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# Predictors of Comorbid Eating Disorders and Association with Other Obsessive-Compulsive Spectrum Disorders in Trichotillomania

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## Abstract

Trichotillomania (TTM) and <u>eating disorders</u> (ED) share many phenomenological similarities, including ritualized <u>compulsive</u> <u>behaviors</u>. Given this, and that <u>comorbid</u> EDs may represent additional functional burden to hair pullers, we sought to identify factors that predict diagnosis of an ED in a TTM population. Subjects included 555 adult females (age range 18–65) with *DSM-IV-TR* TTM or chronic hair pullers recruited from multiple sites. 7.2% (N = 40) of our TTM subjects met criteria for an ED in their lifetime. In univariable <u>regression analysis</u>, <u>obsessive-compulsive disorder</u> (OCD), <u>Yale-Brown Obsessive</u> <u>Compulsive Scale</u> (Y-BOCS) worst-ever compulsion and total scores, certain obsessive-compulsive <u>spectrum disorders</u>, anxiety disorder, <u>attention-deficit/hyperactivity disorder</u> (ADHD), and substance disorder all met the pre-specified criteria for inclusion in the multivariable analysis. In the final multivariable model, diagnosis of OCD (OR: 5.68, 95% CI: 2.2–15.0) and diagnosis of an additional body-focused repetitive <u>behavior disorder</u> (BFRB) (OR: 2.69, 95% CI: 1.1–6.8) were both associated with increased risk of ED in TTM. Overall, our results provide further support of the relatedness between ED and TTM. This finding highlights the importance of assessing for comorbid OCD and additional BFRBs in those with TTM. Future research is needed to identify additional predictors of comorbid disorders and to better understand the complex relationships between BFRBs, OCD and EDs.

#### 1. Introduction

<u>Trichotillomania</u> (TTM) is a disorder of repetitive hair pulling, characterized by hair loss, inability to stop pulling and functional impairment or distress <sup>[1]</sup>. Prevalence estimates vary from 0.6% of the population <sup>[2]</sup> to 3.4% of women and 1.5% of men <sup>[3]</sup>, depending on how the diagnosis was made. While the gender distribution in the community varies, the clinical TTM population tends to be dominated by women <sup>[4]</sup>.

TTM is categorized as an obsessive-compulsive and related disorder in the *DSM-5*<sup>[1]</sup>. It is also considered to be an obsessive-compulsive <u>spectrum disorder</u> (OCSD) along with OCD, <u>body dysmorphic</u> <u>disorder</u> (BDD), <u>hoarding</u> disorder, <u>tic disorders</u>, and <u>excoriation (skin-picking) disorder</u> (SPD). TTM and other OCSDs share <u>phenomenology</u>, neurobiology (i.e. fronto-cortico-striatal circuitry dysfunction),

common <u>comorbidities</u> and familial/genetic features <sup>[5], [6], [7], [8], [9]</sup>. These disorders also share genetic vulnerability and occur in one another with increased prevalences <sup>[10]</sup>.

Comorbid <u>eating disorders</u> (EDs) are not uncommon in TTM. In 1991, Christenson et al. found that about 20% of chronic hair-pullers had eating disorders (comprised of <u>bulimia</u> and "eating disorder not otherwise specified") <sup>[11]</sup>. Houghton and et al. also reviewed the prevalence of EDs in smaller TTM populations, and found that <u>anorexia nervosa</u> ranged from 1.6%–5%, bulimia nervosa ranged from 2%–14%, and <u>binge eating disorder</u> ranged from 6%–10.2% <sup>[9]</sup> (reflecting elevated prevalence rates of EDs than in the general population).

Other disorders are also frequently comorbid in TTM. Houghton et al. found that 78.8% of TTM subjects met criteria for at least one lifetime comorbid psychiatric condition, including OCD (5%–30%), major depressive disorder (32%–55%), generalized anxiety disorder (16.6%–32%), alcohol use disorder (2.6%–19.4%), and <u>substance abuse</u> disorder (8.3%–22%) <sup>[9]</sup>. SPD prevalence rates range from 10%–34% <sup>[12]</sup>. In general, anxiety disorders are common in TTM and are thought by some researchers to be central in both the <u>etiology</u> and maintenance of eating disorders <sup>[13]</sup>. The prevalence of anxiety disorders, including simple phobia (now known as specific phobia), <u>avoidant disorder, separation</u> anxiety, post-traumatic stress disorder (PTSD), and OCD is 37% <sup>[14]</sup>.

