Right care, first time: a highly personalised and measurement-based care model to manage youth mental health
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Supplement

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Right care, first time: a highly personalised and measurement-based care model to manage youth mental health

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Summary

- Mood and psychotic syndromes most often emerge during adolescence and young adulthood, a period characterised by major physical and social change. Consequently, the effects of adolescent-onset mood and psychotic syndromes can have long term consequences.
- A key clinical challenge for youth mental health is to develop and test new systems that align with current evidence for comorbid presentations and underlying neurobiology, and are useful for predicting outcomes and guiding decisions regarding the provision of appropriate and effective care.
- Our highly personalised and measurement-based care model includes three core concepts:
  - A multidimensional assessment and outcomes framework that includes: social and occupational function; self-harm, suicidal thoughts and behaviour; alcohol or other substance misuse; physical health; and illness trajectory.
  - Clinical stage.
  - Three common illness subtypes (psychosis, anxious depression, bipolar spectrum) based on proposed pathophysiological mechanisms (neurodevelopmental, hyperarousal, circadian).
- The model explicitly aims to prevent progression to more complex and severe forms of illness and is better aligned to contemporary models of the patterns of emergence of psychopathology. Inherent within this highly personalised approach is the incorporation of other evidence-based processes, including real-time measurement-based care as well as utilisation of multidisciplinary teams of health professionals.
- Data-driven local system modelling and personalised health information technologies provide crucial infrastructure support to these processes for better access to, and higher quality, mental health care for young people.

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Chapter 1
Multidimensional outcomes in youth mental health care: what matters and why?

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Mood and psychotic syndromes (including anxiety, depression, bipolar disorder and psychosis) present one of the most serious public health challenges in the 21st century. They affect fundamental aspects of human life — our ability to work, function and develop quality social relationships — and too often lead to the early loss of life. About one in every three individuals is affected by such mental disorders over their lifetime, and studies continuously show they are a leading cause of years lost to disability.1–3 Young people in particular are at risk, with over 75% of adult mental disorders emerging before the age of 25 years4,5 and over 45% of the total burden of disease for those aged 10–24 years being attributed to mental disorders.6 Consequently, a key population health priority is to reduce the burden of these disorders so that their impact does not endure a lifetime.7–9

Much of the burden can be attributed to prevalence and early age of onset, which influence the chronicity and secondary risks (eg, suicidal thoughts and behaviours, alcohol or other substance misuse) associated with these disorders. Lifetime prevalence estimates indicate that up to one-third of young people meet diagnostic criteria for a mental disorder,10 while the 12-month prevalence among Australian young people aged 16–24 years was the largest across all age groups at about 26%.11 Studies consistently report such high prevalence rates for mental disorders before the age of 25 years, irrespective of whether or not they adhere to strict diagnostic rules about symptom thresholds and impairment.12–14 The prevalence of mental disorders during youth poses a risk for future health and wellbeing outcomes precisely due to the time at which they tend to emerge.

Adolescence and young adulthood is a critical period of biological and social development. Usually beginning with the onset of puberty, major physical and neurobiological changes occur, characterised by the development of key brain circuits responsible for higher order cognitive and emotional functions that, if suboptimal or disrupted, can have a significant impact on behaviours and the development of disorder.15–22 This period is also characterised by significant social development as young people embark on the early phases of their careers via education and employment, and engage in more complex relationships with friends, family, and intimate and sexual partners. During this time young people face increasing diversity in potential life trajectories as they move from relatively restricted and homogenous environments, such as school and home life, to environments characterised by greater independence and variability in new educational, employment and social environments.23 For some, this transition may occur without major disruption; however for others, this change in context and roles can lead to maladaptive functioning or can manifest and amplify underlying problems.24 Thus, the biological and social complexity of adolescence and young adulthood means that young people are susceptible to the onset of mental health problems that may have a long term impact on outcomes in adulthood.15,25,26

Summary
- Mood and psychotic syndromes present one of the most serious public health challenges that we face in the 21st century. Factors including prevalence, age of onset, and chronicity contribute to substantial burden and secondary risks such as alcohol or other substance misuse.
- Mood and psychotic syndromes most often emerge during adolescence and young adulthood, a period characterised by major physical and social change; thus, effects can have long term consequences.
- We propose five key domains which make up a multidimensional outcomes framework that aims to address the specific needs of young people presenting to health services with emerging mental illness. These include social and occupational function; self-harm, suicidal thoughts and behaviours; alcohol or other substance misuse; physical health; and illness type, stage and trajectory.
- Impairment and concurrent morbidity are well established in young people by the time they present for mental health care. Despite this, services and health professionals tend to focus on only one aspect of the presentation — illness type, stage and trajectory — and are often at odds with the preferences of young people and their families.
- There is a need to address the disconnect between mental health, physical health and social services and interventions, to ensure that youth mental health care focuses on the outcomes that matter to young people.

Evidence for a multidimensional outcomes framework
The impact of mood and psychotic syndromes extends beyond the symptoms that define them. They affect many aspects of human life which typically establish during adolescence and young adulthood (ie, social relationships, education, employment skills and experience). Thus, it is not surprising that 22 years of age is identified as the age at which the maximum negative impact of a disabling illness occurs.27 Since young people are more likely to present with multidimensional needs,28 health service strategies should be in place to identify and respond to a range of health and social issues with the appropriate type and intensity of intervention.29 We propose five key domains that make up a multidimensional outcomes framework to address the specific needs of young people presenting to health services with emerging mental illness (Box 1):
- social and occupational function;
- self-harm, suicidal thoughts and behaviours;
- alcohol or other substance misuse;
and/or medical interventions as part of standard care. Data for longitudinal follow-up were collected for the duration of each participant’s engagement with the clinical services and/or participation in research sub-studies.

**Social and occupational function**

Prospective longitudinal studies have demonstrated that the presence of a mental disorder before the age of 16 years affects economic potential (ie, reduced income by 28%) and social relationships (ie, marriage instability) of adults aged 50 years. Moreover, individuals who had a mental disorder between the ages of 18 and 25 years were more likely to have lower occupational participation, income and living standards by 30 years of age. The effect of mood and psychotic syndromes on these outcomes is greater than the impact of physical health problems among young people, and is present even when the mental disorder is subthreshold or has remitted. This illustrates that even though adolescent-onset mood and psychotic syndromes may dissipate by adulthood, due to the nature of the adolescent and young adulthood period, they may have already affected an individual’s ability to function economically and socially over the course of their life.

Among young people presenting to health services, well established social and occupational functional impairment is common. Rates of disengagement from education, employment and training are about 25%, which is nearly twice the national average for young people, although for those engaged in employment or education, functional impairment due to mental ill health tends to manifest as higher rates of days out of role. While such findings have been common in the literature on individuals at risk of psychosis and those who have experienced first-episode psychosis, they have not been as extensively delineated in these early mood disorder populations. Further, greater functional impairment at entry tends to be associated with neurocognitive problems or difficulties, more severe mood or psychotic symptoms and concurrent substance (notably cannabis) misuse. Over time, while impairment may vary considerably for individuals, the overall pattern is largely one of stable trajectories, whereby the degree of impairment at entry to care is the main predictor of long term course.

Social and occupational function typically varies at entry into care and has a discrete relationship with each of the other key outcomes (Box 2). Most importantly, there is a significant subpopulation (characterised as stage 1b, see Chapter 2) of people who have not yet developed a persistent or full-threshold disorder but are already impaired and often remain largely impaired or deteriorate further despite the provision of standard clinical care. As would be expected, prior research suggests that young

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### 1 Multidimensional outcomes framework for young people with emerging mood and psychotic syndromes

- **Physical health**
- **Illness type, stage, and trajectory.

Some of the studies discussed below come from the University of Sydney’s Brain and Mind Centre’s Optimyse Youth Cohort. This cohort includes 6743 individuals aged 12–30 years, 57% of whom are female. They presented to the Brain and Mind Centre’s youth mental health clinics in the Sydney suburbs of Camperdown and Campbelltown and, after consenting, were recruited to a research register between June 2008 and July 2018. Individuals were either self-referred, referred via a family member or friend, or the community (eg, general practitioner) to these clinics which include primary care services (ie, headspace) as well as more specialised mental health services. Demographic data, clinical data such as presentation by Diagnostic and statistical manual of mental disorders diagnosis, substance use, personal history of mental illness, current treatment and functional data such as scores on a social and occupational functional assessment scale and engagement in education and employment were collected from research and clinical files to assess longitudinal outcomes. Subsets of this cohort have completed neuropsychological and neurobiological assessments as part of additional associated research protocols (Chapter 3). All participants received clinician-based case management and psychological, social,
people who present with greater impairment and further developed mental health syndromes require more intensive treatments and resources, yet are less likely to recover. In contrast, those with milder symptoms and impairment are more likely to recover after a briefer period of care.  

Self-harm, suicidal thoughts and behaviours

Mood and psychotic syndromes are consistently associated with self-harm, suicidal thoughts and behaviours, which increase the risk of death by suicide and the overall burden of these disorders. 51 Lifetime prevalence estimates indicate that almost 10% of the population across the world experience suicidal ideation and about 5% engage in suicidal behaviours (ie, plans or attempts), with the peak age of onset occurring during adolescence and young adulthood. 53,54 The overall rate of these behaviours is up to three times higher among young people than older adults, yet young people are also less likely to recover. In contrast, those with milder symptoms and impairment are more likely to recover after a briefer period of care.  

Alcohol or other substance misuse

Concurrent alcohol or other substance misuse is often recognised as an important comorbid condition for anxiety and depressive disorders but is rarely subject to systematic evaluation, or intervention within mental health care services. 61,62 Up to 15% of young people with a prior mental disorder engage in alcohol or other substance misuse, 63 while about one-third of young people have established alcohol or other substance misuse at entry to health services. 37 More frequent alcohol or other substance misuse is associated with older age, being male and having psychotic or bipolar disorders. 37 Alcohol or other substance misuse contributes to the overall impact of mood and psychotic syndromes, since it tends to be associated with greater disability 64 and impaired productivity and interpersonal functioning. 65 The outcomes are particularly poor among those who start to use alcohol or other substances and they are not restricted to those with more severe illness types. 35,36 This contrasts with data from an Australian survey which showed that 8% of teenagers had expressed suicidal ideation and 2% had attempted suicide in the previous 12 months. 60 While engagement with care is associated with a reduction in repeated suicidal behaviours, new experiences of suicidal thoughts and behaviours emerge during care, particularly among those whose illness course and trajectory is worsening and in association with alcohol or other substance misuse. 24 These findings have important implications for an enhanced focus on reducing self-harm, suicidal thoughts and behaviours throughout the course of clinical care for all of those who present to such services, not just those who are perceived as higher risk.
at an early age, with lower socio-occupational functioning, manic-like experiences, suicidal ideation and risky drinking being more common than among those who start later.

These results emphasise the importance of early assessment regarding the potential contribution of alcohol or other substance misuse to the individual’s current impairment and any self-harming behaviours which may be present, as well as the potential impact on physical health, illness type (particularly bipolar disorders) and illness course. Additionally, these data emphasise the potential for secondary prevention of alcohol or other substance misuse by active management of common mood and psychotic syndromes before the age of likely exposure to such substances. Again, broad-based secondary prevention strategies should be a core feature of service delivery — particularly for younger people (i.e., under the age of 18 years) presenting for care. Active management of comorbid disorders early in the course of illness has the potential to not only reduce longer term substance misuse-determined morbidity and mortality but significantly improve functional outcomes more broadly and reduce the morbidity due to self-harm and suicidal thoughts and behaviours.

Physical health

The pervasive impact of mood and psychotic syndromes extends to other chronic physical illnesses, such as diabetes and cardiovascular disease, and is particularly evident in the relationship between depression and early death due to cardiovascular disease. All mood and psychotic syndromes are associated with an increased risk for the onset of a range of chronic physical health conditions, with population estimates suggesting that the onset of up to 13% of physical health conditions could be attributed to such syndromes. The comorbidity between physical and mental health conditions is associated with an increased burden of disease, with evidence suggesting that comorbidity is more burdensome than physical health conditions alone or in combination. While the adverse physical health consequences of persistent mental illness in middle-aged people is now well recognised, the opportunity to prevent this morbidity and premature mortality in those who present with adolescent-onset mood and psychotic syndromes has not yet been realised. Current data suggest that physical health problems and risk factors for later poor physical health are common in young people presenting to care, with up to one-third smoking daily, which is three times higher than the age-matched Australian population. While the patterns of overweight (20%) and obesity (10%) are comparable to the age-matched Australian population, the rate of women who are underweight is higher than that of the general population at 10%. Youth cohorts engaged in mental health care tend to have increased weight and often develop insulin resistance, and recent evidence suggests that increasing body mass index is associated with emerging insulin resistance.

These data highlight key opportunities, notably related to cessation of smoking tobacco, preventing weight gain and providing early active interventions for metabolic disturbance, hormone dysfunction or concurrent autoimmune and other inflammatory conditions. Given the notable emergence of comorbid physical health problems in those who continue to engage with care, particularly among those who are treatment-resistant or develop significant neurological or metabolic side effects from medications, there is a gap in knowledge and thus a need for more interventional studies that attempt to reduce risks of later onset cardiovascular disease, or more proactive approaches (e.g., metformin therapy) for those at risk of developing insulin resistance. It is likely that we will need to develop and evaluate new screening and active intervention protocols to achieve better outcomes in this at-risk population. While a current focus on dealing with these risks in early psychosis cohorts is laudable, we need to adopt a much more proactive and evidence-informed approach to the clinical care of those with adolescent-onset mood and psychotic syndromes.

Illness type, stage and trajectory

Many mood and psychotic syndromes that emerge early in life persist into adulthood, particularly those with longer duration of illness or recurrent episodes in adolescence. While diagnostic manuals are used to guide the diagnosis and treatment of these disorders, they have been heavily criticised for their lack of validity and inability to account for the huge heterogeneity of disorders among young people. Consequently, there has been a major shift towards transdiagnostic approaches among younger populations, to better match diagnosis and treatment with the common developmental psychopathology of mood and psychotic syndromes and specific service settings. Part of this shift has been to apply clinical staging as an adjunct to formal diagnosis. Clinical staging recognises that the boundaries between common mood and psychotic syndromes are often
unclear and that an approach which accounts for their comorbidity is needed (Chapter 2). 3,7,9,83–87

The comorbidity between different mood and psychotic syndromes has been well established in both clinical and community samples. 88–91 About 40% of adolescents with one mental disorder meet the criteria for two or more lifetime disorders, 89 and studies consistently show that major depression and anxiety disorders are particularly comorbid conditions. 92 The presence of comorbidity is associated with greater illness severity, 75,93 poorer response to treatment, 94 greater role impairment, 92,95 and higher rates of suicidality. 96–98 Thus, young people with mood and psychotic syndromes are not only at risk of persistent disorders in adulthood, but at risk for multiple disorders that often lead to poorer outcomes.

