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Cohort profile: the Brain and Mind Centre *Optymise* cohort: tracking multidimensional outcomes in young people presenting for mental healthcare

Joanne S Carpenter ,[1] Frank Iorfino ,[1] Shane Cross ,[1,2] Alissa Nichles,[1] Natalia Zmicerevska ,[1] Jacob J Crouse ,[1] Jake R Palmer ,[1,3] Alexis E Whitton,[1] Django White,[1] Sharon L Naismith,[1,2,4] Adam J Guastella,[1] Daniel F Hermens ,[1,5] Jan Scott ,[1,6,7] Elizabeth M Scott ,[1,8] Ian B Hickie [1]

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For numbered affiliations see end of article.

Correspondence to
Dr Joanne S Carpenter; joanne.carpenter@sydney.edu.au

ABSTRACT

Purpose The Brain and Mind Centre (BMC) *Optymise* cohort assesses multiple clinical and functional domains longitudinally in young people presenting for mental health care and treatment. Longitudinal tracking of this cohort will allow investigation of the relationships between multiple outcome domains across the course of care. Subsets of *Optymise* have completed detailed neuropsychological and neurobiological assessments, permitting investigation of associations between these measures and longitudinal course.

Participants Young people (aged 12–30) presenting to clinics coordinated by the BMC were recruited to a research register (n=6743) progressively between June 2008 and July 2018. To date, 2767 individuals have been included in *Optymise* based on the availability of at least one detailed clinical assessment.

Measures Trained researchers use a clinical research proforma to extract key data from clinical files to detail social and occupational functioning, clinical presentation, self-harm and suicidal thoughts and behaviours, alcohol and other substance use, physical health comorbidities, personal and family history of mental illness, and treatment utilisation at the following time points: baseline, 3, 6, 12, 24, 36, 48, and 60 months, and time last seen.

Findings to date There is moderate to substantial agreement between raters for data collected via the proforma. While wide variations in individual illness course are clear, social and occupational outcomes suggest that the majority of cohort members show no improvement in functioning over time. Differential rates of longitudinal transition are reported between early and late stages of illness, with a number of baseline factors associated with these transitions. Furthermore, there are longitudinal associations between prior suicide attempts and inferior clinical and functional outcomes.

Future plans Future reports will detail the longitudinal course of each outcome domain and examine multidirectional relationships between these domains both cross-sectionally and longitudinally, and explore in subsets the associations between detailed neurobiological measures and clinical, social and functional outcomes.

Strengths and limitations of this study

- This cohort tracks longitudinally a large number of young people presenting for mental health care and treatment early in the course of common mental disorders. It will provide detailed information about variations in the course of emerging illness over a prolonged, and developmentally sensitive, follow-up period.
- Multiple clinical and functional outcome domains will provide a rich dataset including assessment of social, educational and economic participation, physical health, alcohol and substance use, and deliberate self-harm and suicidal thoughts and behaviours.
- Linkage of longitudinal clinical data with more in-depth assessments from related neuropsychological and neurobiological substudies will increase the potential for greater understanding of the pathophysiological correlates of illness course in young people.
- As data are obtained through extraction of information from clinical files, there is likely to be some under-reporting of items or missing data (both random and non-random). Availability of follow-up data is biassed towards those who remain in contact with mental health services.

INTRODUCTION

The significant excess of premature death and disability attributable to mental disorders is a function of early age of onset, prevalence, chronicity, comorbidity with physical illness and alcohol and substance misuse, and degree of resultant impairment.[1–3] Notably, in those aged 10–24 years, neuropsychiatric disorders contribute more than any other cause to the global burden of disease.[2 4] To reduce this burden, earlier identification and enhanced long-term care of those in the early phases of these disorders are key

priorities.[3 5–9] Although 75% of mental disorders begin before the age of 25 years,[10] current diagnostic thresholds and categories often map poorly onto the earlier phases of mental illness experienced by adolescents and young adults.[11 12] Further, genetic, environmental, and neurobiological risk factor studies call into question the validity of specific diagnostic entities.[13–18] Consequently, services have been developed in Australia to promote and support early intervention for young people with a broad range of mental and substance use disorders. This includes the expansion of *headspace* centres, from a network of 10–110 centres nationally from 2007 to 2018.[19] These services aim to reduce adverse long-term clinical, functional, and other health outcomes.[7 20 21]

This paper reports on the methods, baseline characteristics, preliminary follow-up rates, and initial findings of the Brain and Mind Centre (BMC) *Optymise* (optimising early interventions for young people with emerging mood disorders) cohort. *Optymise* is an observational study tracking demographic, clinical, functional, and comorbid outcomes longitudinally in young people who present to enhanced primary care–based mental health services. These BMC clinics are not diagnostically specific, do not impose a symptoms, severity, or risk-related threshold for receiving care, and incorporate concurrent clinical, neurobiological and interventional research. Research within these services has the specific intent of studying the clinical, functional, and neurobiological correlates of the early phases of emerging mental disorders.[7 20 21] Typically, young people attending these services present with a broad range of anxiety, depressive, manic-like, psychotic-like, or comorbid syndromes.

For in-depth examination of this transdiagnostic cohort, we have proposed that it is essential to use a multidimensional clinical and functional assessment and outcomes framework.[22–24] This framework overtly recognises that mental disorders are part of a broader general health construct, and are embedded within a social and neurodevelopmental context. Consequently, we propose five key clinical and functional dimensions: (1) social and occupational functioning (including social, educational and economic participation); (2) clinical presentation (including illness type, stage and trajectory); (3) self-harm and suicidal thoughts and behaviours (also incorporating concepts of accident and injury); (4) alcohol and other substance use; and (5) physical health comorbidities. Figure 1 shows the key domains of the multidimensional outcomes framework across time points and presents examples of potential cross-sectional and longitudinal relationships with particular emphasis on demonstrating the relationships between domains and not simply within the same domain over time. Social and occupational functioning is the primary outcome within this framework, due to the significance and persistence of impaired functioning in mentally ill populations (even during periods of syndromal remission) and its contribution to the burden of disease.[25–28] Clinical treatments and social and occupational interventions between time periods of assessment are recorded and are then considered in analyses as potential mediating or moderating variables.

