Insulin Restriction and Associated Morbidity and Mortality in Women with Type 1 Diabetes

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OBJECTIVE — To determine whether insulin restriction increases morbidity and mortality in women with type 1 diabetes.

RESEARCH DESIGN AND METHODS — This is an 11-year follow-up study of women with type 1 diabetes. A total of 234 women (60% of the original cohort) participated in the follow-up. Mean age was 45 years and mean diabetes duration was 28 years at follow-up. Mean BMI was 25 kg/m^2 and mean A1C was 7.9%. Measures of diabetes self-care behaviors, diabetes-specific distress, fear of hypoglycemia, psychological distress, and eating disorder symptoms were administered at baseline. At follow-up, mortality data were collected through state and national databases. Follow-up data regarding diabetes complications were gathered by self-report.

RESULTS — Seventy-one women (30%) reported insulin restriction at baseline. Twenty-six women died during follow-up. Based on multivariate Cox regression analysis, insulin restriction conveyed a threefold increased risk of mortality after controlling for baseline age, BMI, and A1C. Mean age of death was younger for insulin restrictors (45 vs. 58 years, $P < 0.01$). Insulin restrictors reported higher rates of nephropathy and foot problems at follow-up. Deceased women had reported more frequent insulin restriction ($P < 0.05$) and reported more eating disorder symptoms ($P < 0.05$) at baseline than their living counterparts.

CONCLUSIONS — Our data demonstrate that insulin restriction is associated with increased rates of diabetes complications and increased mortality risk. Mortality associated with insulin restriction appeared to occur in the context of eating disorder symptoms, rather than other psychological distress. We propose a screening question appropriate for routine diabetes care to improve detection of this problem.

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The Diabetes Control and Complications Trial established that maintaining near-normal blood glucose ranges can delay or prevent serious diabetes complications such as retinopathy, neuropathy, and nephropathy (1). However, despite changes in diabetes education emphasizing this important message, >50% of adult patients do not achieve the American Diabetes Association glycemic targets of <7% A1C (2,3). A number of psychosocial variables have been implicated in the search for barriers to the adoption of intensive diabetes management strategies. They include general psychological distress (such as depression and anxiety), diabetes-specific distress, fear of hypoglycemia, concern about weight gain, and related eating disorder behaviors (4). Such variables may lead patients with type 1 diabetes to restrict necessary insulin doses (i.e., take less insulin than prescribed).

Improvements in diabetes treatment are associated with declining rates in diabetes complications and mortality; however, patients with type 1 diabetes continue to have higher mortality rates when compared with patients without diabetes (5). To date, few reports have examined the connection between insulin restriction and mortality. Those that have investigated this link focused exclusively on populations with eating disorder behaviors. Two studies (6,7) examined samples of adolescent and young adult women with documented diagnoses of anorexia nervosa and reported higher mortality rates among women with comorbid anorexia and type 1 diabetes than either diagnosis alone. A third study (8) assessed the impact of subclinical eating disorder behaviors, including insulin restriction as a form of caloric purging, on diabetes complications and mortality and found it to be related to poor health outcomes.

We sought to extend this small body of research by conducting a follow-up assessment of a large cohort of women with type 1 diabetes who were originally assessed 11 years before. Participants were first evaluated from 1990 to 1991 on diabetes self-care behaviors, diabetes distress, fear of hypoglycemia, psychological symptoms including depression and anxiety, and eating disorder symptoms. Insulin restriction was common in the original cohort (reported by 30.5% of women assessed) and was associated with poorer diabetes self-care, heightened diabetes-specific distress, psychological distress, fear of hypoglycemia, and fear that improved glycemic control would result in weight gain (9). Our primary aim for the follow-up study was to investigate whether insulin restriction reported at baseline predicted higher rates of diabetes complications and increased risk of mortality in women with type 1 diabetes over a decade later.

