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Mood episodes and mood disorders: patterns of incidence and conversion in the first three decades of life

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Abstract

Objectives—Significant questions remain regarding both the incidence patterns of mood episodes in adolescents and young adults from the community and the conversion rate from unipolar to bipolar disorders. We addressed these issues by examining data from a prospective longitudinal community study to (i) determine the cumulative incidence of mood episodes and disorders in the first three decades of life; (ii) determine the risk for first onset of depression among individuals with a previous history of hypomanic/manic episodes and vice versa; and (iii) determine the clinical and treatment characteristics of these subjects.

Methods—Using the Munich-Composite International Diagnostic Interview, clinically trained interviewers assessed mood episodes and mental disorders in 3,021 community subjects (aged 14–24 at baseline and 21–34 at third follow-up).

Results—The estimated cumulative incidence at age 33 was 2.9% for manic, 4.0% for hypomanic, 29.4% for major depressive, and 19.0% for minor depressive episodes; overall, 26.0% had unipolar major depression, 4.0% bipolar depression, 1.5% unipolar mania, and 3.6% unipolar hypomania (no major depression). Overall, 0.6% and 1.8% had unipolar mania or hypomania, respectively, without indication for even minor depression. A total of 3.6% of the initial unipolar major depression cases subsequently developed (hypo)mania, with particularly high rates in adolescent onset depression (< 17 years: 9%). A total of 49.6% of the initial unipolar mania cases subsequently developed major depression and 75.6% major or minor depression. While bipolar cases had more adverse clinical and course depression characteristics and higher treatment rates than unipolar depressed cases, bipolar cases did not significantly differ in mania characteristics from unipolar mania cases.

Conclusions—Unipolar and bipolar mood disorders are more frequent than previously thought in adolescence and young adulthood, a time period when both the recognition and the intervention rates by the healthcare system are rather low. ‘Conversion’ to bipolar disorder is limited in initial unipolar depression, but common in initial unipolar mania. The remaining unipolar mania cases appear to be

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significant in terms of clinical and course characteristics and thus require more research attention to replicate these findings.

Keywords

bipolar disorder; community study; conversion; epidemiology; mood episode

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In the traditional nosology of manic-depressive illness/bipolar disorder (BD), depression and mania are viewed as part of a unitary illness, reflecting dysregulation along a mood dimension (1). The frequency of (hypo)manic episodes without lifetime episodes of depression remains controversial; prevalence data among all bipolar patients range from 1.1 to 47.2% (2). Less controversial is the observation that individuals with unipolar depressive disorder might subsequently develop (hypo)manic episodes, thus converting to BD. The question remains what proportion will convert and whether it is feasible to predict conversion, e.g., by characteristics of the initial depressive episode. The answers to these questions would inform nosology and facilitate early recognition and intervention (3).

While there are a substantial number of large, community-based surveys, most are limited by their cross-sectional nature and inclusion of a broad age spectrum, spanning adolescence (age 16+) to late adulthood (4–[9]). Thus, these studies may be subject to notable recall bias and they typically do not provide an adequately powered sample to estimate the prevalence and incidence of mood episodes in restricted age ranges, such as adolescence and young adulthood. Yet these studies suggest that the highest incidence of mood episodes occurs between ages 15–25 (9–[14]). Ages of first onset may date back to childhood (15,[16]), but childhood studies often differ from those in adolescents and adults in terms of diagnostic criteria and assessment instruments (e.g., self versus parental report). Thus, it is difficult to draw firm conclusions about the frequency of hypomania and mania in childhood and adolescence. Furthermore, little information is available about the probability of longitudinal transitions from depressive to (hypo)manic episodes, and also the reverse direction, in this time period. Beyond major depression, considering minor depression (potential ‘counterparts’ of hypomanic episodes) is important given significant functional impairment (17).

Using data from a prospective, longitudinal community sample of adolescents and young adults, we examined the following questions:

- **i.** What is the cumulative incidence of manic episodes (ME), hypomanic episodes (HE), major depressive episodes (MDE), and minor depressive episodes (MinDE), as well as of unipolar and bipolar mood disorders, in the first three decades of life?
- **ii.** What is the risk for first onset of major or minor depression among individuals with a previous history of HE/ME? And what is the risk for first onset of HE/ME among individuals with a preceding MDE or MinDE?
- **iii.** What clinical and treatment features characterize subjects with unipolar and bipolar mood disorders?

Patients and methods

Sample

The Early Developmental Stages of Psychopathology (EDSP) study is a prospective, longitudinal study in a representative community sample of 3,021 subjects aged 14–24 years at baseline (T0) that was followed prospectively (T1/T2/T3) over up to 10 years (14,[18],[19]). The baseline response rate was 70.8%. The conditional response rates were 88.0% at T1 (interval

since baseline: 1.2–2.1 years), 84.3% at T2 (interval since baseline: 2.8–4.1 years), and 73.2% at T3 (interval since baseline: 7.3–10.6 years).

Diagnostic assessment

Individuals were assessed by trained clinical interviewers (mostly psychologists) with the computer-assisted Munich-Composite International Diagnostic Interview (DIA-X/M-CIDI) (20,[21]). The lifetime DIA-X/M-CIDI was used at baseline and the interval version at follow-ups. Test-retest reliability and validity for the DIA-X/M-CIDI have been previously established (21–[23]).

Diagnoses were computed using the M-CIDI/DSM-IV algorithms. Consistent with DSM-IV and M-CIDI conventions, we studied the following mood episodes: MDE, HE, and ME. We also considered the research category of MinDE, defined as 2–4 depressive symptoms (one of them depressed mood or loss of interest) occurring over at least two weeks with distress/impairment.

In addition to these definitions of episode types, we used the DSM-IV diagnoses: major depressive disorder [(MDD) = *unipolar depression*; MDE but no ME/HE] and *bipolar disorder* [(BD) =ME/HE and MDE]. When DSM-IV ME or HE criteria were met without lifetime presence of MDE, we deviated from the DSM-IV convention by using the terms *unipolar mania* (instead of BD as in DSM-IV) and *unipolar hypomania* (instead of BD not otherwise specified as in DSM-IV). We also labeled cases with ME and MDE, or HE and MDE, as *bipolar depression* to differentiate these cases from DSM BD, which also includes cases with ME but no MDE. Furthermore, we also considered MinDE for broadly defined *bipolar depression*.

