Original Investigation

Familial Liability for Eating Disorders and Suicide Attempts
Evidence From a Population Registry in Sweden

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IMPORTANCE Suicide attempts are common in individuals with eating disorders. More precise understanding of the mechanisms underlying their concomitant occurrence is needed.

OBJECTIVE To examine the association between eating disorders and suicide attempts and whether familial risk factors contribute to the association.

DESIGN, SETTING, AND PARTICIPANTS A Swedish birth cohort including individuals born in Sweden between January 1, 1979, and December 31, 2001, was followed up from age 6 years to December 31, 2009 (N = 2 268 786). Information was acquired from Swedish national registers. All individuals were linked to their biological full siblings, maternal half siblings, paternal half siblings, full cousins, and half cousins. Data analysis was conducted from October 5, 2014, to April 28, 2015.

MAIN OUTCOMES AND MEASURES Eating disorders were captured by 3 variables (any eating disorder, anorexia nervosa, and bulimia nervosa) identified by any lifetime diagnoses recorded in the registers. Suicide attempts were defined as any suicide attempts, including death by suicide, recorded in the registers. We examined the association between eating disorders and death by suicide separately, but the study was underpowered to explore familial liability for this association.

RESULTS Of 2 268 786 individuals, 15 457 females (1.40% of all females) and 991 males (0.09% of all males) had any eating disorder, 7680 females (0.70%) and 453 males (0.04%) had anorexia nervosa, and 3349 females (0.30%), and 61 males (0.01%) had bulimia nervosa. Individuals with any eating disorder had an increased risk (reported as odds ratio [95% CI]) of suicide attempts (5.28 [5.04-5.54]) and death by suicide (5.39 [4.00-7.25]). The risks were attenuated but remained significant after adjusting for comorbid major depressive disorder, anxiety disorder, and substance use disorder (suicide attempts: 1.82 [1.72-1.93]; death by suicide: 2.04 [1.49-2.80]). Similar results were found for anorexia nervosa (suicide attempts: crude, 4.42 [4.12-4.74] vs adjusted, 1.70 [1.56-1.85]; death by suicide: crude, 6.46 [4.38-9.54] vs adjusted, 2.67 [1.78-4.01]) and bulimia nervosa (suicide attempts: crude, 6.26 [5.73-6.85] vs adjusted, 1.88 [1.68-2.10]; death by suicide: crude, 4.45 [2.44-8.11] vs adjusted, 1.48 [0.81-2.72]). Individuals (index) who had a full sibling with any eating disorder had an increased risk of suicide attempts (1.41 [1.29-1.53]). The risk was attenuated for any eating disorder in more-distant relatives (maternal half siblings, 1.10 [0.90-1.34]; paternal half siblings, 1.21 [0.98-1.49]; full cousins, 1.11 [1.06-1.18]; half cousins, 0.90 [0.78-1.03]). This familial pattern remained stable after adjusting for the index individuals' eating disorders. Similar patterns were found for anorexia nervosa and bulimia nervosa.

CONCLUSIONS AND RELEVANCE These results suggest an increased risk of suicide attempts in individuals with lifetime eating disorders and their relatives. The pattern of familial coaggregation suggests familial liability for the association between eating disorders and suicide. Psychiatric comorbidities partially explain this association, suggesting particularly high-risk presentations.

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Eating disorders, including anorexia nervosa (AN) and bulimia nervosa (BN), are severe psychiatric disorders with peak onset during adolescence and early adulthood.[1] The disorders are associated with high premature mortality,[2] including elevated risk of suicide.[3-5] Based on meta-analyses, approximately 1 of 5 premature deaths in patients with AN was due to suicide[2]; suicide-specific standardized mortality ratios were estimated to be 18.1 in AN[4] and 7.5 in BN.[3] However, studies included in the meta-analyses reported considerably varied estimates, possibly owing to differences in follow-up time, source, sample size, and representativeness of the samples.[2,3,6] Large population-based studies are essential to provide more reliable estimates of the risk of suicide in individuals with eating disorders.