RESEARCH DESIGN AND METHODS — The study protocol was approved by the Joslin Diabetes Center

Committee on Human Studies before contacting participants at both time points, and participants provided written informed consent. Further, the protocol was approved by the National Center of Health Statistics for searching the National Death Index database and also by specific state ethics review boards for investigating death information on past participants.

The following were baseline inclusion criteria for study participation: female sex, diagnosis of type 1 diabetes for at least 1 year, between 13 and 60 years of age, not currently pregnant, and no severe visual impairment. Participants were attending routine diabetes appointments at a specialty diabetes treatment center at the time of their baseline assessments.

Each participant from the original study was sent a letter explaining the project and was later contacted by telephone to describe the project in detail and answer questions. Several attempts were made 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. Internet search engines and a private search agency were used to help locate participants' most up-to-date addresses.

Death information, including cause of death, was ascertained through records searches at the Department of Vital Statistics of the Commonwealth of Massachusetts, the Social Security Death Index, and the National Death Index. All names of those lost to follow-up were entered into these three different death record databases. Causes of death for three women were obtained by contacting their families.

The original participant sample consisted of 390 women with type 1 diabetes. Of these, 49 declined to enroll in the follow-up cohort and 107 were lost to follow-up. Thus, the follow-up sample consists of 234 women, including 26 women known to have died during the study period, and represents 60% of the original cohort. Mean age at follow-up was 45 ± 12 years (range 24–72). Mean diabetes duration at follow-up was 28 ± 12 years (11–67). At follow-up, 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, or any of the survey measures administered at baseline. They also showed no differences in rates of diabetes complications at baseline.

Demographic and clinical information

Demographic and clinical information, including age, diabetes duration, BMI, and presence of medical complications, was gathered by chart abstraction at baseline. Most baseline laboratory data used HbA1 assays rather than the current A1C standard. All HbA1 laboratory results were converted to A1C using this formula developed through comparative testing on paired samples: A1C = (HbA1 − 0.19)/1.21 (10). At follow-up, many participants were no longer receiving their medical care at Joslin. For this reason, all follow-up participants completed a brief self-report questionnaire in which they reported current age, diabetes duration, BMI, and medical complications.

Baseline psychosocial assessment

The screening item "I take less insulin than I should" in a self-administered survey developed for the original study was used to determine insulin restriction status in this patient cohort. Based on their responses at baseline, women were categorized as insulin restrictors if they reported restriction at any level of frequency from "rarely" to "always" in response to this statement. They were categorized as appropriate insulin users if they endorsed "never" on this same item.

The Self-Care Inventory (11) was used to measure self-reported frequency of adherence to 14 diabetes self-care tasks (e.g., blood glucose monitoring frequency, insulin administration). Diabetes-specific distress was measured by administering the 20-item Problem Areas in Diabetes survey (12,13), which assesses a broad range of feelings related to living with diabetes and its treatment. The 17-item Hypoglycemia Fear Survey (14) was used to assess the level of worry about hypoglycemia. Higher scores indicate greater level of worry. The 53-item Brief Symptom Inventory (15) was used to measure symptoms of depression, anxiety, and severity of general psychological symptoms by examining scores on the depression and anxiety subscales as well as the global severity index.

Eating and weight concerns were measured two ways. The 36-item Bulimia Test-Revised (16) and the 64-item Eating Disorders Inventory (17) were used to measure attitudes and behaviors central to eating disorders, such as drive for thinness, weight preoccupation, binge eating, and purging behaviors. Both measures have been used in previous diabetes research (18–20).

