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Prévalence croisée entre les troubles des conduites alimentaires et les sous-types de troubles bipolaires : Revue systématique de la littérature

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Conflict of interest

SG and PC declare having received fees for interventions from Janssen, Otsuka, Lundbeck, BMS and Servier. The authors have declared no conflict of interest in connection with this review.

Authors' contributions

SG and ST designed and carried out the bibliographical research; ST drafted the article: NG, PC, SG and LR made comments and improved the manuscript; all the authors approved the manuscript.

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Abstract

Objective: To assess the association between sub-types of bipolar disorder (BD) (types I and II) and sub-types of eating disorders (EDs) (Anorexia Nervosa, Bulimia Nervosa, Binge-eating disorders) as well as their relative order of occurrence. **Methodology**: A systematic review of articles estimating prevalence rates for BD among patients with ED and vice-versa. We also analysed all articles assessing their relative order of occurrence. **Results**: Comorbid BD is common among patients with an ED. From 0.6 to 33.3% of bipolar subjects have an eating disorder. Conversely, from 0 to 35.8% of subjects with an ED can present a BD. This co-occurrence has mostly been observed among patients with anorexia of the bulimic/purging type, with bulimia or with binge-eating disorders. The association is less frequent in cases of anorexia of the restrictive type. In contrast, the BD sub-type does not seem to have an impact on the association with EDs. Whilst age at BD onset is earlier in case of a comorbid ED, age at ED onset does not seem to be impacted by the presence of an associated BD. There has been little data on the relative order of occurrence of the two disorders or on the impact of the thymic phase on the expression of EDs. **Conclusions**: EDs and BD are frequently comorbid, suggesting the need for crossed screening of these pathologies, in particular for EDs with purging behaviours and for patients with early BD onset.

Keywords: bipolar disorder, anorexia nervosa, bulimia nervosa, binge-eating disorders, comorbidity

Résumé

Objectif : Evaluer l'association entre les sous-types de troubles bipolaires (TB) (type I et II) et les sous types de troubles des conduites alimentaires (TCA) (anorexie, boulimie, hyperphagie boulimique) ainsi que leur chronologie relative d'apparition. **Méthodologie** : Revue systématique des articles ayant estimé une prévalence du TB chez des patients souffrant de TCA et réciproquement. Nous avons également analysé tous les articles évaluant leur chronologie relative d'apparition. **Résultats** : Un trouble bipolaire comorbide est fréquent chez les sujets souffrant de TCA. Entre 0.6 et 33.3% de sujets bipolaires présenteraient un TCA. Réciproquement, entre 0 et 35.8% de sujets avec un TCA pourraient présenter un TB. Cette cooccurrence est le plus souvent observée chez les sujets présentant : une anorexie de type crises de

boulimie/vomissements ou prise de purgatifs, une boulimie ou une hyperphagie boulimique. Cette association est moins fréquente en cas d'anorexie de type restrictif. A l'inverse, le sous-type de TB semble ne pas avoir d'impact sur l'association avec un TCA. Alors que l'âge de début du TB est plus précoce en cas de TCA comorbide, l'âge de début du TCA ne semble pas être impacté par l'existence d'un trouble bipolaire associé. Il existe peu de données sur les chronologies d'apparition relatives des deux troubles et l'impact des phases thymiques sur l'expression du TCA. **Conclusions** : TCA et TB sont fréquemment comorbides, ce qui impose un dépistage croisé de ces pathologies, en particulier pour les TCA avec des manifestations purgatives et chez les patients avec un TB à début précoce.

Mots clés : trouble bipolaire, anorexie mentale, boulimie, hyperphagie boulimique, comorbidité

Introduction

Bipolar disorders (BD), like eating disorders (ED), are frequent psychiatric conditions occurring in young adults. The lifetime risk of developing BD is 1.32% (1.29-1.36) for men and 1.84 (1.80-1.88) for women [1], whilst the risk of developing an ED is 3.00% (2.95-3.06) for women and 0.17% (0.16-0.19) for men [1]. Since the nineties, a few literature reviews have raised the issue of a frequent comorbidity between these disorders [2] and have reported that from 5.3% to 31% of patients with BD present an ED; conversely, about 8% of patients presenting an ED develop a BD in the course of their lives [3-6].

There are however many limitations to these reviews. The first limitation results from the heterogeneity of the clinical forms of ED and BD under consideration. Previous studies have thus focused on BD as a whole, without making a distinction between type I BD and type II BD. Given the differences between these BD sub-types, particularly clinical and biological differences, [7,8], it is possible that their respective associations with EDs differ. Similarly, although the most commonly defined ED types – Anorexia Nervosa (AN), Bulimia Nervosa (BN) and Binge-eating disorders (BED) - show differences in frequency of association with BD, they have not always been differentiated in studies. The second limitation is the absence of any synthesis of the published data concerning the relative order of occurrence of these disorders. The interpretation of the data on lifetime prevalence is restricted if the chronological link between these disorders is not known. A third limitation concerns the methodological disparities across studies, in particular the variability in the symptom profiles under study and the diagnostic criteria used to define the disorders [9]. The diagnostic classifications used have thus followed the evolution of the different DSM editions, with the use of the Research Diagnostic Criteria (RDC) for the earliest studies. With time, criteria have become less restrictive, thus leading to an increase in reported prevalence. For instance, the early classifications reported a maximum of 8.5% BD in the general population, whereas the most recent report up to 33.3%. Furthermore, most studies were cross-sectional; it is therefore not possible to establish a chronological sequence of events, which could increase the risk of making incorrect diagnoses in pathologies where the diagnosis is unstable over time. Indeed, depending on the age of the subjects under study, certain BD or ED sub-types with a late onset, such as BED, may not yet have developed. The diagnostic tools used are also very heterogeneous, ranging from simple self-report questionnaires to structured standardised interviews. Finally, these reviews were generally carried out by teams

specialised in one of the disorders, and who consequently lacked knowledge in the other pathology. It therefore seemed necessary to carry out a literature review that addressed these limitations.

The objectives of this systematic review were first to study the respective prevalence of ED and comorbid BD, differentiating their sub-types, and secondly, to study their development through their relative order of occurrence. Methodological differences in the various studies were taken into consideration in order to interpret the relationships between these disorders.

Method

This systematic review followed the PRISMA recommendations (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) [10].

A systematic review on Pubmed was carried out on articles published between 1980 and May 31st 2017. Inclusion criteria were the following: studies published in English, French or Spanish, including patients with EDs and patients with BD, enabling a calculation of the prevalence of these comorbidities. Studies that did not enable the calculation of the prevalence were excluded (figure 1). The method and the article selection procedure are available in the Supplementary Material section.

Results

Seventy-nine studies on the prevalence and co-occurrence of ED/BD were retained. Some had been carried out on clinical populations (hospitalised or ambulatory) with EDs or BD and others on the general population. The studies were divided into 3 categories: general population (6 studies), patient populations with BD (34 studies) and patient populations with EDs (39 studies).

Study on the comorbidity of bipolar disorders/eating disorders in the general population:

Six studies [11-16] in the general population focused on BD/ED comorbidity. **Table 1** gives a summary of these studies: the BD and ED prevalence figures observed were proportionally higher when the definitions of these disorders were less strict (some studies, such as *Angst et al.* [12], considered sub-clinical forms, where BED was defined by the presence of more than 4 episodes a year). Logically, the prevalence of ED and BD also increases with the average age of the samples. Only two studies [11, 15] were carried out on an adult population, the others concerned adolescents or young adults (19-20-year-olds); these two studies found the lowest frequencies of the disorders, using subsyndromal definitions. The prevalence also increased with the number of ED sub-types under study. Frequency was very low if only AN was considered [11], but higher if both AN and BN were considered together [14]. The larger the sample, the greater was the number of cases observed for each disorder. Therefore, the greater the number of cases observed, the greater the probability of observing comorbid cases, which contributes to explaining apparently contradictory results. For instance, in the *Fogarty et al.* study [11], the fact that only AN was taken into account - a

rare disorder in that sample (0.1%) – could explain the absence of any link between BD and ED.

Three studies found a significantly increased frequency of BD among patients with an ED compared to the general population. Among adolescents, Lewinsohn et al [14] reported that the risk of bipolar disorders not-otherwise-specified (BD-NOS) was 4.8 times greater than in case of eating disorders not-otherwise-specified (EDNOS). Swanson [16] estimated this risk to be 7.3 times greater for BN and 3 times greater for BED. Finally, among adults, *Hudson et al.* estimated the risk of BD to be 4.7 times greater for BN, 3.6 times for BED and 3.5 times for any ED subtypes with purging behaviours.

The main limitation of these studies is that the prevalence results were not adjusted on possible confounding factors (psychiatric or addictive comorbidities, history of early abuse, etc.). Another major limitation is the cross-sectional nature of most of these studies. In this sense, Lewinshon's longitudinal study [13] is particularly informative because it involved a prospective follow-up of adolescents up to 24 years of age, thus limiting the risk of underestimating the link (because of late onset age and the possible diagnostic instability).

