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Youth Mental Health Tracker: protocol to establish a longitudinal cohort and research database for young people attending Australian mental health services

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ABSTRACT

Introduction Mental disorders are a leading cause of long-term disability worldwide. Much of the burden of mental ill-health is mediated by early onset, comorbidities with physical health conditions and chronicity of the illnesses. This study aims to track the early period of mental disorders among young people presenting to Australian mental health services to facilitate more streamlined transdiagnostic processes, highly personalised and measurement-based care, secondary prevention and enhanced long-term outcomes.

Methods and analysis Recruitment to this large-scale, multisite, prospective, transdiagnostic, longitudinal clinical cohort study ('Youth Mental Health Tracker') will be offered to all young people between the ages of 12 and 30 years presenting to participating services with proficiency in English and no history of intellectual disability. Young people will be tracked over 3 years with standardised assessments at baseline and 3, 6, 12, 24 and 36 months. Assessments will include self-report and clinician-administered measures, covering five key domains including: (1) social and occupational function; (2) self-harm, suicidal thoughts and behaviour; (3) alcohol or other substance misuse; (4) physical health; and (5) illness type, clinical stage and trajectory. Data collection will be facilitated by the use of health information technology. The data will be used to: (1) determine prospectively the course of multidimensional functional outcomes, based on the differential impact of demographics, medication, psychological interventions and other key potentially modifiable moderator variables and (2) map pathophysiological mechanisms and clinical illness trajectories to determine transition rates of young people to more severe illness forms.

Ethics and dissemination The study has been reviewed and approved by the Human Research Ethics Committee of the Sydney Local Health District (2019/ETH00469). All data will be non-identifiable, and research findings will be disseminated through peer-reviewed journals and scientific conference presentations.

Strengths and limitations of this study

- This study focusses on presentation to care, rather than diagnosis-based, recruitment to establish a comprehensive and transdiagnostic longitudinal cohort and research database of young people attending Australian mental health services.
- We aim to track up to 5000 young people (aged between 12 and 30 years) over a 3-year period.
- The use of our multidimensional outcomes framework enables a comprehensive assessment of young people as well as routine monitoring.
- The study does not yet include standardised objective measures such as biomarkers, data on brain structure and function and neuropsychological assessments.
- The study is part of a clinical trials framework evaluating the utility of our multidimensional outcomes framework as well as our pathophysiological mechanism and illness trajectory model.

INTRODUCTION

Mental disorders are a leading cause of premature death and persistent disability worldwide.[1–4] In those aged 10–24 years, neuropsychiatric disorders contribute more than any other cause to the global burden of disease.[5] In addition to the early age of onset of mental disorders, factors including their prevalence, chronicity, comorbidity with physical illness, risky alcohol or other substance use, and high suicide risk and self-harm behaviour significantly contribute to significant disability and premature mortality.[6–15] Consequently, earlier identification, personalised early interventions, secondary prevention and enhanced long-term care in the

early phases of these disorders are key priorities to reduce persistent disability and premature mortality.[16–18]

In order to better characterise the individual needs and enable highly personalised and measurement-based care, we have proposed the use of a multidimensional outcomes framework.[15 19–21] This framework comprises five key domains, namely:

1. Social and occupational function.
2. Self-harm, suicidal thoughts and behaviours.
3. Alcohol or other substance misuse.
4. Physical health.
5. Illness type, clinical stage and trajectory.

These domains can be assessed by using various freely accessible validated scales and standardised questionnaires.[20] New health information technologies (HIT), such as the InnoWell Platform (Project Synergy, InnoWell Pty),[22] can facilitate the delivery of such comprehensive assessments, as they allow clinicians to implement time-efficient self-report versions of the scales and questionnaires that can often be completed by consumers without guidance.[20]

The assessment and identification of individual needs in each domain may prove to be particularly valuable, as it allows clinicians to develop highly personalised care options targeting specific factors associated with illness persistence and more significant disability across disorders (eg, functional impairment, physical illnesses, risky alcohol or other substance use, and high suicide risk and self-harm behaviour).[19 23]

Young people presenting to mental health services commonly experience a variety of symptoms that are often less specific (eg, anxiety, high level of psychological distress, sleep problems, mood instability and variable psychosocial function) and not yet sufficiently severe to meet thresholds for assigning specific diagnostic categories. Thus, current syndrome-focused classification systems, and their matching clinical guidelines, often map poorly onto the earlier phases of mental illness.[18 24–28] A transdiagnostic clinical staging model has been proposed as an adjunct to formal diagnosis in order to address this problem. The clinical staging model reflects the progression of mental disorders and is based on the staging concept used in general medicine, where more advanced stages are associated with a poorer prognosis and a need for more intensive interventions with a higher risk-to-benefit ratio.[18 29]

