BMC Youth Model Seminar #2: Combining clinical stage and pathophysiological mechanisms to understand illness trajectories in young people

Presented by

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THE UNIVERSITY OF SYDNEY

Acknowledgements

- Of country
- Of lived experience

BMC Youth Model of Care – Seminar Series

1. A highly personalised and measurement-based model of care to manage youth mental health
2. Combining clinical stage and pathophysiological mechanisms to understand illness trajectories in young people
3. A comprehensive assessment framework for youth mental health care
4. Using the BMC Youth Model to personalise care options – best care, first time!
5. A youth mental health service delivery model to support highly personalised and measurement-based care
6. Maximising the use of digiHealth solutions in youth mental health care

Recap of Seminar #1

- Mood and psychotic syndromes most often emerge during adolescence and young adulthood, with effects that can have long term consequences
- The BMC Youth Model is **highly personalised and measurement-based care** that aims to **prevent progression to more complex and severe forms of illness**
- Core concept 1 of the BMC Youth Model is a **multidimensional assessment and outcomes framework** to address the holistic needs of young people presenting for care
- This framework helps to ensure that youth mental health care focuses on outcomes that matter most to young people

Outline for Seminar #2

- Barriers in traditional diagnostic classification systems, and implications to providing care
- Introduction to **transdiagnostic framework** for classifying common adolescent-onset mood and psychotic syndromes, combining two independent but complementary dimensions:
    1. Clinical staging
    2. Three proposed pathophysiological mechanisms → over time have illness trajectories (or pathways)
        1. Neurodevelopmental abnormalities → Psychosis
        2. Hyperarousal → Anxious depression
        3. Circadian dysfunction → Bipolar spectrum disorders

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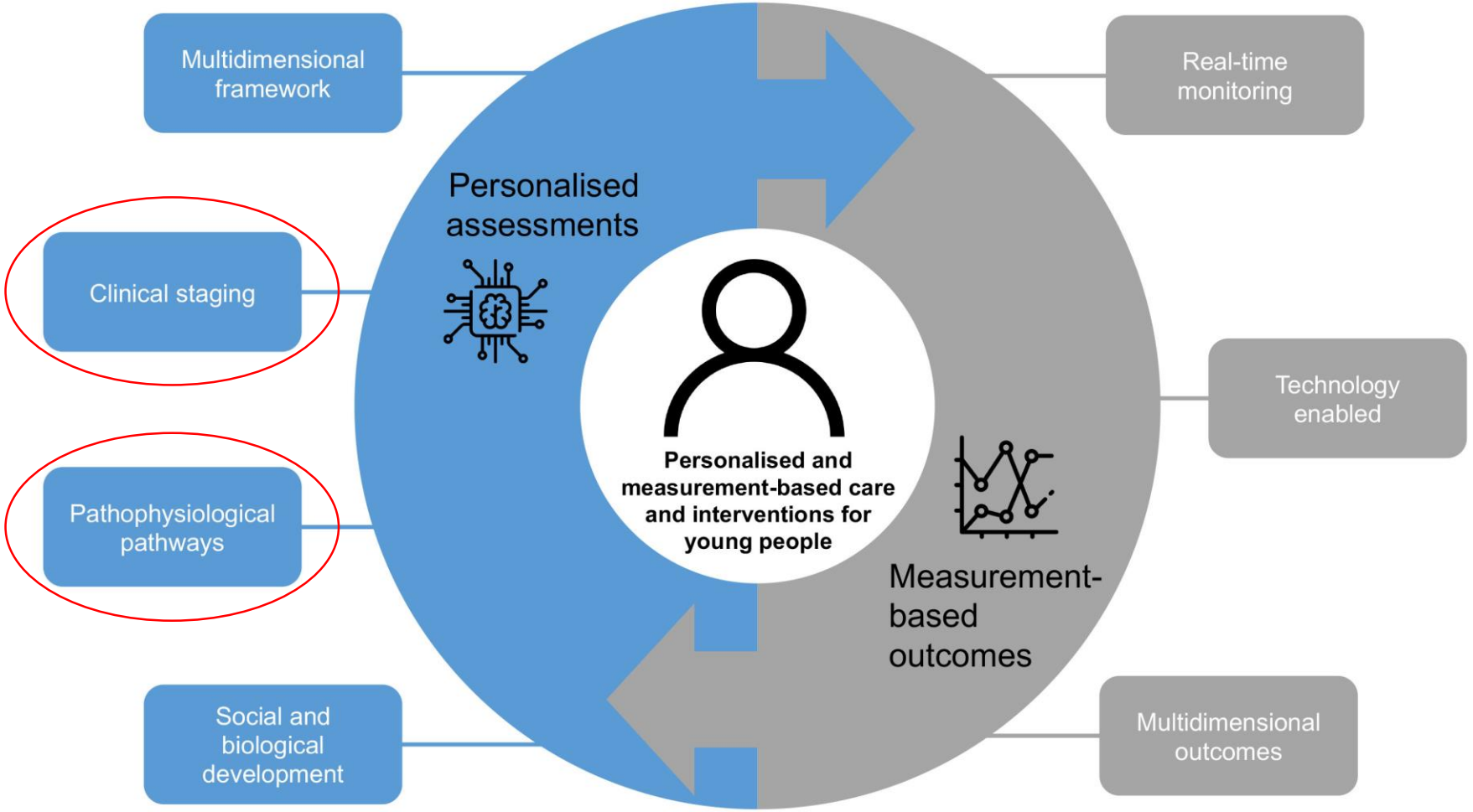
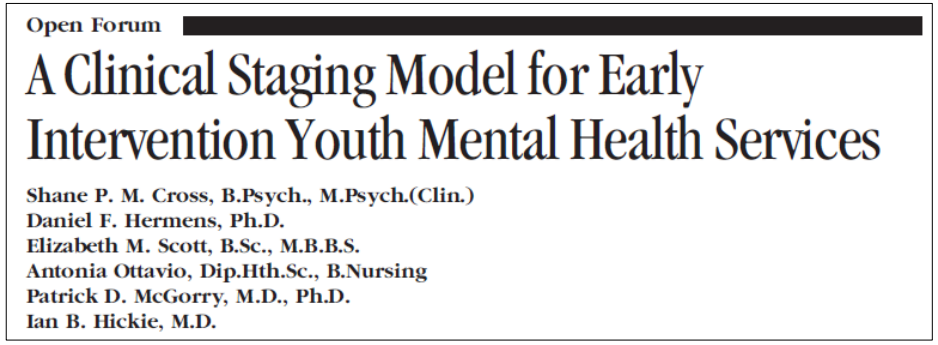


