It is illegal to post this copyrighted PDF on any website. Adding Increased Energy of Activity to Criterion (A) of the DSM-5 Definition of Hypomania and Mania: Effect on the Diagnoses of 907 Patients From the Bipolar Collaborative Network

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ABSTRACT

Objective: According to *DSM-IV*, criterion (A) for diagnosing a hypomanic/manic episode is mood change (ie, elevated, expansive, or irritable mood). Criterion (A) was redefined in *DSM-5*, adding increased energy or activity in addition to mood change. We sought to investigate the effect of adding increased energy or activity to criterion (A) for the diagnosis of hypomania/mania and, thus, bipolar disorder.

Methods: This analysis of prospectively collected data from the Bipolar Collaborative Network (1995–2002) includes 907 *DSM-IV-TR*–diagnosed bipolar outpatients (14,306 visits). The Young Mania Rating Scale (YMRS) was administered monthly and used to define *DSM-IV* and *DSM-5* criterion (A) fulfillment during a hypomanic/manic visit.

Results: Patients were adults (median age = 40; IQR, 33–49), and over half (56%) were women. Median number of contributed visits was 10 (IQR, 4–23). Applying *DSM-5* criterion (A) reduced the number of patients experiencing a hypomanic/manic visit by 34%, compared to *DSM-IV*. Visits fulfilling *DSM-5* criterion (A) had higher odds of experiencing elevated levels of all other mania symptoms, compared to fulfilling *DSM-IV* criterion (A) only. Association between individual symptoms was strongest with mood elevation and energy or activity (OR [95% CL] = 8.65, [7.91, 9.47]).

Conclusions: The 34% reduction in the number of patients being diagnosed with a hypomanic/manic visit shows that the impact of applying *DSM-5* criterion (A) is substantial. Fewer hypomanic/manic episodes may be diagnosed by the stricter *DSM-5* criterion (A), but the episodes diagnosed are likely to be more severe. The *DSM-5* criteria may in general prevent overdiagnosis of bipolar disorder but possibly at the cost of underdiagnosing hypomanic/manic episodes.

J Clin Psychiatry 2019;80(6):19m12834

To cite: Fredskild MU, Mintz J, Frye MA, et al. Adding increased energy or activity to criterion (A) of the *DSM-5* definition of hypomania and mania: effect on the diagnoses of 907 patients from the Bipolar Collaborative Network. *J Clin Psychiatry.* 2019;80(6):19m12834.

To share: https://doi.org/10.4088/JCP.19m12834 © Copyright 2019 Physicians Postgraduate Press, Inc.

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In his early 20th century description of mental disorders, Kraepelin¹ identified 3 core shared features of mania and depression: disturbances of mood, cognition, and motor activity. However, no single feature was ascribed primacy. As modern psychiatric diagnostic systems evolved in the latter part of the 20th century, eg, the *Diagnostic and Statistical Manual of Mental Disorders*² (*DSM*), the term *bipolar* was introduced to describe patients who experienced episodes of depressive and manic states. Bipolar disorder was classified as a mood disorder, establishing mood abnormalities as the key criterion above motor activity.

Several more recent studies have challenged this view, acknowledging that increased energy or activity is a core feature of the manic spectrum^{3,4} and further advocating that this symptom has equal importance to mood change for the diagnosis of manic states.⁵⁻¹¹ Consequently, the revised definition of criterion (A) for mania and hypomania published in DSM-5¹² now states that persistently increased energy or activity must be present in addition to mood change (ie, "abnormally and persistently elevated, expansive, or irritable mood")^(p124) to make the diagnosis of hypomania and mania—the argument being that adding energy or activity to the diagnostic criterion (A) will improve specificity when making the diagnosis.

