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"EARLY DETECTION OF BIPOLAR DISORDERS AND TREATMENT RECOMMENDATIONS FOR HELP-SEEKING ADOLESCENTS AND YOUNG ADULTS: FINDINGS OF THE EARLY DETECTION AND INTERVENTION CENTER"

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ABSTRACT

Background: Bipolar disorder (BD) is a debilitating mental health condition, often undiagnosed for years, which significantly impacts individuals and society. Early detection is crucial for improving treatment outcomes and reducing disability.

Methods: This cross-sectional study involved 300 adolescents and young adults at a private hospital. Participants were assessed using standardized diagnostic procedures and early recognition instruments. Data collected included sociodemographic information, psychiatric history, substance use, and treatment history, analyzed through SPSS version 26.

Results: Among the participants, 70 were identified as at risk for or manifesting BD, while 230 were not. Significant differences were found in substance use, with higher rates of nicotine (40% vs. 26.96%), alcohol (30% vs. 20%), and cannabis (48.57% vs. 33.91%) in the at-risk group. Furthermore, 71.43% of the at-risk group were diagnosed with mood disorders compared to 38.26% in the not-at-risk group. A notable 17.14% of the at-risk group had a diagnosis of manic episodes/Bipolar affective disorder, absent in the not-at-risk group. Individuals at risk showed a greater prevalence of comorbidity and a higher history of psychiatric treatment.

Conclusion: The findings emphasize the importance of early detection and intervention for BD in adolescents and young adults. Identifying at-risk individuals and addressing their unique needs can enhance treatment efficacy and improve long-term outcomes. This study underscores the need for structured early detection programs within healthcare systems.

Keywords: Bipolar disorder, early detection, adolescents, treatment recommendations, mental health, comorbidity.

INTRODUCTION

Bipolar disorder (BD) is a complex mental health condition characterized by a spectrum of symptoms, including manic, hypomanic, depressive, mixed, and psychotic features. These symptoms can lead to chronically debilitating patterns that pose significant challenges for effective treatment. [1] According

to the World Health Organization Global Burden of Disease Study, BD ranks among the top ten causes of disability globally, affecting approximately 3 million individuals within the European Union alone. [2] The prevalence of BD is estimated to be between 1% and 3% of the population [3], highlighting its substantial impact on public health.

Despite the availability of effective therapeutic approaches, there remains a significant delay averaging six years between the onset of BD symptoms and the initiation of appropriate treatment [4, 5, 6] This treatment delay is critically associated with poorer functional outcomes, an increased risk of suicide, and diminished responses to mood-stabilizing medications. [7] Recent findings from early detection centers indicate that individuals at risk for developing BD often exhibit significantly impairing subsyndromal symptoms years prior to the full manifestation of the disorder [8, 2]. Therefore, early identification and timely intervention for at-risk individuals present promising opportunities to improve outcomes for those with BD. [9, 10]

Research indicates that BD is frequently preceded by precursor symptoms. [11, 12] However, identifying at-risk individuals is complicated due to the intricate nature of BD and its varied symptom presentations in adolescents and young adults. [7] A systematic review highlighted that a family history of BD is one of the most potent risk factors for developing the disorder, [13] although it lacks specificity as it may also predict other mental health conditions. [14] Other significant predictors include subsyndromal manic and depressive symptoms as well as mood swings prior to the onset of BD. [7]

Various additional risk factors have been identified, including characteristics of the first depressive episode that may heighten the risk of transitioning to BD such as increased suicidality and feelings of worthlessness. [15] Changes in sleep patterns and circadian rhythms, childhood anxiety, attention-deficit/hyperactivity disorder (ADHD), as well as personality traits like extraversion and novelty-seeking have also been implicated as potential risk factors for BD. [7]

Environmental influences such as stressful life events, substance abuse, and a history of antidepressant use further complicate the landscape of risk factors associated with BD. [7]

In response to this pressing need for early identification, several research groups have developed early detection instruments aimed at identifying young individuals at heightened risk for developing BD. Instruments such as EPIbipolar [16], BPSS-FP, and BARS criteria have shown promising psychometric properties in initial studies. [7] However, previous investigations into the early course and transition rates of BD have varied significantly in terms of methodology and sampling. An overview of prospective studies examining transition rates among help-seeking patients at youth mental health services or early detection centers reveals a critical gap in parallel application of these early detection instruments across diverse cohorts. [17, 18]

This study presents findings from the Early Detection and Intervention Center aims to addressing these gaps through systematic evaluation and treatment recommendations for help-seeking adolescents and young adults.