Statistical analyses

Summary statistics are presented as means ± SDs for continuous variables. Student's *t* tests were used to 1) compare demographic and clinical characteristics of follow-up participants with those women who were lost to follow-up and 2) determine differences in baseline demographic variables and baseline measures of psychosocial functioning between insulin restrictors and appropriate insulin users enrolled in the follow-up cohort. χ^2 tests were used to 1) compare rates of insulin restriction reported at baseline between the group of participants and the group of women who were lost to follow-up and 2) compare rates of complications reported at follow-up by insulin restrictors and appropriate insulin users. Wilcoxon exact tests for small sample sizes were used to test for differences in demographic variables and psychosocial functioning between insulin restrictors and appropriate insulin users who died during follow-up. Wilcoxon exact tests were also used to compare living and deceased insulin restrictors only. Fisher's exact tests were used to compare mortality rates between insulin restrictors and appropriate insulin users during follow-up.

We present unadjusted Kaplan-Meier survival curves to illustrate differences in probability of death between insulin restrictors and appropriate insulin users during the 11-year follow-up period. We also estimated the relative risk of death conferred by baseline insulin restriction after controlling for baseline age, BMI, and A1C using multivariate Cox regression analysis. Statistical analyses were performed using SAS statistical software (version 8.2; SAS Institute, Cary, NC).

RESULTS — Of 234 women followed in the study (208 living and 26 deceased), 71 women (30%) reported insulin restriction at baseline. Analyses examining the subsample of follow-up participants were consistent with findings reported in the original study (9). Insulin restrictors showed distinct clinical differences from women reporting appropriate insulin use. At baseline, insulin restrictors were younger (aged 32 vs. 36 years, *P* < 0.01) and had higher A1C values (9.6 vs. 8.3%, *P* < 0.001) but did not differ from appro-

Table 1—*Multivariate Cox survival analysis modeling death during the study period*

Baseline characteristics	Hazard ratio	P value
Insulin restriction status	3.2	0.05
Age	1.1	0.001
A1C	1.6	0.001
BMI	1.1	0.001

priate insulin users with regard to baseline BMI or diabetes duration. Not surprisingly, insulin restrictors reported lower scores on the baseline measure of diabetes self-care behaviors (Self-Care Inventory 50 vs. 70.4, $P < 0.001$). Insulin restrictors scored higher on baseline measures of diabetes distress (Problem Areas in Diabetes survey 69 vs. 34.5, $P < 0.001$), fear of hypoglycemia (Hypoglycemia Fear Survey 35.1 vs. 26.5, $P < 0.01$), general psychological symptoms (Brief Symptom Inventory–Global Severity Index 60.4 vs. 54.4, $P < 0.001$), and bulimia and other eating disorder symptoms (Bulimia Test-Revised 66.8 vs. 45.6, $P < 0.001$; and Eating Disorders Inventory 37.9 vs. 22.3, $P < 0.001$).

Diabetes complications

Relative to appropriate insulin users, women reporting insulin restriction at baseline were more likely to report nephropathy (25 vs. 10%, $P < 0.01$) and foot problems (25 vs. 12%, $P < 0.05$) at follow-up. Self-reported rates of retinopathy, neuropathy, and cardiovascular complications at follow-up did not differ between insulin restrictors and appropriate insulin users.

Mortality

After controlling for baseline age, BMI, and A1C, multivariate Cox survival analysis (Table 1) showed that self-reported insulin restriction at baseline increased the relative risk of death during the 11-year study period by 3.2 times (Fig. 1).

Causes of death for 10 of 71 women reporting insulin restriction at baseline were as follows: perforated bowel (with gastroparesis) ($n = 1$), cancer ($n = 1$), cardiac events ($n = 3$), hypoglycemia ($n = 1$), renal failure ($n = 2$), sepsis ($n = 1$), and suicide (in the context of retinopathy-related blindness) ($n = 1$). Causes of death for 16 of 163 women reporting appropriate insulin use were as follows: cancer ($n = 1$), cardiac events ($n = 11$), diabetic ketoacidosis ($n = 1$), sepsis ($n = 1$), and unknown cause ($n = 1$).

