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SPECIAL ARTICLE

Transdiagnostic clinical staging in youth mental health: a primer for clinical practice

Letícia Müller **Haas**,[1,2] Pedro Mario **Pan**,[1,2] Ian B. **Hickie**,[3] Letícia Sanguinetti **Czepielewski**[4,5]

[1]*Departamento de Psiquiatria e Psicologia Médica, Universidade Federal de São Paulo (UNIFESP), São Paulo, SP, Brazil.* [2]*Laboratório Interdisciplinar de Neurociências Clínicas, Departamento de Psiquiatria e Psicologia Médica, UNIFESP, São Paulo, SP, Brazil.* [3]*Brain and Mind Centre, Faculty of Medicine and Health, University of Sydney, Sydney, Australia.* [4]*Departamento de Psicologia do Desenvolvimento e da Personalidade, Universidade Federal do Rio Grande do Sul (UFRGS), Porto Alegre, RS, Brazil.* [5]*Programa de Pós-Graduação em Psicologia, UFRGS, Porto Alegre, RS, Brazil.*

Clinical staging models are tools used in healthcare that have the potential to enhance diagnostic precision, improve treatment decisions, articulate more personalized care pathways, and optimize service models. In youth mental health, clinical staging has been increasingly applied to conditions where progression from non-specific symptoms to full-blown syndromes, such as schizophrenia, bipolar disorder, and depression, is possible. However, novel transdiagnostic staging models have also been proposed, recognizing the limitations of current classification systems and the substantial overlap of symptoms, particularly early in the illness course. Models incorporating an appropriate developmental and transdiagnostic lens may offer significant advances for research and clinical practice, supporting early intervention and secondary prevention. This narrative review critically examines theoretical premises and empirical applications of transdiagnostic clinical staging models in youth. Peer-reviewed studies were identified in PubMed using search terms related to clinical staging, focusing on sociodemographic, cognitive, and clinical factors investigated in youth samples (age 12-30 years). Evidence is synthesized in three main sections: progression, extension, and stage-based treatment. Additionally, a stage-based care model and directions for future research are presented. Early findings partially support important assumptions for the model, suggesting stage-related differences in cognition and functionality. Furthermore, new extension features have been recently proposed, including substance use, circadian disturbances, and physical illnesses. The long-term outcomes of stage-based interventions remain an open question. While the transdiagnostic clinical staging model offers a promising alternative for classifying youth psychopathology, further empirical validation is essential before its widespread implementation.

Keywords: Staging; transdiagnostic; mental disorders; psychopathology; prevention

Introduction

The increasing burden of mental disorders is a significant global health, social, and economic concern, especially given its differential impact on youth.[1] Meta-analytical evidence suggests that one in four people worldwide will develop a mental disorder during their lifetime,[2] with 75% of anxiety, mood, and psychotic disorders emerging by age 25.[3,4] The combinations of early onset and high incidence among youth makes mental disorders the leading cause of disability for these age groups.[5] However, current international classification systems fail to account for the early phases of mental disorders, also termed "subthreshold" manifestations, that often precede more severe or persistent illness presentations and are common in youth. Emerging classification systems have been proposed to address these limitations, considering the developmental course of psychopathology in young people. Among these, the transdiagnostic clinical staging model has been highlighted in several recent reviews as a promising framework for this age group, supporting prevention and early intervention in mental health.[1,6-9] This in-depth narrative review aims to provide clinicians and researchers with a comprehensive overview of recent developments in transdiagnostic clinical staging for youth mental health.

The course of mental disorders is dynamic, with initial presentations in youth often characterized by nonspecific anxious and depressed symptoms, attenuated hypomanic or psychotic symptoms, or nonpersistent or nonprogressive syndromes.[10] So, while some young people progress into adulthood with more persistent or disabling

Correspondence: Letícia Sanguinetti Czepielewski, Serviço Social e Comunicação Humana, Instituto de Psicologia, Universidade Federal do Rio Grande do Sul, Rua Ramiro Barcelos, 2600, Santa Cecília, CEP 90035-003, Porto Alegre, RS, Brazil.
E-mail: czepielewski@gmail.com
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syndromes,[11-13] others experience remission and recover functionality.[14] In the latter, transient phenomena may have occurred as typical developmental processes of growth and resilience.[15] Additionally, if symptoms progress, they can follow a homotypic trajectory, staying within the same diagnostic category, or a heterotypic trajectory, crossing into different categories. For instance, subclinical psychotic symptoms in young adults can lead to common mental disorders such as mood, social anxiety, and obsessive-compulsive disorders,[16] or vice versa.[17] At the same time, neurodevelopmental disorders increase the risk of later developing psychotic experiences.[17,18] Considering the complex and dynamic nature of youth mental health, the concept of pluripotentiality has been introduced to describe the various potential input syndromes that define states of risk and the possibility of transition into several full-blown disorders.[19]

Acknowledging the continuities and discontinuities of symptoms across the spectrum of mental disorders, a key challenge is to identify which at-risk young people will progress to more severe and disabling conditions, to provide them with relevant early intervention and secondary prevention strategies. To achieve that, a preventive approach must be developmentally informed,[20] considering the evolution of symptoms across the lifespan as well as social, educational, and occupational changes that occur during youth.[21] Misrecognition of these early stages may result in delayed identification and extended periods of untreated illness, hindering potential indicated or secondary preventive interventions.[22] Thus, accurate characterization of the initial stages of mental disorders is crucial for timely intervention, securing the ''right care, first time.''[21]

Current classification systems for mental disorders have several shortcomings, such as wide heterogeneity within the same diagnosis,[23] non-specificity of diagnostic criteria,[24] high rates of comorbidity,[25] and the use of relatively arbitrary thresholds, such as the number and duration of symptoms.[26] As a result, emerging approaches for classifying mental disorders, including the Research Domain Criteria (RDoC),[27] the Hierarchical Taxonomy of Psychopathology (HiTOP),[28] and clinical staging models,[29,30] have been suggested to replace or complement current manuals. A common characteristic among these proposals is the use of transdiagnostic approaches,[31] which aim to understand the global and shared processes responsible for the etiology and maintenance of psychological suffering, regardless of diagnostic class. Mansell[32] compares this position with the natural selection hypothesis, understanding it as a mechanism that explains variation in all classified living organisms, regardless of species. Evidence for the use of transdiagnostic models in psychopathology has been established in various branches of research, including genetics,[33,34] environmental risk factors,[35] and neuroimaging research.[36]

