KEY REVIEW

Prevalence of Bipolar Disorders: Traditional and Novel Approaches

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Epidemiologie studies using the modern and widely used Composite International Diagnostic Interview, based on the DSM criteria, have reported generaUy low lifetime prevalence rates for bipolar 1 and bipolar II disorders, and cydothymia of between 1% and 2% (range, 0.0-2.4%). These low rates require serious investigation as there is growing evidence from epidemiologie studies in adolescents and young adults of clinically very relevant subdiagnostic hypomanic morbidity. As a consequence of the under-recognition of hypomania, major depressive disorders are over-diagnosed at the expense of bipolar II disorders. There is a similar over-diagnosis of dysthymia, and minor and recurrent brief depression, and under-diagnosis of minor bipolar disorder. New data suggest that 25-50% of all individuals with mood disorders suffer from bipolar illness; this is true for both major and minor depressive syndromes. Accurate recognition of bipolar disorders will have an important impact on decisions about long-term prophylactic medication with mood stabilizers.

Concepts of Bipolar Oisorders

Until the late 19605, Kraepelin's concept of manic-depressive insanity, unifying depressive disorders, and bipolar disorders published in 1899 dominated epidemiologic and clinical research on affective disorders.[1] Though there were some pioneering studies on the incidence of treated cases of mania in Denmark, Iceland, England, and Wales in the 1980s and 1990s,[2-3] manic and bipolar disorders were not cLassified as distinct from depressive affective disorders in epidemiology and clinical psychiatry.

The modern concept of bipolar disorders had already been developed in the mid-19th century,[4-6] and Mendel coined the term hypomania in 1881.[7] Systematic research into pure, well-defined bipolar groups began in the mid-1960s, when genetic and follow-up studies were carried out on large sample populations selected from hospital admissions.[8-10]

In the subsequent decades, the diagnostic concepts of bipolar disorders were refined progressively Dunner *et al.*[11]separated bipolar II disorders (hospitalized for depression, but not for mild mania) from bipolar I disorders (hospitalized for mania and for depression). Klerman[12] went on to distinguish six subgroups of the bipolar spectrum:

- Mania
- Hypomania
- Hypomania or mania precipitated by drugs
- Cycothymic personality
- Depression with a family history of bipolar disorder
- Mania without depression.

Akiskal's most recent list has been expanded to eight subgroups and includes new subtypes, such as schizo-bipolar disorder, chronic refractory hypomania and mood swings associated with substance use/abuse.[13] Recently, an international group of experts strongly recommended expanding the definition of bipolar II disorders,[14] Angst introduced the concepts of recurrent brief hypomania [15-l6] and, more recently, that of minor bipolar disorders (hypomania associated with minor depression,

dysthymia, or recurrent brief depression) as distinct from hyperthymic and cycothymicpersonality.[17]

The bipolar disorder spectrum

Today's complex range of bipolar disorder subtypes, excluding mixed states, are illustrated in Figure 1. There are three subtypes of bipolar I disorder: pure mania (M), predominantly manic bipolar I disorder with mid depression (Md), and the nucLear form of bipolar I, in which sufferers experience both severe mania and severe depression (MD). Under the diagnostic threshold of bipolar II disorder (Dm) lies the group of minor bipolar disorder, defined by the combination (md) of mild depression (d) with hypomania (m) or hypomanic symptoms (mdsx). Though the group experiencing hypomanic symptoms is listed in the normal range of affective phenomena, there is evidence for classifying such cases as very mild bipolars.

Clearly, Lifetime prevalence rates for bipolar disorders are dependent entirely on diagnostic concepts and the instruments tailored to them. As the diagnostic concepts seem to be in flux, this' review will distinguish between epidemiologic findings based on traditional approaches and those founded on unorthodox, novel approaches.

The Traditional Approach: Lifetime Prevalence Rates Based on Current DSM and ICD Diagn9stic Manuals

As in psychopharmacology, most epidemiologic studies have been devoted to the relatively rare bipolar I disorders, while few studies have reported data on bipolar II disorder and other subgroups of the bipolar spectrum that are more prevalent. Most studies have found relatively low prevalence rates for bipolar disorders. Our review of the Literature comprises the studies carried out since the introduction of DSM-III, but will concentrate on the results of the most recent studies using the Comprehensive International Diagnostic Interview (CIDI),18 which was adapted to DSM-III-R and DSM-IV diagnostic criteria.

