Recent Developments in the Epidemiology of Bipolar Disorder in Adults and Children: Magnitude, Correlates, and Future Directions

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During the past decade, there has been increasing recognition of the dramatic personal and societal impact of bipolar disorder I and II (DSM-IV). The estimated disability-adjusted life years of bipolar disorder outranked all cancers and primary neurologic disorders, such as epilepsy and Alzheimer's disease, primarily because of its early onset and chronicity across the lifespan (World Health Report, 2002). The results of numerous international epidemiologic surveys using contemporary diagnostic criteria have strengthened the evidence base on the magnitude, correlates, and consequences of bipolar disorder in representative samples of the general population. Epidemiologic research has also demonstrated the differences between clinical and community samples in terms of demographic factors, comorbidity, patterns of onset, severity, treatment utilization, and response. The aims of this article are (a) to summarize the magnitude of the prevalence of bipolar disorder in adults and children through a comprehensive review of DSM-IV bipolar disorder in the general population; (b) to describe the risk factors and correlates of bipolar disorder in community surveys; and (c) to describe the future directions for the field of epidemiology of bipolar disorder.

Key words: bipolar disorder, future directions, prevalence, risk factors. [Clin Psychol Sci Prac 16: 121–133, 2009]

MAGNITUDE OF BIPOLAR DISORDER IN THE POPULATION-BASED SAMPLES

There have been numerous reviews of the epidemiology of bipolar disorder in adults that provide comprehensive summaries of international studies of the prevalence of bipolar disorder over the past 25 years (Bauer & Pfennig, 2005; Goodwin & Jamison, 2007; Pini et al., 2005; Sherazi, McKeon, McDonough, Daly, & Kennedy, 2006; Waraich, Goldner, Somers, & Hsu, 2004; Weissman et al., 1996). The aggregate cross-study estimate of the lifetime prevalence of bipolar disorder is about 1.0%. Only one of the reviews of the epidemiology of bipolar disorder includes bipolar II and bipolar spectrum disorders (Bauer & Pfennig, 2005). As expected, it was found that the median rates increase with successively less restrictive definitions of bipolar disorder; the median lifetime prevalence rate of bipolar II was 1.2%, and of bipolar spectrum was 2.9%. The only systematic difference that has been found to explain the variation in rates is the actual diagnostic interview employed to generate the criteria for bipolar disorder (Waraich et al., 2004).

During the past decade, the results of three major population surveys of the United States and several international studies have presented prevalence rates of bipolar disorder. The U.S. studies include the National Comorbidity Study-Replication (NCS-R; Kessler et al., 2005), the National Epidemiological Survey on Alcohol and Related
Conditions (NESARC; Grant et al., 2005), and the Third National Health and Nutrition Examination Survey (NHANES III; Jonas, Brody, Roper, & Narrow, 2003). These studies are all nationally representative surveys of mental disorders in the United States. The NCS-R studied 9,282 English-speaking respondents over the age of 18 to assess DSM–IV criteria using Version 3.0 of the World Health Organization’s Composite International Diagnostic Interview (Kessler et al., 2006), a fully structured lay-administered diagnostic interview. It was conducted between February 2001 and April 2003. The NESARC, which used the U.S. Census Bureau to interview 43,093 respondents between 2001 and 2002, used the Alcohol Use Disorder and Associated Disabilities Interview Schedule (Grant et al., 2003) to ascertain DSM–IV criteria for mental disorders. The NHANES III was conducted by the National Center for Health Statistics, Centers for Disease Control and Prevention. This study assessed 7,968 respondents ages 18–39 years from 1988 to 1994 using the Diagnostic Interview Schedule and DSM–III–R criteria. In addition, the results from several international studies and a global collaborative initiative based on the methods of the NCS-R in the United States were also reported during the past few years.

Few studies report rates of bipolar II disorder because of the widely held view that hypomania cannot be assessed reliably in nonclinical samples. Likewise, there are sparse data on bipolar disorder in children from community studies because of the beliefs that it is rare in children and that hypomania cannot be assessed reliably in children. In the next section, we describe the prevalence rates of bipolar disorder in community surveys of adults.

