

# Factors Help Predict Eating Disorders in Diabetes

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KEYSTONE, COLO. — Significant predictors of the onset of disturbed eating behavior within the next several years in girls with type 1 diabetes include concerns with weight and shape, a higher body mass index, depressive symptoms, and poor self-esteem—both globally and specifically with regard to physical appearance, according to a new prospective study.

These are the factors to look out for in clinical practice. Collectively they explained 48% of the variance between young adolescent girls with diabetes who went on to manifest disturbed eating behavior within the next 5 years and those who didn't, Dr. Denis Daneman said at a conference on the management of diabetes in youth.

The study findings raise the possibility that early interventions focused on helping girls who have diabetes develop positive feelings about themselves might protect against later development of disturbed eating behavior.

This hypothesis, however, requires testing, particularly in light of the fact that no successful strategies for the prevention of eating disorders in adolescents and young adults with type 1 diabetes have been reported to date.

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Moreover, treatment of eating disorders in this population of girls with type 1 diabetes has proved extremely difficult, much more so than in patients without diabetes, according to Dr. Daneman, who serves as professor and chair of the department of pediatrics at the University of Toronto and pediatrician-in-chief at the Hospital for Sick Children.

The prospective study involved 126 girls with type 1 diabetes who were enrolled at ages 9-13 years at the pediatric hospital and followed for 5 years. They were interviewed annually using the validated, semistructured Eating Disorder Examination.

The study was designed to identify predictors of disturbed eating behavior by following girls as they moved into the peak years of disturbed eating behavior onset, which is ages 15-25, according to Dr. Daneman, who is a pediatrician.

At entry, 25 girls had disturbed eating behavior, defined by dieting for weight control, self-induced vomiting, binge eating, or using insulin omission, laxatives, intense exercise, or diuretics for weight control. An additional 45 girls developed disturbed eating behavior during follow-up (Diabetes Care 2008 July 15 [doi:10.2337/dc08-0333]).

Eating disorders are a huge problem among girls and young women with type 1 diabetes, said Dr. Daneman, who has

cowritten nearly two dozen publications on the topic.

His own studies, as well as others conducted in Scandinavia, the United Kingdom, France, and the United States, indicate that 10% of girls with type 1 diabetes in their midteens meet formal DSM-IV criteria for an eating disorder and another 14% have subthreshold eating disorders—that is, their disturbed eating behavior doesn't fulfill DSM-IV criteria for an eating disorder but nonetheless has important

clinical consequences, including poor control of blood glucose and early onset of diabetes complications.

The two full-blown DSM-IV eating disorders associated with type 1 diabetes are bulimia nervosa and eating disorder not otherwise specified (EDNOS). Anorexia nervosa is not part of the picture.

"When type 1 diabetes and anorexia nervosa occur together, it's a chance occurrence," Dr. Daneman said at the conference, which was cosponsored by the

Barbara Davis Center for Childhood Diabetes, the University of Colorado, and the Children's Diabetes Foundation at Denver.

Dr. Daneman views it as a major failing of the eating disorders section of DSM-IV that insulin manipulation for the purpose of weight control isn't listed as a major diagnostic criterion.

But he indicated that he is not losing any sleep over the omission, considering what he said is the non-evidence-based nature of the DSM. ■

## IMPORTANT CORRECTION OF DRUG INFORMATION ABOUT EFFEXOR XR® (VENLAFAXINE HCl) EXTENDED-RELEASE CAPSULES

An advertisement in professional journal publications for EFFEXOR XR® (venlafaxine HCl) Extended-Release Capsules for the treatment of major depressive disorder was the subject of a Warning Letter issued by the U.S. Food and Drug Administration (FDA) in December 2007. The FDA stated that the journal ad was misleading because it overstated the efficacy of EFFEXOR XR, made unsubstantiated superiority claims, and contained other unsubstantiated claims regarding EFFEXOR XR.

Wyeth would like to take this opportunity to clarify the content of the advertisement.

### Claims that Reference the Baldomero et al Study and Other Related Claims

The FDA objected to the claim, "In an open-label study of patients who failed previous antidepressant treatment, nearly 60% achieved remission when changed to EFFEXOR XR." The FDA determined that the Baldomero study (the cited reference for this claim) could not be relied upon as substantial evidence to support the claim due to the following reasons: (1) the study was an open-label study, which is not an appropriate study design to measure subjective end points because it fails to minimize potential bias; (2) the study did not include a placebo group, so there was no way to determine the actual effect size of the drug; and (3) the study did not provide information about whether EFFEXOR XR was superior to failed therapy because study subjects were not randomized to their previously failed therapy. Therefore, the FDA stated that the study failed to support the 60% remission rate claim as well as any conclusion that EFFEXOR XR is superior to other antidepressant treatments. In addition to the above claim, the FDA stated that other claims added to the misleading impression that patients who have failed previous antidepressant therapy can expect improvement when switching to EFFEXOR XR.

### Claims from the PREVENT Study

The FDA objected to the claim, "In the PREVENT study, the probability of preventing a new episode of depression was 92% with EFFEXOR XR in maintenance year 2 vs. 55% with placebo." The FDA stated that the cited claim overstated the efficacy of EFFEXOR XR by implying that the general patient population suffering from major depressive disorder can expect a 92% probability of preventing a recurrent depressive episode after two years of treatment when this is not supported by substantial evidence.

The cited study for this claim was a randomized, multicenter, double-blind study (n=1096) comparing EFFEXOR XR with placebo. The study was designed to provide efficacy data regarding recurrence prevention with EFFEXOR XR after two years of maintenance

treatment. It followed patients through 4 different time periods: a 10-week acute period, a 6-month continuation period, an initial 12-month maintenance period (maintenance year 1), and a second 12-month maintenance period (maintenance year 2). At the end of each period, patients were only considered eligible for inclusion in the next period if they were still responding to the drug. Patients dropped out of the study during each of the periods for different reasons (eg, lack of efficacy, adverse events). At the start of each maintenance period, the remaining patients who still showed a response to EFFEXOR XR were re-randomized to EFFEXOR XR or placebo. Because a high percentage of EFFEXOR XR patients were either re-randomized to placebo or were discontinued from the study before entering maintenance year 2 and because only patients who responded to EFFEXOR XR were selected to continue to the next phase of treatment, the FDA determined that the results of the study could not be extrapolated to the general patient population suffering from major depressive disorder.

### Claim Regarding Clinical Experience and Number of Patients

The FDA objected to the claim, "More than 12 years of clinical experience and over 20 million patients treated with EFFEXOR/EFFEXOR XR." The claim of 20 million EFFEXOR/EFFEXOR XR patients was estimated from the number of U.S. prescriptions, average daily consumption, and average length of therapy. The FDA determined that this claim was misleading based on the referenced data because the calculations used did not reflect the number of "unique" patients. Because there are no unique patient-level data available for the entire 14-year period during which EFFEXOR/EFFEXOR XR has been on the U.S. market, the claim is no longer used in EFFEXOR XR promotional materials.

**Please see brief summary of Prescribing Information on adjacent page.**

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