Improvement and Emergence of Insulin Restriction in Women With Type 1 Diabetes

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OBJECTIVE—To determine the distinguishing characteristics of women who report stopping insulin restriction at 11 years of follow-up from those continuing to endorse insulin restriction as well as those characteristics differing in patients who continue to use insulin appropriately from new insulin restrictors.

RESEARCH DESIGN AND METHODS—This is an 11-year follow-up study of 207 women with type 1 diabetes. Insulin restriction, diabetes self-care behaviors, diabetes-specific distress, and psychiatric and eating disorder symptoms were assessed using self-report surveys.

RESULTS—Of the original sample, 57% participated in the follow-up study. Mean age was 44 ± 12 years, diabetes duration was 28 ± 11 years, and A1C was 7.9 ± 1.3%. At follow-up, 20 of 60 baseline insulin restrictors had stopped restriction. Women who stopped reported improved diabetes self-care and distress, fewer problems with diabetes self-management, and lower levels of psychologic distress and eating disorder symptoms. Logistic regression indicated that lower levels of fear of weight gain with improved blood glucose and fewer problems with diabetes self-management predicted stopping restriction. At follow-up, 34 women (23%) reported new restriction, and a larger proportion of new insulin restrictors, relative to nonrestrictors, endorsed fear of weight gain with improved blood glucose.

CONCLUSIONS—Findings indicate that fear of weight gain associated with improved blood glucose and problems with diabetes self-care are core issues related to both the emergence and resolution of insulin restriction. Greater attention to these concerns may help treatment teams to better meet the unique treatment needs of women struggling with insulin restriction.

Diabetes Care 34:545–550, 2011

Restriction of insulin is a problem unique to type 1 diabetes: the patient intentionally takes less insulin than prescribed, which induces hyperglycemia, usually aimed at calorie purging and weight loss. Insulin restriction places patients with type 1 diabetes at increased risk for diabetic ketoacidosis and earlier onset and higher rates of long-term medical complications of diabetes, such as retinopathy, nephropathy, and neuropathy, as well as increased risk of mortality (1–4).

To date, only two published reports have examined the course of insulin restriction and associated eating disturbances by attempting to identify risk factors for both the development and worsening of these problems (5,6). These reports on the same cohort suggest that disturbed eating behaviors become more prevalent and increase in symptom severity into young adulthood; however, only three participants in their sample (2% of the total group) reported insulin restriction.

We conducted a follow-up assessment of a cohort of 207 women with type 1 diabetes, aged 13–60 at baseline, who were originally assessed 11 years earlier. Insulin restriction was reported by 31% of women assessed in the original cohort and was associated with poorer diabetes self-care, heightened diabetes-specific distress, as well as psychologic distress, fear of hypoglycemia, and fear that improved glycemic control would result in weight gain (7). Insulin restriction was associated with a threefold increased risk of death during the 11-year follow-up (3). To better understand the natural course of insulin restriction in women with type 1 diabetes, as it resolves and emerges, we sought to identify the clinical characteristics that changed in those women who reported no longer engaging in insulin restriction at follow-up and also in those women who reported restricting insulin for the first time at follow-up.

RESEARCH DESIGN AND METHODS

Study design

The study protocol was approved by the Committee on Human Studies before participants were contacted at both assessment times. Participants provided written informed consent.

Baseline inclusion criteria for study participation were female sex, diagnosis of type 1 diabetes for at least 1 year, aged between 13 and 60 years, not currently pregnant, and no severe visual impairment. Participants were attending routine diabetes clinic appointments at the time of their baseline assessments.

For the follow-up study, we sent each participant from the original study a letter explaining the project and later contacted her by telephone to describe the project in detail and answer questions. We made several attempts to locate original participants who were lost to follow-up. Clinic records were searched for possible contact information, and we attempted to mail information to all addresses and emergency contacts when listed. We also searched the National Death Index to identify and confirm participants who died during the follow-up period. Finally, we used Internet search engines and a private search agency to help locate participants' most up-to-date addresses.

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Received 10 August 2010 and accepted 17 December 2010.
DOI: 10.2337/dc10-1547

Participants

The original participant sample consisted of 390 women with type 1 diabetes. Of these, 26 were known to have died, 49 declined to enroll in the follow-up study, and 108 were lost to follow-up. Thus, the follow-up sample consisted of 207 women, which represents 57% of the living cohort. All subsequently described data analyses refer to the current study cohort of 207 women, unless described otherwise. At follow-up, mean age was 44 ± 12 years and mean diabetes duration was 28 ± 11 years. Mean BMI was 25 ± 5 kg/m^2, and mean A1C was 7.9 ± 1.3%.