The accumulated evidence suggests there is a pressing need for a new clinical model for young people that captures the broader spectrum of psychopathology and promotes a range of strategies, including indicated prevention, early intervention, and secondary prevention. The transdiagnostic clinical staging model examines disorder courses, acknowledging that transdiagnostic characteristics impact symptom trajectories, just as symptom trajectories influence other clinical manifestations and psychopathological correlates.[30,37] The current literature on transdiagnostic clinical staging is sparse, with no comprehensive review specifically addressing the validity and evidence of this model for young people or providing guidelines on how to implement it in clinical practice. Therefore, this narrative review aims to describe the theoretical assumptions of clinical staging as applied to psychopathology and further discuss the potential implications of the transdiagnostic model for mental health care and reform. Finally, we discuss possible recommendations for future research aiming to test the implementation of this model in clinical practice.

Methods

This narrative review covers theoretical and empirical articles addressing transdiagnostic clinical staging as applied to youth mental health. PubMed was searched for peer-reviewed articles until December 2024, using two search queries: ''clinical staging'' AND ''transdiagnostic OR trans-diagnostic''; and ''clinical staging'' AND ''youth OR young OR adolescent.'' Terms were limited to the title and abstract. We selected full-text articles that involved youth samples (age 12 to 30 years) and investigated sociodemographic, cognitive, and clinical factors, since these are most frequently assessed by health professionals in routine clinical practice. Therefore, studies focusing solely on genetics and biomarkers were excluded. Additionally, we manually searched the references of included studies and previously published review articles clearly related to transdiagnostic clinical staging. The evidence was compiled and is presented here in three theoretical-relevant sections: i) Progression, ii) Extension, and iii) Stage-based treatment. We begin with an introduction to clinical staging, followed by an in-depth presentation of transdiagnostic clinical staging and a synthesis of the selected evidence. Finally, we propose a stage-based model of care and explore future directions.

Clinical staging

Staging is a tool used in medicine to enhance diagnosis and treatment decision-making. It uses predefined criteria to classify a person's position on a disease continuum, considering clinical factors (e.g., symptom progression, chronicity, comorbidity, family history) and physiological abnormalities (e.g., test results, biological analyses, etiology).[29] The selection of criteria for staging is evidence-based and context-dependent, ranging from the absence of disease (at-risk stages) to severe and persistent states, including death (terminal stages). Staging models are commonly applied in a range of chronic diseases, especially cancer, ischemic heart disease, Parkinson's disease, and rheumatoid arthritis.[38] Oncology pioneered staging with the TNM Classification of Malignant Tumors, established by the International Union for Cancer Control in 1958. This system grades the

primary tumor (T), regional lymph nodes (N), and distant metastases (M) from T0 to T4, N0 to N3, and M0 to M1, respectively, to determine cancer progression.[39] Considering the trajectory and development of the disease, staging models aim to promote interventions tailored to the current stage while preventing progression.[38]

While clinical staging is well-established in medicine, it has been largely neglected in psychopathology.[40] However, the foundational ideas of disease progression have been present since the early writings of Emil Kraepelin, who observed that the number of mood episodes was associated with shortening periods of euthymia in manic-depressive patients.[41] One significant influence on the development of staging in psychopathology was the study of early psychosis, which began in the 1990s and introduced the concepts of clinical high risk (CHR-P) and ultra-high risk (UHR-P) for psychosis. These concepts were developed as a prospective version of the idea of ''prodrome,''[42] which refers to the signs or symptoms preceding a disease's development. This shift from a retrospective to a prospective viewpoint was a crucial advance, indicating that progression from an at-risk mental state (ARMS) to full-blown psychosis, although more likely than in the general population, was not inevitable.[42] Therefore, if the transition is probabilistic, there is room for preventive strategies among at-risk individuals.

The study of at-risk states for psychosis has generated a fruitful field of research and intervention,[43,44] which was later extended to include risk status criteria for bipolar disorders[45] and, more recently, to depression[46] and anxiety disorders,[47,48] among others.[49] These initial studies about early psychosis and other at-risk states have ''opened the door to a dynamic clinical staging model'' (p. 131).[42] In psychopathology, a four-stage classification has been utilized, ranging from asymptomatic (stage 0) through help-seeking with nonspecific symptoms and minor distress (stage 1a), attenuated syndromes (stage 1b), full-threshold disorder (stage 2), recurrence and persistence (stage 3), to severe, chronic, and treatment-resistant mental illness (stage 4). This model is based on several predefined assumptions,[50] which are summarized in Box 1. The extent to which these assumptions have been corroborated will be discussed in the following sections.

The translation of clinical staging from general medicine to mental health care brings with it a biomedical perspective of mental illness, emphasizing the idea that the progression of mental disorders follows a natural course with an underlying biological basis and that each stage should be associated with distinct biomarkers. This framing is most evident in the staging of bipolar disorder, where the concept of ''neuroprogression'' – a pathophysiological process involving progressive brain changes – has been central.[51,52] However, evidence indicates that neuroprogression occurs only in a subgroup of individuals with bipolar disorder.[53,54] Unlike other medical conditions, mental health disorders may not adhere to a singular natural history; instead, their trajectories are mostly heterogeneous and pluripotent. Nevertheless, many authors argue that the transdiagnostic staging model offers greater potential for identifying biomarkers and uncovering the biological underpinnings of mental disorders compared to traditional categorical models – an assertion similarly made by other emerging classification systems,[27,28,50] though such findings remain elusive. For clinical staging to be effectively implemented in youth mental health, a shift toward a more integrated biopsychosocial framework is still needed.[9] In this context, we explore sociodemographic, cognitive, and functional correlates that could help formulate stage criteria and guide stage-based treatment across diverse youth populations.

