Suicide Attempts in Anorexia Nervosa

Cynthia M. Bulik, PhD, Laura Thornton, PhD, Andréa Poyastro Pinheiro, MD, PhD, Katherine Plotnicov, PhD, Kelly L. Klump, PhD, Harry Brandt, MD, Steve Crawford, MD, Manfred M. Fichter, MD, Katherine A. Halmi, MD, Craig Johnson, PhD, Allan S. Kaplan, MD, James Mitchell, MD, Detlev Nutzinger, MD, Michael Strober, PhD, Janet Treasure, MD, D. Blake Woodside, MD, Wade H. Berrettini, MD, PhD, and Walter H. Kaye, MD

Objective: To explore prevalence and patterns of suicidal attempts in persons with anorexia nervosa (AN). Methods: Participants were the first 432 persons (22 male, 410 female) enrolled in the NIH funded Genetics of Anorexia Nervosa Collaborative Study. All participants had current or lifetime AN. The participants ranged in age from 16 to 76 (mean = 30.4, SD = 11.3). Suicidal behavior and intent was assessed via the Diagnostic Interview for Genetic Studies. We compared frequency and severity of attempts across diagnostic subtypes and comorbidity, and personality features associated with the presence of suicide attempts in persons with AN. **Results:** About 16.9% of those with AN attempted suicide. Significantly fewer persons with the restricting subtype (7.4%) reported at least one attempt than those with purging AN (26.1%), AN with binge eating (29.3%), and a mixed picture of AN and bulimia nervosa (21.2%). After controlling for major depression, suicide attempts were associated with substance abuse, impulsive behaviors and traits, Cluster B personality disorders, panic disorder, and post-traumatic stress disorder as well as low self-directedness and eating disorder severity. **Conclusions:** Suicide attempts in AN are not uncommon, are frequently associated with the intention to die, occur less frequently in persons with the restricting subtype of the illness, and after controlling for depression are associated with a constellation of behaviors and traits associated with behavioral and affective dyscontrol. **Key words:** anorexia nervosa, bulimia nervosa, eating disorders, suicide.

AN = anorexia nervosa; **BN** = bulimia nervosa; **RAN** = restricting anorexia nervosa; **PAN** = purging anorexia nervosa; **AN(B)** = binging anorexia nervosa; **EDNOS** = eating disorder not otherwise specified; **ANBN** = lifetime history of both AN and BN.

INTRODUCTION

Suicide is a major cause of death among persons with anorexia nervosa (AN). Suicide rates are higher in AN in comparison to the general population. In a meta-analysis, Pompili et al. (1) reviewed nine studies of suicide in AN and reported that the expected mean number of suicides was eight times higher in persons with AN than in a general population of young women (age 14–25). Sullivan (2) examined 42 studies and reported that the mortality rate for AN was 5.6% per decade, with suicide as the second most common cause of death after complications of the eating disorder.

Franko and Keel (3) extensively reviewed the published studies on suicide and suicide attempts in persons with eating disorders, and reported that suicide attempts occur in 3% to 20% of patients with AN, whereas the standardized mortality ratio for suicide ranges from 1.0 to 5.3. In an earlier report (4), this group assessed suicidality in an 8-year prospective longitudinal study with 246 women with AN and bulimia nervosa (BN). They found that women with AN were more likely to attempt suicide than women with BN, and that severity of both depressive symptoms and drug use over the course of the study were the unique predictors of suicide among women with AN. In contrast, Bulik et al. (5) have shown that women with AN are likely to attempt suicide regardless of the presence of lifetime major depression. In terms of eating disorder subgroups and suicide attempts, previous studies (6) indicate that suicide attempts are more likely to occur among patients with binge or purge subtype than restricting AN. Other clinical correlates of suicidality include a history of physical and/or sexual abuse (6,7) and certain personality features such as high persistence, low self-directedness, and high self-transcendence (5).