Many researchers believe that like TTM, EDs should be considered as part of the obsessive-compulsive spectrum <sup>[15], [16], [17], [18]</sup>. OCSDs and EDs are both characterized by difficulties inhibiting <u>repetitive</u> <u>behaviors</u> and a subjective sense of compulsion <sup>[6]</sup>. TTM and EDs are also part of a small group of <u>disorders thought</u> to have both compulsive and impulsive components <sup>[5]</sup>. In addition to sharing similar phenomenology and functionality <sup>[18]</sup>, they may also share <u>pathophysiological</u> mechanisms, including <u>cortico-striatal</u> dysfunction <sup>[15]</sup>. There are elevated prevalences of OCD within ED populations (11%–41%) <sup>[19]</sup>, and of EDs within OCD populations (11%–42%) <sup>[15], [17]</sup>. A recent study by Cederlof et al. showed that females and males with OCD had respective 16-fold and 37-fold increased risks of having a comorbid diagnosis of anorexia nervosa <sup>[17]</sup>. Given that OCD is elevated in relatives of probands with EDs <sup>[16]</sup> and the risk for EDs is elevated in relatives of probands with OCD <sup>[17]</sup>. Cederlof et al. concluded that the comorbid pattern is at least in part due to shared genetic factors <sup>[17]</sup>. This observation is important because the presence of obsessive-compulsive <u>symptomatology</u> has been positively associated with the severity of the ED <sup>[19]</sup>. It also points to the likelihood that OCD may be a <u>predictive factor</u> of the presence of an ED within TTM populations.

Despite many similarities/correlations, there has been limited research thus far on the specific relationships between EDs and TTM <sup>[5]</sup>, and what factors may be predictive of having an ED within a TTM population. Recently, Keuthen et al. looked at the predictive factors of having an OCD diagnosis within a TTM population, and found that having an ED diagnosis was associated with greater risk for OCD <sup>[20]</sup>. In 2011, Zucker et al. assessed the predictive factors of hair pulling within an ED population <sup>[5]</sup>. Five percent of their female ED population had evidence of repetitive hair pulling <sup>[5]</sup>. The significant predictors of hair pulling were (OCD-related) compulsive features and <u>trait anxiety</u> <sup>[5]</sup>.

Given reported comorbidities and traits commonly associated with TTM and EDs, we were tasked with choosing variables a priori that may lead to increased risk of having an ED within a TTM population. In

addition to including OCD diagnosis as a variable, measures of compulsion (i.e. <u>Y-BOCS</u> sub-score) were included. Given the preponderance of the association of anxiety disorders and depression with EDs, generalized anxiety, specific phobia, 'any anxiety disorder,' the <u>Beck Anxiety Inventory</u> (BAI) score, and major depressive disorder were included [14], [21]. ED probands tend to have more tic disorders and substance abuse compared to controls <sup>[16]</sup>, and so tic disorders and substance abuse were included as well. Other body-focused repetitive <u>behavior disorders</u> (BFRBs), such as skin-picking and severe nail biting, were included as potential factors given their strong relationship to TTM and OCD. Lastly, given the impulsive components found in TTM and ED, disorders known for increased <u>impulsivity</u>, such as <u>ADHD</u> and <u>bipolar disorder</u> (in addition to substance abuse disorders) were included <sup>[22]</sup>.

Ultimately, determining which factors are more predictive of having an ED within a TTM population is important to the clinician who works with patients with TTM. The combination of TTM and EDs represents an increased functional burden for the patient, in addition to EDs themselves having a high morbidity/mortality rate <sup>[23], [24]</sup>. Additionally, individuals with EDs may be reluctant to disclose their condition, and so having a more accurate "pre-test probability" could help identify sufferers <sup>[25]</sup>.

## 2. Methods

## 2.1. Participants

Five-hundred fifty-five adult female hair pullers were recruited from both treatment and nontreatment studies at Massachusetts General Hospital (n = 232), the University of Chicago (n = 40), the University of Minnesota (n = 109), the University of Wisconsin-Milwaukee (n = 97), and Stellenbosch University (n = 77) between 2006 and 2015. All subjects were between 18 and 65 years of age and met diagnostic criteria for *DSM-IV-TR*<sup>[2]</sup> TTM or chronic hair pulling (CHP). The latter was defined by meeting *DSM-IV-TR* TTM criteria except for tension before pulling or when attempting to resist (formally criterion B) and/or pleasure, relief, or gratification when pulling (formally criterion C) and is considered analogous to *DSM-5* TTM criteria.