Clinical staging in mental health service delivery

- Concept of clinical staging widely used and accepted in various areas of medicine (e.g. oncology) to place an individual on a continuum to determine treatment using evidence-based pathological boundaries
- Staged care recognises that mental health problems rarely occur in isolation and enhances personalised assessment, intervention and referral so individuals receive the **right level of care at the first point of contact** with a mental health service



Open Forum

A Clinical Staging Model for Early Intervention Youth Mental Health Services

Shane P. M. Cross, B.Psych., M.Psych.(Clin.)
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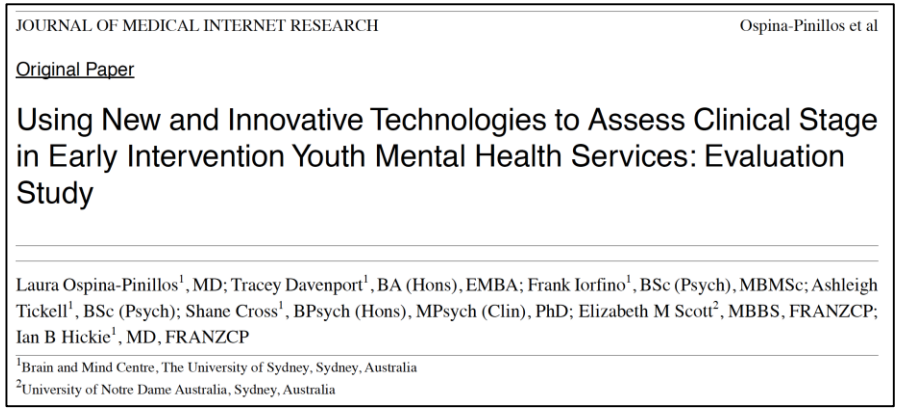
Ian B. Hickie, M.D.



JOURNAL OF MEDICAL INTERNET RESEARCH

Original Paper

Using New and Innovative Technologies to Assess Clinical Stage in Early Intervention Youth Mental Health Services: Evaluation Study

Laura Ospina-Pinillos[1], MD; Tracey Davenport[1], BA (Hons), EMBA; Frank Iorfino[1], BSc (Psych), MBMSc; Ashleigh Tickell[1], BSc (Psych); Shane Cross[1], BPsych (Hons), MPsych (Clin), PhD; Elizabeth M Scott[2], MBBS, FRANZCP; Ian B Hickie[1], MD, FRANZCP

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A Digital Platform Designed for Youth Mental Health Services to Deliver Personalized and Measurement-Based Care

Frank Iorfino[1,2], Shane P. Cross[1], Tracey Davenport[1,2], Joanne S. Carpenter[1], Elizabeth Scott[3], Sagit Shiran[2] and Ian B. Hickie[1]*

Clinical staging summary

Clinical Stage	Description
Stage 0	• Non-help-seeking asymptomatic with risk factors
Stage 1a	• Help-seeking with presenting symptoms which are distressing, but are not specific to one disorder, are or low to moderate severity and have limited impact on functioning.
Stage 1b	• Attenuated syndromes of severe mental disorders, with moderate to severe functional impacts
Stage 2	• Discrete first episode syndromes with major functional impacts
Stage 3	• Recurrent or persistent syndromes with ongoing severe functional impacts
Stage 4	• Syndromes which are severe, persistent and unremitting

Stage 0

ASYMPTOMATIC; RISK FACTORS

- First-degree relatives of individual with illness
- Family history of mental illness
- Preterm delivery or low birthweight
- Childhood physical or sexual abuse
- Presence of a major developmental disorder
- Childhood-onset anxiety or affective disorders

Stage 1a

HELP-SEEKING WITH SYMPTOMS

- Non-specific symptoms of anxiety or depression
- Mild to moderate severity of symptoms
  - Arousal **without** significant or persistent avoidant behaviours for anxiety
  - Depressive ideation **without** specific features of a more disabling disorder
- Mild neuropsychological deficits
- Recent or mild impacts on social, educational or occupational function (SOFAS 70-100)
- May include those with earlier childhood-onset symptoms who have re-presented or worsened during the adolescent period
- May include those with earlier onset neurodevelopmental or attentional disorders who now present with anxiety or depressive symptoms in the adolescent years

Stage 1b

ATTENUATED SYNDROMES

- More specific anxiety, depressive or mixed syndromes of at least moderate severity:
  - Anxiety: more severe symptoms and development of specific avoidant behaviours
  - Depressive syndromes: depressed mood, anhedonia, suicidal ideation or thoughts of self-harm, some neurovegetative features
  - Hypomanic symptoms of less than 4 days' duration during any specific episode
  - Psychotic symptoms of brief duration only
- May include subjective or objective evidence of at least moderate neuropsychological change
- Moderate to severe impact on social, education or employment functioning (typically SOFAS 60-70)
- May meet diagnostic criteria (e.g. MDD, Bipolar II) without characteristics of Stage 2
- Often have mixed symptoms or have features of a number of different diagnostic groups
- The presence of regular, deliberate self-harm without overt suicidal intent may occur in this stage
- Significant circadian disturbance (e.g. prolonged fatigue or sleep disturbance) is common

Stage 2

DISCRETE DISORDERS

Original Article

Applying clinical staging to young people who present for mental health care

Ian B. Hickie, Elizabeth M. Scott, Daniel F. Hermens, Sharon L. Naismith, Adam J. Guastella, Manreena Kaur, Anna Sidis, Bradley Whitwell, Nicholas Glozier, Tracey Davenport ... See all authors

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- Discrete depressive, manic, psychotic or mixed syndromes with more severe symptoms
- Do not necessarily match a single or discrete DSM disorder or correspond to a specific cut-off point on a specific rating scale
- Key symptoms are **no longer transient**
- Must have evidence of **major impacts** on social, educational or occupational functioning
- Importantly, primary discrete syndromes may co-occur:
  - For example, severe anxiety and depression; severe depression complicated by hypomanic periods; severe bipolar depression; and severe depression complicated by a psychotic syndrome
- If patient has been hospitalised for treatment, then typically they would have met criteria for this stage