A detailed description of this transdiagnostic staging model is given in references.[18 29] In brief, the staging model distinguishes five stages. Each stage is defined by a degree of functional impairment and persistence of symptoms. Importantly, clinical stages are not expected to coincide with traditional diagnostic categories. The stages cover early illness phases characterised by non-specific symptoms accompanied by mild to moderate functional impairment (stage 1a) or 'attenuated syndromes' of severe mental disorders, with moderate to severe functional impairments (stage 1b), as well as full-threshold syndromes with clear and ongoing functional impairment (stage 2), and later stages, including recurrent or persistent illnesses with marked worsening in social, educational or occupational function due to persistence or recurrence (stage 3) or severe, persistent and unremitting illnesses with clear evidence of marked functional deterioration (stage 4). The staging model takes also comorbidities into account. In stage 1b cases, syndromes may be mixed in terms of their symptoms or complicated by alcohol and other substance misuse. After transition to stage 2, the syndrome may remain mixed in terms of symptoms, and not necessarily matching a single or discrete Diagnostic and Statistical Manual of Mental Disorders (DSM)-style disorder, or primary discrete syndromes may co-occur. The significant comorbidity may also include alcohol or other substance misuse, abnormal eating behaviour or other relevant psychological syndromes.

General medicine also shows that an understanding of underlying pathophysiological mechanisms is crucial for selecting optimal treatment. Identifying mood and psychotic syndromes (including anxiety, depression, bipolar disorder and psychosis) based on pathophysiology will allow clinicians to select treatment options targeting underlying causes and, thus, eventually lead to improved clinical outcomes.[30]

Based on the results of a cross-sectional study,[31] we have proposed three underlying pathophysiological mechanisms (neurodevelopmental abnormalities, hyperarousal and circadian dysfunction), which over time influence individual illness trajectories to three different illness types, namely psychosis, anxious depression and bipolar spectrum disorders, respectively.[18 31] More precisely, the 'neurodevelopmental-psychosis illness type' is characterised by psychotic features and significant and persistent developmental difficulties, including cognitive impairments, learning difficulties, and autism spectrum disorder. This subtype is based on evidence linking neurodevelopmental abnormalities with the increased risk of developing psychotic phenomena[32–34] and is in line with meta-structures proposed for the redevelopment of diagnostic classification systems.[35 36] The 'hyperarousal-anxious depression' illness subtype includes cases with childhood anxiety, heightened stress sensitivity and adolescent depressive syndromes. Also, cases without clear evidence for a neurodevelopmental-psychosis or circadian-bipolar spectrum illness subtype are allocated to this subtype. It is consistent with models of neural fear circuitry, prolonged stress responses and glucocorticoid-dependent arousal in anxiety and unipolar mood disorders.[37–40] The 'circadian-bipolar spectrum' illness subtype is derived from models linking mood disorders with circadian disturbances and dysregulated activation and energy and is characterised by disrupted sleep-wake behaviours and circadian rhythms, delayed sleep-waking timing and an atypical or bipolar spectrum symptom profile.[41–44]

Current research projects at Brain and Mind Centre (BMC) are investigating the validity and potential implementation of this approach within mental health services.[45 46]

Importantly, there is a degree of overlap between the three pathways at all stages of illness. Previously, we have shown in a similar cohort study that 27% of young people with emerging mental disorders progress across stages and between pathways throughout care. This included 13% progressing between pathways while developing more specific and severe symptoms.[18] Continuous tracking of long-term outcomes will provide detailed information on these individual trajectories and factors influencing them, and, most importantly, will allow for early identification of changing needs that require adjustments of individual interventions. Furthermore, the information on clinical illness trajectories of young people can be used to determine transition rates to more severe illness forms (eg, severe depression, bipolar or psychotic disorder) and may help to better understand which factors drive the progression of illness.

Objectives of the study and conceptual framework

Mental disorders emerge early in life and evolve dynamically over time. The longitudinal 'Youth Mental Health Tracker' study aims to better understand the complex and variable clinical course (trajectories and pathophysiological mechanisms) of mental disorders and their impacts over time by tracking long-term multidimensional outcomes in a youth mental health cohort.