### Prevalence of Bipolar Disorder in Recent General Population Samples of Adults

A summary of the 12-month and lifetime prevalence rates of bipolar I and bipolar II as defined by DSM–IV criteria is presented in Table 1. The aggregate cross-study estimate of the lifetime prevalence of bipolar disorder is 1.2%, with a range of 0.0% in Nigeria (Gureje, Lasebikan, Kola, & Makanjuola, 2006) to 3.3% in the United States (Grant et al., 2005). Despite these outliers, the prevalence rates of bipolar I disorder are highly consistent across studies. The lifetime prevalence rates cluster at about 1.0%, whereas the average 12-month prevalence rate is only slightly lower with a median of 0.8%, with a range from 0.2% to 1.8%. The prevalence of bipolar II was only assessed in a few studies (Merikangas et al., 2007; Szadoczky, Papp, Vitrai, Rihmer, & Furedi, 1998; Wittchen, Nelson, & Lachner, 1998). Two recent studies also reported on prevalence of bipolar disorder defined by ICD-10 criteria. The lifetime prevalence of ICD-10 bipolar I was 1.8 in Ethiopia (Fekadu et al., 2004), and the 12-month prevalence in Ireland was 0.2 (McConnell, Bebbington, McClelland, Gillespie, & Houghton, 2002). Finally, the lifetime prevalence of DSM–III-defined bipolar I and

### Table 1. Rates of DSM–IV Bipolar Disorders in Community Samples of Adults

<table>
<thead>
<tr>
<th>Location</th>
<th>Study</th>
<th>Age (years)</th>
<th>Sample size</th>
<th>Method</th>
<th>Diagnosis</th>
<th>Lifetime prevalence (%)</th>
<th>12-month prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Male</td>
<td>Female</td>
<td>Total</td>
</tr>
<tr>
<td>China</td>
<td>Lee et al. (2007)</td>
<td>18–70</td>
<td>5,201</td>
<td>WMH-CIDI/DSM-IV</td>
<td>Bipolar I/bipolar II</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Germany</td>
<td>Jacobi et al. (2004)</td>
<td>18–65</td>
<td>4,181</td>
<td>M-CIDI/DSM-IV</td>
<td>Any bipolar</td>
<td>0.8</td>
<td>1.2</td>
</tr>
<tr>
<td></td>
<td>Wittchen et al. (1998)</td>
<td>14–24</td>
<td>3,021</td>
<td>M-CIDI/DSM-IV</td>
<td>Bipolar I</td>
<td>1.1</td>
<td>1.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Bipolar II</td>
<td>0.2</td>
<td>0.7</td>
</tr>
<tr>
<td>Japan</td>
<td>Kawakami et al. (2005)</td>
<td>≥20</td>
<td>1,664</td>
<td>WMH-CIDI/DSM-IV</td>
<td>Bipolar I/bipolar II</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Lebanon</td>
<td>Karam et al. (2008)</td>
<td>≥18</td>
<td>2,857</td>
<td>CIDI 3.0/DSM-IV</td>
<td>Bipolar disorder</td>
<td>2.6</td>
<td>2.3</td>
</tr>
<tr>
<td>Mexico</td>
<td>Medina-Mora et al. (2007)</td>
<td>18–65</td>
<td>5,826</td>
<td>WMH-CIDI/DSM-IV</td>
<td>Bipolar I/bipolar II</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>New Zealand</td>
<td>Baxter et al. (2006)</td>
<td>16–64</td>
<td>12,992</td>
<td>CIDI 3.0/DSM-IV</td>
<td>Bipolar disorder</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Bipolar II</td>
<td>–</td>
<td>–</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Bipolar I/bipolar II</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Switzerland</td>
<td>Angst et al. (2005)</td>
<td>≥12</td>
<td>591</td>
<td>SPIKE/DSM-IV</td>
<td>Bipolar I</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>United States</td>
<td>Grant et al. (2005)</td>
<td>≥12</td>
<td>43,093</td>
<td>NESARC/DSM-IV</td>
<td>Bipolar I</td>
<td>3.2</td>
<td>3.4</td>
</tr>
<tr>
<td></td>
<td>Ford et al. (2007)</td>
<td>≥18</td>
<td>6,082</td>
<td>WMH-CIDI/DSM-IV</td>
<td>Bipolar I/bipolar II</td>
<td>0.8</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Merikangas et al. (2007)</td>
<td>≥18</td>
<td>9,282</td>
<td>CIDI/DSM-IV</td>
<td>Bipolar I</td>
<td>0.8</td>
<td>1.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Bipolar II</td>
<td>0.9</td>
<td>1.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Subthreshold</td>
<td>2.6</td>
<td>2.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>bipolar disorder</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>
bipolar II combined was 1.6 in the NHANES survey in the United States (Jonas et al., 2003).