In addition to clinical staging, knowledge of the underlying pathophysiology (Chapter 2) which may be driving the development of a mental disorder is important for guiding treatment decisions. The validity of three common illness subtypes (psychosis, anxious depression and bipolar spectrum) based on proposed pathophysiological mechanisms (neurodevelopmental, hyperarousal and circadian) is supported by demographic, family history and neuropsychological data (Chapter 2). 3,9,42 In the Brain and Mind Centre’s Optymise Youth Cohort, psychotic or bipolar phenomena (including psychosis-like experiences, mania-like experiences and circadian disruption) are common, occurring in 40% of the sample, and are often comorbid, with considerable overlap between these phenomena 43 (Box 3). Our previous work has demonstrated the extent to which

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### 5 Various stakeholder perspectives of what should be the focus for mental health care across multidimensional domains

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Note: The findings presented here are based on a literature review. The shading of each box indicates the priority level for each of the domains across the different stakeholder groups, based on group consensus of the available literature. Dark shading = high priority; medium shading = moderate priority; light shading = low priority.
psychosis-like experiences and circadian disruption predict progression to more severe mood and psychotic syndromes, as determined by clinical staging. In this cohort, these phenomena were measured at a low threshold and were not necessarily sufficient to warrant inclusion in a psychotic or bipolar illness category; however, the data demonstrate the overlap in key characteristics, softening the boundaries between different illness types and trajectories.

Expanding the focus in youth mental health care

Collectively, these studies underscore the broader impact of mood and psychotic syndromes on the capacity of young people to make the transition into adulthood and reach their actual health, social and economic potential. It is also clear that impairment and concurrent morbidity are well established among young people by the time they present for mental health care (Box 4). These results emphasise the extent to which the treatment of mood and psychotic syndromes should not be limited to a discrete set of symptoms, but rather, focus more broadly on outcomes across multiple domains to address the core needs of young people with emerging disorders. Psychological symptoms, such as depression or anxiety, are often reported as the main reason for presentation to services, however, as discussed above, educational, vocational, social and physical health problems are also prevalent issues.

The extent to which the focus of mental health care extends beyond mental illness type or psychological symptoms is variable. The priority for focus differs depending on whether you are a young person, family member or carer, health professional or service provider, policy maker or funder (Box 5). Young people do not tend to rate symptom reduction as high as health professionals in relation to quality of life, whereas they do tend to rate social relationships and physical health as more important for quality of life. This type of mismatch in focus, or expectations about positive outcomes, is often reflected in the outcomes on which services and health professionals traditionally focus. Most outcome measures focus on symptoms, and services tend to focus exclusively on group-level symptom reduction as indicators of improvement or positive outcomes.

The consequences of this are that young people are left to coordinate their own social and physical health needs, which places increased burden on family and carers who try to help them navigate the health system to get the support they require for these areas. Together, this emphasises the need to address the disconnect between mental health, physical health and social services and interventions, to enable mental health care to focus on the outcomes that matter most to young people.

Conclusion

Young people with mood and psychotic syndromes are susceptible to poorer social, physical and mental health outcomes — many of which are already present and well established at their entry into care. This emphasises the need for models of care which prioritise a multidimensional outcomes framework and more closely align to their preferences and needs, as well as those of their families. We believe this will give them the best chance of leading fulfilled and engaged lives in adulthood.

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trajectories for self-reported psychological to depression by age 16 years: examining 
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DSM-5 and RDoC: progress in psychiatry correlates of DSM-IV disorders in the National 

adolescents: a 14-year prospective cohort prognosis of common mental disorders in 
P a t t o n    G C   ,    C o f f e y    C   ,    R o m a n i u k    H   ,  e t  a l .   T h e 

framework for choosing earlier, safer and more staging of psychiatric disorders: a heuristic 


Chapter 2
Combining clinical stage and pathophysiological mechanisms to understand illness trajectories in young people with emerging mood and psychotic syndromes

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Despite the vast majority of major mental disorders having their onset in adolescence or early adulthood,1 current diagnostic frameworks often map poorly onto the early stages of illness. Young people commonly experience less specific syndromes with mixed clusters of symptoms that do not clearly fit within specified categories and thresholds.2–5 Further, diagnostic categories in these frameworks (based exclusively on sets of presenting symptoms) are assumed to represent independent clinical categories. However, comorbidity is the rule rather than the exception in young people, and research regarding genetic, environmental and neurobiological risk factors does not readily support current assumptions regarding classification.6–11

Considering the inadequacies of current diagnostic classification systems, an important clinical challenge is to derive new diagnostic frameworks. These should be consistent with the current understanding of developmental epidemiology and neurobiology, reflect the experiences of individuals across the course of illness, and provide utility when used in a clinical setting for facilitating informed decisions regarding care and treatment. In response to this challenge, we have developed a transdiagnostic framework incorporating two independent but complementary dimensions to classify common mood and psychotic syndromes in young people (Box 1). These two dimensions are clinical stage, reflecting the severity and persistence of illness, and pathophysiological mechanisms, reflecting the proposed underlying mechanisms of illness and their individual trajectories (or pathways). These two dimensions are key tools for the assessment of clinical presentation within our larger multidimensional framework (Chapters 1 and 3) and are intended to be used as adjuncts to formal diagnosis. We describe these dimensions in detail in this chapter, and also present data from the University of Sydney’s Brain and Mind Centre (BMC) Optymise Youth Cohort — a group of young people who were included in a longitudinal study tracking multidimensional outcomes for the duration of their engagement with youth mental health clinics at the BMC (Chapter 1).2,11

Clinical staging

The concept of clinical staging is widely used and accepted in various areas of medicine (eg, oncology) in which it is inappropriate to treat conditions based on an ambiguous illness category (eg, treating all presentations of breast cancer equally). Rather, staging attempts to place an individual on a continuum from risk to end-stage disease and then determines treatment using evidence-based pathological boundaries. Applying the same concept in mental health, it is not optimal to plan preventive, early intervention strategies and/or treatment plans based on broad illness categories such as schizophrenia or major depression. The use of clinical staging in mental health care is supported by preliminary evidence that suggests there are different patterns of response to specific interventions at different points along the continuum of mental illness.14–17 Further, levels of impairment in young people presenting for mental health care are high, despite being at early stages of mental disorders and often not meeting formal diagnostic criteria.18–22 This highlights a need to intervene with stage-appropriate care to reduce this distress and disability, and to prevent progression to later stages. In contrast to previous research (eg, early-psychosis research), the emphasis in our clinical staging framework is on transdiagnostic transition from earlier to later stages of illness, rather than transitions to full-threshold disorders within narrow diagnostic bands. Clinical stages in our model are an adjunct to formal diagnosis, and the demarcation between stages does not equate
to the cut-off points for threshold diagnoses according to standard diagnostic classification systems (eg, *Diagnostic and statistical manual of mental disorders*<sup>23</sup> and International Classification of Diseases<sup>24</sup>).

**Illness progression in clinical staging**

Clinical staging can be applied to young people (aged 12–30 years) with mood and psychotic syndromes (including anxiety, depression, bipolar disorder, psychosis) presenting for mental health care. Earlier stages are characterised by lower rates of impairment and are associated with a lower risk of progression to more severe, disabling or persistent disorders. As with clinical staging in other areas of medicine, intervention at earlier stages is more likely to result in positive treatment outcomes. One key distinction is the differentiation between those in early phases (stages 1a and 1b) and those who have reached a higher threshold of disorder (stage 2 and above). Stage 2 is our proposed cut-off point for more persistent disorders requiring further specific and intensive clinical care and treatment.<sup>5,16,17</sup> Another key distinction is made in the earlier stage 1 disorders where we differentiate “attenuated syndromes” (stage 1b) — which often, but not always, meet criteria for specific mood or anxiety disorders according to diagnostic criteria — from more non-specific anxiety or depressive symptoms (stage 1a). Transitions across stage 1a to 1b and stage 2 are largely driven by severity of illness, whereas transitions to stage 3 and 4 are largely driven by persistence and recurrence of illness. While it is possible to recover from an acute episode of illness, individuals cannot move backwards across clinical stages once a threshold is reached. In instances of uncertainty about the appropriate stage, assessors are encouraged to rate down, assigning the earlier clinical stage until more evidence of progression becomes apparent. A decision tree outlining key clinical decisions (between stage 1 and 2, and between stage 1a and 1b) is provided in Box 2, and detailed descriptors of each stage are provided in Box 3. We have previously demonstrated the inter-rater reliability of clinical staging using this structured approach.<sup>5</sup>

The distinction between early stage 1 syndromes and more developed stage 2+ illnesses represents a key boundary between non-specific syndromes that may or may not progress, and more specific discrete disorders that are expected to persist or recur if appropriate intervention is not provided. This is particularly important across the adolescent period, when transient mood instability is common, and many experiences that may be considered “depressive syndromes” at early adolescent ages will spontaneously remit by late adolescence or early adulthood. In support of this, Box 4 illustrates recent data in a community-based cohort of adolescents showing that most depressive syndromes that meet the criteria for “caseness” in early adolescence (age 12 or 14 years) do not continue into later adolescence (age 16 years).<sup>25</sup> In the context of development, it is thus important to use appropriate levels of monitoring and care for those at early clinical stages with the expectation that most will not experience progressive continuation of illness.

At later clinical stages, recovery is expected to be less common and more difficult. One key aspect of recovery from mental illness is return to a normal level of functioning. Using the Social and Occupational Functioning Assessment Scale (SOFAS) as an indicator of functional recovery in the BMC’s Optymise framework of clinical stages, proposed pathophysiological mechanisms, and illness trajectories for the onset and course of adolescent-onset mood and psychotic syndromes *

Youth Cohort, Box 5 shows differences in recovery rates across stages (unpublished data). A greater proportion of those at earlier stages achieve functional recovery (as indexed by a SOFAS score in the normal range [ie, ≥ 70]) during the course of care, with functional recovery rates of 54% for stage 1a, 32% for stage 1b, and 24% for stage 2+ (Box 5). Further, those at earlier stages who do functionally recover, do so at a faster rate than those at later stages, starting with less functional impairment and achieving functional recovery earlier in the course of care. It should be noted that these data only represent those who continue to engage with care, so they cannot provide insight into recovery rates for young people who are no longer engaged with care. Nevertheless, these results highlight the importance of intervening early in the course of illness to maximise positive outcomes. Thus, the use of clinical staging, as an adjunct to formal diagnosis, may help guide decisions regarding the provision of appropriate and effective care options (Chapter 4).

**Illness extension in clinical staging**

Most clinical staging models employed in mental health settings have evolved primarily as a means of describing disease progression (ie, severity and persistence of illness). Often this means that attempts are made to include other phenomena — such as metabolic disturbances, alcohol or other substance misuse, or other problems that are significantly associated with mental disorders — in the progression dimension. While this approach is understandable, it has created some problems when trying to employ a transdiagnostic framework. An alternative is to try to separate disease extension from disease progression. While disease progression refers to worsening of the syndrome itself, disease extension refers to the spread of the syndrome to have wider reaching effects on multiple outcomes (analogous to the spread of physical disease to other areas of the body). It is important to stress, however, that this idea is an emerging concept. Nevertheless, as is seen in oncology (where, for example, tumour-node-metastasis models chart progression across several dimensions), it is expected that there is a range of disease extension that may occur within each stage. Therefore, in addition to an individual’s clinical stage, the degree of extension may help inform clinical decisions such as additional treatments targeting specific concerns (Chapter 4).

**Clinical and objective validation of clinical staging**

In the BMC’s Optymise Youth Cohort, we previously examined multiple clinical and objective factors in relation to clinical stage. It is clear from our studies that later stages are associated with greater distress and disability, and more functional impairment. Increased functional impairment at later stages is partially to be expected cross-sectionally because current levels of functioning are part of the clinical presentation used to assess clinical stage. However, those at later stages also remain functionally impaired longitudinally, highlighting the need for more intensive care for those at later stages. For example, we have found that, compared with stage 1a, those classified as stage 1b remain significantly impaired following 10 sessions of treatment despite greater service use, modest decreases in psychological distress and improvement in functioning. The first 3 months of treatment has been highlighted as a critical window for intervention in which most transitions from stage 1b to stage 2+ occur. Our data show that by 12 months, about 17% of those at stage 1b will have transitioned to a later stage. Among those classified at stage 1b, there are diverse patterns of symptomatic and functional change, with 25–30% showing reliable improvement, 10% showing reliable deterioration, and most showing neither linear improvement nor deterioration of symptoms and functioning when followed up for 6 months. Recently, we have reported in the BMC’s Optymise Youth Cohort that of those presenting to care at stage 1a, only 3% progress to stage 2+ by time last seen, whereas 13% of those presenting at stage 1b progress to stage 2+. In our longitudinal work, transition to later stages has been found to be predicted by negative symptoms, psychotic-like experiences, manic-like experiences, circadian disturbance, self-harm, lower social functioning, and lower engagement in education or employment.

*This is intended to be used in conjunction with Box 3 to assist in assigning clinical stage to young people receiving mental health care. The first key decision is between stage 1 and stage 2+, with young people at stage 2+ likely to require more specific and intensive interventions. For those at stage 1, the second key decision is between stage 1a and stage 1b, to determine whether the illness is at an early, non-specific stage with a low risk of progression, or has developed into an attenuated syndrome with a greater need for monitoring and intervention to prevent progression. The specification of stage 2, 3 or 4 in those assigned stage 2+ is a secondary distinction that may be made to provide more detail on the illness and treatment history.