Age of onset information for mood episodes over assessment waves was based on the minimum age of onset reported by the respondent (24). This definition agreed well (> 90%) with other age-of-onset aggregation methods (e.g., using the *first* or the *mean* of reported ages of onset), i.e., the absolute value of differences were at most one year. The only exception was that agreement between the mean and minimum method in MDE onset was 72.5%. *Duration of longest episode* was based on the maximum reported number of consecutive weeks with depression or (hypo)mania, respectively, at any assessment. *Number of episodes* was based on the maximum number of reported depressive or (hypo)manic episodes at any assessment; a two-month period of euthymia was required to account for the presence of different episodes. *Professional attention/treatment* was hierarchically assessed (hospitalization, treatment by doctor, treatment by other specialist, medication use) separately for depression and/or (hypo) mania in the respective M-CIDI sections. *Impairment* due to depression or (hypo)mania, respectively, was dichotomized to severe (a fair amount or much) versus nonsevere (a little/none).

Statistical analysis

Data were weighted by age, sex, and geographic location at baseline to match the distribution of the sampling frame; frequencies are reported unweighted. Stata 10.0 (25) was used to compute robust variances, confidence intervals (CI), and p-values (by applying the Huber-White sandwich matrix) required when basing analyses on weighted data (26).

Age-specific cumulative incidence rates (in contrast to observed rates) were estimated with the Kaplan-Meier method (27). Separate Cox regressions with hazard ratios (HR) were used to assess overall differences in the risk of mood episodes between females and males. Cox regressions were also used to assess associations with the risk for MDE and MinDE between those without HE and ME and those with HE and ME, respectively. Conversely, associations

with the risk for HE/ME were assessed between those without MDE or MinDE and those with MDE or MinDE.

Group differences in binary outcomes were assessed with odds ratios (ORs) from logistic regressions. Differences in moderately skewed outcomes (e.g., age of onset) were assessed with median differences from linear regressions. All associations were adjusted for sex and age at last assessment.

Of note, age-of-onset information was missing for two cases with MDE and three cases with HME; these subjects were excluded from all analyses considering temporal order of onset.

Results

Cumulative incidence

Mood episodes—The estimated age-specific cumulative incidence at age 33 was 2.9% for ME (observed n = 84, 2.8%; *note: numbers are unweighted, percentages are weighted*), 4.0% for HE (observed n = 115, 3.8%), 29.4% for MDE (observed n = 822, 28.4%), and 19.0% for MinDE (observed n = 357, 12.4%).

The cumulative incidence for ME was almost the same for males (3.0%) and females (2.9%; HR = 0.92; 95% CI: 0.57–1.49, p = 0.733; Fig. 1A). For both genders, peak incidence period for ME was the mid-teens. With respect to HE, females had a higher estimated cumulative incidence at age 33 (5.2%) than males (3.3%; HR = 1.74; 95% CI: 1.15–2.64, p = 0.009). Some first ME/HE cases occurred in childhood, and a sharp incidence increase was found in adolescence; first onsets after the age of 20 were rare.

Females revealed a higher estimated cumulative incidence at age 33 than males for MDE (females: 35.6%, males: 23.1%; HR = 1.70, 95% CI: 1.44–2.01, p < 0.001), but not for MinDE (females: 18.0%, males: 19.4%) (Fig. 1B). In both genders, some few depression onsets occurred in childhood. Most cases emerged between ages 12 and 25 and, in contrast to the HE/ME curves, both males and females showed continued new onsets of MDE and MinDE up to the mid-30s.

Mood disorders—A total of 33 of the 84 observed ME cases (36.9%) and 76 of the 115 HE cases (67.8%) never had threshold DSM-IV MDE, and thus could be best labeled as *unipolar mania* or *unipolar hypomania*, respectively. Among the 713 MDE cases, 623 (88.0%) did not experience HE/ME (MDD; *unipolar major depression*), while 90 (12.0%) did [*bipolar depression*; i.e., MDE and ME (7.0%; n = 51) or MDE and HE (5.0%; n = 39)]. The estimated cumulative incidences of mutually exclusive mood disorder categories up to age 33 are 1.5% for unipolar mania (ME, no MDE), 3.6% for unipolar hypomania (HE; no MDE), 26.0% for unipolar major depression (MDD; MDE, no HE/ME); and 4.0% bipolar depression (MDE and HE or ME) (Fig. 2A). The age-of-onset patterns suggest that unipolar mania/hypomania occurs earlier than unipolar major depression and that *bipolar* cases reveal earlier onset of first mood episode compared to unipolar major depression cases.

Considering additionally MinDE (no MDE), the more strictly defined estimated cumulative incidence rates were 0.6% for unipolar mania (ME, no MDE/MinDE) and 1.8% for unipolar hypomania (HE, no MDE/MinDE); 0.5% had ME with MinDE but no MDE, and 0.9% had HE with MinDE but no MDE (Fig 2B). Earlier onsets of first mood episode occurred among (hypo)mania cases with MinDE compared to those without MinDE.

Importantly, an examination of ME and HE rates by age (Table 1) did not suggest that unipolar mania/hypomania as compared to bipolar depression cases were overrepresented in the younger

age groups. Subjects with unipolar mania/hypomania appeared as likely as those with bipolar depression to have passed through the period of risk for depression.

Conditional probability and risk for onset of mood episodes

Two types of analyses were used to examine the probability and risk of developing bipolar depression given the presence of initial unipolar mania/hypomania and, conversely, initial unipolar depression. First, conversion numbers and rates were based on observed cases; and second, conversion risk up to age 33 was estimated by using survival analyses that take different ages at final assessment and dropouts into account. Cases with same-year onset of (hypo)mania and depression were not considered for these analyses because information on temporal priority was not available for these cases.

Risk for depressive episodes conditional on prior (hypo)manic episodes— Among the observed temporally primary unipolar (hypo)mania cases (HE/ME without a prior or same-year onset of MDE; n = 154), 45 (29.2%) subsequently developed MDE (Fig. 3), and thus bipolar depression. This rate did not differ by gender or by age of onset of HE/ME. Yet risk for bipolar depression was higher among primary ME cases (n = 30/63, 49.6%) than in primary HE cases (n = 15/91, 15.8%; OR = 5.2, 95% CI: 2.3–12.2, $p < 0.001$). Similar rates occurred when HE/ME cases with prior or same-year MinDE were excluded. Of note, however, rates were considerably higher when also considering subsequent MinDE in addition to MDE.