The mechanism underlying the association between eating disorders and suicide attempts remains unclear. Few studies have been adequately powered to explore the influence of psychiatric comorbidities on the association,[2] although major depressive disorder (MDD), anxiety disorders, and substance use disorder have been associated with both eating disorders and suicide attempts.[7-10] Evaluating the influence of psychiatric comorbidities on the elevated suicide risk in eating disorders can elucidate the mechanism underlying suicide attempts in individuals with eating disorders and inform clinical decision making in suicide prevention.

Both eating disorders and suicide attempts aggregate in families[11,12]; however, their coaggregation in families has not been thoroughly explored, with the exception of investigations on the effect of family history of a range of psychiatric disorders on suicide.[13,14] Genetically informative designs, such as comparison of the coaggregation of disorders across relatives with different degrees of relatedness, can provide information on the extent to which familial risk factors influence the association between eating disorders and suicide attempts.[15,16] Using a genetically informative design and population data from Swedish national registers, we estimated the association between eating disorders and suicide attempts before and after accounting for the effect of psychiatric comorbidities and investigated the extent to which familial risk factors contributed to the association.

Methods

The study was approved by the regional ethics review board in Stockholm, Sweden. The requirement for informed consent was waived because the study was based on population registers. Individuals in the study population were not identifiable at any time.

Study Population and Swedish National Registers

The study population included individuals born in Sweden between January 1, 1979, and December 31, 2001, and had both biological parents identifiable in the population registers; adopted individuals and individuals who had emigrated or died before age 6 years were excluded yielding a final sample of 2 268 786 individuals, of whom 51.4% were males. We followed up the study population until December 31, 2009, when the youngest individuals were aged 8 years and the oldest individuals were aged 30 years. Using unique personal identification numbers, we linked several Swedish registers.[17] In line with previous research based on Swedish population registers,[16] we obtained data on birth year and sex from the Total Population Register (Statistics Sweden). We linked individuals to their biological parents using the Multi-Generation Register.[18] Immigration and emigration data were obtained from the Migration Register (Statistics Sweden). We obtained records from the National Patient Register (NPR) (National Board of Health and Welfare) of psychiatric inpatient (since 1973) and outpatient (since 2001) contacts from across Sweden. Discharge diagnoses were recorded according to the Swedish versions of the *International Classification of Diseases, Eighth Revision* (*ICD-8*) (1973-1986) and *Ninth Revision* (*ICD-9*) (1987-1996) and the *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* (*ICD-10*) (1997 to present).[19] From the Swedish National Quality Assurances Register for Specialized Eating Disorder Treatment (Riksät) (since 1999) and the Internet-based quality assurance system for eating disorders (Stepwise database,[20,21] since 2005), we obtained eating disorder diagnoses from across Sweden. The coverage of the quality registers (Riksät and Stepwise) increased over time.[22] Diagnoses in both quality registers were coded based on the *DSM-IV-TR*,[23] and individuals were registered once intent-to-treat status was established. We acquired causes of death coded according to *ICD*, revisions 8 to 10 from the Cause of Death Register (National Board of Health and Welfare).

Identification of Families and Relatives

Using the Multi-Generation Register, we identified 5 cohorts of biological relatives representing decreasing levels of shared genetic and environmental relatedness: full siblings, maternal half siblings, paternal half siblings, full cousins, and half cousins (offspring whose parents are half siblings). Family identification numbers linked the relatives and were used to statistically control for nonindependence within the data.