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**Clinical decision-making principle:** Assign highest achieved in lifetime, and when in doubt, rate down and re-assess in 4-6 weeks.
### 3 Guidelines and detailed criteria for clinical stage*

<table>
<thead>
<tr>
<th>Clinical stage</th>
<th>Definition and clinical features</th>
<th>Additional information</th>
</tr>
</thead>
</table>
| **Stage 1a:** non-specific symptoms | Functioning — episode of illness is having a mild to moderate impact on social, educational or occupational function  
**plus**  
Depression — mild to moderate levels of depressive ideation without specific features indicative of more disabling syndromes  
**and/or**  
Anxiety — mild to moderate levels of arousal without significant or persistent avoidant behaviour |  
May include those with earlier childhood-onset symptoms who have re-presented or had worsening of symptoms 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  
Typically, adolescent or early adult populations assessed in primary care or educational settings or identified by screening in relevant primary care, employment or educational settings of relevant populations; may be referred to specialist settings for further assessment |
| **Stage 1b:** attenuated syndrome | Functioning — episode of illness is having a moderate to severe impact on social, educational or occupational function  
**plus**  
Depression — depressive syndromes of moderate severity without specific features indicative of a stage 2 syndrome  
**and/or**  
Anxiety — specific and more severe symptoms of anxiety, such as the development of specific avoidant behaviour  
**and/or**  
At-risk mental states — hypomanic symptoms and/or attenuated or brief psychotic symptoms  
Comorbidity — syndromes may be somewhat mixed in terms of their symptoms or complicated by alcohol or other substance misuse |  
May include those who meet diagnostic criteria for specific anxiety disorders, major depressive disorder or bipolar II disorder  
The presence of regular, deliberate self-harm without overt suicidal intent may occur in this stage; this includes impulsive low lethality overdose occurring in the context of psychosocial stressor and in the absence of severe depression  
Treatment may have already commenced and/or the person may have been referred for further specialised assessment  
Some degree of treatment with an antidepressant, antipsychotic or mood-stabilising agent is common, particularly where there has been limited access to specialised psychological therapies |
| **Stage 2:** full-threshold, major and discrete syndrome | Functioning — episode of illness is clearly having an ongoing and major impact on social, educational or occupational function  
**plus**  
Mania — clear manic syndrome during a specific illness event (hypomanic symptoms or brief hypomanic syndromes alone do not constitute a discrete disorder)  
**and/or**  
Psychosis — clear psychotic syndrome for more than 1 week  
**and/or**  
Depression — features indicative of more severe depressive syndromes including psychomotor retardation, marked agitation, impaired cognitive function, severe circadian dysfunction, psychotic features, brief hypomanic periods, severe neuro-vegetative changes, pathological guilt or severe suicidality  
**and/or**  
Anxiety — anxiety complicated by at least moderate to severe concurrent depressive syndromes; typically associated with significant or persistent avoidant behaviour, marked agitation, fixed irrational beliefs, overvalued ideas, attenuated psychotic symptoms, or substantial and persistent substance misuse  
Comorbidity — syndrome may remain mixed in phenomenological terms, not necessarily matching a single or discrete DSM-style disorder or corresponding to a specific cut-off point on a specific rating scale for anxiety, depressive, manic or psychotic symptoms; the primary discrete syndromes may co-occur, including significant and clear symptoms (depressive, manic or psychotic) in the context of a more severe persistent syndrome; and the significant comorbidity may include alcohol or other substance misuse, abnormal eating behaviour or other relevant psychological syndromes |  
Moderately severe mood or anxiety disorders that are complicated by significant and persistent alcohol or other substance misuse may reach this stage  
Typically, patients with discrete disorders have been referred to specialist services for further assessment or have been managed extensively by suitably qualified primary care or other interdisciplinary services  
If the patient has been hospitalised for treatment, then typically they would have met the criteria for this stage  
If the patient required very intensive outpatient care due to suicidal or homicidal intent, plan or history of attempt, florid or persistent psychotic or very severe depressive symptoms (eg, psychomotor change or psychotic features), they would have been likely to have met the criteria for this stage |
| **Stage 3:** recurrent or persistent illness | Functioning — over at least a 12-month period after entry to relevant specialist or enhanced primary care services, there has been clear evidence that the illness course has resulted in marked worsening in social, educational or occupational function due to persistence or recurrence  
**plus**  
Symptoms — either incomplete remission from discrete disorder at 12 months after entry to care following a reasonable course of treatment (of at least 3 months’ duration), or recurrence of discrete disorder after period of complete recovery (having fully recovered for at least 3 months) |  
Includes those with discrete disorders who are assessed and specifically treated for at least 3 months, but with poor response or incomplete response to treatment  
May include those with discrete disorders who have fully recovered but then relapse to the full extent described in Stage 2 |
| **Stage 4:** severe, persistent, and unremitting illness | Functioning — illness course is associated with clear evidence of marked deterioration in social, educational or occupational function due to persistence or recurrence  
**plus**  
Symptoms — 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 |  
Includes those with chronic, deteriorating severe depressive, bipolar, and/or psychotic illness, which may be complicated by alcohol or other substance misuse, that has persisted without remission for at least 2 years |

* DSM = Diagnostic and statistical manual of mental disorders. * Adapted from Hiskie and colleagues. Each stage is defined by a degree of functional impairment as well as severity and persistence of symptoms. Although symptom type is noted in the clinical descriptors, clinical stages are not expected to coincide with traditional diagnostic categories. It is highly likely that young people in the early phases of illness will have mixed symptoms that range across various diagnostic categories. Consequently, young people with the same formal diagnosis (eg, major depressive episode) may be rated as being at different clinical stages based on symptom profile, symptom severity, level of disability, need for hospitalisation and comorbid symptoms.
In our research examining objective factors related to clinical stage, we have used measures of neuropsychological function, brain structure and function, sleep–wake behaviours and circadian rhythms. This research has focused on the two major clinical stages of illness surrounding key transitions (ie, stage 1b and stage 2+) with the aim of determining the objective features that characterise the major demarcation point in adolescent-onset mood and psychotic syndromes. Our key findings to date, linking stage with clinical and objective measures, are summarised in Box 6.

Cross-sectionally, we have reported neuropsychological performance to be impaired in those at stage 2+ relative to controls, with those at stage 1b showing an intermediate profile, and the most prominent impairments being for verbal memory and executive functioning. Longitudinal follow-up of neuropsychological performance indicates that change in these measures is generally similar between those at stages 1b and 2+, despite those at stage 2+ being significantly more impaired at baseline. However, those at stage 1b show significant improvement in verbal memory compared with those at stage 2+, who show slight deterioration in verbal memory at follow-up, suggesting that verbal memory may be a particularly sensitive neuropsychological measure for distinguishing between earlier and later stages.

We have conducted two neuroimaging studies demonstrating structural differences between clinical stages. One of these studies showed that those at stage 2+ presented with decreased grey matter volumes within distributed frontal brain regions compared with controls and those at stage 1b; most prominently, this was in an overlapping region bounded by the superior and middle frontal gyri on the right side. The second study showed that those at stages 1b and 2+ presented with significant disruption in white matter integrity in the left anterior corona radiata, particularly in the anterior thalamic radiation, compared with healthy controls. These studies provide some support for delineating earlier stages from later stages of illness, given that there are measurable changes in the brain associated with stage 2 disorders, which to some degree can be differentiated from stage 1b disorders.

Using actigraphy monitoring to measure average rest and activity timing over several days, we have also found differences in sleep–wake behaviours between those at different clinical stages of illness. This is characterised by delayed sleep timing in those at stage 1b and stage 2+ compared with controls, with more severe delays in those at stage 2+ compared with those at stage 1b. To explore the biological basis of these behavioural sleep–wake delays, we have examined evening dim-light melatonin secretion to quantify circadian rhythm parameters. This study showed that the timing of the evening rise in melatonin secretion did not differ between stages, but reduced levels of evening melatonin and shorter
This provides some initial support for clinical staging as a valid tool in distinguishing stages of illness independent of current mental state. In general, these abnormalities are not associated with clinical or functional markers in the clinical presentation. Any cases with significant mania-like symptoms or significant atypical features (e.g., reduced activation and energy, prolonged sleep or prolonged fatigue) are allocated to the “circadian–bipolar spectrum” illness subtype. This subtype is derived from probabilistic and dimensional models that differentiate mood disorder presentations that are more likely to follow a bipolar course, characterised by atypical features, circadian disturbance, and dysregulated activation and energy including increased need for sleep.45–49 Cases of adolescent-onset mood and psychotic syndromes with a current primary psychotic disorder or a history of childhood-onset significant and persistent developmental difficulties (such as an autism spectrum disorder, specific learning disability, or low intelligence quotient) are allocated to the “neurodevelopmental–psychosis” illness subtype. It is important to note that neurodevelopmental difficulties can also occur outside the context of mood and psychotic syndromes, and that cases are not allocated a position within this framework unless a mood and psychotic syndrome is present. This neurodevelopmental–psychosis subtype is consistent with meta-structures proposed for the redevelopment of diagnostic pathways for young people with mood and psychotic syndromes which may represent underlying pathophysiological mechanisms.5–9 These pathophysiological mechanisms emphasise neurodevelopmental impairments, heightened arousal and stress sensitivity, and circadian rhythm dysregulation (Box 1). In young people presenting with any type of mood and psychotic syndrome, our model is used to allocate one of these three proposed pathophysiological mechanisms on the basis of the clinical presentation.44,45 Any cases with significant mania-like symptoms or significant atypical features (e.g., reduced activation and energy, prolonged sleep or prolonged fatigue) are allocated to the “circadian–bipolar spectrum” illness subtype. This subtype is derived from probabilistic and dimensional models that differentiate mood disorder presentations that are more likely to follow a bipolar course, characterised by atypical features, circadian disturbance, and dysregulated activation and energy including increased need for sleep.45–49

### Proposed pathophysiological mechanisms

A lack of knowledge surrounding the optimal meta-structure for differentiation of major mental disorders has hindered progress in research into objective markers of illness risk, progression, and response to treatment.80–83 Consequently, there is a need to identify pathophysiologically based phenotypes in broad transdiagnostic populations to advance our understanding of how disorders develop and guide decisions regarding the provision of appropriate and effective care options (Chapter 4). This is particularly important in the early stages of mood and psychotic syndromes where clinical phenotypes often do not meet diagnostic thresholds and are not reliably distinguished in conventional frameworks. Focusing on adolescents and young adults close to the onset of these disorders has the added advantage of reducing confounding factors related to chronicity, secondary morbidity and prolonged exposure to treatments.

We propose at least three common illness trajectories (or pathways) in young people with mood and psychotic syndromes.
### 7 Supporting evidence for pathophysiological mechanisms from the Brain and Mind Centre’s Optymise Youth Cohort

<table>
<thead>
<tr>
<th>Illness subtype</th>
<th>Proposed neurobiological features</th>
<th>Key findings</th>
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<tbody>
<tr>
<td>Neurodevelopmental–psychosis</td>
<td>Childhood neurodevelopmental disorders, Cognitive impairment, Psychotic features</td>
<td>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})</td>
</tr>
<tr>
<td>Hyperarousal–anxious depression</td>
<td>Childhood anxiety, Heightened stress sensitivity, Adolescent depressive syndromes</td>
<td>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(^{29})</td>
</tr>
<tr>
<td>Circadian–bipolar spectrum</td>
<td>Disrupted sleep–wake behaviours and circadian rhythms, Delayed sleep–wake timing, Atypical or bipolar spectrum symptom profile</td>
<td>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(^{65}) 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})</td>
</tr>
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**Supplement**

classification systems,\(^{40,50,51}\) and is based on evidence linking neurodevelopmental abnormalities with increased risk of developing psychotic phenomena.\(^{52–55}\) Remaining cases, typically those reporting childhood anxiety and later stress sensitivity with evolving depressive disorder symptoms are allocated to the “hyperarousal–anxious depression” illness subtype. This is also the default subtype for those without clear evidence of a circadian–bipolar spectrum or neurodevelopmental–psychosis subtype. It is aligned with research emphasising stress sensitivity in anxiety and unipolar mood disorders, and with models of neural fear circuitry, prolonged stress responses, and glucocorticoid-dependent arousal.\(^{36–39}\)

It is important to note that the three proposed pathophysiological mechanisms do not represent mutually exclusive pathways, and individuals may shift between pathways over time. Across all stages of illness, there is a degree of overlap between the three pathways, as illustrated in Box 1. In early clinical stage, this is demonstrated by mixed presentations of non-specific symptoms. At later clinical stages, syndromes may be more specific, but are often accompanied by comorbid conditions (such as alcohol or other substance misuse), greater functional impairment and neurobiological effects. Previous research from the BMC’s Optymise Youth Cohort supporting these three proposed pathophysiological mechanisms is summarised in Box 7.

Our previous research has shown that those in the neurodevelopmental–psychosis subtype are more likely to be male, are older at presentation to services, and present with less severe anxiety and depressive symptoms, distress, and suicidality.\(^{29}\) This subtype also presents with poorer social and occupational functioning, lower premorbid intelligence quotient, and poorer performance on neuropsychological measures (including marked dysfunction on tests of mental flexibility and verbal learning and memory). Further, we have found that a cluster of young people with global neuropsychological impairment and poorer functioning over 3 years are more likely to have psychotic illness (unpublished data).

When examining young people in our cohort who have a bipolar course of illness (circadian–bipolar spectrum subtype), we have reported that a greater proportion present with a delayed sleep–wake profile (>60%) compared with those who have unipolar mood disorders and controls\(^{64,65}\). Circadian rhythm abnormalities appear to accompany these sleep–wake delays, with reduced and delayed evening melatonin secretion profiles in young people who have bipolar illness compared with those who have unipolar illness.\(^{65}\) A neurobiological basis for these circadian abnormalities is supported by associations between delayed rhythms and neurochemical alterations.\(^{69,70}\) Analysis of sleep–wake behaviours and circadian rhythms in a transdiagnostic sample further corroborates the presence of this subtype with delayed sleep and circadian rhythms, which is not exclusively restricted to a bipolar diagnosis according to traditional classification systems.\(^{71–73}\) In addition, we have found in our longitudinal research that sleep–wake disturbances are predictive of increased manic symptoms at follow-up.\(^{66}\)

Overall, this research provides initial support for three proposed pathophysiological mechanisms and pathways, with differing objective profiles between groups. The validity of the pathophysiological mechanisms is also supported by our findings that the neurodevelopmental–psychosis subtype is more likely to have a family history of psychotic disorders and less likely to have a family history of depression, while the circadian–bipolar spectrum subtype is more likely to have a family history of anxiety and bipolar disorders, and the hyperarousal–anxious depression subtype is more likely to have a family history of depression.\(^{29}\) A family history of bipolar disorder has also been linked to specific subjective and objective sleep–wake cycle disturbances in our cohort, including increased sleep time and more variable sleep–wake patterns.\(^{67}\) As illustrated in Box 8, the pathways are expected to have different patterns of onset of clinical characteristics across development, with evolving behavioural presentations and increasing comorbidity. The evolution of mood and psychotic syndromes occurs in the context of age-dependent developmental and
environmental influences. That is, genetic predispositions interact with different environmental exposures across the lifespan, including psychosocial stressors, traumatic events, physical health insults, and educational, occupational or socioeconomic pressures. Progressive development of various biological systems, including neural, hormonal, circadian and immune maturation, influence these interactions to generate complex individual presentations with the onset of diverse clinical phenomena at different points along the life course.

