Review Article

Reasons for diagnostic delays in Bipolar Disorder: Systematic review and narrative synthesis

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Background: Bipolar disorder is common, affecting 1% of people. The diagnosis of bipolar disorder is often delayed, which limits access to effective treatment and increases the burden of disease on individuals, families, and society.

Aim: This paper investigates the individual, social, and clinical factors that contribute to delays in diagnosis for people with bipolar disorder, including delays that occur before and after a person presents to a primary care clinician.

Design and setting: Systematic review and narrative synthesis.

Method: Four electronic databases - Embase, Medline, PsychInfo, and Global Health - were systematically searched. This search yielded 3078 studies, 21 of which met the inclusion criteria. The data retrieved were analysed using Braun and Clarke's Thematic Analysis to report a summary of recent research on the delays in the diagnosis of bipolar disorder.

Results: Analysis of the data from the 21 studies identified five main themes as reasons for delays in diagnosis: (1) misdiagnosis, (2) healthcare challenges, (3) mental health stigma, (4) the complex nature of bipolar disorder, and (5) individual factors.

Conclusions: The review demonstrates the importance of educating individuals, families, and clinicians on the symptomatology of bipolar disorder to avoid misdiagnosis. Furthermore, changes in the accessibility and delivery of mental health services are essential to ensure that people with bipolar disorder are diagnosed and treated in a timely manner. In addition, mental health stigma among individuals, families, and clinicians must be addressed to reduce diagnostic delays.

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How this fits in:

- This is the first known systematic review to systematically describe reasons for delays in the diagnosis of bipolar disorder (BD). It found that there are personal, social, and clinical explanations for these delays.
- Social reasons include mental health stigma; personal reasons include demographic factors (e.g., age and socioeconomic status), help-seeking behaviours, and people's knowledge. Clinical reasons include the complexity of BD, the high rate of misdiagnosis, and challenges faced in accessing services.
- Future research should be focused on assessing the health care pathways for diagnosing BD in primary care.

Introduction

Bipolar disorder (BD) is a common illness, affecting 1% of people. It is a lifelong mental illness characterised by recurrent episodes of depression and (hypo)mania.[1] Approximately 60% of people with BD present with symptoms before the age of 21, which disrupts normal development and psychosocial functioning, increasing their risk of suicide, substance misuse disorder, and behavioural difficulties.[2][3]

If BD is left untreated, it can have a negative impact on an individual's well-being – leading to impaired social, occupational, and cognitive functioning, decreased quality of life, danger to self and

others, and increased mortality.[4] Delayed diagnosis can impact the recurrence of mood disturbances, which can worsen an individual's psychological well-being.[5] The misdiagnosis of BD can lead to improper treatment, worsened symptoms, and an increased risk of hospitalisation.[6] In addition, delayed treatment leads to an increase in health care costs due to higher rates of hospitalisation and increased suicide attempts.[7][8] However, when the right treatment is offered, it can help individuals minimise the burden of the illness and function better in society.[9]

To date, there has been limited research addressing the reasons for delays in the diagnosis of people with BD. To our knowledge, no systematic review has been conducted to systematically report reasons for these delays. In this study, we aimed to report the reasons for the delays in the diagnosis of BD and to explore these delays before and after a person presents to primary care, as well as the individual, social, and clinical factors associated with these delays.

Methods

MEDLINE Complete was searched from 1964 to June 2022; Embase Excerpta Medica was searched from 1972 to June 2022; PsycINFO was searched from 1967 to June 2022; and Global Health was searched from 1973 to June 2022. Database searches were conducted by the primary and secondary reviewers on 9th June 2022. Authors searched their own personal libraries. The review protocol was registered with PROSPERO (CRD42022313495).[10]

Inclusion and Exclusion Criteria

Inclusion criteria consisted of qualitative and quantitative studies (original peer-reviewed manuscripts describing research) including participants with BD and those who had experienced a delay in their diagnosis. BD was defined by clinical diagnosis following the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) or the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5)[11][12]. Table 1 details the full list of the inclusion and exclusion criteria.