Comparisons of deceased women who reported insulin restriction at baseline ($n = 10$) and those reporting appropriate insulin use at baseline ($n = 16$) showed that insulin restrictors were younger when they died (aged 44 vs. 58 years, $P < 0.01$) and scored higher on measures of diabetes-specific distress as well as bulimia and other eating disorder symptoms. Insulin restrictors also reported lower frequency of diabetes self-care behaviors than women reporting appropriate insulin use. They did not differ in their levels of hypoglycemia fear or general psychological distress (Table 2).

Insulin restrictors who died during follow-up reported more frequent insulin restriction than their living counterparts at baseline. Specifically, 40% of those who died vs. 7% of those still living reported "always" taking less insulin than they should at baseline ($P < 0.05$). Deceased insulin restrictors had significantly higher baseline BMI and A1C values. Additionally, they scored higher on baseline bulimia symptoms than living insulin restrictors. There was a trend suggesting that those who died also endorsed higher levels of diabetes-specific distress at baseline ($P = 0.07$). The two groups did not show statistically significant differences in fear of hypoglycemia or general psychological distress (Table 3).

CONCLUSIONS — This study is the largest project examining the long-term impact of insulin restriction on the morbidity and mortality of women with type 1 diabetes. After controlling for the impact of baseline age, A1C, and BMI, insulin re-

striction at baseline conveyed more than a threefold increase in the relative risk of death during the 11-year study period. Age of death was younger among insulin restrictors, with a mean age of death of 45 years in women who restricted insulin compared with 58 years among that reporting appropriate insulin use. At follow-up, insulin restrictors reported higher rates of nephropathy and foot problems than appropriate insulin users.

Reasons for insulin restriction may extend beyond eating disorder symptoms and weight-related concerns and can be driven by other factors. Comparisons of the follow-up group, living and deceased, showed that insulin restriction was associated with greater eating disorder symptoms, diabetes-specific distress, overall psychological symptoms, and fear of hypoglycemia at baseline.

The importance of frequency of insulin restriction is highlighted by the fact that insulin restrictors who died during the 11-year follow-up period reported restricting insulin more frequently at baseline. Deceased insulin restrictors also had higher BMI and A1C values and reported more symptoms of bulimia and higher levels of diabetes-specific distress than their living counterparts at baseline. Although formal diagnoses of bulimia were not made in this study and are outside of its scope, the mean BMI for deceased insulin restrictors was consistent with the normal to slightly overweight BMI ranges typically seen in patients with bulimia (21).

Comparisons of both groups of deceased women found deceased insulin re-
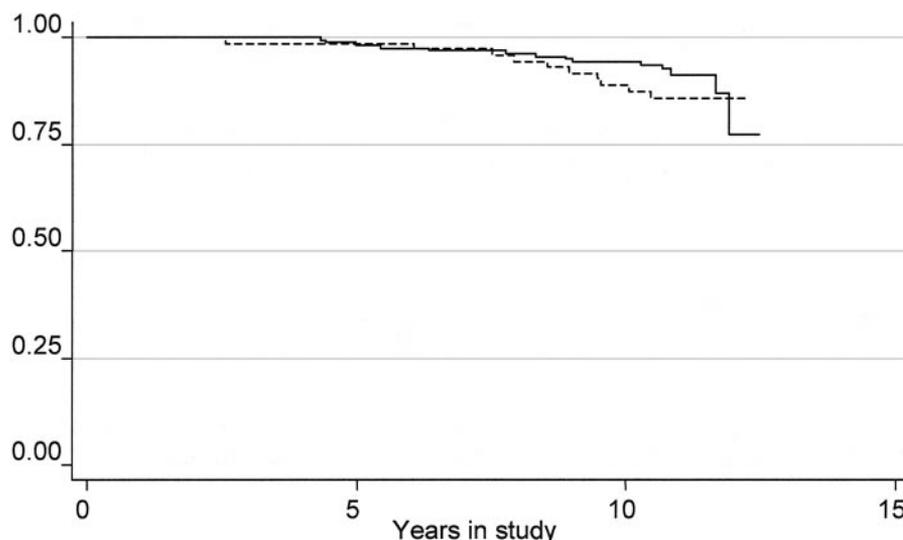
Figure 1—*Unadjusted Kaplan-Meier survival plot of deaths during the study. —, appropriate users; ---, insulin restrictors.*