The *DSM-5* is a diagnostic tool used by clinicians every day. A change in diagnostic criterion (A) may impact the number of diagnostically confirmed hypomanic/manic episodes and, consequently, the diagnosis of bipolar disorder. To our knowledge, only a few studies^{13,14} have investigated the impact of the modification in *DSM-5* criteria and with conflicting results. The Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) study¹³ found that applying *DSM-5* criteria reduced the identified number of hypomanic/manic episodes by 48% when looking at baseline visits only. However, the UK Bipolar

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Clinical Points

- In DSM-5, the primary criterion for diagnosing hypomania/ mania was changed, now requiring increased energy or activity in addition to mood change. The impact of the modification in criterion (A) has not been thoroughly investigated.
- A 34% reduction in the number of patients being diagnosed with a hypomanic/manic visit in this study shows that the impact of applying DSM-5 criterion (A) is substantial.
- If the clinician observes a mood change coupled with increased energy or activity in a patient suffering from bipolar disorder, the certainty that the patient is destabilizing into a full hypomanic/manic episode is high.

Disorder Research Network (BDRN) study¹⁴ found that up to 94% of patients with a lifetime diagnosis of DSM-IV¹⁵ bipolar disorder also met lifetime DSM-5 criteria for bipolar disorder.

To elucidate the clinical consequences of the modification to the current DSM-5 criterion (A), we conducted a post hoc analysis of prospectively collected data on 907 bipolar outpatients from the Bipolar Collaborative Network (BCN).^{16,17} We sought to estimate the number of patients fulfilling criterion (A) for at least 1 hypomanic/manic episode according to DSM-IV and DSM-5 definitions throughout the patient's follow-up time in the study. We hypothesized that applying the stricter DSM-5 criterion (A) would lower the number of patients diagnosed with bipolar disorder. We investigated if any of the covariates measured could predict DSM-5 diagnosis. On the basis of visits, we compared the severity of manic symptoms between visits fulfilling DSM-5 criterion (A), visits fulfilling DSM-IV criterion (A) only, and visits fulfilling no criteria. Last, we explored the association between the individual manic symptoms available from the Young Mania Rating Scale¹⁸ (YMRS). Understanding the effect of adding increased energy or activity to the diagnostic criterion (A) is important for the future diagnosis of hypomanic/manic episodes and, consequently, bipolar disorder.

METHODS

Details on the methods and procedures used in the BCN are more fully described elsewhere.^{16,17} All patients provided written informed consent through procedures approved by their individual institutions before entering the multicenter study.

Sample

Clinical data were available on 907 subjects who volunteered for an observational follow-up study conducted from 1995 to 2002 in which their clinical characteristics and medications were prospectively assessed.^{19,20} Included in this study are only those patients enrolled in the observational follow-up study from the BCN; thus, subjects

that specific inclusion or exclusion criteria from those trials might alter the likelihood of co-occurrence of symptoms.¹⁹ At baseline, all diagnoses of bipolar disorder were validated using the Structured Clinical Interview for DSM-IV Axis I Disorders-Research Version.²¹ Diagnoses were based on the DSM-IV-TR²² criteria set and included bipolar I disorder (BD I), bipolar II disorder (BD II), bipolar disorder not otherwise specified (BD NOS), or schizoaffective disorderbipolar type (SA BD).

Procedures

Patients were seen monthly as part of their clinical care and for longitudinal evaluation of their course of illness, and ongoing medication changes were made based on need. At each visit, the 11-item YMRS¹⁸ and the 30-item Inventory of Depressive Symptomatology-Clinician-Rated Version (IDS-C)^{23,24} were administered to assess mania and depression symptoms, respectively. Both scales have been extensively validated.18,23,24

Patients were required to have at least 1 visit with a completed YMRS and IDS-C to be included in this study, as these were the basis of inclusion criteria.

Interrater reliability was regularly assessed across the 4 US and 2 non-US sites, and rater training was reinforced as needed to maintain consistent performance (k values were 0.7 for the YMRS and 0.85 for the IDS-C).¹⁹

Definitions

The clinician's rating on the distinct Items 1, 2 and 5 on the YMRS will allow an evaluation of the separate symptoms: mood, energy or activity, and irritability, respectively.

