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Is recurrence in major depressive disorder related to bipolarity and mixed features? Results from the BRIDGE-II-Mix study

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Abstract. *Background.* Current classifications separate Bipolar (BD) from Major Depressive Disorder (MDD) based on polarity rather than recurrence. We aimed to determine bipolar/mixed feature frequency in a large MDD multinational sample with (High-Rec) and without (Low-Rec) >3 recurrences, comparing the two subsamples. *Methods.* We measured frequency of bipolarity/hypomanic features during current depressive episodes (MDEs) in 2,347 MDD patients from the BRIDGE-II-mix database, comparing High-Rec with Low-Rec. We used Bonferroni-corrected Student's *t*-test for continuous, and *chi*-squared test, for categorical variables. Logistic regression estimated the size of the association between clinical characteristics and High-Rec MDD. *Results.* Compared to Low-Rec (n=1084, 46.2%), High-Rec patients (n=1263, 53.8%) were older, with earlier depressive onset, had more family history of BD, more atypical features, suicide attempts, hospitalisations, and treatment resistance and (hypo)manic switches when treated with antidepressants, higher comorbidity with borderline personality disorder, and more hypomanic symptoms during current MDE, resulting in higher rates of mixed depression according to both DSM-5 and research-based diagnostic (RBDC) criteria. Logistic regression showed age at first symptoms <30 years, current MDE duration ≤1 month, hypomania/mania among first-degree relatives, past suicide attempts, treatment-resistance, antidepressant-induced swings, and atypical, mixed, or psychotic features during MDE to associate with High-Rec. *Limitations.* Number of MDEs for defining recurrence was arbitrary; cross-sectionality did not allow assessment of conversion from MDD to BD. *Conclusions.* High-Rec MDD differed from Low-Rec group for several clinical/epidemiological variables, including bipolar/mixed features. Bipolarity specifier and RBDC were more sensitive than DSM-5 criteria in detecting bipolar and mixed features in MDD.

Key words. Recurrence; Cyclicity; Major Depressive Disorder; Mixed features.

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