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Crossed clinical features between eating disorders and types of bipolar disorder: Results from the FondaMental Advanced Centers of Expertise - Bipolar Disorder cohort

Short title: Eating disorders and bipolar disorder

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Abstract (250 words)

Background: Eating disorders (EDs) are liable to alter the disease course of bipolar disorder (BD). We explored the crossed clinical features between EDs and BD, particularly as a function of BD type (BD1 vs. BD2).

Methods: 2,929 outpatients attending FondaMental Advanced Centers of Expertise were assessed for BD and lifetime EDs with a semi-structured interview, and their sociodemographic, dimensional and clinical data were collected according to a standardized procedure. For each ED type, bivariate analyses were used to investigate associations between these variables and the type of BD type followed by multinomial regressions with the variables associated with EDs and BDs after Bonferroni correction.

Results: Comorbid EDs were diagnosed in 478 (16.4%) cases, and were more prevalent in patients with BD2 than in those with BD1 (20.6% vs. 12.4%, $p < 0.001$). Regression models showed no difference according to the subtype of bipolar disorder on the characteristics of patients with anorexia nervosa (AN), bulimia nervosa (BN) or binge eating disorder (BED). After multiple adjustments, the factors differentiating BD patients with versus without ED were primarily age, gender, body mass index, more affective lability and comorbidity with anxiety disorders. BD patients with BED also scored higher regarding childhood trauma. BD patients with AN also showed higher risk of past suicide attempts than those with BED.

Conclusions: In a large sample of patients with BD, we found a high prevalence of lifetime EDs, especially for the BD2 type. EDs were associated with several severity indicators, but not with BD type-specific characteristics. This should prompt clinicians to carefully screen patients with BD for EDs, regardless of BD and ED types.

Keywords: bipolar disorder, eating disorders, comorbidity, types

Introduction

Bipolar disorder (BD) is a frequent (1-2% of the general population)¹ and disabling condition that has particularly high comorbidity rates with other psychiatric disorders², including eating disorders (EDs). Thus, the estimated lifetime prevalence of EDs in people with a primary BD was found to be 12.7% in a meta-analysis of 47 original studies³.

EDs often appear during adolescence and in early adulthood (i.e. typically before BD onset), resulting in an immediate burden for individuals⁴ and a particularly high rate of health service use^{5,6}. There is growing evidence that, compared with individuals with BD alone, individuals with both BD and EDs have a more severe clinical profile, including increased mood instability, alcohol use disorders, anxiety disorders, more depressive episodes, more rapid cycling, increased suicidality, and poorer response to medication⁷⁻¹¹. EDs therefore represent major modifiers of the BD disease course, and worsen the prognosis for both disorders in patients with a primary diagnosis of BD. However, they may be associated with BD type 1 and BD type 2 in different ways, resulting in either different clinical profiles or different impacts on the BD disease course.

Several studies of BD type-specific prevalence of EDs have yielded discrepant results. A meta-analysis³ highlighted an increased risk of EDs in BD2 versus BD1, but others have reported the opposite finding (see review by Thiebault et al.¹¹). A recent study in a French sample of BD patients (independent from the current study)¹² found that the prevalence and sequence of onset of psychiatric comorbidities (including EDs) differed substantially according to BD type. However, despite its clinical importance, the issue of the clinical associations between EDs and BD according to BD type has so far been overlooked. Improving our understanding of this comorbidity requires large samples of extensively-characterized patients, in order to yield fine-grained descriptions of clinically relevant subgroups of patients. In order to explore the clinical associations between EDs and BD, particularly according to BD and ED

types, we analyzed data from 2929 patients with confirmed BD and valid data regarding EDs, drawn from the FondaMental Advanced Centers of Expertise – Bipolar Disorder (FACE-BD) cohort. We hypothesized that (i) the raw prevalence of EDs in BD would differ between BD1 and BD2, and (ii) the clinical characteristics of patients' EDs would vary according to BD and ED types.

Methods

We conducted a post hoc analysis of a large sample of patients with BD who had been assessed using a standard procedure implemented in the FACE-BD network, which was set up to better characterize the lifetime and current profile of individuals with BD in order to support optimized treatment choices.

Clinical sample

We analyzed de-identified patient-level data from the FACE-BD national network. The present study was carried out in accordance with ethical principles for medical research involving humans (Declaration of Helsinki). The assessment protocol was approved by the relevant institutional review board (CPP-Ile de France IX, 18 January 2010). Although the committee waived the requirement for written informed consent, patients received a letter informing them about the study and asking whether they agreed to participate.