Survival analysis revealed that the estimated risk for a first onset of MDE (Fig. 4A) was greater among cases with prior ME [estimated percentage at age 25 (no stable estimates after that age): 71.2%; HR = 4.25; 95% CI: 2.83–6.40, $p < 0.001$] relative to cases without prior HE/ME (28.5%), both in males (HR = 3.94; 95% CI: 2.18–7.12, $p < 0.001$) and in females (HR = 4.61; 95% CI: 2.61–8.12, $p < 0.001$). Initial HE cases, however, did not reveal an increased estimated risk for temporally secondary MDE (estimated weighted percentage at age 33: 27.8%; HR = 0.89; 95% CI: 0.51–1.54, $p = 0.580$) compared to cases without prior HE/ME. Considering subsequent onset of MinDE (no MDE; Fig. 4B), similar findings occurred with ME (estimated percentage of MinDE at age 33: 27.6%; HR = 3.26; 95% CI: 1.64–6.46, $p = 0.001$) but not HE cases (estimated percentage of MinDE at age 33: 24.5%; HR = 1.46; 95% CI: 0.84–2.53, $p = 0.177$) showing a significantly increased risk compared to cases without prior HE/ME (estimated percentage of MinDE at age 33: 18.5%).

Risk for (hypo)manic episodes conditional on prior MDE—Among temporally primary MDE cases without prior or same-year onset of HE/ME (n = 649), 3.6% (n = 26) reported a subsequent onset of HE/ME (Fig. 3), with no significant gender difference. ‘Conversion’ rates to BD were highest among subjects with early MDE onset (age < 17: 9.0%) and lower among those with MDE onset at ages 17–20 (0.5%; OR = 0.05; 95% CI: 0.01–0.35, $p = 0.003$), 21–25 (0.7%; OR = 0.07; 95% CI: 0.01–0.56, $p = 0.012$), or 26 and above (0.0%). Compared to MDE, ‘conversion’ rates for MinDE were lower, particularly due to lower rates of ME onset (1.0%).

Survival analyses (age span 5–33; Fig. 4C) showed that the estimated risk for the onset of HE/ME tended to be higher among cases with prior MDE (estimated weighted percentage at age 33: 10.4%; HR = 1.54; 95% CI: 0.94–2.52, $p = 0.089$) compared to cases without prior MDE (6.3%). The risk for onset of HE/ME among cases with no prior MDE but MinDE was numerically similar (estimated weighted percentage at age 33: 11.4%) but not significantly increased compared to cases with neither MDE nor MinDE (6.3%; HR = 1.37; 95% CI: 0.65–2.89, $p = 0.406$).

Clinical and treatment characteristics of unipolar and bipolar cases

Course—Unipolar (hypo)mania cases (HE/ME, no MDE) did not differ from bipolar cases (HE/ME and MDE) in reported number of HE/MEs, duration of longest HE/ME, or age of onset of first HE/ME (Table 2; p-values > 0.1). Similar findings occurred when MinDE was considered in HE/ME cases, i.e., HE/ME cases *with* versus *without* MinDE did not differ in these characteristics. However, bipolar cases (MDE and HE or ME) were more likely to have a higher number of MDEs relative to unipolar depression cases (unweighted median difference: 2.0, $p < 0.001$; three or more episodes relative to only one episode: OR = 2.3, 95% CI: 1.3–3.8, $p = 0.003$; Table 3). They also had a longer episode duration of depression (unweighted median difference: 2.3, $p = 0.051$; 6–10 versus 2–5 weeks: OR = 3.5, 95% CI: 1.7–7.1, $p = 0.001$; 11 + versus 2–5 weeks: OR = 2.7, 95% CI: 1.4–4.9, $p = 0.002$), and an earlier age of onset of first MDE (unweighted median difference: –1.1, $p = 0.030$). This pattern was particularly pronounced for individuals with ME and MDE as opposed to those with HE and MDE.

Among the total 90 bipolar cases with MDE and HE or ME, the first mood episode was hypomanic/manic in 45 cases (50.1%), with ME cases being more frequently temporally primary (n = 30/51, 57.6%) than HE cases (n = 15/39, 39.5%). A same-year MDE onset occurred equally as frequent in ME (n = 10/51, 21.8%) and HE (n = 9/39, 23.9%).

Impairment—There were no significant differences in severity of impairment due to ME between bipolar cases with ME and MDE and those with unipolar ME (severe impairment: 90.9% versus 78.0%). However, there were higher rates of impairment due to hypomania in bipolar HE/MDE as compared to unipolar HE (severe impairment: 60.3% versus 43.4%; OR = 3.01, 95% CI: 1.70–7.24, $p = 0.001$). Among unipolar HE/ME cases, impairment rates due to (hypo)mania did not significantly differ in subjects *with* versus *without* MinDE.

In terms of impairment due to depression, bipolar subjects with ME and MDE (but not HE and MDE) tended to be more severely impaired than unipolar depressed individuals (severe impairment: 96.1% versus 89.5%; OR = 2.90, 95% CI: 0.87–9.68, $p = 0.084$). Similar findings occurred when also considering MinDE.

Professional attention and treatment—Unipolar hypomania/mania cases were as likely to receive any treatment for HE/ME (hospitalization, treatment by doctor/other specialist, medication use) as bipolar cases (ME/MDE: 25% versus ME alone: 14.8%, $p = 0.366$; HE/MDE: 6.9% versus HE alone: 3.3%, $p = 0.511$). However, a trend for higher rates of hospitalizations for mania occurred in bipolar cases (ME and MDE) compared to unipolar ME cases (11.6% versus 1.8%; OR = 6.91, 95% CI: 0.78–61.03, $p = 0.081$).