To sum up, the study of comorbidity between EDs (particularly AN) and BD in the general population is difficult because of the low frequency of these two types of disorders. There are however arguments in favour of an increased frequency of BD in patients with BN or BED. Two studies carried out on large samples of adults [15] or adolescents [14] showed that the risk of presenting type I or type II BD was significantly greater in case of BN (alone or associated with AN) or BED, compared to the general population. AN or BED-NOS, on their own, do not increase this risk.

Compared to the general population, adolescent patients presenting BD-NOS have an increased risk of having an ED (AN or BN) [16]. Adults presenting hypomania seem to more frequently present BED (4 episodes a year) [12].

Studies on the lifetime prevalence of EDs among patients with BD.

Table 2 gives a summary of the thirty-four studies [8,17-49] assessing the prevalence of EDs in patient populations presenting BD.

The prevalence of AN, BN and BED in the general population is about 0.9%, 1-2.3% and 1.9-3.5% respectively [50]. Figure 2 gives a summary of BD prevalence rates overall (Figure 2a), followed by prevalence rates per sub-type (BD I and BD II) differentiating the different EDs (Figures 2b and 2c). Figure 1a clearly suggests that in a population with BD, these prevalence figures are higher, with up to 8.6% for AN, 24.6% for BN and 28.8% for BED according to studies. This comorbidity seems to be more frequent in disorders presenting bingeing episodes: BN and BED.

Results are very heterogeneous across studies: AN prevalence varies from 0 to 8.6%, BN prevalence from 2.3 to 24.6% and BED prevalence from 0 to 28.8%. The range of the different values found for AN is thus smaller than for BED.

In type I BD, a prevalence of EDs from 2.3 to 35.2% was found, from 0 to 8.6% for AN, from 2.3 to 24.6% for BN and from 8.9 to 17.6 for BH. Figure 2b suggests that, across studies, the prevalence of BED is higher than for AN. As for BN, the inter-study variability is

substantial. However, the prevalence of AN in patients suffering from type I BD seems lower than the prevalence of BN and BED across all studies considering the three types of ED. A BN/BED comparison was not possible given the diversity of the results.

In type II BD, the prevalence of EDs ranged from 5.6 to 40%: 0.5 to 4.2% for AN, 5.4 to 15.8% for BN and 5.6 to 13.7% for BED. The prevalence of AN among patients presenting type II BD is systematically lower than the prevalence figures for BN and BED (figure 2c). A BN/BED comparison was not possible given the diversity of the results.

Patient age does not seem to be a contributory factor to explaining the variations observed, as most studies focused on populations between 30 and 45 years of age. In the study by *Martin et al.* [49], the average age of 16 could explain the absence of BED, for which onset occurs much later [15].

For women, Zerwas et al. [51] found a peak of occurrence at 15 years of age for AN, and 22 for BN.

It is interesting to see that the highest ED prevalence figures – up to 33.3% - have all been based on recent classifications, whereas earlier classifications (up to the DSM-III-R) only yielded 8.5% ED. The early studies only took one ED (BN) or two EDs (AN and BN) into account, and quite often did not consider BED, which appeared later in the DSM IV classification. The use of the DSM 5 criteria increased the frequency of the different ED sub-types at the expense of EDNOS (deletion of the amenorrhea criterion, decrease in the numbers of bingeing episodes for BN and BED episodes [52]). With time, classifications have become less restrictive and have led to an increase in the reported prevalence of EDs.

Studies that excluded patients presenting substance abuse, psychosis or suicidal behaviour, or even personality disorders [18,23,27,29,33,37,44] found a lower prevalence of EDs, ranging from 6.6 to 15.2%. These studies probably underestimated the prevalence of the association, due to frequent comorbidities between the different diagnoses.

The study populations comprised 43 to 100% women. However, EDs occur more frequently in women than in men. Therefore, for the same number of sub-types considered, and with similar diagnostic criteria, the frequency is greater if the percentage of women is high. The study by *Azorin et al.* [40] is in this respect interesting, because it makes a distinction between prevalence figures for men and women.

No differences in prevalence were found in relation to whether the patients recruited were ambulatory or hospitalised.

To sum up, if we analyse the studies that have focused on AN, BN and BED at the same time, the frequency of EDs among patients presenting BD varies from one study to another from 9.9 to 28.8%. According to these same studies, it ranges from 14.4 to 24.7% for type I BD and from 13.7 to 30% for type II BD.

Only one study [49] included a control group and found a greater prevalence of bulimic episodes induced by stress and emotion-related eating behaviours in young people with bipolar disorder ($p=0.001$).

The eating disorder for which the prevalence is the lowest in patients presenting type I or type II BD is AN. BED –8.3 to 28.8% - and Bulimia – 2.3 to 24.6% - are more frequent.

The studies that make a distinction between type I BD and type II BD do not allow a conclusion to be drawn on the prevalence of EDs according to BD sub-type, as no statistical test was carried out to make these comparisons. Some studies [8,26,30,44,47] found prevalence figures for EDs that are higher in type II BD compared to type I BD. However, other studies [20,33,37] found the opposite trend, with more EDs in type I BD compared to type II BD.

Studies on the lifetime prevalence of BD among patients with an ED.

Table 3 gives a summary of the thirty-nine studies [53-91] that assessed the prevalence of BD in patient populations with an ED.

20 studies included control groups and 5 studies [77, 86, 88-90] found a significantly greater frequency of BD among patients with an ED compared to the control groups. Because these studies were carried out on the largest samples, *Tseng et al.* [89] were able to evidence significant differences in the comparisons of groups of AN, BN, BED and EDNOS subjects with control groups ($p<0.0001$). Among patients with AN, ten years after hospitalisation, a greater frequency of BD-NOS was found compared to a control group ($p<0.01$) [77]. Godart et al. [88] also found a significantly greater frequency of BD in the purely restrictive AN (AN-r) group compared to control subjects.

Figure 3 summarises the prevalence rates for BD and its sub-types. The prevalence of BD is about 1% in the general population (0.6% for type I BD and 0.4% for type II BD) and 2.4% across the bipolar spectrum [92]. In an ED population, whatever the ED sub-type, the prevalence appears much higher, with up to 26.1% for type I BD and 26.7% for type II BD.

In the overall population presenting EDs, the prevalence of type I BD ranges from 0 to 26.1%, type II BD from 0 to 19.8% and BD-NOS from 0 to 9.7%. It is worth noting that the 9 studies [54, 55, 60, 64, 68, 71, 80, 85, 91] that did not find any type II BD were carried out on 50 or fewer subjects for six of them (and 78, 98 and 171 subjects for the other three studies [60, 64, 91]). The 8 studies [53, 54, 56, 68, 80, 84, 85, 91] that did not find any type II BD were carried out on 50 patients or fewer for 5 of them (with 51, 90 and 98 patients for the other three [53, 84, 91]), which suggests a probable lack of statistical power.

In AN, the prevalence figures found were the following: from 0 to 12.6% for type I BD, from 0 to 5.6% for type II BD and from 0 to 9.7% for BD-NOS. It seems that in a population with AN, type I BD is the most common, compared to type II BD and BD-NOS. Studies focusing on the prevalence of several ED sub-categories and differentiating purely restrictive anorexia from binging-purging anorexia are rare, but they all found the same results: a apparently higher prevalence of BD in the AN-BN sub-group compared to the restrictive sub-group [57, 58, 60, 61, 69, 88], although no significant difference was found, probably due to a lack of statistical power.

In the AN-r category, the prevalence figures found were the following: from 0 to 6.3% for type I BD, 0 to 1.8% for type II BD and 0% (only one study) for BD-NOS. In the AN-BN category, the prevalence figures were: 0 to 25.5% for type I BD, 1 to 5.6% for type II BD and 0 to 3.3% for BD-NOS.

In the BN category, the prevalence figures found were the following: from 0 to 20% for type I BD, 0 to 21.6% for type II BD, and 0 to 9% for BD-NOS. The prevalence values for type I and type II BD among patients presenting BN are fairly similar. As for BD-NOS, the prevalence was not as high as for type I and type II BD and was fairly close to that found in AN.

In the BED category, only 10 studies gave prevalence figures, making it difficult to draw any conclusions. The prevalence figures range from 0 to 22.7% for type I BD and 0 to 26.7% for type II BD.

Samples of patients presenting an ED mainly concern women; no study was specifically focused on men.

Studies that only focused on hospitalised patients found a prevalence of BD ranging from 2.5 to 8.3%. Studies focusing on both hospitalised and ambulatory patients did not make the distinction in the analyses.

Classifications have evolved. The prevalence figures found in the recent studies are higher. If we consider all studies up to the DSM-IIIR, we find prevalence figures for BD ranging from 0 to 18.5%, versus prevalence figures ranging from 0 to 35.8% for post-DSM-IV studies.

Certain studies presented more restrictive exclusion criteria, such as substance abuse, patients with unstable BD, suicide risk or serious psychosomatic disorder [55, 62, 63, 76, 85, 87-89, 93]. The prevalence figures found for these studies were mostly in the lower bracket of the prevalence figures observed.