With increased interest in evaluating the validity of the thresholds of mania and its core components, investigators are beginning to test different thresholds in general community samples. Application of the concept of subthreshold bipolarity to the Zurich Cohort Study demonstrated the enormous consequences of varying definitions of diagnostic criteria for symptoms, duration, and impairment. The broader criteria yielded rates of 5.3% for bipolar II disorder, 3.2% for minor bipolar disorder, and 3.3% for hypomania (Angst, Gamma, & Lewinsohn, 2002). Similar rates emerged from a reanalysis of the Epidemiologic Catchment Area study by Judd and Akiskal (2003), who reported that 5.1% of the population met the criteria for lifetime subthreshold mania/hypomania. Likewise, expansion of the definition of hypomania in the NCS-R study yielded a lifetime prevalence rate of 4.5% (Kessler et al., 2006; Merikangas et al., 2007). Evidence for the validity of the expanded definition was provided by the clinical significance, severity, and impairment associated with subthreshold bipolar disorder. Of particular interest, the severity of symptoms of depression and mania associated with subthreshold bipolar disorder suggested that the latter category did tap clinically significant manifestations of bipolar disorder that were comparable to people seeking treatment for these conditions in outpatient settings (Kessler et al., 2006).

**Incidence Rates**

Most of the evidence on incidence rates (e.g., new cases in a defined population over a specified time period) of bipolar disorder has been derived from information on first admissions for bipolar disorder. Sherazi et al. (2006) reported a range of annual incidence rates of first-episode mania and bipolar I from 1.7 to 6.5 per 100,000 per year. Although some studies did report that men and women had different incidence rates, there are no consistent patterns of sex difference across studies.

**Bipolar Disorder in Youth**

Although there has been substantial research on the epidemiology of mental disorders in children and adolescents in specific regions of the United States, there is still a striking lack of information on the national estimates of the prevalence and distribution of mental disorders in children in the U.S. population. There is also a lack of data on the prevalence of bipolar disorder in youth from international studies as well. Most of the information on bipolar disorder in adolescents can be derived from ongoing longitudinal studies that have followed a sample of youth from adolescence through adulthood. These studies include community surveys of children and adolescents in New York State (Cohen et al., 1993), North Carolina (Costello et al., 1996), and Oregon (Lewinsohn, Rohde, Seeley, & Hops, 1991) in the United States, in Munich, Germany (Wittchen et al., 1998), and Dunedin, New Zealand (Newman et al., 1996). However, very few of these studies have had sufficient sample sizes to identify cases of bipolar disorder. There are also a limited number of international population surveys that have provided information on the magnitude of bipolar disorder in youth.

Table 2 shows the prevalence rates of mania, hypomania, and bipolar disorder in population-based studies of youth that employed standardized diagnostic criteria for bipolar disorder. There was substantial variability in the age ranges of the samples, with some including only one age group in the sample, and most others assessing a broader age range of youth. Furthermore, some examined young children (7–11 years), while others examined adolescent samples (14–24 years). These methodological differences make it difficult to summarize the findings across studies.

The studies show a wide range of prevalence rates for bipolar disorder. A 2003 UK study found no cases of mania among children ages 5–15 years (Ford, Goodman, & Meltzer, 2003), whereas a Dutch study found lifetime prevalence rates as high as 1.9% in cross-sectional studies of adolescents (Verhulst, van der Ende, Ferdinand, & Kasius, 1997). Overall, the lifetime prevalence rates for bipolar disorder estimated in cross-sectional surveys ranged from 0% to 1.9%, 0.1% to 0.9% for hypomania, and 0.4% to 1.9% for mania.