Stage 2

DISCRETE DISORDERS

- For depression:
  - psychomotor retardation, agitation, impaired cognitive function, severe circadian dysfunction, psychotic features, brief hypomanic periods, severe neurovegetative changes, pathological guilt, severe suicidality
- For anxiety disorders:
  - complicated by at least moderately severe and concurrent depressive disorders, typically marked agitation, fixed irrational beliefs, overvalued ideas or attenuated psychotic symptoms, or substantial and persistent substance misuse
- For manic disorders:
  - Must clearly have had manic syndromes (not just symptoms) for more than 4 days during a specific illness event; hypomanic symptoms or brief hypomanic syndromes alone do not constitute a discrete disorder
- For psychotic disorders:
  - Must have had a clear psychotic syndrome for more than a week
- For mixed or ‘comorbid’ syndromes:
  - Must have had significant symptoms (depressive, manic or psychotic) within the context of a more severe syndrome that is persisting and having a major impact on function. At some points, the significant co-morbidity may include alcohol or substance misuse, abnormal eating behaviour or other relevant psychological disorders

Stage 3

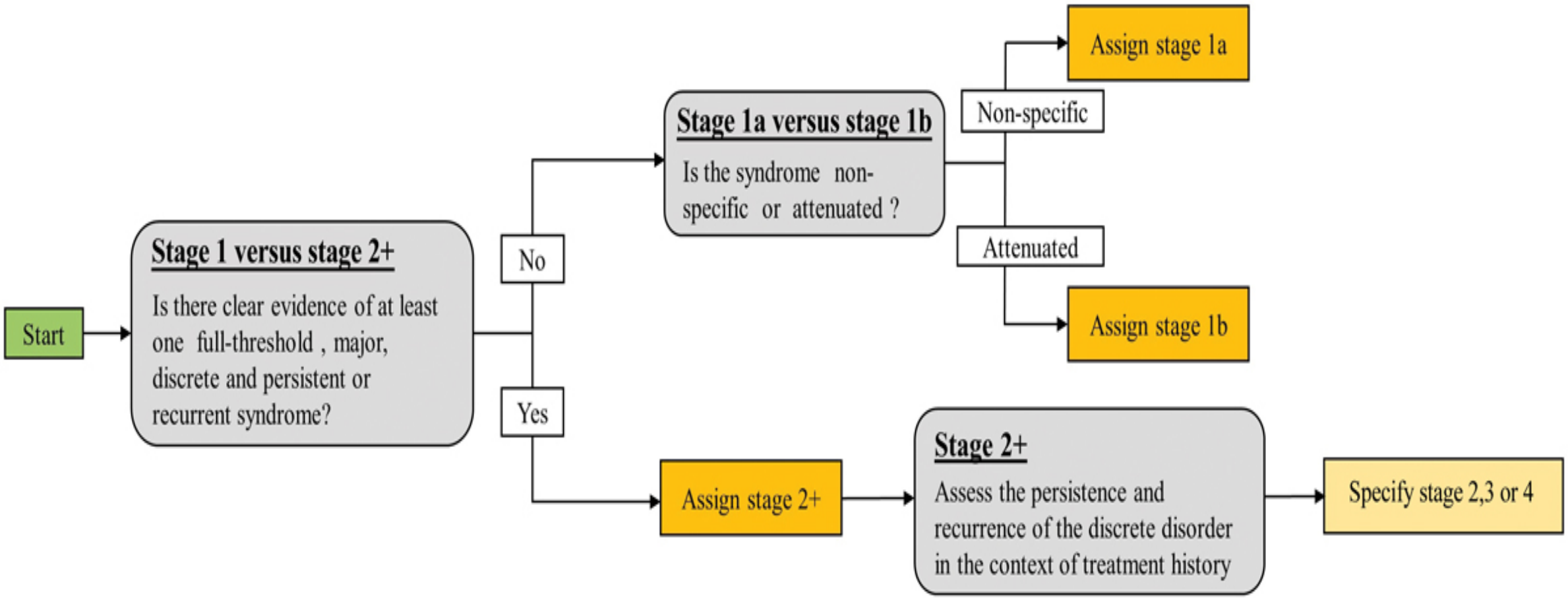
RECURRENT OR PERSISTENT DISORDER

- **Incomplete remission** from discrete disorder at 12 months after entry to care following reasonable course of treatment (of at least 3 months' duration)
- **Recurrence** of discrete disorder after period of complete recovery (having fully recovered for at least 3 months)
- Illness course is associated with objective evidence of deteriorating neuropsychological function
- Illness course is associated with deteriorating social, education or occupational function due to persistence or recurrence
- Typically SOFAS <40