Women who participated in the follow-up study and those who declined participation or who were lost to follow-up did not differ with respect to insulin restriction status, age, diabetes duration, A1C, BMI, diabetes complications, or any of the survey measures administered at baseline. Baseline characteristics of participants who died are described elsewhere (3).

Demographic and clinical information

We gathered demographic and clinical information by record abstraction at baseline, including age, diabetes duration, BMI, and presence of diabetes complications. Baseline laboratory data used HbA_1 assays rather than the current A1C standard. All HbA_1 laboratory results were converted to A1C using a formula developed through comparative testing on paired samples: A1C = (HbA_1 − 0.19)/1.21 (8).

At follow-up, we completed record abstractions on participants who were still receiving their care at the clinic. Those no longer being treated at the clinic received a brief record review form to be completed by their health care team. Data gathered using both methods included the most recent A1C and BMI assessments and the presence of diabetes complications.

Psychosocial assessment

We used responses to the screening statement, "I take less insulin than I should," to determine insulin restriction status in this cohort. Responses were on a 6-point Likert scale ranging from "never," "rarely," "sometimes," "often," "usually," to "always." We decided on the following definition of insulin restriction, because we believed that social desirability pressures could influence women to underreport insulin restriction as a symptom, particularly as part of research being done in a specialty diabetes center. This decision is described further in a prior article (3). We used their responses at baseline to categorize women as insulin restrictors if they reported any form of restriction from, "rarely" to "always." They were categorized as appropriate insulin users if they endorsed "never." We used a similar approach to classify participants into four categories according to their responses to the same screening question at follow-up:

Those who did not endorse insulin restriction at baseline and continued not to endorse insulin restriction at follow-up were categorized as "never restricted."

Those who did not endorse insulin restriction at baseline but did endorse insulin restriction at follow-up were categorized as "new insulin restriction."

Those who endorsed insulin restriction at baseline and continued to endorse insulin restriction at follow-up were categorized as "continued insulin restriction."

Those who endorsed insulin restriction at baseline but no longer endorsed insulin restriction at follow-up were categorized as "stopped insulin restriction."

Participants completed the same battery of psychosocial surveys at baseline and follow-up; however, they completed a revised version of the Self-Care Inventory (SCI-R) at follow-up. For all surveys described subsequently, higher scores indicate higher levels of the variable being measured.

The SCI-R (9,10) measures self-reported frequency of adherence to diabetes self-care tasks, including blood glucose monitoring frequency and insulin administration.

The Problem Areas in Diabetes (PAID) survey (11,12) is a 20-item Problem questionnaire that assesses a broad range of feelings related to living with diabetes.

The Hypoglycemia Fear Survey–Worry Subscale (13) is a 17-item questionnaire that assesses level of worry about hypoglycemia.

The Brief Symptom Inventory (BSI) (14) is a 53-item questionnaire that measures psychiatric symptoms. Here, we examined scores on the depression and anxiety subscales as well as the global severity index.

Bulimia Test-Revised (15) is a 36-item questionnaire to measure attitudes and behaviors central to eating disorders, such as weight and shape preoccupation, fear of weight gain, restrictive eating, binge eating, and purging behaviors. This measure has been used in previous diabetes research (16).

We measured self-reported diabetes-specific eating and weight concerns on a 5-point and 6-point Likert scale survey created specifically for the original project. Participants rated how much their weight or body shape influenced how they felt about themselves as people ("not at all influenced," "slightly influenced," "somewhat influenced," "moderately influenced," "very much influenced"). Attitudes toward diabetes treatment and its relationship to weight were assessed using answers to two statements: "I am afraid that getting my blood sugars in good control will cause me to gain weight" ("never," "rarely," "sometimes," "often," "usually," "always," for some analyses "never" was coded as "no" and "rarely" through "always" were coded as "yes"). "Taking insulin makes me gain weight" ("no" or "yes"). This survey also included four items evaluating problems with diabetes self-management, such as poor blood glucose control, not monitoring blood glucose frequently, not taking medications at the recommend times, and not following nutrition or exercise recommendations.

