



Eating disorder recovery is associated with absence of major depressive disorder and substance use disorders at 22-year longitudinal follow-up

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ABSTRACT

Background: Psychiatric comorbidity is common in eating disorders (EDs) and associated with poor outcomes, including increased risk for relapse and premature death. Yet little is known about comorbidity following ED recovery. **Methods:** We examined two common comorbidities, major depressive disorder (MDD) and substance use disorder (SUD), in adult women with intake diagnoses of anorexia nervosa and bulimia nervosa who participated in a 22-year longitudinal study. One hundred and seventy-six of 228 surviving participants (77.2%) were interviewed 22 years after study entry using the Eating Disorders Longitudinal Interval Follow-up Evaluation to assess ED recovery status. Sixty-four percent ($n = 113$) were recovered from their ED. The Structured Clinical Interview for DSM-IV was used to assess MDD and SUD at 22 years.

Results: At 22-year follow-up, 28% ($n = 49$) met criteria for MDD, and 6% ($n = 11$) met criteria for SUD. Those who recovered from their ED were 2.17 times more likely *not* to have MDD at 22-year follow-up (95% CI [1.10, 4.26], $p = .023$) and 5.33 times more likely *not* to have a SUD at 22-year follow-up than those who had not recovered from their ED (95% CI [1.36, 20.90], $p = .008$).

Conclusion: Compared to those who had not fully recovered from their ED, those who had recovered were twice as likely not to be diagnosed with MDD in the past year and five times as likely not to be diagnosed with SUDs in the past year. These findings provide evidence that long-term recovery from EDs is associated with recovery from or absence of these common major comorbidities. Because comorbidity in EDs can predict poor outcomes, including greater risk for relapse and premature death, our findings of reduced risk for psychiatric comorbidity following recovery at long-term follow-up is cause for optimism.

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1. Introduction

Eating disorders (EDs) are often associated with chronic course and time to recovery is protracted [1]. Comorbidity with other psychiatric disorders occurs in 56–98% of those with eating disorders [2,3]. Individuals with EDs and comorbidity have a longer duration of illness and poorer outcomes compared to those without comorbidity, including increased risk for ED relapse [4,5], premature death, and suicide [6]. Mood disorders are among the most common comorbidities, occurring in an estimated

28–95% of those with EDs [2,3]. Depression has been identified as a predictor of poor ED outcome in patients with anorexia nervosa (AN) in many studies [6–8], but not in all [9]. Substance use disorder (SUD) is also a common comorbidity, with estimates ranging from 17 to 46% [3,10]. Comorbid EDs and SUDs have proven to be a lethal combination, with previous research finding that alcohol use disorder increases the risk for mortality in AN by twofold [11].

Less is known, however, about whether major depressive disorder (MDD) and SUD persist following recovery from an ED, particularly in the long-term. Several studies have found that, compared to individuals with active EDs, those who had achieved recovery for greater than 12 months had fewer depressive symptoms [12,13] and were less likely to have major depressive disorder [14]. However, despite improvements in mood, evidence suggests that after ED recovery, levels of depression remain higher in those with ED histories than in healthy controls. For instance, Holtkamp and colleagues [15] found greater depressive symptoms in adolescents who were recovered for three years from AN

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compared to those adolescents with no ED history. Three additional studies also reported higher levels of depressive symptoms in those recovered from AN or bulimia nervosa (BN) for one year relative to those without ED histories [16–19]. Importantly, all [13–19] but one [12] of these studies were restricted to adolescent or young adult samples and most relied on self-report measures of depressive symptoms [15–19]. To our knowledge, no studies have examined the frequency of SUD following ED recovery.

Given that these psychiatric comorbidities have been identified as poor prognostic indicators, increasing risk for ED relapse and premature death, and less is known about whether comorbidity—particularly SUDs—persists or emerges following ED recovery, we examined two common comorbidities in adult women at long-term follow-up. Our team has recently published data from the same study demonstrating that nearly two-thirds of women with AN and BN achieved full ED recovery at a 22-year follow-up [1]. Herein, we aimed to extend these findings by examining the co-occurrence of depression and SUD in adult women who were recovered, relative to those who were not, at 22 years. We hypothesized that at 22 years post-study enrollment, those who achieved full recovery from their EDs would also have lower rates of MDD and SUD comorbidity compared to those who remained ill with AN or BN at 22-year follow-up.