Transdiagnostic clinical staging

Clinical staging in mental health initially incorporated a transdiagnostic perspective, addressing symptoms of psychosis, depression, and bipolar disorder.[29,55] Despite the proliferation of diagnosis-specific staging models,[49] such as for depression,[46] bipolar,[41] schizophrenia,[56] social anxiety,[48] and others, the field is now moving back to transdiagnostic models.[30,37,57] This shift is relevant because it enhances early intervention in youth mental health and accommodates pluripotent trajectories. The transdiagnostic clinical staging model acknowledges that

Box 1 Assumptions of the clinical staging model

Assumption	Description
Transition	• Transitions between stages are probabilistic, not inevitable. • Transition between stages is associated with increased severity, functional impairment, abnormalities in biomarkers, and change in treatment approach - that is, the transition reflects significant gradual changes in the clinical picture, which starts to differ quantitatively and qualitatively from the previous stage. • There is a unidirectionality of the transition from earlier to later stages, so even after remission of symptoms, it is not possible to return to a previous stage, and the person is assigned the highest stage ever reached. • The earlier the stage, the lower the risk of transition to subsequent stages.
Treatment	• Patients at early stages have a better response to treatment and better prognosis than those in more advanced stages, although recovery and positive outcomes are possible at all stages. • Interventions in the first stages should be simpler and safer than treatments offered in the subsequent stages, which are generally more intensive, invasive, and with more adverse effects. • The primary function of stage-based interventions is first, to address current needs and improve immediate and short-term impacts, and second, to reduce the risk of progression (transition to subsequent stages) or extension (development of complications or physical and psychiatric comorbidities) through preventive interventions.

Box 2 Transdiagnostic clinical stages: description and potential interventions based on expert consensus

Stage	Definition	Intervention
0	Asymptomatic individuals at risk for psychopathology not seeking mental health treatment. Risk attribution may occur due to genetic (e.g., family history) and environmental (e.g., sexual abuse) risk factors known to be associated with mental disorders.	Informal mental health literacy, family psychoeducation, drug advice, brief socio-emotional skills training
1a	Individuals seeking help with mild and nonspecific symptoms	Formal mental health literacy, family psychoeducation, psychotherapy, reduction of psychoactive substance use
1b	People with attenuated syndromes, often with mixed symptoms	Family psychoeducation, psychotherapy, reduction of psychoactive substance use, psychopharmacotherapy
2	Persons with severe and persistent symptoms	Family psychoeducation, psychotherapy, reduction of psychoactive substance use, psychopharmacotherapy, and vocational guidance
3	People with recurrent (recurrence of episodes after periods of remission) or persistent (incomplete remission of symptoms after treatment) disorders	Same as stage 2, with added emphasis on medical and psychosocial strategies to achieve complete remission of symptoms, relapse prevention, and early-warning-signs strategies for long-term stabilization
4	Individuals with severe, treatment-resistant, or chronic disorders whose symptoms have persisted for 2 years without remission, even after specialist mental health treatment	Same as stage 3, emphasizing tertiary treatments, social and functional rehabilitation, and family management

Adapted from Scott et al.[30] and Hickie et al.[55]

i) transdiagnostic micro-phenotypes in youth can evolve into diagnosable syndromic macro-phenotypes as symptoms become more severe, specific, and impairing[50]; and ii) this process is non-linear and heterogeneous, allowing for pluripotent trajectories and supporting preventive strategies for multiple potential outcomes.[50,57] McGorry et al.[57] state that this paradigm addresses many shortcomings of the CHR-P approach, broadening transitions to severe mental disorders and framing attenuated psychotic symptoms within general psychopathology. Complementarily, Shah et al.[37] observed that this approach facilitates prognosis prediction by considering diverse symptom trajectories and progression and extension patterns. Current transdiagnostic staging models range from stages 0 to 4, as detailed in Box 2.

In 2020, an International Working Group on Transdiagnostic Clinical Staging in Youth Mental Health released its first international consensus statement, articulating the assumptions that underpin the model and its operationalization.[37] The authors criticize the distinction between threshold and subthreshold disorders since the so-called subthreshold manifestations rarely fit into a single diagnostic category, being compositions of symptoms that change over time. This dependence on current diagnostic systems creates an ''artificial notion of diagnostic purity'' (p. 235).[37] Hence, there is a need to evaluate a set of signs, symptoms, and ''thresholds'' not based exclusively on existing manuals that frame psychopathology differently than the clinical staging model.

Recently, the same group updated the model to elucidate further the distinction between progression and extension in transdiagnostic clinical staging.[30] First, they disaggregated functionality and cognition from the other symptoms, retaining the severity of psychopathology as the core criterion for assignment of stages. Progression, which refers to significant gradual changes in clinical status,[37] indicates a higher probability of transition from earlier to later stages, as well as deterioration in functioning, cognition, and other relevant biomarkers. Extension, on the other hand, signifies the illness process acquired new and more complex characteristics, such as the emergence of physical and mental comorbidities, including substance misuse.[30] A representation of the clinical staging model in psychopathology, along with the distinction between progression and extension, is exemplified and presented in Figure 1.

Although associated, extension can occur regardless of progression. This distinction is essential for clinical decision-making: progression requires more intensive interventions, while extension requires broader or additional treatments. The current model suggests rating progression and extension as stage modifiers that range from 0 to 2 (0, no/minimal; 1, moderate; 2, severe). For instance, a young person might be classified as stage 1b, P = 1, E = 1, reflecting an attenuated syndrome with moderate functional and cognitive impact and some comorbidities.[30] Since these aspects are separate, it is possible for a person to receive any rate of progression and extension regardless of the allocated stage. However, this proposition still needs empirical validation.