In France, patients with ascertained or suspected BD are referred to one of the 12 centers of excellence in the FondaMental network by general practitioners or psychiatrists to get diagnostic or therapeutic advice. Participants with ascertained BD undergo a 2-day assessment of their sociodemographic and clinical history by trained nurses, psychologists and physicians, in order to provide both them and their treating physician with personalized therapeutic/diagnostic guidance. The FACE-BD network procedures have been described in detail elsewhere¹³. For the present study, we included all patients who had attended a center

between 2009 and August 2020 (date of data extraction from the centralized data management system), and for whom the presence or absence of lifetime EDs was available. We then excluded all participants with BD-not otherwise specified and/or ED-not otherwise specified, resulting in a final study sample of $N = 2,929$.

Assessments

Throughout the study, we focused on the lifetime prevalence of EDs, diagnosed on the basis of the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision*¹⁴. We considered three ED types of interest: anorexia nervosa (AN), bulimia nervosa (BN), and binge eating disorder (BED). Although it has been reported that different ED types can occur successively (or co-occur) across the lifespan¹⁵, a lifetime diagnosis of ED in the consensual assessment procedure of the FACE-BD network refers to the most impactful disorder according to both the participant and the investigator, and a specified disorder (AN, BN, BED) is preferred and rated over an unspecified one. Thus, to ensure the reliability of cross-prevalence investigations between subsamples of BD types and comorbid diagnoses (e.g., EDs, anxiety, and substance use disorders), we excluded DSM *not otherwise specified* diagnoses for both BD and EDs. The diagnoses of BD, EDs and other psychiatric comorbidities were made using the Structured Clinical Interview for DSM-IV Axis I Disorders¹⁶. Age at onset of BD was defined as the age at which participants reported having their first mood episode, which was further used to compute BD duration (age at interview - age at BD onset). Polarity at onset referred to the same first BD episode, further dichotomized into *up* [(hypo)manic or mixed] versus *down* (depressive). The number of mood episodes was also collected, dichotomized on the same basis, and used as a rate per year of bipolar illness. The presence of any psychotic symptoms during a mood episode (hereafter termed *history of psychosis*) was also collected. Age at ED onset was considered as the age at which participants first met DSM-IV criteria for any ED. Comorbid anxiety disorders, tobacco-smoking status (never, former or current smoker) and substance use

disorders (DSM-IV abuse or dependence) were also considered on a lifetime basis. Any disorders related to cocaine and other stimulants were pooled to form a lifetime *stimulant use disorder* variable.

During the interviews, data were collected on age, gender, and education level (number of years since elementary school). The following well-validated dimensional scales were also used for the present study. Current functioning was assessed with the Functional Assessment Short Test (FAST)¹⁷, using the total score from the six specific areas of functioning. The higher the score, the poorer the functioning. The Montgomery-Åsberg Depression Rating Scale (MADRS)¹⁸ was used to assess current depressive symptoms. The Young Mania Rating Scale (YMRS)¹⁹ was used to assess current manic symptoms. Patients also completed the short forms of the Affective Lability Scale (ALS)²⁰, and the Childhood Trauma Questionnaire (CTQ)²¹. For this scale, to assess trauma load, we also chose to use the total score, in order to limit the multiplication of tests, especially given that trauma was not our main focus in this study. General medical history was collected via standardized questions on major disease categories, supplemented by open questions. Finally, in addition to body mass index (BMI), waist circumference was measured in centimeters using a standard procedure²². Given that BMI is by definition extremely variable in EDs, with individuals ranging from extreme thinness to severe obesity, we used the dummy variable *abnormal BMI*, deemed to be present when the BMI was below 18.5 kg/m² or above 30 kg/m², according to the WHO specifications, to better detect clinically meaningful associations with EDs.

Internal consistency was good to excellent, with standardized Cronbach's $\alpha = 0.78$ for MADRS, 0.75 for YMRS, 0.9 for FAST, 0.92 for CTQ, and 0.98 for ALS.

Statistical analyses

Continuous variables were described by medians (interquartile range), given that most had non-Gaussian distributions (Shapiro-Wilk test p value < 0.05). Categorical data were described by counts (frequency).