A score on Item 1 (mood) \geq 2 is considered reflective of objectively "elevated mood," Item 2 (energy/activity) ≥ 2 is considered objectively "increased energy or activity," and Item 5 (irritability) \geq 4 is considered objectively "increased irritability."18

Thus, study definition of fulfilling DSM-IV criterion (A) for a hypomanic/manic visit (the "DSM-IV-All group") was defined as Item $1 \ge 2$ and/or Item $5 \ge 4$, presumably adequate to meet the DSM-IV definition of criterion (A): "a distinct period of abnormally and persistently elevated, expansive [Item 1], or irritable mood [Item 5]."^{15(p332)} Study definition of DSM-5 criterion (A) for a hypomanic/manic visit (the "DSM-5 group") was defined as (Item $1 \ge 2$ and/or Item $5 \ge 4$) AND Item $2 \ge 2$, presumably adequate to meet the *DSM-5* definition of criterion (A): "a distinct episode of abnormally and persistently elevated, expansive [Item 1], or irritable mood [Item 5] AND persistently increased activity or energy [Item 2]."^{12(p124)} A No Symptoms group (reference group) was defined for visits fulfilling neither DSM-IV nor DSM-5 criterion (A). Finally, a DSM-IV-Only group was defined for visits fulfilling study-defined DSM-IV criterion (A) but lacking the DSM-5 criterion (A), which requires increased energy or activity.

Depressive symptoms were defined as an IDS-C score \geq 15 based on cut points of previous studies.^{19,20}

It is illegal to post this copyrighted PDF on any web Table 1. Demographic and Clinical Characteristics of Patients Fulfilling Criteria for at Least 1 Hypomanic/Manic Visit According to DSM-5, DSM-IV-Only, and DSM-IV-All Groups

	DSM-5 Group, ^a	DSM-IV-Only Group,b	DSM-IV-All Group Total, ^c	
Variable	n=342 (66%)	n=176 (34%)	n=518 (100%)	
Diagnosis, n (%)				
BD-I	273 (79.8)	129 (73.3)	402 (77.6)	
BD-II	59 (17.3)	39 (22.2)	98 (18.9)	
BD-NOS	2 (0.6)	2 (1.1)	4 (0.8)	
SA-BD	8 (2.3)	6 (3.4)	14 (2.7)	
Sex, n (%)				
Female	174 (50.9)	101 (57.4)	275 (53.1)	
Male	168 (49.1)	75 (42.6)	243 (46.9)	
Age, median (IQR), y	41.0 (34.0, 50.0)	39.0 (31.0, 49.5)	41.0 (33.0, 50.0)	
No. of visits contributed, median (IQR)	18.0 (9.0, 32.0)	9.0 (4.0, 20.5)	15.0 (7.0, 28.0)	
No. of visits with depressive symptoms, ^d median (IQR)	6.0 (3.0, 13.0)	4.0 (1.0, 8.0)	6.0 (2.0, 11.0)	
Modified YMRS score, ^e median (IQR)	2.3 (1.3, 3.7)	1.3 (1.0, 8.0)	2.0 (1.0, 3.4)	

^aSubjects with ≥ 1 visit fulfilling *DSM-5* criterion (A) for hypomania/mania. Fulfilling *DSM-5* criterion (A): scores for (Item 1 [mood] ≥ 2 and/or Item 5 [irritability] ≥ 4) AND Item 2 (energy/activity) ≥ 2 on the YMRS.

^bSubjects with no visits fulfilling DSM-5 criterion (A) for hypomania/mania. Fulfilling DSM-IV criterion (A) but NOT fulfilling DSM-5 criterion (A): scores for (Item 1 [mood] ≥ 2 and/or Item 5 [irritability] ≥ 4) AND Item 2 (energy/activity) < 2 on the YMRS.</p>
^cFulfilling DSM-IV criterion (A): scores for Item 1 (mood) ≥ 2 and/or Item 5 (irritability) ≥ 4 on the YMRS.

^dDepressive symptoms defined as an IDS-C score \geq 15.

^eMean YMRS score minus Items 1, 2, and 5 by patient (all visits).

Abbreviations: BD-I = bipolar I disorder, BD-II = bipolar II disorder, BD-NOS = bipolar disorder not otherwise specified, IDS-C = 30-item Inventory of Depressive Symptomatology–Clinician-Rated Version, IQR = interquartile range,

SA-BD = schizoaffective disorder-bipolar type, YMRS = Young Mania Rating Scale.

Statistical Analysis

A total of 14,306 study visits for the 907 patients were analyzed.