Combining clinical staging and proposed pathophysiological mechanisms for a transdiagnostic framework

The combination of clinical staging and the proposed pathophysiological mechanisms into one transdiagnostic framework is shown in Box 1. Assigning individuals to a location in the framework is intended to assist in clinical decisions regarding appropriate care and treatment (Chapter 4). Tracking movement or progression in the framework over time will enable a greater understanding of individual illness trajectories and key intervention points. Box 9 shows the distribution and movement of the BMC’s Optymise Youth Cohort across clinical stages and proposed pathophysiological mechanisms (unpublished data). At baseline, 28% are at stage 1a, 61% are at stage 1b and 10% are at stage 2+; 78% are classified as being in the hyperarousal–anxious depression pathway, 11% in the circadian–bipolar spectrum pathway and 11% in the neurodevelopmental–psychosis pathway. Over the course of care, 27% progress across stages and between pathways, including 14% progressing to later stages within the same trajectory and 13% progressing between pathways (typically through the development of psychotic, hypomanic or manic phenomena, or without stage progression). Accordingly, while the three proposed pathophysiological mechanisms represent common pathways in which most individuals remain over time, there are multiple unique trajectories
within the model that an individual may take across the course of their illness. Box 10 illustrates three case examples of potential illness trajectories over time, reflecting movement from non-specific symptoms into more specific and severe syndromes.

**Limitations**

This transdiagnostic framework is intended to be applied to adolescent-onset mood and psychotic syndromes in young people presenting for mental health care. It does not encompass all mental illness presentations (eg, eating disorders) or young people who have persistence of their childhood onset disorders (eg, autism spectrum disorders and attention deficit hyperactivity disorder) without development of a subsequent adolescent-onset mood and psychotic syndrome, although these may exist as precursors or comorbid conditions. While the research to date is promising, further validation of the objective underpinnings of clinical stages and pathophysiological mechanisms is necessary to support the framework and inform treatment implications. The potential utility of this framework for improving clinical care for mental illness in young people is a focus of ongoing research at the BMC.

**Conclusion**

Our transdiagnostic framework combining two independent but complementary dimensions of clinical staging and pathophysiological mechanisms in common adolescent-onset mood and psychotic syndromes is supported by clinical, neuropsychological, neuroimaging, sleep–wake behaviour and circadian rhythm evidence from the BMC’s Optymise Youth Cohort. It is important that future research clarifies any longitudinal relationships between objective correlates of both clinical stages and the proposed pathophysiological mechanisms in young people with mental illness. Prospective biological research is
also needed to validate the distinctions between stages and pathways in our model and compare our proposed boundaries to other clinical or data-driven subtypes. Further elaboration of this framework could provide a greater understanding of the underlying clinical and objective features of these disorders. It also has the potential to inform advances in treatment development and personalising care options. Compared with the use of traditional diagnostic classification systems in isolation, it could underpin the development of much more personalised, youth-relevant models of care.

43 Hickie IB, Scott J, Hermens DF, et al. Clinical classification in mental health at the

Right care, first time

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Chapter 3
A comprehensive assessment framework for youth mental health: guiding highly personalised and measurement-based care using multidimensional and objective measures

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The burden of mental disorders is due to a combination of factors including illness onset during adolescence, population prevalence, chronicity, comorbidity with physical illness, and concurrent alcohol or other substance misuse.1,2 To reduce this burden, earlier identification and enhanced long term care of those who are most at risk have been prioritised.3–6 However, young people often present with subthreshold mental health disorders that are not yet sufficiently severe to meet traditional diagnostic criteria. Moreover, the clinical presentations of young people are often further complicated by normative developmental changes in mood, sleep and neurobiology which drive changes to symptoms and functioning. Consequently, young people rarely get the appropriate level of care matched to their unique personal needs.7–11 Enhanced personalised care must be underpinned by a thorough and comprehensive assessment from the very first presentation to services, which in addition to documenting the clinical syndrome requires an evaluation of the broader impacts on: social and occupational function; self-harm, suicidal thoughts and behaviour; alcohol or other substance misuse; physical health; and illness type, stage and trajectory.12,13 The assessments we recommend are based on their importance to functioning and physical and mental health outcomes (Chapter 1), as well as a consideration of the pathophysiological mechanisms underlying an individual’s illness trajectory or pathway (Chapter 2). Innovation in clinical services requires expanding assessments beyond mental health symptoms to facilitate the development of highly personalised and measurement-based care plans13–15 (Chapter 4), which may represent a more cost-effective approach to current models of mental health care.7 The multidimensional outcomes framework (Chapter 1) and the pathophysiological mechanism and illness trajectory model (Chapter 2) are novel tools which facilitate the capture of a comprehensive clinical picture and aim to guide highly personalised and measurement-based care (Chapter 4). The multidimensional outcomes framework comprises five key domains that overtly recognise that mental disorders are part of a broader general health construct and are embedded within a social and neurodevelopmental context (Chapter 1). The pathophysiological mechanism and illness trajectory model attempts to describe the processes underlying the development of common adolescent-onset mood and psychotic syndromes (Chapter 2). Evaluation of these pathophysiological mechanisms is based on objective assessments including neuropsychological function, sleep–wake behaviours and circadian rhythms, metabolic and immune markers, and brain structure and function. Finally, clinical staging aims to establish where a young person is along an illness continuum, which is then used to guide interventions that are commensurate to that stage (Chapters 2 and 5).

Assessments targeting multidimensional outcomes, pathophysiological mechanisms and illness trajectories

The multidimensional outcomes framework is used to guide the standardised assessment of five key domains (Chapter 1):

- social and occupational function;
- self-harm, suicidal thoughts and behaviours;
- alcohol or other substance misuse;
- physical health; and
- illness type, stage and trajectory.

Numerous validated scales and questionnaires have been developed to assess a broad spectrum of features which are associated with these five key domains. Box 1 provides a panel of established measures which can be used to obtain a comprehensive evaluation...
### 1 Multidimensional measures, with prioritised assessments in bold

<table>
<thead>
<tr>
<th>Domain</th>
<th>Self-report or clinical measures</th>
</tr>
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<tbody>
<tr>
<td><strong>Social and occupational function</strong></td>
<td>Education or employment engagement: ie. Not in Education, Employment or Training (NEET) status</td>
</tr>
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<td><strong>Social and Occupational Functioning Assessment Scale (SOFAS)</strong>: a global rating of current functioning ranging from 0 to 100, with lower scores denoting lower functioning. The SOFAS differs from the similar Global Assessment of Functioning (GAF) scale by focusing on social and occupational functioning independent of the overall severity of the individual’s mental health symptoms. It also differs from the GAF by including impairments that are caused by both physical and mental disorders, thereby making a useful and holistic assessment tool for traumatic brain injury and other neurological disorders. To be scored, impairments need to be directly effects of mental and physical health problems rather than a consequence of lack of opportunity or environment. A self-rating adaptation of this questionnaire can be used if necessary.</td>
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<td></td>
<td><strong>Everyday function and daily activity</strong>, for example:</td>
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<td></td>
<td>- <strong>World Health Organization Disability Assessment Schedule (WHO-DAS 2.0)</strong>: a 36-item generic assessment instrument for health and disability that assesses standardised disability levels and profiles across all diseases, including mental, neurological and addictive disorders.</td>
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<td></td>
<td>- <strong>Work and Social Adjustment Scale (WSAS)</strong>: a five-item scale of functional impairment attributable to an identified problem.</td>
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<td><strong>Social relationships and support</strong>, for example:</td>
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<td>- Schuster’s Social Support Scale (SSSS): a 15-item measure of social support used to examine an individual’s social relationships with others (relatives, friends, spouse) and the associated impact on their emotional functioning.</td>
</tr>
<tr>
<td><strong>Self-harm, suicidal thoughts and behaviour</strong></td>
<td><strong>Suicidal ideation frequency and severity</strong>, for example:</td>
</tr>
<tr>
<td></td>
<td>- <strong>Suicidal Ideation Attributes Scale (SIDAS)</strong>: a five-item self-report questionnaire assessing the frequency, controllability, closeness to attempt, distress and interference with daily activities over the past month.</td>
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<td><strong>Engagement in self-harm and suicidal behaviours</strong>, for example:</td>
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<td></td>
<td>- <strong>Columbia-Suicide Severity Rating Scale (C-SSRS)</strong>: a questionnaire used for suicide assessment developed by multiple institutions, including Columbia University, with National Institute of Mental Health support. This scale is intended to be used by individuals who have received training in its administration. The questions contained in the C-SSRS are suggested probes. Ultimately, the determination of the presence of suicidal ideation or behaviour depends on the judgement of the individual administering the scale. The scale comprises three sections: suicidal ideation, intensity of ideation, and suicidal behaviour. A self-rating adaptation of this questionnaire can be used if necessary.</td>
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<td></td>
<td>- <strong>Brief Non-Suicidal Self-Injury Assessment Tool (B-NSSI-AT)</strong>: the short version of the NSSI-AT to assess primary (such as form, frequency and function) and secondary (including but not limited to NSSI habituation, contexts in which NSSI is practised, and NSSI perceived life interference, treatment and impacts) characteristics.</td>
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<tr>
<td><strong>Alcohol or other substance misuse</strong></td>
<td><strong>Alcohol misuse</strong>, for example:</td>
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<td></td>
<td>- <strong>Alcohol Use Disorders Identification Test (AUDIT)</strong>: a ten-item translucal screening tool to detect excessive alcohol consumption, dependence and alcohol-related problems, first developed by the WHO in 1989. Both clinician-administered and self-report versions are provided.</td>
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<td><strong>Alcohol and substance misuse</strong>, for example:</td>
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<tr>
<td></td>
<td>- <strong>WHO-ASSIST</strong> (see description above)</td>
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<tr>
<td></td>
<td>- <strong>Hooked on Nicotine Checklist (HONC)</strong>: a measure of the loss of autonomy over tobacco use in youths. It comprises 10 questions that assess if the sequelae of tobacco use, either psychological or physiological, present a barrier to quitting.</td>
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<tr>
<td><strong>Physical health</strong></td>
<td><strong>Height, weight and waist circumference</strong></td>
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<td><strong>Physical activity</strong>, for example:</td>
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<td></td>
<td>- <strong>International Physical Activity Questionnaire (IPAQ) – short version</strong>: a seven-item questionnaire providing internationally comparable data on health-related physical activity</td>
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<td>- <strong>activity trackers, such as Fitbit</strong></td>
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<tr>
<td></td>
<td>- <strong>WHO-ASSIST</strong> (see description above)</td>
</tr>
<tr>
<td></td>
<td>- <strong>Hooked on Nicotine Checklist (HONC)</strong>: a measure of the loss of autonomy over tobacco use in youths. It comprises 10 questions that assess if the sequelae of tobacco use, either psychological or physiological, present a barrier to quitting.</td>
</tr>
<tr>
<td><strong>Illness type, stage and trajectory</strong></td>
<td><strong>Lifetime mental illness history and current psychiatric symptoms</strong> (including previous Diagnostic and statistical manual of mental disorders or International Classification of Diseases diagnoses)</td>
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<td></td>
<td><strong>Clinical staging</strong> (see Chapter 2)</td>
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<td></td>
<td><strong>Further illness type specific measurements</strong> (see Box 2)</td>
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<td><strong>Medical history</strong></td>
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<td><strong>Family history of mental illness</strong></td>
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<td><strong>Treatment utilisation history</strong>, for example:</td>
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<td></td>
<td>- <strong>previous hospitalisation</strong></td>
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<td></td>
<td>- <strong>previous pharmacological and psychological interventions</strong></td>
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<td></td>
<td><strong>Other mental health syndromes</strong>, for example:</td>
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<td></td>
<td>- <strong>Primary Care PTSD Screen for DSM-5 (PC-PTSD-5)</strong>: a five-item screen designed for use in primary care settings. The measure begins with an item designed to assess whether the respondent has had any exposure to traumatic events. If a respondent denies exposure, the PC-PTSD-5 is complete with a score of 0. However, if a respondent indicates that they have experienced a traumatic event over the course of their life, five additional yes/no questions need to be completed about how that trauma exposure has affected them over the past month. The PC-PTSD-5 was designed to identify respondents with probable PTSD. Those screening positive require further assessment.</td>
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<td><strong>Eating Disorder Examination Questionnaire (EDE-Q)</strong>: a 28-item self-report questionnaire based on the EDE structured, respondent-based clinician-rated interview. It is a widely used measure to assess eating disorder attitudes and behaviours. The EDE-Q uses a seven-point forced-choice rating scale (0–6) with scores of 4 or higher indicative of clinical range. The subscale and global scores reflect the severity of eating disorder psychopathology.</td>
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</tbody>
</table>
of impairments across the domains. Box 2 summarises validated scales and questionnaires which can be used to assess three proposed pathophysiological mechanisms and their illness trajectories, namely neurodevelopmental–psychosis, hyperarousal–anxious depression, and circadian–bipolar spectrum (Chapter 2). These measures capture specific dimensions of mental health disorders including anxiety, depression, bipolar disorder and psychosis.

