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Improving the Diagnosis of Mood Disorders: A Mini-Review of Recent Approaches

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Abstract

This mini-review summarizes information from eight recent (21st century) articles focused on the improvement of diagnoses for mood disorders. Authors of all articles recognized that a problem in diagnosis exists (**Table 1**) and made suggestions for improvements in existing systems (**Table 2**). Most of the research employed predictive analytical schemes and many of the proposed diagnostic symptoms were biological (**Table 3**). A model for success in diagnosis is applied to mood disorders. It is noted that an increase in diagnostic accuracy depends on both better identification of symptoms and better delineation of disorders.

Keywords

Mood Disorders, Diagnostic Issues, New Approaches

1. Introduction

Diagnostic systems such as the DSM family (e.g., DSM-5, American Psychiatric Association, 2013) and the ICD family (International Statistical Classification of Diseases, World Health Organization, 2004) are employed worldwide in the diagnosis of mood disorders. In DSM-5, there are two overarching categories of mood disorder (Bipolar and Depressive), each of which contains several specific disorders (e.g., Bipolar 1 and Cyclothymic Disorders in the first case and Major Depressive Disorder and Premenstrual Dysphoric Disorder in the second). One of the main benefits of diagnosing mental disorders is that appropriate treatments can be identified. DSM and ICD are based on sets of diagnostic classifications for disorders such as MDD (Major Depressive Disorder) and BD (Bipolar Disorder). Sets of diagnostic criteria accompany each classification. "Depressed mood" and "insomnia or hypersomnia", for example, are criteria for both Major Depressive

Disorder and the depressed phase of Bipolar 1 Disorder in DSM-5. The use of the DSM and ICD classification systems for the diagnosis of disorders in the professions of medicine, psychiatry, and psychology has led to wide-ranging congruence among diagnoses. This congruence did not exist (for example) in the early 1900s when the systems were not available. In spite of congruence, problems are still present in the diagnosis of mood disorders. Some problems reside in difficulties with differential diagnoses. It is challenging to distinguish one mood disorder from another, especially when the diagnoses reference overlapping symptoms. Difficulties also arise when professionals attempt to distinguish a disorder from a different class of disorder (e.g., a depressive disorder from an anxiety disorder). Another issue of concern is the fact that although the current DSM and ICD classifications for mood disorders overlap in some respects, they are not identical: diagnoses and the criteria employed to reach them differ between systems.

Researchers in the area of mood disorders have recognized the presence of problems in diagnosis (see **Table 1**), and are attempting to address them by improving diagnostic systems. This mini-review examines 21st century articles concerned with the diagnosis of mood disorders that were published in English between 2021 and the summer of 2025 (inclusive). The review describes various suggestions that researchers have offered for improving the manner in which mood disorders are diagnosed. It also addresses how success in diagnosis might be conceptualized, and what types of improvements promote greater success.

2. Selection of Articles for the Mini-Review

Articles were selected for inclusion in this mini-review with the help of Google Scholar®. A search was performed in August 2025 with the search phrase *diagnosis of mood disorders*. The publication date was set as 2021 or later. Articles were sorted according to relevance by a metric developed by Google®. This proprietary metric is influenced by the number of times an article was cited, and by the status of its source (journal) and author. It is entirely likely that past computer searches for an article also contribute to its relevance, but this was not stated explicitly. According to the Google® AI (8/13/2025), the metric was designed to imitate the manner in which scholars assign relevance to articles. Articles selected for study were those published in English that addressed the issue of diagnosis in mood disorders directly. Most of the articles focused either on identifying differences among mood disorders or on identifying the presence of a single mood disorder. Articles simply employing the extant diagnostic systems were excluded, as were articles comparing articles focused on treatment. This search procedure employed in this review might be biased: it represents what scholars employing Google® would discover, but it might miss articles accessible through other search engines.