Based on the aforementioned, the goal of the present study was to examine the prevalence and severity of suicide attempts in a sample of phenotypically well-characterized women with AN ascertained for a genetic study, and also to assess differences in suicidal behavior (number of attempts, severity, and premeditation), psychiatric comorbidity, and personality features across distinct AN subtypes. One goal of this study is to optimize phenotyping for genetic analysis. Because there is evidence that approximately 45% of the variability of suicidal thoughts and behavior may be explained by genetic factors (95% confidence interval, 33%–51%) (8), investigating suicidal behavior in eating disorder subtypes may help to refine diagnostic phenotypes for future molecular studies of vulnerability genes and environmental mediators of the major eating disorders.

From the Department of Psychiatry, University of North Carolina, Chapel Hill, North Carolina (C.M.B., L.T., A.P.P.); Department of Psychiatry, University of Pittsburgh, Pittsburgh, Pennsylvania (K.P., W.H.K.); Department of Psychology, Michigan State University, East Lansing, Michigan (K.L.K.); Department of Psychiatry, University of Maryland School of Medicine, Baltimore, Maryland (H.B., S.C.); Klinik Roseneck, Hospital for Behavioral Medicine and University of Munich (LMU), Munich, Germany (M.M.F.); New York Presbyterian Hospital-Westchester Division, Weill Medical College of Cornell University, White Plains, New York (K.A.H.); Laureate Psychiatric Clinic and Hospital, Tulsa, Oklahoma, (C.J.); Department of Psychiatry, The Toronto Hospital, Toronto, Canada (A.S.K., D.B.W.); Department of Psychology, Neuropsychiatric Research Institute, Fargo, North Dakota (J.M.); Bad Bramstedt Hospital for Behavioral Medicine and University of Lübeck, Lübeck, Germany (D.N.); Neuropsychiatric Institute and Hospital, School of Medicine, University of California at Los Angeles, Los Angeles, California (M.S.); Department of Psychiatry, Institute of Psychiatry, Kings College, London, United Kingdom (J.T.); Department of Psychiatry, University of Pennsylvania, School of Medicine, Philadelphia, Pennsylvania (W.H.B.).

Address correspondence and reprint requests to Cynthia M. Bulik, PhD, Department of Psychiatry, University of North Carolina at Chapel Hill, 101 Manning Drive, CB #7160, Chapel Hill, NC 27599-7160. E-mail: cbulik@med.unc.edu

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METHOD

Participants

Participants were the first 432 persons enrolled in the NIH funded Genetics of Anorexia Nervosa Collaborative Study. Data were collected between March 2003 and March 2005. Probands provided informed consent to participate and permission for the contact of their willing affected relatives and parents in accordance with institutional review board requirements of each participating site. All probands and affected relatives signed informed consent. The full methods for this investigation are presented in a separate publication (9). Briefly, probands were male or female, age 16 or older, ill or recovered. They must have met a lifetime diagnosis of DSM-IV AN, with or without amenorrhea, at least 3 years before study entry and by age 45. The amenorrhea criterion was waived because of its lack of applicability to men and the unreliability of its retrospective assessment in women. The threshold for low weight was defined as a body mass index (BMI) at or below 18 kg/m^2 for women and 19.6 kg/m^2 for men, which correspond to the 5th percentile BMI values of the NHANES epidemiological sample of women and men, respectively, for the average age range (27–29 years) of the probands in our previous studies (10). No probands had regular binge eating, defined in accordance with the DSM-IV guidelines for "regular" binge episodes in BN, as at least twice a week for at least 3 months. They were required to have at least one first-, second-, or third-degree relative with AN, excluding parents and MZ twins, who was willing to participate in the study. Potential probands were excluded from the study if they had a history of severe CNS trauma, psychotic disorders, or developmental disability, or if they had a medical, neurological, or substance use disorder that could confound the diagnosis of AN or interfere with their responding cogently to assessments. Those with a maximum lifetime BMI exceeding 30 kg/m^2 were excluded, as were those who did not speak either English or German.