MATERIALS AND METHODS

The present study was a cross-sectional analysis conducted at a private hospital, involving a total of 230 participants. These participants were divided into two groups: those not at risk for and without manifest mania or bipolar disorder (N=230) and those at risk for or with manifest mania/bipolar disorder (N=70). Comprehensive assessments were performed by trained clinical psychologists and/or psychiatrists using a standardized, stepped diagnostic procedure. Patients were assessed by clinical psychologists and/or psychiatrists using a comprehensive standardized, stepped diagnostic procedure that included early recognition instruments when indicated. Treatment was based on the best available evidence, with recommendations potentially covering pharmacotherapy, psychotherapy,

sociotherapy, and additional specialized diagnostics. The individuals at risk for or with manifest mania or bipolar disorder involved a comprehensive approach. Initial assessments included collecting sociodemographic data such as age, gender, and education level, as well as documenting the reasons for seeking help. A detailed psychiatric history was obtained, covering family history, past treatment experiences, and substance use.

Structured clinical interviews using the German version of the Structured Clinical Interview for DSM-IV Axis I and II disorders were conducted by trained clinicians. Additionally, risk assessment tools like the Early Phase Inventory for Bipolar Disorders (EPIbipolar) and the Bipolar Prodrome Symptom Scale-Full Prospective (BPSS-FP) were utilized to evaluate subthreshold manic and depressive symptoms. Participants were diagnosed according to DSM-IV criteria. A follow-up procedure was implemented for individuals diagnosed with bipolar disorder or identified as at risk, potentially offering additional support or treatment recommendations. Quality assurance measures included regular training for clinicians to maintain consistency and reliability in diagnostic practices and assessments.

DATA ANALYSIS:

Statistical analyses included t-tests and chi-square tests to compare means and categorical data, respectively. Data were compiled using Microsoft Excel and analyzed with SPSS version 26 (IBM Corp., Armonk, NY). Quantitative data were presented as mean \pm standard deviation, while categorical data were summarized using frequencies and percentages. Chi-square tests were used for comparing categorical variables, and t-tests were employed for continuous variables, with p < 0.05 considered statistically significant.

RESULTS

Table-1: Distribution according to Age, Gender and Education

Age	Not at-risk for a Bipolar Disorde	manifest	or or mania/ Disorder	t-test	P-value	
	Mean	SD	Mean SD			
	24.01	6.3	24.3	4.7	0.356	0.72
Gender	No. of Cases	%	No. of Cases	%	Chi-Sq	P-value
Female	101	43.91%	40	57.14%	2.75	0.052
Male	129	56.09%	30	42.86%	3.75	
Education						
Studies not fnished (yet)	23	10.60%	5	7.94%		
9th or 10th grade	82	37.79%	19	30.16%		
a-level	80	36.87%	34	53.97% 6.3		0.17
University level	25	11.52%	4	6.35%		
No educational degree	7	3.23%	1	1.59%		

The analysis revealed no significant age difference between the not at-risk and at-risk/manifest mania groups (p = 0.72). Gender showed a trend towards significance (p = 0.052), with a higher proportion of females in the at-risk group. Educational attainment did not significantly differ between the groups (p = 0.17).

Table-2: Distribution according to First contact to the health care system for present symptoms

First contact to the health care system for present symptoms	Not at-risk for and no manifest mania/ Bipolar Disorder (N=230)		At-risk for or manifest mania/ Bipolar Disorder (N=70)		Chi-Sq	P- value
	No. of Cases	%	No. of Cases	%		
General practitioner or specialist physician	41	30.83 %	28	47.46 %		
Counselling center	24	18.05 %	9	15.25 %	<i>C</i> 200/	0.098
Early Recognition Center	66	49.62 %	20	33.90 %	6.28%	0.098
Other	2	1.50 %	2	3.39 %		

The analysis of first contact with the healthcare system revealed no significant difference between the not at-risk and at-risk/manifest mania groups (p = 0.098). A higher percentage of individuals in the at-risk group consulted a general practitioner or specialist (47.46% vs. 30.83%), while those not at-risk were more likely to contact an Early Recognition Center (49.62% vs. 33.90%). Contacts with counseling centers and other options were similar between the groups.