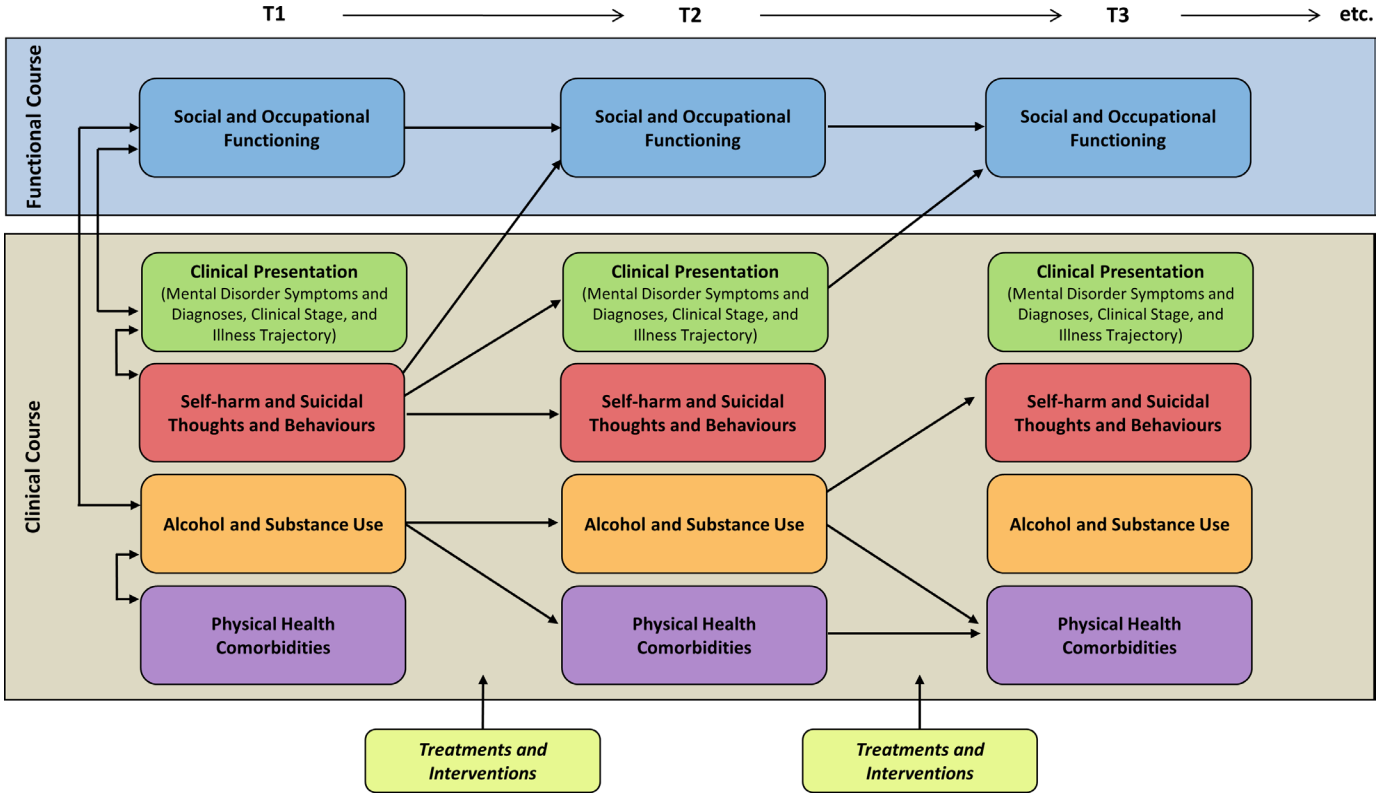

Figure 1 The multidimensional outcomes framework and examples of the potential relationships that operate across the various domains over time.

The *Optymise* cohort has been established to provide longitudinal multidimensional outcomes data from a large, transdiagnostic sample of young people, who are typically presenting in the early stages of common mental illness syndromes. Recruitment is based on presentation for care and treatment rather than specific diagnostic criteria or severity thresholds, thus the findings are likely to translate well to other broadly based youth mental health and primary care settings. This focus on setting rather than diagnosis, severity, or risk-based recruitment is consistent with National Institute of Mental Health recommendations to conduct more inclusive clinical research in cohorts drawn from the same or similar settings.[29–32] These inclusive cohorts are then more appropriate for the study of clinical or neurobiological constructs or dimensions of interest, and are also more likely to inform the development of more meaningful classification systems for common mental disorders.

Within the *Optymise* cohort, selected subgroups have been invited to take part in substudies with more in-depth measures of neuropsychological performance, structural and functional brain imaging, physical health (including anthropometric metabolic and immune function), and sleep–wake and circadian rhythms. These measures have been collected in large subsets of this population in various observational, longitudinal, and interventional studies conducted at the BMC. The *Optymise* cohort has been set up to maximise the use of data in these substudies by collecting broad information on individuals presenting to care, and linking individual clinical data between these associated studies and the cohort. This will enable more detailed investigation of the underlying neurobiology of mental illness in young people, as well as examination of the predictive value of such neurobiological measures in determining a range of long-term outcomes.