In summary, EDs with purging/compulsive behaviours are the disorders the most commonly associated with BD. BN is the most frequently associated disorder with BD. If we exclude studies with small samples, the prevalence varies from 0.8% to 36%. For BED, there are fewer studies. Excluding small sample studies, the prevalence of BD ranges from 0.4% to 49.3%. Concerning AN as a whole, the prevalence of BD, excluding small sample studies, is 0 to 16.7%. For the AN-BN subtype, we find prevalence figures for BD from 0 to 29.1%. The purely restrictive AN subtype shows prevalence figures ranging from 0 to 8.1%, which is much lower than for the AN type involving episodes of bulimia. There is no data enabling a comparison between the frequency of occurrence of BD for AN, BN and BED, or their sub-types.

Relative order of occurrence of ED/BD

Table 4 gives a list of the relevant studies. In a population presenting EDs with a mean age of 21 years, *Godart et al.* [88] found onset of BD occurring around the same time as or later than ED onset. Conversely, other studies [28, 33] found BD onset occurring before the ED onset among patients with a mean age of 40-41 years. This preliminary data does not enable any conclusions to be drawn, given the small size of the samples.

Concerning the impact of comorbidity on age at BD onset: five studies on almost 3000 subjects presenting BD found similar results for significantly earlier age at BD onset in the case of a comorbid ED [33, 34, 47, 48, 94]. *McElroy et al.* [47] also found an age at BD onset

significantly earlier in case of a comorbid ED (p=0.02). However, when stratification was performed on ED sub-categories, the results were no longer significant, probably because of a lack of statistical power (p=0.06). This early onset could be aggravated by the presence of substance abuse. *Becker et al.* [95] have thus reported that in a population of 347 patients presenting BH, the presence of substance abuse comorbid with the mood disorder was associated with an earlier age at BH and BD onsets.

To sum up, age at BD onset is earlier in patients with a comorbid ED and even earlier in case of AN. Subjects with BD before or around puberty are more likely to have a comorbid ED. Age at ED onset does not seem to be affected by a comorbid BD.

Discussion

In this systematic review of the literature, whatever the methodological approach (general population, bipolar population, or ED population), the lifetime comorbidity of ED/BD is frequent.

Studies involving general populations found a significantly increased frequency of BD among patients presenting EDs compared to the general population, whether for adolescents or adults. This frequency is 4.7 to 7.3 times greater for BN, 3 to 3.6 times greater for BH and 3.5 times greater for any ED with purging.

In clinical populations, if we consider the studies covering 80% of the largest samples, we find an ED prevalence among patients with BD ranging from 0.6% to 33.2%, and a prevalence of BD in patients with EDs ranging from 0 to 26.1% for type I and 0 to 19.8% for type II BD.

The EDs for which this co-occurrence is the most frequent, are: AN-BN, BN and BED. BD comorbidity is less present in case of purely restrictive AN, whether for type I or type II BD. The presence of purging behaviours therefore seems to be a risk factor with respect to this lifetime comorbidity. The recent study by *Godart et al.* [88] differentiating purging forms (BN P+) and non-purging forms (BN P-) of BN found BD prevalence rates of 25.6% and 10.5% respectively. We could therefore hypothesise that the presence of purging behaviours is even more closely associated with BD than the presence of bulimic episodes. Conversely, BD sub-types do not seem to have an impact on the association with EDs.

Regarding the onset of disorders, in clinical populations of patients presenting BD, female patients with a comorbid ED had earlier BD onset; patients with a form of BD occurring before or around puberty are more likely to have a comorbid ED. The data is still too limited to draw any conclusion on the respective order of occurrence of the two disorders.

The marked comorbidity between BD and EDs requires systematic screening for the other disorder in each of these pathologies. A number of simple screening tools available in the French language can be used. The Mood Disorders Questionnaire (MDQ) has proved efficacious in screening for bipolar disorders among patients presenting EDs [64]. Similarly, a simple screening tool used for EDs such as the SCOFF questionnaire [96] could be of use. Screening should be all the more systematic when dealing with sub-populations that are at risk (purging EDs, early-onset bipolar disorders).

The joint treatment of these disorders is needed, since an eating disorder can lead to the deterioration of BD: poorer daily functioning between mood episodes, more serious anxiety disorders, more frequent thymic episodes, particularly depressive episodes [34][97]. The impact of BD on ED characteristics is more difficult to assess in the light of the current literature. The existence of an ED comorbid with BD could increase suicide risk (47.4% among BD patients with a lifetime ED versus 27.8% among BD patients without an ED, $p<0.01$), particularly in type I patients (61.8% versus 35.7% in type II patients) [8]. Finally, this comorbidity increases mortality, as was shown by a recent study [70] on patients with AN where the standardised mortality ratio (SMR) was 3.2 (95% IC=2.7-3.9) in the absence of a psychiatric comorbidity, 8.2 (95% IC=7.3-9.2) in case of a psychiatric comorbidity and 8.5 (95% IC= 5-13.4) in case of comorbid BD. In particular, women with AN and comorbid BD had mortality rates from non-natural causes 40 times higher than women in the general population. This comorbidity should guide prescriptions in BD, as anti-psychotic drugs have negative consequences on eating behaviours, especially increased food craving and loss of dietary control [98].

The dynamics and the order of occurrence of these two disorders remain understudied. There are probably crossed vulnerability factors that trigger the emergence of both disorders. Studies on families have thus shown that among parental psychiatric disorders, BD is the most frequently associated disorder with an increased risk of ED in children [99].
Although the data consistently suggests that the existence of an ED in case of BD is associated with early-onset BD, it is currently insufficient regarding the impact of this comorbidity on age at ED onset. Similarly, it is not currently possible to determine whether certain forms of ED chronologically precede and trigger the emergence of BD, or vice-versa. A number of methodological difficulties could explain this issue. Firstly, the mean age of ED onset varies from one form to another: anorexia, in the general population, has an earlier age at onset than BD, and BED an older age at onset than BD. Secondly, BD, whatever the thymic phase, is associated with frequent changes in eating behaviour: anorexia, hypophagia, weight loss, hyperphagia, and increase in appetite all interfere with ED diagnosis. Ramaccioti et al [28] found 4 patients for whom an ED had started during a manic episode, 7 during depressive episodes and 1 during a euthymic episode. *Mantere et al.* [100] found an association between EDs and depression ($r= 0.150.32$, $p<0.05$). *Seixas et al.* [36] and Torrent et al. [101] found more frequent EDs in depressive episodes. Similarly, people presenting EDs often present thymic symptoms interfering with the diagnosis of a thymic disorder. People with BED thus often describe depressive and anxious symptoms before a binging episode, followed by relief during the episode, later followed by depressive affects, self-depreciation and guilt after the episode has ended. Similarly, among people with AN, elation, slowing down, irritability, mood changes, hyperactivity, logorrhoea, and sleep disorders have all been observed, and are possibly linked to undernourishment. These different crossed symptoms make it difficult to study BD/ED chronologies.

Future studies should differentiate ED sub-types to confirm the risk-prone populations we have evidenced. Particular attention should be given to the order of occurrence of the two disorders so as to understand it more fully. Indeed, respective age at onset for the two disorders is of great clinical and prognostic interest, and unfortunately there is still a lack of studies on the subject.

Beyond the objectives of this review, the association between BD and EDs raises the issue of the link between AN and BD. McElroy et al. [3], as well as Godart et al (not yet published), suggest two reasons for this comorbidity: (1) ED and BD are two distinct entities, or they

share aetiological mechanisms that constitute risk factors one for the other; (2) there could be vulnerability factors that are common to both disorders. Data from a variety of sources currently supports this hypothesis. A bipolar disorder could thus be the parental psychiatric pathology that most increases the risk of the children developing an eating disorder [99]. BD and EDs share certain common clinical characteristics, such as emotional dysregulation, high suicide risk or common neuropsychological deficits, such as those affecting decision-making processes [102, 103]. Finally, there are pre-morbid personality traits, such as impulsiveness and emotional dysregulation which are frequently found in bipolar disorder or certain eating disorders (especially BN and BED) [3]. This data overall suggests that there is a vulnerability common to the two disorders, and that further investigation is required.

In AN, there is a high frequency of early major depressive episode. This occurrence should alert clinicians to the risk of developing BD. Indeed, as pointed out by Akiskal [32], the occurrence of depression before the age of 20 signals an increased risk of developing BD thereafter. 25% of children or adolescents presenting a major depressive episode thus develop BD in the 2 to 5 years following [32].

There are many advantages to our review (systematic review, inclusion of studies on clinical and general populations, etc.); there are nevertheless limitations. The use of different definitions and concepts for BD and ED diagnoses, and the changes in these definitions have made it difficult to compare studies. Successive changes in ED and BD diagnostic criteria have undeniably impacted patient selection and the prevalence figures found. Furthermore, there were weaknesses in the methodology of some studies, for instance, the size of the samples or the inclusion criteria (inclusion of women only, exclusion of patients with addictive comorbidities, etc.). As for studies on clinical populations, the recruiting establishments also could have impacted the prevalence results. In line with the results reported by *Hudson et al.* [53], the prevalence of BD among hospitalised patients was much higher than for ambulatory patients; as *Godart et al.* [6] remarked, patients who are treated are not representative of all the patients with EDs, as a result of a filtering effect in access to care. Furthermore, patients with multiple diagnoses are more likely to see a doctor and ask to be treated, and this trend is commonly known as *Berkson's paradox*.