Table 2—*Characteristics of women who died during follow-up*

	Appropriate insulin users	Insulin restrictors
n	16	10
Age at death	57.7 ± 11	44.7 ± 11*
Diabetes duration at death	33.2 ± 12	26.5 ± 11
Baseline characteristics		
A1C (%)	9.4 ± 1.5	11.1 ± 2.1†
BMI (kg/m^2)	29 ± 8	28 ± 7
Problem Areas in Diabetes Survey	48.4 ± 38.6	83.8 ± 27.6†
Hypoglycemia Fear Survey	41.4 ± 24.3	41.9 ± 24.2
Self-Care Inventory	65.3 ± 17.7	46 ± 20.1†
Brief Symptom Inventory (depression)	58.5 ± 10.6	58.6 ± 14.5
Brief Symptom Inventory (anxiety)	55.8 ± 11.5	60.5 ± 11.8
Brief Symptom Inventory–Global Severity Index	56.7 ± 13.4	62.1 ± 10.1
Bulimia Test-Revised	55 ± 24	85 ± 30*
Eating Disorders Inventory (drive for thinness)	3.6 ± 3	5.9 ± 3
Eating Disorders Inventory (bulimia)	1.5 ± 2	4.1 ± 4‡
Eating Disorders Inventory (body dissatisfaction)	9.3 ± 6	11.6 ± 5
Eating Disorders Inventory (total score)	29.6 ± 19.5	47.6 ± 24‡

Data are means ± SD. *$P < 0.01$; †$P < 0.05$; ‡trend $P = 0.07$ (P values associated with Wilcoxon exact tests).

strictors to have higher baseline A1C values, poorer diabetes self-care behaviors, increased levels of diabetes-specific distress, and higher scores on measures of bulimia and other eating disorder symptoms than appropriate insulin users who died during the study period. The two groups of deceased participants did not differ on measures of hypoglycemia fear, depression, anxiety, or general psychiatric symptoms. These data suggest that mortality associated with insulin restriction occurred in the context of eating disorder symptoms, rather than other psychological distress. Studies documenting the high rate of mortality in eating disorders (22) suggest that diabetic patients with significant eating disorder symptoms and any insulin restriction should be carefully monitored.

Factors associated with type 1 diabetes treatment, such as careful attention to food portions and choices, regular exercise, regular blood glucose monitoring, and treatment of hypoglycemia, may contribute to eating and weight concerns in this population (23) and may predispose individuals with diabetes to develop diabetes-specific disordered eating attitudes and behaviors. Indeed, weight gain is a common side effect of intensive insulin treatment (1,24). Individuals with type 1 diabetes possess a uniquely dangerous tool for rapid weight loss—restricting insulin to purge calories through glycosuria. Insulin restriction was associated with a number of psychosocial variables in this sample of women; however, ratings of eating disorder symptoms, and not other measures of psychological distress, were significantly higher in insulin restrictors who died during follow-up.

Clearer understanding of the unique determinants of insulin restriction among individual patients would require in-depth evaluations by a mental health professional, ideally with specialized training in diabetes. Unfortunately, such specialty services are rarely available to individuals with type 1 diabetes. As a result, detection of insulin restriction may be unlikely until after the problem has become habitual and entrenched. Our data suggest that insulin restriction as captured by a single screening item ("I take less insulin than I should") is associated with increased mortality. Use of this question in routine clinical practice has the potential to identify at-risk women so that interventions may be provided. Further research is needed to assess the clinical utility of adopting such a question as a screening tool for identifying insulin restrictors in need of further psychological evaluation. This in turn could increase the likelihood of earlier detection and improve access to specialty treatment referrals for these high-risk patients.