Participant data was drawn from TTM genetics, imaging, and treatment studies and as a result, some differences in site exclusion criteria were present. Subjects from Massachusetts General Hospital and Stellenbosch University were excluded if they met criteria for a lifetime diagnosis of <u>psychosis</u>, <u>autism</u>, or <u>mental retardation</u>. Subjects at the University of Chicago and the University of Minnesota were excluded if they were pregnant or met lifetime criteria for <u>bipolar disorder</u> or psychosis. Subjects at the University of Wisconsin-Milwaukee, University of Chicago and University of Minnesota were excluded if they had unstable medical illness, bipolar disorder, psychotic disorder, <u>dementia</u>, current substance dependence, mental retardation or <u>pervasive developmental disorder</u>, or were evaluated to be a <u>suicide risk</u>. Participants were also excluded if they were pregnant or lactating, had an estimated IQ < 85, had a head injury/neurological disorder (i.e. epilepsy), had a medication change within the prior 8 weeks or were currently in <u>psychotherapy</u> for another condition. Of note, other analyses have been conducted on this dataset in part and/or in its entirety <sup>[20]</sup>.

Participants were recruited from multiple sources including the TLC Foundation for BFRBs (the national advocacy organization for body-focused repetitive behaviors), local mental health clinics, hospital

intranets, and flyers in the community. Study approval was received from the Institutional Review Boards of all relevant institutions prior to study initiation. All subjects gave informed consent prior to study participation. Modest financial compensation was offered to participants at each study site with some variability across the sites. Data were de-identified according to the Safe Harbor method for de-identification prior to data sharing (§164.514(b))<sup>[26]</sup>.

#### 2.2. Assessment materials

Semi-structured interviews were utilized for the diagnosis of TTM or CHP and assessment of <u>psychiatric</u> <u>comorbidities</u> and family history. The diagnostic interviews were performed by MD or PhD faculty at each site or by study staff trained to reliability on the structured interviews. A self-report measure was used to assess TTM and OCD severity. The relevant scales are described below.

#### 2.2.1. Semi-structured interviews

2.2.1.1. The structured clinical inventory for DSM-IV axis I disorders, patient edition [27] (SCID-I/P)

The SCID-I/P is a structured clinical interview with well-accepted reliability and validity. It is currently considered the gold standard for <u>psychiatric diagnosis</u>. The SCID was used at all sites to assess for current and lifetime eating, other <u>comorbid</u> and exclusionary disorders. The EDs diagnosed in this population include <u>anorexia nervosa</u>, <u>bulimia nervosa</u> and <u>binge eating disorder</u>.

#### 2.2.1.2. Schedule for affective disorders and schizophrenia-present and lifetime version [28] (K-SADS-PL)

The K-SADS-PL is a semi-structured diagnostic interview designed to assess current and past episodes of <u>psychopathology</u> in children and adolescents utilizing both DSM-III-R and DSM-IV diagnostic criteria. The <u>attention deficit hyperactivity disorder</u> (ADHD) module was used at Massachusetts General Hospital, University of Chicago, University of Minnesota, and Stellenbosch University for assessment of <u>ADHD</u> (inattention, hyperactivity, and impulsivity) in adults.

#### 2.2.1.3. The trichotillomania diagnostic inventory-revised [29] (TDI-R)

The TDI-R is a clinician-based semi-structured interview modeled after the SCID and is an updated version of the original TDI to be consistent with *DSM-IV-TR* TTM criteria. The TDI-R consists of 3-point ratings of responses to six items. It was utilized in the present study to diagnose TTM or CHP.

#### 2.2.1.4. The skin picking diagnostic inventory [30] (SPDI)

The SPDI is a clinician-administered interview for skin picking that is analogous to the TDI-R. The diagnostic criteria for SPD and CSP (a diagnosis largely parallel to *DSM-5* SPD) are modeled after DSM-IV criteria for TTM and CHP. The SPDI consists of 3-point ratings of responses to six items assessing these diagnostic criteria. The SPDI was used to assess for the presence of SPD and CSP.

