstrated that modest weight reduction of approximately 7% over a six-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.<sup>6,7</sup> The ongoing Look AHEAD (Action for Health in Diabetes) study is also exploring the health outcomes associated with modest weight loss maintained over 10 years following 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 type 2 diabetes. The Look AHEAD study group recently published their first-year results, which are encouraging.<sup>8</sup> The study found that participants randomized to ILI lost an average of 8.6% of their initial bodyweight compared with 0.7% in the DSE group. Although both groups experienced blood glucose reductions compared with baseline, HbA<sub>1c</sub> improvement in the ILI group was significantly greater than that observed in the DSE group (absolute HbA<sub>1c</sub> reduction: -0.64% [ILI] versus -0.14% [DSE];  $p < 0.001$ ; baseline HbA<sub>1c</sub> for both groups: ~7.3%). Notably, glycosylated hemoglobin (HbA<sub>1c</sub>) lowering was observed in the context of decreased glucose-lowering medication use in the ILI group and increased medication use in the DSE group. Therefore, the available data indicate that short-term weight loss of 7–10% in patients with diabetes is metabolically beneficial. More substantial weight loss (23.4% at two years and 16.1% at 10 years) has recently been reported post-operatively in severely obese patients treated with bariatric surgery; this was associated with diabetes remission in 72% of patients at two 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 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.<sup>9,10</sup>

## The Why WAIT Program

Weight Achievement and Intensive Treatment (WAIT) 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.



Osama Hamdy, MD, PhD, is Medical Director of the Joslin Obesity Clinical Program, a Clinical Investigator and a Staff Endocrinologist at the Joslin Diabetes Center, and an Assistant Professor of Medicine at Harvard Medical School. His research focuses on the effects of lifestyle modification on cardiovascular risk factors in obese individuals with or without type 2 diabetes. His research contributed to the discovery of the contribution of obesity to insulin resistance, atherosclerosis, inflammation, coagulation, and coronary artery disease in obese patients with type 2 diabetes. Dr Hamdy is studying the long-term effects of sustained weight loss on cardiovascular health, distribution of body fat, and circulating adipokines.

E: Osama.Hamdy@joslin.harvard.edu

**Table 1: Weight-specific Effects of Available Classes of Diabetes Medication**

Diabetes Medications Associated with Weight Gain (Weight Fury)	Diabetes Medications Associated with Weight Loss or Weight-neutral (Weight-friendly)
Sulfonylureas Glyburide, glipizide, glimepiride: ~4.4lb weight gain	Metformin Weight-neutral or up to ~6.6lb weight loss
Glinides Nateglinide: 0.7–2.0lb weight gain; repaglinide: ~2.2–6.6lb weight gain	Amylin analog Pramlintide: ~3.3lb weight loss
Thiazolidinediones Pioglitazone, rosiglitazone: ~2.2–6.6lb weight gain	Glucagon-like peptide-1 receptor agonist Exenatide: short-term: ~3.3lb weight loss; long-term: ~8.8lb weight loss
	Dipeptidyl peptidase-4 inhibitor Sitagliptin: weight-neutral

### Intensive and Interactive Diabetes Medication Adjustments

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 that are weight-neutral or associated with minimal weight gain (weight-friendly diabetes medications) (see 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 others that promote weight gain. In patients treated with insulin and with prior good diabetes control ( $HbA_{1c} < 7\%$ ), hypoglycemia is an immanent risk that may aggravate hunger and consequently slow weight reduction. Such participants were advised to reduce their prandial insulin by ~20–30% 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. As 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, not on what they presumed to eat. This tactic minimized both hypoglycemic risk and the consumption of unneeded calories to cover pre-planned prandial insulin. When post-prandial short-acting insulin was preferred, we used glulisine insulin for its quicker onset of action.<sup>11</sup> Despite the controversy, glargine insulin and neutral protamine Hagedorn (NPH) insulin were frequently changed to detemir insulin for its weight advantage.<sup>12,13</sup> Regarding oral medications, both metformin and sitagliptin were preferred for their weight neutrality. Metformin dose was frequently increased. On the other hand, sulfonylureas, glinides, and thiazolidinediones were reduced or eliminated. Exenatide was frequently added to oral medications for its weight benefit; pramlintide was frequently added to mealtime 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/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 two hours after each meal.