COHORT DESCRIPTION

Participants

Study participants are drawn from a larger cohort of n=6743 individuals aged between 12 and 30 years who presented to the BMC's youth mental health clinics in the Sydney suburbs of Camperdown and Campbelltown and were recruited to a research register between June 2008 and July 2018. These clinics include primary care services branded as *headspace*,[7 20 21] as well as more specialised psychiatric services. The clinics primarily attract young people with a range of mental health problems (commonly anxious, mood, or psychotic syndromes) including those with subthreshold and full-threshold mental disorders. Young people may have been self-referred, referred via a family member or friend, or else via the community including external general practitioner, school, or university.[7] All participants received clinician-based case management and relevant psychological, social, and/or medical interventions as part of standard care. This may have also included referral to more specialised mental health services, or hospitalisation, for those whose need exceeded the capacity of the primary care services.

All participants (and/or their guardians) gave written informed consent for the use of routinely collected clinical data for research purposes. No personally identifying information is recorded in the proforma in order to protect the privacy of the participants.

Patient and public involvement

Our *headspace* centres have an active patient advisory panel who are consulted regarding the development and application of research projects within our service. Findings from research studies are fed back to our young persons advisory group and to the users of our services. Results are also shared with regional and national health agencies, to assist with ongoing development of novel youth mental health services.

Data collection

Research staff were trained through individual and group training sessions to extract key data from clinical and research files and code inputs according to a specifically designed clinical research proforma (see 'Clinical proforma' below). Clinical files included all available notes and records from standard clinical care, and research files included various assessments as part of participation in substudies (which may include structured or unstructured clinical interviews and the use of symptom rating scales). The proforma records demographic, clinical, and functional information at predetermined time points. The first available clinical assessment at the service is taken as the baseline time point (T1) for each participant and the date of this assessment is used to determine each of the follow-up time points: T2 (3 months), T3 (6 months), T4 (12 months), T5 (2 years), T6 (3 years), T7 (4 years), and T8 (5 years). If there is no clinical information available for any time point (ie, the participant did not attend the service during that time), then that entry is left missing. A 'time last seen' (TLS) entry is also used to capture clinical information from the most recent presentation to the clinical service, which does not always align with one of the prespecified time points. All clinical and research notes from the preceding time points, up to and including the current time point are used to inform and complete the current proforma entry. The clinical research team responsible for collecting the data consult regularly to resolve ambiguities regarding any of the proforma items and ensure these are dealt with consistently.

As of December 2018, phase 1 of data entry has been completed, with 2767 participants included in the cohort and 78 excluded due to insufficient data. These participants were prioritised due to the richness of clinical and research data available, as a consequence of their participation in more detailed clinical or neurobiological substudies. Available data from the remaining 3898 will be entered progressively in phase 2 (commencing in 2019). New systematic data collection to determine

long-term outcomes from all original participants, using novel digital technologies, is planned for 2020.

Clinical proforma

The clinical proforma captures key clinical information regarding the following:

Demographics

Biological sex is specified at baseline (T1), and age is calculated at each time point.

Current engagement in part-time or full-time education or employment is recorded to determine Not in Education, Employment, or Training (NEET) status. NEET is assigned if there was no full-time or part-time education, employment, training or volunteer work. Current receipt of any government benefits is also recorded.

Social and occupational functioning

The Social and Occupational Functioning Assessment Scale (SOFAS)[33] is assessed at each time point. The SOFAS is a clinician-rated measure that assesses functioning on a 0–100 scale, with lower scores suggesting more severe impairment. The instructions emphasise that the rater should aim to avoid confounding the rating with clinical symptoms (which has been noted as an issue with the Global Assessment of Functioning[33–35]). A SOFAS score of below 70 is considered to be clinically significant impairment.[36]

Clinical presentation

Mental disorder diagnoses

Mental disorder diagnoses at each time point are classified according to The Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria[37] and specified as either full-threshold or subthreshold. Diagnoses are also labelled as either primary, secondary, or tertiary based on judgement of which was the dominant presenting problem at that time point.

Clinical stage

Information about the course of illness is also used to assign a clinical stage at each time point according to a previously established model.[6 38 39] This model provides a framework to assess the clinical stage of mental illness based on current and previous severity and frequency of symptoms; characteristic mental features; age of onset and clinical course of illness prior to presentation; current level of risks of harm due to illness; previous treatment and hospital admissions; suicide attempts or other risk behaviours; and current levels of social, educational and economic participation.[6] These stages are an adjunct to formal diagnosis and the demarcation between stages does not equate to the cut-offs for threshold diagnoses according to DSM-5 or other classification systems. Descriptions of the criteria for key stages (1a, 1b, and 2+) within this model are outlined in online supplementary appendix A and are detailed elsewhere.[6] A decision tree outlining the clinical staging process is provided in figure 2. While stages 3 and 4 are also specified elsewhere for recurrent, persistent and chronic illness courses, stage 2 is our proposed cut-point for more persistent disorders requiring more specific and intensive clinical care and treatment.[6 38 39] Consistent with other models of clinical staging used elsewhere in medicine (eg, in oncology), while an individual may experience clinical remission across longitudinal assessment, they cannot go back across stages when assessed at follow-up points.