Prospective studies of child and adolescent samples from population surveys are the best source of incidence rates of bipolar disorder. Lewinsohn, Seeley, Buckley, and Klein (2002) found that the incidence of bipolar disorder peaks at age 14 in both males and females and decreases gradually thereafter. By age 21, the rate of bipolar disorder rose to 2% in the prospective cohort studies of youth who were followed for several years (Cannon et al., 2002; Lewinsohn et al., 2002). There is also
a growing number of studies that evaluate the incidence of first onset mania in clinical samples of youth. Incidence rates from these studies range from 1.7 to 2.2 per 100,000 per year, with a weighted average of 1.4% (Soutullo et al., 2005).

**Treatment Rates**

The studies summarized in Tables 1 and 2 have also provided substantial information about differential treatment patterns among samples identified from the general population. The findings indicate that about 60% of those with bipolar I in U.S. community samples receive mental health treatment. Although more variable, more than half of those with bipolar in other countries receive treatment as well. This also suggests that half of those with bipolar disorder in the general population are not represented in mental health treatment, thereby limiting the generalizability of research conducted in these settings.

Treatment rates in children have also been reported from prospective surveys. Newman et al. (1996) found that approximately half of those youth in New Zealand with a 12-month episode of mania had received treatment. Moreno et al. (2007) examined data from the National Ambulatory Medical Care Survey to show that most visits by both youth and adult patients with a diagnosis of bipolar disorder included the prescription of at least one psychotropic medication, with use of mood stabilizers (generally anticonvulsants) in approximately two thirds of the visits, and antidepressants in approximately one third of the visits.

**Age of Onset**

Although estimates of the average age of onset of bipolar disorder from clinical samples was believed to occur in the third decade of life, retrospective estimates from the population surveys reveal that the average first onset of manic episodes occurs in the late teens to early 20s (Merikangas et al., 2007). Emerging evidence from prospective studies of adolescents converges in demonstrating that the first onset of bipolar disorder generally begins in adolescence (possibly preadolescence) or early adulthood, with a mean age of onset of 18 years (Lewinsohn, Duncan, Stanton, & Hautzinger, 1986). Waraich et al. (2004) showed that there was remarkable stability in the lifetime prevalence of bipolar disorder across adulthood, thereby demonstrating the chronicity of this condition across the lifespan.

**CORRELATES AND RISK FACTORS**

**Sex**

The finding of equal rates of bipolar disorder in men and women from epidemiologic surveys was confirmed in all
of the recent U.S. population surveys (Grant et al., 2005; Jonas et al., 2003; Merikangas et al., 2007). Although there is consistent evidence for an equal sex ratio for bipolar I disorder, several studies have shown that more women manifest the bipolar II subtype (Benazzi, 2006). The lack of a sex difference demonstrates one of the sources of bias in clinical samples, which tend to have a greater proportion of women in psychiatric care for bipolar disorder (Blanco, Laje, Olafson, Marcus, & Pincus, 2002). Studies of youth also confirm the lack of sex differences in the rates of bipolar disorder and its components during adolescence (Soutullo et al., 2005). However, caution should be exercised in drawing conclusions regarding the lack of sex differences in prevalence rates because there may be differential manifestations of bipolar disorders in males and females. Whereas males may be more likely to exhibit mania, females are more likely to present with depression (Duax, Youngstrom, Calabrese, & Findling, 2007).

Other Demographic Factors
Although many early studies of treated samples suggest that bipolar disorder was more common in upper socioeconomic classes, the most recent U.S. epidemiologic studies have consistently found that there are higher rates among those with lower income and education (Grant et al., 2005; Jonas et al., 2003; Merikangas et al., 2007). Likewise, rates of bipolar disorders are greater among those who were separated, divorced, or widowed compared to those who are married or never married in all of the recent U.S. population surveys. In contrast, a comparison of rates of bipolar disorder in high-income and low-income countries from the World Mental Health Survey showed that bipolar disorder was more common in high-income than in low-income countries (1.4% vs. 0.7%), as was disability associated with bipolar disorder (Ormel et al., 2008). Moreover, people from high-income countries were nearly three times more frequently likely to enter treatment than their low-income counterparts.