Inclusion criteria
Studies were considered for the review if they met the following criteria: • Peer reviewed published studies from journals • Studies of all dates • Studies of all languages • Humans of all ages • No geographical restrictions • Quantitative methodologies reporting original data such as: randomised controlled trial, non-randomised controlled trial, cohort, case-control, cross-sectional, case-series and chart review studies • Qualitative methodologies reporting original data such as: in-depth interviews, focus groups, one-to-one interviews, ethnographic research, case studies and record keeping • Participants who have a diagnosis of BD • Participants who have experienced a delay in their diagnosis of BD
Exclusion criteria
Studies were excluded if they met the following criteria: • Studies that do not focus on BD • Letters to journals, editorials, or opinion pieces • Not reporting original empirical data • Unpublished / grey literature • Duplicate studies that report data on a similar study population • Studies not written in English

Table 1. Inclusion and exclusion criteria

Search Strategy

The search strategy was developed using key terms that were built around the three main concepts: BD, delays, and diagnosis. The formation of the search terms was influenced by previous search strategies used by a systematic review that focused on BD and provided guidance on which key terms would provide relevant information for the review.[13] The database searches for Embase can be found in Supplementary Table S1. Following the search, eligible studies were transferred to EndNote (version 20.3) and de-duplicated. These libraries were then reviewed for relevant studies and information. The PRISMA flow diagram for studies selected is illustrated in Figure 1.
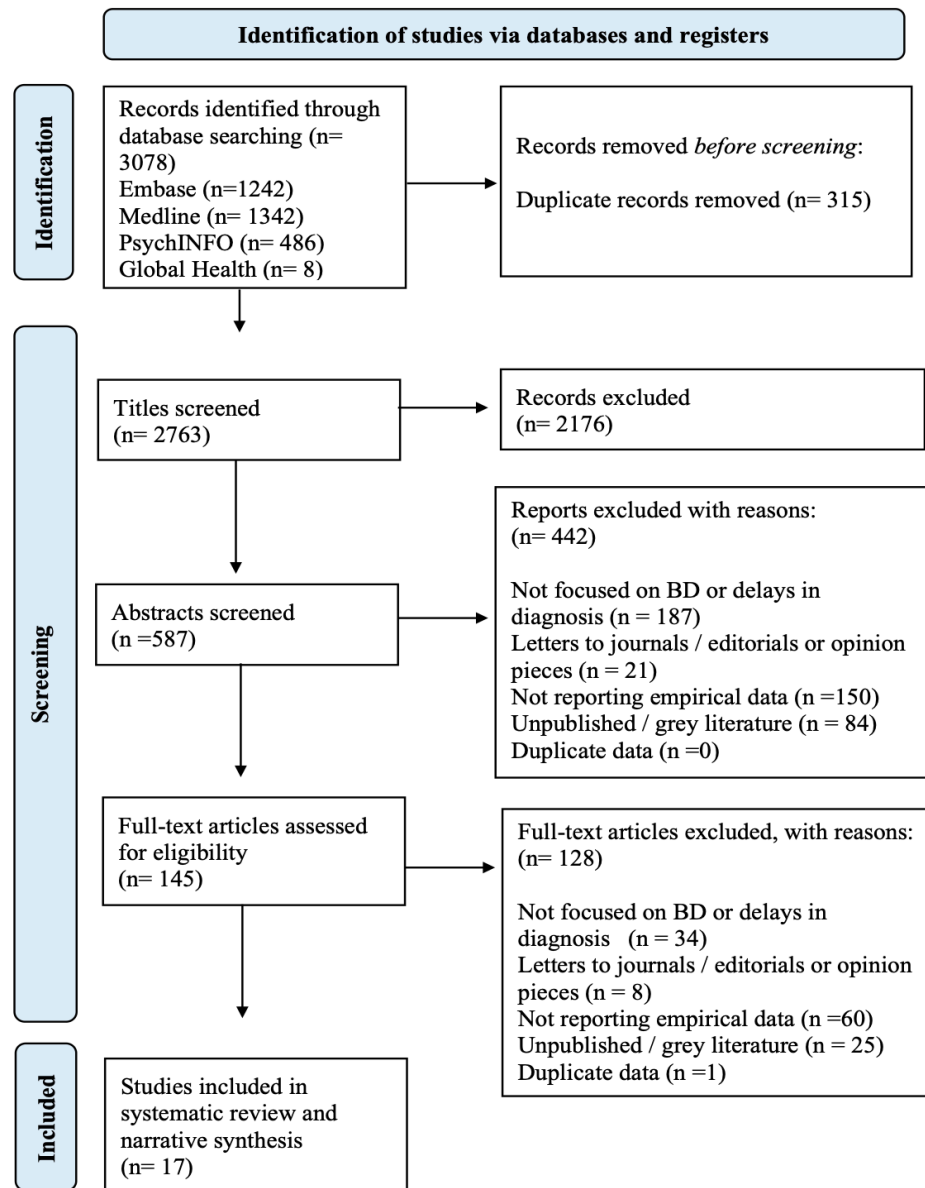
Figure 1. PRISMA flowchart