All affected relatives also had AN and were required to meet the same inclusion criteria as probands with the exception that regular binge eating was permitted. Although they need not have met AN criteria 3 years before the study, they were required to have had a minimal duration of at least 3 months at the low weight as outlined above. Affected relatives could have had a diagnosis of BN.

Thus, probands (n = 194) and affected relatives (n = 219) included in this study had the following eating disorder subtypes: restricting anorexia nervosa (RAN) defined as no lifetime binge eating or purging; purging anorexia nervosa (PAN) defined as having engaged in purging behaviors (vomiting, laxative, or diuretic abuse) but no binge eating; and binging anorexia nervosa [AN(B)] defined as having had irregular or regular (affected relatives only) binging behavior with or without purging. Seventy of the participants had a current eating disorder diagnosis, the remaining participants had not had an eating disorder symptom in at least 12 months.

There were no exclusion criteria for biological parents. Additional affected relatives with the diagnosis of AN, BN, or Eating Disorder Not Otherwise Specified (EDNOS) were included as long as the family already had a fully ascertained proband and affected paired relative. Any individual who had a lifetime history of both AN and BN was classified as subtype ANBN.

Assessments

In this section, we present an overview of the assessment instruments used for this analysis. A complete treatment including rationale for inclusion of all measures can be found in Kaye et al. (9).

Eating Disorder Pathology

Three interviews were used to assess eating disorder pathology. The Extended Screening instrument, an expanded modified version of Module H of the Structured Clinical Interview for Axis I Disorders (SCID-I) (11) was used to establish the diagnoses of eating disorders and assess for all other inclusion and exclusion criteria. In addition, The Structured Interview for Anorexia Nervosa and Bulimic Syndromes (SIAB) was administered to confirm the eating disorder diagnosis and to obtain additional information on core eating disorder behaviors. The SIAB (12) is a detailed structured interview schedule that derives information relevant to lifetime severity of psychopathological factors, including body image and slimness ideal, bulimic symptoms, measures to counteract weight gain, fasting and substance abuse, and atypical binges www.epi.med.uni-muenchen.de. The internal consistency of the SIAB subscales on the lifetime version of the instrument has been shown to be moderate to high with Cronbach's alpha ranging from 0.78 to 0.91 for five of the six components (12). Likewise, the inter-rater reliability for these same subscales has been shown to be excellent, ranging between 0.86 and 0.96 (12). Participants were asked to report worst lifetime symptoms. Finally, the Yale-Brown-Cornell Eating Disorder Scale (YBC-EDS) (13), was used to assess core obsessions and compulsions specific to eating disorders (e.g., those related to food, eating, weight, and exercise) and to rate the current and lifetime severity of the eating disorder. Excellent inter-rater reliability, internal consistency, and convergent validity have been demonstrated (14).

General Psychopathology

The Diagnostic Interview for Genetic Studies (DIGS) (15) was used to assess lifetime psychotic symptoms and affective disorders in accordance with other NIMH-sponsored genetic studies. It has a) polydiagnostic capacity; b) a detailed assessment of the course of illness, chronology of psychotic and mood syndromes, and comorbidity; c) additional phenomenologic assessments of symptoms; and d) algorithm scoring capability. The two-phase test-retest reliabilities (within-site, between-site) have been shown to be excellent (0.73–0.95), except for schizoaffective disorder (15). Subsequent studies have revealed good to excellent inter-rater test-retest reliability for mood disorders, schizophrenia, and substance use disorders (16–18). Section O of the DIGS includes an extensive evaluation of suicidal ideation and behavior. Items in Section O include Have you ever tried to kill yourself? How many times have you tried to kill yourself? How many attempts led to medical care? How old were you when you first tried to kill yourself? How did you try to kill yourself? Did you want to die? Did you think you would die from what you had done? Did the suicidal behavior described above occur during an episode of depression, bipolar, alcohol abuse, drug abuse, psychosis, or other? In addition, the interviewer was asked to rate the intent, lethality, and premeditation of the most serious attempt. Responses from Section O form the basis of the analyses for this investigation.