Several study limitations should be noted. Other variables, which were not assessed, could have contributed to mortality over the 11-year period between baseline and follow-up. Further, despite the lack of baseline differences in participants lost to follow-up and those for whom we have data, only 60% of the original sample is included in this report. Finally, important differences may exist among women along the continuum of severity and frequency of insulin restriction. However, social desirability biases may lead diabetic patients, especially

Table 3—*Baseline characteristics of living versus deceased (insulin restrictors only)*

	Living	Deceased
	61	10
Age	30.6 ± 10.4	36.6 ± 12
Diabetes duration	26.1 ± 9.4	26.5 ± 10.6
Baseline characteristics		
A1C (%)	9.3 ± 1.9	11.1 ± 2.1*
BMI (kg/m^2)	23 ± 3	28 ± 7*
Problem Areas in Diabetes Survey	66.4 ± 25.7	83.8 ± 27.6†
Hypoglycemia Fear Survey	34 ± 20.4	41.9 ± 24.2
Self-Care Inventory	50.7 ± 17.9	46 ± 20.1
Brief Symptom Inventory (depression)	60 ± 9.9	58.6 ± 14.5
Brief Symptom Inventory (anxiety)	58.8 ± 9.4	60.5 ± 11.8
Brief Symptom Inventory–Global Severity Index	60.2 ± 10.6	62.1 ± 10.1
Bulimia Test-Revised	63.8 ± 25	85.1 ± 29.6‡
Eating Disorders Inventory (drive for thinness)	5.3 ± 3.2	5.9 ± 3.4
Eating Disorders Inventory (bulimia)	2.6 ± 2.8	4.1 ± 3.7
Eating Disorders Inventory (body dissatisfaction)	10.4 ± 6.2	11.6 ± 4.8
Eating Disorders Inventory (total score)	36.3 ± 20.9	47.6 ± 24.4

Data are means ± SD. *$P < 0.01$; †trend $P = 0.07$; ‡$P < 0.05$ (P values associated with Wilcoxon exact tests).

those being treated at a specialty diabetes center, to underreport or minimize their pattern of insulin restriction. In the majority of our analyses, we chose to define insulin restriction as being present if it was reported at any level of frequency for this reason; however, this decision could not eliminate the limitation that study analyses relied on participant's willingness to report insulin restriction.

The problem of insulin restriction is an important health issue for women with type 1 diabetes, and our data demonstrate that this behavior is associated with increased rates of diabetes complications, shortened lifespan, and increased mortality risk. We propose a brief method for assessing this dangerous practice. Further research is needed to validate this screening method in clinical practice and to determine the best treatment strategies for women struggling with this problem. The health and wellness of women with type 1 diabetes is likely to be promoted by greater attention to the problem of insulin restriction in future research and in clinical practice.

References

1. The Diabetes Control and Complications Trial Research Group: The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med* 329:977–986, 1993

2. Saaddine JB, Cadwell B, Gregg EW, Engelgau MM, Vinicor F, Imperatore G, Narayan KM: Improvements in diabetes processes of care and intermediate outcomes: United States, 1988–2002. *Ann Intern Med* 144:465–474, 2006

3. Resnick HE, Foster GL, Bardsley J, Ratner RE: Achievement of American Diabetes Association clinical practice recommendations among U.S. adults with diabetes, 1999–2002. *Diabetes Care* 29:531–537, 2006

4. Jacqueminet S, Masseboeuf N, Rolland M, Grimaldi A, Sachon C: Limitations of the so-called "intensified" insulin therapy in type 1 diabetes mellitus. *Diabetes Metab* 31:4S45–44S50, 2005

5. Pambianco G, Costacou T, Ellis D, Becker DJ, Klein R, Orchard TJ: The 30-year natural history of type 1 diabetes complications: the Pittsburgh Epidemiology of Diabetes Complications Study experience. *Diabetes* 55:1463–1469, 2006