Developments in operationalization of transdiagnostic stages notwithstanding, it remains a major challenge due to the absence of universally accepted objective markers and overreliance on clinical interpretation and experience.[58] An important contribution in this regard was the proposition of the Clinical High At-Risk Mental State (CHARMS) criteria,[59] which is a transdiagnostic adaptation of the at-risk criteria for psychosis. CHARMS comprises four at-risk states, which could be seen as stage 1b: attenuated psychotic symptoms, subclinical

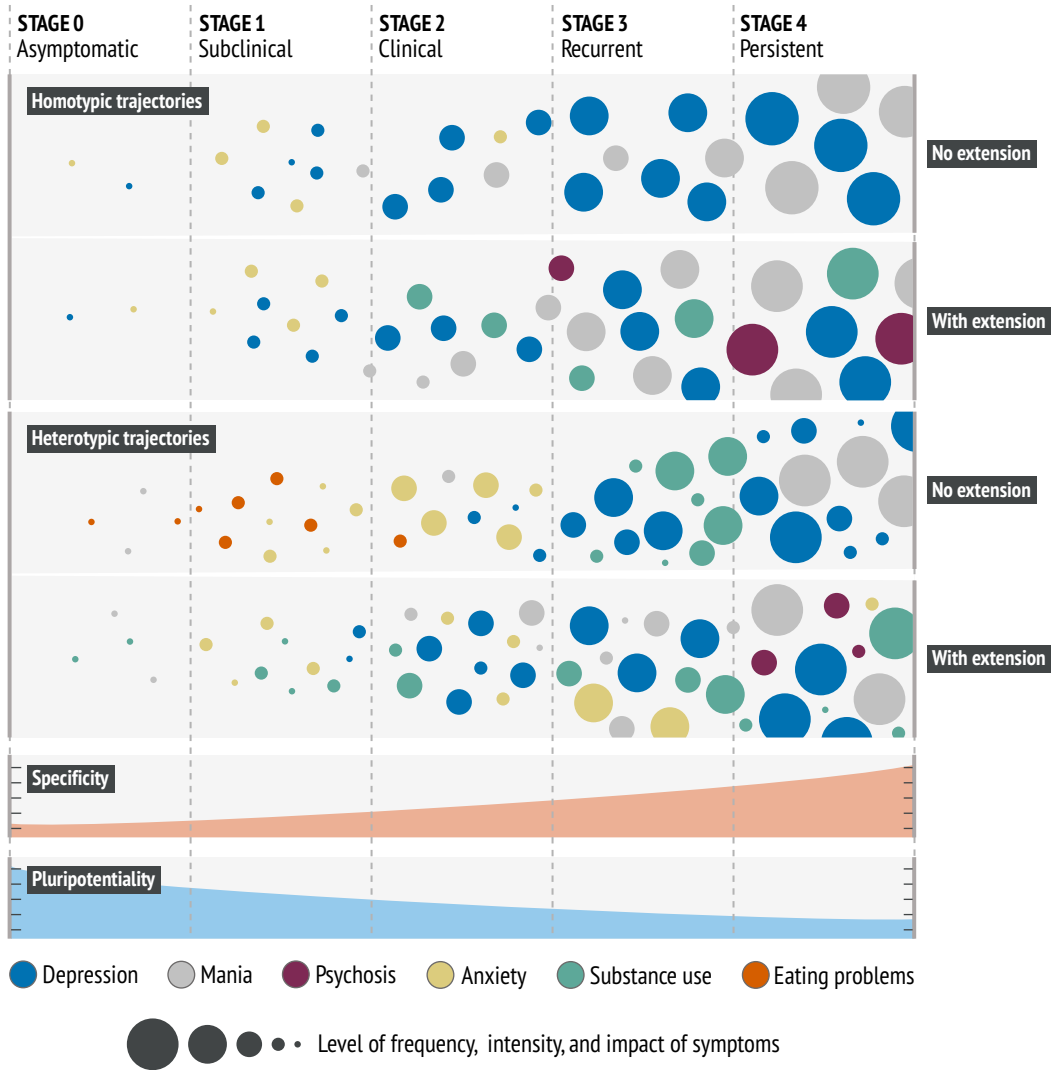


Figure 1 Clinical staging in psychopathology. Representation of different symptom trajectories that progress towards a mania macrophenotype. Homotypic and heterotypic trajectories refer, respectively, to the flow of symptoms within or between diagnostic categories. Extension refers to the development of associated factors that add complexity to the current stage, such as mental and physical comorbidities, including alcohol and substance misuse. As stages progress, it is expected that specificity increases while pluripotentiality decreases.

bipolar states, mild to moderate depression, and subthreshold borderline personality features. Validation studies of CHARMS indicate that a transdiagnostic risk identification approach is feasible, improving the identification of transitions to severe mental disorders and favoring the follow-up of homotypic and heterotypic trajectories.[19,60] Moreover, in their study, half of the participants aged between 13 and 25 years met the criteria for more than one at-risk group,[60] underscoring symptom overlap in the early stages of youth psychopathology.

The CHARMS assessment includes multiple diagnostic interviews and self-report questionnaires, which could be challenging to implement across diverse health systems and contexts.[58] To improve reliability and ensure model fidelity, Iorfino et al.[61] developed a protocol for staging young people seeking mental health care. Based on a multidimensional assessment, the algorithm can be integrated into services using health information technologies. However, their criteria rely heavily on functionality, which is not considered core criteria in transdiagnostic staging updates.[30] Other authors have either adapted the CHARMS criteria for their context[62] or developed their own set of criteria.[63] Notably, Ratheesh et al.[63] were the first to test the transdiagnostic staging in a non-clinical sample, transposing this research from high-risk or first-episode clinics to an epidemiological sample. Although research with nonclinical samples has previously been contraindicated,[37] this design can provide important clues about the distribution of transdiagnostic stages at the population level, informing preventive interventions. This is still a topic of debate. To establish an international consensus on criteria for transdiagnostic stages, further research is needed to understand progression and extension better and to test the suggestions of the "staging 2.0" framework.[30]