Standardised multidimensional clinical information will be routinely and confidentially collected across participating services. The study involves multiple longitudinal assessments so that key illness outcomes (ie, social and occupational function, self-harm, suicidal thoughts and behaviour, alcohol or other substance misuse, physical health, and illness type, clinical stage and trajectory) can be measured and tracked over time. Importantly, this allows for the detection of treatment non-responders at an early stage of illness; that is, before extensive exposure to interventions and chronic manifestation of illness.

In summary, such standardised data collection will enable improved identification, characterisation and profiling of mental disorders in young people, thus, enabling the identification of new targets and mechanisms that can be translated into more streamlined transdiagnostic processes, the development of the next generation of highly personalised interventions and health service strategies that greatly enhance care for young people.

METHODS AND ANALYSIS

Study design and setting

This is a large-scale, multisite, prospective, transdiagnostic, longitudinal clinical cohort study (Youth Mental Health Tracker), with the Brain and Mind Centre (including headspace Camperdown and Early Intervention and High-Intensity Services, public health organisations) at the University of Sydney (Sydney, Australia), being the lead site for this study. Further, St Vincent's Private Hospital (USpace) (private health organisation) will be another participating site in Sydney, Australia. Thus, this study involves both specialist (USpace) and enhanced primary-care (headspace Camperdown and Early Intervention and High-Intensity Services) youth mental health services.

For the collection and storage of routine clinical data across sites, a HIT system will facilitate the data extraction and use in a de-identified manner for research purposes.

The study is expected to start in late 2020. Participants will be tracked over 3 years with standardised assessments occurring at baseline and 3, 6, 12, 24 and 36 months.

Patient and public involvement

The HIT system (InnoWell Platform (InnoWell Pty))[22] that will be used by sites participating in the study for self-report assessments was developed with the patient and public involvement and has been approved as a medical device by the Australian Register of Therapeutic Goods (ID: 315030).[47] Although young people were consulted during the development of the technology used to measure relevant outcomes of the study, they were not invited to comment on the study design.

Study population

This study focusses on young people seeking treatment for emergent mood and psychotic syndromes and aims to establish a comprehensive transdiagnostic, longitudinal clinical cohort. Therefore, the recruitment is based on the presentation to care and is not restricted by specific diagnostic criteria. That is, young people presenting with non-specific anxiety or depressive symptoms according to diagnostic criteria (stage 1a), attenuated syndromes (stage 1b) or full-threshold, major and discrete syndromes (stage 2+) will be included.

This diagnosis-independent recruitment is consistent with the National Institute of Mental Health recommendations to conduct more inclusive clinical research in cohorts drawn from similar standard service settings[48] and facilitate translation of the findings to other youth mental healthcare settings.

However, the vast majority who presents to the participating ambulatory-care clinical services have 'internalising' disorders (anxiety, depression, mood, psychotic disorders and so on), often associated with role impairment, comorbid substance misuse and suicidal thoughts and behaviours. The proportion of persons with major 'externalising' disorders as their primary difficulty is low.

Inclusion and exclusion criteria

Participation in this study will be offered to all young people, presenting to participating youth mental health service sites that provide mental health support to young people between the ages of 12 and 30 years. Young people who do not have proficiency in the English language or have an intellectual disability (at investigator's discretion, based on standard procedures at each site) will be excluded due to inability to accurately complete study scales and questionnaires.

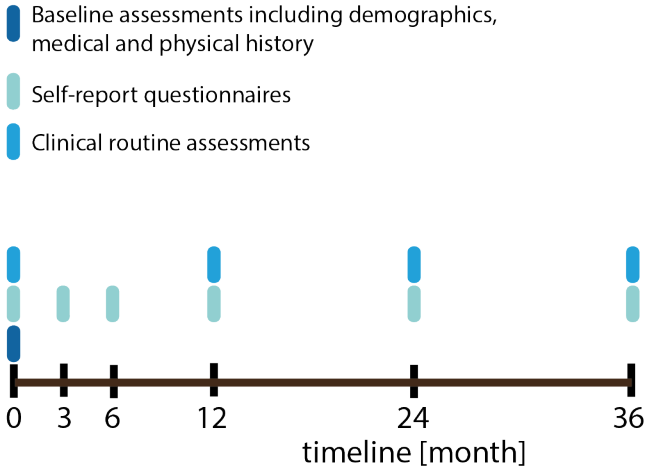

Figure 1 Overview of study visits. After completing the baseline visit, participants will be followed-up once yearly. During each visit, self-report questionnaires and clinical routine assessments have to be completed. In addition, participants will be asked to complete self-report questionnaires also 3 and 6 months after study start.