Eating Disorders

Based on lifetime diagnoses of eating disorders in the NPR and the quality registers, we defined 3 analytic sets that were not mutually exclusive: (1) any eating disorder, defined as *ICD-9* codes 307B or 307F and *ICD-10* codes F50.0, F50.1, F50.2, F50.3, or F50.9 in the NPR, or meeting *DSM-IV* criteria for eating disorders (AN, atypical AN, BN, atypical BN, or eating disorders not otherwise specified) in the quality registers; (2) AN, defined as any diagnosis of AN or atypical AN, identified with *ICD-9* code 307B and *ICD-10* codes F50.0 or F50.1 in the NPR, or meeting *DSM-IV* criteria for AN or atypical AN in the quality registers (other lifetime eating disorders could be present); and (3) BN, defined as any diagnosis of BN or atypical BN, identified with *ICD-10* codes F50.2 or F50.3 in the NPR, or meeting *DSM-IV* criteria for BN or atypical BN in the quality registers (other lifetime eating disorders could be present). The period of BN diagnosis was shorter than that of any eating disorder and AN because BN was not an independent eating disorder category in the Swedish versions of *ICD* before *ICD-10*.[24]

Suicide Attempts

Suicide attempts were defined as any suicide attempt reported in the NPR or death by suicide reported in the Cause of Death Register, based on *ICD-9* codes E950 through E959 and E980 through E989 and *ICD-10* codes X60 through X84 or Y10 through Y34.[16] We examined the association between eating disorders and death by suicide separately, but the study was underpowered to explore familial liability for this association.

Comorbid Psychiatric Disorders

Psychiatric comorbidities were identified from the NPR and included MDD (*ICD-9* codes 296.3, 300.4, or 311 and *ICD-10* codes F32-F39 [except F34.0]), anxiety disorder (*ICD-9* codes 300, 300.09, or 300.29 and *ICD-10* codes F40-F41), and substance use disorder (*ICD-9* codes 303-304, 305.0, or 305.9 and *ICD-10* codes F10-F16 or F18-F19).[25]

Statistical Analysis

Association Between Eating Disorders and Suicide Attempts

We applied a cohort design to evaluate the association between eating disorders and suicide attempts; the results are presented as odds ratios (ORs) with 95% CIs. We first fitted logistic regressions to the total population (adjusted for sex), and to females and males separately, to obtain crude ORs. We then adjusted the models for psychiatric comorbidities to obtain adjusted ORs. In all models, we adjusted for birth year and used a robust (sandwich) estimator of SEs to account for nonindependence owing to familial clustering.[26] Death by suicide was analyzed as a separate outcome.

Familial Liability for the Association

To explore the extent to which familial risk factors contribute to the association between eating disorders and suicide attempts, we fitted a logistic model in each of the 5 relative cohorts to estimate the ORs of suicide attempts in individuals who had 1 or more relatives in the cohort with an eating disorder compared with those whose relatives in the cohort did not have the eating disorder. A significantly increased OR (ie, an increased risk of suicide attempts in people who had ≥1 relative with an eating disorder compared with those whose relatives did not have an eating disorder) suggests that familial risk factors shared among relatives contribute to the association between eating disorders and suicide attempts. Furthermore, a higher OR in full siblings than in maternal half siblings suggests that genetic factors are operative because the 2 types of siblings are assumed to share a similar family environment, whereas full siblings are more genetically similar than maternal half siblings. A higher OR in maternal half siblings than in paternal half siblings suggests that family environmental factors are operative because the 2 types of half siblings have equivalent genetic sharing, whereas maternal half siblings are assumed to share more family environment than paternal half siblings because children more often remain with their mothers after parental divorce.[15,16,27] In each model, we adjusted for birth year, sex, and number of relatives in the specific cohort and used a robust (sandwich) estimator of SEs to account for nonindependence due to familial clustering.

Sensitivity Analysis

In each of the 5 relative cohorts, we repeated the analyses, adjusting for eating disorders in the index individual (the person from whom we acquired information on suicide attempts and relatives' eating disorders). If the ORs remained significant after adjustment, the contribution of common familial risk factors to eating disorders and suicide attempts would be further supported (explained in eFigure in the Supplement).[28] We also adjusted for MDD, anxiety disorder, and substance use disorder in index individuals and in relatives to further test whether the comorbidities were associated with the familial liability.

Data analysis was conducted from October 5, 2014, to April 28, 2015. Data management was performed using SAS, version 9.3 (SAS Institute, Inc); analyses were performed using Stata, version 13.0 (StataCorp).