Lifetime ED was coded as the following categorical variable: ‘no ED’, ‘Anorexia nervosa’, ‘Bulimia Nervosa’ and ‘Binge eating disorder’. Firstly, bivariate analyses were used to investigate associations between the collected variables and the absence *vs.* type of lifetime ED, extended with pairwise comparisons to assess whether ED types differ for each independent variable of interest when the global test across ED types was significant. We used Kruskal-Wallis H and Mann-Whitney U for continuous data and Chi^2 for categorical data. Secondly, each of these independent associations between lifetime ED type(s) and clinical and sociodemographic data was entered in four multinomial regression models that included intercepts and where the dependent variable was the type of ED. This yielded six pairwise comparisons since the reference level (*i.e.*, the ED type) was different in each model (**Supplementary Table 1**). The center of inclusion (12 sites) was used as a random term in the regression models, after checking that they were more informative than fixed effects models, that is, with a lower Akaike’s Information Criterion (AIC). Bonferroni correction was applied for multiple testing, yielding a p -value cutoff for significance $=0.05/20$ tests (20 variables) $=0.0025$ for bivariate analyses – further corrected for pairwise analyses between ED types. Multinomial regression model p -values were also Bonferroni-corrected for six comparisons, yielding $p < 0.0083$ to consider statistical significance. Given the large number of odds ratios elicited, we chose to present the findings from multinomial regression as a heatmap (**Figure 3**). Multicollinearity was assessed by computing the general variance inflation factor (gVIF) of each independent variable. We ran dummy linear regression using ED types as a numeric variable to be able to properly use the function, as previously suggested. A gVIF above the “balanced” threshold of 2.5²³ was deemed problematic and, in that case, the model was run

again without the variable, until all gVIF values became satisfactory. R version 4.1.2²⁴ through R studio version 1.4.17²⁵ were used to compute statistics under Mac OS X.12.3.1 system²⁶. The R session summary is available as a supplementary file.

Results

After exclusion of participants with the *ED – not otherwise* and *BD – not otherwise specified* diagnosis, the final sample comprised 2,929 patients ($M_{\text{age}} = 40.5$ years, $SD = 12.8$) with BD1 or BD2 with reliable data on EDs. There were 1,765 (61%) women, and 1,424 (48.6%) patients had BD2. Comorbid EDs were diagnosed in 479 (16.4%) patients, including 186 with BD1 (12.4%) and 293 with BD2 (20.6%) ($p < 0.001$) (**Table 1**). ED types were as follows (percentages based on total number of participants with any lifetime ED): AN ($n = 143$, 30%); BN ($n = 63$, 13%); and BED ($n = 272$, 56%).

<Insert Table 1 about here>

Demographic and clinical features of patients with BD as a function of the presence and type eating disorders

Comparisons between BD with *vs.* without ED are displayed **Table 1**. The characteristics of patients as a function of ED type are displayed **Table 2**.

Compared to those without ED, patients BD with ED were more likely to be women (77% *vs.* 55%; all ED types significant *vs.* no ED), further significant for AN *vs.* BED (95% *vs.* 82%) (**Figures 1 and 2**). BD patients with ED were younger than without ED (37 *vs.* 41 years; all ED types significant *vs.* no ED), also further significant for AN *vs.* BED (34 *vs.* 38 years). They also reported more frequent history of suicide attempts (50% *vs.* 35%; all ED types significant *vs.* no ED), which was further significant for AN *vs.* BED (61% *vs.* 46%), including regarding age at first suicide attempt (24 years *vs.* 30 years). BD patients with AN and BN also had a lower

age of first suicide attempt than without ED (respectively 24 years-AN- and 22 years-BN- vs. 31 years-no ED).

Patients BD with ED reported higher levels of depressive symptoms than without ED (MADRS score 13 vs. 10; all ED types significant vs. no ED). History of psychosis was less frequent for BD patients suffering from AN (26%) and BED (26%) than BD without ED (40%). BD patients with ED had greater affective lability (ALS score 1.6 vs. 1.2; all ED types significant vs. no ED) and higher levels of childhood trauma than non-ED BD patients, especially when comparing AN and BED to BD patients without ED (CTQ total scores =49 and 48 vs. 42, respectively).

<Insert figure 1 and 2 here>

BD patients with ED reported an earlier age at BD onset, notably for anorexia nervosa (19 vs. 24 years without ED) and BED (21 vs. 24 years without ED). Approximately half of the patients with a history of ED had an active disorder. The presence of a current ED was more frequent in patients with BED than in patients with AN. Patients BD suffering from AN and BED had poorer daily functioning than BD without ED. More specifically and importantly, there was a gradient of decreasing current functioning from BD without ED (FAST =18) to BD with AN (FAST =21) to BD with BN (FAST =24), the worst functioning being found for BD with BED (FAST =26). Interestingly, all EDs, but AN, had poorer functioning than non-ED patients and BED patients had poorer functioning than AN patients.