Recruitment procedure

All young people presenting to participating youth mental health services and meet inclusion and exclusion and exclusion criteria will be invited to participate in this Youth Mental Health Tracker study.

Study course and procedures

All participants recruited to this Youth Mental Health Tracker study will undergo a standardised baseline assessment (t_0, details see below), which will routinely be conducted by a mental health professional at the service. Standard information on demographics, medical history and physical history will be collected, and a range of clinician-administered assessments will be conducted. The young person will also complete a suite of online self-report questionnaires.

Participants that complete the baseline assessment will be followed up and invited to complete an online assessment that will consist of the self-report questionnaire pack (completed online at home). These follow-up assessments will be done at 3 and 6 months following the baseline assessment (t_3, t_6).

To ensure that optimal participant care is maintained, all participants will be invited to attend the service they initially presented to, for annual clinical routine assessments (t_{12}, t_{24}, t_{36}). Clinician administered assessments and self-report questionnaires will be repeated to track individual outcomes. That is, young people will be tracked on at least an annual basis over 36 months (figure 1).

Assessments

In order to provide improved characterisation and profiling of the Australian youth mental health population, multidimensional self-report and clinician-administered measures (outlined below) will be deployed. These cover the five key domains of the multidimensional assessment and outcomes framework.[15 20]

The self-report questionnaires (see table 1) collect information regarding social and occupational function, self-harm, suicidal thoughts and behaviours, alcohol or other substance misuse, physical health as well as lifetime and current psychiatric symptoms, family history of mental illness and medical history. The questionnaires will be hosted online by using the InnoWell Platform (InnoWell Pty).[22]

As part of the clinical routine assessments,[20] clinicians will record additional information regarding functioning, clinical stages, common illness subtypes and possible underlying pathophysiological mechanisms. More precisely this includes:

1. Social and Occupational Functioning Assessment Scale reflecting the clinician's judgement of overall social and occupational function.
2. Clinical Global Improvement, providing an overall clinician-rated summary measure that takes information on the patient's history, psychosocial circumstances, symptoms, behaviour and the impact of the symptoms in the patient's ability to function into account.
3. Common illness subtypes (psychosis, anxious depression, bipolar spectrum) and possible underlying pathophysiological mechanisms (neurodevelopmental, hyperarousal, circadian).[18 31]
4. Clinical Staging.[18 25 29 49] Based on the clinical staging assessment,[18 25 29 49] participants will be distinguished as those in the earliest phases with non-specific clinical presentations (stages 1a 'seeking help') from those at greater-risk with more specific, sub-threshold presentations (stage 1b) or experiencing first major illness episodes (stages 2+).

Following the continuation of this Youth Mental Health Tracker study, this may further include neuropsychological and neurobiological (genetic, metabolic, circadian and imaging) assessments in a subset of participants as required by their clinicians based on need, to reflect an approach that is patient-centred care and highly personalised.

Table 1 Overview of self-report questionnaires

Health domain	Psychometric tool
Distress	► Kessler Psychological Distress Scale-10 [62 63]
Suicidal thoughts and behaviour	► The Suicidal Ideation Attributes Scale [64] ► The Columbia–Suicide Severity Rating Scale[65]
Psychosis-like experiences	► Prodromal Questionnaire-16[66]
Mania-like experiences	► Altman Self-Rating Mania Scale[67]
Daily activities	► Youth not in education or employment, Organisation for Economic Co-operation and Development ► Census of Population and Housing, Australian Bureau of Statistics ► WHO Disability Assessment Schedule-2.0 [68]—'unable to carry out usual activities' question ► Work and Social Adjustment Scale [69] ► Social and Occupational Functioning Assessment Scale—[70]adapted for self-report
Self-harm	► Brief Non-suicidal Self-Injury Assessment Tool[71]
Tobacco	► The Alcohol, Smoking and Substance Involvement Screening Test (ASSIST)[72 73]
Alcohol	► ASSIST[72 73] ► Alcohol Use Disorder Identification Test - Consumption (AUDIT-C)[74]
Relationships	► 'Perceived social support' and 'conflict in close relationships' were measured by an adapted version of the Schuster's Social Support Scale [75]
Depression	► Quick Inventory of Depressive Symptomatology—self-report[76]
Anxiety	► Overall Anxiety Severity and Impairment Scale[77]
Physical health	► Height, weight and waist circumference ► International Physical Activity Questionnaire[78 79]
Sleep-wake cycle	► Sleep timing items are based on the Pittsburgh Sleep Quality Index[80] and Munich ChronoType Questionnaire[81 82] ► Sleep quality items are based on expert consensus in the literature
Post-traumatic stress	► Primary Care Posttraumatic Stess Disorder (PTSD) Screen for Diagnostic and Statistical Manual of Mental Disorders Version 5 (DSM-5)[83]
Eating behaviours and body image	► Modelled on the Eating Disorder Examination.[84] Derived from structured interview questions from the Health Omnibus Surveys
Cannabis	► ASSIST[72 73]