The first 10 pages of the Google Scholar® search contained information for 100 articles. The 10th and 11th pages contained no candidates for inclusion. Eight articles matched the criteria for inclusion; they are listed in **Table 1**. Two additional articles were included in some discussions because they addressed the use of novel variables in the diagnosis of mood disorders. Six of the 10 articles were published in medical journals, three were published in psychiatric journals, and one was published in the *International Journal of Molecular Science*. Two or more authors were associated with each article. Authors of multiple articles were affiliated with institutions in Bulgaria, the Republic of Korea, and Thailand. Authors of one article apiece were affiliated with institutions in the US, UK, Poland, and China. Three of the articles were described as review articles.

3. Problems in the Diagnosis of Mood Disorders

The eight key articles covered in this mini-review are listed in **Table 1**. The order of their appearance in the table was determined by their relevance ranking at the time of sampling. Authors of all articles recognized the existence of problems in the diagnosis of mood disorders. These problems included the unreliability of the present diagnostic systems (DSM and/or ICD), difficulty in obtaining accurate differential diagnoses, the heterogeneity of symptoms, and disagreements among system users (**Table 1**).

Table 1. Issues in the diagnosis of mood disorders, as noted by the authors of each article.

First Author & Year	Issues in the Diagnosis of Mood Disorders
Maes and Stoyanov (2022)	The current understanding of major depressive disorder (MDD) and bipolar disorder (BD) is plagued by a cacophony of controversies, as evidenced by competing schools to understand MDD/BD. (Abstract)
Le-Niculescu et al. (2021)	Due to the lack of objective tests and the perceived presence of stigma, mood disorders are often underdiagnosed or misdiagnosed (depression instead of bipolar disorder). (Abstract)
Todeva-Radneva et al. (2021)	Major Depressive Disorder (MDD) and Bipolar Disorder (BD) have a high prevalence and detrimental socio-economic consequences for patients and the community. Furthermore, the depressive symptomatology of both disorders is essentially identical, thus rendering the clinical differential diagnosis between the two significantly more difficult considering the concomitant lack of objective biomarkers. (Abstract)
Song et al. (2024)	Differentiating between the diagnoses of mood disorders and other psychiatric disorders, and predicting treatment response in depression, has long been a concern for clinicians. (Abstract)
Zheng et al. (2024)	Mood disorders are characterized by great heterogeneity in clinical manifestation. (Abstract)
Tomasik et al. (2021)	The vast personal and economic burden of mood disorders is largely caused by their underdiagnosis and misdiagnosis, which is associated with ineffective treatment and worsening outcomes. (Abstract)
Maes et al. (2021)	Nevertheless, the case definitions of both MDD [Major Depression Disorder] and MDE [Major Depressive Episode] according to DSM (American Psychiatric Association, APA) and ICD (World Health Association, WHO) criteria are rather unreliable … (Introduction)
Kim et al. (2021)	Mood disorders are the most common mental disorders worldwide; they present difficulties in early detection, go undiagnosed in many cases, and have a poor prognosis (Abstract).

Note: These are exact quotations from each article, with the source appearing in brackets.

4. Purpose of the Articles, Variables, and Analytical Techniques

Having identified what they perceived were issues with the diagnosis of mood disorders, the authors proceeded to explain the purpose of their work and to outline how they planned to address these issues. Table 2 includes direct quotations from the eight key articles in which the authors describe their planned approach. In general, the purpose of each article was the offering of evidence that would lead to improvements in the diagnosis of mood disorders. Most articles pointed to the inclusion of symptoms beyond the traditional ones (from DSM and ICD). Novel variables and measurements (e.g., neuroimaging data, genetic data) and complex analytical techniques (e.g., Machine Learning, Convergent Functional Genomics) were employed in predictive schemes. Details of each approach are included in Table 3.

Table 2. The purpose of each article, as stated by the authors of the eight key articles.