Bipolar I disorders

Twenty-one studies reported lifetime prevalence rates of bipolar I disorders between 0% and 2.4%, with most rates below 1.0% (Table 1). The largest studies, which were carried out in the USA, identified a Lifetime prevalence rate of 1.6% using the CIDI,[19] and 0.45% with clinical interviews.[20] European studies have demonstrated slightly higher prevalence rates: a Hungarian study reported a rate *bf* 2.4%,[21] The Netherlands Mental Health Survey

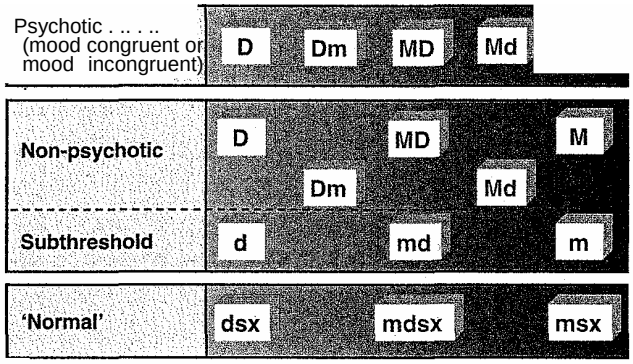

Figure 1: Subgroups of the bipolar spectrum. M, mania; m, hypomania; D, major depressive episode; d, mild depression (minor depression [three or four of nine symptoms for 2 or more weeks], dysthymia, recurrent brief depression); msx, manic symptoms under the diagnostic threshold; dsx, depressive symptoms under the diagnostic threshold; mdsx, manic and depressive symptoms under the diagnostic threshold

and Incidence Study (NEMESIS) reported1.8%,[22] and the rate was 1.4% in a German study of adolescents and young adults.[23]

In contrast with depression, bipolar I disorders appear to affect males and females equally.[24]

Bipolar II disorders

Eleven studies reported lifetime prevalencerates of bipolar II disorders between 0.3% and 3.0%. In eight of these studies, the rate was below 1.0%. Wittchen *et al..*[23] reported a rate of 1.4% in adolescents and young aduLts, while Szadoczky *et al.*[21] found the prevalence to be 2.4% in Hungary,

Cyclothymia

Cyclothymia is defined in DSM-IV and ICD-l0 by analogy with dysthymia as a chronic form of mild bipolar disorder. Of five studies reporting Lifetime prevalence rates for cyclothymia, three reported rates between 1.4% and 2.8%,

TabLe 1: Review of prevalence rates in the epidemiologic literature .

Diagnosis	No. of studies reviewed	Range of reported lifetime prevalence rates (%)
Bipolar I		0.0-2.4
Bipolar II		0.3-3.0
Cyclothymia		0.5-2.8
Hypomania		2.2-5.7
Spectrum		2.6-7.8 (10.8)

Bipolar spectrum disorders defined by **DSM** criteria

In agreement with the generally low lifetime prevalence rates found for bipolar I disorder, bipolar II disorder and cyclothymia, five studies have published rates of between 2.6% and 3.4% for the total bipolar spectrum.[24] There are exceptions, however. Heun and Maier[25] reported a higher rate of 6.5% from a relatively small study, as did Szadoczky et al.,[21] who observed a rate of 5.1 % in a large Hungarian study. On the basis of a softer definition of hypomania, our earlier results demonstrated a rate of 7.8%.26

The conclusion to be drawn from most studies is that, compared with depressive disorders, bipolar disorders are rare. White this is certainly true for bipolar 1 disorder, we need to ask whether it is also true for bipolar II disorder and cyclothymia, or whether the low prevalence rates are not merely an artifact of a questionable definition of hypomania (Table *1).*[17,27]

Novel Diagnostic Approaches: Subthreshold Syndromes and New Concepts of Hypomania

More unorthodox approaches do not confine themselves to the criteria found in the diagnostic manuals, but examine subthreshold syndromes and test the clinical validity of those diagnostic criteria. For the new concepts of hypomania, clinical validators included:

The positive predictive power for bipolar I and bipolar II disorders[28]

- A positive family history of mania
- Association with major depression
- Treatment for depression
- Suicidality
- Substance abusey,[27]