#### 2.2.1.5. The Schedule for Tourette's Syndrome and other behavioral syndromes [31,32] (STOBS)

This interview includes symptom checklists and severity ratings based on the <u>Yale Brown Obsessive</u> <u>Compulsive Scale</u> (Y-BOCS) for documentation of OC symptoms and the Yale Global Tic Severity Scale (YGTSS) for documentation of tics. It also has a BFRB section for the assessment of hair pulling, skin picking, and nail biting. OCD and <u>Tourette's Syndrome</u> (TS) were diagnosed using the *DSM-IV-TR* criteria. Those who endorsed repetitive nail biting that caused significant distress were deemed to have clinical levels of nail biting. The interviews have been shown to be both valid and reliable for the diagnosis of OCD, TS, and chronic tics <sup>[33]</sup>. The STOBS was used at Massachusetts General Hospital and Stellenbosch University to assess comorbid diagnoses of OCD, TS, chronic tics, and nail biting plus OCD severity.

#### 2.2.2. Self-reports scales

#### 2.2.2.1. Beck anxiety inventory [34] (BAI)

This 21-item self-report measure asks participants to assess their anxiety symptoms during the past week on a four-point <u>Likert scale</u> from 0 to 3. Higher scores indicate more severe anxiety. The BAI has demonstrated good internal consistency, with alpha coefficients of 0.90–0.92 <sup>[34]</sup>. This measure was used at Massachusetts General Hospital and University of Wisconsin-Milwaukee to assess anxiety severity.

## 2.3. Statistical analyses

All statistical analyses were performed in IBM SPSS Statistics for Windows, Version 20.0 <sup>[35]</sup>. Inspection of variable plots suggested largely normal distributions for the majority of variables. Initial analyses were used to assess significance of candidate predictor variables. Univariable logistic regression was used to determine the <u>odds ratios</u> and 95% confidence intervals for categorical and continuous candidate predictors. Beta significance levels were set at 0.20. Clinical predictors from the univariable analyses with p < 0.10 were subsequently included in the final multivariable models predicting comorbid EDs in TTM/CHP. Age at interview was also included as a covariate in the final multivariable models to control for some participants not yet having passed through the risk periods for development of some comorbid disorders. In the final model, multivariable logistic regression was used and variables were considered to be independently associated with comorbid EDs at a threshold of p < 0.05.

## 2.4. Sample description

The mean (SD) age of the participants was 32.6 (11.7) years. (see <u>Table 1</u> for a description of the sample). Of the 40 individuals diagnosed with lifetime EDs, 10 were diagnosed with anorexia nervosa, 12 were diagnosed with bulimia nervosa, 14 were diagnosed with binge eating disorder, and 4 had non-specific diagnoses.

Table 1. Sample characteristics.

Factor	n	%
Race		
White/Caucasian	474	85.4
Black/African American	23	4.1
Asian	8	1.4
Multi-Racial	18	3.2
Other	9	1.6
Ethnicity		
Hispanic/Latino	10	1.8
Marital status		
Single/never married	310	55.9
Married	184	33.2
Separated	7	1.3
Divorced	27	4.9
Widowed	15	2.7
Education		
High school or less	142	25.6
College or some college	304	54.8
Graduate degree	85	15.3
Comorbid lifetime diagnoses		
OCD	105	18.9
SPD/chronic skin picking	108	19.5
Nail biting	71	12.8
Body-dysmorphic disorder	15	2.7
Eating disorder	40	7.2
Anxiety disorder	200	36.0
Substance use disorder	88	15.9
Tic disorder	16	2.9
Major depressive disorder	277	49.9
Bipolar disorder	5	0.9

OCD = <u>obsessive-compulsive disorder</u>; SPD = skin picking disorder; <u>eating disorder</u> = <u>anorexia nervosa</u>, <u>bulimia nervosa</u>, and/or <u>binge eating disorder</u>; anxiety disorder = <u>panic disorder</u> without <u>agoraphobia</u>, panic disorder with agoraphobia, agoraphobia, specific phobia, social <u>anxiety disorder</u>, <u>separation</u> anxiety, <u>general anxiety disorder</u>, and <u>post-traumatic stress</u> <u>disorder</u>.

Mean (SD) onset of hair pulling was 12.7 (5.9) years. The mean (SD) score for <u>Y-BOCS</u> worst ever compulsions was 4.6/20 (5.6) and the mean (SD) score for Y-BOCS worst ever obsessions and compulsions was 8.7/40 (10.5). For those who met criteria for OCD, the mean (SD) score for Y-BOCS

worst ever compulsions was 10.5/20 (3.8), and the mean (SD) score for Y-BOCS worst ever total was 20.2/40 (7.0). The mean (SD) total score for the BAI was 10.6/63 (9.5).