The SCID-1 (Research Version) (11) and the Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SCID-II) are semistructured clinical interviews designed to make the major DSM-IV Axis I diagnoses and to assess personality disorders, respectively. For the current study, SCID I was used to assess substance disorders and anxiety disorders. An individual was assigned a positive score for any of the psychoactive substances if they had a history of either abuse of or dependence for alcohol, stimulants, sedatives, cannabis, cocaine, opiates, hallucinogens, other, or polysubstance. SCID II was used to obtain information regarding Cluster B personality disorders.

Personality and Symptom Assessments

Temperament and Character Inventory (19) measures seven dimensions of temperament and character of which five were utilized for this report: novelty seeking, harm avoidance, persistence, self-directedness, and self-transcendence. The Barrett Impulsivity Scale (BIS-11) (20) is a 30-item self-report measure of impulsiveness. This scale provides three measures of impulsivity: motor, cognitive, and nonplanning. The Eatatelife Phenotype (EATATE), Version 2.1, January 19, 2001 (21), was administered as another measure of personality traits. This instrument assesses childhood perfectionism and rigidity retrospectively. The data gathered on 12 impulsive behaviors—binge eating, excessive alcohol consumption, shoplifting or stealing, gambling, hitting someone or breaking things, provoking fights or arguments, firesetting, self harm, overdosing, using street drugs, excessive spending, disinhibited or reckless sexual activities—were evaluated in the present study.

Statistical Analyses

All statistical analyses were performed using SAS/STAT 9.1 software (22). Differences by AN subtype in whether a person attempted suicide were evaluated by PROC MULTTEST. Fisher exact tests were used to assess differences across AN subtypes in intent, premeditation, degree of violence, and seriousness of attempt.

Logistic regressions were used to assess whether the presence of suicide attempts could be predicted from measures of eating disorder severity, impulsivity, impulsive behaviors, harm avoidance, novelty seeking, persistence, self-directedness, self-transcendence, anxiety disorders, Cluster B personality disorders, and substance use disorder. It should be noted that those who attempted suicide had a significantly ($\chi^2 = 21.1, p < .001$) higher prevalence of lifetime major depression (87.1%, $n = 61$) than those that had no suicide attempt (62.8%, $n = 214$). Thus, the dichotomized diagnostic variable of lifetime major depression was added to all models as a covariate as was age at interview. All continuous variables were standardized.

Generalized Estimating Equations corrections were used in the logistic regressions to account for the nonindependence of the data due to the inclusion of affected relatives in the analyses (23–25). These statistical analyses were conducted using the GENMOD procedure of SAS version 8.1 (22). All tests were two-tailed. Chi-square and p values were given for the models. p values were adjusted for multiple testing using the method of false discovery rate (26).

RESULTS

Of the first 432 persons enrolled in the study, 19 did not have information from Section O of the DIGS. Seventy (16.9%) of the remaining 413 participants reported at least one suicide attempt, representing 66 separate families—four families had two sisters with an eating disorder who both attempted suicide. Usable data from the DIGS section O were available for 69 of these who constitute the suicide sample for this report.

Significantly fewer persons with RAN [7.4%; (15/202)] reported at least one attempt than those with PAN [26.1%; (30/115), $p < .001$], AN(B) [29.3%; (17/58), $p < .001$], and ANBN [21.2%; (7/33) $p = .01$].

Of those who had attempted suicide, 36 persons (52.2%) reported one attempt, 27 persons (39.1%) reported between 2 and 4 attempts, and 6 persons (8.7%) reported ≥5 attempts. The following results describe the worst attempt at suicide.