Study Selection and Data Extraction

The titles and abstracts of each study were analysed by a master's student for inclusion (NM), and a second master's student (VA) reviewed 5% of the titles and abstracts of the studies. Following this, both reviewers reviewed the full text of the remaining studies. It was decided that disagreements about which studies met the inclusion criteria should be resolved by consensus or, if necessary, with the assistance of a third author (VP). In addition, a forward and backward citation search was performed using Connected Papers.[14]

Quality appraisal

The full-text manuscripts of the selected quantitative studies were assessed using the National Institute of Health (NIH) assessment tools. The two assessment tools used were: The Quality Assessment of Case Series Studies and The Quality Assessment of Cohort and Cross-sectional Observational Studies.[15] Whereas the selected qualitative studies were assessed using the Critical Appraisal Skills Programme Tool.[16] Due to the scarcity of the studies discussed in this review, it was

concluded that studies would not be excluded based on their quality assessment. Although from the assessment, none of the studies were identified as being low in quality.

Data synthesis

The data were synthesised to report the similarities and differences between studies, the observation of relationships within the data, and the strength of the findings. A thematic methodology was used to become familiar with the data extracted from the studies and to search, review, and define themes that report on the reasons for delays in the diagnosis of BD.[17] Due to the methodological and clinical diversity (e.g., heterogeneity in the participants) of the included studies, meta-analysis was not possible.

Results

Database searches retrieved 3,078 studies. Following de-duplication and title and abstract screening, 145 studies were assessed in full text for eligibility. Four additional studies were identified in the co-authors' library, and no new studies were observed in the forward and backward citation searches, leading to a final total of 21 included publications (Figure 1).

Characteristics of included studies

The included publications consisted of 21 original studies, using qualitative (n=3), quantitative (n=17), and mixed method designs (n=1). The research was conducted in the United States (n=4), the United Kingdom (n=2), Canada (n=1), Australia (n=3), Hungary (n=1), Sweden (n=1), Spain (n=1), Singapore (n=1), Vietnam (n=1), South Korea (n=1), Brazil (n=1), Germany (n=1), Japan (n=1), Morocco (n=1), and Chile (n=1). Studies were published between 2004 and 2022. Supplementary Table S2 summarises the included publications.

Common themes identified

In this review, there were patterns in the findings throughout the included studies that may explain the causes of delays in the diagnosis of BD, which have been translated into themes. The topics have been divided into five primary themes, each of which has been further subdivided into subthemes. Supplementary Table S3 illustrates the generation of initial codes, and Table 2 presents the identified themes.