First Author and Year	Purpose of the Article
(Maes & Stoyanov, 2022)	The aim of this review is to discuss the false dogmas that reign in current MDD/BD research with respect to the new data-driven, machine learning method to model psychiatric illness, namely nomothetic network psychiatry (NNP). (Abstract)
(Le-Niculescu et al., 2021)	We endeavored to use a similar [to their previous work] comprehensive approach to identify more definitive biomarkers for mood disorders that are transdiagnostic, by studying mood in psychiatric disorder patients. (Abstract)
(Todeva-Radneva et al., 2021)	Therefore, the aim of this review is to explore a more multidimensional framework in the scientific research of mood disorders, including epigenetic and neuroimaging data, in order to shape an outline for their translational capacity in clinical practice. (Abstract)
(Song et al. 2024)	This study will review the research on the use of ML techniques to differentiate diagnoses and predict treatment responses in mood disorders based on electroencephalography (EEG) data. (Abstract)
(Zheng et al., 2024)	Uncovering … heterogeneity [in clinical manifestation] using neuroimaging-based individual biomarkers, clinical behaviors, and genetic risks might contribute to elucidating the etiology of these diseases and supporting precision medicine. (Abstract)
(Tomasik et al., 2021)	Here, we aimed to develop a diagnostic algorithm, based on an online questionnaire and blood biomarker data, to reduce the misdiagnosis of bipolar disorder (BD) as major depressive disorder (MDD). (Abstract)
(Maes et al., 2021)	The aim of the current paper is to explain how machine learning techniques can be used to a) construct a model that ensembles risk/resilience (R/R), adverse outcome pathways (AOPs), staging, and the phenome of mood disorders, and b) disclose new classes based on these feature sets. (Abstract)
(Kim et al., 2021)	In this study, we explore the MMPI-2's effectiveness in screening for mood disorders and whether it can be improved through ML techniques with predictive efficiency. (Introduction)

Notes: These are exact quotations from each article, with the source indicated within brackets. 1 Nomothetic Network Psychiatry is an approach that relies on machine learning and develops causal models for psychiatric disorders.

Predictive schemes were central to most of the articles in Table 3. In these schemes, the main criteria were either the presence of a mood disorder or the distinction of one mood disorder from another. Predictors employed in different articles included metabolic information, genetic information, brain structure and activity, blood biometric markers, information related to inflammation, and standardized questionnaires. In general, authors supported the employment of complex diagnostic systems that included variables of different types. Although questionnaires and interviews were employed in several articles, the novel aspects of the approaches discussed were generally biological. The combination of different kinds of predictors is in the spirit of the NIMH Research Domain Criteria approach (Insel et al., 2010), where mental disorders are assumed to be caused by brain functions and to involve a complex set of actions that are assessed for diagnosis in a multidimensional manner (Maes & Stoyanov, 2022). The Research Domain Criteria approach relies heavily on data, and valorizes the collection of it from different situations: this approach is quantitative in nature while the symptom-based diagnostic approaches tends to be qualitative. Authors either reported, reviewed, or foresaw success in the use of their predictors in the diagnosis of mood disorders. Success was defined as improvement rather than perfection in diagnostic accuracy.

Table 3. The main analytical and predictive techniques employed and the focus variables for the eight key articles and two subsidiary articles.