Results

Descriptive Statistics

More females than males had a lifetime history of eating disorders (**Table 1**). Of 2 268 786 individuals, 15 457 females (1.40% of all females) and 991 males (0.09% of all males) had any eating disorder, 7680 females (0.70%) and 453 males (0.04%) had AN, and 3349 females (0.30%), and 61 males (0.01%) had BN. In both sexes, the prevalence of suicide attempts and psychiatric comorbidities was higher in individuals with eating disorders than in those without eating disorders.

Association Between Eating Disorders and Suicide Attempts

Individuals with any eating disorder had an increased risk of suicide attempts, reported as OR (95% CI) (5.28 [5.04-5.54]), and death by suicide (5.39 [4.00-7.25]) (**Table 2**). The associations remained significant even after adjusting for comorbid MDD, anxiety disorder, and substance use disorder (1.82 [1.72-1.93] for suicide attempts; 2.04 [1.49-2.80] for death by suicide). Adjustment for each comorbid disorder decreased the magnitude of the effect, with the greatest reduction associated with MDD followed by anxiety disorder and substance use disorder (eTable 1 in the Supplement). Similar patterns were found for AN and BN in both sexes, except that the adjusted OR of death by suicide in BN became nonsignificant, possibly owing to the lack of power. Bulimia nervosa presented stronger crude associations with suicide attempts compared with AN, and AN presented slightly stronger crude associations with death by suicide compared with BN.

We did not find support for sex differences in the association between eating disorders and suicide. Results of the tests for interaction between sex and eating disorders are reported in eTable 2 in the Supplement.

Familial Liability for the Association

Because we did not find support for sex differences in the association between eating disorders and suicide attempts (eTable 2 in the Supplement), we collapsed and adjusted for sex to increase the power in the analyses addressing familial

Table 1. Distribution of Suicide Attempts Stratified by Sex and Eating Disorder Diagnosis[a]