6. Walker JD, Young RJ, Little J, Steel JM: Mortality in concurrent type 1 diabetes and anorexia nervosa. *Diabetes Care* 25:1664–1665, 2002

7. Nielsen S, Emborg C, Molbak AG: Mortality in concurrent type 1 diabetes and anorexia nervosa. *Diabetes Care* 25:309–312, 2002

8. Peveler RC, Bryden KS, Neil HA, Fairburn CG, Mayou RA, Dunger DB, Turner HM: The relationship of disordered eating habits and attitudes to clinical outcomes in young adult females with type 1 diabetes. *Diabetes Care* 28:84–88, 2005

9. Polonsky WH, Anderson BJ, Lohrer PA, Aponte JE, Jacobson AM, Cole CF: Insulin omission in women with IDDM. *Diabetes Care* 17:1178–1185, 1994

10. Krolewski AS, Laffel LM, Krolewski M, Quinn M, Warram JH: Glycosylated hemoglobin and the risk of microalbuminuria in patients with insulin-dependent diabetes mellitus. *N Engl J Med* 332:1251–1255, 1995

11. Greco P, LaGreca AM, Ireland S, Wick P, Freeman C, Agramonte R, Gutt M, Skyler JS: Assessing adherence in IDDM: a comparison of two methods (Abstract). *Diabetes* 39 (Suppl. 1):165A, 1990

12. Polonsky WH, Anderson B, Lohrer P, Welch G, Jacobson AM, Aponte JE, Schwartz CE: Assessment of diabetes-related distress. *Diabetes Care* 18:754–760, 1995

13. Welch GW, Jacobson AM, Polonsky WH: The Problem Areas in Diabetes scale: an evaluation of its clinical utility. *Diabetes Care* 20:760–766, 1997

14. Cox DJ, Irvine A, Gonder-Frederick L, Nowacek G, Butterfield J: Fear of hypoglycemia: quantification, validation, and utilization. *Diabetes Care* 10:617–621, 1987

15. Derogatis LR, Melisaratos N: The Brief Symptom Inventory: an introductory report. *Psychol Med* 13:595–605, 1983

16. Thelen MH, Farmer J, Wonderlich S, Smith M: A revision of the bulimia test: the BULIT-R. *Psychol Assess* 3:119–124, 1991

17. Garner DM, Olmsted MP, Polivy J: Development and validation of a multidimensional eating disorder inventory for anorexia nervosa and bulimia. *Int J Eat Disord* 2:15–34, 1983

18. Steel JM, Young RJ, Lloyd GG, Macintyre CC: Abnormal eating attitudes in young insulin-dependent diabetics. *Br J Psychiatry* 155:515–521, 1989

19. Jones JM, Lawson ML, Daneman D, Olmsted MP, Rodin G: Eating disorders in adolescent females with and without type 1 diabetes: cross sectional study. *BMJ* 320:1563–1566, 2000

20. Affenito SG, Backstrand JR, Welch GW, Lammi-Keefe CJ, Rodriguez NR, Adams CH: Subclinical and clinical eating disorders in IDDM negatively affect metabolic control. *Diabetes Care* 20:182–184, 1997

21. American Psychiatric Association: *Diagnostic and Statistical Manual of Mental Disorders.* Washington, DC, American Psychiatric Association Press, 1994

22. Keel PK, Dorer DJ, Eddy KT, Franko D, Charatan DL, Herzog DB: Predictors of mortality in eating disorders. *Arch Gen Psychiatry* 60:179–183, 2003

23. Daneman D, Olmsted M, Rydall A, Maharaj S, Rodin G: Eating disorders in young women with type 1 diabetes: prevalence, problems and prevention. *Hormone Res* 50:79–86, 1998

24. The DCCT Research Group: Weight gain associated with intensive therapy in the diabetes control and complications trial. *Diabetes Care* 11:567–573, 1988