The age of first attempt for all persons with at least one suicide attempt was 7 to 40 years. Of all participants who attempted suicide, 38 (55.1%) required medical attention for the most serious (or only) attempt and 32 (46.4%) were hospitalized. Of the 32 who were hospitalized, 16 went to a medical hospital exclusively (6 to the emergency room, 10 were admitted), 4 went to a psychiatric hospital (3 voluntary, 1 involuntary), and 12 were at both types of institutions.

For those who had more than one attempt, 8 (26.7%) reported no attempts requiring medical care, 21 (70.0%) reported one to four attempts that required medical care, and one individual (3.3%) reported six attempts that required medical care.

In terms of intent, 54 (78.3%) wanted to die (2 did not know). Thirty-nine (56.5%) thought they would actually die, 4 (5.8%) did not know, and 26 (37.7%) did not think they would die. Moderate or serious attempts were defined as those attempted by the persons who had a definite intent to die but were ambivalent or who definitely expected to die. By this definition, 50 (72.4%) had a moderate or serious intent score. Eleven (15.9%) were considered violent attempts (e.g., gunshot, stabbing, hanging, jumping from a high place).

Moderate (e.g., briefly unconscious) to extreme (e.g., prolonged coma or respiratory arrest) severity was reported in 37 (53.6%) persons who attempted suicide.

In terms of premeditation of the event, 33 (49.2%) were impulsive, 17 (25.4%) were somewhat premeditated, and 17 (25.4%) were thoroughly premeditated.

When asked about active comorbid disorders at the time of attempt, 56 (81.2%) reported that the worst (or only) attempt occurred during a depressive episode, 12 (17.4%) reported alcohol abuse at the time of the attempt, 6 (8.7%) reported drug abuse at the time of the attempt, and 4 (5.8%) reported some other disorder at the time of the attempt. There were no reports of bipolar illness or psychosis. Of those who had no suicide attempts, 62.8% (214) had lifetime major depression. For those who had suicide attempts, 87.1% (61) had lifetime major depression ($\chi^2 = 21.16$, $p < .001$, OR = 4.05, 95% confidence interval, 1.96, 8.37).

We explored whether intent, premeditation, degrees of violence, and seriousness of attempt differed across AN subtypes, and no significant differences were observed.

Table 1 presents the frequencies, means, and statistical comparisons between those who had and had not attempted suicide for various impulsivity variables, measures of anxiety, and personality measures.

After controlling for depression, those who attempted suicide were significantly more likely to drink excessively, overdose, use illicit substances, steal or shoplift, and engage in self-injurious behavior. They were also more likely to have a history of substance abuse or dependence, panic disorder, PTSD, and were more likely to have Cluster B personality disorders. These persons also had lower self-directedness scores and higher scores for harm avoidance and the cognitive scale of the BIS. They exhibited greater severity of eating disorders symptoms on the YBC-EDS than those who did not attempt suicide.

DISCUSSION

Although considerable data exist confirming that persons with AN are at increased risk for suicide, this report highlights that suicide attempts are frequent occurrences in this population, are often severe, and associated with an intention to die. Of those who attempted suicide, more than two thirds required medical care, three quarters wanted to die, and more than half fully intended to die as a result of their worst attempt. A previous investigation (5) examined suicidal intent and medical lethality in a sample of women with AN, BN, and major depression and reported a trend for more serious intention to die in women with AN and major depression than those with BN, although no difference in the degree of medical threat across the three groups was detected. In light of these results, careful assessment of not only the presence of suicidal ideation, but the degree of lethality and intention to die should be a routine aspect of evaluation and treatment efforts in women with AN.