Characteristic	Any Eating Disorder		Anorexia Nervosa		Bulimia Nervosa	
	Yes	No	Yes	No	Yes	No
Eating Disorders						
No.	16 448	2 252 338	8133	2 260 653	3410	2 265 376
Female	15 457	1 088 136	7680	1 095 913	3349	1 100 244
Male	991	1 164 202	453	1 164 740	61	1 165 132
Prevalence, %	0.72	NA	0.36	NA	0.15	NA
Female	1.40	NA	0.70	NA	0.30	NA
Male	0.09	NA	0.04	NA	0.01	NA
Age at first diagnosis, mean (SD), y	18.4 (4.0)	NA	17.4 (3.6)	NA	21.0 (3.4)	NA
Female	18.5 (4.0)	NA	17.4 (3.6)	NA	21.0 (3.4)	NA
Male	16.1 (4.5)	NA	15.9 (3.6)	NA	21.0 (4.0)	NA
Suicide Attempts						
Any suicide attempts, No. (%)	2148 (13.1)	44 293 (2.0)	923 (11.3)	45 518 (2.0)	595 (17.4)	45 846 (2.0)
Female	2077 (13.4)	23 491 (2.2)	895 (11.6)	24 673 (2.3)	581 (17.3)	24 987 (2.3)
Male	71 (7.2)	20 802 (1.8)	28 (6.2)	20 845 (1.8)	14 (23.0)	20 859 (1.8)
Age at first suicide attempts, mean (SD), y	18.9 (3.5)	18.0 (4.8)	18.7 (3.4)	18.0 (4.8)	19.6 (3.3)	18.0 (4.8)
Female	18.8 (3.5)	17.6 (4.4)	18.7 (3.4)	17.7 (4.4)	19.6 (3.3)	17.7 (4.4)
Male	19.3 (3.8)	18.4 (5.2)	18.8 (3.8)	18.4 (5.2)	20.3 (3.1)	18.4 (5.2)
Death by suicide, No. (%)	48 (0.29)	1467 (0.07)	27 (0.33)	1488 (0.07)	11 (0.32)	1504 (0.07)
Female	43 (0.28)	400 (0.04)	23 (0.30)	420 (0.04)	10 (0.30)	433 (0.04)
Male	5 (0.50)	1067 (0.09)	4 (0.88)	1068 (0.09)	1 (1.6)	1071 (0.09)
Age at death by suicide, mean (SD), y	20.8 (3.5)	21.2 (3.9)	20.3 (3.2)	21.2 (3.9)	22.0 (3.0)	21.2 (3.9)
Female	20.8 (3.5)	20.3 (3.9)	20.2 (3.1)	20.3 (3.9)	22.1 (3.1)	20.3 (3.9)
Male	20.4 (3.5)	21.5 (3.8)	20.3 (4.0)	21.5 (3.8)	21.0 (NA)	21.5 (3.8)
Psychiatric Comorbidities						
Major depressive disorder, No. (%)	5247 (31.9)	49 255 (2.2)	2320 (28.5)	52 182 (2.3)	1349 (39.6)	53 153 (2.3)
Female	5011 (32.4)	30 358 (2.8)	2217 (28.9)	33 152 (3.0)	1323 (39.5)	34 046 (3.1)
Male	236 (23.8)	18 897 (1.6)	103 (22.7)	19 030 (1.6)	26 (42.6)	19 107 (1.6)
Anxiety disorder, No. (%)	3742 (22.8)	45 684 (2.0)	1506 (18.5)	47 920 (2.1)	958 (28.1)	48 468 (2.1)
Female	3544 (22.9)	28 602 (2.6)	1439 (18.7)	30 707 (2.8)	934 (27.9)	31 212 (2.8)
Male	198 (20.0)	17 082 (1.5)	67 (14.8)	17 213 (1.5)	24 (39.3)	17 256 (1.5)
Substance use disorder, No. (%)	1731 (10.5)	52 897 (2.4)	741 (9.1)	53 887 (2.4)	507 (14.9)	54 121 (2.4)
Female	1655 (10.7)	23 813 (2.2)	709 (9.2)	24 759 (2.3)	494 (14.8)	24 974 (2.3)
Male	76 (7.7)	29 084 (2.5)	32 (7.1)	29 128 (2.5)	13 (21.3)	29 147 (2.5)

Abbreviation: NA, not applicable.

[a] The diagnostic period for bulimia nervosa (BN) differed from any eating disorders and anorexia nervosa (AN). Any eating disorder and AN were identified based on the Swedish version of the *International Classification of Disease, Ninth Revision* (*ICD-9*) (1987-1996) and *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* (*ICD-10*) (1997-2009) diagnoses in the National Patient Register (NPR) and *DSM-IV* diagnoses in the quality registers (Swedish National Quality Assurances Register for Specialized Eating Disorder Treatment [Riksät, 1998-2009] and Stepwise [2005-2009]); BN was identified based on only *ICD-10* diagnoses in NPR and *DSM-IV* diagnoses in the quality registers.

liability for the association (**Table 3**). The risk of suicide attempts, reported as OR (95% CI), was significantly increased in individuals with any full sibling with any eating disorder compared with those without full siblings with any eating disorder in the full sibling cohort (1.41 [1.29-1.53]). The risk was also increased in individuals with any full cousin with any eating disorder compared with those without full cousins with any eating disorder in the full-cousin cohort (1.11 [1.06-1.18]). These results suggest that familial risk factors underlie the association between eating disorders and suicide attempts. The OR in full siblings was higher than that in full cousins, further supporting the importance of familial risk factors in accounting for the association. We did not detect significant ORs in half siblings. Similar patterns were observed for individuals with relatives with AN (full siblings: 1.21 [1.06-1.37]; full cousins: 1.13 [1.04-1.22]), and individuals with relatives with BN (full siblings: 1.56 [1.31-1.86]; full cousins: 1.20 [1.07-1.34]) (Table 3). For any eating disorder, the OR in full siblings was slightly higher than the OR in maternal half siblings (P = .02), suggesting that some common familial risk factors for any eating disorder and suicide attempts may be genetic. We did not detect significant differences between the OR in maternal and pater-