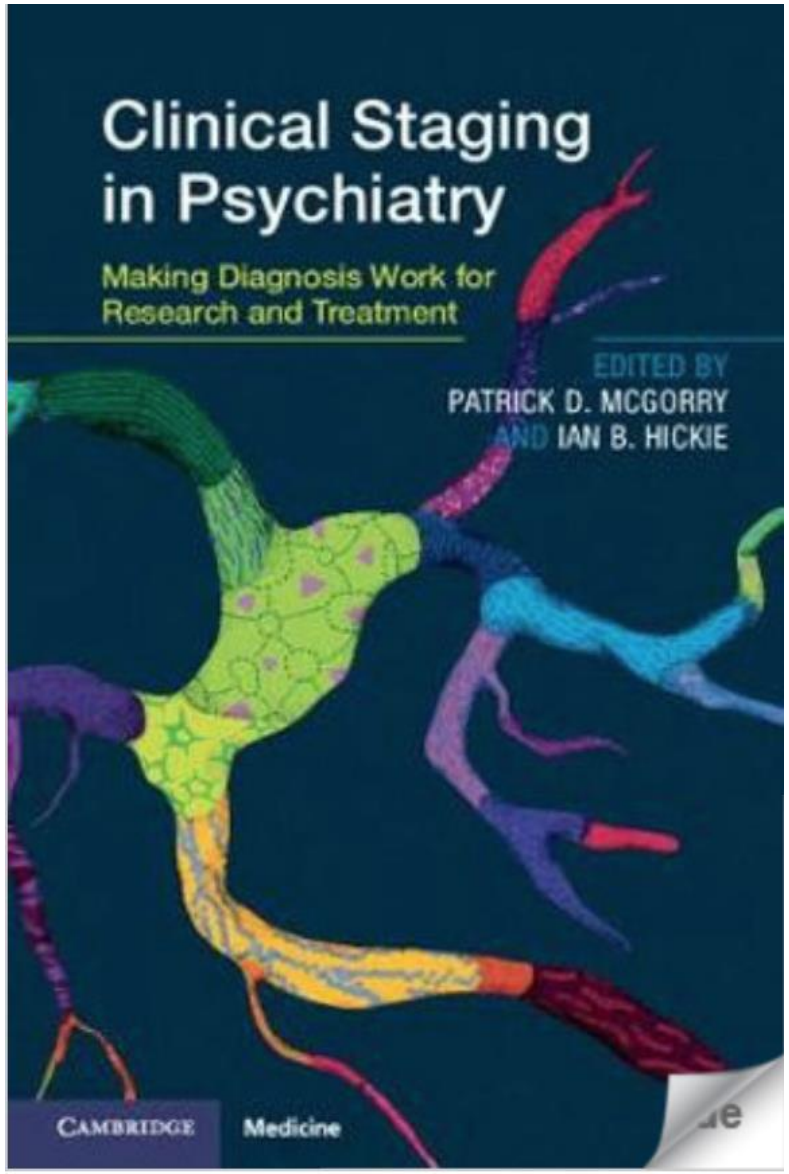
Stage 4

SEVERE, PERSISTENT AND UNREMITTING ILLNESS

- Severe, persistent and unremitting illness assessed after at least 24 months of engagement with relevant specialised clinical services and provision of a reasonable range of medical, psychological and social interventions
- Illness course is associated with objective evidence of severe deterioration in neuropsychological function
- Illness course is associated with clear evidence of marked deterioration in social, education or occupational function due to persistence or recurrence
- Typically SOFAS <30



Clinical decision-making principle: *Assign highest achieved in lifetime, and when in doubt, rate down and re-assess in 4–6 weeks.*


Clinical Staging in Psychiatry
Making Diagnosis Work for Research and Treatment
EDITED BY
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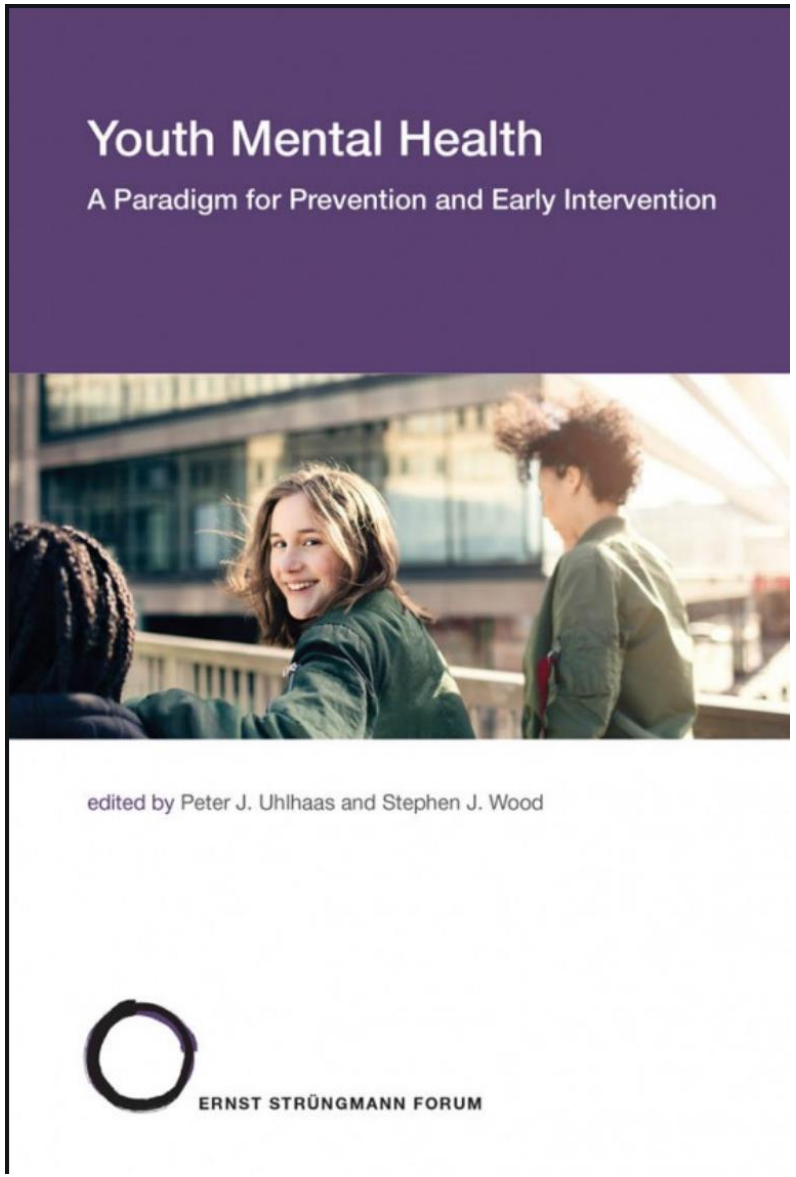
Medicine