Pathophysiological mechanisms

Participants with any type of mood syndrome are also allocated to one of three proposed pathophysiological mechanisms on the basis of the description of the clinical presentation. Any cases with significant manic-like symptoms (manic, hypomanic, or brief hypomanic phenomena) or significant atypical features (eg, reduced activation and energy, prolonged sleep, prolonged fatigue) are allocated to the 'circadian-bipolar spectrum' subtype. Cases with a primary psychotic disorder or significant and persistent developmental difficulties (such as autism spectrum disorder (ASD), specific learning disability, or low IQ) are allocated to the 'neurodevelopmental-psychosis' subtype. Remaining cases–typically those reporting childhood anxiety and later stress–sensitivity with evolving depressive disorder symptoms are allocated to the 'hyperarousal-anxious depression' subtype. Allocation to these pathophysiological mechanisms is intended as an adjunct to the clinical staging model and has been described in detail previously.[40–42] The clinical presentation is reviewed at each time point to assess the emergence of mania-fatigue or developmental-psychosis syndromes. As the entire clinical history is used to inform allocation to these categories, individuals assigned a circadian-bipolar spectrum or neurodevelopmental-psychosis phenotype cannot be assigned to the anxiety-depression phenotype at a later time point.

At-risk mental states

Clusters of symptoms that have been previously indicated as risk factors for progression to more severe mental disorders[43–48] are recorded in all individuals regardless of diagnosis. This includes psychotic-like experiences (the presence of any psychotic symptoms including perceptual abnormalities, bizarre ideas, disorganised speech, psychotic-like unusual language or thought content, or psychotic-like disruptive or aggressive behaviour), manic-like experiences (the presence of any manic/hypomanic symptoms including abnormally elevated mood or irritability; increased motor activity, speech, or sexual interest; manic-like disruptive or aggressive behaviour; manic-like unusual language or thought content; increased goal directed behaviour; or decreased need for sleep), and circadian disturbance (the presence of significant disruption in sleep–wake or circadian cycles including the presence of a severe sleep–wake disorder or chronic fatigue). The distinction between psychotic-like and manic-like symptoms is judged within the context of the clinical notes.

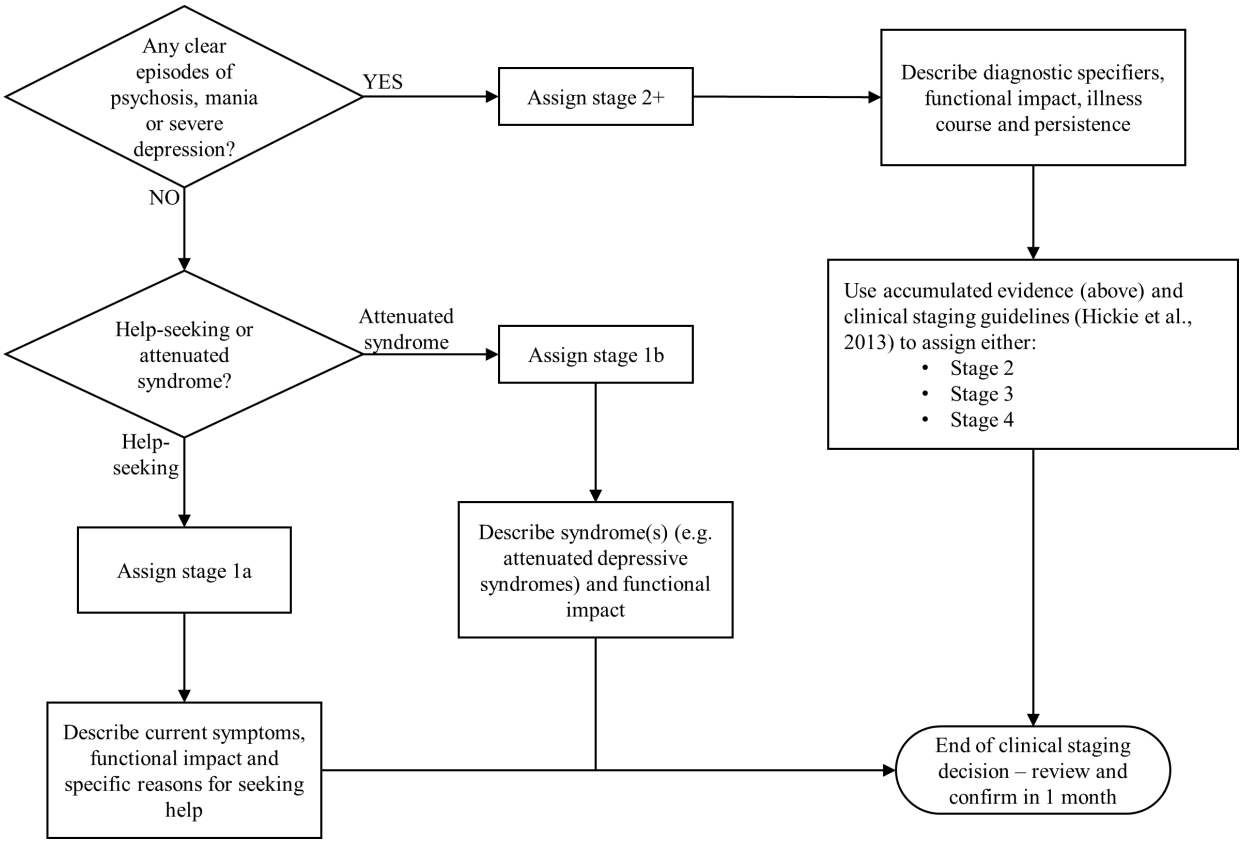

Figure 2 The stepwise process taken to assign those presenting for mental health care and treatment to the appropriate clinical stage.

Self-harm and suicidal thoughts and behaviours

The presence of suicidal ideation, suicide planning, suicide attempts, and deliberate self-harm since the previous available time point is recorded. A suicide attempt is recorded when a young person has actually taken steps to take their own life. If an individual harms themselves via cutting, hitting themselves, burning themselves, or scratching with the intention to self-harm only and not to take their life, then this is included as self-harm and not a suicide attempt. If a suicide attempt occurs it is also recorded whether the attempt resulted in hospitalisation or presentation to a hospital emergency department.