Importantly, the assessments listed in Box 1 and Box 2 are freely accessible and predominantly available as self-report questionnaires. As some of the assessments are detailed and take

<table>
<thead>
<tr>
<th>Illness subtype</th>
<th>Self-report or clinical measures</th>
<th>Objective measures</th>
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</thead>
<tbody>
<tr>
<td>Neurodevelopmental–psychosis</td>
<td>Psychotic syndrome, for example:</td>
<td>• Neuropsychology</td>
</tr>
<tr>
<td></td>
<td>• Prodomal Questionnaire (PQ-16):33 a brief 16-item version of the 92-item Prodomal Questionnaire.32 This self-report screen is used to select subjects for interviewing for psychosis risk. The PQ-16 consists of three subscales: “perceptual abnormalities (hallucinations),” “unusual thought content/delusional ideas (paranoia),” and “negative symptoms.”</td>
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<td>• Community Assessment Psychiatric Experiences (CAPE-42):34 a 42-item questionnaire that evaluates the positive, negative and depressive dimensions of psychotic symptoms.</td>
<td>• Neuropsychology</td>
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<td></td>
<td>• Comprehensive Assessment of At Risk Mental States (CAARMS):35 a semi-structured interview that assesses psychopathology thought to indicate imminent development of a first-episode psychotic disorder and determines if an individual meets criteria for being at ultra-high risk for onset of first psychotic disorder.</td>
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<td>Social cognition, for example:</td>
<td>• Social cognition (eg, reading the mind in the eyes test)</td>
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<td>• Empathy Quotient (EQ-15):37,38 a short version of the 60-item self-report EQ questionnaire measuring empathy.</td>
<td>• Neuropsychology</td>
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<td></td>
<td>• Social Responsiveness Scale (SRS):39 a 65-item screening tool to identify social impairment associated with autism spectrum disorders and quantifies its severity. A self-report version is available.</td>
<td>• Neuroimaging</td>
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<td></td>
<td>Neurodevelopment, for example:</td>
<td>• Metabolic</td>
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<td></td>
<td>• Autism Spectrum Quotient questionnaire (AQ-10):40 a ten-item self-report questionnaire for adolescents or adults with a possible autism spectrum disorder who do not have a moderate or severe learning disability. The AQ-10 helps to identify whether an individual should be referred for comprehensive autism assessment.</td>
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<tr>
<td>Hyperarousal–anxious depression</td>
<td>Depressive syndrome, for example:</td>
<td>• Psychophysiology (eg, startle responses, heart rate variability)</td>
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<td></td>
<td>• Quick Inventory of Depressive Symptomatology (QIDS):41 a rating scale that assesses the nine criterion symptom domains (sleep, sad mood, appetite/weight, concentration/decision making, self-view, thoughts of death or suicide, general interest, energy level, and restlessness/agitation) designated by DSM-IV to diagnose a major depressive episode. The short version includes 16 questions with equivalent weightings (0–3) for each symptom item and is available as a clinician-rated and self-report scale.</td>
<td>• Neuropsychology</td>
</tr>
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<td></td>
<td>• Patient Health Questionnaire (PHQ-9):42 a nine-item self-report questionnaire for common mental disorders, which scores each of the nine DSM-IV depression criteria as 0 (not at all) to 3 (nearly every day).</td>
<td>• Neuroimaging</td>
</tr>
<tr>
<td></td>
<td>Anxiety syndrome, for example:</td>
<td>• Metabolic</td>
</tr>
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<td></td>
<td>• Overall Anxiety Severity and Impairment Scale (OASIS):43 a five-item self-report measure assessing severity and impairment associated with any anxiety disorder or multiple anxiety disorders. It evaluates frequency of anxiety, intensity of anxiety symptoms, behavioural avoidance and functional impairment associated with anxiety. The instructions ask the patient to consider a variety of experiences such as panic attacks, worries and flashbacks, and to consider all of their anxiety symptoms when answering the questions. The OASIS is therefore potentially applicable to any anxiety disorder and should be able to simultaneously assess severity and impairment associated with multiple anxiety disorders.</td>
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<td>• Generalised Anxiety Disorder Questionnaire (GAD-7):44 a seven-item, self-report screening tool and severity indicator for generalised anxiety disorder, developed to increase the recognition of the disorder in primary care settings.</td>
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<tr>
<td>Circadian–bipolar spectrum</td>
<td>Manic syndrome, for example:</td>
<td>• Actigraphy monitoring</td>
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<td></td>
<td>• Altman Self-Rating Mania Scale (ASRM):44 a five-item self-rating scale designed to assess the presence and/or severity of manic symptoms. Each question measures a specific manic symptom (ie, elevated mood, inflated self-esteem, decreased need for sleep, pressured speech and psychomotor agitation). Items are rated in increasing severity from 0 (absent) to 4 (present to a severe degree).</td>
<td>• Neuroimaging</td>
</tr>
<tr>
<td></td>
<td>Sleep–wake behaviours and circadian rhythms, for example:</td>
<td>• Metabolic</td>
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<td></td>
<td>• Pittsburgh Sleep Quality Index (PSQI):46 a nine-item self-report questionnaire to measure the quality and patterns of sleep, whereby seven domains are assessed (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction).</td>
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<td>• Munich Chronotype Questionnaire (MCTQ):47,48 a 13-item self-report questionnaire to assess the individual phase of entrainment on work and work-free days. The tool collects primary sleep times, such as bed and rise times, plus the clock time of becoming fully awake as well as sleep latency and inertia, in addition to other time points; individuals rate themselves as one of the seven chronotypes.</td>
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considerable time to complete, we emphasise that health professionals should aim to achieve an overall assessment that is comprehensive but minimises burden to consumers (eg, time, cognitive load). We therefore recommend that health professionals select at least one measure from each domain and pathophysiological mechanism/illness trajectory.

However, practical benefits of self-report scales and questionnaires are that they can be time-efficient, can often be completed by consumers without guidance and can therefore be implemented within health information technologies (HITs) such as the InnoWell Platform (Project Synergy, InnoWell Pty Ltd). The InnoWell Platform is an emerging HIT which aims to support prevention, early intervention, treatment and continuous monitoring of mental ill health and maintenance of wellbeing (https://www.innowell.org/). It has been developed to improve the delivery of mental health care by services and health professionals and for consumers, and validation of the Platform is currently underway in a clinical trial. Such novel HITs can facilitate the delivery of comprehensive assessments, reduce the burden on the face-to-face system, ease disclosure of embarrassing problems, expedite an earlier response to risk, enhance consumer engagement, simplify longitudinal monitoring and create the potential for highly personalised and measurement-based care (Chapter 4). While the inclusion of self-report assessments in clinical services and HITs (such as the InnoWell Platform) is intended to reduce health professional and consumer burden, we recognise that health professionals may need to guide some consumers through self-report scales and questionnaires, which may require greater effort and time — health professionals should therefore aim to achieve an appropriate balance.

In addition to self-report assessments, objective measures provide crucial insights into the potential pathophysiological mechanisms underpinning illness trajectories and facilitate informed intervention and treatment decisions (Chapter 4). For example, neuropsychological evidence of an impairment in verbal memory may be used to personalise cognitive training interventions, while actigraphic evidence of a sleep–wake cycle disturbance may guide treatments targeting specific disturbances of sleep–wake behaviours and/or circadian rhythms (eg, light therapy or melatonin supplementation). A panel of recommended objective measures is summarised in Box 2 and discussed in depth in the following sections.

**Objective measures to understand the drivers of multidimensional outcomes, pathophysiological mechanisms and illness trajectories**

Objective measures offer health professionals and researchers the ability to characterise an individual’s phenotype (ie, their clinical phenomena and objective markers) at any given time along an illness trajectory, and develop understanding of the factors driving the evolution of mental illness and the associated impacts on multidimensional outcomes. An enhanced identification of such abnormalities in young people with mental disorders will facilitate highly personalised and measurement-based care as interventions can be tailored to their unique characteristics (Chapter 4). Consider, for example, two young people presenting to clinical services with an emerging mood disorder. Both report symptoms of moderate depression (persistently depressed mood, anhedonia); however, one shows abnormalities in sleep–wake behaviour, while the other reports normal sleep behaviour but shows deficits in verbal memory and attention. A highly personalised and measurement-based care plan would include interventions and treatments designed to recalibrate sleep–wake behaviours and circadian rhythms in one young person (eg, light therapy), while the other may benefit from cognitive training targeting specific neuropsychological impairments (Chapter 4). In the following section, we discuss previous findings with a focus on how incorporation of measures of neuropsychological function, sleep–wake behaviours and circadian rhythms, metabolic and immune markers, and brain structure and function can refine the understanding of an individual’s phenotype and illness trajectory over time and reveal novel areas for targeted assessment, intervention and treatment.

Standard and further assessments for key neuropsychological, sleep–wake behaviours and circadian rhythms, metabolic and immune markers, and brain structure and function are summarised in Box 3.

**Neuropsychological function**

Neuropsychological assessment is an invaluable tool which aims to determine an individual’s abilities on a range of tests indexing functions such as speed of processing, immediate and delayed memory, sustained attention, decision making, and social cognitive functions such as theory of mind (ie, the ability to infer mental states of others) and facial and emotion recognition. While assessment of these functions is typically conducted by a clinical neuropsychologist, neuropsychological assessments are increasingly more accessible via online technology-based platforms such as the Cambridge Automated Neuropsychological Assessment Battery (https://www.cambridgecognition.com/cantab/), which affords greater accessibility and reduced burden on consumers. Performance on these measures is strongly linked to outcomes such as social and occupational functioning, and repeated measures of these functions can be used to understand changes in an individual’s illness (eg, advance toward a more severe, full threshold disorder).

In a cohort of over 1000 young people — one of the largest studies modelling the relationships between neuropsychological and social and occupational functioning — it was demonstrated that general neuropsychological performance is a better predictor than symptoms and alcohol or other substance misuse. Notably, about half of the variability in social and occupational functioning at follow-up (average, 22 months) is predicted by baseline neuropsychological functioning, with time series evidence suggesting a causal model whereby neuropsychological function is causally primary to functional outcome, consistent with previous reports. Further, the impaired performance on a measure of cognitive flexibility seems to be related to lesser improvement in social and occupational functioning over a 5-year period (unpublished data), which highlights the importance of identifying and targeting executive impairments alongside other recovery-oriented functional interventions.

The use of data-driven statistical techniques which use machine learning algorithms to uncover novel patterns in data are an emerging method of grouping individuals based on neuropsychological functioning, and may map more closely to objective or social and occupational outcomes than traditional diagnostic groupings. A longitudinal study showed that in two subgroups, improvements in verbal memory and sustained attention, respectively, were associated with greater improvements in social and occupational functioning compared with a third subgroup characterised by psychomotor slowing. Further, a subgroup characterised by global impairment had a poorer course of social and occupational functioning over a 3-year period (unpublished data). Importantly, this subgroup comprised individuals with all of the major mental disorders; however,
there was an over-representation of individuals with neurodevelopmental and psychotic syndromes, consistent with previous work.60 Additionally, individuals with more advanced stages of illness (ie, stages 2 and 3) have more impairments in neuropsychological function compared with those in an earlier stage (ie, stage 1b),39,67 highlighting the importance of assessing neuropsychological and neurophysiological domains in individuals with subsyndromal presentations to determine non-normative changes in brain function or structure.

There is increasing evidence that social cognition is strongly associated with social and occupational functioning and is a significant mediator of the relationship between neurocognitive and functioning.61 Deficits in social cognitive functions such as emotion perception (ie, inferring the emotional state of an individual), attributional style (ie, how one explains the causes of events), and theory of mind are common in psychotic and neuropsychological syndromes, consistent with previous research focus because of their sensitive developmental stages 2 and 3 have more impairments in neuropsychological and neurophysiological domains in individuals with subsyndromal presentations to determine non-normative changes in brain function or structure.

Sleep–wake behaviours and circadian rhythms

Sleep–wake behaviours and circadian rhythms have been a particular research focus because of their sensitive developmental maturation across adolescence and their key links to mental health and illness.64,65 Several assessment modalities to monitor the activity of various sleep–wake behaviours and circadian rhythms and guide further interventions targeting specific abnormalities are available. Actigraphy is a non-invasive method of monitoring cycles of rest and activity; it involves the wearing of an actigraph unit (usually in wristwatch form) over a period of days and weeks in which gross motor activity (and possibly light) is continuously measured. Rhythms of rest and activity are subsequently used alongside additional information (eg, sleep diaries) to infer parameters such as sleep onset and offset times, sleep midpoint, the time awake after sleep onset, and the total sleep time. Importantly, this assessment can be used to determine abnormalities in these parameters and evaluate the presence of a circadian rhythm sleep disorder (eg, phase delay), which is commonly reported in young people.64 Other laboratory-based assessments of sleep–wake behaviours and circadian rhythms include measurement of dim-light salivary melatonin concentration and timing of release; overnight core body temperature using ingestible temperature sensors; polysomnographic assessment of nocturnal sleep parameters; vigilance monitoring using neuropsychological or neurophysiological assessments.

Using such assessment techniques, abnormalities in sleep–wake behaviours and circadian rhythms have been reported to be common in mood and psychotic syndromes,66,67 with delayed timing of rest and activity a characteristic feature in adolescents and young adults.66 Abnormalities in sleep–wake and circadian parameters have important links with clinical state and the course of illness, with reports of associations between delayed circadian profiles and more severe depressive symptomatology,68 and associations between residual sleep–wake cycle disturbances and...
both persistent mood symptoms\textsuperscript{69} and increased risk of relapse.\textsuperscript{70} Increasing evidence indicates that identification and targeted correction of abnormalities in these parameters may assist in the resolution of symptoms.\textsuperscript{2} For instance, there are some reports of correction of circadian abnormalities following antidepressant treatment.\textsuperscript{71} Moreover, we have recently reported preliminary evidence that realignment of the circadian system is associated with the degree of response to agomelatine, a melatonin agonist antidepressant.\textsuperscript{72} Thus, knowledge of circadian disturbance in a young person presenting with a mood and psychotic syndrome may in future guide novel interventions and treatments targeting this potential pathophysiological mechanism (Chapter 4).

**Metabolic and immune markers**

There is global recognition of the premature death and disability costs attributable to common mental disorders.\textsuperscript{73,74} Chronic diseases of physical health such as cardiovascular disease and diabetes are common in individuals with full-threshold mental disorders.\textsuperscript{75} However, more research, mapping various risk factors against cardiovascular, metabolic and other health measures in young people at the earliest phases of illness, is urgently needed. These data are key to advancing our understanding of pathways to premature physical disease and the planning of treatment programs to redirect those illness trajectories. Measurement of metabolic, immune and physical health characteristics including body mass index, central obesity, pro-inflammatory cytokines (eg, interleukin 1 and 6, tumour necrosis factor-\textalpha{}, C-reactive protein) and fasting glucose and insulin levels are critical to furthering our understanding of these pathways.