No ethnic or racial differences in the rates of bipolar disorder have been reported in recent population surveys of the United States (NHANES, NCS-R, and NESARC). However, there are only a limited number of studies that can truly distinguish ethnic differences because of the inclusion of sufficiently large multiethnic samples. The large sample size of the NESARC study enabled inclusion of several distinct ethnic subgroups in the U.S. population. This study found that Native Americans reported higher rates of bipolar I disorder (Grant et al., 2005) than the other subgroups included in the survey. Another study that examined cultural subgroups is the New Zealand Mental Health Survey (Baxter, Kokaua, Wells, McGee, & Browne, 2006) that yielded higher rates of bipolar disorder among the Maori (3.4%) and Pacific Island people (2.7%) compared to European and other Whites (1.9%).

Comorbidity
Recent epidemiologic surveys have highlighted the striking magnitude of comorbidity between bipolar disorder and other Axis I DSM-IV disorders. Data from the NCS-R revealed that more than 90% of those with lifetime bipolar I or bipolar II disorder also meet criteria for another lifetime disorder, and that 70% of those with bipolar spectrum disorders have a history of three or more disorders (Merikangas et al., 2007). The disorders that are most strongly associated with bipolar disorder are anxiety disorders and substance use disorders. The strong link between anxiety disorders and bipolar disorder described in clinical samples has been consistently confirmed in population surveys. The NCS-R study revealed that more than 80% of those with bipolar disorder also have a lifetime history of DSM-IV anxiety disorders, particularly panic attacks (e.g., 70%) and social phobia (e.g., 50%; Merikangas et al., 2007).

Prospective studies of community samples provide valuable information on the temporal patterns of association between bipolar disorder and comorbid conditions. Follow-up studies of children have shown that bipolar disorder is associated with multiple other disorders, including attention-deficit/hyperactivity disorder (ADHD; Biederman et al., 2004; Lewinsohn et al., 2002; Moreno et al., 2007; Youngstrom et al., 2005), anxiety disorders and/or oppositional defiant disorder (Youngstrom et al., 2005), and conduct disorder (Lewinsohn et al., 2002). An eight-year follow-up study of a population sample of youth from New York State revealed that childhood anxiety disorders and depression, and to a lesser extent disruptive behavioral disorders, were significantly associated with the development of bipolar disorder in early adulthood (Cohen et al., 2000; Johnson & Nowak, 2002).

Recent results of a study of offspring of parents with bipolar disorder confirm the anxiety–bipolar link. Duffy,
Alda, Trinneer, et al. (2007) found that rates of anxiety disorders and sleep disturbances were significantly elevated among offspring of bipolar probands compared to those of controls (Duffy, Alda, Milin, & Grof, 2007). The latter work suggests that anxiety disorders may constitute an early form of expression of the developmental pathway of bipolar disorders. Future studies should attempt to distinguish whether anxiety disorders represent manifestations of the same etiologic factors or independently elevate the risk for development of bipolar disorder. For example, one possible explanation for comorbidity in high-risk samples could be parental concordance for these disorders (e.g., paternal bipolar disorder and maternal anxiety disorder).

The strong association between bipolar disorder and substance use disorders has also been widely described in both community and clinical samples. Retrospective research has shown that the onset of bipolar disorder generally precedes that of the substance use disorder. For example, Merikangas et al. (2008) used data from a 20-year prospective cohort study to demonstrate the dramatic increase in risk of alcohol dependence associated with symptoms of mania and bipolar disorder in early adulthood. Thus, bipolar disorder can be considered a risk factor for the development of substance use disorders.

**Physical Disorders**

Comorbidity of physical diseases with bipolar disorder has been well recognized in clinical settings (McIntyre & Keck, 2006; McIntyre et al., 2006). The recent generation of large psychiatric epidemiology studies has begun to include assessment of medical conditions that can be used to examine whether the associations that have been reported in clinical samples are associated with biases associated with either sampling or treatment. The disorders that have been most strongly associated with bipolar disorder in clinical settings include cardiovascular disorders, diabetes, and migraine. Several studies of population-based samples and the recent results of the NCS-R have confirmed the strong association between migraine and bipolar symptoms/disorder (Merikangas & Stevens, 1997; Saunders, Merikangas, Low, Von Korff, & Kessler, 2008). Evaluation of physical-mental comorbidity in World Mental Health countries showed that heart disease, hypertension, and back/neck pain are associated with bipolar disorder in both high- and low-income countries, whereas associations with arthritis, asthma, and cancer are limited to high-income countries. In contrast, severe headaches/migraine are more strongly associated with bipolar disorder in low-income countries (Ormel et al., 2008).