To conclude, this review suggests a non-negligible comorbidity between BD and EDs of the purging type, leading to very serious consequences for patients. A screening for EDs is therefore paramount in case of BD, particularly in early onset, and vice-versa a screening for BD in presence of an ED. Because the association is even more marked, the screening for BD should be particularly careful in cases of the ED with purging/compulsive behaviour.

Conflicts of interest:

SG and PC have received payment for various interventions with Jansse, Otsukan Lundbeck, BMS and Servier. The other authors do not have any conflicts of interest to declare in connection with this review.

Authors' contributions:

SG and ST designed the review and carried out the bibliographical search. ST wrote the article; NG, PC, SG, LR provided comments and improved the manuscript; all the authors approved the manuscript.

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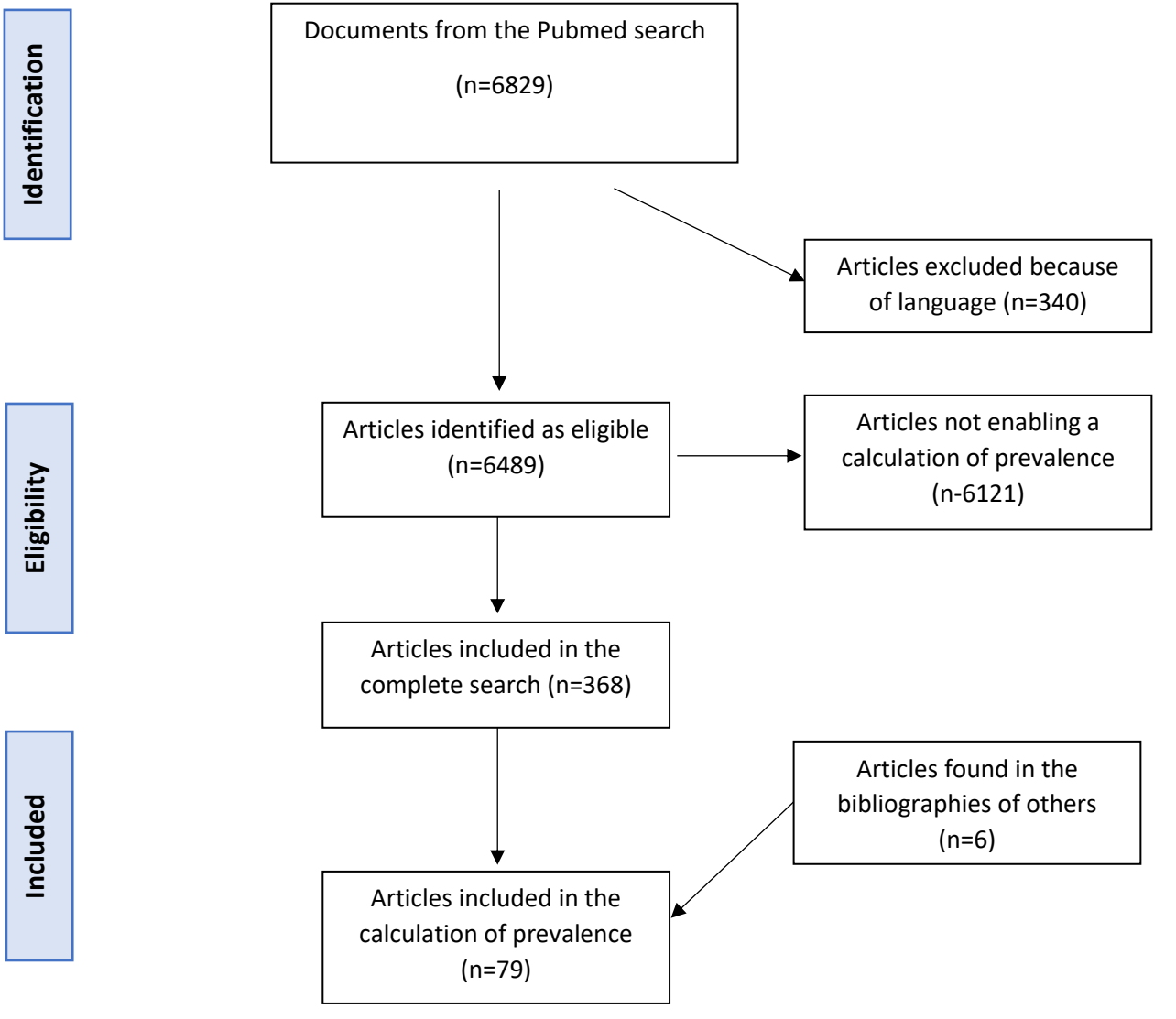
Figure 1. Flow Chart



Lifetime prevalence studies on ED among patients presenting a BD

Figure 2a. BD

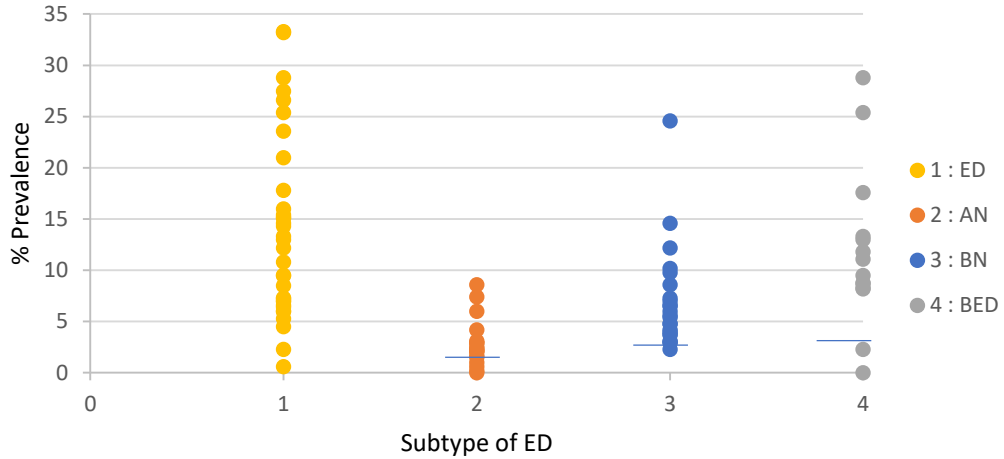


Figure 2b. BD I

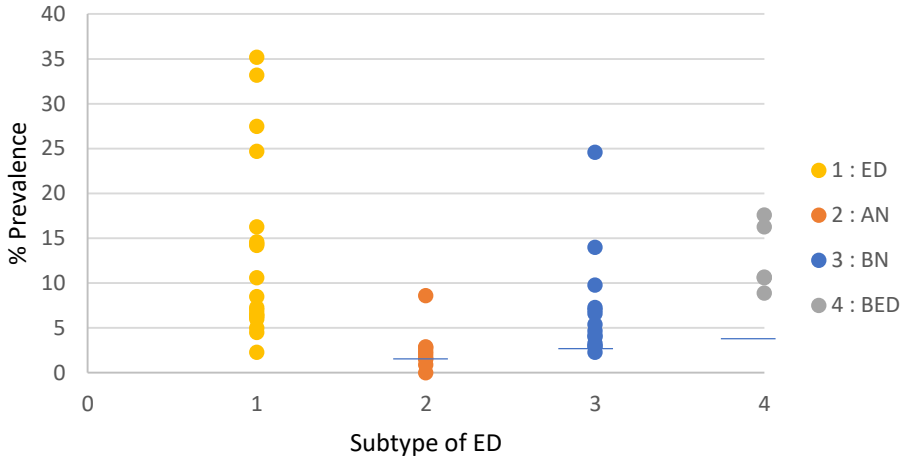
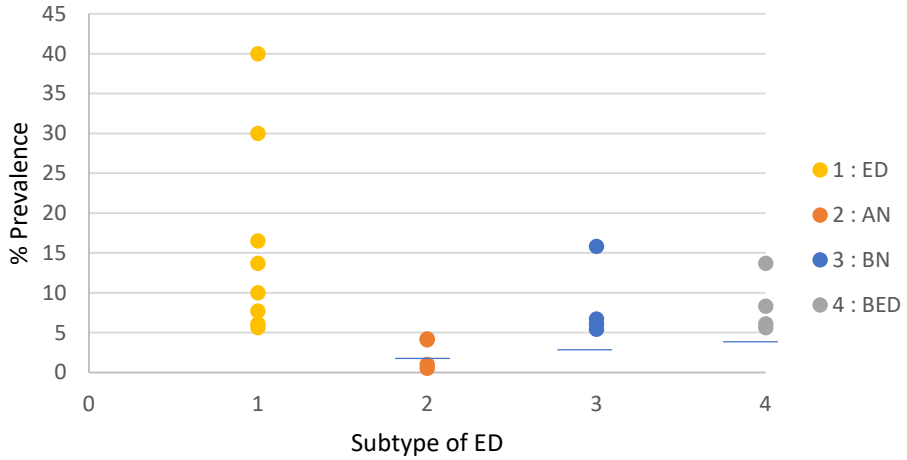