Table-3: Distribution according to Substance use

Not at-risk for and no manifest mania/ Bipolar Disorder (N=230)			At-risk for mania/ Bipo (N=70)	or manifest lar Disorder	Chi-Sq	P-value
	No. of Cases	%	No. of Cases	%		
Nicotine usea	62	26.96%	28	40.00%	12.84	0.0003
Alcohola	46	20.00%	21	30.00%	9.32	0.0023
Cannabis usea	78	33.91%	34	48.57%	17.28	< 0.0001
Amphetamine useb	24	10.43%	10	14.29%	5.76	0.016
Hallucinogen useb	14	6.09%	8	11.43%	1.63	0.2
Cocaine useb	11	4.78%	5	7.14%	2.25	0.13

The analysis of substance use revealed significant differences between the not at-risk and at-risk/manifest mania groups. The at-risk group had higher rates of nicotine (40.00% vs. 26.96%; p = 0.0003), alcohol (30.00% vs. 20.00%; p = 0.0023), cannabis (48.57% vs. 33.91%; p < 0.0001), and amphetamine use (14.29% vs. 10.43%; p = 0.016). No significant differences were found for hallucinogen (p = 0.2) and cocaine use (p = 0.13).

Table-4: Distribution according to Diagnoses according to DSM-IV (current or lifetime)

Diagnoses according to DSM-IV (current or lifetime)	Not at-risk manifest Bipolar (N=230)	for and no mania/ Disorder	At-risk for or manifest mania/ Bipolar Disorder (N=70)		Chi-Sq	P-value
	No. of Cases	%	No. of Cases	%		
Mental/behavioral dis. due to psychoactive substance use (F1x.x)	26	11.30%	12	17.14%	5.15	0.023

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Mental/behavioral dis. due to use of alcohol (F10.x)	10	4.35%	9	12.86%	0.05	0.81
Mental/behavioral dis. due to use of cannabis (F12.x)	10	4.35%	6	8.57%	1	0.31
Mood (Affective) Disorders (3x.x)	88	38.26%	50	71.43%	10.46	0.0012
Manic episode/Bipolar affective disorder (wo Hypomania) (F30.x-F31.x)	0	0.00%	12	17.14%	12	0.0005
Depressive episode (F32.x)	42	18.26%	13	18.57%	15.29	0.0001
Recurrent depressive disorder (F33.x)	40	17.39%	24	34.29%	4	0.045
Persistent mood (Affective) disorders (F34.x)	12	5.22%	3	4.29%	5.4	0.0201
Neurotic, stress-related and somatoform disorders (F4x.x)	69	30.00%	19	27.14%	28.4	< 0.0001
Phobic anxiety disorders and other anxiety disorders (F40.x-F41.x)	49	21.30%	14	20.00%	19.44	< 0.0001
Obsessive–compulsive disorder (F42.x)	8	3.48%	3	4.29%	2.27	0.13
Reaction to severe stress, adjustment disorder (F43.x)	12	5.22%	4	5.71%	4	0.045
Eating disorders (F50x)	4	1.74%	5	7.14%	0.11	0.73
Specifc, mixed & other personality disorders (F60.x-F61.x)	10	4.35%	4	5.71%	2.57	0.108
ADHD/ hyperkinetic disorderc (F90.x)	9	3.91%	7	10.00%	0.25	0.61

The analysis of DSM-IV diagnoses revealed significant differences between the not at-risk and at-risk/manifest mania groups. The at-risk group had higher rates of mental/behavioral disorders due to psychoactive substance use (17.14% vs. 11.30%; p = 0.023) and mood disorders (71.43% vs. 38.26%; p = 0.0012). Notably, manic episodes/bipolar affective disorder were present in 17.14% of the at-risk group, while absent in the not at-risk group (p = 0.0005). Higher rates of recurrent depressive disorder (34.29% vs. 17.39%; p = 0.045) were also found. Other disorders, such as neurotic and phobic anxiety disorders, were more prevalent in the not at-risk group.