Statistical analyses

Data are presented as means ± SDs for continuous variables and percentages for categoric variables. We used Wilcoxon two-sample rank sum tests to compare differences in means. The χ^2 and Fisher exact tests were used to compare proportions in categoric variables between *1*) women who continued to report insulin restriction and those who stopped insulin restriction at follow-up and 2) women who never reported insulin restriction and those with new insulin restriction at follow-up. Paired *t* tests were used to compare mean differences in change scores within the four groups described previously. Because of multiple analyses, we used a conservative *P* value of < 0.01 to indicate statistical significance and *P* values between 0.01 and 0.05 to indicate statistical trends for group comparisons. Finally, we used logistic regression analyses to predict insulin restriction status at follow-up. Statistical analyses were performed using SAS 9.2 software (SAS Institute, Cary, NC).

RESULTS—A total of 60 women endorsed insulin restriction at baseline; of these, 40 continued insulin restriction at

follow-up, and 20 stopped insulin restriction. Of those women who continued insulin restriction at follow-up, 55% reported doing so "sometimes," "often," or "usually." At baseline, 147 women reported appropriate insulin use, and at follow-up, 113 continued to report appropriate insulin use; however, 34 women endorsed new insulin restriction, of whom 53% reported the behavior occurred "sometimes" or "often."

Distinguishing characteristics of women who no longer reported insulin restriction

Table 1 reports comparisons between women who continued to endorse insulin restriction and those who stopped insulin restriction at follow-up. The groups did not differ at baseline. At follow-up, however, women who no longer endorsed insulin restriction reported less diabetes-specific distress ($P < 0.01$), fewer problems with diabetes self-management ($P < 0.001$), higher levels of diabetes self-care ($P < 0.01$), lower levels of overall psychologic distress ($P < 0.01$), and lower levels of eating disorder symptoms ($P < 0.01$). Women who stopped insulin restriction did not differ from women who continued to restrict with regard to the number who reported commercial weight loss attempts in their lifetimes (35 vs. 33%, $P = 0.85$). However, the two groups did differ in diabetes and weight-related attitudes. Specifically, relative to women who continued insulin restriction, a smaller percentage of those who stopped restricting endorsed the statement that they were "afraid that getting my blood sugars in good control will cause me to gain weight" (55 vs. 82%, $P < 0.01$). Women who stopped insulin restriction were also less likely to agree with the statement, "taking insulin makes me gain weight" (20 vs. 58%, $P < 0.01$).

Prescribed diabetes management plans did not differ between groups. Both reported an average of two prescribed insulin injections per day at baseline and an average of three at follow-up. Those women who stopped insulin restriction reported an average of four diabetes medical appointments per year at baseline compared with six at baseline in the other group, but this was not statistically significant. The two groups also did not differ on this variable at follow-up, with a respective average of 4.8 and four diabetes medical appointments per year at follow-up. No additional differences were found between diabetes treatment plans at follow-up: 27% reported insulin pump use, 58% reported using carbohydrate counting, and 28% reported using the exchange method for meal planning. No differences were noted in the reported average number of mild hypoglycemic events in the past month, with 6.7 reported by those who stopped insulin restriction and 7.1 reported by those who continued to restrict. At baseline and follow-up, the two groups did not have different rates of women reporting one or more diabetes complications (47% at baseline and 63% at follow-up).

Within-group analyses of women who stopped insulin restriction showed that they also reported improvements in diabetes self-care ($P < 0.01$), diabetes-specific distress ($P < 0.001$), and problems with diabetes self-management ($P < 0.001$) at follow-up. Within-group analyses of continued insulin restrictors also showed lower average A1C ($P < 0.01$); however, their average BMI increased by 2.3 points ($P < 0.001$), whereas the average BMI of women who stopped restricting insulin remained stable at follow-up. Between-group analyses showed that problems with diabetes self-management improved more among those who stopped insulin restriction than those who continued (−0.9 vs. 0.2, $P < 0.001$).

After we controlled for age and follow-up BMI in a logistic regression model, fewer problems with diabetes self-management reported at follow-up (odds ratio [OR] 0.59 for each 10-point increase, $P < 0.03$) and less fear of weight gain associated with healthier blood glucose ranges reported at follow-up (OR 0.4, $P < 0.02$) predicted stopping insulin restriction. The overall model was 86% concordant.