The mean modified YMRS score for each patient (ie, a mean of all their contributed visits) was calculated based on the total YMRS score (at each visit) minus Item 1, Item 2, and Item 5, since these items were used to define the outcome, ie, *DSM-IV* and *DSM-5* criterion (A).

Age information was missing for 1 male participant, which led to single imputation (median age = 40 years).

Multivariable logistic regression was used to investigate if any of the covariates were independently associated with the outcome. For these models, the outcome was defined as being *DSM-5*-diagnosed or not. Results from these models were presented unadjusted and adjusted for sex, age, number of visits contributed, number of visits with depressive symptoms, and mean modified YMRS score. Bonferroni correction was applied for multiple comparison correction.

To understand whether the associations were evident in particular diagnostic subgroups, we repeated the multivariable logistic regression, this time stratifying based on the type of bipolar disorder (BD I vs BD other, including BD II, BD NOS, and SA BD).

A separate analysis was performed using all visit data in contrast to individual patient data used in the prior models. We performed repeated measures analysis of longitudinal data on 14,306 visits. We compared the 3 diagnostic groups, *DSM-IV*–Only, *DSM-5*, and No Symptoms (based on visits), and their odds of experiencing elevated levels of the different YMRS items. The outcome was defined as the individual YMRS items dichotomized, defining a score of ≥ 2 as increased. For each analysis, we used the generalized linear mixed effects model, specifying each participant as random effect and the different diagnostic groups as fixed effect.

Last, we used the correlated mixed-distribution model by Tooze²⁵ to evaluate the association between individual items on the YMRS. We used this model because it is intended for zero-inflated, longitudinal, repeated-measures data. The occurrence-model from the correlated-mixed distribution model was used to investigate the odds of experiencing elevated levels of manic symptoms evaluated by the YMRS (dependent variable) for visits with any mood elevation above zero versus visits with no mood elevation. The analysis was repeated for irritability. The model was specified with mood and irritability as predictors, the different YMRS items as dependent variables, and a random intercept for each participant to account for multiple observations made on the same subject. All statistical analyses were performed using software programs (SAS University Edition version 9.4, SAS Institute, Cary, North Carolina; RStudio version 1.1.463, RStudio, Inc, Boston, Massachusetts).

RESULTS

Characterization of 907 Patients

We identified 907 outpatients (median age = 40; IQR, 33–49; 56% were women [n = 506]), including BD I (n = 680), BD II (n = 187), BD NOS (n = 18) or SA BD (n = 22). A total of 14,306 visits by the 907 patients were included in this study. Less than 0.03% of total visits from the original data set¹⁹ were excluded due to missing YMRS scores, which did not lead to exclusion of any subjects. Across a period of 7 years, the median follow-up time was 60 weeks (IQR, 15–138). The median number of visits contributed was 10 (IQR, 4–23).

DSM-IV and DSM-5 Criterion (A) (N = 907)

Of the 907 patients, 57% (n = 518) had at least 1 visit fulfilling the study-defined *DSM-IV* criterion (A) for a hypomanic/manic visit, ie, elevated, expansive, or irritable

Fredskild et al **It is illegal to post this copyrighted PDF** mood (the DSM-IV-All group). The remaining 43% YMRS score) are present

(n = 389) had no visits fulfilling the DSM-IV criterion (A) for a hypomanic/manic visit (the No Symptoms group).

We extracted the *DSM-IV*-All group (n = 518) and investigated how many had at least 1 visit fulfilling the studydefined *DSM-5* criterion (A) for a hypomanic/manic visit, ie, both a mood change and increased energy or activity. Among the 518 patients, 66% (n = 342) had at least 1 visit fulfilling *DSM-5* criterion (A) for a hypomanic/manic visit (the *DSM-5* group). Demographic and clinical characteristics (sex, age, type of bipolar disorder, number of visits contributed, number of visits with depressive symptoms, and mean

Table 2. Odds Ratios for Different Clinical Characteristics and Predicting *DSM-5* Diagnosis: Analyzing 518 Patients from Table 1