The meters were downloaded at the beginning of each weekly session. Diabetes medications were adjusted by a diabetes nurse practitioner and a certified diabetes educator according to the weekly blood glucose pattern. 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 for hypoglycemia that might prevent further weight loss. Patients were also medically evaluated for 30 minutes at weeks four and eight by a nurse practitioner and at week 12 by a diabetologist.

### Structured Modified Dietary Intervention

All participants received dietary evaluation by 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 comply with 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 1,200, 1,500, or 1,800 calorie level. With few exceptions, most men started on an 1,800-calorie diet plan and most women on a 1,500-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 130gm per day, 30% from protein (to minimize lean-mass loss during weight reduction), and the remaining 30% from fat.<sup>14,15</sup> Trans-fats were entirely eliminated and saturated fat was reduced to 10% in general, and to 7% in patients with elevated low-density lipoprotein cholesterol (LDL) ( $>100\text{mg/dl}$ ). 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 Medical Nutrition, Inc., Minneapolis). Participants were encouraged to eat two snacks between meals. A list of six choices of 100- 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 1,200-, 1,500-, and 1,800-calorie meal plans. The full meal plan was consistent with Joslin Nutrition Guidelines, had a low glycemic index, and was high in fiber (~30g), particularly from fresh fruits and vegetables, and low in sodium ( $<800\text{mg}$ ). 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 fourth week or 5% by the eighth week were advanced to the lower caloric level (e.g. 1,800–1,500 or 1,500–1,200). This approach was rarely used as most patients achieved targets in that time-frame. 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 follow 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.

#### **Graded, Balanced, and Individualized Exercise Plan**

Prior to starting the exercise plan, an evaluation of exercise capacity, an ophthalmological examination, an electrocardiogram, and, in most cases, an exercise stress test were conducted. Participants met individually with an exercise physiologist (EP) to construct an individualized exercise plan responsive to their lifestyles. The exercise plan was based on each participant's health status and exercise capacity. As 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 for injury. The exercise plan included a weekly 60-minute exercise session under the supervision of 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) four days/week to 60 minutes six days/week. On completion of the initial 12 weeks, they were instructed to continue to exercise independently for 60 minutes/day, six days/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 of injuries.<sup>16</sup> This modality of exercise has been proved to improve glucose disposal in patients with diabetes<sup>17</sup> and maintain bone mineral density and content during weight loss.<sup>18</sup> As 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 the main components of cognitive-behavioral therapy for weight loss already validated in other clinical trials.<sup>19,20</sup> 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.

#### **Adult Group Education**

Group didactic sessions were conducted each week for 30 minutes by diabetologist, an EP, an RD, or psychologists during the initial 12 weeks.

Participants were provided with hand-outs 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 co-payments. Out-of-pocket expenses were limited to the \$100 enrollment fee to cover the additional administrative costs plus the regular co-payment at each of the initial 12 visits.