Table-5: Distribution according to Comorbidity of above mentioned diagnoses and History of child psychiatric treatment

Comorbidity of above mentioned	Not at-risk for and no manifest mania/ Bipolar Disorder (N=230)		At-risk for or manifest mania/ Bipolar Disorder (N=70)		Chi-Sq	P-value
diagnoses	No. of Cases	%	No. of Cases	%		
0	81	35.22%	11	15.71 %		
1	101	43.91%	28	40.00 %	18.02	0.0001
2+	48	20.87%	31	44.29 %		
History of child psychiatric treatment	18	7.83%	11	15.71 %	1.68	0.19

The analysis of comorbidity of diagnoses revealed significant differences between the not at-risk and at-risk/manifest mania groups. A higher proportion of individuals in the not at-risk group had no comorbid conditions (35.22% vs. 15.71%; p = 0.0001), while the at-risk group exhibited a greater

prevalence of multiple diagnoses, with 44.29% having two or more comorbidities compared to 20.87% in the not-at-risk group. Additionally, the rates of history of child psychiatric treatment were higher in the at-risk group (15.71% vs. 7.83%), though this difference was not statistically significant (p = 0.19).

Table-6: Distribution according to History of psychiatric treatment/ medication treatment

	Not at-risk for and no manifest mania/ Bipolar Disorder (N=230)		At-risk for mania/ Disorder (N	or manifest Bipolar N=70)	Chi-Sq	P-value	
	No. of Cases	%	No. of Cases	%			
Outpatient	10	4.35%	5	7.14%	1.66	0.196	
Inpatient	8	3.48%	9	12.86%	0.05	0.808	
History of psychiatric treatment/ psychotherapy	93	40.43%	37	52.86%	24.12	< 0.0001	
Outpatient	78	33.91%	31	44.29%	20.26	< 0.0001	
Inpatient	52	22.61%	16	22.86%	19.05	< 0.0001	
History of medication treatment							
Antidepressant	49	21.30%	18	25.71%	14.34	0.0002	
Mood stabilizer	2	0.87%	2	2.86%	0	1	
Antipsychotic	32	13.91%	6	8.57%	17.78	< 0.0001	

The treatment history analysis indicates significant differences between the not at-risk and at-risk/manifest mania groups. A higher proportion of individuals in the at-risk group reported a history of psychiatric treatment or psychotherapy (52.86% vs. 40.43%; p < 0.0001), particularly in outpatient settings (44.29% vs. 33.91%; p < 0.0001). Additionally, the at-risk group had greater use of antidepressants (25.71% vs. 21.30%; p = 0.0002) but lower rates of antipsychotic medications (8.57% vs. 13.91%; p < 0.0001). Overall, these findings suggest a higher demand for psychiatric care among individuals at risk for or experiencing mania.

DISCUSSION

This analysis examined sociodemographic, clinical and psychopathological characteristics as well as treatment histories of help-seeking persons who were seen at the Early Detection. Based on the characteristics, differential at-risk groups for BD were compared and treatment recommendations analyzed. In a study comparing individuals not at risk for or without manifest mania/bipolar disorder (N=230) and those at risk for or with manifest mania/bipolar disorder (N=70), the mean age for both groups was similar (24.01 \pm 6.3 years vs. 24.3 \pm 4.7 years; t-test = 0.356, P = 0.72). Gender distribution showed a higher percentage of females in the at-risk group (57.14% vs. 43.91%), though the difference approached but did not reach statistical significance. Educational levels were also compared, with a notable proportion of those at risk having completed A-levels (53.97%) compared to those not at risk (36.87%), but no significant differences were found. These results were comparable to the study by Martini J. et al., [2] which included 582 patients. While age differences between the at-risk and nonat-risk groups for bipolar disorder (BD) were not significant, there was a significant difference in gender distribution, with more females in the at-risk group (57.0% vs. 44.9%, P = 0.011). Additionally, a significantly higher proportion of individuals at risk for BD had completed A-levels (55.6% vs. 37.5%, P = 0.008), indicating distinct demographic and educational patterns in the at-risk population.

Individuals at risk for or manifesting mania/bipolar disorder were more inclined to contact a general practitioner or specialist (47.46% vs. 30.83%), though this difference was not statistically significant (p = 0.098). In contrast, those not at risk demonstrated a higher tendency to engage with Early

Recognition Centers (49.62% vs. 33.90%). **Martini et al. [2]** reported that among 149 individuals at risk for or manifesting mania/bipolar disorder, the mean percentage of first contacts to healthcare providers revealed no significant differences between the two groups, with 37.1% of the at-risk group seeking help from general practitioners or specialists compared to 45.2% in the not-at-risk group (433) = 3.607, p = 0.307), highlighting a similar trend in help-seeking behavior across both studies.