Variable	OR	95% CL	P Value	
Number of visits contributed				
Unadjusted	1.037	1.023, 1.051	<.0001	
Adjusted ^a	1.039	1.020, 1.057	<.0001*	
Mean modified YMRS ^b				
Unadjusted	1.115	1.024, 1.213	.0118	
Adjusted ^a	1.221	1.109, 1.344	<.0001*	
Number of visits with depressive				
symptoms ^c				
Unadjusted	1.064	1.034, 1.094	<.0001	
Adjusted ^a	1.034	0.998, 1.070	.06	
Age				
Unadjusted	1.012	0.996, 1.028	.15	
Adjusted ^a	1.005	0.988, 1.022	.57	
Sex				
Unadjusted	1.300	0.901, 1.875	.16	
Adjusted ^a	1.126	0.756, 1.676	.56	

^aIntercept for adjusted model = -1.14. Adjusted for number of visits contributed by each patient, mean modified YMRS scores for each patient over all their visits, number of visits with depressive symptoms for each patient, age, and sex. ROC area for adjusted model = 0.70.

^bMean YMRS scores without Item 1 (mood), Item 2 (energy/activity), and Item 5 (irritability).

^cDepressive symptoms defined as IDS-C score \geq 15.

*Reaching statistical significance after Bonferroni correction (P = .01).

Abbreviations: CL = confidence limit, IDS-C = 30-item Inventory of Depressive Symptomatology–Clinician-Rated Version, OR = odds ratio, ROC = receiver operating characteristic, YMRS = Young Mania Rating Scale. group, the *DSM-5* group, and the remaining group of 176 patients who fulfilled *DSM-IV* criteria but never had a visit that met the *DSM-5* criterion (A) (the *DSM-IV*-Only group).

Multivariable Logistic Regression of the *DSM-IV*-All Group (n = 518)

Evaluating the 518 *DSM-IV*–All patients from Table 1, we investigated if any of the covariates measured could predict *DSM-5* diagnosis of hypomania/mania criterion (A). The multivariable logistic regression analysis revealed that the mean modified YMRS score and number of visits contributed were statistically significant predictors of *DSM-5* diagnosis (Table 2). For every 1-unit increase in the mean modified YMRS score, the odds of *DSM-5* diagnosis increased by 22.1% (adjusted OR [95% CL] = 1.221 [1.109, 1.344]). For each visit contributed, the odds of *DSM-5* diagnosis increased by 3.9% (adjusted OR [95% CL] = 1.039 [1.020, 1.057]). There was no effect of sex and age.

Stratified Analysis of the DSM-IV-All Group (n = 518)

Stratification based on type of bipolar disorder (BD I vs BD other) revealed that the mean modified YMRS and the number of visits contributed remained statistically significant predictors of *DSM-5* diagnosis for the BD I patients after analysis adjustment and Bonferroni correction (number of visits contributed: OR [95% CL] = 1.036 [1.016, 1.056], P = .0004; mean modified YMRS: OR [95% CL] = 1.252 [1.114, 1.406], P = .0002). However, for the BD other group, none of the predictors remained statistically significantly associated with *DSM-5* diagnosis after adjustment.

Characterization of 14,306 Visits

Comparing elevated levels of manic symptoms among diagnostic groups. Using the 3 study-defined diagnostic groups (*DSM-IV*-Only, *DSM-5*, and No Symptoms) to separate the 14,306 visits, we compared the 3 groups' odds of experiencing elevated levels of the different manic symptoms

Table 3. Comparing the Odds of Experiencing Increased Levels of Manic Symptoms	
Between the Different Diagnostic Groups: Analyzing 14,306 Patient-Visits	
	-