To date, it has been shown that several key behavioural and cardiovascular risk factors are already present at the early phases of mental disorders. Use of alcohol, tobacco and cannabis are common and frequent,\textsuperscript{76} with an estimated one-third of young people accessing mental health services engaging in daily cigarette smoking,\textsuperscript{77} approximately three times the rate of the age-based Australian general population.\textsuperscript{78} These high rates of alcohol or other substance misuse are likely to contribute to increased risk of poor physical and/or mental health outcomes, especially if sustained. Further, associations between current use of psychotropic medication and increased body mass index have been observed,\textsuperscript{77} in addition to other metabolic disturbances such as glucose dysregulation.\textsuperscript{78} Importantly, there is evidence of emerging insulin resistance in a significant proportion of young people with emerging mental disorders, with about 10% of cases in one study having a homeostasis model of insulin resistance score greater than two (indicating development of insulin resistance).\textsuperscript{80} While fewer than 1% of this cohort had abnormally high fasting plasma glucose levels, continued monitoring of these parameters is necessary to identify at-risk individuals and pathways to pre-diabetes. One such major modifiable risk factor in this population is body mass index. However, a significant proportion of the variance in body mass index was not accounted for by other demographic, clinical or treatment factors, and further exploration using longitudinal monitoring of other factors such as disrupted circadian rhythms and 24-hour sleep–wake and activity patterns, concomitant inflammatory or immune processes, and dietary patterns are needed in order to address the unacceptable disparities in physical health and mortality between the general population and those experiencing mental health disorders.\textsuperscript{81,82}

Moreover, considerable research is needed to clarify the extent to which metabolic and immunological abnormalities represent side effects of medication usage or whether they are also related to underlying pathophysiological mechanisms.\textsuperscript{79,83}

**Brain structure and function**

Abnormalities in brain structure and function are likely to represent key drivers of poor clinical and multidimensional outcomes. Associations between magnetic resonance-based imaging of brain structure, connectivity and neurochemistry, and clinical symptoms, neuropsychological function, alcohol or other substance misuse and clinical stage may be used to guide the selection of interventions and treatments, with the aim of preventing neuroprogression and encouraging neuroprotection.

A number of objective abnormalities are evident at the earliest phases of illness and map to key clinical factors.\textsuperscript{84–86} With respect to clinical symptomatology, it has been demonstrated that reduction in grey matter volume in the anterior insula is associated with greater severity of general psychiatric symptoms and positive symptoms specifically.\textsuperscript{87} Moreover, reductions in measures of white matter integrity (connections between brain regions) that are indicative of disorganisation, reduction and/or loss of axons are associated with greater general psychiatric symptoms and worse positive, negative and depressive symptoms.\textsuperscript{88} Neuropsychological functioning has also been shown to be related to a number of objective measures across mental disorders,\textsuperscript{89,90} with important impacts on executive and memory domains, which are key predictors of social and occupational functioning. With respect to brain structure, reduced grey matter volume in the left anterior insula is associated with poorer attentional set-shifting\textsuperscript{87} (the ability to switch between one task and another), while cortical thinning in inferior parietal regions is associated with worse performance on tasks indexing visual sustained attention, semantic verbal fluency, and verbal learning and memory.\textsuperscript{91} Finally, reductions in white matter integrity in a key association tract (left superior longitudinal fasciculus) has been shown to be associated with impaired attention and semantic fluency.\textsuperscript{88}

Proton magnetic resonance spectroscopy can be used to explore the impacts of alcohol or other substance misuse on the brain’s major antioxidant, glutathione, and major excitatory neurotransmitter, glutamate. Robust associations have been observed between level of alcohol use and glutathione in the anterior cingulate cortex\textsuperscript{92,93} and hippocampus,\textsuperscript{94} as well as between level of alcohol use and glutamate in the hippocampus.\textsuperscript{95} These findings demonstrate that higher levels of alcohol use are related to lower levels of glutathione and higher levels of glutamate in key brain regions, which may in turn lead to aberrant brain changes associated with oxidative stress and excitotoxicity, respectively. Importantly, a longitudinal study showed that decreases in alcohol consumption and frequency of tobacco use are associated with normalisation of glutathione levels,\textsuperscript{95} indicating a modifiable treatment target for reducing oxidative stress and possibly neuroprogression.

Interestingly, there is evidence that individuals with differing clinical stages of illness (ie, stage 1b versus stages 2 and 3) may be differentiated by objective factors which may explain differences in clinical severity (Chapter 2). For instance, individuals with a more advanced stage of illness exhibit greater frontal grey matter loss\textsuperscript{86} and greater signs of white matter disruption.\textsuperscript{77} The gradients in grey matter loss and disruption to white matter organisation across clinical stages support the model of intense neuroprogression.

The presentation aiming to prevent transition to a more clinically and functionally impacted disorder, as has been demonstrated in early psychosis.\textsuperscript{96,97}
Genetic risk and polygenic risk scores

Our understanding of the genetic pathways underlying the major mental disorders has improved dramatically in recent years with the explosion in large international genetic consortia and genome-wide association studies. Contrary to expectations that there would be a specific mapping of genetic risk factors to specific mental health diagnoses, there is now strong evidence implicating many genes of pleiotropic effect across disorders, with significant overlap across major depressive disorder, bipolar disorder and schizophrenia, challenging the validity of the boundaries separating these diagnostic categories. Importantly, there also appears to be genetic continuity between individuals with full-threshold mental disorders and milder variation in characteristic traits for psychiatric phenotypes in the general population, indicating an important distributed gradient of risk.107

The key insight that considerable genetic heritability is shared across mental disorders suggests that polygenic risk scores may be used in psychiatry for risk prediction, prognosis and stratification. Polygenic risk scores summarise genome-wide data into a single composite variable which indexes an individual's genetic liability to a trait or disorder.108,109 Polygenic risk scores are increasingly used in other areas of clinical medicine such as cancer and heart disease,110 and the nature of their potential in psychiatry will become clearer with further identification of risk loci and evaluation of risk prediction in larger studies.111

Conclusion

The use of multidimensional and objective measures in research settings has allowed unprecedented opportunity to refine our understanding of some important clinical features in individuals with mental disorders. Further investigation of such parameters may continue to uncover novel subgroups of individuals who may be responsive to personalised therapies targeting their particular phenotypes (Chapter 4). A crucial next step is to determine whether translation of these measures into clinical practice leads to improved outcomes for consumers. We acknowledge that calls for more comprehensive assessment inherently require clinical support and expertise as well as more time and effort from consumers. We therefore recommend that health professionals carefully balance the benefits and costs of incorporating such measures into their clinical services until evidence becomes available to support their positive impact on consumer outcomes.

There are some important limitations to the comprehensive assessments framework detailed above. First, there are a number of illness- and recovery-related factors which are beyond the scope of the framework but may nonetheless warrant clinical attention because of their impacts on clinical and functional outcomes (eg, sexual trauma history, social support, and attitudes and beliefs about health and recovery). Second, we acknowledge that the utility of the multidimensional outcomes framework and pathophysiological mechanism and illness trajectory model has to date not been evaluated in clinical trials. However, a clinical trial of the InnoWell Platform (which incorporates this framework and model) is underway at the University of Sydney’s Brain and Mind Centre.17 If this new framework and model of care are validated, it will be a major step towards enabling highly personalised and measurement-based care which helps target interventions and treatments for young people with mood and psychotic syndromes.

22 van Spijker BA, Batterham PJ, Callear AL, et al. The suicidal ideation attributes scale (SIDAS): community-based validation study of a new scale for the measurement of suicidal ideation. Suicide Life Threat Behav 2014; 44: 408–419.
Parallel changes in mood and melatonin rhythm following an adjunctive multimodal chronobiological intervention with melatonin in people with depression: A proof of concept open label study. *Front Psychiatry* 2018; 9: 1–8.


Walsh T, McLellan JM, McCarthy SE, et al. Rare structural variants disrupt multiple genes in neurodevelopmental pathways in schizophrenia. *Science* 2008; 320: 533–543.


Chapter 4
Personalising care options in youth mental health: using multidimensional assessment, clinical stage, pathophysiological mechanisms, and individual illness trajectories to guide treatment selection

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M ajor mood and psychotic syndromes (ie, anxiety, depression, bipolar disorder, psychosis) typically have their onset in late childhood or early adolescence and emerge as a function of complex and bidirectional interactions between genetic and environmental factors. While a portion of these disorders remit after a single episode, many are recurrent and continue progressively into adult life.¹ Each individual follows genetic and environmental factors. While a portion of these as a function of complex and bidirectional interactions between disorder comorbidities, and ongoing functional impairment.⁶ hospitalisation, accumulation of greater physical and mental presentations to emergency departments, use of crisis services, suicidality, and ongoing functional impairment.⁶

However, current service delivery models are limited, resulting in young people frequently receiving no care or care that is not well matched to their individual needs.²⁻⁴ This can have adverse consequences including worsening of the syndrome,⁵ acute presentations to emergency departments, use of crisis services, hospitalisation, accumulation of greater physical and mental disorder comorbidities, and ongoing functional impairment.⁶

Poor matching of individuals to intervention occurs for a variety of reasons:

- current syndrome-focused classification systems, and matching clinical guidelines, are largely generic and often fit poorly to young people presenting with subthreshold mental disorders (eg, clinical features of one disorder may overlap with those of other diseases, or the most prominent presenting symptoms may not be those that most clearly define the established phase of the disorder)²⁻¹⁰
- multidimensional assessment and indicators of illness extension including social and occupational function, self-harm, suicidal thoughts and behaviours, alcohol or other substance misuse, and physical health are often neglected (Chapter 1);¹¹⁻¹³
- objective assessment profiles (Chapter 3) and pathophysiological mechanisms (Chapter 2) are often not recognised¹⁴⁻¹⁵ and selected interventions do not recognise the significance of clinical stage¹⁶⁻¹⁸ (ie, severity and persistence of the illness; Chapter 2).

Hence, a reorientation towards selecting active interventions considering the core concepts of multidimensional outcomes, clinical stage, underlying pathophysiological mechanisms and individual illness trajectories is critical to improving care for young people with emerging mood and psychotic syndromes (Chapters 1, 2 and 5).²⁻¹¹,¹² This new youth model of care could be described as stage-appropriate, transdiagnostic, effective, highly personalised and measurement-based. We believe this model would not only benefit young people with emerging disorders, but also people presenting with more severe and discrete mental disorders.

In a national survey conducted by beyondblue, it was shown that consumers and carers interacting with health professionals and

Summary
- New models of mental health care for young people require that interventions be matched to illness type, clinical stage, underlying pathophysiological mechanisms and individual illness trajectories. Narrow syndrome-focused classifications often direct clinical attention away from other key factors such as functional impairment, self-harm and suicidality, alcohol or other substance misuse, and poor physical health.
- By contrast, we outline a treatment selection guide for early intervention for adolescent-onset mood and psychotic syndromes (ie, active treatments and indicated and more specific secondary prevention strategies). This guide is based on experiences with the Brain and Mind Centre’s highly personalised and measurement-based care model to manage youth mental health.
- The model incorporates three complementary core concepts:
  - A multidimensional assessment and outcomes framework including: social and occupational function; self-harm, suicidal thoughts and behaviours; alcohol or other substance misuse; physical health; and illness trajectory.
  - Clinical stage.
  - Three common illness subtypes (psychosis, anxious depression, bipolar spectrum) based on three underlying pathophysiological mechanisms (neurodevelopmental, hyperarousal, circadian).
- These core concepts are not mutually exclusive and together may facilitate improved outcomes through a clinical stage-appropriate and transdiagnostic framework that helps guide decisions regarding the provision of appropriate and effective care options.
- Given its emphasis on adolescent-onset mood and psychotic syndromes, the Brain and Mind Centre’s model of care also respects a fundamental developmental perspective — categorising childhood problems (eg, anxiety and neurodevelopmental difficulties) as risk factors and respecting the fact that young people are in a period of major biological and social transition. Based on these factors, a range of social, psychological and pharmacological interventions are recommended, with an emphasis on balancing the personal benefit-to-cost ratio.

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service providers frequently experienced a fundamental lack of understanding of their situations, a sense of not being taken seriously, and an unwillingness to address their specific needs. Further, a survey of consumers presenting to psychiatric emergency services emphasised the importance of medical staff listening to their patients and involving them in shared decision making regarding treatment. These perspectives and reports of the factors that are most important to consumers are addressed by this new youth model of care.

Since the mid-2000s, stepped care has been promoted to improve the detection, treatment and outcomes of mental disorders. However, as described in Chapter 5 in more detail, prevailing service delivery models often operate using a “fail-first” approach, where the initial level of care is of low intensity and is only increased if the individual does not respond. New clinical staged care models that move beyond stepped care ensure that more intensive interventions are offered in a timely way and, thus, that young people receive the “right care, first time” (Chapter 5).

In this chapter, we outline a treatment selection guide for early intervention for adolescent-onset mood and psychotic syndromes, including active treatments and more specific secondary prevention. It is based on experiences with the Brain and Mind Centre’s (BMC’s) highly personalised and measurement-based care model to manage youth mental health (Box 2, and Chapters 1, 2, 3 and 5) and includes three complementary core concepts:

- a multidimensional assessment and outcomes framework (Chapters 1 and 3);
- personal illness onset and course, severity of illness and functional impairment to guide the nature of the intensity, duration and complexity of interventions (clinical staging model, Chapter 2); and
- individual illness trajectories, reflecting the putative underlying pathophysiology of common adolescent-onset mood and psychotic syndromes (illness trajectory model, Chapter 2).

These core concepts can be combined with tracking of measurement-based outcomes to help guide decisions regarding the provision of appropriate and effective care options — “right care, first time”. Service delivery using this approach is described in Chapter 5.
Interventions based on the BMC’s youth model of care

1. Interventions targeting the multidimensional outcome domains

To better address the individual needs of young people, we have developed a multidimensional assessment and outcomes framework\(^1,2,3\) (summarised in Chapters 1 and 3, particularly Box 1 in Chapter 1 and Boxes 1–3 in Chapter 3). This framework aims to capture a comprehensive and holistic representation of an individual’s presentation and broaden the scope of clinical attention to include other important factors. More precisely, it comprises five domains that specifically address the needs of young people with emerging mental illness:\(^1,2,3\)

- social and occupational functioning;
- self-harm and suicidal thoughts and behaviour;
- alcohol or other substance misuse;
- physical health; and
- illness type, stage and trajectory.

These domains are equally critical to preventing premature death or ongoing disability.\(^1,2,3,4\) Assessment and identification of individual needs in each of the outcome domains is a critical step in developing personalised care options, which we have described in greater detail elsewhere (Chapter 3). Recommended interventions targeting the first four of these domains are shown in Box 3, and interventions targeting the fifth domain are shown in Box 4. Importantly, interventions targeting specific multidimensional assessment and outcome domains are likely to also have indirect effects on other outcome domains. These direct and indirect effects are likely to cascade over time. A schematic representation of three hypothetical treatment paths and their longer term impacts is shown in Box 5.