Overall, depressive episodes received greater professional attention than did HE/ME. Bipolar cases with MDE and ME were more likely to receive any treatment for depression than unipolar depression cases (70.6% versus 45.6%; OR = 2.53, 95% CI: 1.24–5.16, $p = 0.010$). Among the treatments for depressive episodes, hospitalizations (16.4% versus 7.8%; OR = 2.26, 95% CI: 0.95–5.37, $p = 0.065$) and treatments by other healthcare professionals (psychologists, psychotherapists; 16.4% versus 14.5%; OR = 3.12, 95% CI: 1.19–8.19, $p = 0.021$) were overrepresented in bipolar cases with ME and MDE relative to unipolar depression cases. In contrast, bipolar cases with HE and MDE tended to have lower overall treatment rates for depression than unipolar depression cases (34.7% versus 45.6%; OR = 0.53, 95% CI: 0.26–1.10, $p = 0.090$). Considering MinDE as well, there were no differences in professional attention among HE/ME cases with MinDE in comparison to cases with MinDE alone.

Discussion

Using data from a large, representative community sample of subjects aged 14–24 that were followed over 10 years, the present investigation provides novel insights regarding the incidence patterns of mood episodes and mood disorders, the risk for conversion from unipolar disorder to BD, and the clinical and treatment characteristics of unipolar and bipolar mood disorders in the critical time period of adolescence and young adulthood.

Cumulative incidence of mood episodes and mood disorders in the first three decades of life

Unlike previous contributions, our study provides an incidence characterization of mood episodes and mood disorders from puberty into early adulthood. The cumulative incidence estimates of HE and ME, and of DSM-IV BD up to age 33, were higher than the lifetime prevalence estimates reported by previous cross-sectional community studies, which covered a considerably broader age range (e.g., 28, 29). Yet they resemble the findings reported by Angst et al. (30) in their longitudinal cohort study, providing support for the suggestion that cross-sectional lifetime studies may underestimate the prevalence of ME and HE. Consistent with earlier studies in adult samples (e.g., 12), peak onset for mania was in the mid-teen period. Our finding that manic cases revealed numerous indications of being clinically severe (impairment and course characteristics) underlines the credibility of these mania cases. For hypomania, the incidence pattern showed two peak onset periods: one as early as childhood, and then a second, sharper increase in adolescence. Here caution is warranted because of the challenges inherent in assessing hypomania in childhood and early adolescence, and in particular because the childhood assessments were done retrospectively.

The estimated cumulative incidence for (unipolar) major depression up to age 33 was higher than retrospective lifetime rates from adult community surveys (4,[28]), but in the range of estimates from multiwave prospective studies (12,[31]). A further considerable proportion meets criteria for MinDE. First onsets of depression occurred rarely in childhood. Quite different from HE/ME, depression was characterized by a fairly steady rate of new-onset cases from early adolescence up to the mid-30s. Our findings are consistent with previous clinical studies that report the mean age of onset of unipolar depression in the mid- to late-20s (5) and of BD within the age range of 15–19 years [median age of onset of 17.5 years (see 32)]. They are also in agreement with other epidemiological studies in comparable age groups (4,[33],[34]) that typically reveal slightly lower mean onsets than do clinical samples.

Particularly noteworthy is our finding of relatively high rates of unipolar mania/hypomania without indication for threshold DSM-IV MDE in the first three decades of life. The occurrence of unipolar mania has been rarely examined and its existence remains controversial. Our findings, however, are in agreement with some other epidemiological longitudinal studies (35,[36]) as well as recent long-term follow-up data (2), indicating considerable rates of unipolar (hypo)mania. Although these rates substantially decreased when additionally considering MinDE or dysthymia, further explorations of unipolar (hypo)mania are warranted. In particular, the unipolar mania cases without MDE did not significantly differ from bipolar cases in terms of clinical and course characteristics, impairment severity, professional help seeking, and treatment for the ME, suggesting that these cases are clinically relevant. This conclusion holds when minor depression is also considered, because these characteristics did not significantly differ in unipolar mania cases with and without minor depression. Because of the restricted follow-up period and the relatively young age of our sample, however, these cases might be best diagnosed as ‘provisional unipolar mania’, even though we ruled out the possibility that the cases were overrepresented in younger age groups that had not passed the first core incidence period for depression in a similar way as older individuals.

Conditional probability and risk for onset of mood episodes

Consistent with traditional thinking, we observed considerable rates of subsequent MDE onsets among primary hypomania (15.8%) and particularly mania cases (49.6%), with no indication that conversion to 'true' BD differed by age of (hypo)mania onset. These proportions increased when subsequent minor depression (44.3% of HE and 75.6% of ME cases developed MDE or MinDE) was also considered, or when projecting the lifetime risk (as opposed to the observed rates) by using survival analyses (27.8% of primary HE and 71.2% of primary ME cases were estimated to have developed MDE by age 33). Angst and Zimmermann (37) reported a conversion rate of 2.7 per year in patients whose disorder started with mania. Of note, compared to individuals without (hypo)mania, the depression onset risk was significantly increased only in mania but not hypomania cases.

In contrast, the conversion rate from unipolar depression to bipolar depression appears to be overall relatively low. A total of 3.6% of all initial MDD cases were observed to have a subsequent first ME or HE, with indications that the conversion risk is remarkably high (9%) in early-onset depression (< 17 years). In a recent analysis of a sample of unipolar depressive and bipolar patients, Benazzi (38) showed a close association between an early onset of the mood disorder and bipolarity (history of hypomania, family history of mania/hypomania). Of note, the overall projected estimated (as opposed to the observed rate) conversion risk up to age 33 is about 10% in both our patients with initial MDD and in subjects with MinDE but no MDE, and thus substantial for the age range considered. Although 90% did not convert in the observation period, and despite our finding that the risk rates were not significantly higher when compared to subjects with no depression, this finding confirms cautionary notes by some authors (11,[39]) who consider the diagnosis of unipolar depression in adolescence as provisional. Angst and colleagues (40) reported a conversion rate of 39% in patients with unipolar depression followed prospectively for an average of 20 years from the onset of the disorder. As the age range and follow-up period in our study was restricted to the mid-30s, further conversions are conceivable, yet rates are expected to be very limited as the core risk period for first (hypo)mania onset appears to be adolescence. Unfortunately, due to the fairly low number of conversion cases, our study was not sufficiently powered to determine whether these cases reveal substantially different course characteristics that might help to identify early cases at risk. It is unlikely that epidemiological research will provide useful information in that way. A combination of retrospective assessment and prospective observation of children and adolescents at risk, as determined by prodromal syndromes or newly diagnosed depression, should provide more opportunities. Also, studies focussing on those with a familial risk for BD may be beneficial.