The present study highlights significant implications for the healthcare system regarding the treatment of individuals at risk for or with manifest bipolar disorder (BD). Our findings indicate that these individuals exhibit notably higher rates of substance use, including nicotine (40.00% vs. 26.96%, P = 0.0003), alcohol (30.00% vs. 20.00%, P = 0.0023), and cannabis (48.57% vs. 33.91%, P < 0.0001). Furthermore, at-risk individuals also demonstrated increased amphetamine use (14.29% vs. 10.43%, P = 0.016), while differences in hallucinogen and cocaine use were not statistically significant. The finding of substance use among a significant proportion of at-risk patients and those diagnosed with manifest mania/bipolar disorder, particularly with cannabis and alcohol being the most frequently used substances, aligns with existing study study by **Brietzke et al., 2012**; **Goldstein et al., 2013**; **Leopold et al., 2012**; **van Meter et al., 2016**. [19-22] These results suggest an early onset of substance misuse or substance use disorders in individuals who later develop bipolar disorder **Beesdo-Baum et al., 2015**. [23] Additionally, patients with substance use disorders often demonstrate low utilization of mental health care services **Mack et al., 2014**. [24]

The present study analysis of DSM-IV diagnoses shows significant differences between individuals at risk for or with manifest bipolar disorder (BD) and those not at risk, reflecting findings from **Martini J. et al. [2]** In the present study, the at-risk group demonstrated higher rates of mental/behavioral disorders due to psychoactive substance use (17.14% vs. 11.30%, p = 0.023) and mood disorders (71.43% vs. 38.26%, p = 0.0012). Additionally, 17.14% of at-risk individuals met the criteria for manic episodes or bipolar affective disorder (p = 0.0005), while recurrent depressive disorder was more prevalent among the at-risk group (34.29% vs. 17.39%, p = 0.045). Similarly, **Martini J. et al. [2]** reported higher rates of mental/behavioral disorders due to psychoactive substance use (17.4% vs. 11.3%, p = 0.054) and alcohol use disorders (13.4% vs. 4.6%, p < 0.001). These findings emphasize the complex mental health challenges faced by those at risk for BD and underscore the need for targeted interventions.

The analysis of comorbidity shows that only 15.71% of individuals at risk for or with manifest bipolar disorder (BD) reported no comorbid diagnoses, compared to 35.22% in the non-at-risk group (P=0.001). Additionally, 44.29% of the at-risk group had two or more comorbid conditions, significantly higher than the 20.87% in the non-at-risk group. While 43.91% of non-at-risk individuals had one comorbid diagnosis, this was slightly lower at 40.00% for the at-risk group. Furthermore, 15.71% of at-risk individuals had a history of child psychiatric treatment, compared to 7.83% in the non-at-risk group, though this difference was not statistically significant (P=0.19). Anticonvulsants and other mood stabilizers may be especially helpful in treating BD patients with significant comorbidity. [25] The treatment history analysis indicates that individuals at risk for or with manifest bipolar disorder (BD) have significantly higher rates of psychiatric treatment (52.86% vs. 40.43%, P<0.0001) and outpatient treatment (44.29% vs. 33.91%, P<0.0001) compared to those not at risk. Additionally, 25.71% of the at-risk group received antidepressants, whereas 21.30% of the non-at-risk group did (P=0.0002). Conversely, antipsychotic use was more common in the non-at-risk group, reported by 13.91% compared to only 8.57% in the at-risk group (P<0.0001).

These findings underscore the increased assignation in psychiatric treatment among individuals at risk for BD, highlighting the necessity for targeted interventions. In comparison, a study by **Martini et al.** [2] found that 45.5% of individuals not at risk for and without manifest mania or BD had a history of psychiatric treatment or psychotherapy. This contrasts with 53.0% of individuals at risk for or with

manifest mania or BD (N = 149), further emphasizing the greater treatment engagement among those at risk

CONCLUSION

The findings of the present study highlight significant differences in demographics, substance use, psychiatric treatment history, and comorbidity between individuals at risk for or with manifest bipolar disorder (BD) and those not at risk. Notably, while there was no significant difference in age, a higher proportion of females was observed in the at-risk group. The at-risk individuals also exhibited higher rates of substance use, particularly for nicotine, alcohol, and cannabis. Additionally, they showed a greater engagement in psychiatric treatment, including psychotherapy and antidepressant use. The analysis of diagnoses revealed that mood disorders and comorbidities were more prevalent among the at-risk group, highlighting the complexity of their mental health needs. These results emphasize the importance of early identification and targeted interventions to support adolescents and young adults at risk for bipolar disorder.