2. Staged-based interventions targeting pathophysiological mechanisms and individual illness trajectories

Conventional models of mental health care place great emphasis on the presenting constellation of symptoms when deciding which treatments to select and reaching an arbitrary threshold for active interventions. This focus on symptoms and thresholds is of limited usefulness in young people, where symptoms are fluid over time and impairment is often well established in those who are subthreshold for any specific disorder.\(^2,5\) In addition, the syndromal categories (eg, major depression and generalised anxiety), as traditionally defined, are only based on symptoms and group together apparent symptoms of similar presentations, but are not linked with any proposed underlying pathophysiological mechanisms.\(^6,7,8\) However, based on experiences in general medicine (eg, cancer, heart disease and infectious diseases), the identification and classification of syndromes based on pathophysiology should eventually improve outcomes.\(^9\)

Accordingly, we have proposed a reorientation towards individual illness trajectories based on three pathophysiological mechanisms — which we argue underlie a substantial proportion of common adolescent-onset mood and psychotic syndromes.\(^1,2,3\) This transdiagnostic framework is described in depth in Chapter 2 and summarised in Box 1 of the Supplement.
Chapter 2). Briefly, three illness subtypes are based on the clinical presentation (significant psychotic-, depressive- or manic-like symptoms) and underlying pathophysiological alterations (neurodevelopmental impairments, heightened arousal or stress sensitivity, and circadian rhythm dysregulation, respectively).

A cross-sectional study provided preliminary support for the three pathophysiological mechanisms, and current research projects at the BMC are investigating the validity and potential implementation of this approach within mental health services.

Importantly, we do not claim that the three illness subtypes represent clearly defined and mutually exclusive pathways, but the framework allows individuals to shift across pathways over time (Chapter 2, particularly Box 1). Thus, the emphasis is on

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**4 Recommended psychological, social and pharmacological interventions based on illness trajectory**

<table>
<thead>
<tr>
<th>Illness subtype</th>
<th>Psychological or social interventions</th>
<th>Pharmacological interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurodevelopment–psychosis</td>
<td>- Social skills training(^{(18)})</td>
<td>- Fish oil(^{(53,54)})</td>
</tr>
<tr>
<td></td>
<td>- Social recovery therapy(^{(29)})</td>
<td>- Aripiprazole(^{(65)})</td>
</tr>
<tr>
<td></td>
<td>- Physical activity(^{(40,61)})</td>
<td>- Quetiapine(^{(66)})</td>
</tr>
<tr>
<td></td>
<td>- Education engagement</td>
<td>- Other atypical antipsychotics(^{(67)})</td>
</tr>
<tr>
<td>Hyperarousal–anxious depression</td>
<td>- Transdiagnostic CBT-based interventions(^{(69)})</td>
<td>- Lamotrigine (add-on)(^{(68)})</td>
</tr>
<tr>
<td></td>
<td>- E-health-based anxiety management(^{(83)})</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Education engagement</td>
<td></td>
</tr>
<tr>
<td>Circadian–bipolar spectrum</td>
<td>- CBT focusing on sleep–wake behaviours and circadian rhythms(^{(83,84)})</td>
<td>- Selective serotonin reuptake inhibitors (eg, fluoxetine, sertraline, escitalopram)(^{(6–81)})</td>
</tr>
<tr>
<td></td>
<td>- Behavioural regulation of sleep–wake timing(^{(85)})</td>
<td>- Selective serotonin and norepinephrine reuptake inhibitors (eg, venlafaxine, duloxetine)(^{(80–82)})</td>
</tr>
<tr>
<td></td>
<td>- Physical activity(^{(40,85)})</td>
<td></td>
</tr>
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<td></td>
<td>- Education engagement</td>
<td></td>
</tr>
</tbody>
</table>

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**5 Cascading direct and indirect impacts of interventions on multidimensional outcome domains**

- **Interventions**
  - Employment support and placement
  - Self-harm and suicidal thoughts and behaviours
  - Alcohol or other substance misuse
  - Physical health comorbidity

- **Functional Course**
  - Social and occupational function
  - Physical health comorbidity

- **Clinical Course**
  - Illness type, stage, and trajectory
  - Self-harm and suicidal thoughts and behaviours
  - Alcohol or other substance misuse

**Icons from www.flaticon.com: alarm bell, bicycle and magnifying glass/brain made by Freepik; wine bottle/glass made by srip; team education made by Eucalyp. Interventions which target individual multidimensional outcome domains are likely to have specific and direct impacts, as well as indirect impacts which cascade over time (indicated by time points \([T]\) 1 to 3). Here, we demonstrate three hypothetical paths stemming from three distinct targeted interventions. Path 1 (green) demonstrates that employment support and placement can have a direct effect on social and occupational function that is sustained over multiple time points and has flow-on effects on the future illness type, stage and trajectory, and alcohol or other substance misuse. Path 2 (blue) shows that harm reduction can have a direct and enduring effect on self-harm, suicidal thoughts and behaviours, and also has downstream impacts on social and occupational function and physical health. Path 3 (grey) demonstrates that an exercise intervention can directly improve physical health with future positive effects on social and occupational function, self-harm, suicidal thoughts and behaviours, and alcohol or other substance misuse.**
transdiagnostic transition from earlier to later clinical stages of illness, rather than transitions to full-threshold disorders within narrow diagnostic bands (Chapter 2). A key strength of the framework is its longitudinal perspective and attempts to track over time the development of mood and psychotic syndromes within the pathways. The selection of treatments targeting the three illness subtypes places a strong emphasis on the pathophysiological mechanisms that are thought to underpin individual illness trajectories over time (Box 4). Crucially, this approach also emphasises a careful consideration of the clinical stage of an individual within their illness trajectory. This enables a selection of treatments that are commensurate with the severity and complexity of illness, the pathophysiological mechanisms most affected in each subtype, and the functional impacts associated with an individual’s presentation. A key aspect of the clinical staged care model is that interventions offered at earlier stages of illness are not lower grade versions of interventions offered to those with established illness; rather, interventions offered at earlier stages are expected to be more benign and have a greater benefit-to-risk ratio.

The staged care model of intervention selection advocates a prioritisation of psychological and social therapies as first line interventions for individuals with a less advanced stage of illness (ie, those at stage 1a, who benefit in general from brief generic interventions). For individuals with a syndromal presentation that suggests an attenuated or more discrete syndrome form of adult-type illness (ie, those at stage 1b or 2+), treatment options are extended to include more type-specific and targeted psychological and social therapies as well as psychotropic medications. Critically, we hypothesise that young people traverse a significant illness (and potentially neurobiological) threshold when they transition from stage 1b to stage 2. Hence, recognising and preventing this transition is of paramount importance. Accordingly, both clinical and research attention, as well as preventive efforts, are concentrated at this early (or attenuated syndrome) stage. The two equally important goals of the staged care model are therefore to effectively manage the current clinical stage and to prevent illness progression (Box 1).

2.1. Non-specific primary interventions and secondary prevention strategies

Before discussing interventions that are specific to pathophysiological mechanisms and individual illness trajectories, it is important to note that a range of primary psychological and social interventions are likely to provide benefits relating to non-specific illness factors across all illness subtypes (Box 6). Further, non-specific secondary prevention strategies may have the added benefit of reducing the risk of illness persistence and relapse (Box 7). However, emphasis should be placed on interventions which map more closely to pathophysiological based phenotypes (ie, clinical phenomena and objective markers), especially on a greater usage of objective markers. Together, these clinical and laboratory-based measures should assist with the selection of more specific and targeted interventions (Box 4).

2.2. Interventions specific to the neurodevelopmental–psychosis subtype (Box 4)

2.2.1 First and second line psychological and social interventions

The neurodevelopmental–psychosis subtype is hypothesised to be underpinned primarily by aberrant brain development and/or functioning. Accordingly, psychological and social interventions primarily target brain health and impaired neurocognitive and social and occupational functioning. Social skills training targets aspects of social behaviour that are commonly impaired in individuals with psychotic disorders. These interventions aim to teach both verbal communication skills (eg, conversation skills, appropriate volume and tone, appropriate emotional responses) and non-verbal communication skills (eg, eye contact, expression and understanding of body language). Social recovery therapy involves multi-systemic assertive outreach and case management to connect with socially withdrawn individuals and encourage them to re-engage in social settings. Increasing physical activity is a key intervention which may result in improvements in psychiatric symptoms, enhancement of brain and neurocognitive function and, potentially, minimisation of the adverse cardiometabolic effects of medication.

For individuals with more advanced stages of illness (stage 1b+), interventions targeting functional disability and neurocognitive impairment are recommended. Cognitive training has been demonstrated to improve neurocognitive performance and psychosocial functioning, with improvements in social and occupational functioning greatest when cognitive training is implemented alongside functional rehabilitation efforts.

2.2.2. First and second line pharmacological interventions

Pharmacological interventions for this subtype primarily aim to prevent neuroprogression and manage psychotic symptoms. There are effective conventional (typical) and more recently developed atypical antipsychotics that affect dopaminergic and serotonergic receptors and, thus, target mainly positive symptoms. However, patients often suffer from adverse effects including extrapyramidal symptoms, sexual dysfunction and metabolic complications. A shared decision-making process that considers efficacy, adverse effects, cost and mechanism of action is necessary to develop an effective treatment strategy. Shared decision making has been shown to have positive effects on satisfaction with treatment and treatment adherence, health status and health inequalities. It is particularly important to prevent medication non-adherence, which is linked with poor prognosis of patients on treatment.

Atypical antipsychotic medications such as aripiprazole and quetiapine are well tolerated and effective at managing symptoms in the early phases of psychotic disorders, and are therefore...
recommended as first line treatments. However, as antipsychotics of both generations do not sufficiently ameliorate negative symptoms and cognitive impairments in most cases, recent drug development efforts have focused on several new targets such as the glutamatergic, nicotinergic and endocannabinoid systems. These new drugs with new innovative mechanisms of action aim to treat negative symptoms and cognitive impairments more effectively and might also be a beneficial alternative for treatment resistant cases. Lamotrigine is an anticonvulsant that has been used primarily to treat epilepsy. However, it is an antagonist of postsynaptic voltage-sensitive sodium channels, so it decreases presynaptic release of glutamate and is therefore considered to be a potential treatment for schizophrenia, especially as augmentation therapy in patients who do not fully respond to clozapine.

Interestingly, there is also emerging evidence that administration of omega-3 rich fish oils may reduce the risk of transition to treat patients who do not fully respond to clozapine.

### 2.3. Interventions specific to the hyperarousal–anxious depression subtype (Box 4)

#### 2.3.1 First and second line psychological and social interventions

The hyperarousal–anxious depression subtype is hypothesised to be underpinned by abnormalities in central nervous system arousal and reactivity. First line interventions teach individuals to self-regulate these systems. E-health-based anxiety management interventions are scalable and highly accessible treatments that are likely to be effective in individuals presenting primarily with mild to moderate anxiety and mood symptoms.

Cognitive behaviour therapy and meta-cognitive therapy teach individuals to monitor and evaluate their cognition, and then draw links between thoughts and behaviour. Interpersonal therapy aims to improve the quality of interpersonal relationships and social functioning. Specific psychological therapies may be required for specific phenotypes, such as exposure therapy for social anxiety disorder and exposure and response prevention therapy for obsessive compulsive disorder. Individuals with more advanced presentations (stage 1b+) may require extensions of the above therapies with greater intensity and longer duration, and involving multidisciplinary and team-based care with multiple concurrent interventions.

#### 2.3.2 First and second line pharmacological interventions

Patients with more advanced stages of illness (stage 1b or 2+) may benefit from pharmacological intervention. As a first line therapy, selective serotonin reuptake inhibitors (SSRIs) should be considered. Such medications may dampen heightened stress-reactivity, enhance neuroplasticity, and improve functioning of neural circuits that regulate mood. As a second line option, serotonin norepinephrine inhibitors may be effective in those unresponsive to SSRIs.

### 2.4. Interventions specific to the circadian–bipolar spectrum subtype (Box 4)

#### 2.4.1 First and second line behavioural, lifestyle and biological interventions

The circadian–bipolar spectrum subtype is hypothesised to involve dysregulation of sleep–wake behaviours and biological circadian rhythms. Cognitive behaviour therapy or behavioural regulation therapy focusing on sleep–wake behaviour and resynchronisation of circadian rhythms are two key first line treatments which aim to encourage behaviour that boosts circadian synchrony. These therapies encourage a range of behaviours including appropriate timing of meals, engagement in physical activity, adequate exposure to light (particularly morning light), minimisation of intake of caffeine, alcohol and other substances during the evening, and timing of sleep onset and offset.

For individuals with more advanced presentations (stage 1b+), several chronobiological treatments are available. Light therapy acutely increases an individual’s daytime exposure to light in the blue spectrum to entrain the circadian period to a 24-hour cycle. Sleep deprivation (during a depressive episode) may be used as a rapid-onset antidepressant therapy, which may be supplemented by other circadian-based interventions (eg, light therapy). Dialectical behaviour therapy may be useful in presentations accompanied by complicating problems such as interpersonal difficulties, alcohol or other substance misuse, self-harm, and suicidal thoughts and behaviours. Ruminations-focused cognitive behaviour therapy may also have benefit in individuals with perseverative negative cognition that commonly accompanies fatigue and sleep problems.

#### 2.4.2 First and second line pharmacological interventions

For individuals with a more advanced stage of illness (eg, evidence of a discrete bipolar syndrome) or those with a depressive disorder with additional phenotypic, actigraphic or laboratory-based evidence of underlying circadian disturbances (Chapter 3), pharmacological intervention may be required. Melatonin-based antidepressants (eg, agomelatine) may assist in realigning the circadian rhythm and its regulation of the sleep–wake cycle and other systems (eg, daytime activity, thermoregulation).

While preliminary, there is evidence from an open label trial demonstrating that resolution of depressive symptoms in individuals with a circadian-type depressive phenotype is strongly correlated with the correction of abnormal underlying circadian parameters (specifically, laboratory-determined dim-light melatonin onset times). A second line pharmacological approach could include mood-stabilising medications such as lithium and lamotrigine or stimulant drugs such as modafinil.

### Discussion

While the three core concepts we have described may appear complex, we emphasise that they can be used concurrently to narrow the broad array of available interventions to those that: limit the extension of key illness factors including functional impairment, self-harm, suicidal thoughts and behaviours, alcohol or other substance misuse, and poor physical health; carefully balance personal risk and benefit as informed by an individual’s current phenotype and its evolution.

The interventions described may be used to directly modify social and occupational functioning, or may indirectly affect social and occupational functioning through other multidimensional outcome domains, including illness type, alcohol or other substance misuse, self-harm, suicidal thoughts and behaviours, and physical health (Box 8). The selection of these direct or indirect interventions can be further guided by using clinical staging.