Clinical and treatment characteristics of unipolar and bipolar mood disorders

Consistent with results from Perlis et al. (41), our study showed evidence that unipolar and bipolar depression differ with respect to course, impairment, and treatment. Individuals with ME and MDE in particular reported a greater number and duration of depressive episodes and earlier depression onset than unipolar depression cases. Bipolar ME/MDE subjects, unlike bipolar HE/MDE cases, were also more frequently severely impaired due to depression than were unipolar depressed individuals and received inpatient and outpatient treatment for depression more frequently. This underscores the fact that bipolar I disorder is a particularly severe and clinically significant condition.

In contrast to our finding of more adverse clinical and treatment characteristics in bipolar versus unipolar depression, our characterization of (hypo)manic episodes suggests that bipolar cases do not significantly differ from unipolar mania cases in terms of critical mania course characteristics and impairment as well as treatment due to mania. This finding holds even when additionally considering minor depression, providing support for the validity of our unipolar

mania group. Despite the fact that the size of this group was small compared to unipolar and bipolar depression, together with our finding that (hypo)mania receives, in general, little professional attention and treatment, these findings indicate the strong need to further explore this patient group in terms of special diagnostic and treatment needs.

Limitations

First, we examined the incidence patterns and conversion rates only up to the mid-30s; thus, no conclusions can be drawn for 'true lifetime' incidence and conversion rates. Second, our data did not allow for analyses regarding temporal order of onset of (hypo)manic and depressive episodes emerging within the same year; our conversion rates refer to cases with onsets in different years (minimum one year). Third, the symptom and diagnostic assessment was exclusively based on a standardized diagnostic interview (DIA-X/M-CIDI) administered by trained clinical interviewers (psychologists or MDs), with the limitation of imperfect reliability and validity. Fourth, despite the prospective longitudinal design of the EDSP study, data are based on retrospective recall of participants for the time before baseline assessment and variable time intervals between the respective follow-up interviews. Fifth, some of the subgroup comparisons were based on small numbers, and thus should be interpreted with caution. Finally, our analyses were conducted by strictly applying the DSM-IV criteria as operationalized in the DIA-X/M-CIDI. We deliberately did not manipulate the threshold definitions of mood episodes, with the exception that we included additional analyses on the research category of minor depression. We did not examine overlap with cyclothymia or various types of personality disorders because these data were not available in our study.

Conclusions

Mood episodes are frequent conditions among youth from the community, with adolescence being the core incidence phase for mania and hypomania, whereas depression incidence continues into the third decade of life. Risk of 'conversion' to BD in the course of initial unipolar depression is limited, but is particularly elevated among adolescent-onset depression cases. In contrast, initial mania cases frequently develop depression. However, there is also evidence for the significance of a (small) group of patients remaining unipolar (hypo)manic at least up to their mid-30s. In particular, unipolar mania cases were found to have similar clinical and course characteristics of mania as bipolar cases. Further research is needed to replicate these findings, especially as our study indicates particularly low treatment rates for this patient group that may require more specific diagnostic and professional attention. Overall, our study suggests that both unipolar and bipolar mood disorders seem to be more frequent than previously thought in adolescence and young adulthood, a time period when both the recognition and the intervention rates by the healthcare system have remained relatively low.

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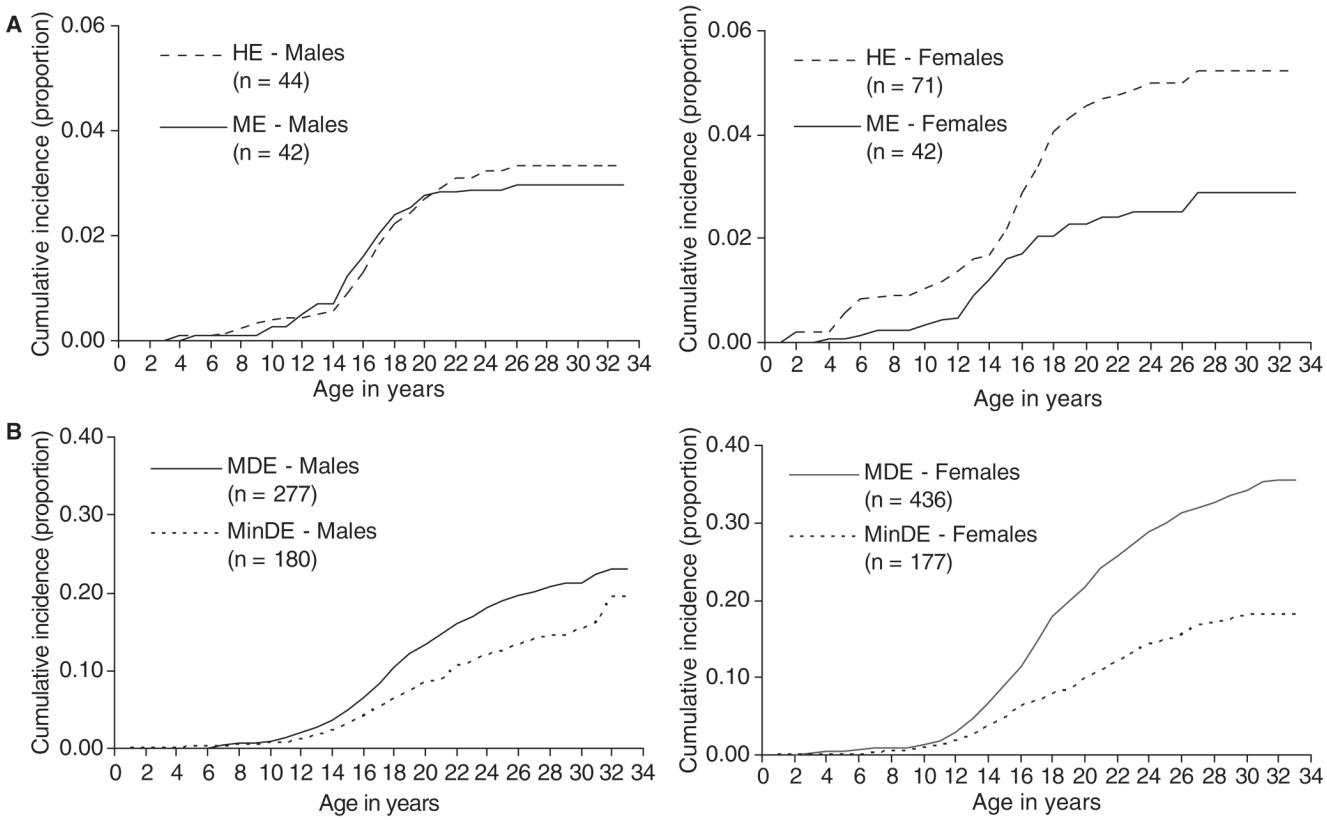

Fig. 1.