Themes	Misdiagnosis	Healthcare Challenges	Mental Health Stigma	Complex nature of Bipolar Disorder	Individual factors
Subthemes	Diagnostic tool limitations	Poor continuity of care	Societal attitudes towards mental illness	Comorbidities	Personal demographics
	Misdiangosed with another psychiatric disorder	Accesability issues	Strugllling to accept a diagnosis	Depressive polarity	Help-seeking behaviour
	Incorrect treatment given	Role of clincian			Lack of knowledge

Table 2. Themes and subthemes

Misdiagnosis

There were 18 papers that suggested that the misdiagnosis of BD occurred due to diagnostic tool limitations, patients being misdiagnosed with another psychiatric disorder, and patients receiving an incorrect treatment.[18][19][20][21][22][23][24][25][26][27][28][29][30][31][32][33][34][35] The studies convey

how the DSM-5 criteria have inherent restrictions, which require the existence of manic and hypomanic episodes – leading to a misdiagnosis of major depressive disorder (MDD) for individuals only presenting with depressive symptoms.[19][21][22] It is reported that the most common misdiagnoses given were schizoaffective disorder, ADHD, unipolar depression, and/or psychosis.[26][28][32] Furthermore, the administration of drugs that may potentially induce mania can lead to misdiagnosis and further delays.[24][26][27]

Healthcare challenges

It was highlighted by 11 of the studies that BD patients may face challenges in accessing mental health treatments. In addition, they are not being seen by competent mental health clinicians and are experiencing poor continuity of care.[18][19][20][36][27][28][29][30][31][33][35] It was reported that troubles in finding a suitable clinician resulted in long waiting times to be seen and in being provided with limited treatments.[29][30] Moreover, it was conveyed how patients felt that clinicians were unable to make a specific diagnosis or lacked the skills to treat their condition and did not take their concerns seriously.[28][29] Along with the inability to establish stable long-term care relationships due to the constant rotation of psychiatrists in the public system.[32]

Mental health stigma

Across eight studies, it was suggested that societal attitudes towards mental illness and the inability of individuals to accept their diagnosis led to diagnostic delays.[22][23][31][32][33][37][35][38] Stigma was shown to act as a barrier for individuals to seek help from mental health services; patients expressed that the fear associated with mental health stigma discouraged them from seeking a diagnosis.[22][23] Moreover, patients would struggle to accept their diagnosis as their symptoms were different from the stereotypical ideas about what BD is.33

Complex nature of BD

Among 12 studies, it was explained that the presence of comorbidities and patients having a depressive polarity increased diagnostic delays.[18][19][21][39][22][25][26][27][28][32][37][35] The greatest delays were seen in individuals with high rates of comorbidities due to BD symptoms overlapping with psychiatric disorders such as ADHD, anxiety, substance use disorders, and primary psychotic disorders.[19][39][26][27][28] Moreover, patients presenting with first depressive episodes, with no history or prominent symptoms of mania or hypomania, were more likely to be misdiagnosed with MDD.[22]

Individual factors

Across 14 of the studies, personal demographics, patients' help-seeking behaviours, and lack of knowledge were shown to contribute to greater diagnostic delays.[19][36][21][39][23][24][26][27][28][29][30][31][33][34] The studies demonstrated that socioeconomic status was linked with delays in seeking help as patients would be faced with healthcare costs.[36] Moreover, participants were reluctant to seek help for manic or hypomanic symptoms as they did not perceive them as abnormal.[30] And a lack of understanding of BD in patients, the community, and healthcare practitioners was shown to heighten these delays.[36][29]

Discussion

Summary

The literature addressing the reasons for delays in the diagnosis of BD has highlighted that individual, social, and clinical factors contribute to this delay. Available data indicate that BD is often misdiagnosed as other psychiatric disorders due to the complexity of the condition. In addition, patients are faced with barriers to accessing care due to healthcare challenges; patients may also delay seeking help due to mental health stigma and individual factors. The limited evidence offers a variety of reasons for these delays that are all intertwined.