#### **Support Session**

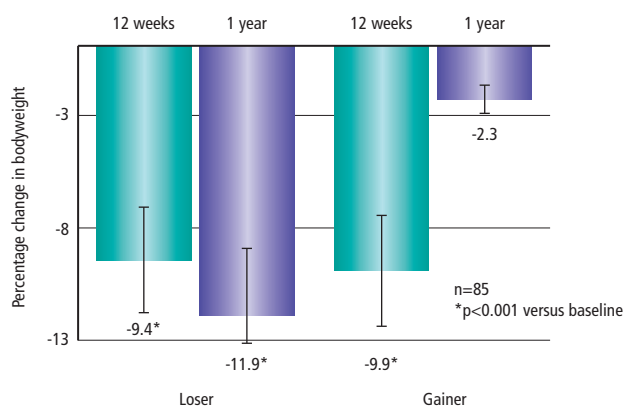
Upon completion of the program, participants were advised to come each month for a one-hour group support session. As attendance was unexpectedly poor in the first year, we switched the support program to one-on-one. Participants were advised to continue their follow-up with one provider of the intervention team on a monthly basis. In this support model, participants who needed ongoing support in one particular component of this multidisciplinary approach was 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 10–15 participants. Application of this multidisciplinary intervention model in routine clinical practice resulted in a significant reduction in bodyweight and waist circumference. Eighty-five participants with mean age of 54.2.8±1.2 years (mean standard error [SE], approximately 20% above 70 years of age), diabetes duration of 9.8±1.1 years, weight of 237.7±4.6lb, body mass index (BMI) of 38.4±0.6kg/m<sup>2</sup>, HbA<sub>1c</sub> of 7.5±0.14%, and waist circumference of 46.7±0.6 inches were followed for an average duration of 357 days.

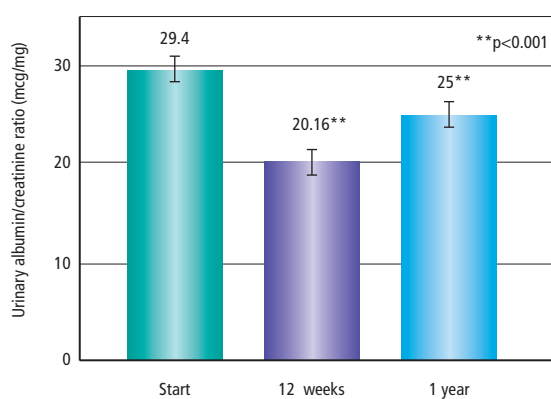
After 12 weeks, they were able to reduce their initial weight by an average of 24.6±1.2lb (-10.3%;  $p<0.001$ ), and their waist by 3.6±0.24 inches ( $p<0.001$ ). Except for the first week, weight loss was steadily progressive over time and ranged from 1.2 to 2.5lb/week. The reduction in waist circumference was associated with a significant reduction in the waist-hip ratio (0.932±0.01–0.916±0.01;  $p<0.001$ ), indicating that weight loss was predominantly from the central area. Although we did not quantify visceral or intra-hepatic fat in this cohort, the significant reduction in liver transaminases at 12 weeks ( $p<0.001$ ) appears to suggest their reduction.<sup>21,22</sup> After approximately one year, weight remained lower by 18.2±2.2lb (-7.6±0.9%;  $p<0.001$ ) from baseline. Fifty-five percent of participants continued to lose weight or gained fewer than 5lb from the end of the initial 12 weeks. The remaining 45% regained >5lb, but their one-year weight remained lower than baseline by -2% (see *Figure 1*). Due to 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.

**Figure 1: Change in Bodyweight After 12 Weeks and One Year of the Why WAIT Program in Patients with Diabetes**



Losers refer to those who continue to lose weight or who gained <5lb from the end of the initial 12 weeks. Gainers refer to those who regained >5lb after the initial 12 weeks.

**Figure 2: Change in Urinary Albumin/Creatinine Ratio After 12 Weeks and One Year of the Why WAIT Program in Patients with Diabetes**



HbA<sub>1c</sub> decreased significantly from 7.5±0.14 to 6.6±0.12% (p<0.001). At 12 weeks, 82.3% achieved the target HbA<sub>1c</sub> of <7% and 69.4% were able to reduce their HbA<sub>1c</sub> to <6.5%. Reduction in HbA<sub>1c</sub> 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<sub>1c</sub>. Systolic blood pressure (BP) was reduced significantly at both 12 weeks and one year from a baseline of 128.1±1.7mmHg (-5.5±1.7mmHg; p<0.01, -5.5±1.8mmHg; p<0.01, respectively). Similarly, diastolic BP reduced significantly from a baseline of 75.5±0.8 mmHg (-3.3±1.1mmHg; p<0.01, -3.4±0.9 mmHg; p<0.001, respectively).