Overall age-specific cumulative incidence of mood episodes for males (n = 1,533) and females (n = 1,488). (A) hypomanic episode (HE) and manic episode (ME); (B) major depressive episode (MDE) and minor depressive episode (MinDE).

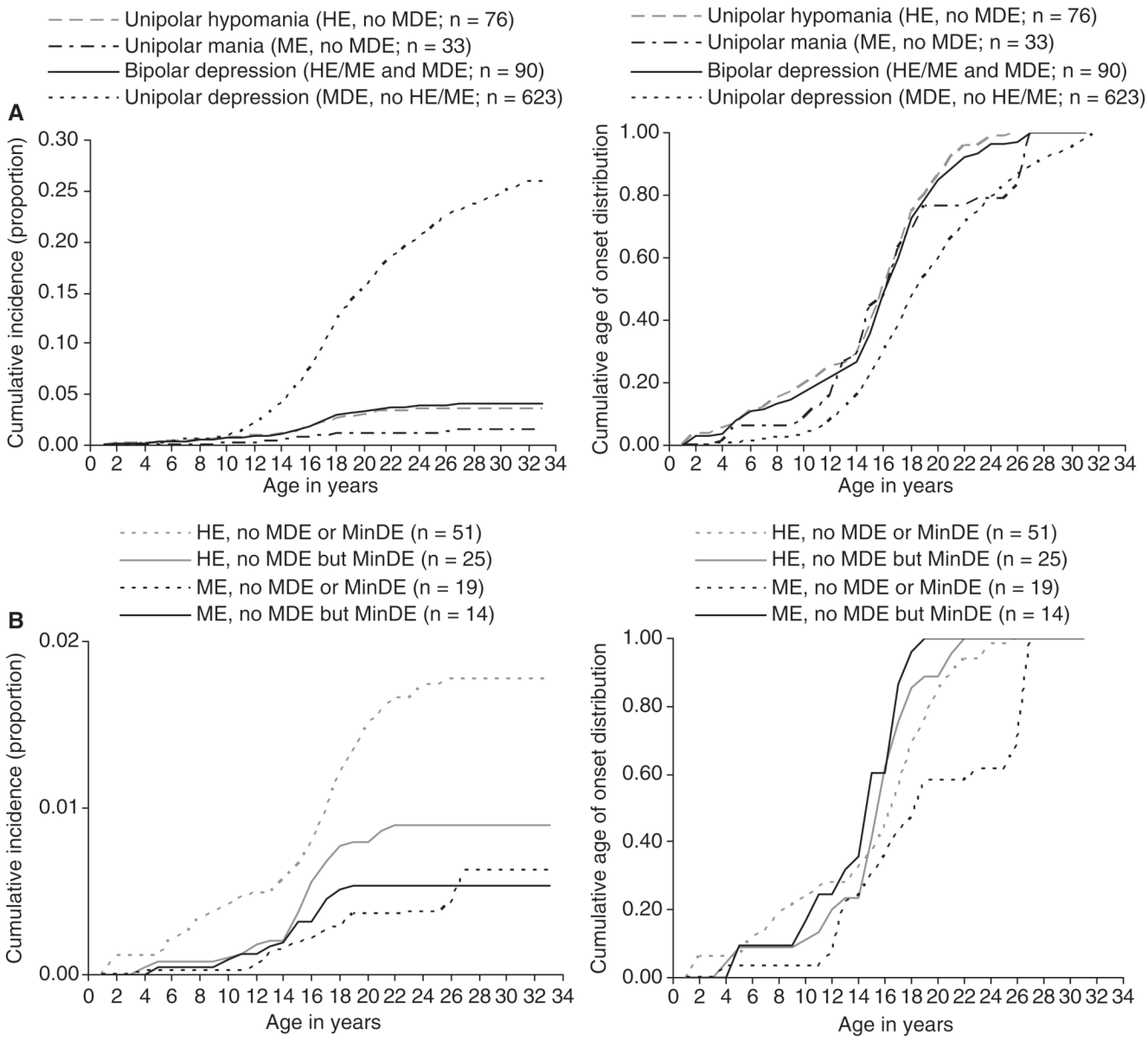

Fig. 2.

Age-specific cumulative incidence and age-of-onset distribution of (A) unipolar hypomania/mania, unipolar depression, and bipolar depressiona and of (B) unipolar hypomania/mania with or without minor depressiona. HE = hypomanic episode; ME = manic episode; MDE = major depressive episode; MinDE = minor depressive episode.

[a]For bipolar depression cases (A) and (hypo)mania with minor depression cases (B), age of onset is defined as the minimum age of onset of HE/ME and MDE (A) and MinDE (B).