Evidence for progression

Transition rate and risk factors

The transition from high-risk states to first-episode mental disorder is well documented in psychosis research, with transition rates reaching 35% at 10 years.[64] Importantly, recent studies have extended this research to transdiagnostic samples. Iorfino et al.[65] examined young people (age 12-25 years) with symptoms of anxiety, mood disorder, and psychosis. They found transition rates of 36.9% from stage 1a to 1b, 12.8% from stage 1b to 2, and 2.6% from stage 1a to 2 over 14 months. Risk factors for transitioning from stage 1a to 1b included lower social functioning, low educational/employment engagement, manic and psychotic experiences, self-injury, and older age. Additionally, attention-deficit/hyperactivity disorder (ADHD) was associated with a lower risk of transition. From stage 1b to 2, risk factors were psychotic experiences, circadian disorders, psychiatric medication, childhood psychiatric disorders, and older age.[65] Studies using CHARMS criteria also demonstrated a greater transition of stage 1b to 2 during 12-month follow-up (34%) vs. a transition rate of 3% from 1a to 2.[19] In one study including 121 participants aged 13 to 25 years, those meeting the CHARMS criteria had a 27.6% transition rate at 12 months, compared to 8.5% for the control group of help-seeking young people not meeting the CHARMS threshold.[60] Depression score on the Quick Inventory of Depressive Symptomatology (QIDS) scale was the only significant risk factor. Most transitions were to severe depression (96%). Some participants subsequently developed psychosis (9%) and borderline personality disorder (4%),[60] which might suggest heterotypic trajectories with depression as an intermediary for other disorders.

In Canada, the Canadian Psychiatric Risk and Outcome (PROCAN) study included youth (age 12-25 years) with a family history of serious mental illness (stage 0), early mood symptoms (stage 1a), and subthreshold psychotic symptoms (stage 1b).[66] The overall transition rate was 17.8%, with most transitions (87%) to major depressive disorder.[67] Regarding stages, 11% of participants in stage 1a and 24.5% of those in stage 1b transitioned. Significant risk factors included female gender, higher distress scores on the Kessler Psychological Distress Scale (K-10), and higher attenuated psychotic symptoms as assessed with the Scale of Psychosis-Risk Symptoms (SOPS).

Another study in South Korea adapted the CHARMS criteria and included 90 high-risk individuals (age 15-45 years) followed over 48 months, finding a 53.3% transition rate to severe psychiatric disorders. Bipolar disorder was the most common outcome (45.7%).

Finally, Grierson et al.[68] who sought to investigate transdiagnostic mechanisms associated with the transition to stage 2. They showed that a principal component factor named "anergia," reflecting the commonalities between depression severity, rumination, and sleep-wake disturbance, significantly differentiated cases that transitioned to stage 2 vs. those that did not.

Cognition and neuropsychological functioning

The initial operationalization of clinical staging in psychopathology included cognitive deficits as important characteristics for stage allocation.[29,55] It is well established that individuals at CHR-P exhibit significant neurocognitive impairments, with verbal learning and verbal memory associated with later transition to psychosis.[69] Similarly, cognitive impairments have been reported for bipolar and depression first episodes (for a review, see Allot[70]). Recently, Millman et al.[71] conducted a meta-analysis on neuropsychological performance among individuals at CHR-P compared to peers with other psychopathologies (clinical comparators [CC]). They found significant neuropsychological impairments in both groups relative to healthy controls, with minimal differences between them. Notably, cognitive functioning in non-transitioning CHR-P individuals was similar to that of the CC group, while those who transitioned to psychosis exhibited greater impairments, especially in working memory, verbal memory, and semantic and phonemic fluency, with effect sizes exceeding Hedges' g of 0.4 when compared to CC. The authors suggest that cognitive difficulties may reflect a transdiagnostic vulnerability to various disorders when moderate but, more specifically, signal a risk for psychosis when neuropsychological functioning is severely impaired. These results have important implications for transdiagnostic clinical staging, supporting the incorporation of cognition and neuropsychological impairment as progression criteria and potentially as a stage specifier.

Four studies using data from the Brain & Mind Youth Cohort (BMC) (ages 12-30) and the PROCAN study (ages 12-25) examined cognitive and neuropsychological impairment in transdiagnostic samples.[66,72] Hermens et al.[73] found that individuals in stages 2/3 had the greatest neuropsychological deficits (z scores ranging between 0 and -1 below the norm), especially in verbal memory and executive functions, followed by those in stage 1b (z scores between 0.0 and -0.5), which showed an intermediate impairment profile compared to controls (z scores between 0.4 and -0.3). Romanowska et al.[74] also noted that individuals at stage 1b performed worse in multiple neurocognitive domains than controls, especially in the composite score of neurocognitive performance, processing speed, working memory, attention, reasoning, and problem-solving tasks. The authors suggested that the composite cognitive functioning score supports the transdiagnostic clinical staging model.[74] A longitudinal study by Tickell et al.[75] corroborated that, cross-sectionally, there is greater neuropsychological impairment in stage 2+ compared to stage 1b, namely in verbal learning, verbal memory, visual memory, set shifting, and cognitive flexibility scores, which are clinically relevant (z scores below -0.5). Over time, most neuropsychological measures improved in both groups, except for verbal memory, which worsened in those at stage 2+ but improved in stage 1b. These improvements may arise from the effects of early intervention in those with attenuated presentations, given that all participants were engaged in mental health treatment, including psychotherapy and psychopharmacology. However, practice

effects cannot be ruled out. Finally, Crouse et al.[76] used cluster analysis to derive neurocognitive subgroups among help-seeking young people. They found that neurocognitive impairment may span along a continuum of severity (global impairment, z scores between -2 and -1; intermediate impairment, z scores -1 to 0; normal range, z scores 0 to 0.5) across major mental disorders and serve as a transdiagnostic predictor of social and occupational functioning over a 3-year period. Cognitive dysfunction may be conceptualized as deficits in specific cognitive functions or as a generalized impairment, referred to as the C factor.[77] Whether a general measure of cognitive impairment or specific deficits should be incorporated as stage modifiers in the transdiagnostic staging model to inform assessment, treatment, and monitoring is still unclear.