Table 2. ORs of Suicide Attempts and Death by Suicide in Individuals With Eating Disorders[a]

Characteristic[b]	Crude OR (95% CI)	*P* Value	Adjusted OR (95% CI)	*P* Value
Suicide attempts				
Total population (N = 2 268 786)				
Any eating disorder	5.28 (5.04-5.54)	<.001	1.82 (1.72-1.93)	<.001
Anorexia nervosa	4.42 (4.12-4.74)	<.001	1.70 (1.56-1.85)	<.001
Bulimia nervosa	6.26 (5.73-6.85)	<.001	1.88 (1.68-2.10)	<.001
Female (n = 1 103 593)				
Any eating disorder	5.29 (5.04-5.56)	<.001	1.66 (1.56-1.77)	<.001
Anorexia nervosa	4.40 (4.10-4.72)	<.001	1.55 (1.42-1.70)	<.001
Bulimia nervosa	6.19 (5.65-6.78)	<.001	1.68 (1.50-1.89)	<.001
Male (n = 1 165 193)				
Any eating disorder	3.86 (3.03-4.91)	<.001	1.57 (1.19-2.06)	.001
Anorexia nervosa	3.29 (2.25-4.82)	<.001	1.49 (0.97-2.27)	.07
Bulimia nervosa	11.24 (6.22-20.32)	<.001	2.88 (1.40-5.93)	.004
Death by suicide				
Total population (n = 1 919 114)				
Any eating disorder	5.39 (4.00-7.25)	<.001	2.04 (1.49-2.80)	<.001
Anorexia nervosa	6.46 (4.38-9.54)	<.001	2.67 (1.78-4.01)	<.001
Bulimia nervosa	4.45 (2.44-8.11)	<.001	1.48 (0.81-2.72)	.20
Female (n = 891 434)				
Any eating disorder	5.36 (3.91-7.36)	<.001	1.81 (1.28-2.56)	.001
Anorexia nervosa	5.93 (3.89-9.03)	<.001	2.18 (1.39-3.42)	.001
Bulimia nervosa	4.39 (2.34-8.23)	<.001	1.29 (0.68-2.45)	.44
Male (n = 938 205)				
Any eating disorder	5.36 (2.21-12.97)	<.001	2.27 (0.90-5.72)	.08
Anorexia nervosa	9.96 (3.69-26.89)	<.001	4.62 (1.59-13.40)	.005
Bulimia nervosa	9.56 (1.30-70.65)	.03	2.44 (0.32-18.71)	.39

Abbreviation: OR, odds ratio.

[a] When estimating crude ORs, we adjusted for birth year, sex (for total population), and used a robust (sandwich) estimator of SEs to account for nonindependence owing to familial clustering. When estimating adjusted ORs, we additionally adjusted for psychiatric comorbidities including major depressive disorder, anxiety disorder, and substance use disorder. Individuals with any eating disorder, anorexia nervosa, and bulimia nervosa had significantly increased risk of both suicide attempts and death by suicide. Most of the associations remained significant even after adjusting for psychiatric comorbidities, except a few, possibly owing to limited power resulting from the rarity of the eating disorder and death by suicide in the corresponding population. Individuals in some birth-year strata were excluded from analyses for death by suicide (females born in 1997-2001 and males born in 1996 and 1998-2001), because there were no deaths by suicide in those years. This exclusion resulted in a smaller number of observations used in analyses for death by suicide than that used in analyses for suicide attempts in which no individual was excluded.

[b] Numbers represent the observations used in analyses.