First Author & Year	Analytical & Predictive Techniques	Variables (Measurements) and Their Role in the Article
(Maes & Stoyanov, 2022)	Discussion Article: Supports use of Nomothetic Network Psychiatric Model	Suggested Predictors: ROI (recurrence of illness), the most important predictor that mediates others, e.g., nitro-oxidative stress pathways, early lifetime trauma. Suggested Criteria: Phenome (expression) of mood Disorder
(Le-Niculescu et al., 2021)	Convergent Functional Genomics (Bayesian technique) 1	Predictors: Blood biomarkers Criteria: Depression Scales Mood State
(Todeva-Radneva et al., 2021)	Review of Predictive Value	Predictors: Non-coding RNAs fMRI Data MRS Data (magnetic resonance spectroscopy) Criteria: Major Depressive Disorder Bipolar Disorder
(Song et al., 2024)	Review of Machine Learning	Predictors: EEG data Criteria: Diagnosis Response to Treatment
(Zheng et al., 2024)	Quantile Normative Modeling Maturational Curves Hierarchical Clustering	T1 MRI imaging data Grey Matter Volume Clinical symptoms Neurocognitive assessments Genetic information
(Tomasik et al., 2021)	Machine Learning - Trained Diagnostic Algorithm	Predictors: PHQ-9 (Patient Health Questionnaire) Purpose-built questionnaire Blood Measures (biomarkers) World Mental Health Composite International Diagnostic Interview Criterion: MDD versus BD
(Maes et al., 2021)	Pathway analysis Model Involving Risk-Resilience, Adverse Outcome Pathways: Phenome	Predictors: Measures related to the PON1 gene Early lifetime trauma Criteria: HDL-PON1 complex Reactive oxygen and nitrogen species Nitro-oxidative stress toxicity Staging (#episodes) Phenome (test scores)
(Kim et al., 2021)	Machine learning Discriminant Analysis Random Forest Classification	Predictors: MMPI-2-RF PHQ-9 (Patient Health Questionnaire) MDQ (Mood Disorder Questionnaire) Criteria: Diagnosis
(Lee et al., 2023)	Random Forest Algorithm	Predictors: Direct measures taken by smart phones and devices (related to circadian rhythms) Questions Criteria: Phenotype (episodes of mania, Hypomania, and Depression)
(Sakrajda & Szcze-pankiewicz, 2021)	Review Article	Predictors: Inflammation Microglia activation Energy metabolism Criteria: Mood disorders

Notes: 1 Convergent Functional Genomics employs Bayesian statistics to build a model of genetics (to identify genes) based on data from both humans and animals. 2 These two articles are subsidiary articles, which did not meet the criteria for inclusion in the mini-review but demonstrated novel diagnostic approaches.

Authors discussed why they selected various criteria for inclusion in their diagnostic schemes. For example, Lee et al. (2023) mentioned the importance of circadian rhythms and their relationship to sleep disturbance in mood disorders: these authors represented some of their diagnostic measures as reflections of day-night cycles. Song et al. (2024) noted that EEG recordings could be employed to diagnose mood disorders because these recordings are sensitive to neurocognitive function and alterations in neurotransmission that accompany such disorders. Valid additions to the list of symptoms employed in the diagnosis of mood disorders might be related to the causes of these disorders, or to their effects. The only real requirement for the inclusion of a symptom in a diagnostic scheme is that the symptom should increase success in diagnosis.

5. The Definition of Success in Diagnosis

	Disorder X is Present	**Disorder X is Absent**
Disorder X is Diagnosed	Outcome 1: Success (Sensitivity)	Outcome 2: Failure
Disorder X is Not Diagnosed	Outcome 3: Failure	Outcome 4: Success (Specificity)

Figure 1. Model of diagnostic success and failure.

Figure 1 depicts a model that quantifies diagnostic success. In the figure, there are two possible states for a disorder, X. It is either present or absent in individual cases. There are two possible predictions (diagnoses) provided by the presence of symptom Y (or set of symptoms Y). The symptoms predict either that the disorder is present or that it is absent. The crossing of these two sets of categories results in four possible outcomes, two of which represent success and two failure. Success is defined as a congruence between the disorder X and the diagnosis predicted by symptoms Y. If the symptoms suggest a disorder should be present and it is present (Outcome 1), this registers as a success. If the symptoms suggest that a disorder should not be present and it is not present (Outcome 4), the diagnostic scheme again registers a success. The two failures involve predicting the presence of a disorder when it is absent and predicting the absence of a disorder when it is present. A diagnostic tool or system shows sensitivity when the proportion of Outcome 1 in the top row is high, and it shows specificity when the proportion of Outcome 4 in the second row is high.

For example, if the disorder being diagnosed were Major Depressive Disorder (X) and the symptom used to predict this disorder was sleep disturbance (insomnia or hypersomnia, Y), then the symptom would be considered 100% successful if sleep disturbance were present in all cases of Major Depressive Disorder and absent in all other cases. This is unlikely to be true. Sleep disturbance not only characterizes more than one mood disorder but also appears in criterion lists for other types of disorders (e.g., Generalized Anxiety Disorder, DSM-5). This symptom is also present in medical disorders with no associated mental disorder. Sleep disturbance alone would be a very poor predictor of a Major Depressive Disorder.