## 3. Results

## 3.1. Univariable analyses

In the univariable analyses predicting <u>comorbid</u> EDs in TTM/CHP, we investigated a number of variables including age, <u>Y-BOCS</u> worst ever compulsions score, Y-BOCS worst ever total score, BAI total score, diagnosis of OCD, diagnosis of GAD, diagnosis of any anxiety disorder, diagnosis of SPD/CSP, diagnosis of nail biting, diagnosis of an additional BFRB, diagnosis of BDD, diagnosis of <u>ADHD</u>, diagnosis of a substance disorder, diagnosis of any <u>tic disorder</u>, diagnosis of MDD, and diagnosis of <u>bipolar</u> <u>disorder</u> (<u>Table 1</u>). "Any BFRB" included those with SPD/CSP and/or severe nail biting. Y-BOCS worst ever total score, diagnosis of any anxiety disorder, diagnosis of an additional BFRB, diagnosis of OCD, diagnosis of any anxiety disorder, diagnosis of an additional BFRB, diagnosis of OCD, diagnosis of any anxiety disorder, diagnosis of an additional BFRB, diagnosis of OCD, diagnosis of any anxiety disorder, diagnosis of an additional BFRB, diagnosis of BDD, diagnosis of ADHD, and diagnosis of a substance disorder each met the pre-specified criteria for inclusion in the multivariable analysis (<u>Table 2</u>).

Table 2. Univariable predictors of <u>comorbid eating disorders</u> in a TTM population.

Continuous predictors	Mea	n (SD)	OR (95% CI)	<i>p</i> -Value
Age	33.25 (	11.68)	1.00 (0.98–1.03)	0.74
Y-BOCS worst ever compulsion	8.65 (6	.09)	1.15 (1.07–1.24)	< 0.001
Y-BOCS worst ever obsessions and compulsio	ns 15.42 (	11.77)	1.06 (1.02–1.10)	0.001
BAI total score	12.81 (	9.61)	1.02 (0.99–1.06)	0.17
Categorical predictors	N (%)		OR (95% CI)	<i>p</i> -Value
OCD	19 (47.5)	4.47 (2	2.30–8.67)	< 0.001
Generalized anxiety disorder	8 (20.0%)	1.12 (0	).50–2.51)	0.78
Any anxiety disorder	21 (52.5%)	2.06 (1	08–3.92)	0.03
SPD/CSP	11 (27.5%)	1.59 (0	).75–3.37)	0.22
Nail biting	5 (12.5%)	0.94 (0	).35–2.56)	0.91
SPD/CSP and/or severe nail biting	16 (40.0%)	1.99 (0	).91–4.32)	0.08
Body dysmorphic disorder	3 (7.5%)	3.28 (0	).88–12.25)	0.08
ADHD	6 (15.0%)	2.68 (1	03–6.97)	0.04
Substance use disorder	12 (30.0%)	2.62 (1	26–5.48)	0.01
Any tic disorder	3 (7.5%)	2.05 (0	).55–7.63)	0.28
Major depressive disorder	25 (62.5%)	1.71 (0	).88–3.32)	0.11
Bipolar disorder	1 (2.5%)	3.24 (0	).35–29.73)	0.30

SD = standard deviation; OR = <u>odds ratio</u>; <u>Y-BOCS</u> = <u>Yale-Brown Obsessive Compulsive Scale</u>; BAI = <u>Beck Anxiety Inventory</u>; OCD = <u>obsessive-compulsive disorder</u>; SPD/CSP = skin picking <u>disorder/chronic</u> skin picking; <u>ADHD</u> = <u>attention-</u> <u>deficit/hyperactivity disorder</u>.

#### 3.2. Multivariable analyses

Due to multicollinearity with diagnosis of OCD, Y-BOCS worst ever compulsions score (tolerance = 0.108; VIF = 0.282) and Y-BOCS worst ever total score (tolerance = 0.108; VIF = 0.282) were not included in the final multivariable model. In the final multivariable model of comorbid EDs in TTM/CHP (Table 3), diagnosis of OCD (OR = 5.7, CI [2.16–14.99], p < 0.001) and diagnosis of an additional BFRB (OR = 2.7, CI [1.07–6.76], p = 0.035) remained significant predictors of increased risk of comorbid EDs in TTM/CHP (Table 3).