BMI was significantly lower for patients with AN and higher for patients with BED compared to BD patients without ED (21 and 29 vs. 24, respectively). We also observed that BD patients with AN had more frequent alcohol use disorder compared to BD patients without ED (36% vs. 23%), and that those with bulimia and/or BED had more frequent sedative use disorders than

non-ED BD patients (13 and 11% vs. 4%, respectively). Finally, BD patients with ED had increased prevalence of comorbid anxiety disorders than non-ED patients (67% vs. 39%; all ED types significant vs. no ED).

<Insert table 2 here>

The multinomial regressions (**Figure 3** and **Supplementary Table 1**) showed that, comparing BD patients suffering from AN and BD without ED, patients were younger (OR=0.97, 95% CI [0.95,0.99]), more likely to be women (OR=9.47, 95% CI [3.97, 22.59]) and suffer from comorbid anxiety disorder (OR=2.22, 95% CI [1.35,3.66]), with lower BMI (OR=0.89, 95% CI [0.84,0.95]) and greater affective lability (OR=2.15, 95% CI [1.43,3.23]).

Secondly, comparing BD patients suffering from BN and BD without ED patients were more women (OR=5.15, 95% CI [1.95,13.63]), had a BMI more important (OR=1.1, 95% CI [1.04,1.16]), and greater affective lability (OR=3.2, 95% CI [1.75,5.87]).

Thirdly, BD patients suffering from BED vs. without ED were younger (OR=0.96, 95% CI [0.95,0.98]), more likely to be women (OR=3.27, 95% CI [2.18,4.93]), with higher levels of childhood trauma (OR=1.02, 95% CI [1.01,1.03]), increased BMI (OR=1.15, 95% CI [1.12,1.18]), greater affective lability (OR=1.27, 95% CI [0.94,1.71]), and more prevalent anxiety disorders (OR=1.91, 95% CI [1.34,2.73]).

BD patients with AN had greater risk for suicide attempts than BD patients without ED (OR =2.4, 95% CI [1.4-3.2]). This difference was also significant vs. BD patients with BED, who had lower risk for suicide attempt than Bd patients with AN (OR=0.41, 95% CI [0.23,0.72]).

The same pattern was observed regarding affective lability, which was higher in BD + AN patients compared to those with BD alone, and lower for BD+BED patients compared to BD+AN (OR=0.39, 95% CI [0.2,0.74]).

The global association between EDs and BD2 type was not evidenced for specific ED types, whether considered against the absence of ED or against each other.

<Insert Figure 3 here>

Discussion

We investigated the prevalence of EDs in each BD type, separately. Using standardized procedures implemented within the national FACE-BD network, we first showed that 16% of patients with BD had lifetime ED, which is roughly twice as high as the figure found for the general population in a recent review²⁷, where the weighted means of lifetime EDs were 8% for women and 2.2% for men. The prevalence we found is similar to - although slightly higher than - the 13% calculated in a review of 10 studies for a pooled sample of 4,856 individuals with a primary diagnosis of BD³. These differences may arise from the heterogeneity of the included studies (some had been performed before BED became a separate ED category), as well as from the higher age of the patients included in our cohort (our prevalence estimates were not weighted by sociodemographic characteristics). When we examined the prevalence of ED types as a function of BD type, all ED types were homogeneously overrepresented in the BD2 vs. BD1 subsample.

A further aim was to investigate the clinical characteristics of BD types in relation to comorbid EDs. Fornaro et al.'s meta-regression³ indicated that patients with BD2 are more likely to exhibit comorbid ED than patients with BD1 cases. Overall, EDs were independently associated with a worse BD disease course in our study. Severity indicators were very similar for both BD types: younger age at BD onset (for BD with AN or BED), suicide attempts, higher likelihood of depression, higher likelihood of comorbid substance use and anxiety disorders, abnormal BMI (lower for AN and higher for BED, with strong effect sizes), and higher affective lability

for BD+ED patients with versus without ED. We also observed higher levels of childhood trauma for patients with BD and AN or BED compared to the absence of ED. After controlling for other variables, the independent factors differentiating BD patients with versus without ED were primarily younger age, female gender, abnormal BMI, increased affective lability and higher comorbidity with anxiety disorders.

The different patterns of adjusted association between clinical and sociodemographic features and ED types in BD suggest different pathway that mediate the presence of ED and the resulting clinical severity. For instance, in the regression models, increased CTQ was eventually only associated with BED compared to the absence of ED, BED being also associated with younger age, comorbid anxiety disorders and with female gender. BD patients with vs. without AN showed similar gender, age and comorbid anxiety disorder profile than BED vs. no ED, yet with a particular association with increased lifetime SA risk and increased affective lability. The association between AN and risk of past suicide attempts in BD is similar to the risk conferred by AN in non-BD populations AN²⁸⁻³⁰. Importantly, no other ED was associated with additional risk for SA in BD, which is already a high-risk population for SA³¹. It is noteworthy that most of the associations related to AN and BED showed strong effect sizes.