REFERENCES

- Jeong JH, Bahk WM, Woo YS, Yoon BH, Lee JG, Kim W, Sohn I, Park SY, Shim SH, Seo JS, Choo IH, Yang CM, Jung MH, Jon DI, Kim MD. Korean Medication Algorithm Project for Bipolar Disorder 2022: Comparisons with Other Treatment Guidelines. Clin Psychopharmacol Neurosci. 2023 Feb 28;21(1):32-48. doi: 10.9758/cpn.2023.21.1.32. PMID: 36700310; PMCID: PMC9889890.
- 2. Martini J, Leopold K, Pfeiffer S, Berndt C, Boehme A, Roessner V, Fusar-Poli P, Young AH, Correll CU, Bauer M, Pfennig A. Early detection of bipolar disorders and treatment recommendations for help-seeking adolescents and young adults: Findings of the Early Detection and Intervention Center Dresden. Int J Bipolar Disord. 2021 Jul 2;9(1):23. doi: 10.1186/s40345-021-00227-3. PMID: 34215910; PMCID: PMC8253866.
- 3. Bauer M, Pfennig A. Epidemiology of bipolar disorders. Epilepsia. 2005;46 Suppl 4:8-13. doi: 10.1111/j.1528-1167.2005.463003.x. PMID: 15968806.
- 4. da Silva Lima AF, Cruz L, Cohen M, Zimmermann JJ, de Sousa Miguel SR. Cost-effectiveness of treatment for bipolar disorders. Mental health economics: The costs and benefits of psychiatric care. 2017:299-311.
- 5. Dagani J, Signorini G, Nielssen O, Bani M, Pastore A, Girolamo GD, Large M. Meta-analysis of the interval between the onset and management of bipolar disorder. The Canadian Journal of Psychiatry. 2017 Apr;62(4):247-58.
- 6. Pfennig A, Correll CU, Leopold K, Juckel G, Bauer M. Early recognition and intervention for bipolar disorders: state of research and perspectives. Der Nervenarzt. 2012 Jul;83:897-902.
- 7. Martini J, Bröckel KL, Leopold K, Berndt C, Sauer C, Maicher B, Juckel G, Krüger-Özgürdal S, Fallgatter AJ, Lambert M, Bechdolf A. Young people at risk for developing bipolar disorder: Two-year findings from the multicenter prospective, naturalistic Early-BipoLife study. European Neuropsychopharmacology. 2024 Jan 1;78:43-53.
- 8. Leopold K, Ratzer S, Correll CU, Rottmann-Wolf M, Pfeiffer S, Ritter P, Bauer M, Pfennig A. Characteristics, symptomatology and naturalistic treatment in individuals at-risk for bipolar disorders: baseline results in the first 180 help-seeking individuals assessed at the Dresden high-risk project. Journal of affective disorders. 2014 Jan 1;152:427-33.
- 9. Collins C, Copeland B, Croucher M. Bipolar affective disorder, type II, apparently precipitated by donepezil. International psychogeriatrics. 2011 Apr;23(3):503-4.
- 10. Forsman AK, Ventus DB, van der Feltz-Cornelis CM, Wahlbeck K. Public mental health research in Europe: a systematic mapping for the ROAMER project. The European Journal of Public Health. 2014 Dec 1;24(6):955-60.