Figure 2c. BD II



Approximate prevalence in the general population

1 dot = 1 study

Lifetime prevalence studies on BD among patients presenting an ED

Figure 3a. ED

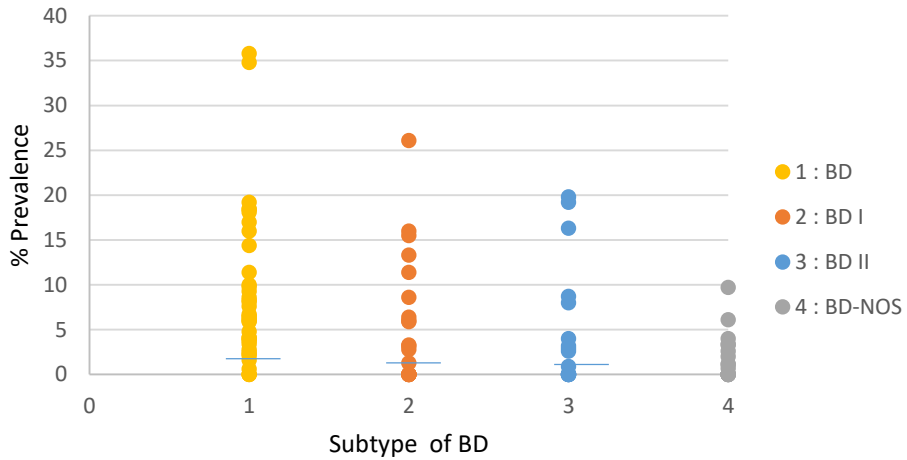


Figure 3b. AN

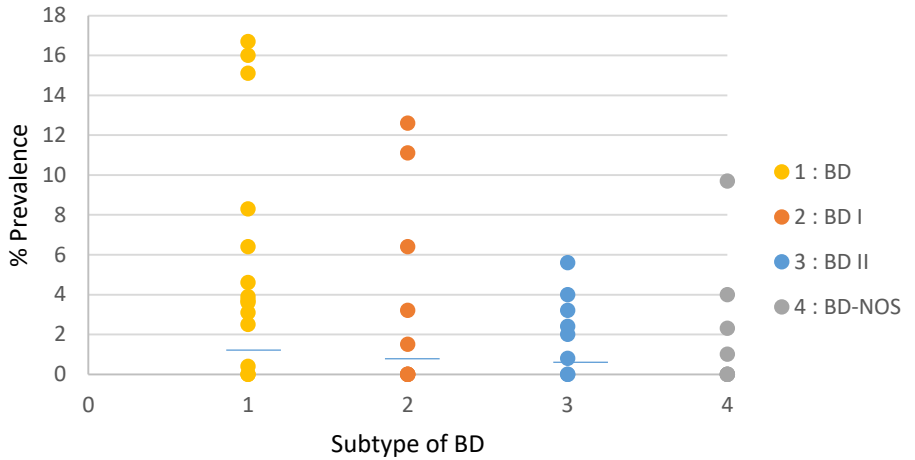


Figure 3c. BN

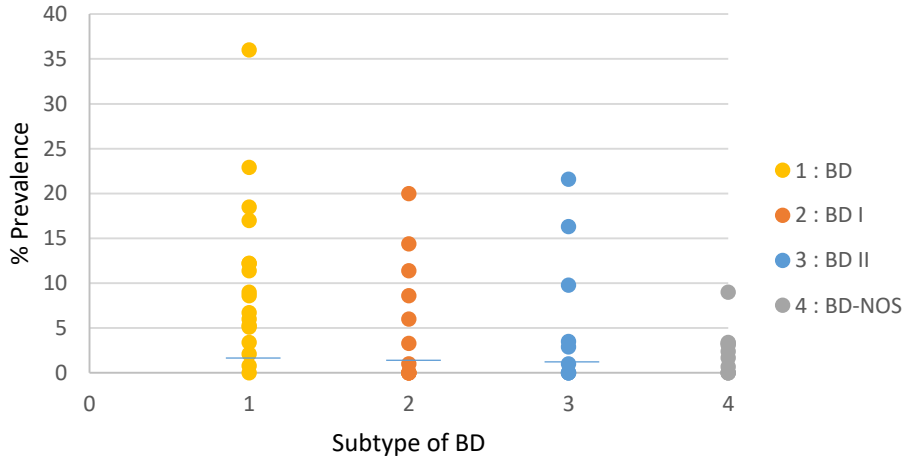
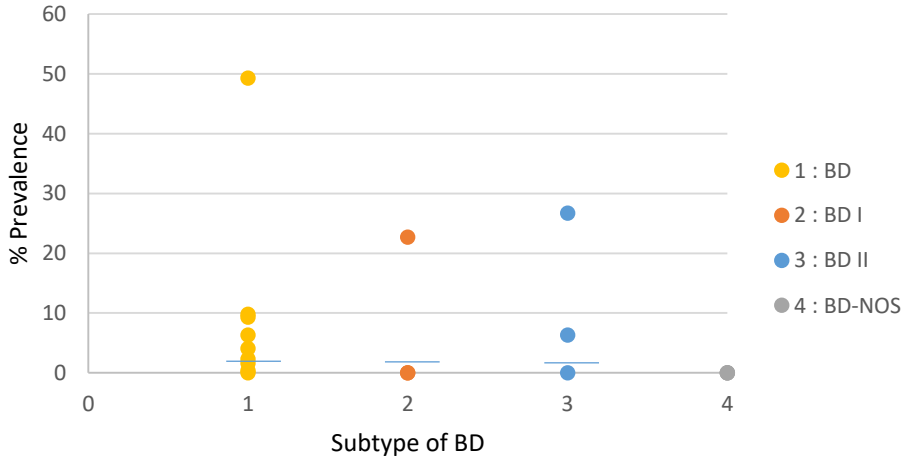


Figure 3d. BED



Approximate prevalence in the general population

1 dot = 1 study

Lifetime prevalence studies on BD among patients presenting AN

Figure 3e. AN-R

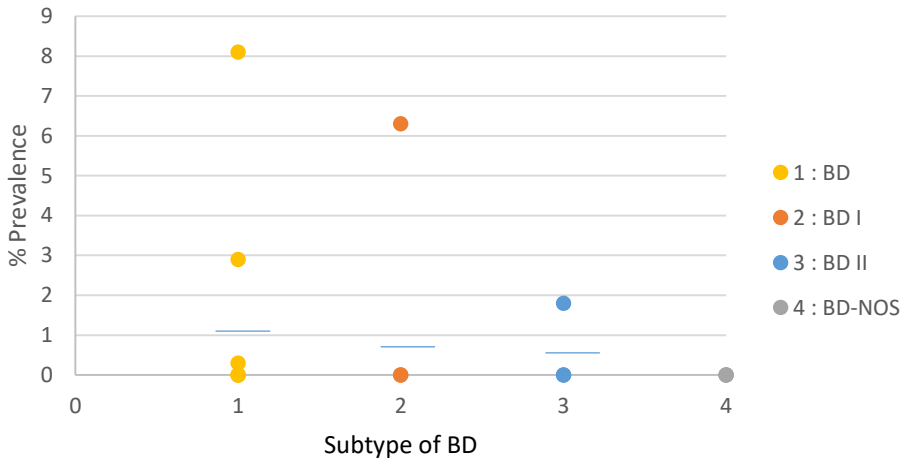
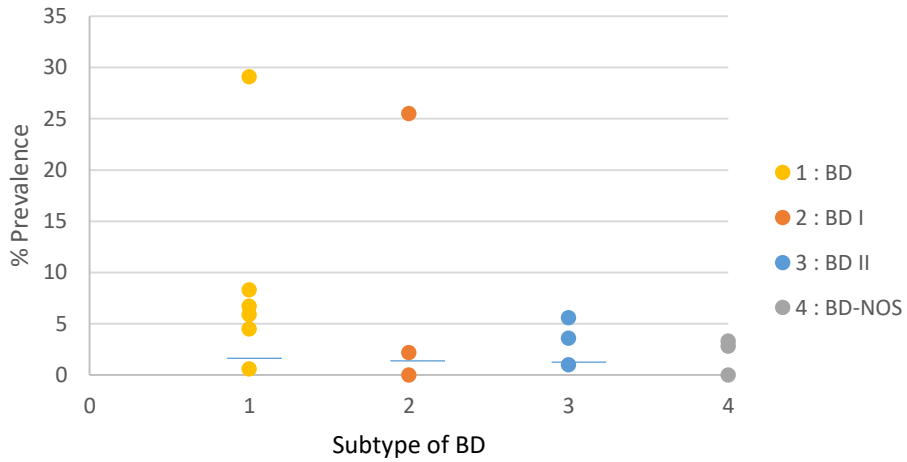