Alcohol and substance use

The presence of any reported use of tobacco, alcohol, cannabis, stimulants, or other drugs since the previous available time point is recorded.

Physical health comorbidities

Any major physical illness is recorded and assigned to a category based on type of illness.

Personal mental illness history

Known childhood-onset disorders (ie, with clear onset prior to 12 years old) are recorded in addition to current diagnoses.

Family history of mental illness

Known family history of mental illness in first-degree relatives is recorded.

Treatment utilisation

Exposure to classes of medication (antidepressant, antipsychotic, mood stabiliser, or stimulant medication) since the previous available time point, and hospitalisation overnight or longer due to a mental health problem since the previous available time point (including specification of hospitalisation due to illness severity or suicidality) are recorded.

Inter-rater reliability

An inter-rater reliability (IRR) analysis was performed using T1 proforma recordings for 66 participants that were completed independently by three raters. Fleiss' kappa was computed for nominal variables, and intraclass correlation coefficient (ICC) was computed for ordinal and continuous variables (see online supplementary appendix B).[49]

IRR estimates generally indicated moderate (kappa>0.4) to substantial (kappa>0.6) agreement, with excellent agreement (kappa>0.8) for some variables, typically those with clear defining features that would be expected to be well documented in clinical notes, such as psychotic illness, obsessive compulsive disorder, ASD and use of antidepressant or antipsychotic medication.

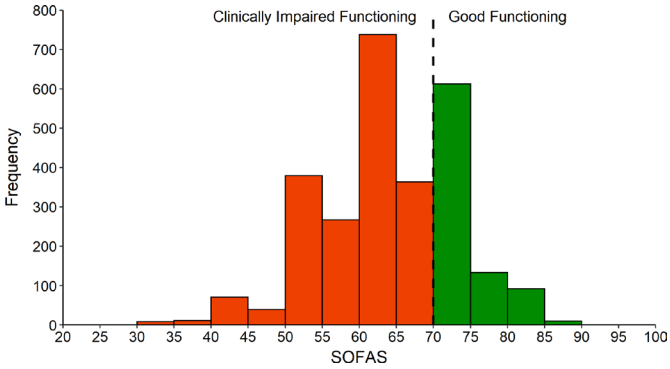

Figure 3 Distribution of Social and Occupational Functioning Assessment Scale (SOFAS) scores in the *Optymise* cohort at baseline.

Lower reliability estimates (in the fair range: kappa 0.2–0.4) were found for some variables, including receipt of government benefits, the presence of a trauma-related or personality disorder syndrome, suicide attempts, the presence of circadian disturbance, and the receipt of psychological therapy. Reliability estimates for childhood anxiety or other neurodevelopmental disorders (ie, other than ASD or attention deficit hyperactivity disorder) were in the poor range (kappa≤0.2). This indicates some variation in the scoring of these items between raters. The prevalence of some variables was too low to warrant calculation of IRR indices; caution should be exercised in the interpretation of analyses involving these variables.

Baseline characteristics

Of the 6743 individuals in the research register (mean age at presentation to clinical services±SD: 18.4±3.8 years, 57.3% female), 2767 participants have been included in phase 1 of data entry for the current study (mean age at study baseline±SD: 18.8±3.8 years, 58.2% female) based on the availability of at least one time point of clinical data, 78 have been excluded due to insufficient data, and 3898 are yet to be entered in phase 2 of data entry for this cohort.

Occupational status indicated that 17.4% (n=481) were NEET; 63.7% (n=1763) were engaged in full-time education, employment and/or training; 14.3% (n=397) were engaged in part-time education, employment and/or training; and for 4.6% (n=126) it was unclear whether there was any current occupational engagement. Ratings on the SOFAS ranged from 30 to 90, with a mean of 62.1±9.4. The distribution of baseline SOFAS scores is shown in figure 3; 68.6% (n=1876) had a SOFAS score less than 70, indicating clinically significant impairment.

Presenting syndromes at baseline are reported in table 1, with more detailed full-threshold and subthreshold diagnoses reported in online supplementary appendix C. Clinical stage, proposed pathophysiological mechanisms, and at-risk mental states are reported in table 2; the prevalence of self-harm and suicidal thoughts and behaviour, alcohol and substance use, and physical health comorbidities are reported in table 3; and the prevalence of clinical course characteristics are reported in table 4.

Preliminary follow-up rates

Of the 2767 included participants, 2336 had at least one follow-up time point (that was in the range of T2 or later, that is, at least 1 month after baseline). The median duration of follow-up from baseline to time last seen was 14.4 months (range 1–127 months; mean 22.9±23.2). The number of participants with available data and demographic characteristics for those with data at each time

Table 1 Presenting syndromes in the *Optymise* cohort at baseline

	Primary presenting syndrome		Any presenting syndrome	
	N	Percentage of sample	N	Percentage of sample
Depressive disorder	1203	43.5%	1821	65.8%
Anxiety disorder	576	20.8%	1633	59.0%
Bipolar or related disorder	232	8.4%	288	10.4%
Schizophrenia spectrum or other psychotic disorder	183	6.6%	245	8.9%
Neurodevelopmental disorder	158	5.7%	388	14.0%
Disruptive, impulse-control or conduct disorder	81	2.9%	195	7.1%
Trauma-related or stressor-related disorder	109	3.9%	223	8.1%
Substance-related or addictive disorder	58	2.1%	272	9.8%
Obsessive-compulsive or related disorder	40	1.5%	139	5.0%
Eating disorder	27	1.0%	135	4.9%
Personality disorder	24	0.9%	93	3.4%
Other disorder	57	2.1%	114	4.1%
No psychiatric syndrome	19	0.7%		

Any presenting syndrome includes any full-threshold or subthreshold primary, secondary, or tertiary diagnoses. 'Other disorder' includes gender dysphoria, dissociative disorders, sleep–wake disorders, and somatic disorders.