Improvements in diagnostic success involve improvements in both sensitivity and specificity. Practitioners need to know when a disorder is present and when it is not present. Most of the key articles studied in this mini-review addressed the improvement and expansion of sets of diagnostic symptoms. They attempted to improve the rows in **Figure 1**. However, researchers should also focus on the problem of an accurately defined diagnostic category. There is a need for improvement in the definition of the columns of **Figure 1**. Maes and Stoyanov (2022), for example, conclude both that the use of ROI (Return of Illness) would contribute to better prediction of mood disorders, and that the definition of mood disorders embodied in present systems is invalid. The first of these improvements focuses on better data for defining rows and the second on better data for defining columns (**Figure 1**). According to Maes and Stoyanov, "The DSM/ICD classifications of mood disorders are not only unreliable but their dogma-like nature prevents inductive (as top-down) and deductive (as incontrovertible) remodeling of the case-definitions" (Maes & Stoyanov, 2022, Conclusions). If the diagnosis one were trying to predict were "not a thing" (i.e., if it were invalid), then prediction would be doomed at the outset. It could never be better than random.

Improvements in diagnostic success should be directed both at the rows of **Figure 1** (better diagnostic testing) and at its columns (greater accuracy in the definition of individual disorders). A more accurate assessment of symptoms leads to a better understanding of the character of a disorder. The converse is also true. A better understanding of the disorder being diagnosed leads to the employment of a more accurate set of symptoms. The DSM manuals, for example, show evidence of both column-wise improvement (with the refinement of diagnoses, the exclusion of some diagnoses, and the introduction of others) and row-wise improvement (with the development of better lists of symptoms or criteria) across editions.

6. Application to Practice

Can practitioners draw any immediate pragmatic inferences from the articles reviewed here and apply them directly to the improvement of their own diagnostic activities? Probably not. There is little information that practitioners can apply directly to their own work, primarily because many of the improved diagnostic measures suggested (e.g., genetic information, fMRI) are costly and difficult to obtain, and secondarily because the addition of these new measures, while it increases diagnostic success somewhat, does not perfect it. Additionally, practitioners are not free to make revisions in the diagnostic categories of existing and widely used systems such as DSM and ICD. The authors of the articles studied here are not offering a fully developed system of diagnosis; rather, they are pointing the way to what such a system might be employed in the future. In order for the diagnostic symptoms covered in the reviewed articles to be of practical use, they would have to be widely studied, and their reliability and validity would have to be established in different situations. Furthermore, they would have to be systematized in some way so that practitioners could take advantage of them.

7. Conclusion

This mini-review examined articles addressing issues in the diagnosis of mood disorders. Eight such articles and two subsidiary articles were examined in terms of (a) their recognition that a problem in the diagnosis of mood disorders exists and (b) their plan or suggestion for improvements in diagnostic success. Several symptoms of different kinds were proposed on the assumption that they would lead to improvements in the diagnosis of mood disorders. Most authors employed predictive schemes in their research, with diagnosis as the criterion. Cutting-edge predictive techniques were employed, with a strong focus on machine learning. In very rough terms, a machine learning (ML) program takes both symptoms and diagnoses as input, proposes a predictive scheme, receives automated feedback as to the accuracy of the scheme, and improves prediction based on feedback, all without human intervention. Authors criticized the present state of diagnosis and noted that improvements were needed in defining disorders as well as in identifying symptoms.

There is a common two-part meme recognized by most graduate students defending their dissertations. This is the meme that "more participants (or more data) would improve the research" and "longitudinal studies would improve the research". This meme is trite but true. More studies on the diagnosis of mood disorders need to be conducted in different settings around the world to ensure generalizability of symptoms. Additionally, longitudinal studies would provide strong evidence of success in prediction. The ability to see a symptom today and predict a problem tomorrow (or next year) would make it easier for practitioners to both recognize and treat disorders.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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