DSM-IV-On No Symp		Only Group ^b vs nptoms (Ref) ^c	<i>DSM-</i> No Syn	<i>DSM-5</i> Group ^d vs No Symptoms (Ref) ^c		DSM-5 Group vs DSM-IV–Only Group	
YMRS Items ^a	OR	95% CL	OR	95% CL	OR	95% CL	
Item 3 (sexual interest)	6.80	5.33, 8.69	17.95	14.76, 21.81	2.64	2.03, 3.42	
Item 4 (sleep)	3.75	3.12, 4.52	10.32	8.85, 12.04	2.75	2.21, 3.42	
Item 6 (speech)	8.31	7.15, 9.65	42.81	35.09, 52.23	5.15	4.07, 6.53	
Item 7 (language-thought disorder)	4.89	4.05, 5.84	13.43	11.50, 15.69	2.76	2.23, 3.43	
Item 8 (content)	5.84	4.83, 7.07	13.33	11.33, 15.69	2.28	1.83, 2.84	
Item 9 (disruptive-aggressive behavior)	5.32	4.30, 6.58	10.95	9.16, 13.08	2.06	1.62, 2.62	
Item 10 (appearance)	3.90	2.41, 6.32	7.87	5.44, 11.38	2.02	1.19, 3.43	
Item 11 (insight)	7.99	4.71, 13.54	24.90	16.83, 36.84	3.12	1.89, 5.15	
Mean ^e	5.85		17.70		2.84		
Median ^e	5.58		13.38		2.70		

^aAll YMRS items (outcomes) are dichotomized at 2, defining a score \ge 2 as increased.

^bDSM-IV–Only Group: Fulfilling DSM-IV criterion (A) but not DSM-5 criterion (A), n = 793 visits.

^cNo Symptoms (reference group): Not fulfilling DSM-IV criterion (A) or DSM-5 criterion (A), n = 12,668 visits.

^dDSM-5 Group: Fulfilling DSM-5 criterion (A), n = 845 visits.

^eMean and median odds ratios across all 8 items evaluated (sexual interest, sleep, speech, language-thought disorder, content, disruptive-aggressive behavior, appearance, insight).

Abbreviations: CL = confidence limit, YMRS = Young Mania Rating Scale.

It is illegal to post this copyrighted PDF on any website Figure 1. Odds of Experiencing Elevated Levels of Different Manic Symptoms: 14,306 Patient-Visits Evaluated With YMRS



^aAny mood elevation defined as Item 1 > 0. No mood elevation defined as Item 1 = 0. Elevated levels of the different YMRS items defined as any score above 0. ^bAny irritability defined as Item 5 > 0. No irritability defined as Item 5 = 0. Elevated levels of the different YMRS items defined as any score above 0. Abbreviation: YMRS = Young Mania Rating Scale.

evaluated by the YMRS. Of the 14,306 visits, 845 visits (5.9%) met criteria for the *DSM-5* group, 793 visits (5.5%) for the *DSM-IV*-Only group, and 12,668 visits (88.6%) for the No Symptoms group (reference group). Presented in Table 3, both *DSM-IV*-Only and *DSM-5* visits increased the odds of experiencing elevated levels of all other manic symptoms when compared with the No Symptoms reference group. When comparing the *DSM-5* visits to the *DSM-IV*-Only visits, the *DSM-5* visits were associated with higher odds of experiencing elevated levels of all other manic symptoms (mean increase in odds across all YMRS items = 2.84) (Table 3).

Association Between Individual Hypomanic/Manic Symptoms in 14,306 Visits

Elevated mood. To analyze the association between mood (Item 1) and the additional manic symptoms evaluated by the YMRS, the correlated mixed distribution model was applied.

The odds of experiencing elevated levels of the additional manic symptoms evaluated by the YMRS were all statistically significantly increased if patients had elevated mood versus no mood elevation (Figure 1A). The highest odds ratio was associated with energy or activity. If patients had elevated mood, they were almost 8.65 times more likely to experience increased energy or activity compared with those with no mood elevation (OR [95% CL] = 8.65 [7.91, 9.47], P<.0001).

Irritability. The strongest association was observed between irritability (Item 5) and disruptive-aggressive behavior (OR [95% CL] = 2.42 [2.29, 2.56], P < .0001) (Figure 1B).

Sensitivity Analysis

Sensitivity analysis, analyzing visits by BD I and BD II separately, did not change the results of the association between mood and the additional manic symptoms evaluated by the YMRS, and it did not change the association between irritability and the manic symptoms.