Table 2 Clinical stage, developmental trajectories, and at-risk mental states in the *Optymise* cohort at baseline

	N	Percentage of sample
Clinical stage		
Stage 1a	804	29.1%
Stage 1b	1625	58.7%
Stage 2+	338	12.2%
Proposed pathophysiological mechanism		
Hyperarousal-anxious depression	2024	73.2%
Neurodevelopmental-psychosis	346	12.5%
Circadian-bipolar spectrum	303	11.0%
No mood syndrome	94	3.4%
At-risk mental states		
Psychosis-like experiences	599	21.7%
Mania-like experiences	460	16.6%
Circadian disturbance	410	14.8%

Table 3 Prevalence of self-harm and suicidal thoughts and behaviour, alcohol and substance use, and physical health comorbidities in the *Optymise* cohort at baseline

	N	Percentage of sample
Self-harm and suicidal thoughts and behaviour		
Deliberate self-harm	1013	36.6%
Suicidal Ideation	1240	44.8%
Suicide planning	489	17.7%
Suicide attempt(s)	379	13.7%
Hospitalisation for suicide attempt	219	7.9%
Alcohol and substance use		
Any alcohol or substance use	1853	67.0%
Alcohol use	1724	62.3%
Cannabis use	1083	39.1%
Tobacco use	1048	37.8%
Stimulant use	570	20.6%
Other drug use	432	15.6%
Physical health comorbidities		
Any major physical illness	447	16.2%
Respiratory illness	129	4.7%
Neurological illness	87	3.1%
Endocrine illness	77	2.8%
Metabolic illness	49	1.8%
Infective illness	28	1.0%
Immune illness	26	0.9%
Gastrointestinal illness	24	0.9%
Musculoskeletal illness	20	0.7%
Gynaecological illness	19	0.7%
Pain-related illness	19	0.7%
Cardiovascular illness	12	0.4%
Skin-related illness	13	0.5%
Blood-related illness	10	0.4%
Allergic illness	9	0.3%
Cancer or tumour-related illness	7	0.3%
Renal or urinary illness	4	0.1%
Hearing-related illness	3	0.1%
Ophthalmic illness	2	0.1%

point are shown in table 5. Follow-up data will be reported in more detail in subsequent publications.

FINDINGS TO DATE

The BMC *Optymise* cohort includes individuals between 12 and 30 years old, and the mean age at baseline was approximately 19 years old, consistent with the target demographic of the early intervention youth services. The gender distribution of this cohort was similar to that reported generally in young Australians with mental disorders,[50] with around 58% female, but there was a slightly smaller proportion of females than estimated in the national population of individuals presenting to *headspace* centres.[51] The sample with available data at each of the longitudinal follow-up time points were fairly similar to the baseline sample in terms of age; however, the percentage of female participants increased at longer follow-up intervals, suggesting that females in this population may engage with care for longer periods of time.

Baseline social and occupational functioning as measured by SOFAS ranged from good functioning to a complete inability to function, with the average in the range of moderate impairment and close to 70% of the sample in the range of clinically significant impairment, demonstrating the widespread nature of functional impairment early in the course of mental illness.[52–54] Further, approximately 17% were already not engaged in education, employment or training at baseline, similar to the rate reported in *headspace* clients nationally[55] and higher than general population estimates in this age group (11.4% of Australians aged 15–29 years old).[56] Our initial report on changes in social and occupational functioning across the course of care in this cohort[57] indicates that only around a quarter of participants experience reliable improvement, with functioning either deteriorating or remaining the same in the majority. This chronic functional impairment should be a high priority target for intervention efforts, given the significant contribution of poor functioning to the burden of disease,[25 27] and associations between poor functioning and other adverse outcomes.[58–60]

Baseline diagnostic information indicates that the most common primary presenting problem was a depressive syndrome, followed by anxiety, bipolar, and psychotic

Table 4 Clinical course characteristics in the *Optymise* cohort at baseline

	N	Percentage of sample
Personal mental illness history		
Any childhood disorder	364	13.2%
Childhood ADHD	151	5.5%
Childhood ASD	77	2.8%
Childhood anxiety disorder	66	2.4%
Other childhood neurodevelopmental disorder	56	2.0%
Childhood depression	41	1.5%
Childhood behavioural or conduct disorder	24	0.9%
Childhood OCD	12	0.4%
Other childhood disorder	11	0.4%
Family history in first-degree relatives		
Any family history of mental illness	1270	45.9%
Family history of depressive disorder	835	30.2%
Family history of anxiety disorder	404	14.6%
Family history of alcohol use disorder	249	9.0%
Family history of bipolar disorder	216	7.8%
Family history of substance use disorder	184	6.7%
Family history of psychotic disorder	126	4.6%
Family history of suicide	44	1.6%
Treatment Utilisation		
Psychological therapy	1501	54.3%
Any psychiatric medication	1373	49.6%
Antidepressants	1068	38.6%
Antipsychotics	475	17.2%
Stimulants	244	8.8%
Mood stabilisers	209	7.6%
Any hospitalisation	635	23.0%
Hospitalisation due to severity	281	10.2%
Hospitalisation due to suicidality	218	7.9%

ADHD, attention deficit hyperactivity disorder; ASD, autism spectrum disorder; OCD, obsessive compulsive disorder.