Health information collected in the NHANES data showed that those with bipolar disorder were more likely to rate themselves as in fair or poor health than those without affective disorders; however, other subtypes of mood disorders, including major depression and dysthymia, tended to have even stronger associations with poor health than bipolar disorder (Jonas et al., 2003). In the same study, associations emerged between all mood disorder subtypes with hypertension, but asthma was only significantly associated with major depression (Jonas et al., 2003). Although there is scant information on medical comorbidity in children with bipolar disorder, some studies of children have reported links between bipolar disorder and diabetes and cardiovascular diseases (Scheffer & Linden, 2007).

There are also several studies of systematic samples, such as the Veteran’s Administration (Kilbourne et al., 2004) and health insurance claims databases (Carney & Jones, 2006), that provide strong evidence that people with bipolar disorder have high rates of physical disorders (McIntyre et al., 2007). The study of healthcare claims by Carney and Jones (2006) found that nearly every medical disorder was more common among those with bipolar disorder; however, the extremely large database, lack of correction for multiple comparisons, and failure to conduct multivariate analysis reduced the ability of this study to address the specificity of these associations.

**Family History**

A family history of bipolar disorder is one of the strongest and most consistent risk factors for the development of bipolar disorder. Controlled family studies of bipolar disorder yield an average tenfold increased risk of bipolar disorder among adult relatives of probands with bipolar disorder compared to relatives of controls (Merikangas & Yu, 2002), as well as a 3.5-fold increased risk of bipolar disorder among relatives of probands with nonbipolar major depression. Results of a small number of twin studies yield an aggregate estimate of threefold greater risk among monozygotic compared to dizygotic twins, indicating that a significant proportion of the familiality of bipolar disorder can be attributed to genetic factors...
However, there is a remarkable lack of twin studies of bipolar disorder defined by modern diagnostic criteria (Merikangas & Yu, 2002). Existing twin studies yield an average concordance rate for monozygotic twins of 40% compared to 5% for dizygotic twins, thereby suggesting a complex mode of inheritance of this condition (Smoller & Finn, 2003).

Despite the strong evidence for familial and genetic factors underlying bipolar disorder, there is still a lack of information on susceptibility genes that have been consistently shown to have significant predictive value for the development of bipolar disorder. Although there have been many studies designed to identify candidate genes underlying bipolar disorder through either linkage (segregating within family) or association (differences between cases and controls), there are still no replicated genetic markers for bipolar disorder. The results of recent genome-wide association studies did not identify any of the candidate genes found in earlier studies, but it is anticipated that combined results of several large studies now underway may yield more presumptive evidence for susceptibility genes in the next few years (Smoller & Finn, 2003). Irrespective of whether the family history represents increased genetic or environmental risk, or more likely elements of both, it is one of the most important predictors of the development of bipolar disorders in particular and mood and anxiety disorders in general among youth.

There are a growing number of studies of offspring of parents with bipolar disorder that have contributed substantial information on developmental influences in the expression of bipolar disorder among youth (Chang, Steiner, & Ketter, 2000; Duffy et al., 2002; Duffy, Alda, Kutcher, Fusee, & Grof, 1998; Duffy, Alda, Trinner, et al., 2007; Gershon et al., 1985; Hammen, Burge, Burney, & Adrian, 1990; Henin et al., 2005). Controlled studies of offspring of parents with bipolar disorder have revealed an increased risk of a range of disorders, including depression, anxiety disorders, and ADHD, suggesting a lack of specificity of early manifestations of bipolarity (Duffy, 2007). Rates of mania and bipolar disorder are generally low due to the young age of adolescent offspring in these studies; however, children of bipolar parents show greater specificity of transmission of affective disorders than do children of parents with unipolar depression (Merikangas & Angst, 1995). The increased rates of ADHD that have been reported in some studies have been interpreted as evidence that symptoms of ADHD may be manifestations of a common underlying diathesis with bipolar disorder (Biederman et al., 1996, 2004, 2008; Chang et al., 2000; Hirschfeld et al., 2002). The prospective design of many of these studies will enable investigators to evaluate the prognostic significance of the symptoms and syndromes manifested by these children across development.