DISCUSSION

We revealed 3 overall findings. First, of 518 patients who experienced at least 1 hypomanic/manic visit according to

It is illegal to post this copy criterion (A) *DSM-IV* definition, only 66% fulfilled the additional requirement of increased energy or activity for a *DSM-5* diagnosis of hypomania/mania (a 34% reduction). Second, fulfilling *DSM-5* criterion (A) increased the odds of experiencing elevated levels of all other manic symptoms evaluated by the YMRS, compared to fulfilling *DSM-IV* criterion (A) only. Third, among all manic symptoms (according to scores on the YMRS), increased energy or activity and mood elevation showed the strongest association.

The 34% reduction in the number of patients being diagnosed with a hypomanic/manic visit shows that the impact of applying *DSM-5* criterion (A) is substantial. Fewer hypomanic/manic episodes will be diagnosed by the stricter *DSM-5* criteria, but the episodes diagnosed are more severe. The stricter *DSM-5* criteria may, in general, prevent overdiagnosis of bipolar disorder but possibly at the cost of underdiagnosing hypomanic/manic episodes.

It is unknown whether the group of patients that no longer meets the stricter DSM-5 criterion (A) for a diagnosis of hypomania/mania (in our study, n = 176) would still be diagnosed in the mood disorder spectrum. The STEP-BD study¹³ suggested that a large percentage of patients who no longer met DSM-5 criteria for bipolar disorder met criteria for a major depressive episode with mixed features, which could have important clinical implications for their treatment course (mood stabilizers vs antidepressants or antipsychotics).

Interestingly, we found that for each additional visit contributed, the odds of being *DSM-5*–diagnosed increased by 3.9% (95% CL, 1.020, 1.057), showing that patients over time become more likely to get *DSM-5*–diagnosed, which is in concordance with findings from the UK Bipolar Disorder Research Network.¹⁴

Evaluating our cohort based on visits (n = 14,306), we found that visits fulfilling *DSM-5* criterion (A) had higher odds of experiencing elevated levels of all other manic symptoms compared with the *DSM-IV*-Only group. To our knowledge, our study is the first to definitively show that visits fulfilling *DSM-5* criteria are associated with more severe manic symptoms evaluated by YMRS.

The strongest individual association between symptoms was observed between mood elevation and increased energy or activity, supporting findings from the STEP-BD study.¹³ Other studies^{11,26} have even suggested that energy or activity may supersede mood as a cardinal, defining feature of mania.

Strengths and Limitations of the Study

Our study design has several strengths. Importantly, our cohort includes a large sample of well-characterized patients with bipolar disorder who were followed prospectively over 7 years. The multicenter study design and broad inclusion criteria help optimize generalizability. The use of standardized, validated rating scales for clinical assessments and the high interrater reliability across US and European sites furthermore improves internal and external validity of **anted PDF on any website**. findings. The diagnostic numbers we found based on visits were consistent with findings from the STEP-BD study,¹³ despite that the STEP-BD study used different rating scales for evaluating mood symptoms.

Our study also has limitations. Results presented in this study were collected prospectively (1995–2002) and subject to analysis post hoc. These data were not collected for the purpose of comparing *DSM-IV* and *DSM-5* criteria. However, this shortcoming may also be regarded as a strength since data were collected with no influence of the *DSM-5* definition of hypomania/mania.

The assessment of the *DSM-5* criterion (A) was based on YMRS scores, which served as proxies for evaluating mood states. The YMRS and also the IDS-C rating scales do not serve as diagnostic tools; however, they are reliable and valid measures of overall symptom severity and thus provide indirect approximates of the presence or absence of *DSM*-defined mood episodes in this study. Because of the different time frames of the symptom assessment for the YMRS (3 days) and IDS-C (7 days), we could not distinguish symptoms occurring simultaneously versus in close juxtaposition.

When more symptoms are required to diagnose hypomania/mania, one could anticipate a higher correlation with the remaining manic symptoms, as these symptoms are part of the same clinical phenomenon. Our analysis based on visits showed that visits fulfilling *DSM-5* vs *DSM-IV*-Only criteria were associated with higher levels of the different mania symptoms (YMRS). These results may possibly reflect that the bar is simply set higher for the *DSM-5* group. However, this association was not upheld when we applied different YMRS items instead of Item 2 (energy or activity) to test the diagnostic groups.