Adolescent psychiatry

In adolescent psychiatry, a longitudinal study by Lewinsohn *et* al.[28] found not only the usual 1.0% prevalence rate for bipolar disorders (consisting mainly of bipolar II and cyclothymia), but also reported 'core manic symptoms' in 5.7% of adolescents. These symptoms were a distinct period of abnormally and persistently elevated, expansive or irritable mood, even though these individuals never met the diagnostic criteria for bipolar disorder. In this prospective study, the core manic symptoms were highly predictive of bipolar disorder. The authors also stressed that juvenile bipolar is typically characterized by high rates of rapid cycling (e.g. >365 cycles per year) and very high rates of co-morbidity with attention deficit hyperactivity disorder[29] and conduct disorder.[30]

Adults

Recent research on bipolar disorders in adults has also seriously questioned the established diagnostic criteria of hypomania with respect to:

- The diagnostic primacy of mood changes and the exclusion of hyperactivity
- The minimum number of diagnostic symptoms
- The required minimum duration of 4 days per episode.

The findings of the adolescent psychiatric study mentioned above are in clear conflict with the third point, not requiring a minimum duration to define a hypomanic episode.

In the recent systematic validation of diagnostic criteria (Zurich criteria),[17] the authors demonstrated that a new hard operational definition of hypomania should:

- Include hyperactivity as a stem criterion
- Not limit the required duration of hypomanie manifestations
- Include only three of the seven criterial symptoms.

They also provided evidence that cases of depression (major depression, minor depression, dysthymia, recurrent brief depression) associated with symptoms of hypomania below the diagnostic threshold (soft definition) are likely to be cases of bipolar II and minor bipolar disorders.

A prevalence rate for bipolar II disorders in the community of 11% was reported .[17] Of these cases, 63% were treated for depression, and this graup was characterized by a high rate of family history of mania. In addition, they found that 9% of adults between 20 and 40 years of age suffered from minor bipolar disorders.[17] Rapid cycling was also found to be very common, but these subjects could not be considered cyclothymics as most did not meet the chonicity criterion.

Applying the Zurich criteria for hypomania indicates that at least one in every four individuals suffering from major depressive episodes is in fact a bipolar II case, with a further quarter being probable bipolar II cases. These criteria suggest that approximately half of all patients suffering from major depressive episodes may have been misdiagnosed and are likely to be suffering from bipolar II disorders. Furthermore, the same proportion of mild depressives under the threshold of major depressive episodes would appear to be minor bipolars (Figure 2). The same observations have been made in the French EPIDEP survey, which included major depressives seen in clinical psychiatric settings.[31,32]