Table 3. ORs of Suicide Attempts in Individuals With at Least 1 Relative With an Eating Disorder[a]

	Any Eating Disorder		Anorexia Nervosa		Bulimia Nervosa	
Relative Cohort[b]	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Full sibling (n = 1 680 658)	1.41 (1.29-1.53)	<.001	1.21 (1.06-1.37)	.004	1.56 (1.31-1.86)	<.001
Maternal half sibling (n = 253 172)	1.10 (0.90-1.34)	.36	1.09 (0.81-1.47)	.56	1.13 (0.74-1.73)	.57
Paternal half sibling (n = 248 939)	1.21 (0.98-1.49)	.08	1.25 (0.91-1.72)	.17	1.36 (0.89-2.06)	.15
Full cousin (n = 1 753 065)	1.11 (1.06-1.18)	<.001	1.13 (1.04-1.22)	.003	1.20 (1.07-1.34)	.001
Half cousin (n = 384 222)	0.90 (0.78-1.03)	.14	0.82 (0.67-1.00)	.54	1.01 (0.77-1.33)	.92

Abbreviation: OR, odds ratio.

[a] Outcome was defined as suicide attempts (any suicidal attempt or death by suicide). The models estimated the risk of suicide attempts in people with at least 1 relative with an eating disorder. We controlled for birth year, sex, and number of the type of relatives in the models, and used a robust (sandwich) estimator of SEs to account for nonindependence owing to familial clustering. A significantly elevated risk of suicide attempts was found in individuals with any full sibling with any eating disorder, anorexia nervosa, and bulimia nervosa, and in individuals with any full cousin with any eating disorder, anorexia nervosa, and bulimia nervosa.

[b] Numbers represent the observations used in analyses.

nal half siblings. For AN or BN, the ORs did not differ significantly between full siblings and maternal half siblings or between half siblings.

Sensitivity Analysis

The ORs of suicide attempts in individuals (index) with any full sibling or full cousin with an eating disorder remained statis-

tically significant even after adjusting for the index individuals' eating disorders (eTable 3 in the Supplement), further supporting familial liability for eating disorders and suicide attempts. Controlling for MDD, but not for other comorbidities, in the index individuals as well as in relatives reduced the familial liability for any eating disorder, AN, and BN and suicide attempts (eTable 4 and eTable 5 in the Supplement).

Discussion

Using nationwide register data, we thoroughly explored the association between eating disorders and suicide attempts and revealed a familial liability for the association. In line with previous research,[2] we found strong associations between any eating disorder, AN, and BN and suicide attempts. We extended previous studies by adjusting for comorbid psychiatric disorders. The associations remained significant, suggesting the elevated risks of suicide attempts in eating disorders are not entirely accounted for by psychiatric comorbidity. We did not observe sex differences in the association between eating disorders and suicide attempts.

Although previous research[29,30] has suggested familial influences on both eating disorders and suicide separately, whether these outcomes have common familial risk was unclear. We addressed this uncertainty by demonstrating an elevated risk of suicide attempts in individuals with any full sibling or full cousin with any eating disorder, AN, and BN compared with individuals without any full sibling or full cousin with the eating disorders (Table 3) even after controlling for the index individuals' eating disorders (eTable 3 in the Supplement). This finding reveals that the association between eating disorders and suicide is influenced by familial risk factors. By comparing the ORs across different types of relatives, our design allowed deeper exploration of the origin of the familial liability. If the familial liability was genetic, higher ORs would be expected in full siblings than in maternal half siblings because these relatives share similar family environments, but full siblings share more genetic factors than do maternal half siblings.[15,16] We observed a slightly higher OR in full siblings than in maternal half siblings for any eating disorder (P = .02), suggesting genetic influence on the association between any eating disorder and suicide attempts. If the familial liability originated from the family environment, higher ORs would be expected in maternal half siblings than in paternal half siblings because these relatives have equivalent genetic sharing, but maternal half siblings share greater family environment.[15,16] We did not observe this pattern, which could be the result of (1) the absence of family environmental effects, consistent with twin studies reporting minimal family environmental effects on either eating disorders or suicide[29-32]; (2) inadequate statistical power; or (3) changes in custody arrangements that led to fewer differences in shared family environment between maternal and paternal half siblings than expected.[33] Our pattern of results reflects those of a recent twin study[34] reporting common genetic, but not family environmental, influence on both eating disorders and suicide. These results suggest that heritable and common risk factors for both eating disorders and suicide attempts may exist and be useful for risk identification.