From a clinical point of view, the results of the present study firmly underline the need to screen for EDs in the BD population with variable issues depending on the type of ED. Comorbid AN were independently associated with more frequent past suicide attempts than comorbidity with BED, after adjustment for multiple confounders that are also known to enhance rate of suicidal attempts (e.g., comorbid anxiety, and substance use disorders). On the other hand, half of the comorbid patients still had active ED (past-month symptoms) and this rate was almost 2/3 among patient with BED. A rigorous evaluation of BED would allow a specific management of BED associated in our sample as in previous study with a high functional impairment, but also to include in the benefit-risk balance of the choice of the optimal mood stabilizer, some

treatments can necessarily aggravate the binge eating episode³². One typical patient profile that should be carefully screened is a younger female patient with BD2 and an abnormal BMI (i.e. below 18.5 or above 30). A high proportion of patients with BD have a BMI > 25^{32,33}, and the prevalence of lifetime EDs among our patients with BD cases who had a BMI > 30 was 30%, compared with 13% in those who had a BMI < 30. Our findings therefore suggest that, among patients with BD who have an abnormal BMI, a substantial proportion of this weight problem may be due to comorbid EDs, and not simply to BD lifestyle and medication. This would substantially improve our ability to prevent and/or manage metabolic syndrome, a dramatic issue for morbidity and mortality in BD³⁴.

EDs were independently associated with comorbid mental disorders in BD. The link between anxiety disorder and EDs had already been demonstrated³⁵, and it seems particularly important to identify the type of comorbid anxiety disorder, in order to propose more targeted treatments. Anxiety disorders and—to a lesser extent—comorbid substance/sedative use disorders were both associated with EDs. These other comorbid disorders may have a greater influence than EDs on daily functioning, suicidality, and current depressive symptoms. However, if EDs are a precipitating factor for either anxiety or substance/sedative use disorders, increased prevention measures should be put in place to reduce the burden associated with these complex comorbidity patterns. Overall, our findings also further highlight the pivotal role of anxiety disorders in the most complex comorbidity patterns exhibited by BD patients³⁶.

Interestingly, despite the overall profile of increased severity, the number of inpatient stays did not differ in the presence or absence of EDs after adjustment for multiple confounders. This may reflect the fact that comorbid EDs worsen BD features that alter the mid- to long-term disease course of BD, rather than being associated with acute instability in the form of, say, manic episodes (as is seen with other comorbid conditions such as severe substance use

disorder³⁷). This interpretation is supported by the absence of association between EDs (as a whole and type-specific) and the rate of mood episodes /year in our sample.

The study had two main strengths. First, the sample was consecutively recruited, and both BD and EDs were ascertained using well validated assessments applied by trained clinicians in a structured interview. Second, the sample size was equivalent to more than half the sample size of the recent meta-analysis by Fornaro et al.³, and about three times more than the single study with the largest sample published to date. This large sample allowed us to perform reliable subsample analyses that could not previously be performed. Our study also had limitations. First, the lack of a control group with non-BD individuals limited the specificity of our findings. Second, the ED diagnosis was considered on a lifetime basis, so investigators were advised to retain the most impactful EDs across the lifespan. In addition, there were few BNs in our sample which does not allow precise statistical analyses on this specific population. We believe that this limitation will require further investigation. Third, our study was only cross-sectional and not longitudinal, preventing causal inference.

Conclusions

Results of a standard procedure revealed a particularly high prevalence of EDs in patients with BD who underwent a standard assessment procedure. ED comorbidity was also associated with severity indicators, and was independently more frequent in BD2. It is essential to adapt the management of patients with BD who exhibit this comorbidity, by providing integrated BD and ED care. The impact of ED on BD course and presentation was similar when considering BD types, but showed interesting patterns when considering ED types, including on possibly lethal events such as suicidal behavior. Future studies should therefore now focus on the evolution of these disorders as a function of comorbidities and subtypes of BD and ED to better understand their mutual interactions.

Author statement

Contributors

VF, RI, LS and SG wrote the first draft of the manuscript. PML, VA, RS, PR, MP, PC, EO, CH, EH, BE, ML, FB, RB and OG obtained the initial funding for recruitment and designed the overall assessment strategy. RI, SGa, KMB, IB, LS, GB, JL, IC, NM and SGu designed the specific methodology of the current study and reviewed the first draft of the manuscript. All authors critically reviewed and approved the final version of the manuscript before submission.

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Declaration of Competing Interest

The authors declare that they have no competing interests with regard to the manuscript.