The lipid profile improved significantly at 12 weeks (total cholesterol by -10.8±1.5% from a baseline of 166.9±3.4mg/dl; p<0.001, triglycerides by -18.2±3.8% from a baseline of 130.1±7.1mg/dl; p<0.001, LDL by -9.6±2.4% from a baseline of 101.2±3.3mg/dl; p<0.001), but were mostly back to baseline at one year except high-density lipoprotein (HDL), which was significantly higher than the baseline of 42.8±1mg/dl (+9.5±3.4%; p<0.01). While most clinical trials of weight loss showed significant reductions in triglycerides and increases in HDL cholesterol, there were minimal or no changes seen in the LDL cholesterol and the non-HDL cholesterol.<sup>6,8,23</sup> In this intervention model, both 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 the use of meal replacements with controlled fat content. Reduced saturated fat and increased mono- and polyunsaturated fat and dietary fiber may also contribute to such lipid outcomes. A similar reduction in LDL was seen in one trial that used a comparable dietary composition.<sup>24</sup>

While HDL cholesterol showed minimal but significant reduction at 12 weeks (-3.6±1.5%; p<0.01), 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 at 12 weeks from an average of 6.0±0.85 to 4.2±0.65mg/l (p<0.01), and was found to correlate with percentage weight loss (r=0.3; p<0.05). Such changes in the CRP serum level may indicate a possible reduction in cardiovascular risk.

Due to the higher percentage of calories from protein in the Why WAIT meal plan, we excluded patients with renal impairment (serum creatinine >1.5mg/dl and/or severe microalbuminuria). Both blood urea nitrogen (BUN) and serum creatinine did not change with this intervention, while a significant improvement in urinary albumin/creatinine ratio was noticed at 12 weeks (p<0.01). This significant improvement was maintained after one year of follow-up (see Figure 2). Such improvement may be explained by a reduction of the mean BP. 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.<sup>25</sup> The use of a formula diet has also been shown to improve kidney function in patients with diabetic nephropathy.<sup>26</sup>

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 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.<sup>27</sup> Meanwhile, increasing the percentage of calories from protein to 30% was associated with a significant decrease in the 24-hour integrated glucose area and percentage HbA<sub>1c</sub> irrespective of weight loss or the carbohydrate-to-fat ratio.<sup>28</sup> In a one-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.<sup>29</sup>

Significant changes in diabetes medications were also seen in response to weight reduction in the Why WAIT program (see Table 2). 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 the remaining patients on insulin therapy, the daily dose of long-acting analog insulins was reduced by an average of 55% and of short-acting analog 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 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/ patient, which is projected to be \$561.37/patient/year. A systematic review of 11 long-term studies with a follow-up of more than two years showed that mortality risk was reduced by 25% in patients with diabetes who intentionally lost a significant amount of weight.<sup>30</sup> It is important to observe this cohort for a much longer duration before drawing such a conclusion, and to try to determine which factors are specifically associated with long-term positive results.