In addition to the main findings, our study has 2 important contributions. First, we confirmed and further quantified the effect of comorbid MDD, anxiety disorder, and substance use disorder on suicide risk in individuals with eating disorders. Our finding is in line with previous studies reporting associations between the comorbidities and both eating disorders and suicide attempts[9,10,35] as well as studies showing an elevated suicide risk in individuals with eating disorders with greater comorbid psychiatric burden.[36,37] In addition, the decreased familial risk when adjusting for MDD in family members suggests that the familial liability may partly relate to MDD (eTable 4 and eTable 5 in the Supplement). However, whether the association is genetic and/or environmental requires further study.

Second, we found that BN presented a higher crude OR of suicide attempts and a lower, yet comparable, crude OR of death by suicide compared with AN (Table 2). This observation differs from the results of a meta-analysis showing a lower suicide risk in BN than AN[3] but is in line with a Danish study reporting a higher hazard ratio of suicide attempts in BN than AN[38] and an outpatient-based mortality study reporting comparable suicide-specific standardized mortality ratios for AN and BN.[39] In aggregate, these findings encourage vigilance for suicidality in both AN and BN.

Our findings should be contextualized by considering the limitations of our design. First, the lifetime prevalence of eating disorders that we observed in the register data was lower than the survey-based lifetime prevalence in other studies,[1] including one based on Swedish adult twins.[31] This difference could be the result of (1) register data capturing only treatment-seeking cases (and treatment seeking can differ across eating disorders), (2) the coverage of the eating disorder quality registers increasing over time,[22] and (3) for BN particularly, the diagnosis being unavailable in the Swedish version of the *ICD-9*.[24] Such underdetection might dilute the association if the underdetection were nondifferential between people with and without suicide attempts. However, the effect should be minor since eating disorders were relatively rare. Nevertheless, the association might be overestimated if suicide attempts were overrepresented in treatment-seeking individuals compared with those who did not seek treatment, or if the diagnosis of eating disorders facilitated the discovery of suicide attempts and vice versa. In addition, the generalizability of our findings might be limited as the registers captured only treatment-seeking cases. Similar limitations could be attributed to possible misclassification in the diagnosis of suicide attempts.[40] Second, it is possible that confounding effects remain after adjusting for comorbidities and that the adjustment may overcorrect the association or may introduce bias owing to the complexity of the correlations between psychiatric disorders. Therefore, the adjusted OR should not be overinterpreted. Nevertheless, the adjusted OR suggests particularly high-risk groups in eating disorders. Potential problems related to overadjustment do not influence our main conclusion about familial liability between eating disorders and suicide attempts. Third, despite the large sample size and long follow-up period, the study remained underpowered

to clearly distinguish genetic from family environmental effects. This limitation is illustrated by the wide 95% CIs for ORs in half siblings. Larger studies and more effective designs are needed to distinguish genetic from family environmental factors with greater certainty. In addition, the inference of the origin of familial liability by comparing different types of siblings was based on an assumption that full siblings shared equal family environment with maternal but not paternal half siblings.[15,16] The assumption was supported by the fact that most (91%) children live with their mother after parental divorce.[27] However, more children now spend equal amounts of time with both parents after parental divorce than before.[33] Nevertheless, this trend was less likely to influence the older individuals in the study population. Finally, identification of the comorbid conditions might be incomplete since only diagnoses captured via health care contacts were included in the register.

Conclusions

To our knowledge, this is one of the largest studies investigating the association between eating disorders and suicide attempts and their coaggregation in families. Use of data from the total Swedish population guaranteed the representativeness, improved the precision of the estimates, and eliminated potential recall bias. Furthermore, the genetically informative design allowed us to examine the familial liability for eating disorders and suicide attempts. The study represents an important step toward understanding the mechanism underlying the association between eating disorders and suicide, and it encourages future studies to distinguish between genetic and environmental risk factors and examine their interaction.

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