Youth Mental Health
A Paradigm for Prevention and Early Intervention
edited by Peter J. Uhlhaas and Stephen J. Wood
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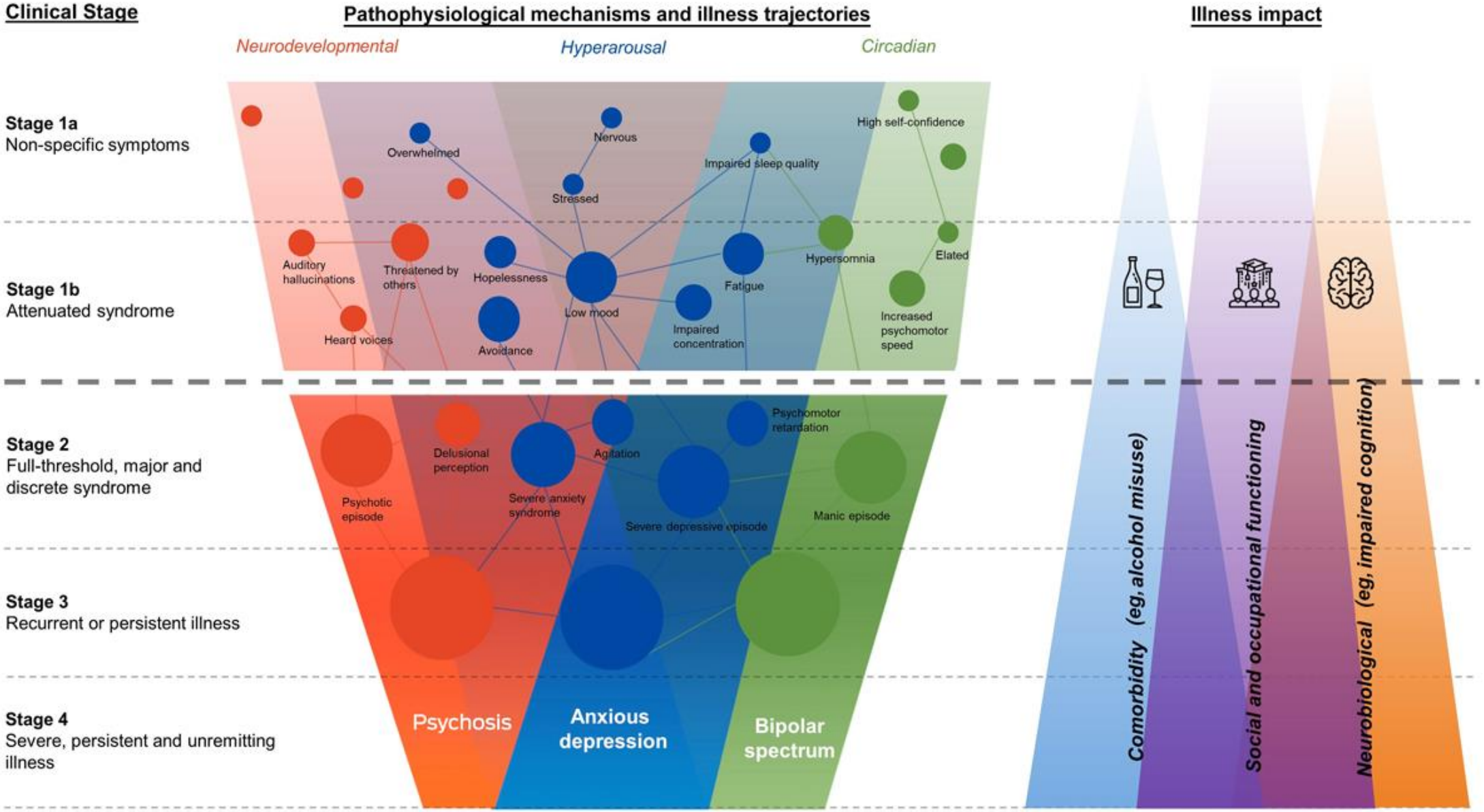
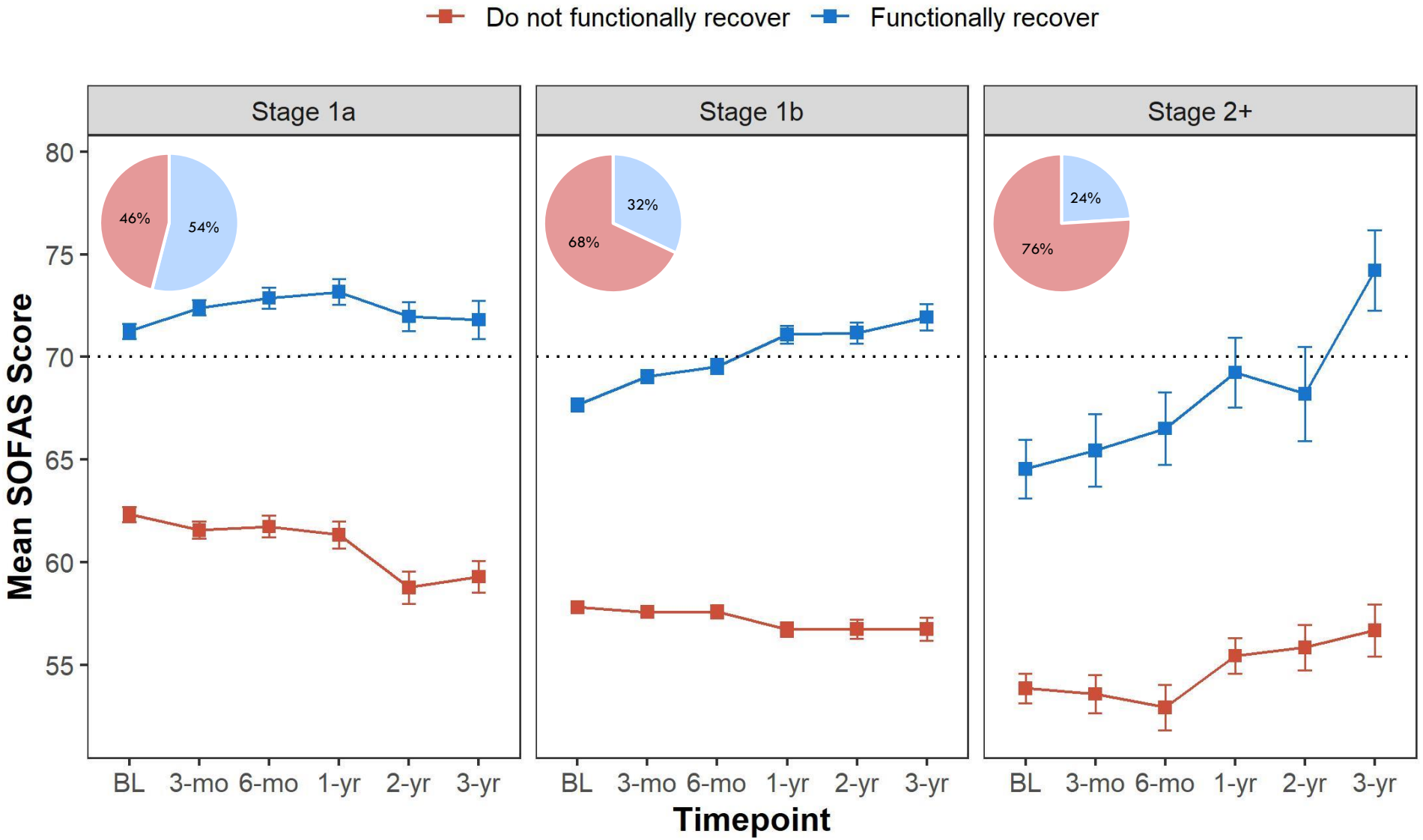