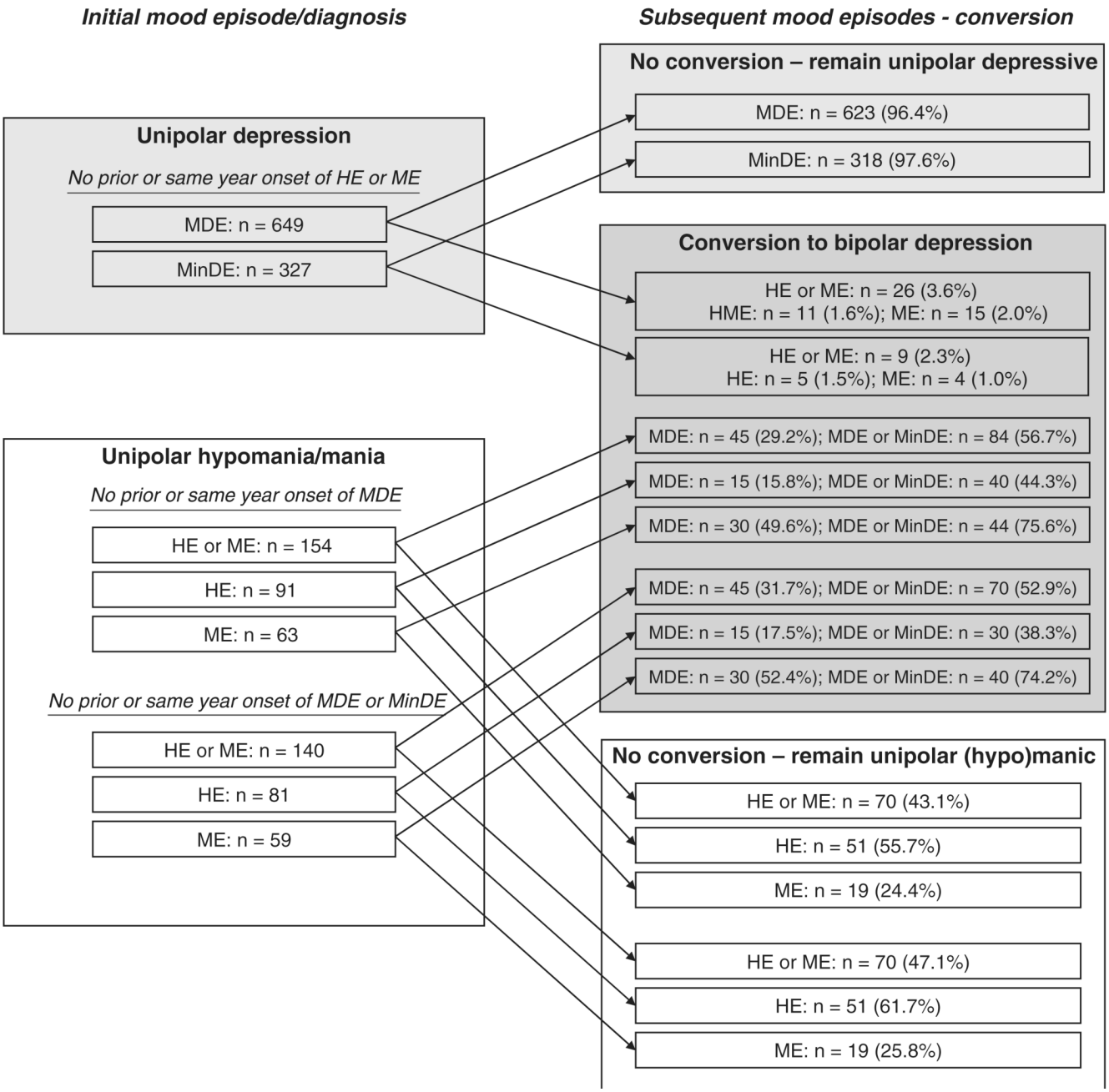

Fig. 3.

Conversion from unipolar to bipolar disorders. Shading: white = unipolar mania; light gray = unipolar depression; dark gray = bipolar depression. MDE = major depressive episode; MinDE = minor depressive episode; HE = hypomanic episode; ME = manic episode.

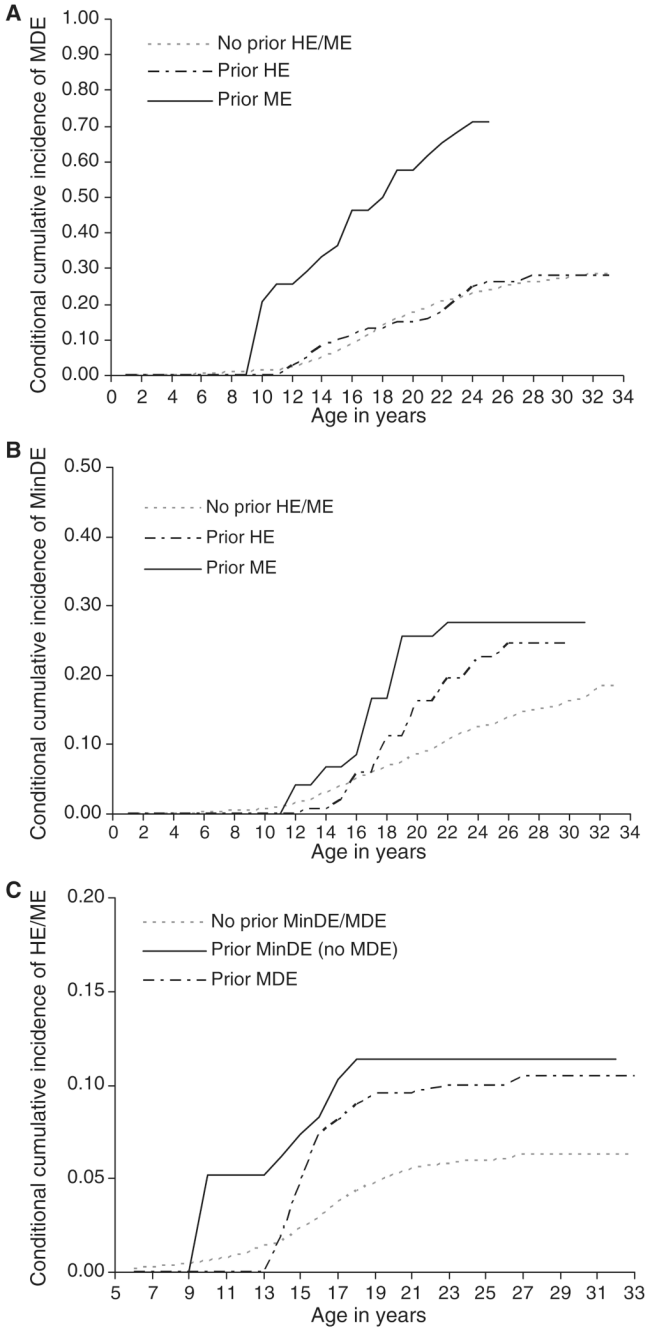

Fig. 4.

Conditional cumulative incidence of major depressive episode (MDE) (A) and minor depressive episode (MinDE) (B) by prior hypomanic episode (HE)/manic episode (ME), and conditional cumulative incidence of HE/ME by prior MDE and MinDE (C)a.

[a]In (C) analyses are restricted to age range 5–33 due to unstable estimates because of low case numbers.