Distinguishing characteristics of women newly reporting insulin restriction

Table 2 summarizes comparisons between women who never endorsed insulin restriction and those who reported new insulin restriction. These two groups did not differ at baseline. At follow-up,

Table 1—*Characteristics of women who continue to endorse insulin restriction and those who stopped insulin restriction at follow-up*

	Continued insulin restriction (n = 40)			Stopped insulin restriction (n = 20)		
Characteristic	Baseline	Follow-up	Mean change	Baseline	Follow-up*	Mean change
Diabetes duration (years)	29.9 ± 8.9	—	—	28.9 ± 10.1	—	—
Age (years)	30.0 ± 9	—	—	32.5 ± 12.8	—	—
Married	54	63	—	54	65	—
A1C (%)	9.2 ± 1.7	8.3 ± 1.0	−0.9†	9.4 ± 2.2	7.9 ± 1.2	−1.5‡
Years of education	14.8 ± 2	15.4 ± 1.6		14 ± 2	14.5 ± 1.7‡	
BMI (kg/m^2)	23.2 ± 3	25.5 ± 4.8	2.3§	22.7 ± 2.3	23 ± 2.5	0.4
Problem Areas in Diabetes score	51 ± 20	43.6 ± 20.9	−7.9†	44.9 ± 18.4	25.7 ± 22†	−19.3§
Diabetes self-management problems	52 ± 21	47 ± 27.3	−4.6	54.7 ± 26	18.3 ± 14.3§	−36.6§
Fear of hypoglycemia	34 ± 20.2	33.5 ± 18.8	−1.3	32.4 ± 20.4	30.2 ± 15.9	−3.2
Self-Care Inventory score	51 ± 18	53.7 ± 12.3	1.4	49.6 ± 18.6	66.8 ± 14.9†	16.7†
Brief Symptom Inventory score						
Depression	59.8 ± 10.5	59.3 ± 11.3	−1.3	60 ± 8.9	54 ± 10.7	−7.2‡
Anxiety	58.9 ± 9.7	58.6 ± 10.9	−0.9	58 ± 9.2	52.4 ± 10.7‡	−5.7
Global severity	60.3 ± 11	61.1 ± 10.2	0.5	59.5 ± 9.8	52.6 ± 9.8†	−6.9
Bulimia Test-Revised	63.6 ± 23.3	64.6 ± 23.7	0.9	62.6 ± 28	46.2 ± 16.9†	−16.4‡

Continuous data are shown as mean ± SD, and categoric data as percentage. *P value symbols in this column indicate differences between means for the two groups at follow-up. †$P < 0.01$; ‡$P < 0.05$; §$P < 0.001$.

Table 2—*Characteristics of women who never endorsed insulin restriction and those who newly endorse it at follow-up*

	Never restricted (n = 113)			New insulin restriction (n = 34)		
Characteristic	Baseline	Follow-up	Mean change	Baseline*	Follow-up†	Mean change
Diabetes duration (years)	29 ± 12.7	—	—	24 ± 9	—	—
Age (years)	35 ± 13	—	—	32 ± 11.4	—	—
Married	54	80	—	54	82	—
A1C (%)	8.2 ± 1.4	7.7 ± 1.3	−0.4‡	8.2 ± 1.5	8.4 ± 1.4‡	0.2
Years of education	14 ± 2.6	15.3 ± 2.1		14.6 ± 2.5	15.4 ± 1.5	
BMI (kg/m^2)	23.5 ± 3.5	25.4 ± 5.1	1.9§	23.2 ± 2.4	24.9 ± 3.4	1.8‡
Problem Areas in Diabetes score	24.3 ± 17	18.8 ± 17	−5.6§	26.2 ± 17	24.7 ± 17‡	−1.8
Diabetes self-management problems	25 ± 21	17.8 ± 16.9	−7.3§	28.2 ± 21	32.7 ± 23.5§	4.6
Fear of hypoglycemia	25 ± 17	24.3 ± 20.6	−0.7	25 ± 14.6	24.8 ± 16.9	−0.8
Self-Care Inventory score	72.2 ± 13.4	70 ± 12.8	−2.1	66.5 ± 12.2‡	60.2 ± 17.8‖	−5.2‡
Brief Symptom Inventory score						
Depression	53.4 ± 9.9	51.4 ± 10.1	−2.3‡	53.6 ± 9.8	52.8 ± 9.6	0.7
Anxiety	53.4 ± 10.3	50.3 ± 10	−3.2‖	53.4 ± 9.5	53.2 ± 9.3	0.7
Global severity	54.3 ± 10.3	53 ± 10.1	−1.6	53.9 ± 10.9	54.8 ± 9.2	0.7
Bulimia Test-Revised score	43.9 ± 14.8	43.7 ± 14	−0.4	46.9 ± 16.7	48.4 ± 17	0.5