In the present study, suicide attempts were reported by 16.9% of participants which is lower than some previous reports (4,5,27) and comparable to others (28). This inconsistency may be due to several factors, including the source of the samples and the study design. Participants in the present

TABLE 1. Results From Logistic Regressions Predicting Presence or Absence of Suicide Attempts From Measures of Impulsivity, Impulsive Behaviors, and Personality[a]

Variable	No Suicide Attempts (n = 343), % (n) or Mean (SD)	At Least 1 Suicide Attempt (n = 69), % (n) or Mean (SD)	χ^2 (p)	OR (95% CI)
EATATE phenotype				
Binge eating	22.2% (76)	32.4% (22)	2.16 (.200)	—
Excessive drinking	17.0% (58)	41.2% (28)	10.82 (.004)	3.09 (1.73, 5.53)
Shoplifting or stealing	8.5% (29)	19.1% (13)	5.55 (.044)	3.14 (1.54, 6.42)
Gambling	0.3% (1)	0.0% (0)	—	—
Hitting someone or breaking things	7.6% (26)	17.6% (12)	4.18 (.079)	—
Provoking fights/arguments	9.7% (33)	17.6% (12)	2.25 (.198)	—
Firesetting	0.3% (1)	1.5% (1)	0.83 (.433)	—
Cutting/burning/hitting/biting yourself	16.4% (56)	58.8% (40)	29.10 (<.001)	7.56 (4.07, 14.07)
Overdosing	3.2% (11)	36.8% (25)	21.96 (<.001)	15.47 (7.04, 33.97)
Substance use	7.4% (25)	22.1% (15)	8.04 (.016)	3.55 (1.79, 7.04)
Over spending	9.4% (32)	20.9% (14)	4.63 (.066)	—
Reckless or disinhibited sexual activity	5.6% (19)	13.2% (9)	3.11 (.142)	—
Structured Clinical Interview for DSM Axis I and Axis II Disorders				
Agoraphobia	1.8% (6)	2.9% (2)	0.05 (.856)	—
Generalized anxiety disorder	9.7% (33)	15.7% (11)	1.03 (.400)	—
Overanxious disorder	29.7% (102)	46.4% (32)	2.88 (.155)	—
Obsessive-compulsive disorder	42.6% (146)	61.4% (43)	4.60 (.067)	—
Panic disorder	9.1% (31)	24.3% (17)	6.19 (.035)	2.74 (1.43, 5.25)
Post-traumatic stress disorder	7.4% (25)	33.8% (23)	13.33 (.002)	5.48 (2.73, 11.02)
Separation anxiety disorder	7.4% (25)	15.9% (11)	2.77 (.163)	—
Social phobia	18.4% (63)	27.1% (19)	0.78 (.435)	—
Specific phobia	9.6% (33)	11.4% (8)	0.02 (.898)	—
Any anxiety disorder	63.9% (218)	85.7% (60)	7.33 (.020)	2.48 (1.20, 5.12)
Psychoactive substance abuse and dependence	20.1% (68)	55.1% (38)	18.37 (<.001)	4.70 (2.59, 8.55)
Cluster B personality disorders	3.3% (11)	14.5% (10)	5.47 (.046)	4.25 (1.63, 11.11)
Barratt Impulsivity Scale-11				
Cognitive	16.6 (4.4)	19.2 (4.6)	11.34 (.004)	1.67 (1.26, 2.21)
Motor	20.0 (4.0)	20.7 (5.1)	1.31 (.341)	—
Nonplanning	22.8 (4.7)	24.0 (5.7)	2.56 (.163)	—
Temperament and Character Inventory				
Harm avoidance	18.9 (7.7)	24.9 (5.9)	23.69 (<.001)	2.31 (1.67, 3.19)
Novelty seeking	17.0 (6.4)	17.2 (6.9)	0.29 (.634)	—
Persistence	5.9 (1.9)	5.7 (2.2)	0.98 (.401)	—
Self-directedness	29.6 (8.2)	23.6 (7.8)	17.18 (<.001)	0.50 (0.37, 0.67)
Self-transcendence	12.4 (6.5)	13.4 (6.5)	0.61 (.482)	—
Yale-Brown-Cornell Eating Disorders Scale				
Worst total score	22.6 (6.2)	25.7 (6.2)	7.92 (.016)	1.64 (1.07, 2.53)

[a] Age at interview and history of major depression were entered as covariates in all models. p values have been corrected for multiple testing by FDR.

study were ascertained for a genetic investigation of eating disorders and were recruited both from treatment centers and from community advertisements. Treatment seeking was not necessarily related to participation, whereas many other studies focus on treatment samples.