- 11. Faedda GL, Baldessarini RJ, Marangoni C, Bechdolf A, Berk M, Birmaher B, Conus P, DelBello MP, Duffy AC, Hillegers MH, Pfennig A. An International Society of Bipolar Disorders task force report: Precursors and prodromes of bipolar disorder. Bipolar disorders. 2019 Dec;21(8):720-40.
- 12. Van Meter AR, Burke C, Youngstrom EA, Faedda GL, Correll CU. The bipolar prodrome: metaanalysis of symptom prevalence prior to initial or recurrent mood episodes. Journal of the American Academy of Child & Adolescent Psychiatry. 2016 Jul 1;55(7):543-55.
- 13. Scott J, Marwaha S, Ratheesh A, Macmillan I, Yung AR, Morriss R, Hickie IB, Bechdolf A. Bipolar at-risk criteria: an examination of which clinical features have optimal utility for identifying youth at risk of early transition from depression to bipolar disorders. Schizophrenia bulletin. 2017 Jul 1;43(4):737-44.
- 14. Vieta E, Salagre E, Grande I, Carvalho AF, Fernandes BS, Berk M, Birmaher B, Tohen M, Suppes T. Early intervention in bipolar disorder. American Journal of Psychiatry. 2018 May 1;175(5):411-26.
- 15. Pfennig A, Ritter PS, Höfler M, Lieb R, Bauer M, Wittchen HU, Beesdo-Baum K. Symptom characteristics of depressive episodes prior to the onset of mania or hypomania. Acta Psychiatrica Scandinavica. 2016 Mar;133(3):196-204.
- 16. Leopold K, Ritter P, Correll CU, Marx C, Özgürdal S, Juckel G, Bauer M, Pfennig A. Risk constellations prior to the development of bipolar disorders: rationale of a new risk assessment tool. Journal of affective disorders. 2012 Feb 1;136(3):1000-10.
- 17. Bechdolf A, Ratheesh A, J Wood S, Tecic T, Conus P, Nelson B, M Cotton S, M Chanen A, P Amminger G, Ruhrmann S, Schultze-Lutter F. Rationale and first results of developing at-risk (prodromal) criteria for bipolar disorder. Current pharmaceutical design. 2012 Feb 1;18(4):358-75.
- 18. Fusar-Poli P, De Micheli A, Rocchetti M, Cappucciati M, Ramella-Cravaro V, Rutigliano G, Bonoldi I, McGuire P, Falkenberg I. Semistructured interview for bipolar at risk states (SIBARS). Psychiatry research. 2018 Jun 1;264:302-9.
- 19. Brietzke E, Mansur RB, Soczynska JK, Kapczinski F, Bressan RA, McIntyre RS. Towards a multifactorial approach for prediction of bipolar disorder in at risk populations. Journal of affective disorders. 2012 Sep 1;140(1):82-91.
- 20. Goldstein BI, Strober M, Axelson D, Goldstein TR, Gill MK, Hower H, Dickstein D, Hunt J, Yen S, Kim E, Ha W. Predictors of first-onset substance use disorders during the prospective course of bipolar spectrum disorders in adolescents. Journal of the American Academy of Child & Adolescent Psychiatry. 2013 Oct 1;52(10):1026-37.
- 21. Leopold K, Ritter P, Correll CU, Marx C, Özgürdal S, Juckel G, Bauer M, Pfennig A. Risk constellations prior to the development of bipolar disorders: rationale of a new risk assessment tool. Journal of affective disorders. 2012 Feb 1;136(3):1000-10.
- 22. Van Meter AR, Burke C, Youngstrom EA, Faedda GL, Correll CU. The bipolar prodrome: metaanalysis of symptom prevalence prior to initial or recurrent mood episodes. Journal of the American Academy of Child & Adolescent Psychiatry. 2016 Jul 1;55(7):543-55.
- 23. Beesdo-Baum K, Knappe S, Asselmann E, Zimmermann P, Brückl T, Höfler M, Behrendt S, Lieb R, Wittchen HU. The 'Early Developmental Stages of Psychopathology (EDSP) study': a 20-year review of methods and findings. Social Psychiatry and Psychiatric Epidemiology. 2015 Jun;50:851-66.
- 24. Mack S, Jacobi F, Gerschler A, Strehle J, Höfler M, Busch MA, Maske UE, Hapke U, Seiffert I, Gaebel W, Zielasek J. Self-reported utilization of mental health services in the adult German population—evidence for unmet needs? Results of the DEGS1-Mental Health Module (DEGS1-MH). International journal of methods in psychiatric research. 2014 Sep;23(3):289-303.
- 25. Krishnan KR. Psychiatric and medical comorbidities of bipolar disorder. Psychosomatic medicine. 2005 Jan 1;67(1):1-8.