syndromes. This is consistent with reports that, although anxiety disorders are the most prevalent mental illnesses in young people,[50 61] mood disorders are generally associated with greater help-seeking and service use.[62 63] The prevalence rates of full-threshold diagnoses were slightly higher in our sample than those reported in *headspace* clients nationally.[51] For almost all diagnostic categories, the prevalence of subthreshold or unspecified cases was greater than the prevalence of full-threshold disorders (see online supplementary appendix C), highlighting that, despite being help-seeking, the majority of our sample experience syndromes that do not meet formal diagnostic criteria at presentation to care. This illustrates the inadequacy of traditional diagnostic classification systems for describing the experiences of young people at early stages of mental disorders, in whom levels of distress and disability are high, clearly warranting intervention even in the absence of such formal diagnoses.[7 51 64–66]

Further, the prevalence of at-risk mental states was more substantial than both full-threshold and subthreshold bipolar and psychotic diagnoses, suggesting that such features are common in those presenting to youth mental health services, occurring much more frequently than overt psychotic or bipolar disorders. The prevalence of psychosis-like experiences in this sample is higher than the 6%–12% reported in adults and adolescents in the general population[67–69] but lower than previous reports in young people presenting for mental healthcare, which have found prevalence closer to 50% even in non-psychotic samples.[70 71] The more conservative prevalence in the current study is likely due to the method of data collection, as less severe psychosis-like symptoms may not have been specifically assessed or recorded by clinicians.

The distribution across clinical stages of young people presenting to our early intervention services has varied somewhat across previous reports[7 64 66 72]; however, the broadly consistent pattern of the majority of cases presenting at earlier stages (1a or 1b) is reproduced in the present sample. The present study provides the largest sample to date with clinical stage data using this model, and assessment at the earliest available clinical time point provides an estimate of the distribution across stages as close to first presentation to care as possible. Our report on longitudinal transition rates from earlier to later clinical stages in the *Optymise* cohort indicates a low risk of progression to later stages in those presenting at stage 1a, and a more substantial risk of progression in those presenting at stage 1b.[73] A number of baseline factors are associated with these transitions including manic-like and psychotic-like experiences and lower social and occupational functioning for stage 1a to 1b transitions, and psychotic-like experiences and circadian disturbance for stage 1b to 2+ transitions.[73]

The proportion of individuals assigned to the three proposed pathophysiological mechanisms (hyperarousal-anxious depression, circadian-bipolar spectrum, and neurodevelopmental-psychosis) differed somewhat from previous reports,[40 74] with a greater proportion of the current sample in the hyperarousal-anxious depression subtype. This is likely due to the fact that the current report describes the profile of individuals at the first available clinical time point, whereas previous reports have used all available information, and have not been

Table 5 Key baseline characteristics of included participants at each time point

	Baseline	3 months	6 months	12 months	24 months	36 months	48 months	60 months
N	2767	1690	1257	1074	691	466	288	199
Sex (% female)	58.2	59.6	61.7	61.6	59.2	63.1	63.5	63.3
Baseline age (mean±SD)	18.8±3.8	18.4±3.6	18.4±3.6	18.4±3.6	18.7±3.8	18.6±3.8	18.5±3.7	18.4±3.7
Baseline SOFAS (mean±SD)	62.1±9.4	62.3±9.1	62.3±9.0	61.7±9.4	61.4±9.1	61.1±8.8	60.9±9.0	61.0±8.6

SOFAS, Social and Occupational Functioning Assessment Scale.

restricted to this early point in clinical care. The emergence of circadian, manic, or psychotic phenomena may occur at various points across the course of illness; therefore, a greater proportion of individuals in the circadian-bipolar spectrum and neurodevelopmental-psychosis subgroups would be expected at later time points. Accordingly, initial longitudinal data indicate that around 13% of those in the *Optymise* cohort transition across these pathophysiological mechanism pathways during the course of care, with an additional 14% transitioning to later clinical stages within the same pathway.[42] Clinical staging and pathophysiological mechanisms are independent but complementary classification systems, with clinical stage reflecting the severity and persistence of illness, and proposed pathophysiological mechanisms reflecting the type of illness.

Deliberate self-harm and suicidal thoughts and behaviour were common at baseline, with rates concordant with previous studies in mentally ill samples[75 76] and much higher than the general adolescent population.[77 78] The presence of such high rates of deliberate self-harm and suicidal thoughts and behaviour early in the course of care highlights the specific need for risk reduction strategies and ongoing management of these thoughts and behaviours during care and treatment. A report on suicide attempts in this cohort[79] found that the presence of a prior suicide attempt at baseline increases not only the risk for subsequent deliberate self-harm and suicidal thoughts and behaviours but also other negative outcomes including onset of alcohol or substance use disorder and bipolar disorder. This demonstrates the utility of this dataset in assessing prospective risk for multiple outcome domains in relation to baseline features.

STRENGTHS AND LIMITATIONS

The *Optymise* cohort will provide an important resource to evaluate outcomes and understand the course of mental illness in young people presenting for mental health care and treatment. The large transdiagnostic sample, and selection based on presentation for care rather than specific diagnostic, severity, or risk-related criteria, allows for appropriate variance along dimensions of interest and provides a sample representative of those presenting to clinical services. This approach maximises the potential for clinically meaningful conclusions to be drawn. The assessment of multidimensional outcomes affords an important level of detail. It will allow examination of inter-relationships between these domains and inform appropriate confounding factors to be considered in subsequent analyses. Longitudinal assessment, using all available data will be another strength of this study, with standardised follow-up time points as well as a 'time last seen' time point capturing information across the full duration of time in care. The linkage of this longitudinal data with more in-depth assessments from related neuropsychological and neurobiological studies will further strengthen the richness of this dataset and increase the potential for greater understanding of the underpinnings of the development of mental illness in young people.