Social and occupational functioning

Functional impairment is already noticeable in the early stages of psychosis and affective disorders, often affecting social, educational, and occupational roles before young people seek mental health care.[78,79] Studies using transdiagnostic samples of youth observed that functioning, measured by the Social and Occupational Functioning Assessment Scale (SOFAS), declined progressively as stages increased.[65,80,81] One exception was a study by Romanowska et al., which noted a decline in social functioning across stages 0, 1a, and 1b using the Global Functioning: Social (GF:Social) and Role (GF:Role) scales, though role functioning did not differ between stages.[82] Moreover, Cross et al. highlighted that, although stage 1b patients improved after 10 treatment sessions, they remained functionally impaired,[81] suggesting the need for treatment to emphasize functional rehabilitation not only for late-stages but also for young 1b patients.[79] This proposition is strengthened by recent evidence in youth indicating that social and occupational functioning might significantly impact suicidality, with direct effects on ideation and self-harm and an indirect effect on suicide attempts.[83]

Evidence for extension

In the current transdiagnostic staging model, physical and mental comorbidities are considered an extension of the symptom continuum, independent of disease progression.[30,37] Empirical studies on extension are scarce. One contribution is the study of Capon et al.,[84] who investigated clinical outcomes in young people (age 12-25 years) across stages 1a, 1b, and 2+ over 12 months. They found that circadian disturbances increased with stages, but there was no association between the clinical stage and the emergence of substance misuse or physical comorbidities. However, Iorfino noted higher rates of substance-related disorders in participants at stage 1b (16.6%) vs. 1a (10%), but no significant difference between stages 1b and 2+.[65] Interestingly, major physical illnesses were present in 15 to 24% of youths across stages 1a, 1b, and 2+.[65] Another aspect evaluated in relation to transdiagnostic stages was personality traits. Santesteban-Echarri[85] found that participants at stages 1a and 1b scored higher in neuroticism and lower in extraversion and conscientiousness compared to controls and those in stage 0. Future research should also investigate suicidal behaviors, as these might serve as an important specifier in the model.[86] Replication of studies about comorbidities, personality, and other characteristics is important to distinguish between progression and extension criteria.

Evidence for stage-based treatment

Evidence that stage-appropriate interventions can change the progression of psychotic disorders comes from a meta-analysis of early intervention studies.[87,88] After the successful implementation of high-risk psychosis clinics, Australia pioneered the creation of a primary-level mental health service providing care for youth (12 to 25 years) with transdiagnostic symptoms. These "headspace" clinics were founded in 2006 through a government initiative,[89] offering a broad range of interventions, including mental and physical health care, vocational and educational support, and substance use interventions.[90] The interventions are stage-based, usually consisting of brief psychotherapies as a first-line treatment.[89] Similar efforts have been implemented in the United Kingdom, Canada, Ireland, Israel, Denmark, and the Netherlands, with promising results.[91] The most recent national evaluation of headspace suggests that the program has successfully increased access to mental health services for young people, particularly in underserved areas, improving their mental health and well-being.[92] Nevertheless, there are criticisms about this service model, especially its cost-effectiveness and scalability.[93]

Additional studies have begun to emerge testing stage-based treatments for youth at transdiagnostic risk. Weintraub et al.[94] piloted the Unified Protocol (UP), a transdiagnostic cognitive-behavioral therapy protocol, on adolescents aged 13-17 at high risk for psychosis (n=7) or bipolar disorder (n=3). Initial findings demonstrate its feasibility and acceptability and suggest potential efficacy in reducing psychiatric symptoms, improving quality of life, and enhancing emotion regulation. Similarly, the EMIcompass, a transdiagnostic ecological momentary intervention design for early intervention, was applied over 6 weeks alongside treatment as usual (TAU) to 92 individuals in stages 1a (psychological distress), 1b (CHARMS), or 2 (first episode of severe mental disorder).[95,96] The results indicate feasibility and potential positive effects on stress reactivity and quality of life.

Summary of evidence

The reviewed evidence on progression partially supports the assumptions of the transdiagnostic clinical staging model summarized in Box 1. Indeed, there are differences between stages regarding cognition and neuropsychological impairment, with verbal memory as a potential treatment target in stage 1b.[75] Furthermore, functional impairments are significant at early stages and do not

necessarily improve as expected with treatment,[81] suggesting a need to provide functioning-specific interventions. The transition from stages 1a and 1b to 2 occurs in 18-53% of high-risk individuals, suggesting that not all young people progress to severe mental disorders. Additionally, those in stage 1b presented a higher transition rate than those in stage 1a.[60,62,65,67] To date, no meta-analysis has summarized the transdiagnostic risk of transition in psychopathology, though a scoping review suggested similarities between the clinical antecedents of psychosis, bipolar disorder, and depression.[10] In conclusion, identifying markers capable of accurately and reliably predicting transdiagnostic risk of onset and progression of mental disorders is essential for improving personalized mental health care. This is still only an aspiration,[50] but evidence is starting to accumulate. Regarding extension, there is much work to be done. It is not clear if a three-point classification from no/minimal (1) to moderate (2) and severe (3), as suggested in Staging 2.0,[30] is the most valid and informative way to convey information about patient comorbidities and clinical complications. Additionally, which clinical characteristics need to be monitored and how they relate to progression is a topic that needs to be investigated and better described in the transdiagnostic clinical staging model. Promising targets include substance use, circadian disturbances, major physical illnesses, personality traits, and suicidal behavior.[65,84-86] Finally, evidence for transdiagnostic stage-based treatment is emerging,[94-96] although the assumptions highlighted in Box 1 still need to be empirically tested, specifically to verify long-term symptomatic, functional, and staging outcomes of these interventions.

Translating transdiagnostic clinical staging into action: insights from the clinician's perspective

The development of staging models is strongly associated with validity and clinical utility, a premise that popularized staging as a clinical tool in medicine. In the case of the TNM system, for instance, cancer treatment becomes progressively more intensive, invasive, and extensive at later stages, when the odds of mortality are greater.[39] The same principle may apply to mental disorders. Treatment must respect the ethical principles of non-maleficence and avoidance of excessive treatment and stigmatization while also addressing undertreatment, which is ubiquitous in mental illness. Clinical staging may allow for more personalized mental health care as it addresses the needs of each patient at their stage, aiming to mitigate current suffering and impairment while simultaneously preventing progression to subsequent stages.[37] International agencies have emphasized staging and early intervention as key innovative models to guide the future of psychiatry on a global scale. The Lancet Commission on Global Mental Health and Sustainable Development and the Lancet Commission on Youth Mental Health highlighted the importance of staging models for delivering a broader range of interventions as early as possible in the course of mental health conditions.[1,9,97] Similarly, the World Psychiatric Association (WPA) underscored the value of early intervention and advocated for sustained recovery support for those at later stages.[98]