** Circles represent symptoms. Some examples of symptoms in the model, symptom clustering and illness trajectories (shown by joining lines) are provided. Increasing symptom burden occurs as syndromes progress to later clinical stages of illness and more discrete disorders (represented by larger circles and a more solid background). Colours represent proposed pathophysiological mechanisms with three key pathways to illness subtypes: neurodevelopmental–psychosis, hyperarousal–anxious depression, and circadian–bipolar spectrum. Progression to later stages of illness is also accompanied by increasing illness impacts including comorbidity, impairment in social and occupational functioning, and neurobiological deficits.*



** Unpublished data from 2162 young people with at least 1 month of follow-up after presentation to care. Those who do functionally recover (blue lines) are compared with those who do not functionally recover (red lines) for each clinical staging group. Pie charts indicate the proportions of young people at each stage who do and do not functionally recover, in blue and red, respectively. Functional recovery is indexed by a SOFAS score of ≥70 by time last seen. Squares represent mean values and error bars indicate standard error of mean.*

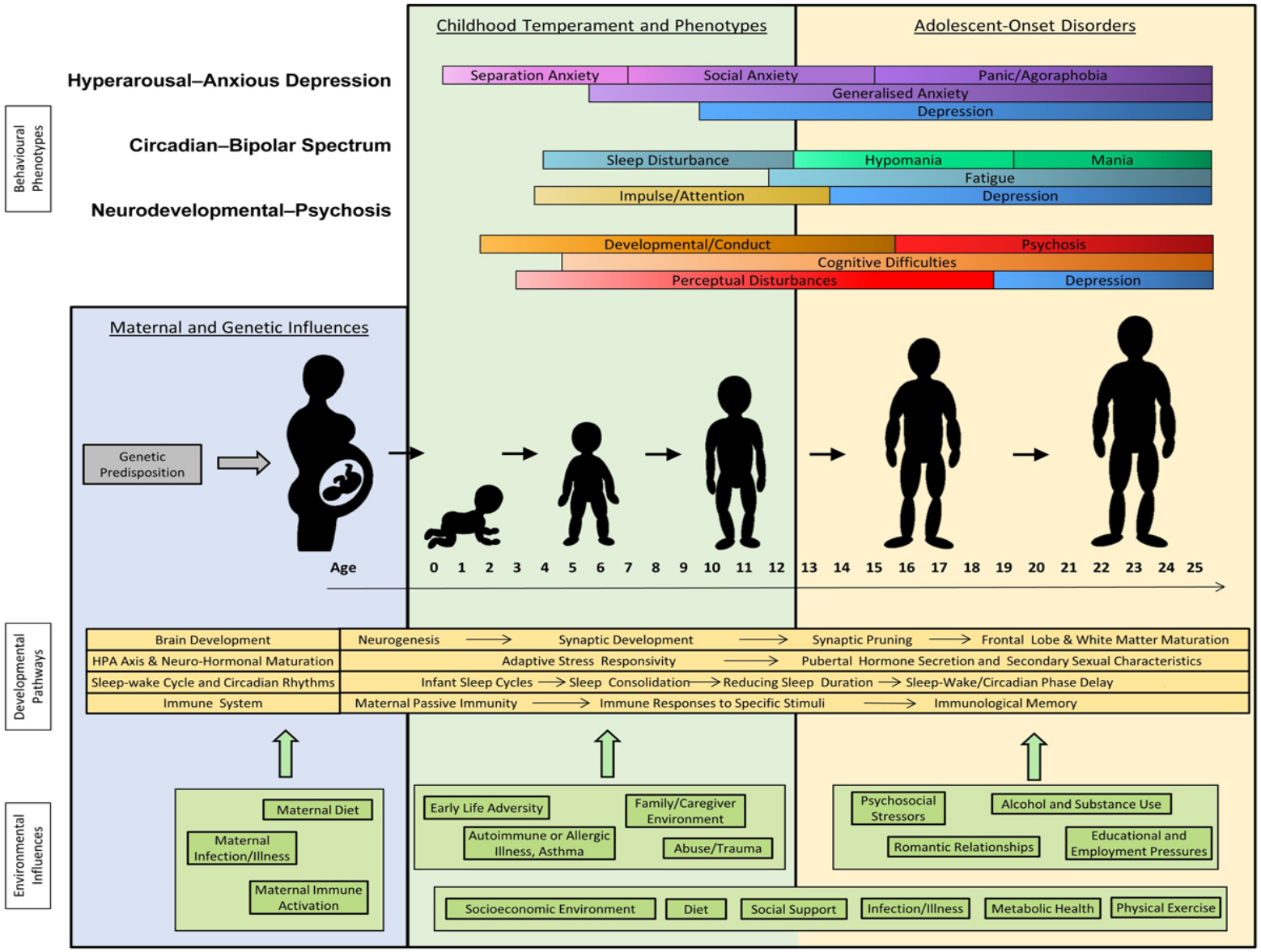
6 Supporting evidence for clinical staging from the Brain and Mind Centre's Optymise Youth Cohort