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Captions

Figure 1: % patients with any lifetime ED as a function of BD type and gender. N =2929. Ns are shown in bars and % in x-axis. BD, bipolar disorder; AN, anorexia nervosa (bingeing and restrictive subtypes combined); BN, bulimia nervosa; BED, binge eating disorder.

Figure 2: % patients with each ED type as a function of BD type and gender. N =2929. % shown in y-axis. BD, bipolar disorder; AN, anorexia nervosa (bingeing and restrictive subtypes combined); BN, bulimia nervosa; BED, binge eating disorder.

Figure 3: Effect sizes (scaled Z values) of differences between ED types as a function of clinical and sociodemographic variables. BD, bipolar disorder; SA, suicide attempt; MADRS, Montgomery-Asberg Depression Rating Scale; FAST, Functional Assessment Short Test; CTQ, Childhood Trauma Questionnaire; ALS, Affective Lability Scale; BMI, AUD, alcohol use disorder; SedUD, sedative use disorder; AN, anorexia nervosa (bingeing and restrictive subtypes combined); BN, bulimia nervosa; BED, binge eating disorder. * $p < 0.00833$, ** $p < 0.00167$, *** $p < 0.00017$.

Supplementary Table: full data from multinomial regression with ED types as the dependent variable.

Table 1: Comorbid eating disorders in patients with BD Type 1 and BD Type 2.

	BD 1	BD 2	p
	N=1,504	N=1,424	
No eating disorder	1,319 (88%)	1132 (80%)	
Anorexia nervosa	54 (34%)	89 (6%)	<0.001
Bulimia nervosa	28 (2%)	35 (3%)	
Binge eating disorder	103 (7%)	168 (12%)	

BD, bipolar disorder

ED type		N	no ED (WED) N=2,765	Anorexia (AN) N=168	Bulimia nervosa (BN) N=69	Binge eating disorder (BED) N=301	Uncorrected p across ED types ^a	Significant pairwise differences ^b
Women (vs. men)***		2927	1,352 (55%)	136 (95%)	54 (86%)	223 (82%)	<0.00001	ALL vs. WED; AN vs. BED
Age***		2928	41 (13)	34 (12)	36 (10)	38 (11)	<0.00001	ALL vs. WED; AN vs. BED
Years of education		2445	14 (3)	14 (2)	15 (2)	14 (3)	0.09265	
Marital status	Never married		906 (39%)	64 (44%)	26 (43%)	102 (39%)		
	With partner	2506	1,183 (50%)	62 (43%)	27 (45%)	120 (46%)	0.3371	
	Divorce/separated		266 (11%)	19 (13%)	7 (12%)	39 (15%)		
BD subtype	Type 1	2928	1319 (54%)	54 (38%)	28 (44%)	103 (38%)	<0.00001	AN vs. WED; BN vs. WED
	Type 2		1132 (46%)	89 (62%)	35 (56%)	168 (62%)		
AAO BD***		2928	24 (9)	19 (6)	21 (8)	21 (8)	<0.00001	AN vs. WED; BED vs. WED
AAO ED**		408	N/A	17 (7)	20 (8)	21 (10)	0.00037	AN vs. BED
Past-month ED symptoms**		443	N/A	57 (42%)	26 (44%)	153 (62%)	0.00032	AN vs. BED
History of suicide attempt***		2859	836 (35%)	86 (61%)	31 (51%)	121 (46%)	<0.00001	ALL vs. WED; AN vs. BED
Age at first suicide attempt***		997	31 (14)	24 (13)	22 (12)	30 (13)	<0.00001	AN vs. WED; BN vs. WED; AN vs. BED
Past-year BD episode		2676	1751 (77%)	104 (84%)	45 (82%)	197 (83%)	0.07798	
Rate of MDE per year of BD		2255	0.3 [0.2-0.5]	0.3 [0.2-0.7]	0.3 [0.2-0.5]	0.3 [0.2-0.5]	0.02805	
Rate of (hypo)manic or mixed episodes per year of BD		2807	0.2 [0.1-0.4]	0.2 [0-0.4]	0.2 [0.1-0.4]	0.1 [0-0.3]	0.05339	
History of psychosis***		2517	840 (40%)	32 (26%)	14 (28%)	60 (26%)	0.00001	AN vs. WED; BED vs. WED
MADRS total***		2891	10 (9)	13 (9)	13 (11)	13 (10)	<0.00001	ALL vs. WED
YMRS total		2885	2 (4)	3 (4)	1.7 (2.3)	3 (4)	0.0028	
FAST total***		2784	18 [8-30]	21 [10-29]	24 [15-35]	26 [14-38]	<0.00001	BN vs. WED; BED vs. WED; BED vs. AN;
CTQ total***		2795	42 (14)	49 (18)	46 (14)	48 (17)	<0.00001	AN vs. WED; BED vs. WED
ALS total***		2755	1.2 (0.7)	1.6 (0.6)	1.6 (0.7)	1.5 (0.6)	<0.00001	ALL vs. WED
BMI (kg.m ⁻²)***		2769	24 [22-28]	21 [19-23]	25 [22-30]	29 [24-34]	<0.00001	AN vs. ALL; AN vs. WED; BED vs. WED; BN vs. BED
Waist circumference (cm)***		2628	91 (15)	81 (13)	91 (15)	100.5 (18)	<0.00001	AN vs. ALL; AN vs. BN; BED vs. BN; BN vs. BED
Substance use disorders	Anxiety disorder***	2840	927 (39%)	95 (68%)	41 (65%)	173 (66%)	<0.00001	ALL vs. WED
	Tobacco (vs. never smoked)		282 (12%)	20 (15%)	10 (17%)	282 (12%)		
	Former	2783	1072 (46%)	66 (49%)	30 (51%)	1072 (46%)	0.4969	
	Current							
	Cannabis use disorder		457 (19%)	37 (27%)	13 (21%)	51 (19%)		
	Alcohol use disorder **	2881	567 (23%)	49 (36%)	23 (37%)	79 (30%)	0.00024	AN vs. WED
	Sedatives use disorder ***		90 (4%)	10 (7%)	8 (13%)	28 (11%)	<0.00001	BN vs. WED; BED vs. WED
Stimulant use disorder			125 (5%)	14 (10%)	5 (8%)	17 (6%)	0.05989	