In a stage-based model of care, the indication of treatment is made considering the current stage (e.g., risk and protection factors, symptoms, functionality, severity, comorbidity) and prognostic factors (e.g., risk of progression and extension, risk of negative outcomes including suicide behavior, decreased functionality, and neuroprogression). This reasoning unites diagnosis and prognosis. Possible interventions suitable for each stage according to the transdiagnostic clinical staging model are exemplified in Box 2. The stage-based model of care, illustrated in Figure 2, consists of the following steps: i) comprehensive assessment; ii) clinical stage allocation; iii) evidence-based treatment planning, including stage-matched interventions and shared decision-making; iv) routine outcome assessment, with integration with specialized mental health services if needed; and v) service exit planning.[50]

Regarding assessment, instruments for evaluation and diagnosis of CHR for psychosis and bipolar disorder are available, such as the Comprehensive Assessment of At-Risk Mental States (CAARMS),[99] the Structured Interview for Prodromal Syndromes (SIPS)[100] (see Fusar-Poli et al.[44] for other measures in psychosis), and the Bipolar Prodrome Symptom Interview (BPSS).[101] Recently, Patterson et al.[102] developed the Youth Experience Tracker Instrument (YETI), a transdiagnostic self-report measure to evaluate developmental antecedents of severe mental disorders, including affective lability, anxiety, basic symptoms, depressive symptoms, psychotic-like experiences, and sleep. Other resources for a comprehensive assessment include the Brain and Mind Centre (BMC) multidimensional framework, which proposes evaluating a range of behaviors outlined in Figure 2.[21] Whichever the instruments selected, the principles of evidence-based assessment should guide all evaluations.[103] From all the results collected, using the decision tree in Figure 2 and the description provided in Box 2, the practitioner is able to assign the patient a transdiagnostic clinical stage.

Treatment planning and monitoring should be stage-based, developmentally appropriate, and prioritize shared decision-making independently of the stage allocated.[104] Treatment should aim to reduce symptoms, substance use, and suicidal risk, but also improve functional outcomes and physical health, promoting global quality of life. Besides, modifiable transition risk factors should be addressed to prevent progression. Measurement-based care can be used to monitor treatment outcomes, as well as disease progression and extension.[105] Upon recognizing that treatment goals are not being met, intensive or broader interventions and integration with other health services should be considered to intervene as early as possible in the disease trajectory and thus prevent deterioration. Finally, the patient and their friends/family/community should agree on exit planning. In this phase, self-care and relapse prevention should be promoted, and monitoring should be planned according to patient needs. If early warning signs arise after treatment discontinuation, the patient and clinician should have a plan of action, which may include a return to the health service.[21]