Sample size calculation

The clinics that are participating in the project provide early intervention mental health services along with assistance in promoting young peoples' well-being. As such, there is no set sample size for the establishment of this cohort. Based on the previous recruitment numbers of past research studies in these settings, the annual number of young people enrolled in the study is expected to be a minimum of 1000. This number will sufficiently detect even the smallest effect sizes to investigate prospectively, over 3 years, the course of multidimensional functional outcomes (social and occupational function; self-harm, suicidal thoughts and behaviours; alcohol or other substance misuse and physical health) [15 19] in young people presenting to youth-specific mental health services.

Data analysis plan

This Youth Mental Health Tracker study will allow us to determine prospectively, over 3 years, the course of key multidimensional functional and clinical outcomes, in young people presenting to youth mental health services. This includes:

1. Modelling the impacts of demographic, treatment and other key potentially modifiable moderator variables, on functional and clinical outcomes.
2. Mapping the clinical illness trajectories and pathophysiological mechanisms of young people to determine transition rates to more severe illness forms (eg, severe depression, bipolar or psychotic disorder).
3. Investigating the differential effects of duration of exposure to antipsychotic, antidepressant, or mood-stabilising medications on physical health, clinical outcomes, and risks to self-harm or suicidal behaviour.

We will make use of high-level statistical techniques, including mixed-effects/multilevel modelling, Bayesian modelling,[50–52] structural equation modelling[53] and data-driven techniques,[54–56] such as hierarchical cluster analysis,[57–59] latent profile analysis[60] and group-based trajectory modelling.[61]

ETHICS AND DISSEMINATION

The study has been reviewed and approved by the Human Research Ethics Committee (HREC) of the Sydney Local

Health District (2019/ETH00469, protocol version V.1-2, 01/07/2019). Protocol modifications will only be implemented after HREC approval.

This is a research database study; therefore, the consent process is entirely concerned with permissions regarding the storage and use of routinely collected data. For this reason, an opt-out consent process has been implemented. Potential participants presenting to the service at the participating sites will be in-depth informed by the clinicians about the study. The opt-out consent will be conducted at an 'arm's length approach'. Participants will have sufficient time to consider whether they would like to participate in the research project. Young people under the age of 15 years will initially undergo the standard consent process. However, the young participants who do not opt-out of the study will be required to obtain additional parent/guardian consent. Participants can withdraw from the study at any time. Participants will be assured that their decision to participate will not affect their treatment, nor the current or future relationship with their treating clinician or researchers at the service. All participant data will be de-identified and stored in accordance with applicable security standards; therefore, the privacy of all participants will be protected.

Research findings will be disseminated through peer-reviewed journals and scientific conference presentations, and participant data will be non-identifiable.

This study allows to build a large transdiagnostic clinical cohort. The data can be used to model the clinical course and long-term functional outcomes of young people who present for clinical care before extensive exposure to interventions or chronic illness course. The study aims to improve identification, characterisation, and profiling of adolescent-onset mental disorders to enhance personalised interventions, and health service strategies that greatly enhance care for young people.

Contributors IBH conceived the research idea, designed the study and is the principal investigator. CR and YJCS contributed to study conception and wrote the study protocol with input of IBH, JC, TAD, FI, BH, NZ, AN, JSC, AMT, CW, SC, AJG, DK, FML and EMS. CR wrote the manuscript with input of IBH, YJCS, JC, TAD, FI, BH, NZ, AN, JSC and AMT. All authors critically reviewed content and approved the final version of the publication.

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Competing interests Professor Ian Hickie was an inaugural Commissioner on Australia's National Mental Health Commission (2012-18). He is the Co-Director, Health and Policy at the Brain and Mind Centre (BMC) University of Sydney. The BMC operates an early-intervention youth services at Camperdown under contract to *headspace*. He is the Chief Scientific Advisor to, and a 5% equity shareholder in, InnoWell Pty Ltd. InnoWell was formed by the University of Sydney (45% equity) and PwC (Australia; 45% equity) to deliver the $30 M Australian Government-funded Project Synergy (2017-20; a three-year program for the transformation of mental health services) and to lead transformation of mental health services internationally through the use of innovative technologies.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

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