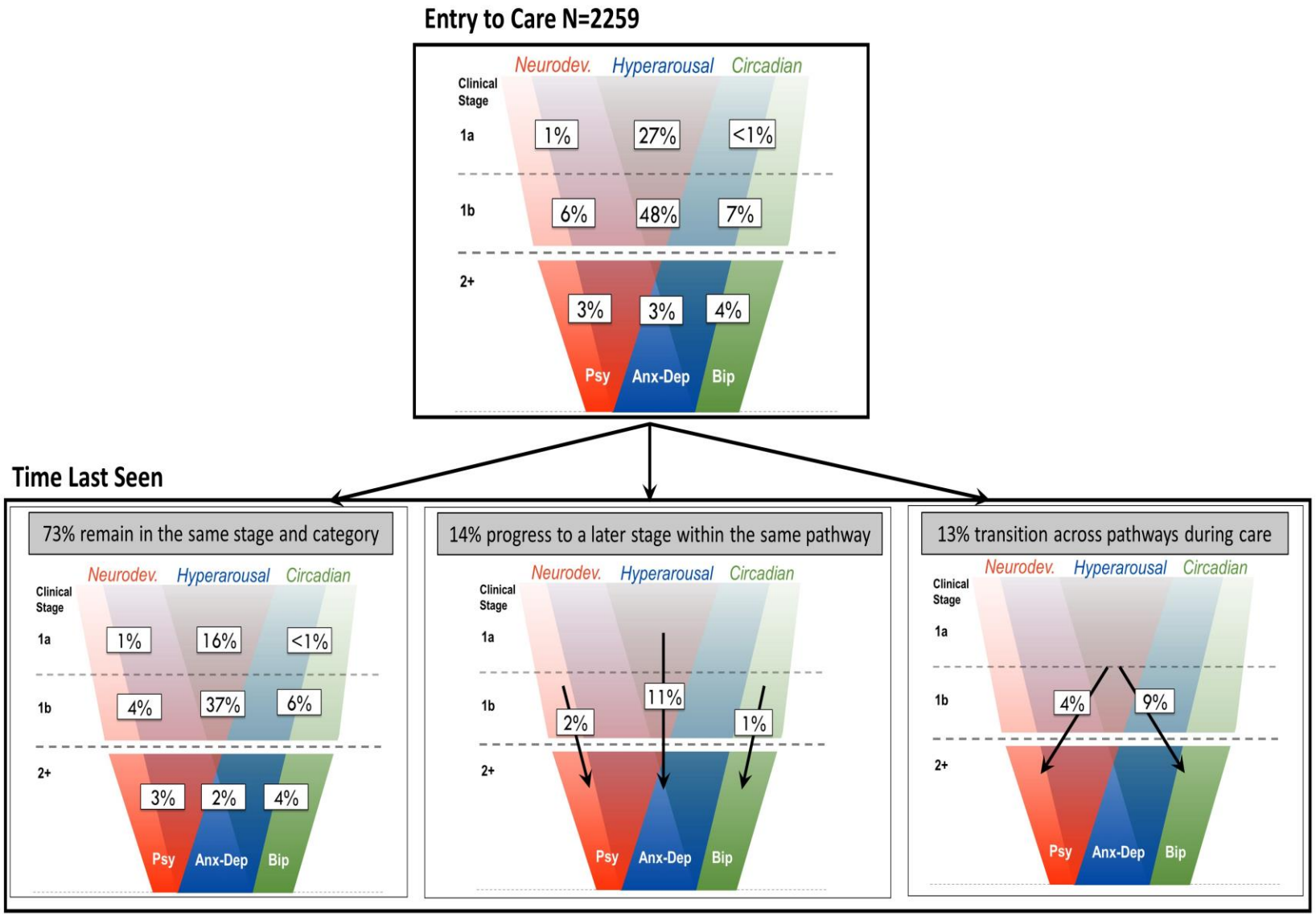
Measurement domain and study design	Key findings
Clinical domain, cross-sectional design	• Later clinical stages are associated with greater impairment in social and occupational functioning,[18,19,22,29] greater symptom severity,[22,29] greater distress[18,19] and greater disability[19]
Clinical domain, longitudinal design	• Psychological distress abates and functioning improves in stage 1 patients following 6–10 sessions of care, but stage 1b patients remain impaired[30] • Stage 1b patients make and miss more appointments than stage 1a patients[33] • Those who present at later stages have a greater rate of transition[5,13] • Predictors of transition include being female, negative symptoms, psychotic-like experiences, manic-like experiences, circadian disturbance, self-harm, lower social functioning, and lower engagement in education or employment[13,30] • Within stages, there are diverse ranges of individual symptomatic and functional change over time with only a small proportion of patients showing reliable deterioration or improvement at 6-month follow-up[5,32]
Neuropsychological domain, cross-sectional design	• Stage 1b and 2+ patients are both impaired across neuropsychological measures compared with controls, with greater impairments in stage 2+ patients compared with stage 1b patients[34,35] • The greatest impairments in stage 2+ patients are found in tests of verbal memory and executive functioning[34,35]
Neuropsychological domain, longitudinal design	• Neuropsychological measures either improved or did not significantly change at follow-up in stage 1b and 2+ patients[35] • Verbal memory improved in stage 1b patients relative to stage 2+ patients at follow-up[35] • The proportion of young people showing improvement or deterioration in neuropsychological variables did not differ between stages 1b and 2+[35]
Neuroimaging domain, cross-sectional design	• Both stage 1 and 2+ patients have a reduction in grey matter volume in frontal brain regions compared with controls[36] • Stage 2+ patients have more extensive grey matter loss in frontal brain regions compared with stage 1 patients, with the greatest loss occurring in a region bounded by the right superior and middle frontal gyri[36] • Diffusion tensor imaging showed both stage 1 and 2+ patients have disrupted white matter integrity in the left anterior corona radiata, with a greater extent of these white matter microstructural changes in stage 2+ patients[37]
Circadian domain, cross-sectional design	• There is a progressive increase in the proportion of young people with delayed sleep phase at later clinical stages, with significantly later sleep times in stage 1b and 2+ patients compared with controls[38] • Stage 2+ patients have reduced evening melatonin secretion and altered timing of melatonin onset relative to sleep compared with stage 1b patients;[39] this reduced melatonin secretion is also associated with lower subjective sleepiness and impaired verbal memory in those at stage 2+

7 Supporting evidence for pathophysiological mechanisms from the Brain and Mind Centre's Optymise Youth Cohort

Illness subtype	Proposed neurobiological features	Key findings
Neurodevelopmental–psychosis	• Childhood neurodevelopmental disorders • Cognitive impairment • Psychotic features	• More likely to be male and older at presentation to services[29] • Lower premorbid intelligence quotient and performance on neuropsychological measures, especially mental flexibility and verbal learning and memory[29] • Disproportionately represented in a data-driven cluster characterised by global neurocognitive impairment and lower functioning over 3 years (unpublished data) • Poorer social and occupational functioning at baseline and over the first 6 months of care, and less likely to be at early clinical stages of illness[29,60] • More likely to have a family history of psychotic disorders[29]
Hyperarousal–anxious depression	• Childhood anxiety • Heightened stress sensitivity • Adolescent depressive syndromes	• Those who have unipolar depressive disorders are more likely to report social anxiety compared with those who have bipolar-type illness[61] • More likely to have a family history of depressive disorders[29] • Reduced rates of alcohol or other substance misuse in those without psychotic or bipolar syndromes[62]
Circadian–bipolar spectrum	• Disrupted sleep–wake behaviours and circadian rhythms • Delayed sleep–wake timing • Atypical or bipolar spectrum symptom profile	• More likely to be female[63] • Delayed sleep–wake timing common and more pronounced in those who have bipolar-type illness compared with those who have unipolar mood disorders and controls[64,65] • Other sleep disturbances in bipolar-type illness include long sleep duration and more disturbed sleep[64] • Abnormal melatonin secretion patterns also reported in those who have bipolar-type illness[65] • Sleep–wake cycle disturbances predict increases in manic symptoms longitudinally[66] • More likely to have a family history of bipolar and anxiety disorders[29] • Family history of bipolar disorder is also associated with sleep–wake cycle disturbances[67] • Suicidal thoughts and behaviours have also been linked to bipolar-type illness[68]