**KEY ISSUES FOR FUTURE EPIDEMIOLOGIC RESEARCH**

This review demonstrates the maturity of descriptive epidemiology of bipolar disorder based on the rather consistent findings of large cross-sectional epidemiologic studies that have now provided sufficient descriptive data on the prevalence, social and demographic correlates, and comorbidity of bipolar disorder as well as other major disorders. Therefore, the next stage of epidemiologic research should shift to a focus on the application of the tools of analytic epidemiology in order to pursue the clues generated in the large descriptive studies reviewed above (Weich & Araya, 2004; Wittchen, Muhlig, & Pezawas, 2003). Application of nested case–control and cohort study designs, particularly prospective studies, can begin to incorporate these new concepts that can advance our understanding of the classification, risk factors, and consequences of bipolar disorder. There are several contemporary issues that warrant further study, including the diagnostic thresholds and boundaries of bipolar disorder; key components, particularly trait measures underlying bipolar disorder; the developmental manifestations of bipolar disorder across the lifespan; identification of nondemographic environmental correlates, and potential biologic factors that may index sources of heterogeneity of this disorder; and explanations for nonrandom patterns of comorbidity. Therefore, future epidemiologic research may be valuable in addressing the following contemporary issues concerning the classification, manifestations, and risk factors for bipolar disorder.

**Is Bipolar Disorder Better Characterized by the Spectrum Concept?**

The evolving definition of the spectrum of bipolar disorder described by Akiskal (2002), Angst et al. (2003), and Dunner (2003) has generated substantial interest in assessing the thresholds between major depression and bipolar disorder. As described above, recent studies have begun...
to expand the diagnostic criteria for mental disorders to collect information on the spectra of expression of particular conditions (Angst, 2007; Angst et al., 2002; Judd et al., 1998). Although expansion of diagnostic thresholds would naturally lead to increased prevalence rates of bipolar disorder, Angst (2007) notes that it would not lead to an increase in affective disorders in general because the cases shift from nonbipolar to bipolar disorder. However, comparable expansion of mood disorders to include subthreshold manifestations of depressive symptoms would actually lead to an increased prevalence of mood disorders in the general population.

The distinction between bipolar I and bipolar II is also related to the spectrum concept since these subtypes of bipolar disorder are based on differences in duration and impairment rather than to distinct qualitative manifestations. Several recent reviews of the validity of bipolar II have summarized the evidence for this distinction (Benazzi, 2006; Vieta et al., 2000; Vieta & Suppes, 2008) and concluded that bipolar II is an important entity that may either constitute a distinct subtype or be a manifestation of the same underlying spectrum of bipolar I. Finally, few studies have expanded the information collected in community samples to include affective temperament as defined by Akiskal, Brieger, Mundt, Angst, and Marneros (2002).

Future epidemiologic studies can address these issues by inclusion of assessment of the full spectrum of expression of mood disorders rather than solely ascertaining categorical diagnostic criteria in place at the time of the survey (Ruscio, Zimmerman, McGinley, Chelminski, & Young, 2007). The addition of dimensional scales to supplement diagnostic interviews can enhance the information on the symptom criteria included in the diagnostic interview. In addition, collection of independent information on severity, impairment, duration, and recurrence will allow inspection of thresholds and boundaries of mood disorders in general population samples.