Table 3. Multivariable predictors of comorbid eating disorders in a trichotillomania population.

Variable	В	S.E.	Wald	df	<i>p</i> -Value	OR (95% CI)
Age	0.006	0.02	0.074	1	0.78	1.01 (0.97–1.05)
OCD	0.495	0.495	12.339	1	< 0.001	5.68 (2.16–14.99)
Any anxiety disorder	0.906	0.474	0.906	1	0.34	1.57 (0.62–3.97)
SPD/CSP and/or severe nail biting	0.989	0.47	4.423	1	0.04	2.69 (1.07–6.76)
Body dysmorphic disorder	1.43	0.825	3.002	1	0.08	4.18 (0.83–21.06)
ADHD	0.872	0.612	2.031	1	0.15	2.39 (0.72–7.94)
Substance use disorder	0.183	0.539	0.116	1	0.73	1.02 (0.42–3.45)
Constant	- 4.338	0.807	28.878	1	< 0.001	

B = beta coefficient; S.E. = standard error; df = degrees of freedom; OR = <u>odds ratio</u>; CI = confidence interval; OCD = <u>obsessive-compulsive disorder</u>; SPD/CSP = skin picking <u>disorder/chronic</u> skin picking; <u>ADHD</u> = <u>attention-deficit/hyperactivity</u> <u>disorder</u>.

## 4. Discussion

This study examined the largest sample of clinically diagnosed individuals with TTM/chronic hair pulling to date. The results overall provide evidence to support the relatedness between TTM, OCD and EDs.

The prevalence of <u>comorbidities</u> in this cohort of individuals with <u>trichotillomania</u> was similar to that found in other studies examining prevalence <sup>[9]</sup>. Individuals with lifetime EDs made up 7.2% of this TTM population. While that proportion of TTM individuals with comorbid EDs is lower than the 20% found by Christenson et al. <sup>[11]</sup>, it is consistent with the ED prevalence rates found in Houghton et al.'s more recent study in which the prevalence of <u>anorexia nervosa</u>, <u>bulimia</u> and <u>binge eating disorders</u> was 4.7%, 1.2% and 1.2%, respectively <sup>[9]</sup>. The prevalence of OCD in this sample, 18.9%, is in the 5%–30% range compiled by Houghton et al. <sup>[9]</sup>. The percentage of individuals with chronic skin-picking/SPD is consistent with prior findings as well.

From the univariable analysis, greater <u>Y-BOCS</u> worst ever compulsion and greater Y-BOCS worst ever total score, and diagnoses of OCD, any anxiety disorder, any BFRB, BDD, <u>ADHD</u> and <u>substance abuse</u>

were all associated with increased risk of having an ED within a TTM population. This is consistent with Sallet et al.'s finding, which showed greater prevalence of anxiety disorders and BDD, in addition to SPD and ADHD (pre-Bonferroni correction), in an OCD and ED population vs. in an OCD population without comorbid EDs <sup>[15]</sup>. Greater Y-BOCS worst ever total scores, and greater prevalence of OCD and any anxiety disorder being associated with EDs in a TTM population was consistent with Zucker et al., who found that increased trait anxiety and compulsions (as part of the obsessive-compulsive spectrum) were associated with increased risk of TTM in an ED population between EDs and OCD, it is not surprising that they too were associated with an increased risk of having an ED in a TTM population. This also supports Sallet et al.'s finding that individuals with OCD and EDs had higher rates of BDD compared to those with only OCD <sup>[15]</sup>. It is interesting, though not surprising, that ADHD and substance abuse both represent the impulsive components on the impulsive-compulsive spectrum found in both EDs and TTM.

When the above factors were all compiled into a multivariable regression equation, it was determined that diagnosis of OCD and diagnosis of another BFRB (other than TTM) were associated with increased risk of ED in a TTM population. This finding is consistent with and a corollary to Keuthen et al.'s recent paper, which showed that a diagnosis of ED is associated with increased risk of OCD within a TTM population <sup>[20]</sup>. Is it also consistent with Fernández-Aranda et al., who showed that individuals with EDs (specifically binge eating) and <u>impulse control disorders</u> were more likely to have OCD symptoms than those with EDs without impulse control disorders <sup>[21]</sup>.