Figure 3f. AN-P



Approximate prevalence in the general population

1 dot = 1 study

Table 1. Studies on Bipolar Disorder/Eating Disorder comorbidity in the general population									
Study Author, year [reference]	**Instruments Criteria**	**Population**	**% F**	**Age**	**Type of ED assessed**	**Prevalence BD among ED subjects**	**Prevalence BD among non-ED subjects % (N)**	**Prevalence ED among BD subjects % (N)**	**Prevalence ED among non-BD subjects % (N)**
Fogarty et coll. [11]	DIS DSM-III	3258 inhabitants of Edmonton Canada	59	>18	AN	0 (NS)	0.6% (22 manic episodes)	0%(NS)	0,1% (2 AN)
Angst et coll [12]	SPIKE DSM-IV	4547 inhabitants of Zurich	ND	19-20	BH (4 episodes per year	ND	ND	12.8% (5) Hypomania 14.3% (8) manic symptoms (p=0,06)	4.7% (11) BH
Lewinsohn et coll. [13]	K-SAD DSM-III-R	810	52	16.6	23 ED -NS 19 ED	BD 0 % among ED and 4,3 % (1) ED-NS BD-NS 26,3% (5) among ED and 21,7% (5) among ED-NS	BD 1,2% (9) BD-NS 3,8% (29)	ND	ND
Lewinsohn et coll. [14]	K-SAD DSM-III-R	1704	52,1	16.6	23 ED-NS 13 ED (AN or BN)	BD-NS 17.4% (4) OR : 4.8 (1, 1–20,4) among ED NS TB 0% chez TCA-NS NS	BD 0,88 % (15) BD-NS 4,4% (75)	ED : 4% (3) among BD-NS OR 6.7 (1, 2–37,8) TCA-NS ND	0,76% (13) ED - NS ED 1,3% (23)
Hudson et coll. [15]	CIDI DSM-IV	2980 USA	59%	>18	23AN 52 BN 115 BH 46 BH-NS 192 any B-ED	BD 1 or 2 3% AN (NS) 17,7% BN (OR: 4.7 (2,1–10,8)) 12,5% BH (OR 3,6 (2,1–6,3)) 10,5% BH-NS(NS) 12% Any B-ED 3,5 (2,0–6,1)	ND	ND	AN: 0,6% BN: 1,0% BH: 2,8% BH-NS:1,2% Any B-ED: 4,5%
Swanson et coll [16]	CIDI DSM-IV	10123	ND	13-18	N	2,1 % BD 1 or 2 among AN (NS) 8,1% BD 1 or 2 among AN NS (NS) 18,5% BD 1 or 2 among BN (AOR : 7.3 (3.1-17.2)) 9% BD 1 or 2 among BH (AOR 3.0 (1.5-5.7)), 2,6 % BH-NS (NS)	2,8%	ND	0,3 % AN, 0,8% AN-NS, 0.9% BN, 1,6% BH, 2,5% BH-NS i.e. 4,5% ED

Significant differences between the general population and the ED population for the prevalence of BD (and vice versa) are given as odds ratios (OR) or adjusted odds ratios (AOR), otherwise NS is specified

AN : anorexia nervosa; Any B-ED: any ED with bulimic episodes; infra diagnostic BD: defined as having had a distinct period of abnormal mood, persistent, marked, expansive or irritable, in addition to having one or several manic symptoms, but never having met the full criteria for bipolar disorder; BN: bulimia nervosa; CIDI: Composite International Diagnostic Interview; DIS: Diagnostic Interview Schedule; DSM: Diagnostic and Statistical Manual of Mental Disorders; BH: bulimic hyperphagia; BH-NS : bulimic episodes at least twice a week over several months with loss of control, without meeting the full criteria for bulimic hyperphagia; ND: no data available; SPIKE: structured psychopathological interview and rating of the social consequences of psychic disturbances for epidemiology; ED: Eating Disorders BD: Bipolar Disorder; BDI ; type I bipolar disorder; BDII: type II bipolar disorder; ED-NS: cases are generally defined by refusal to maintain adequate weight (85% of the norm) for AN and by the presence of recurrent compulsive eating behaviours for BN without having sufficient other ED symptoms to meet the diagnostic criteria; YMRS: Young Mania Rating Scale

Table 2. Studies on the lifetime prevalence of ED among subjects presenting a bipolar disorder

Studies Author, year [reference]	Instruments, Criteria	Patients	Status	Age	N	F %	ED N (%)	AN N (%)	BN N (%)	BH N (%)
Strakowski et coll. 1992 [17]	SCID, DSM-III-R	BD, 1st manic episode	H	32	41	61	3(7.3%)	ND	3(7.3%)	ND
Strakowski et coll. 1993 [18]	SCID, CGI, BPRS, DSM-III-R	BD 1st manic episode	H	29	60	52	4(6.6%)	ND	4(6.6%)	ND
McElroy et coll. 1995 [19]	SCID, DSM-III-R	BD	H	35	71	55	6(8.5%)	ND	ND	ND
Krüger, Shugar & Cooke 1996 [20]	Semi-structured interviews, SADS, DSM-IV	BD BD I BD II	A	40	61 43 18	63	8(13 %), 23(38%)* 7(16.3%), 18(41.8%)* 1(5.6%), 5(33.3%)*	ND	ND	8(13 %), 23(38%)* 7(16.3%), 18(41.8%)* 1(5.6%), 5(33.3%)*
Schuckit et coll. 1996 [21]	SAGA, DSM-III-R	BD	M	40	14	100	1(7%)	0	1(7%)	ND
Edmonds et coll. 1998 [22]	DIGS, RDC, DSM-IV	BD BD I BD II	A	41	55 44 11	47	4(7.3%)	ND	ND	ND
Cassano et coll. 1998 [23]	SCID, DSM-III-R	BD, psychotic	H	34	47	56	3(6%)	1(2.1%)	2(4.2%)	ND
Pini et coll. 1999 [24]	SCID, DSM-III-R	BD, psychotic	H	35	125	59	8(6.4%)	3(2.4%)	5(4%)	ND
Vieta et coll. 2001 [25]	SCID-II, RDC, YMRS, DSM-IV	BD I	A	40	129	59	3(2.3%)	ND	3(2.3%)	ND
McElroy et coll. 2001 [26]	SCID, DSM-III-R	BD BD I BD II	A	44	288 239 49	56	17(6%) 12(5%) 5(10%)	6(2.1%) 4(1.7%) 2(4.1%)	11(3.8%) 8(3.3%) 3(6.1%)	ND
MacQueen et coll. 2003 [27]	SCID, YMRS, DSM-IV	BD BD I BD II	A	40	138 97 41	68	21(15.2%)	4(2.9%)	9(6.5%)	12(8.7%)
Ramacciotti et coll. 2005 [28]	SCID, BEDCI, DSM-IV	BD I	A	40	51	43	14(27.5 %)	ND	5(9.8%)	9(17.6%)
Alciati et coll. 2007 [29]	SCID, HCL-32 QEWP-R, DSM-IV-TR	Obesity + pre-bariatric BD	A	44	83 74	70	11(13.3%) 21(25.3%)*	0 0	0 0	11(13.3%) 21(25.3%)*
Wildes, Marcus & Fagiolini 2007 [30]	SCID, CGI-S-TB, DSM-IV,	BD BD I BD II BD-NS SAD BD	A	42	72 54 15 2 1	62	17(23.6%) 26(36%) ** 19(35.2%) ** 6(40%) ** 1(50%) ** 0	3(4.2%) 6(8.3%) ** ND ND ND ND	4(5.6%) 7(9.7%) ** ND ND ND ND	6(8.3%) 9(12.5%) ** ND ND ND ND
Wildes, Marcus & Fagiolini 2008 [31]	SCID, BDVF, DSM-IV,	BD BDS I BD II BD-NS	A		81 59 17 5	65	17(21%) ND ND ND	6(7.4%)** ND ND ND	7(8.6%) ** ND ND ND	9(11.1%)** ND ND ND
Lunde et coll. 2009 [32]	DSM-IV	Mood disturbances BD MDE	M	37	201 87 114	69	33(16 %) ND ND	12(6%) 22(12.9%) *** ND ND	11(5.4%) 21(10.4%) *** ND ND	ND ND ND
McElroy et coll. 2011 [33]	SCID, DSM-IV	BD BD I BD II	A	41	875 707 168	56	125(14.3%) 102(14.4%) 23(13.7%)	27(3.1%) 20(2.8%) 7(4.2%)	42(4.8%) 33(4.7%) 9(5.4%)	77(8.8%) 63(8.9%) 14(8.3%)
Brietzke et coll. 2011 [34]	SCID, DSM-IV	BD I	A	36	137	100	20(14.6%)	4(2.9%)**	4(2.9%)**	ND
Schoofs et coll. 2011	YMRS, DSM-IV	BD	A	37	52	100	15(28.8%)	0	0	15(28.8%)