Compliance with the Why WAIT program was high. The attendance of patients 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 (5–7pm) might have improved compliance as it would not have conflicted with the working schedules of participants. 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 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 one-year total healthcare cost saving following a 1% weight loss in patients with type 2 diabetes was \$213, and the diabetes-related healthcare cost saving was \$131.<sup>31</sup> These numbers project to an annual decrease in total healthcare cost of ~\$1,619, with a diabetes-related cost of ~\$996 with implementation of the Why WAIT Program. HbA<sub>1c</sub> decreased by an average of 1%. Previous reports showed that a ~1% drop of HbA<sub>1c</sub> leads to cost savings of \$776/patient/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 as most institutions do not 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:

- 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 of carbohydrates to 40% and increasing percentage of protein to 30%;
- use of meal replacement with controlled diet composition;
- increase percentage of resistance exercise and gradual increase of exercise duration;

**Table 2: 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)
<b>Sulfonylureas</b>			
Glyburide	6 (9.5mg/d)	2 (6.2mg/d)	-67 (-35%)
Glipizide	8 (11.25mg/d)	3 (6.6mg/d)	-63 (-41%)
<b>Thiazolidinediones</b>			
Pioglitazone	8 (28.1mg/d)	1 (15mg/d)	-88 (-47%)
Rosiglitazone	7 (7.4mg/d)	2 (5mg/d)	-71 (-33%)
Metformin	46 (1,664.1mg/d)	47 (1,862mg/d)	2 (12%)
Exenatide	8 (15mcg/d)	25 (17.6mcg/d)	213 (17%)
<b>Insulin</b>			
NPH	6 (47.5 unit/day)	3 (41.7 unit/day)	-50 (-12%)
Long-acting analog	10 (60.9 unit/d)	13 (27.2 unit/day)	30 (-55%)
Short-acting analog	14 (52.1 unit/d)	11 (24.1 unit/day)	-21 (-54%)
Pramlintide	2 (45 unit/d)	11 (47.3 unit/d)	450 (5%)

NPH = neutral protamine Hagedorn.

**Table 3: Comparison Between Two Models of Diabetes Management**

	Classic Model (Targeting HbA <sub>1c</sub> )	Alternative Model (Targeting High Bodyweight)
Medications	Increase over time	Possible reduction or stoppage
Cost	Long-term increases	Long-term decreases
Weight	Mostly increases	Decreases or stationary
HbA <sub>1c</sub>	May temporally decrease Target may be achieved	Frequently decrease More patients on target
Cardiovascular risk	May decrease (currently questionable?)	Possibly decreases (improved lipids, lowered blood pressure, decreased C-reactive protein, increased adiponectin)
Quality of life	Less than optimal	Improves

HbA<sub>1c</sub> = glycated hemoglobin.

- availability of a gymnasium in the intervention facility;
- use of several motivational tools throughout the process of weight loss;
- structured design of intervention with limited options; and
- conducting the program in group sessions and between 5 and 7pm.

It remains a challenge to simplify the Why WAIT intervention model for application in primary care practice, where time and resources are traditionally limited. Development of useful written or recorded material that can be handed to patients plus 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 exercise facilities may be another option. The collaborative effort of academic institutions, governmental agencies, and the insurance and pharmaceutical industries is needed to stem the progression of the epidemic of obesity and diabetes problems in the US.

Based on the Why WAIT program results and the early results of the Look AHEAD study, we propose that targeting bodyweight as the prime tool to control diabetes may evolve in the future as a valid alternative model to targeting HbA<sub>1c</sub> in today's diabetes practice. A comparison of the classic model of targeting HbA<sub>1c</sub> versus the alternative model of targeting bodyweight is summarized in Table 3. In this suggested model, providers will focus on helping their patients with diabetes to lose weight in many



ways. This may be achieved through changing diabetes medication 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 over time, providers may tighten these measures, add anti-obesity medications, or even refer some patients for bariatric surgeries. Considering that obesity is a major root cause of type 2 diabetes, any weight loss achievement may improve diabetes control better than the current method of increasing medication dosing or adding more medications over time.

## Conclusion

Multidisciplinary weight management approaches are emerging as viable and potentially cost-effective solutions to overweight and obesity management in type 2 diabetes. Applying weight loss as a type 2 diabetes treatment can delay or reduce the need for medications, reduce cardiovascular risk, and improve quality of life. When resources are limited, important 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 type 2 diabetes; any weight loss achieved may contribute to both long-term health outcomes and reduced costs.