2. Methods

2.1. Participants

Between 1987 and 1991, we recruited 246 women who met criteria for AN or BN (based on the 3rd Revised Edition of the Diagnostic and Statistical Manual of Mental Disorders [20]) and sought treatment at Massachusetts General Hospital and other Boston-area clinics. After reclassification with DSM-IV criteria [21], the sample included 136 women with a baseline diagnosis of AN and 110 women with a baseline diagnosis of BN. Participants were interviewed every 6–12 months for a mean of 9.1 ($SD = 1.6$) years starting in 1987. Of the 228 surviving participants, 176 (77.2%) completed a one-time follow-up assessment at a mean of 22.1 ($SD = 1.1$) years after study initiation. The average age of participants at 22-year follow-up was 46.3 ($SD = 6.6$) years. The study was approved by the Institutional Review Board of Massachusetts General Hospital (MGH). Full sample characteristics and methods have been previously described (see [1,22]).

Women who participated in the 22-year follow-up did not differ from those who dropped out of the study on age at baseline, prevalence of depression at baseline, or SUD at baseline (all ps were not statistically significant).

2.2. Measures

Throughout the course of the MGH Longitudinal Study of Eating Disorders, we used the Eating Disorders Longitudinal Interval Follow-up Evaluation (LIFE-EAT II) – a semi-structured interview based on the LIFE [23] – to assess weekly longitudinal ED pathology and assign diagnosis. ED severity was assessed with a Psychiatric Status Rating (PSR) score (coded 0–6) that corresponded to the Research Diagnostic Criteria ratings for both AN and BN wherein 0 = no lifetime diagnosis, 1 and 2 = full remission, 3 and 4 = partial criteria, and 5 and 6 = full criteria (see [1]). Participants with a PSR score of 2 or less for a full year on the AN and BN PSR scales were considered recovered from their eating disorder [1]. At the 22-year follow-up assessment, we used the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) to assess MDD and SUD, which we rated as present or absent over the past year.

2.3. Data analysis

We conducted all analyses in SPSS version 23 [24]. First, we examined the frequency of MDD and SUD at 22-year follow-up across the entire sample. To determine whether recovery from ED (yes vs. no) was associated with the absence of MDD and SUDs at 22-year follow-up, we conducted chi-square (X^2) analyses and calculated relative risk ratios for presence/absence of MDD and EDs, and for presence/absence of SUDs and EDs.

3. Results

Frequencies and proportions for the absence/presence of ED, MDD, and SUD at 22-year follow-up are reported in Table 1. Of the 176 individuals who completed the 22-year follow-up, 36% ($n = 63$) met criteria for an ED in the past year; 28% ($n = 49$) met criteria for MDD in the past year; and 6.3% ($n = 11$) met criteria for SUD in the past year.

Recovery from an ED at 22 years was associated with the absence of MDD at 22 years, $X^2(1, N = 176) = 5.14, p = .04$. Likewise, recovery from an ED at 22 years was associated with the absence of SUDs at 22 years, $X^2(1, N = 176) = 6.96, p = .02$. Specifically, those who had recovered from their ED were 2.17 times more likely *not* to have MDD at 22-year follow-up (95% CI [1.10, 4.26], $p = .023$) and 5.33 times more likely *not* to have a SUD at 22-year follow-up (95% CI [1.36, 20.90], $p = .008$) than those who had not recovered from their ED. In other words, when comparing those who had recovered from their ED to those with active ED, 22% v. 38% were diagnosed with MDD and 3% v. 13% had a substance use disorder.

4. Discussion

Twenty-two years after entering a longitudinal study, most women with AN and BN achieved full recovery from their ED and, likewise, were free from MDD and SUD. Compared to those who had not fully recovered from their ED, those who had recovered were twice as likely *not* to be diagnosed with MDD in the past year and five times as likely *not* to be diagnosed with SUDs in the past year. These findings provide evidence that long-term recovery from EDs is likely to be full such that improvements in ED psychopathology are associated with an absence of these common comorbidities.