[35]		BD I BD II			23 29		ND ND	0 0	0 0	ND ND
Seixas et coll. 2012 [36]	SCID, YMRS, DSM-IV,	BD	M	41	356	70	19(5.3 %)	8(2.2%)	11(3.1%)	ND
McElroy et coll. 2013 [37]	SCID, BIB-CQ, BIB-PQ, DSM-IV,	BD BD I BD II SAD-TBD	H	42	717 547 163 7	58	68(9.5%) 58(10.6%) 10(6.1%) 0	ND ND ND ND	ND ND ND ND	68(9.5%) 58(10.6%) 10(6.1%) 0
Jen et coll. 2013 [38]	YMRS, ASRM, DIGS, DSM-IV-TR, DSM-V	BD BD IBD II BD NOS, SAD-BD	A	39	354 263 59 23 9	67	63(17.8 %) ND ND ND ND	6(1.7%) 22(6.2%) ** ND ND ND ND	13(3.7%) 49(13.8%) ** ND ND ND ND	29(8.2%) ND ND ND ND
Gao et coll. 2013 [39]	MINI STEP BD DSM-IV	BD	A	38	166	54	18(10.8%)	1(0.6%)	17(10.2%)	ND
Azorin et coll. 2013 [40]	SCID, DSM-IV	BD I	H	43	1090	58	362(33.2%)	94(8.6%) M : 13(1.2%) F : 81(7.4%)	268(24.6%) M : 31(2.8%) F : 237(21.7%)	ND
Perugi et coll. 2013 [41]	YMRS, DSM-IV	BD I	H	45	202	60	9(4.5%)	3(1.5%)	6(3%)	ND
Nery et coll. 2014 [42]	SCID, DSM-IV	BD BD I BD II BD-NOS	A	40	483 434 36 13	71	46(9.5%) ND ND ND	12(2.5%) ND ND ND	23(4.8%) ND ND ND	11(2.3%) ND ND ND
Asaad et coll. 2014 [43]	SCID, DSM-IV	BD	?	33	350	45	2(0.6%)	ND	ND	ND
Baek et coll. 2014 [44]	SCID, DSM-IV	BD BD I BD-II	M	35	417 222 195	67	29(7%) 14(6.3%) 15(7.7%)	4(1%) 2(0.9%) 2(1%)	25(6%) 12(5.4%) 13(6.7%)	ND ND ND
Eich et coll. 2014 [45]	SCID, DSM-IV	BD BD I BD II	M	42	24 17 7	67	8(33.3%) ND ND	ND ND ND	ND ND ND	ND ND ND
Woldeyohannes et coll. 2015 [46]	YMRS, MDQ, DSM-IV	BD	M	39	307	59	78(25.4%)	ND	ND	78(25.4%)
McElroy, Crow, Blom, Biernacka, et coll. 2016 [47]	EDDS, DSM-5	BD BD I BD II	A	43	1092 699 393	62	291(26.6%) 173(24.7%) 118(30%)	2(0.2%) **** 0 2(0.5%)	160(14.6%) 98(14%) 62(15.8%)	129(11.8%) 75(10.7%) 54(13.7%)
Goffin et coll. 2016 [8]	SCID, DSM-IV-TR	BD BD I BD II	A	36	494 240 254	58	76(15.4%) 34(14.2%) 42(16.5%)	ND ND ND	ND ND ND	ND ND ND
Holtzman et coll. 2016 [48]	SCID II, DSM-IV	BD BD II	A	42	502 260	58	76(15.1%)	ND	ND	ND
Martin et coll. 2016 [49]	*KSADS-PL, DSM-IV*	*BD* *BD I* *BD II* *BD-NOS*	*A*	*16*	*82* *19* *39* *24*	*66*	*10(12.2%)*[a]	*0*	*10(12.2%)*	*0*

*Patients presenting bulimic episodes more than twice a week

**Patients presenting infra-diagnostic forms

*** Multiple diagnoses of ED

**** BMI data missing for 32 patients

a : p=0.001

ND : no data available

AN : Anorexia Nervosa; ASRM : Altman Self-Rating Mania Scale; BN: Bulimia Nervosa; BDVF : Bipolar Disorder Visit Form; BEDCI : Binge Eating Disorder Clinical Interview; BPRS : Brief Psychiatric Rating Scale; CGI-S-TB : Clinical Global Impressions – Severity; DIGS: Diagnostic Interview for Genetic Studies; DSM: Diagnostic and Statistical Manual of Mental Disorders; EDDS: Eating Disorder Diagnostic Scale; BH: bulimic hyperphagia; HCL-32: Hypomania/Mania Symptom Checklist; KSADS-PL: Kiddie-Schedule for Affective Disorders and Schizophrenia for School Age Children, Present and Lifetime Version; MDQ: Mood Disorder Questionnaire; MINI STEP BD: Mini International Neuropsychiatric Interview Systematic Treatment Enhancement Program for Bipolar Disorder; Pre-bariatric: under assessment for bariatric surgery; QEWP-R : The Questionnaire on Eating and Weight Patterns-5; RDC : Research Diagnostic Criteria; SCID : Structured Clinical Interview for DSM; Status : (M : Mixed, H: Hospitalised, A: Ambulatory); BD: Bipolar Disorder; BD I : type I bipolar disorder; BD II: type II bipolar disorder; ED: Eating Disorder; YMRS : Young Mania Rating Scale; MDE Major Depressive Episode.

Table 3. Studies on the lifetime prevalence of bipolar disorder among subjects presenting an ED										
Studies Author, year [reference]	**Instruments, Criteria**	**Patients**	**Status**	**Age**	**N**	**F %**	**BD** N (%)	**BD I** N (%)	**BD II** N (%)	**BD-NS** N (%)
Hudson et coll. 1983 [53]	DIS, DSM-III	ED AN-R AN-P BN	M	28	90 16 25 49	94	13(14.4%) ND ND ND	12(13.3%) ND ND ND	0 0 0 0	1(1.1%) ND ND ND
Piran et coll. 1985 [54]	SADS, DSM-III	ED AN BN	M	22	49 14 33	100	3(6.1%) 0 3(9%)	0 0 0	0 0 0	3(6.1%) 0 3(9%)
Walsh et coll. 1985 [55]	SADS, DSM-III et RDC	ED AN BN	M	25	50 9 41	100	5(10%) 0 5(12.2%)	0 0 0	4(8%) 0 4(9.8%)	1(2%) 0 1(2.4%)
Powers et coll. 1988 [56]	SCID, DSM-III-R	BN	A	29	30	100	2(6.7%)	1(3.3%)	0	1(3.3%)
(Herzog et coll. 1992) [57]	SADS, DSM-III-R	ED AN-R AN-P BN	A	24	229 41 90 98	100	11(4.8%) 0 6(6.7%) 5(5.1%)	3(1.3%) 0 2(2.2%) 1(1%)	2(0.9%) 0 1(1%) 1(1%)	6(2.6%) 0 3(3.3%) 3(3.1%)
Braun, Sunday & Halmi 1994 [58]	SCID, DSM-III-R	ED AN-R AN-P BN	H	25	105 34 22 49	100	8(7.6%) 1(2.9%) 1(4.5%) 6(12.2%)	ND ND ND ND	ND ND ND ND	ND ND ND ND
Brewerton et coll. 1995 [59]	SCID, DSM-IV	BN	A	28	59	100	2(3.4%)	ND	ND	2(3.4%)
Iwasaki et coll. 2000 [60]	SCID, DSM-III-R	ED AN-R AN-P BN BH	A	22	171 62 36 57 16	100	7(4.1%) 0 3(8.3%) 3(5.3%) 1(6.3%)	0 0 0 0 0	5(2.9%) 0 2(5.6%) 2(3.5%) 1(6.3%)	2(1.2%) 0 1(2.8%) 1(1.7%) 0
Eddy et coll. 2002 [61]	DSM-III-R	ED AN-R AN-P	A	22	136 51 85	100	5(3.7%) 0 5(5.9%)	ND ND ND	ND ND ND	ND ND ND
McElroy et coll. 2003 [62]	SCID, DSM-IV	BH	A	40	61	87	6(9.8%) **	ND	ND	ND
Joyce et coll. 2004 [63]	SCID, DSM-III-R	BN	A	31	135	100	23(17%)	(excluded)	22(16.3%)	1(0.7%)
Nagata et coll. 2013 [64]	SCID, MDQ, BSDS, DSM-IV	TCA AN-R AN-P BN ED-NOS	A	29	78 11 24 27 16	100	15(19.2%) ND ND ND ND	0 ND ND ND ND	15(19.2%) ND ND ND ND	0 ND ND ND ND
Campos et coll. 2013 [65]	SCID, DSM-IV	ED	A	28	69	100	24(34.8%)	18(26.1%)	6(8.7%)	0
Rodríguez Guarín et coll. 2013 [66]	DSM-IV	ED AN BN BH	A	21	908 328 327 155	95	167(18.4%) ND ND ND	ND ND ND ND	ND ND ND ND	ND ND ND ND
Franko et coll. 2013 [67]	DSM-IV	ED AN-R AN-P BN	A	24	186 51 85 50	100	15(8.1%) ND ND ND	ND ND ND ND	ND ND ND ND	ND ND ND ND
Lähteenmäki et coll. 2014 [68]	SCID, DSM-IV-TR	ED AN BN	A	27	29 10 11	100	0 0 0	0 0 0	0 0 0	0 0 0
Ulfvebrand et coll. 2015 [69]	SCID, DSM-IV-TR, DSM-5	ED AN-R AN-P BN ED-NOS BH	M	26	7154 926 466 2337 2899 526	97	43(0.6%) 3(0.3%) 3(0.6%) 18(0.8%) 17(0.6%) 2(0.4%)	ND ND ND ND ND ND	ND ND ND ND ND ND	ND ND ND ND ND ND
Kask et coll. 2016 [70]	DSM-IV	AN	H	18	8069	100	204(2.5%)	ND	ND	ND
Gershon et coll. 1984	*SADS, DSM-III et RDC*	*AN*	*H*	*25*	*24*	ND	*2(8.3%)*	*0*	*1(4%)*	*1(4%)*