There are important limitations of this study. Due to the method of data collection (ie, data extraction from clinical and research files), there is considerable variability in the quantity and quality of clinical information available. This has an adverse impact on the consistency of the measures. It is important to note that this will likely result in some under-reporting or conservative estimates of the incidence of certain parameters, as the absence of clinical information may mean the information is unavailable or missing, not assessed by the clinician, or simply not clinically relevant. However, the data most consistently available in clinical files likely reflect the measures that are most widely used by treatment providers in an everyday context. This will increase the generalisability of the findings and take advantage of existing approaches to clinical assessment. It is also important to note that those with available follow-up time points are drawn from those continuing to engage with clinical care over a longer period. This may introduce some bias in the follow-up sample towards those individuals with more severe, persistent, or recurrent illness.

CONCLUSION

This paper reports on the methods, baseline characteristics, follow-up rates, and initial findings of the BMC *Optymise* cohort, an observational study tracking a range of demographic, clinical, functional, and comorbid risk outcomes longitudinally in young individuals presenting for mental health care and treatment. The cohort is broadly representative of young people presenting to mental health care services in terms of demographic and clinical features. Initial publications from the cohort indicate a number of factors are associated with transition to

later clinical stages, long-term social and occupational function typically remains poor, and that prior suicide attempts at baseline are predictive of a range of negative outcomes. Further work in this cohort will follow the longitudinal course of mental illness and associated multidimensional outcome domains in young people presenting for mental health care and treatment, and will allow for testing of the relative predictive validity of various illness characteristics and outcome domains. Future plans include exploring the bidirectional longitudinal relationships between functional recovery and other adverse outcomes, characterising longitudinal transitions across clinical stages and pathophysiological mechanisms to provide greater insight into the emergence and development of specific syndromes across the course of care, and analysing the predictive value of at-risk mental states in relation to multidimensional outcomes. Characterising the longitudinal relationships between the clinical, functional, and other associated risk factors in this population (including associated neurobiological factors) and investigating their predictive value across multiple outcomes domains is important for the development of prevention and intervention strategies to improve mental health care and address the broad range of outcomes contributing to the burden of disease.

COLLABORATION

The BMC welcomes collaboration involving the *Optymise* cohort, subject to appropriate ethical approval, permissions and research agreements. This may include collaboration on analysis of the currently available data, as well as collaboration on collection of new data at follow-up time points and further substudies with measures in a specific domain. Interested parties should contact ian.hickie@sydney.edu.au with details of the proposed collaboration.

Author affiliations
[1]Brain & Mind Centre, The University of Sydney, Camperdown, New South Wales, Australia
[2]School of Psychology, The University of Sydney, Camperdown, New South Wales, Australia
[3]Department of Psychology, Macquarie University, Sydney, New South Wales, Australia
[4]Charles Perkins Centre, The University of Sydney, Camperdown, New South Wales, Australia
[5]Thompson Institute, University of the Sunshine Coast, Birtinya, Queensland, Australia
[6]Department of Academic Psychiatry, Newcastle University, Newcastle, United Kingdom
[7]Diderot University, Sorbonne City, Paris, France
[8]School of Medicine, University of Notre Dame, Sydney, New South Wales, Australia

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Contributors IBH, DFH, JC, EMS, SLN, AJG, FI, and JSC were involved in study conception, design and planning, and are involved in ongoing planning, analysis, and publication of the data from this cohort. SC, JJC, JRP, and AEW are also involved in ongoing planning, analysis, and publication of the data from this cohort. AN, NZ, JJC, and DW are involved in study coordination and data collection. JSC drafted the manuscript. All authors contributed to and have approved the final manuscript.

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Competing interests Professor Sharon Naismith has received honoraria for an educational seminar for Lundbeck. A/Professor Elizabeth Scott is the Medical Director, Young Adult Mental Health Unit, St Vincent's Hospital Darlinghurst, Discipline Leader of Adult Mental Health, School of Medicine, University of Notre Dame, Research Affiliate, The University of Sydney and Consultant Psychiatrist. She has received honoraria for educational seminars related to the clinical management of depressive disorders supported by Servier and Eli-Lilly pharmaceuticals. She has participated in a national advisory board for the antidepressant compound Pristiq, manufactured by Pfizer. She was the National Coordinator of an antidepressant trial sponsored by Servier. Professor Ian Hickie has been a Commissioner in Australia's National Mental Health Commission since 2012. 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. Professor Hickie has previously led community-based and pharmaceutical industrysupported (Wyeth, Eli Lily, Servier, Pfizer, AstraZeneca) projects focused on the identification and better management of anxiety and depression. He is a Board Member of Psychosis Australia Trust and a member of Veterans Mental Health Clinical Reference group. He is the Chief Scientific Advisor to, and an equity shareholder in, InnoWell. InnoWell has been formed by the University of Sydney and PwC to administer the $30M Australian Government Funded Project Synergy. Project Synergy is a 3-year programme for the transformation of mental health services through the use of innovative technologies.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not required.

Ethics approval The study was approved by the University of Sydney Human Research Ethics Committee (project numbers 2008/5453 and 2012/1626).

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ORCID iDs
Joanne S Carpenter http://orcid.org/0000-0002-9766-6700
Frank Iorfino http://orcid.org/0000-0003-1109-0972
Shane Cross http://orcid.org/0000-0002-5413-8342
Natalia Zmicerevska http://orcid.org/0000-0001-7649-4711
Jacob J Crouse http://orcid.org/0000-0002-3805-2936
Jake R Palmer http://orcid.org/0000-0001-8253-0483
Daniel F Hermens http://orcid.org/0000-0002-8570-2663
Jan Scott http://orcid.org/0000-0002-7203-8601
Elizabeth M Scott http://orcid.org/0000-0003-3907-0324
Ian B Hickie http://orcid.org/0000-0001-8832-9895

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