Prevalence of Bipolar Disorders

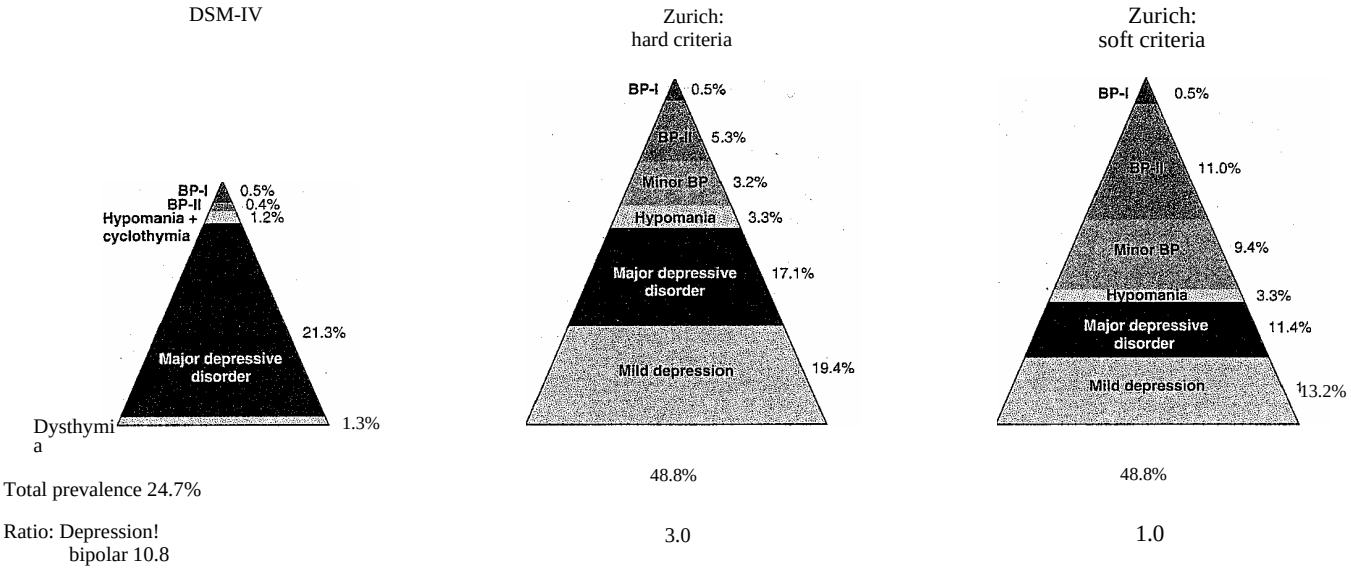

Figure 2: Bipolar versus depressive spectrum according to DSM-IV and Zurich criteria. BP, bipolar disorder

Prevalence of Bipolar Disorders

- Epidemiologic studies using the Composite International Diagnostic Interview based on DSM criteria report low lifetime prevalence rates ~f between 1% and 2% for bipolar l disorder, bipolar II disorder, and cyclothymia
- Lifetime prevalence depends on the diagnostic concepts applied and the instruments based on them
- Hypomania is under-recognized: there is growing evidence that many adolescents and young people have clinieally very relevant subdiagnostie hypomanic morbidity
- Major depressive disorders are being over-diagnosed at the expense of bipolar II disorders. Similarly, dysthymia and minor and recurrent brief depression are being overdiagnosed, and minor bipolar disorder under-diagnosed
- New criteria for hypomania suggest that 25-50% of patients with mood disorders 5uffer from bipolariUness
- Accurate identification of bipolar disorders is needed to ensure the most effective long-term prophylactic medication is prescribed

Conclusions

Epidemiologic studies using the CIDI diagnostic interview and conventional DSM diagnostic criteria report generally low lifetime prevalence rates. for bipolar l disorder, bipolar II disorder, and cyclothymia (between 1% and 2%; range, 0.0-2.4%). Several factors should cause us to question these low rates. Lifetime prevalence rates in these studies were assessed in retrospect, and are therefore subject to inaccuracies in recalling information. ln addition, it is well known that hypomanic subjects are not aware of their symptoms, and are therefore not able to report them reliably in direct diagnostic interviews. The highest rates of bipolar disorders and subthreshold morbidity were found in prospective epidemiologic studies of adolescents and young adults;[17,23,26,28] such data have undoubted advantages over that collected through cross-sectional and retrospective investigations. .

Clinical and epidemiologic studies have demonstrated the relevance of the subthreshold morbidity ofhypomania and hypomanic symptoms. In large clinical samples, bipolar II disorders with hypomanic manifestations of only 2 days' duration were found to be very common. In a recent French follow-up study, a careful systematic search for hypomanic symptoms resulted in a considerably increased rate of bipolar II disorders (from 22% to 39%) at the expense of major' depressive disorders.[32] The Zurich study demonstrates that major depressive disorder is over-diagnosed and bipolar II disorder under-diagnosed if DSM-IV criteria or ICD-l0 criteria are applied; these criteria have not been validated clinically and are too strict. *Half of all subjects with mood disorders are bipolars.*

Further research is needed to clarify whether the less rigid diagnostic criteria suggested by an international expert group33 or the soft Zurich criteria17 is preferable. Our data suggest that every depressive individual manifesting signs of hyperactivity, irritability, euphoria, or mood instability could well be a bipolar. Rapid cycling and ultra-rapid cycling are very common in subthreshold hypomania17.27 and clearly require prophylaxis. A dimensional approach to hypomania and cyclothymia could complement the categoric classification of the bipolar spectrum.[31.34.35]

From a therapeutic perspective, correct identification of bipolar illness is highly relevant as it determines, to a great extent, the optimal choice of long-term treatment. There is currently insufficient evidence; however, to indicate that bipolar II disorder and milder forms of bipolar disorders can be treated successfully in the same way as bipolar l disorder. Further research in this area is very much needed.

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