Previous studies on clinical samples have also yielded somewhat contradictory results in terms of differences across subgroups with some finding no differences across AN and BN (5,27,28); more frequent attempts in persons with BN than AN (6,29); and more frequent attempts in persons with AN than BN (4). Franko and Keel (3) underscored the importance of dividing participants into restricting versus binge or purge subtype in calculating suicide rates. Indeed, when this distinction is made, some consistency emerges in that suicide attempts are more likely to occur in the binge or purge than the restricting subtype of AN (6,27), which we also observed in the present study.

Our observations of higher major depression in those who attempt suicide corroborate previous reports (6,7,30,31). Given the ubiquity of this observation, we opted to control for depression in our analyses. This yielded a clearer picture of comorbid psychopathology independent of depression revealing elevated panic disorder, post-traumatic stress disorder, substance abuse or dependence, Cluster B personality disorders, and various impulse-control disturbances including self-harm, stealing, and shoplifting in those who attempted suicide. This anxious impulsive comorbid profile was further illuminated by the personality profiles marked by lower self-direct-

edness, higher harm avoidance, and higher scores on the cognitive subscale of the BIS. Current evidence suggests that suicidality is associated with anxious personality traits such as harm avoidance and neuroticism in various psychiatric and community samples (5,32–35). Moreover, impulsivity, high novelty seeking and low self-directedness have also been reported in those who attempt or complete suicide (36–38). The coexistence of anxious and impulsive traits may converge to increase suicidal risk.

These comorbid and personality profiles may be reflected in the rather high percentage of those who reported that their suicide attempts were impulsive (i.e., not premeditated). Thus, although depression may be a major contributing factor to suicide attempts in persons with AN, other factors associated with impulsivity and behavioral and affective dyscontrol also seem to play a role. Although the presence of such multi-impulsive traits has been noted in BN (39) and associated with suicide attempts in that group (40), our results underscore that a similar constellation may influence suicidal behavior in AN.

Several limitations of this study should be acknowledged. In addition to describing the prevalence and severity of suicide attempts, we also examined correlates of suicidal behavior. As ours was a cross-sectional design, our assessments were not necessarily made at a time point near the suicide attempt. Second, we did not have either a pathological control or a healthy comparison group, which precluded comparisons of suicide attempt rates and severity with other psychiatric disorders, including BN and EDNOS. Our assessments did not include information about traumatic life events and treatment status of the participants at the time of the suicide attempt. In addition, participants originated from families with more than one affected member. Persons from multiplex families may differ in systematic ways from sporadic cases. The impact of suicide in one affected family member on the risk of another affected family member attempting suicide is unknown. Therefore the generalizability of the present results to other AN samples might be limited.

As stated by Franko and Keel (3), although the frequency of suicide attempts is not consistently different between persons with AN and BN, completed suicides are much more common in those with AN. Although by the nature of our design, we did not include observations of those who had completed suicide, our findings confirm and extend previous studies in that a substantial proportion of women with AN attempt suicide and that these attempts are severe and pose serious threats to their lives. Clinicians who treat eating disorders should remain attentive to the presence of comorbid disorders and traits (e.g., depression, substance abuse, impulsivity, and low self-directedness) and suicidal risk throughout the treatment of persons who suffer from AN. Intervention studies can also assist in tailoring treatments aimed at reducing the occurrence of suicide attempts. Finally, genetic studies may shed light on the complex interaction of genes and environmental factors that contribute to suicidal vulnerability in women with eating disorders.

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