Continuous data are presented as mean ± SD, and categoric data as percentage. *P value symbols in this column indicate differences between means for the two groups at baseline. †P value symbols in this column indicate differences between means for the two groups at follow-up. ‡$P < 0.05$; §$P < 0.001$; ‖$P < 0.01$.

more new insulin restrictors than those never restricting endorsed the statement that they were "afraid that getting my blood sugars in good control will cause me to gain weight" (62 vs. 36%, $P < 0.01$). Only 23% of women who never reported insulin restriction versus 50% of women who endorsed new reported restriction reported commercial weight loss attempts in their lifetimes ($P < 0.01$).

Prescribed diabetes management plans did not differ between groups. Both reported an average of two prescribed insulin injections per day at baseline and an average of three at follow-up. They also reported an average of 3.5 diabetes medical appointments per year at baseline and four at follow-up. In addition at follow-up, 36% reported insulin pump use, 60% reported using carbohydrate counting, and 30% reported using the exchange method for meal planning. Despite this lack of differences in prescribed diabetes management plans, there was a difference at follow-up in the reported average number of mild hypoglycemic events in the past month, with 8.4 ± 7.9 reported by those who stopped insulin restriction and 5.6 ± 5.6 reported by those who continued to restrict ($P < 0.05$). At baseline and follow-up, the rates of women reporting one or more diabetes complications (36% at baseline and 64% at follow-up) were similar in the two groups.

Within-group analyses of women newly reporting insulin restriction showed that these women had an increase in BMI ($P < 0.01$) and also reported an increase in fear that improved glycemia would result in weight gain (0.7 vs. 0.2, $P < 0.001$). Within-group analyses of women who never reported insulin restriction also showed increased BMI ($P < 0.001$), improvements in diabetes-specific distress ($P < 0.001$), improved anxiety ($P < 0.01$), and fewer reported problems with diabetes self-management ($P < 0.001$).

Between-group analyses showed that women who never reported insulin restriction showed improvements in self-reported problems with diabetes self-management ($P < 0.01$). Women endorsing new insulin restriction indicated more fear of weight gain associated with healthier blood glucose ranges relative to women who never endorsed insulin restriction who showed little change ($P < 0.01$).

After controlling for age and follow-up BMI in a logistic regression model, problems with diabetes self-management predicted new insulin restriction (OR 1.5 for each 10-point increase, $P < 0.001$). The overall model was 74% concordant.

CONCLUSIONS—To our knowledge, this study is the first to address the natural course of insulin restriction by examining factors associated with both its resolution and new emergence over time. These findings may help inform current treatment of patients struggling with insulin restriction by providing evidence that the behaviors can improve and by identifying characteristics associated with improvement.

Logistic regression analyses revealed that fear of weight gain associated with improved blood glucose and problems with diabetes self-care are core issues related to both the emergence and resolution of insulin restriction. Women who stopped insulin restriction and those who continued the behavior showed no between-group differences at baseline; however, the two groups did differ at follow-up. Notably, women who stopped restricting reported a higher frequency of diabetes self-care behaviors and lower levels of diabetes-specific distress and problems with self-management than women still restricting insulin at follow-up. Women who stopped also endorsed fewer eating disorder symptoms and lower levels of overall psychologic distress. More importantly, among women who stopped insulin restriction, a smaller proportion continued to endorse fears that improving blood glucose control or even taking insulin would cause weight gain.

Although it did not reach statistical significance ($P < 0.01$), the mean A1C improved in women who stopped insulin restriction from 9.4% at baseline to 7.9% at follow-up, and their BMI was maintained during the same period. Paradoxically, mean AIC levels also improved in women who continued to restrict insulin, from 9.2 to 8.3%; however, their BMIs increased from 23.2 to 25.5 kg/m^2. A1C improvements in both groups may reflect

the emphasis clinicians are placing on improved glycemic control since the publication of the Diabetes Control and Complications Trial results (17).

At follow-up, new insulin restrictors endorsed higher levels of problems with diabetes self-management and lower levels of overall diabetes self-care. More new insulin restrictors acknowledged using their weight as a means of judging their self-worth and also endorsed fears that improving blood glucose control would result in weight gain. Despite insulin restriction, new insulin restrictors had an increase in BMI between baseline and follow-up. In fact, both groups of insulin restrictors—those who continued and those newly restricting—endorsed fear of weight gain associated with improved blood glucose; however, both groups actually experienced weight gain despite insulin restriction.