The Why WAIT model was effective in improving main metabolic abnormalities observed in patients with diabetes. The achieved weight

reduction after 12 weeks of intervention was maintained for an additional one 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, and the insurance and pharmaceutical industries in order to halt the progression of the epidemic of obesity and diabetes problems in the US. ■

## Acknowledgments

The author would like to recognize the extraordinary effort of the Why WAIT team, who conceived and implemented this intervention model: Cathy Carver, NP, CDE; Gillian Arathuzik, RD, CDE; Jacqueline Shahar, RCEP, CDE; Ann Goebel-Fabbri, PhD; Joan Beaton; Stacey O'Donnell, RN, CDE; Voula Mentzelopoulos, MD; Amanda Kirpitch, RD, CDE; Michael See, EP; John Zrebiec, PhD; Pamela Needle, RN, CDE; Amr Morsi, MD; and Ahmed El-Shebiny. The author also acknowledges the support of Martin Abrahamson, MD, and Ranch C Kimball and the rest of the Joslin Clinic providers and supporting staff.

## Disclaimer

Dr Hamdy is on the speaker's bureau for Amylin Pharmaceuticals, Inc., Eli Lilly and Company, Merck & Co, Inc., Novo Nordisk A/S, sanofi-aventis, and Takeda Pharmaceuticals North America, Inc. This work is not funded by any outside sources; however, the Why WAIT program received non-restricted grant contribution from Nestlé Medical Nutrition.

- King H, Aubert RE, Herman WH, Global burden of diabetes, 1995–2025: prevalence, numerical estimates, and projections, *Diabetes Care*, 1998;21(9):1414–31.
- Flegal KM, Carroll MD, Ogden CL, Johnson CL, Prevalence and trends in obesity among US adults, 1999–2000, *JAMA*, 2002; 288:1723–7.
- 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(1):35–9.
- 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(21):2005–12.
- 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(1):21–31.
- 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(7):2119–25.
- Monzillo LU, Hamdy O, Horton ES, et al., Effect of lifestyle modification on adipokine levels in obese subjects with insulin resistance, *Obes Res Sep*, 2003;11(9):1048–54.
- 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(6):1374–83.
- Price JH, Desmond SM, Krol RA, et al., Family practice physicians' beliefs, attitudes, and practices regarding obesity, *Am J Prev Med*, 1987;3(6):339–45.
- Hill JO, Wyatt H, Outpatient management of obesity: a primary care perspective, *Obes Res*, 2002;10(Suppl. 2):1245–1305.
- Becker RH, Frick AD, Clinical pharmacokinetics and pharmacodynamics of insulin glulisine, *Clin Pharmacokinet*, 2008;47(1):7–20.
- Dornhorst A, Lüddecke HJ, Sreenan S, et al., PREDICTIVE Study Group, 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(4): 659–65
- 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(3):408–16.
- 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(5):405–8.
- Campbell A, Tackling 'diabesity' head-on. Joslin Diabetes Center's new nutrition guideline, *Diabetes Self Manag*, 2005;22(6):40, 42–44.
- 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(3):284–9.
- 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(11):2977–82.
- 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(12):1703–12.
- 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(6):393–403.
- Wadden TA, Osei S, The treatment of obesity: An overview. In: Wadden TA, Stunkard AJ (eds), *Handbook of Obesity Treatment*, New York, New York: Guilford Press, 2002:229–48.
- 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(3):413–19.
- 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(10):1278–86.
- Hsieh CJ, Wang PW, Effectiveness of weight loss in the elderly with type 2 diabetes mellitus, *J Endocrinol Invest*, 2005;28(11): 973–7.
- 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(3):425–30.
- 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):S213–217.
- 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(9):1115–20.
- 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(11): 1170–77.
- 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.
- 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(10):1677–86.
- Accott 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(2): 85–94.
- 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(9):2157–69.