Table 1

Observed cases with hypomanic episode (HE) or manic episode (ME) in the total sample (n = 3,021) and by lifetime presence of major depressive episode (MDE) and minor depressive episode (MinDE)

			Gender				Age at last assessment							
			Male		Female		≤ 20 years		21–25 years		26–30 years		31–34 years	
		N	n	% w	n	% w	n	% w	n	% w	n	% w	n	% w
Total sample														
	Total	3,021	1,533	49.4	1,488	50.6	424	9.9	1,259	31.9	956	36.5	382	21.8
	HME or MNE	199	86	42.6	113	57.4	28	14.1	80	40.2	67	33.7	24	12.1
	HME	115	44	36.2	71	63.8	15	9.9	46	30.4	44	45.2	10	14.6
	MNE	84	42	51.5	42	48.5	13	11.6	34	26.5	23	32.3	14	29.7
By MDE and MinDE														
MDE	Total	713	277	38.2	436	61.8	70	6.6	266	27.2	269	42.1	108	24.1
	HME or MNE	90	34	38.6	56	61.4	12	9.4	38	30.5	23	28.1	17	31.9
	HME	39	13	26.7	26	73.3	4	9.4	18	35.5	11	29.6	6	25.5
	MNE	51	21	47.1	30	52.9	8	9.4	20	27.0	12	27.1	11	36.5
No MDE	Total	2,308	1,256	53.1	1,052	46.9	354	10.9	993	33.5	687	34.6	274	21.0
	HME or MNE	109	52	45.9	57	54.1	16	11.6	42	27.3	44	49.3	7	11.8
	HME	76	31	40.7	45	59.3	11	10.1	28	27.9	33	52.6	4	9.4
	MNE	33	21	59.1	12	40.9	5	15.3	14	25.6	11	41.1	3	18.0
MinDE	Total	357	180	47.9	177	52.1	29	5.5	130	25.6	145	45.2	53	23.6
	HME or MNE	39	18	43.2	21	56.8	6	12.1	12	22.6	18	52.2	3	13.1
	HME	25	10	36.0	15	64.0	3	7.8	10	31.9	11	53.8	1	6.6
	MNE	14	8	55.1	6	44.9	3	19.3	2	7.1	7	49.7	2	24.0
No MinDE	Total	1,951	1,076	54.1	875	45.9	325	12.0	863	35.1	542	32.5	221	20.5
	HME or MNE	70	34	47.6	36	52.4	10	11.3	30	30.2	26	47.5	4	11.1
	HME	51	21	43.1	30	56.9	8	11.3	18	25.9	22	52.0	3	10.9
	MNE	19	13	63.2	6	36.8	2	11.1	12	45.4	4	31.9	1	11.7

N/n = unweighted number; % w = weighted row percentage.

Table 2

Course characteristics of unipolar and bipolar (hypo)mania [n = 199 individuals with hypomanic episode (HE) or manic episode (ME) at any assessment]

	Unipolar (hypo)mania (no MDE)						Bipolar (hypo)mania (with MDE)					
	HE/ME n = 109[a]		HE n = 76[a]		ME n = 33[a]		HE/ME n = 90[a]		HE n = 39[a]		ME n =51[a]	
	n	% w	n	% w	n	% w	n	% w	n	% w	n	% w
Number of HE/MEs												
1–7	29	32.8	18	29.4	11	40.1	27	38.2	12	40.9	15	36.5
8–15	30	37.2	18	34.8	12	42.7	21	28.7	10	27.7	11	29.4
16+	28	30.0	22	35.8	6	17.3	25	33.0	8	31.5	17	34.1
Total	87	100.0	58	100.0	29	100.0	73	100.0	30	100.0	43	100.0
Median number of HE/MEs		10		10		10		10		10		10
Duration of HE/ME (length of longest HE/ME in days)												
4–7	32	34.1	23	36.3	9	29.1	24	32.8	12	41.4	12	27.3
8–14	27	29.1	17	27.7	10	32.4	17	20.2	6	17.2	11	22.1
15+	29	36.8	19	36.0	10	38.4	32	47.0	12	41.4	20	50.6
Total	88	100.0	59	100.0	29	100.0	73	100.0	30	100.0	43	100.0
Median length of longest HE/ME in days		14		14		14		14		14		21
Age of onset of HE/ME												
<16	53	44.2	34	40.0	19	54.9	45	44.6	14	32.2	31	53.3
≥16	53	55.8	39	60.0	14	45.1	45	55.4	25	67.8	20	46.7
Total	106	100.0	73	100.0	33	100.0	90	100.0	39	100.0	51	100.0
Median age at onset of first HE/ME		16		16		15		16		17		15

[a] Slightly reduced n for some variables due to missing information.

n = unweighted number; % w = weighted row percentage; MDE = major depressive episode.

Table 3

Course characteristics of unipolar and bipolar depression [n = 713 individuals with major depressive episode (MDE) at any assessment]

	Unipolar depression				Bipolar depression			
	No HE/ME n = 623[a]		HE/ME n = 90[a]		HE n = 39[a]		ME n = 51[a]	
	n	% w	n	% w	n	% w	n	% w
Number of MDEs								
1	313	50.2	31	33.1	19	48.7	12	22.0
2	46	6.8	5	4.9	3	5.9	2	4.2
3 or more	264	43.0	54	62.0	17	45.4	37	73.8
Total	623	100.0	90	100.0	39	100.0	51	100.0
Median number of MDEs	1		3		2		4	
Duration of MDE (length of longest MDE in weeks)								
2–5 weeks	241	41.7	22	20.4	13	33.2	9	11.5
6–10 weeks	98	17.2	23	28.4	9	19.0	14	34.9
11 or more weeks	228	41.2	41	51.2	15	47.9	26	53.6
Total	567	100.0	86	100.0	37	100.0	49	100.0
Median length of longest MDE in weeks	8		12		8		12	
Age of onset of MDE								
< 16	191	26.8	42	39.7	18	39.4	24	40.0
≥ 16	430	73.2	48	60.3	21	60.6	27	60.0
Total	621	100.0	90	100.0	39	100.0	51	100.0
Median age at onset of first MDE	18		16		17		16	

[a] Slightly reduced n for some variables due to missing information.

HE = hypomanic episode; ME = manic episode; n = unweighted number; % w = weighted row percentage.