### Conclusion

The validity and clinical utility of the three core concepts — that are based on experiences with the BMC’s youth model of care and the resulting transdiagnostic, stage-appropriate framework — are currently under investigation. Refining and integrating these core concepts into a useful and simple treatment selection guide is a key priority. The ultimate aim is to prevent illness progressing to more severe, specific and persistent later stages by offering the right care at the earliest emergence of adult-type disorders.

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butes-care-may-improve-cost-effectiveness


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Metacognitive training for young subjects

Usoorio D, Giusti L, Wittink DE, et al.


Chapter 5
A service delivery model to support highly personalised and measurement-based care in youth mental health

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Mental health services in Australia are characterised by service fragmentation, late intervention, a lack of focus on an individual’s needs, and inequitable distribution of scarce resources.¹ These factors perpetuate poor experiences of care and suboptimal outcomes for individuals.¹ For young people, additional challenges include: presentations of sub-threshold disorders,²–⁴ high rates of deterioration,⁵ and illness progression,⁶,⁷ high rates of self-harm and suicidality; impacts on social, educational, or vocational participation; comorbid physical health problems; and alcohol or other substance misuse.⁹–¹¹ Consequently, there is a need to create person-centred and transdiagnostic youth mental health models of care that respond directly to these challenges.¹¹–¹９

Current Australian health policy promotes a stepped-care service approach, designed to make the best use of available workforces and new technologies.⁰,¹¹ Stepped-care models hierarchically arrange service provision based on proposed treatment intensity.²²,²³ Typically, individuals are stratified by current symptoms (or syndromes), functional impairment and risk assessment. However, such approaches tend to be generic and therefore result in broad, non-specific categories such as mild, moderate or severe.⁰,²¹ Typically, this categorisation does not detect the types of issues which can be identified by a highly personalised approach to care, which incorporates transdiagnostic youth models, multidimensional needs, likely underlying pathophysiological mechanisms, and individual illness trajectories and complex comorbidities (Chapters 1–3).

Under simple stepped-care models, differentiation in level of service provision usually occurs after the initial episode of care, largely by identifying those who do not respond. So only individuals who do not respond to the initial episode of care move to more intensive interventions (ie, this can be described as a “fail-first” approach to care). Consequently, these models will persistently fail to reduce disability associated with early onset mental health problems that are already associated with functional impairment or those that progress to more persistent, recurrent or severe forms of illness.

Incorporation of a highly personalised model (ie, one that includes transdiagnostic clinical staging, multidimensional assessment, underlying pathophysiological mechanisms, and individual illness trajectories and comorbidities) into youth mental health service planning would represent a significant enhancement to stepped care. Such a model is not simply an initial assessment and then allocation of service based on type and intensity of symptoms. In addition, it includes real-time clinical decision making based on continuous feedback on the effectiveness of interventions, or intensity of service, provided. Hence, it also includes measurement-based care. This highly personalised and measurement-based model of care, linked to relevant service structures, has the potential to better match treatment type and intensity (defined by cost, time and risk). The clear goals are to prevent illness progression and promote recovery.⁷,¹⁰,²⁴–²⁹

The transdiagnostic clinical staging component of the model overtly respects the often progressive, heterotypic, and recurring or persisting nature of more severe mental health disorders.²⁴,³⁰–³⁴ Clinical staging principles enhance each of the established key features of our model,¹⁰,²⁷ which are outlined in Box 1.

Key features of our model

1. Multidimensional assessment

The primary purpose of multidimensional assessment (Chapters 1 and 3) is to match the ascertained level of need with the appropriate type, intensity and duration of intervention. Ideally, this step would occur before starting to provide care, and at a time and location that suits the young person and their family.

Clinical assessment (ie, diagnostic) practices that are too narrow and shallow run the risk of missing vital signs that an individual requires immediate and more sophisticated care. Consequently, youth mental health services require health professionals with sufficient skills and experience in the complex task of multidimensional assessment to be accessible earlier in the care pathway. This not only ensures the young person accesses timely and appropriate intervention from the outset, but also better

Summary

- Over the past decade, we have seen a growing focus on creating mental health service delivery models that better meet the unique needs of young Australians. Recent policy directives from the Australian Government recommend the adoption of stepped-care services to improve the appropriateness of care, determined by severity of need.
- Here, we propose that a highly personalised approach enhances stepped-care models by incorporating clinical staging and a young person’s current and multidimensional needs. It explicitly aims to prevent progression to more complex and severe forms of illness and is better aligned to contemporary models of the patterns of emergence of psychopathology.
- Inherent within a highly personalised approach is the incorporation of other evidence-based processes, including real-time measurement-based care and use of multidisciplinary teams of health professionals.
- Data-driven local system modelling and personalised health information technologies provide crucial infrastructure support to these processes for better access to, and higher quality of, mental health care for young people.

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1. Multidimensional assessment
2. Service level review and treatment planning
3. Interventions, duration of care and multidisciplinary approaches
4. Continuous and ongoing outcome monitoring
5. Planned exit, promoting full recovery and stopping secondary prevention

**Key features and pathways of a highly personalised and measurement-based care model for youth mental health service delivery**

supports and guides more junior and less experienced staff in the face of commonly encountered clinical complexity or diagnostic uncertainty. Where this skilled workforce is unavailable, health information technologies may play a role in supporting this process.

**2. Service level review and treatment planning**

The intensity, complexity and duration of interventions should match the level of need at the time of presentation to care. Here we define intensity in terms of costs and risks at the service and health professional level and at the young person (and their family) level. Costs for all stakeholders can either be financial or related to time — for example, a young person (and often their family) needing to take time out of education or employment to travel to attend a service, the required frequency of attendance, the number of health professionals involved, the duration of the episode of care, and the setting in which care is provided (inpatient versus outpatient). Risks can be defined as unintended consequences of interventions, such as adverse effects of psychological and pharmacological therapies.

Most stepped-care models simply define need based on current severity of symptoms, illness or impairment, and perceived risk. By contrast, our model uses a combination of current severity of symptoms, illness or impairment, and perceived consequences of interventions, such as adverse effects of psychosocial uncertainty. Where this skilled workforce is unavailable, health information technologies may play a role in supporting this process.

Ideally, all young people should have their multidimensional assessment results reviewed at the service level by a multidisciplinary team trained in this model. Common transdiagnostic and clinical stage language can unite and support this multidisciplinary approach to clinical care. Once consensus regarding clinical stage, multidimensional needs and likely illness trajectory is reached, a draft treatment plan is created and, shortly afterwards, discussed with the young person using shared decision-making principles. Broad assessment ensures that the young person receives an optimal combination and sequence of interventions that is aimed at preventing poor outcomes and illness progression. For example, because disengagement from education or employment increases the risk of illness progression, sometimes it is necessary to prioritise return to education or work (eg, via “non-mental health” interventions). In addition, assessing a young person’s strengths and their personal, family and external resources is helpful in personalised treatment planning.

**3. Interventions, duration of care and multidisciplinary approaches**

Current interventions are often limited by time, intensity, or lack of access to more specialised or multidisciplinary care options. Typically, there is a lack of differentiation of immediate aims from a secondary preventive agenda. In contrast, our model organises levels of intervention-based clinical characteristics defined by clinical stage, illness type and trajectory in the context of an individual’s multidimensional needs (Chapter 4). Early stage treatments are less specific, are lower risk, have lower costs and are proven to be effective. Early stage interventions, which are mainly psychological and behavioural, have a transdiagnostic focus rather than a specific disorder focus. Illness-specific medical or psychological therapies should be reserved for those with more clearly established illnesses who better align to the cohorts in which the therapy’s evidence base was obtained.

As a guide, the spectrum of services matched against need (Box 2) could include:

- self- and carer-directed monitoring and management, via online psychoeducation, health information or self-managed interventions;
- low intensity services, such as clinician-supported or -assisted online interventions, group-based psychological interventions, and brief face-to-face psychological therapy;
- moderate intensity services, such as longer term psychological therapy with assertive case management including social and vocational (education, employment, training) support, with consideration of first line pharmacotherapy where appropriate;
- high intensity services, such as lengthy or intensive psychological, social and vocational intervention that may involve multidisciplinary support, assertive case management, second line pharmacotherapy or polypharmacotherapy; or
- acute and specialist community services, such as highly specialised mental health care typically provided by secondary or tertiary mental health services, possibly including inpatient hospitalisation when appropriate.

Decisions about the duration, intensity, sequence and multidisciplinary nature of care provision, and assertive follow-up and monitoring, should logically match the young person’s
assigned clinical stage, illness type and trajectory. For example, young people at stage 1b with moderate symptom severity and functional impairment are at higher risk of persistent disability and progression to more severe illnesses — about one in five progress to a more severe syndrome within 12 months. According to emerging evidence, the emphasis for young people at this stage would be a 12-month program of clinical care and assertive follow-up. In contrast, those at stage 1a have been shown to benefit from brief interventions and those at stage 2 should stay connected to care for 2–5 years.

In light of the risks of chronicity of impairment and illness progression, services must be cognisant of the challenges of keeping these young people in care. Despite having greater treatment needs, young people at stage 1b have been shown to have poorer rates of service attendance than those with less intensive treatment needs (stage 1a).

4. Continuous and ongoing outcome monitoring

Continuous and ongoing outcome monitoring is central to a youth-focused model of care, yet it is often absent in treatment planning and service funding. Studies of treatment outcomes in community-based youth mental health services show quite consistent findings: 10–25% deteriorate significantly in care over about 6 months, 20–30% show reliable improvement, and the majority are left with persistent distress and/or impairment. No single clinical, demographic or treatment factor is a reliable predictor of treatment response or outcome.

Changing needs should correspond with changing interventions (ie, changes in type, focus, degree of specialisation or intensity of intervention). However, this can only be achieved by careful and regular monitoring in care, which is often not done, so rates of change in treatment intensity tend to be low. Further, an over-reliance on subjective clinical judgement, which often conflicts with objectively tracked outcome data, can lead to inappropriate service provision.

Services can instil processes that mandate the routine use of outcome monitoring, and this has been shown to reduce rates of deterioration and improve treatment outcomes. These data should be accessible by the young person and their treating health professional to facilitate shared treatment planning decisions and be the centrepiece of multidisciplinary clinical review meetings. Service providers should have access to such data in aggregate form to inform decisions regarding service resource allocation, identify service gaps, and perform quality and safety improvement initiatives.

5. Planned exit, promoting full recovery and ongoing secondary prevention

A substantial number of young people exit care prematurely. These young people (depending on their clinical stage, illness type and trajectory) are at risk of experiencing ongoing distress and impairment or, worse still, deterioration without ongoing support. Efforts must be made by service providers to develop
systems that ensure exits from care are individually planned by supporting the young person and their family to make informed decisions about treatment cessation. Part of this process involves identifying factors that may impede service delivery, such as access difficulties or therapeutic relationship breakdowns.\textsuperscript{39,39} Where appropriate, full recovery and relapse prevention plans are put in place (self- and carer-directed monitoring and management) making the best use of online mental health services and resources. While many young people may leave care after symptom or functional improvement, some (especially those at higher stages) will require preferential and timely re-entry into care at the first signs of relapse. Further, arrangements for ongoing support to minimise and prevent risk factors associated with illness progression (eg, unemployment) are critical.

**Creating locally connected care systems**

The mental health system in Australia is a collection of siloed, independent services with different funding sources and entry criteria.\textsuperscript{3} These separate, closed and disconnected systems create situations where young people with long term needs receive episodic rather than continuous care. As a result, young people end up stuck in services, meaning that they may be at risk of overtreatment or undertreatment or, as their needs change, may find it difficult to transfer between appropriate services.

The adoption of our model would provide an opportunity for interservice cooperation and higher quality care for young people. The application of innovative data-driven approaches, such as dynamic systems modelling (a computer simulation approach that can be used to test likely impacts on the health system of different intervention combinations over the short and long term), has recently created new insights into complex patient flows and can highlight gaps in service provision within locally connected care systems rather than within a single service.\textsuperscript{48} These insights can identify service gaps and assist in building robust connections between previously separate and closed systems, to ensure that mental health services address the complete spectrum of needs for young people over time. Locally connected care systems then have more efficient and effective pathways between services, common assessment protocols and more timely clinical information sharing. This ensures that all young people along the “current clinical staging” and “current clinical need” spectrum (Box 2) are supported by the most appropriate level of service for the appropriate period.

**Role of technology in our model**

Today, one of the biggest enablers for achieving significant improvements in quality of mental health service delivery is through the integrated use of health information technologies that can support the functions outlined above.\textsuperscript{49–51} The InnoWell Platform is an Australian example of health information technology that has been co-designed to be integrated within locally connected care systems with the aim of improving access, efficiency, outcomes and care continuity.\textsuperscript{52} It does this by enabling real-time and comprehensive online assessment (including the determination of clinical stage and multidimensional needs),\textsuperscript{53,54} self-monitoring and routine outcome monitoring, and facilitation of access to high quality online psychological interventions. Such new and innovative technologies allow health professionals and services to provide highly personalised and measurement-based care.\textsuperscript{55} They can also help individuals overcome traditional barriers to care, such as those caused by geography, socioeconomic disadvantage, or service preference for face-to-face care.

In conventional services, extensive time is often spent conducting thorough face-to-face assessments rather than providing skilled interventions.\textsuperscript{22} When used in partnership with young people and appropriately matched to their capacity, health information technologies can support and enhance initial assessment processes to help uncover a wide range of needs. Technology used in this way, where real-time health data are immediately made available to young people and their health professionals, results in shorter face-to-face clinical interviews, leads to more timely responses to risk, and allows service resources to be re-directed towards providing a wider range of intervention options.\textsuperscript{50,54,56} Despite these benefits, there are also several barriers — at the levels of the individual, health professional and service provider — that need to be addressed for successful integration and uptake of such health information technologies.\textsuperscript{51}

**Conclusion**

Over the past decade, new service delivery models have been developed to better meet the unique mental health needs of young people. The first task of simply making youth mental health services more accessible has been a substantial achievement. However, the more challenging task of delivering services which meet the requirements of “right care, first time” remains elusive. Policy directives from the Australian Government now recommend the adoption of stepped-care models to improve the appropriateness of care, determined by severity of need. Here, we propose that these stepped-care models can be significantly enhanced by a highly personalised and measurement-based approach to youth services. Importantly, creating locally connected care systems will reduce service fragmentation, and better integrate previously siloed services to achieve person-centred and continuous care over the life course.


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