Increases in BMI in the context of body image concerns may reinforce a cycle of negative diabetes self-care behaviors that will, for some women, include insulin restriction and disordered eating. Unlike the women who never restricted insulin, whose BMIs increased over time, those women who stopped insulin restriction did not increase their average BMI between baseline and follow-up. This may be due to a relative lack of weight concern among those who never restricted insulin as opposed to continued, albeit significantly healthier, weight concerns among those women who stopped insulin restriction.

This interpretation may be supported by our data showing that more insulin restrictors endorse lifetime participation in commercial weight loss programs than those women who do not report insulin restriction. Other studies report higher BMI as a child or teen as a risk factor for developing eating disorder behaviors (5,6); however, we did not find this in the adults who newly restricted at follow-up. In fact, baseline BMI did not differ among the four groups in our study. Perhaps by older adolescence through adulthood, higher BMI is no longer observed as a risk factor because eating disorder behaviors have already begun by this point in women's development.

This study confirms earlier research indicating that body weight and shape concerns are strongly related to insulin restriction women with type 1 diabetes (18,19). Indeed, clear differences emerged between women who stopped insulin restriction and those who newly restricted or continued to restrict; namely, those reporting restriction identified weight as an important marker of self-worth and reported fears about insulin treatment and improvements in glycemia causing weight gain. Women who stopped insulin restriction were less likely to endorse these types of weight and shape concerns relative to women who were newly restricting insulin or continuing to restrict.

These findings highlight the importance of diabetes clinicians taking women's weight concerns seriously and addressing them as part of their overall diabetes treatment plans. Diabetes treatment teams can actively engage women who they believe may be newly struggling with adherence problems and insulin restriction in open communication about their weight and shape concerns as they relate to diabetes adherence and insulin use. Our data indicate that women who restricted insulin experienced increases in BMI, while those who stopped restricting did not. These findings could be used by diabetes clinicians as a potential tool for psychoeducation to prevent or help women to stop insulin restriction. We strongly recommend closer follow-up with nurse educators and dietitians and referrals to mental health specialists with expertise in eating disorders when needed. Unfortunately, our research did not evaluate potential differences in diabetes self-care behaviors as they might pertain to the nature of the patient-diabetes team relationships and continuity of care versus transitioning between multiple care providers. We regret that our data did not allow us to analyze the influence of these factors as they may relate to the emergence or improvement of insulin restriction over time.

Our findings are limited by low power due to small group sizes and unbalanced numbers in each of the four comparison groups and through the use of a cross-sectional design. In addition, our data are based on self-report assessments and did not include the opportunity for interviews to more formally establish active insulin restriction. For this reason, we were also unable to ask women about their own understanding of how and why their insulin use changed over time. It may be that by limiting our evaluations to questionnaire assessments, we have missed important and as yet unrecognized variables.

Thus, we see a need for prospective, longitudinal research of this issue that includes frequent assessments throughout such a study's duration. There is also a need for qualitative research involving focus groups or open-ended interview questions, or both, to gain a better understanding of how women themselves understand what led them to stop insulin restriction and also what led them to start the behavior. Given the important changes in attitudes about diabetes treatment, insulin use, and its relationship to weight, we also see an additional need for future research evaluating intervention strategies that directly address these core attitudes among women with type 1 diabetes who restrict insulin. Such strategies could include cognitive restructuring of fears that appropriate insulin use and improved glycemia lead to weight gain and of the importance that these women place on weight as a marker of their self-worth. Designing and empirically validating such treatments is critical for this high-risk population.

Acknowledgments—This project was funded by a grant from the Center of Excellence in Women's Health, Harvard Medical School and the National Institute of Diabetes and Digestive and Kidney Diseases (R01-DK-060115 and P30-DK-36836). The original work was supported by grants from the National Institutes of Health-supported Diabetes and Endocrinology Research Center at Joslin Diabetes Center and the Herbert Graetz Fund.

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

A.E.G.-F. researched data, contributed to discussion, and wrote the manuscript. B.J.A. edited the manuscript. J.F. researched data, contributed to discussion, and edited the manuscript. D.L.F. and K.P. contributed to discussion and edited the manuscript. K.W. researched data, contributed to discussion, and edited the manuscript.

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