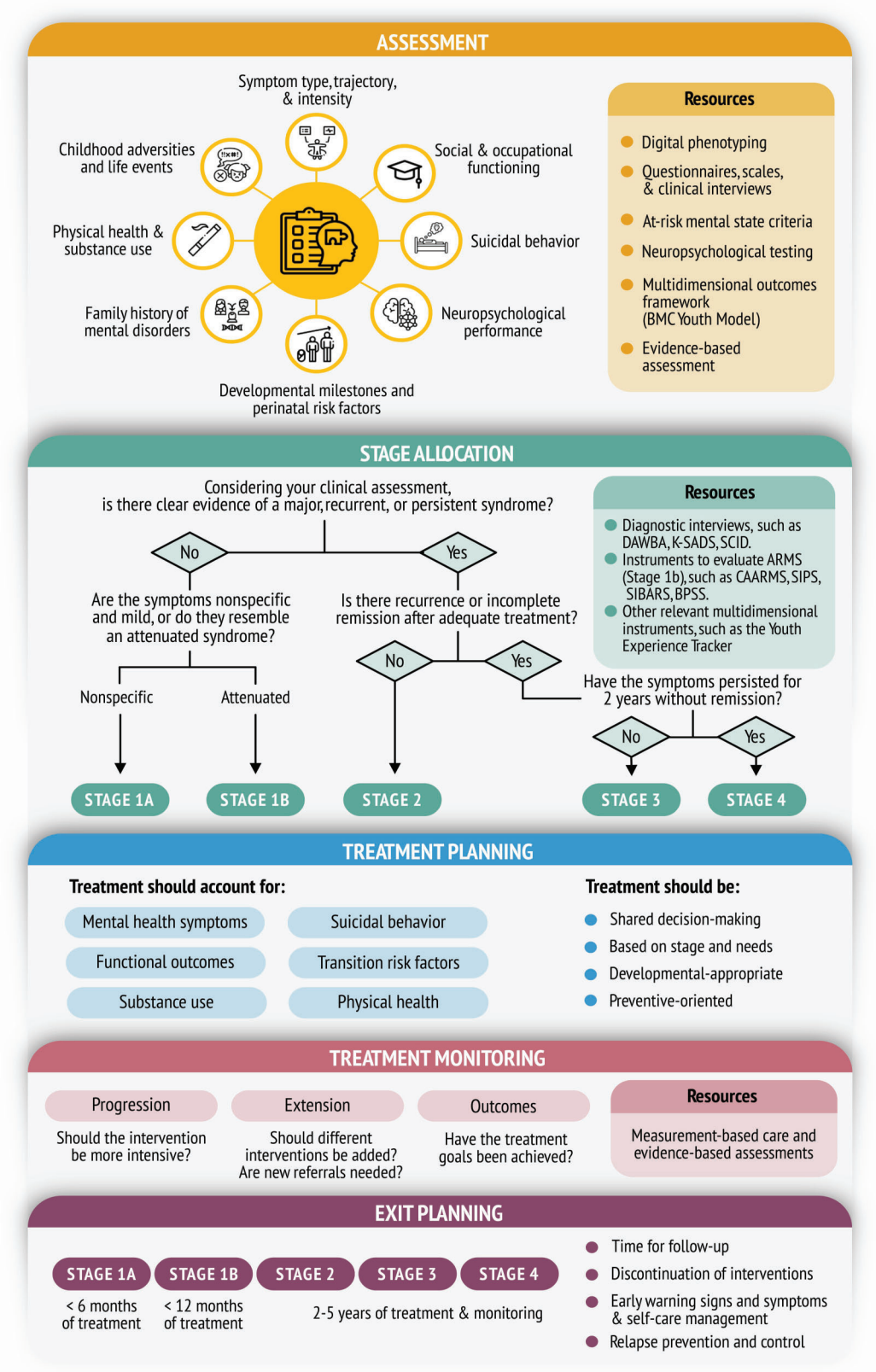


Figure 2 Stage-based model of care. The icons are from Flaticon. ARMS = at-risk mental state; BMC = Brain and Mind Centre; BPSS = Bipolar Prodrome Symptom Interview; CAARMS = Comprehensive Assessment of At-Risk Mental States; DAWBA = Development and Well-Being Assessment; K-SADS = Kiddie Schedule for Affective Disorders and Schizophrenia; SCID = Structured Clinical Interview for DSM; SIBARS = Semistructured Interview for Bipolar At-Risk States; SIPS = Structured Interview for Prodromal Syndromes.

Despite being heuristically consistent, this model needs to be further corroborated, comparing different stage-based models of care.

Recent developments in the transdiagnostic staging model include the distinction between progression and extension, along with the introduction of stage modifiers.[30] This framework has the potential to significantly enhance mental health care by encouraging clinicians to move beyond a focus on symptoms and severity alone. It emphasizes the importance of considering functionality, cognition, suicidality, personality traits, neurophysiological changes, interpersonal and socioenvironmental risk factors, and other transdiagnostic features that transcend the boundaries of stages and specific disorders, holding intrinsic value independent of symptom severity and course. This is particularly relevant in the early stages, because, although symptoms are mild and nonspecific, other impairments might already be clinically significant. However, clear treatment guidelines have yet to be established for addressing varying levels of extension or specific stage modifiers.

Conclusions and future directions

The transdiagnostic clinical staging model is based on testable assumptions, mainly that prognosis can benefit from early diagnosis and intervention. Clinical research is needed to validate this model by evaluating the efficacy, effectiveness, and adherence to stage-specific interventions. One way forward consists of stratifying participants into clinical stages, which requires an objective and comprehensive operationalization of stages to achieve high inter-rater reliability. Furthermore, any characteristic used for stage allocation should have a clear relationship with treatment response, as the progression of stages should be associated with significant changes in the intensity or type of proposed interventions. As new evidence emerges, stages could be allocated based on phenotyping and comprehensive neurobiological, psychological, and clinical assessments, providing the basis for personalized prevention and prognostication,[50] as done in other areas of medicine. To achieve this goal, the predictive value of risk criteria should be investigated, along with the risk and protective factors associated with transition, remission, and persistence in each stage.

Additionally, the role of comorbidities and the process of disease extension need to be better described in terms of their influence on progression and vice versa. Any staging model must also account for between and within-stage variability over time, considering that psychopathology may follow different trajectories.[41] What explains such heterogeneity and how the staging model can incorporate this are questions for future research. Moreover, another line of inquiry is whether the model applies to all mental disorders, particularly those that do not follow a progressive trajectory, such as neurodevelopmental disorders. Recent discussions have emphasized the need to incorporate a neurodevelopmental spectrum into transdiagnostic psychiatric frameworks.[106] Finally, the potential use of clinical staging to classify childhood mental health (5-11 years), particularly internalizing and externalizing problems, has been proposed.[107] While it is evident that childhood mental health issues may have long-term implications for youth, how these should be integrated into the transdiagnostic staging model for young people remains unclear. Further theoretical, feasibility and cost-benefit studies are needed to determine this model's validity and clarify the position of neurodevelopmental conditions within it. Promising research databases incorporating clinical staging include the Youth Follow-up Study[108] and the Youth Mental Health Tracker (YMHT).[109]

Transdiagnostic clinical staging must face other major challenges. First, the progressive nature of staging and the transition between stages may result from the interplay of biological, psychological, and social factors affecting symptom trajectories and functionality, rather than reflecting a disease's natural (and deteriorating) course. Multidimensional data and causal modeling are needed to disentangle these effects, addressing mental health as a complex, dynamic system.[110,111] Second, while there is a growing shift toward transdiagnostic perspectives in psychopathology, the clinical superiority of the transdiagnostic staging model over diagnosis-specific approaches still requires empirical validation, particularly in demonstrating improved care outcomes for youth. Otherwise, both models may coexist, as symptom specificity tends to increase in later stages.

This narrative review critically examined theoretical and empirical articles on transdiagnostic clinical staging in youth mental health, providing an overview of the evidence base for this field. As new evidence emerges, systematic reviews must be conducted to answer specific questions. In conclusion, transdiagnostic clinical staging addresses the limitations of current classification systems, aiding in treatment selection and disorder prognosis. It assumes that stage-appropriate interventions could modify risk factors and states, thereby altering individual prognoses. As a transdiagnostic perspective that goes beyond categorical diagnosis, it supports the prevention of multiple target disorders. While the transdiagnostic clinical staging model offers a promising alternative for classifying youth psychopathology, further empirical validation is essential before its widespread implementation.

Disclosure

PMP received payment or honoraria for lectures and presentations in educational events for Sandoz, Daiichi Sankyo, Eurofarma, Abbot, Libbs, Instituto Israelita de Pesquisa e Ensino Albert Einstein, and Instituto D'Or de Pesquisa e Ensino. IBH is the Co-Director of Health and Policy at the Brain and Mind Centre (BMC), University of Sydney, which operates early-intervention youth services at Camperdown under contract to headspace; is the Chief Scientific Advisor to, and a 3.2% equity shareholder in, InnoWell Pty Ltd, which aims to transform mental health

services through the use of innovative technologies. The other authors report no conflicts of interest.

Author contributions

LMH: Conceptualization, Methodology, Investigation, Writing – original draft, Writing – review & editing.
PMP: Writing – review & editing.
IBH: Writing – review & editing.
LC: Conceptualization, Methodology, Writing – review & editing, Supervision.
All authors have approved the final manuscript.

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