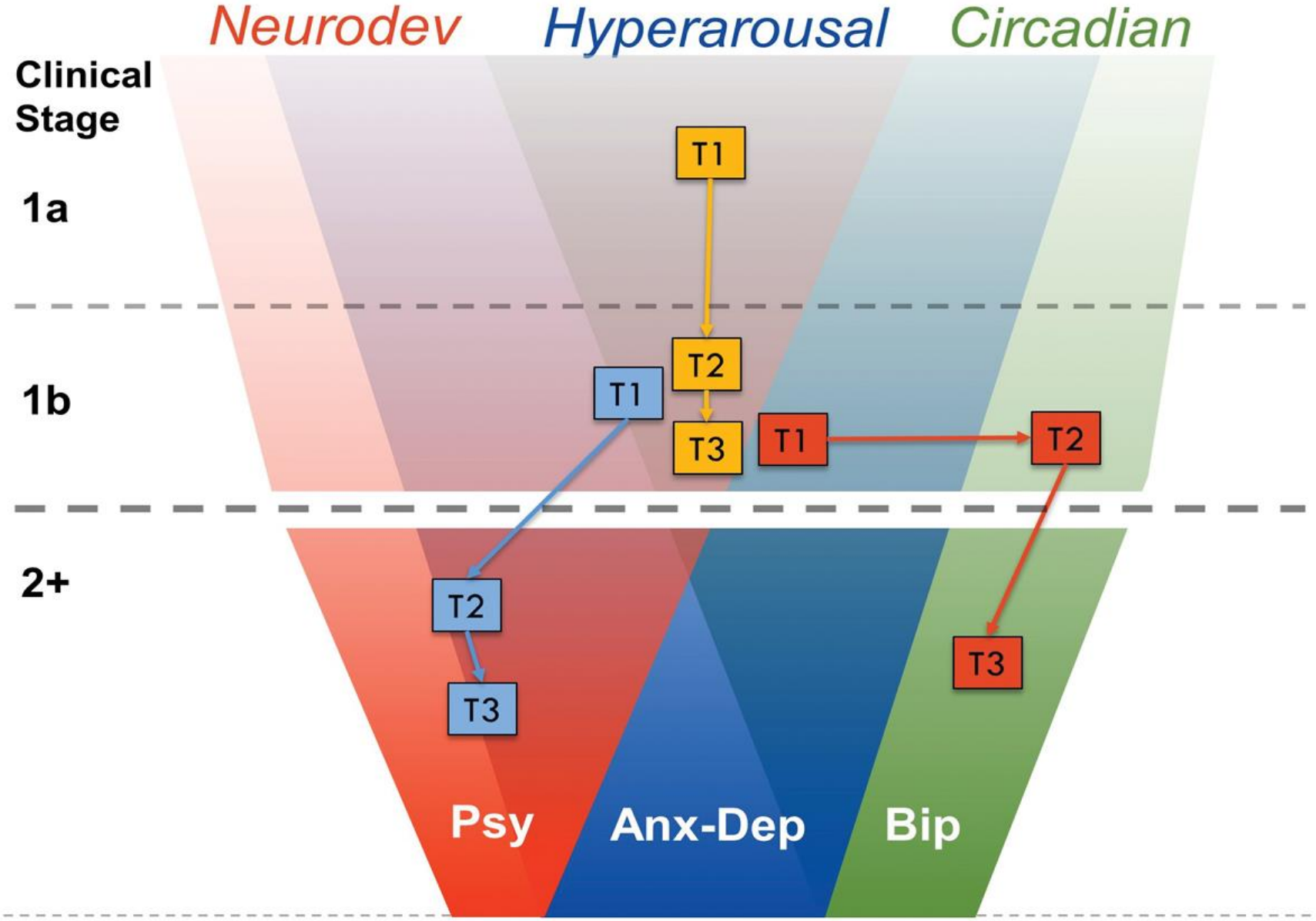
- The behavioural phenotypic expression of mood and psychotic syndromes typically follows one of three proposed pathophysiological mechanisms with different presenting syndromal features across development
- The development and maturation of biological systems provides an age-dependent context in which these interactions occur
- Genetic predispositions interact with various environmental influences across development from the prenatal period to young adulthood
- Some environmental influences are specific to certain developmental periods (e.g. early life adversity) while others may be present across development or may have varied influence at different phases (e.g. socioeconomic environment, diet, etc, as shown in green box at base of figure, are influences during both childhood and adolescence)





**Unpublished data from 2259 young people with at least 1 month of follow-up after entry to care.*

- Most young people first present in the hyperarousal–anxious depression pathway, and at earlier clinical stages
- Across the course of care, 14% progress to a later stage within the same pathway, and 13% transition across pathways, typically from earlier stages of hyperarousal–anxious depression to later stages of circadian–bipolar spectrum or neurodevelopmental–psychosis pathways



T1, T2 and T3 represent time points. Yellow indicates a typical hyperarousal–anxious depression illness trajectory, developing from non-specific to attenuated syndrome but not progressing to a discrete disorder. Blue indicates a typical neurodevelopmental–psychosis illness trajectory, initially presenting with stage 1b general depressive syndrome and then progressing to more severe psychotic-type illness. Red indicates a typical circadian bipolar spectrum illness trajectory, initially presenting with stage 1b anxious-depressive symptoms, then developing a presentation of circadian disturbance before progressing to a more distinct later stage bipolar-type syndrome.

Summary…

- The BMC Youth Model's transdiagnostic framework is supported by clinical, neuropsychological, neuroimaging, sleep-wake behavior and circadian rhythm evidence from our longitudinal database of young people (Optymise Youth Cohort)
- Compared to the use of traditional diagnostic classification systems in isolation, this framework could underpin the development of much more personalised, youth-relevant models of care

Thank you!

CPD points can be claimed for psychologists, psychiatrists, social workers, occupational therapists, and mental health nurses.
Please contact ***tanya.jackson@sydney.edu.au*** *for more information.*

The Brain and Mind Centre would like to thank our research partners, such as

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