Table 2. Characteristics of ED patients in the FACE-BD sample at baseline, by ED type (p-values are considered significant after Bonferroni correction for 20 tests and further corrected for pairwise comparisons wherever applicable). N (%), mean (SD) or median [IQR] are shown. "ALL" denotes significant difference against each ED type. ^aKruskal-Wallis or Chi² or Fisher exact tests. Significance level across the five groups: **p* < 0.0025, ***p* < 0.0005, ****p* < 0.00005; ^b*p* < 0.0025 / number of pairs tested. AAO - Age at onset, MADRS - Montgomery-Åsberg Depression Rating Scale,

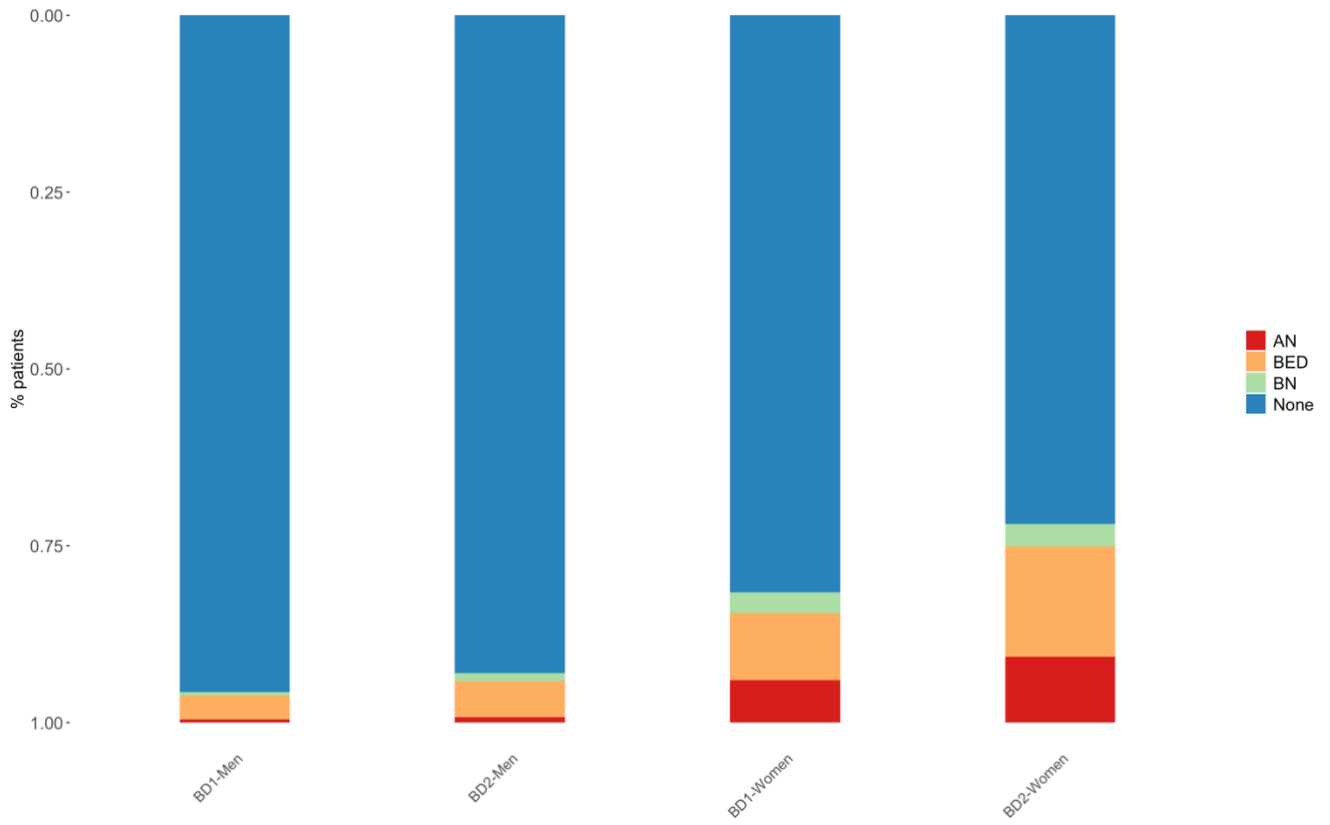


Figure 1

% patients with any lifetime ED
as a function of BD type and gender
N = 2928. Ns are shown in bars and % in x-axis.

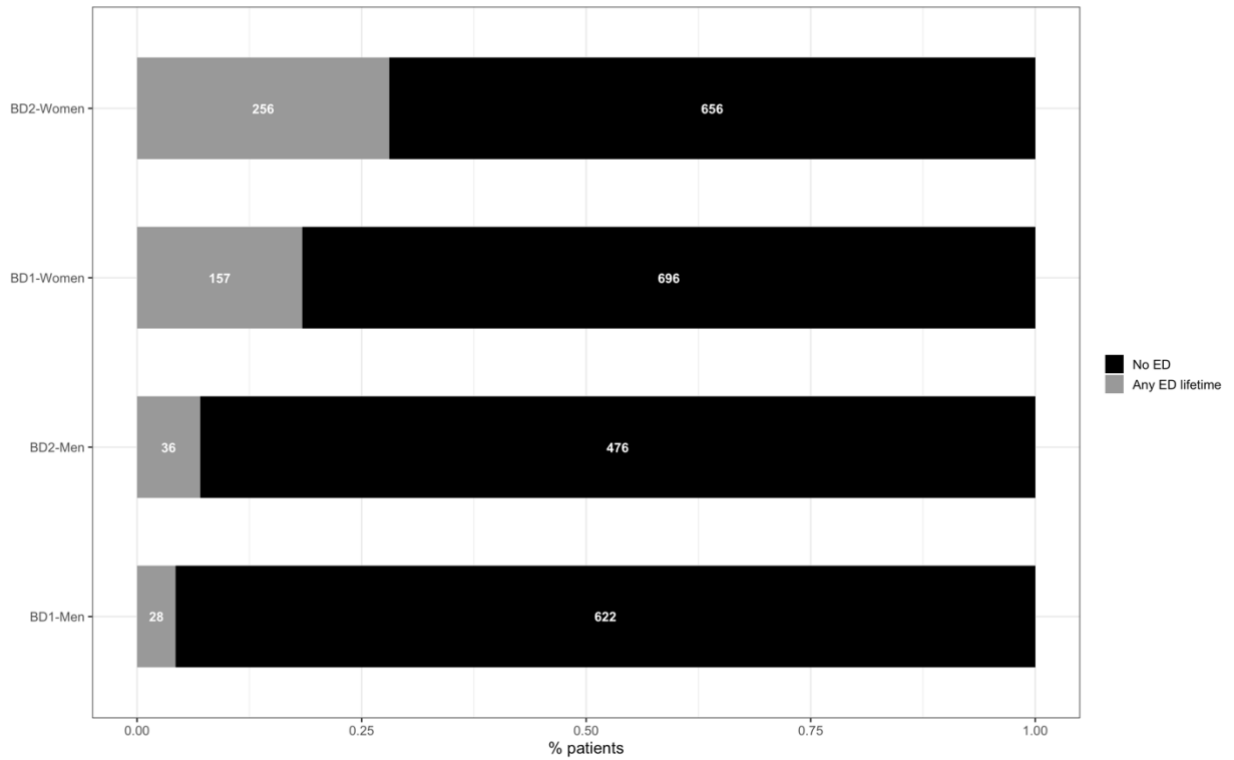


Figure 2.