It is interesting to note that it was the diagnoses that are part of the obsessive-compulsive spectrum disorders (OCD and an additional BFRB) that were ultimately significant in predicting increased risk of EDs in our TTM population. The marginal association between BDD and EDs in TTM may have been due to the low prevalence of BDD in general in our sample. These findings further support the relatedness between EDs and OCSDs, including BFRBs, and support the idea of EDs being on the obsessive-compulsive disorder spectrum. This finding is also consistent with Monzani et al.'s recent report of a shared heritability between all of the obsessive-compulsive and related disorders including, OCD, BDD, hoarding, skin picking and hair pulling <sup>[10]</sup>. It would be interesting for future research to examine the heritability factors of OCSDs and EDs together.

It is important to note study limitations. First, this sample included only females. Replication of the findings in future studies that include males is warranted, especially as gender itself may likely be a predictor of EDs in a TTM population. Also, there were differences in exclusion criteria and measures across sites, which could add heterogeneity to the analyses. Although this study utilized a very large sample size, future research would benefit from even larger samples in order to increase the power to detect associations with more modest <u>effect sizes</u>, and similarly to estimate the observed associations with more accuracy.

An additional limitation is that because this study was conducted in adults, one has to be careful about generalizing any findings to adolescents or other age groups. However, given that the most common age of onset of TTM is early adolescence, and the symptoms/course in adolescence continues into and

is akin to that in adulthood <sup>[4], [11]</sup>, one may be able to prudently apply some of these findings when working with adolescent patients. That said, conducting a similar study with adolescent patients would be very helpful in further examining the relatedness between <u>eating disorders</u> and TTM. Additionally regarding limitations, all ED diagnoses were grouped together in this study. This approach is common, especially given the limited number of subjects with EDs, though future studies would benefit from examining which factors may be predictive of specific EDs given the known differences between anorexia nervosa, bulimia nervosa and <u>binge eating</u> disorder. It is also important to note that Eating Disorder - Not Otherwise Specified (ED-NOS), *DSM-IV* diagnosis, was not screened for in the treatment studies analyzed. Given that <u>ED-NOS</u> was known to be a very common condition, it is possible that estimate of those with EDs in a TTM population is higher <sup>[36]</sup>. Future studies utilizing <u>DSM-5</u> ED criteria (including Avoidant/Restrictive Food Intake Disorder) should help ameliorate that problem. Finally, it is important to note that our cohort consisted of participants in TTM research studies, and that they therefore may not accurately represent the TTM population as a whole. Thus, it is possible that our findings may not generalize to the entire TTM community. For future research, it would be helpful to conduct analyses in community/non-treatment seeking samples.

These findings highlight the importance of assessing for comorbid OCD and additional BFRBs in those with TTM when considering which patients may be most at risk for EDs. Compared to individuals with just OCD, those with OCD and EDs are more likely to have higher lifetime prevalence of comorbid conditions, higher anxiety and depression scores, and higher frequency of suicide attempts <sup>[15]</sup>. Additionally, even after controlling for subtype of ED, the presence of an impulse-control disorder is associated with greater severity of ED and worse general psychiatric morbidity and psychopathology <sup>[21]</sup>. These findings ultimately will allow clinicians to identify which of their patients with TTM may be at greatest risk and have greatest psychiatric burden given that patients with EDs may not reveal their condition secondary to shame and/or are disinclined to seek treatment <sup>[25]</sup>.

Further research is needed to identify additional predictors of comorbid disorders and to better understand the complex relationships between BFRBs, OCD and EDs. This study should help to direct future research on the relationship between TTM and EDs, and help inform <u>pathophysiology</u>, <u>phenomenology</u> and treatment models.

## 5. Conclusion

In this <u>trichotillomania</u> cohort of 555 adult females, 7.2% had a (lifetime) <u>eating disorder</u> diagnosis, including <u>anorexia nervosa</u>, <u>bulimia nervosa</u> and/or <u>binge eating disorder</u>. Using multivariable regression, we determined that having OCD and having an additional body-focused repetitive <u>behavior</u> <u>disorder</u> (such as skin-picking disorder or severe nail-biting), was associated with increased risk of having an eating disorder within a trichotillomania population. This study helps support the relationship between obsessive-compulsive <u>spectrum disorders</u> and eating disorders, and can help physicians identify patients at increased risk for eating disorders, a dangerous psychiatric condition.

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## Contributions

NK and EG designed the study. EC, JS and EG undertook the statistical analyses. NK, JG, CL, DW, DS, ET, SR, EC were involved in data management. EG wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

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