[71]										
Stern et coll. 1984 [72]	*Semi-structured interviews, RDC*	*BN*	*A*	*24*	*27*	*100*	*5(18.5%)*	*ND*	*ND*	*ND*
Hudson et coll. 1987 [73]	*DIS, DSM-III*	*BN*	*A*	*26*	*70*	*100*	*8(11.4%)*	*8(11.4%)*	*ND*	*ND*
Hudson et coll. 1988 [74]	*DIS et SADS, DSM-III*	*BN*	*A*	*33*	*70*	*100*	*6(8.6%)*	*6(8.6%)*	*ND*	*ND*
Toner, Garfinkel & Garner 1988 [75]	*DIS, DSM-III*	*AN (in remission, asympto or sympto)*	*A*	*?*	*47*	*100*	*3(6.4%)*	*3(6.4%)*	*ND*	*ND*
Keck et coll. 1990 [76]	*SCID, DSM-III-R*	*BN*	*A*	*28*	*67*	*100*	*4(6%)*	*4(6%)*	*ND*	*ND*
Halmi et coll. 1991 [77]	*DIS, DSM-III-R*	AN after 10 yrs follow-up Controls	*H*	*27*	*62* *62*	*100* *100*	*10(16%)* *1(1.6%)*	*2(3.2%)* *1(1.6%)*	*2(3.2%)* *0*	*6(9.7%)[a]* *0*
Yanovski et coll. 1993 [78]	*SCID, DSM-III-R*	*BH*	*A*	*37*	*43*	*76*	*1(2.3%)*	*ND*	*ND*	*ND*
Råstam et coll. 1995 [79]	*SCID-II, DSM-III-R*	*AN 6.7 yrs after AN onset*	*A*	*21*	*51*	*94*	*2(3.9%)*	*ND*	*ND*	*ND*
Bushnell et coll. 1994 [80]	*DIS, DSM-III*	*BN*	*A*	*27*	*25*	*100*	*0*	*0*	*0*	*0*
Grilo et coll. 1996 [81]	*SADS et SCID, DSM-IV*	*ED* *AN* *BN* *ED-NOS*	*H*	*20*	*31* *11* *9* *11*	*100*	*2(6.5%)* *ND* *ND* *ND*	*ND* *ND* *ND* *ND*	*ND* *ND* *ND* *ND*	*ND* *ND* *ND* *ND*
Lilenfeld et coll. 1998 [82]	*SADS, DSM-III-R*	*ED* *AN* *BN*	*A*	*25*	*73* *26* *47*	*100*	*1(1.4%)** *0* *1(2.1%)*	*ND*	*ND*	*ND*
Telch & Stice 1998 [83]	*SCID, DSM-III-R*	*BH*	*A*	*43*	*61*	*100*	*1(1.6%)*	*ND*	*ND*	*ND*
Ivarsson et coll. 2000 [84]	*SCID, DSM-III-R*	*AN*	*A*	*16*	*51*	*94*	*3(5.9%)*	*3(5.9%)*	*0*	*0*
Fontenelle et coll. 2003 [85]	*SCID, DSM-IV*	*BH*	*A*	*34*	*33*	*97*	*0*	*0*	*0*	*0*
Javaras et coll. 2008 [86]	*SCID, DSM-IV*	*BH*	*A*	*50*	*150*	*76*	*14(9.3%)[a]*	*ND*	*ND*	*ND*
Aspen et coll. 2014 [87]	*DSM-5*	*ED* *Clinical ED* *ED-NOS*	*A*	*21*	*107* *40* *67*	*100*	*3(2.8%)* *1(2.5%)* *2(3%)*	*3(2.8%)* *1(2.5%)* *2(3%)*	*ND* *ND* *ND*	*ND* *ND* *ND*
Godart et coll. 2015 [88]	*DSM-IV-TR*	*ED* *AN-R,* *AN-P,* *BN NP* *BN P* *p>0.05 compared to controls*	*M*	*23*	*271* *111* *55* *19* *86*	*100*	*49(18.1%)* *9(8.1%)[a]* *16(29.1%)* *2(10.5%)* *22(25.6%)*	*42(15.5%)* *7(6.3%)* *14(25.5%)* *2(10.5%)* *19(22.1%)*	*7(2.6%)* *2(1.8%)* *2(3.6%)* *0* *3(3.5%)*	*0* *0* *0* *0* *0*
Tseng et coll. 2016 [89]	*DSM-IV-TR, DSM-5*	*ED* *AN* *BN* *BH* *ED-NOS*	*A*	*28*	*288* *54* *125* *75* *34*	*88.2*	*103(35.8%)[a]* *9(16.7%)* *45(36%)* *37(49.3%)* *12(35.3%)*	*46(16%)* *6(11.1%)* *18(14.4%)* *17(22.7%)* *5(14.7%)*	*57(19.8%)* *3(5.6%)* *27(21.6%)* *20(26.7%)* *7(20.6%)*	*0* *0* *0* *0* *0*
Welch et coll. 2016 [90]	*DSM-IV*	*BH*	*M*	*24*	*850*	*95.4*	*35(4.1%)[a]*	*ND*	*ND*	*ND*
Marzola et coll. 2017 [91]	*DSM-5*	*AN* *AN-R* *AN-P*	*H*	*25*	*98* *64* *34*	*100*	*0*	*0*	*0*	*0*

In italics: studies [71 to 91) comprising control groups

[a] : p< 0.0001

*Following contact with the author, one patient for 1997 was omitted – same two patients.

**Exclusion of non-stable bipolar disorders.

ND : No data available

AN: Anorexia Nervosa; AN-R: Anorexia Nervosa, restricting type; AN-P: Anorexia Nervosa, purging type; B: Bulimia Nervosa; BN-N Bulimia Nervosa, non-purging type; BN-P: Bulimia Nervosa, purging type; BSD : Bipolar Spectrum Diagnostic Scale; DIS: Diagnostic Interview Schedule; DSM: Diagnostic and Statistical Manual of Mental Disorders; BH: Bulimic Hyperphagia ; MDQ : Mood Disorder Questionnaire; RDC: Research Diagnostic Criteria; SAD: Schedule for Affective Disorders and Schizophrenia; SCID: Structured Clinical Interview for DSM; Status: (M : Mixed, H : Hospitalised, A: Ambulatory); ED: Eating Disorders ; BD: Bipolar Disorder; BD I: Type I bipolar disorder; BD II: type II bipolar disorder; BD-NS: non-specified bipolar disorder; MDE: Major Depressive Episode

Table 4. Chronology of the onset of bipolar disorder							
Study	**Subjects**	**Age**	**N**	**Pathology**	**More than one year before ED**	**In the same year**	**More than one year after ED**
Ramacciotti et coll. 2005 [28]	BD I	40	14	BN, BH	8*(57.1%)	4*(28.6%)	2*(14.3%)
Godart et coll. 2015 [88]	ED	21	31	Manic or hypomanic episode	8(25.8%)	12(38.7%)	11(35.5%)
	AN-R	19	4		1(25%)	2(50%)	1(25%)
	AN-P	21	11		2(18.2%)	4(36.4%)	5(45.5%)
	BN P	23	15		5(33.3%)	5(33.3%)	5(33.3%)
	BN NP	25	1		0	1(100%)	0
McElroy et coll. 2011 [33]	BD	41	70	ED	39(55.7%)	7(10%)	24(34.3%)
			9	AN	5(55.6%)	1(11.1%)	3(33.3%)
			16	BN	8(50%)	1(6.2%)	7(0.44%)
			45	BH	26(57.8%)	5(1.1%)	14(3.1%)

*The number of years is not specified, only the relative chronology of onset.
AN: Anorexia Nervosa; AN-P: Anorexia Nervosa, purging type; AN-R: Anorexia Nervosa, restricting type; BN: Bulimia Nervosa; BN NP: Bulimia Nervosa, non-purging type; BN P: Bulimia Nervosa, purging type; BH: Bulimic Hyperphagia ; BD: Bipolar Disorder; ED: Eating Disorder