**Do the Clinical Components or Endophenotypes Provide More Valid Classification of Bipolar Than Current Diagnostic Nomenclature?**

There is also increasing focus on the extent to which bipolar disorder may also be a reflection of underlying dimensions of regulation of mood, sleep, and activity levels. Studies of schizophrenia and bipolar disorder have begun to deconstruct clinical phenotypes by their component features or subtypes and endophenotypes (e.g., intermediate expression between the underlying biologic/genetic diathesis and the phenotype). Several summaries of potential endophenotypes of bipolar disorder suggest a range of candidate domains that warrant future research (Bora, Yucel, & Pantelis, 2008; Hasler, Drevets, Gould, Gottesman, & Manji, 2006; Lenox, Gould, & Manji, 2002; MacQueen, Hajek, & Alda, 2005; Merikangas et al., 2002). Progress in understanding the pathogenesis of the mood disorders and their component features, such as diurnal rhythm dysregulation, enhanced stress reactivity, and executive attentional function (Hasler et al., 2005; Lenox et al., 2002), may then provide a more fertile ground for interaction with basic science. Prospective studies of each of these domains in both adults and high-risk youth may yield valuable information on whether these domains provide better indices of the pathogenesis of bipolar disorder than the aggregate clinical diagnostic entity.

**Do the Manifestations of Bipolar Disorder Differ Across the Lifespan?**

There has been considerable controversy about the existence of bipolar disorder in young children. Whether the rapid mood changes and behavioral dysregulation that characterize children in clinical samples are truly a manifestation of bipolar disorder that has been fairly well operationalized in adults has been widely discussed (Duffy, Alda, Trinneer, et al., 2007; Parry & Allison, 2008). In a comprehensive review of the phenomenology of bipolar disorder in outpatient samples, Youngstrom, Birmaher, and Findling (2008) describe similarities and differences between the manifestations of mania in adults and children. Since the samples of children have been identified in a range of specialty clinics that may not be representative of the general population of children, future research will require systematic sampling and longitudinal follow-up to address the issue of continuity and discontinuity of the early manifestations of bipolar illness.

**Are Differential Patterns of Comorbidity Sources of Heterogeneity in Bipolar Disorder?**

The confirmation of comorbidity of bipolar disorder with a broad range of other mental disorders reported in clinical studies in population surveys suggests that comorbidity is
a real phenomenon rather than an artifact of sampling bias. Results of prospective and high-risk studies of children described above provide preliminary evidence regarding potential mechanisms for comorbidity and suggest that comorbidity could comprise an important source of heterogeneity of bipolar disorder. For example, future studies should attempt to distinguish whether anxiety disorders represent manifestations of the same etiologic factors or independently elevate the risk for development of bipolar disorder. Additional research on possible explanations for comorbidity with physical disorders, particularly migraine and cardiovascular disease, is also highlighted by recent findings in epidemiologic research.

SUMMARY

This article provides a comprehensive review of the magnitude of bipolar disorder in adults (DSM–IV) and children in community surveys across the world. The major finding is the consistency between estimates derived from large population-based studies of adults during the past decade and those reported from earlier reviews. Epidemiologic research during the past decade has contributed new information on the subtypes of bipolar disorder as well as on subthreshold bipolar disorder in general population samples. Recent findings indicate that bipolar I disorder affects approximately 1 of every 100 adults in the United States, and when taken together with bipolar II and subthreshold bipolar, may affect up to 4% of adults in the community. Equivalent proportions of men and women suffer from this condition, but women tend to exhibit more depressive symptoms and bipolar spectrum disorders than men in the general population. The onset of bipolar disorder generally occurs in adolescence, with the peak onset in the early to mid-20s. In contrast to adults, information on the prevalence of bipolar disorder in children and adolescents is quite limited. The most compelling data on youth derives from prospective follow-up studies of adolescents that converge in demonstrating a prevalence rate of bipolar disorder of 2.0% in young adults. There is a striking degree of comorbidity with other mental disorders, suggesting disturbances in multiple systems of emotion, cognition, and behavior. Evidence suggests that substance use disorders are a consequence of mania, thereby providing an important target for prevention. Bipolar disorder also tends to co-occur with a range of physical disorders, but the causes for this association are not well understood. Finally, we identify several contemporary issues that should be addressed in ongoing and future population-based surveys, including the diagnostic thresholds and boundaries of bipolar disorder; the developmental manifestations of bipolar disorder across the lifespan; identification of nondemographic environmental correlates, and potential biologic factors that may index sources of heterogeneity of this disorder; and explanations for nonrandom patterns of comorbidity.

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