Finally, it should be noted that our sample includes patients from tertiary care, which limits generalizability to the general public, and that the role of comorbidities and medications were not evaluated but may influence mood as well as energy or activity.

To fully understand the impact of changing *DSM-5* criterion (A) for the diagnostic spectrum of mood disorders, further studies in large, generalizable samples are required.

CONCLUSIONS

In summary, little is known about how the modified *DSM-5* criterion (A), requiring increased energy or activity in addition to mood change, affects the diagnosis of hypomania/mania and, consequently, bipolar disorder. In a large sample of well-characterized bipolar outpatients who were followed for up to 7 years, we showed that applying *DSM-5* criteria reduced the number of patients being diagnosed with a hypomanic/manic visit by 34% but concomitantly predicted the visits with the most severe mania symptoms. In-depth understanding of the effect of the current modification to *DSM-5* criterion (A) possesses great importance for future diagnosis and treatment of bipolar disorder.

submitted: March 15, 2019; accepted May 22, 2019.

Published online: October 29, 2019. Author contributions: Ms Fredskild and Drs Mintz and Suppes had full access to all the Bipolar

Collaborative Network data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Potential conflicts of interest: Ms Fredskild was supported by a research scholarship (DARE fellowship) sponsored by the Lundbeck Foundation. Dr Suppes has in the past 36 months reported grants from National Institutes of Health, National Institute of Mental Health, National Institute on Drug Abuse, Palo Alto Health Sciences, Pathways Genomics, Stanley Medical Research Institute, VA Cooperative Studies Program, Merck, and VA OR&D PRIME Care; consulting fees from Allergan and Sunovion; honoraria from CMEology, Global Medical Education, and Medscape Education; royalties from Jones and Bartlett, Hogrefe Publishing, and Wolters Kluwer Health (UpToDate): and travel reimbursement from CMEology, Global Medication Education, and Sunovion. Dr Kessing has within the preceding 3 years been a consultant for Sunovion and Lundbeck, Dr Grunze, in the past 3 years, received grants/research support, consulting fees, or honoraria from GedeonRichter, Genericon, Janssen Cilag, Lundbeck, Otsuka, Pfizer, and Servier. Dr Post has spoken for AstraZeneka, Sunovion, Takeda, Validus, Pamlabs, and Janssen. Dr Frye, in the past 3 years, has received grant research support from Assurex Health, Mayo Foundation, Medibio; provided consultation for Mayo to Actify Neurotherapies, Allergan, Intra-Cellular Therapies, Janssen, Myriad, Neuralstem, Sunovian, Takeda, and Teva; received CME/travel reimbursement/ honoraria from American Physician Institute, CME Outfitters, and Global Academy for Medical Education. Dr Keck, in the past 3 years, has received consulting fees or honoraria from Otsuka/ Lundbeck, Janssen, and Sunovion; and receives royalties as Section Editor of Bipolar Disorders for UpToDate. Drs Kupka, Nolen, Mintz, and McElroy report no potential conflicts of interest.

Funding/support: Ms Fredskild was supported by the Danish American Research Exchange (DARE) fellowship, sponsored by the Lundbeck Foundation, for a research scholarship of 10 months at Stanford University (August 2018 to June 2019).

Role of the sponsor: The funding for the original data collection (1995–2002) was sponsored by the Stanley Foundation Medical Research Institute. The study sponsors had no role in the study design; collection, analysis, or interpretation of data; or writing of the report or the decision to submit for publication.

Acknowledgments: Gabriele S. Leverich, LCSW, National Institute of Mental Health (NIMH), Biological Psychiatric Branch, is acknowledged for her contribution to the Bipolar Collaborative Network. Ms Leverich reports no financial relationships with commercial interests. Dr Altshuler, who died in November 2015, is acknowledged for her contribution to the Bipolar Collaborative Network. Dr Altshuler was on an advisory board for Takeda and Lundbeck and attended an editorial board meeting sponsored by Sunovion; she received an honorarium as part of the 2014 Award for Research in Mood Disorders given by the American College of Psychiatrists; she performed a medical records review for the law offices of Hughes Socol Piers Resnick and Dym; and she was principal investigator and coinvestigator on research studies sponsored by NIMH.

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