Consistent with prior studies [12–14], we found that individuals who had recovered from their EDs were less likely to be depressed than those who were actively ill with their ED. It is possible that the lower frequency of comorbid MDD observed in individuals who had recovered from their EDs could be a result of the disappearance of the negative consequences of eating disorders on mood. For example, some of the symptoms of major depression may be exacerbated by, or even secondary to, the eating disorder symptoms themselves (e.g., starvation, distress about shape and weight). At 22-year follow-up, whereas 38% of those with active ED met criteria for MDD, just 22% of those without an active ED met criteria for MDD. However, the frequency of MDD in the recovered group was double the population prevalence of MDD reported in epidemiological studies, which is approximately 10% [25,26]. Given that depression has been shown to increase risk for relapse and premature death in those with EDs, it may be that this subset of women with MDD following ED recovery at long-term follow-up represents a vulnerable patient subgroup who warrants heightened clinical monitoring.

To our knowledge, this is the first study to document that those who have recovered from their EDs were less likely to have SUDs than those who were actively ill with EDs at long-term follow-up. Prevalence of SUDs at 3% in our recovered sample is comparable to that reported in epidemiological studies [25,26]. Given the grave risks of comorbid SUDs in those with EDs, our finding that SUDs were reduced in those who achieved ED recovery, and occurred at comparable rates to those in the general population, is positive. Whereas some psychodynamic

Table 1

Associations between eating disorders and major depressive disorder and substance use disorders at 22-year follow-up.

	No ED	ED	Total
MDD (n, %)	25 (22%)	24 (38%)	49 (28%)
No MDD (n, %)	88 (78%)	39 (62%)	127 (72%)
SUD (n, %)	3 (3%)	8 (13%)	11 (6%)
No SUD (n, %)	110 (97%)	55 (87%)	165 (94%)
Total (n, %)	113 (64%)	63 (36%)	176

ED = Eating Disorder, MDD = Major Depressive Disorder, SUD = Substance Use Disorder.

theorists have suggested that symptom substitution will occur [27], such that as eating disorder symptoms remit, other behavioral expressions of symptoms—often particularly impulsive ones—may emerge or intensify, our findings do not support this model in ED recovery based on 22-year data.

Contemporary transdiagnostic conceptualization of psychopathology suggests that certain pathophysiology may underlie a spectrum of psychiatric disorders [28]. In addition to arguing for a potential shared etiology, this approach supports the idea of transdiagnostic maintaining mechanisms of illness which may be targeted in treatment to reduce more than one psychiatric disorder. For example, the systematic review conducted by Sloan et al. [29] supports the conceptualization of emotion regulation as a transdiagnostic construct underlying depression, substance use, eating pathology, and other psychopathologies. Similarly, a recent network analysis [30] identified that sensitivity to physical sensations, including a lack of interest in sex and abnormalities in appetite, as well as irritability, were highly central to both BN and depression symptom networks bridging the comorbidities, suggesting that interventions that target these sensitivities may reduce both illnesses.

Study strengths included the prospective longitudinal design with a well-retained cohort (77% of the original sample) and the use of structured clinical interviews to evaluate ED and two common psychiatric comorbidities 22 years after study initiation. One limitation was the narrow focus on females who met full criteria for AN and BN and were seeking treatment in the greater Boston area in the late 1980s, which may render findings less generalizable to those not seeking treatment or even to those receiving currently available evidence-based interventions. Further, although our sample retention was high, we do not have data for all of our participants. In addition, as our study was not powered sufficiently to do so, future research might investigate diagnosis-specific risk for comorbidities in eating disorders.

4.1. Conclusions

Because comorbidity in EDs can predict poor outcomes, including greater risk for relapse and premature death, our findings of reduced risk for psychiatric comorbidity following recovery at long-term follow-up is cause for optimism. Perhaps when achieved in the long-term (i.e., more than two decades post-presentation for an ED) recovery is not only full, but may also, in turn, be more durable. Whether those women with comorbidity even following ED recovery indeed represent a patient subgroup at increased risk over time warrants further study. Prospective longitudinal follow-up studies have the potential to shed light on durability of ED recovery and long-term survival.

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