Strengths and limitations

To the authors' knowledge, this is the first systematic review of the reasons for delays in diagnosis for people with BD. The manual search of the databases and the reference lists of the included studies provided confidence in the conclusion that all relevant research was collected. Furthermore, the use of a second reviewer during the screening process guaranteed that the research inclusion criteria were being applied consistently. Additionally, there was international coverage of previous research, as studies from all geographical locations were reviewed. Contrastingly, the use of only four databases and the exclusion of grey literature may have resulted in publication bias and missing relevant information. We also acknowledge that the search terms omitted older terms, such as 'manic depressive psychosis,' which may conceivably mean older manuscripts were omitted. It may have been useful to collect further data from included papers, such as the severity, extent, and episodes of illness and treatments used. Other diagnoses (such as personality disorder) may be ambiguous with BD. However, these were not part of the original scope of this work. Lastly, due to the methodological diversity of studies, a meta-analysis was not suited; therefore, conclusions are formed from qualitative evidence, which may lack generalisability and not be as reproducible.

Comparison with existing literature

The review highlights that unipolar depression is the most common misdiagnosis for BD patients, which is supported by observations from the National Depressive and Manic Depression Association Survey, which reports that 60% of people with BD received a misdiagnosis of unipolar depression. [6] The review explains that this occurs due to symptom overlaps, which is similarly reported in a study where individuals who were misdiagnosed with unipolar depression had a higher frequency of depressive episodes and a higher incidence of comorbidities.[38] Additionally, the review stipulates that the complexity of BD causes a low index of suspicion among clinicians. Likewise, research reports that most people with BD experience a depressive first episode that lasts longer than manic or hypomanic episodes, leading to the disorder being misclassified as MDD.[40] Furthermore, the review provides insight into mental health stigma from family, friends, and physicians, as well as how internalised stigma can discourage an individual from seeking a diagnosis. Similarly, evidence indicates that stigmatising attitudes against people with mental illnesses are frequent among primary care clinicians, and that this can act as a barrier to patients receiving adequate treatment. [41] Lastly, this review suggests that diagnostic delays may be caused by a lack of awareness and education concerning BD in the population and among clinicians, leading to symptoms going unrecognised in assessments.[42]

Implications for research and practice

There are many advances that need to be made for future research, public health and policy, and clinical practice. These advances may help to reduce diagnostic delays and improve health outcomes in the community. Future research needs to focus on prospective studies to enable the follow-up of BD patients in the long term to understand the process of diagnosing and receiving a diagnosis. It also needs to address the perceptions of clinicians, which may be related to the misdiagnosis and diagnostic delays of BD, and to highlight learning needs in clinical practice. An exploration of reasons for misdiagnosis and treatment failures would help inform clinical practice. More studies need to be conducted with a diverse sample of individuals and consider ethnicity and socio-economic status. Furthermore, public health policy needs to target awareness-raising and training in schools and communities on the signs and symptoms of BD. This paper highlights the need for pivoting resources towards tackling diagnostic delays in BD on a systemic level. Lastly, clinicians need to be mindful that patients will generally report depressive symptoms and not hypomanic or manic ones.[5] The findings of this study indicate the utility of detailed history-taking on the indicators of BD and assessing all patients with depression for previous manic or hypomanic episodes, as well as gathering collateral information from caregivers. Moreover, continuity of care when seeing BD patients ought to be upheld, and information should be accurately relayed about patients who are being referred from primary care to secondary care.

Statements and Declarations

Data Availability

The search strategy details for the Embase database are available in the Supplementary Material (Table S1). Further details regarding the search strategies for other databases, the PRISMA flow

diagram (Figure 1), and the data extraction summaries supporting the conclusions of this systematic review are available from the corresponding author upon reasonable request.

Author Contributions

Conceptualization: VP, NM, SA; Methodology: NM, AB, SA, MK, DHP, VA, VP; Software: Not applicable; Validation: NM, VA, AB, VP, SA; Formal Analysis: NM, AB; Investigation (Literature Search, Screening, Data Extraction): AB, NM; Resources: NM, AB; Data Curation: NM, AB; Writing − Original Draft Preparation: AB, NM, MK, DHP, SA, VP; Writing − Review & Editing: VP, SA, MK, DHP; Visualization: Not applicable; Supervision: VP, SA; Project Administration: AB, NM.

Acknowledgements

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Declarations