

## Appendix A Description of Key Clinical Stages

	Definition and Clinical Features
<b>Stage 1a</b> Help-Seeking Subjects with Symptoms	<ul style="list-style-type: none"> <li>• Non-specific symptoms of anxiety or depression</li> <li>• Mild to moderate severity of symptoms</li> <li>• Symptoms may include subjective or objective evidence of mild neuropsychological deficits</li> <li>• Evidence of only recent or mild impacts of illness on social, educational, or occupational functioning</li> <li>• May include those with earlier childhood-onset symptoms who have re-presented or worsened during the adolescent period</li> <li>• May include those with earlier onset neurodevelopmental or attentional disorders who now present with anxiety or depressive symptoms in the adolescent years</li> </ul>
<b>Stage 1b</b> Attenuated Syndromes	<ul style="list-style-type: none"> <li>• Specific symptoms of severe anxiety, moderate depression, brief hypomania, or brief psychotic phenomena</li> <li>• Persisting syndromes that may meet diagnostic criteria for specific anxiety disorders, major depressive disorder, or bipolar II disorder</li> <li>• May include subjective or objective evidence of at least moderate neuropsychological change</li> <li>• Moderate to severe impact of illness on social, education, or occupational functioning</li> <li>• May have syndromes that are somewhat mixed in terms of their symptomatology or have features of a number of different diagnostic groups, or may have 'comorbidity' of anxiety, depressive, and substance misuse disorders</li> <li>• May include the presence of regular, deliberate self-harm without overt suicidal intent including impulsive low lethality overdose occurring in context of a psychosocial stressor and in the absence of severe depression</li> <li>• Treatment may have already commenced and/or the person may have been referred for further specialized assessment</li> <li>• Some degree of treatment with an antidepressant, antipsychotic, or mood-stabilizing agent is common for subjects in this stage, particularly where there has been limited access to specialized psychological therapies</li> </ul>
<b>Stage 2</b> Discrete Disorders	<ul style="list-style-type: none"> <li>• Clear episodes of psychotic, manic, or severe depressive disorders</li> <li>• 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.</li> <li>• Full-threshold disorder with moderate-severe symptoms and persistence over time, characterized by key symptoms that are no longer transient</li> <li>• Typically associated with significant neuropsychological deficits</li> <li>• Illness is clearly having a major impact on social, educational, or occupational functioning</li> <li>• The 'discrete disorder' stage generally corresponds with the clinical point at which specific medical treatments would be considered an essential part of clinical management (e.g. prescription of antipsychotic or mood-stabilising agents)</li> <li>• If the patient has been hospitalized for treatment, then typically they would have met criteria for this stage</li> <li>• 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 (e.g. psychomotor change, psychotic features), they would have been likely to have met criteria for this stage</li> <li>• Moderately severe mood or anxiety disorders that are complicated by significant and persistent alcohol or other substance misuse may reach this stage</li> <li>• 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</li> </ul>

**Appendix B** Inter-rater Reliability Statistics

		ICC	Fleiss' Kappa
Demographics	NEET Status		0.75
	Receipt of Government Benefits		0.23
Social and Occupational Functioning	SOFAS	0.65	
Clinical Presentation			
<i>Mental Disorder Diagnoses</i>	Primary Presenting Syndrome		0.52
	<u>Any Presenting Syndrome:</u>		
	Depressive Disorder		0.58
	Bipolar or Related Disorder		0.72
	Schizophrenia Spectrum or Other Psychotic Disorder		0.83
	Anxiety Disorder		0.61
	OCD		0.84
	Trauma- or Stressor-related Disorder		0.23
	Neurodevelopmental Disorder		0.75
	Eating Disorder		0.65
	Disruptive, Impulse-control, or Conduct Disorder		0.56
	Personality Disorder		0.24
	Substance-related or Addictive Disorder		0.59
	Other Disorder		0.66
<i>Clinical Stage</i>	Clinical Stage	0.54	
<i>Proposed Pathophysiological Mechanism</i>	Proposed Pathophysiological Mechanism		0.74
<i>At-risk Mental States</i>	Psychotic-like Experiences		0.75
	Manic-like Experiences		0.74
	Circadian Disturbance		0.23
Self-harm and Suicidal Thoughts and Behaviours	Deliberate Self-harm		0.59
	Suicidal Ideation		0.46
	Suicide Planning		0.43
	Suicide Attempt(s)		0.28
	Hospitalisation for Suicide Attempt		0.46
Alcohol and Substance Use	Alcohol Use		0.51
	Cannabis Use		0.76
	Tobacco Use		0.56
	Stimulant Use		0.55
	Other Drug Use		0.52
Physical Health Comorbidities	Any Major Physical Illness		0.45
	Neurological Illness		0.66
	Endocrine Illness		0.50
	Respiratory Illness		0.38
	Metabolic Illness <sup>a</sup>		
	Infective Illness <sup>a</sup>		
	Immune Illness <sup>a</sup>		
	Gastrointestinal Illness <sup>a</sup>		

	Gynaecological Illness <sup>a</sup>	
	Musculoskeletal Illness <sup>a</sup>	
	Pain-related Illness <sup>a</sup>	
	Cardiovascular Illness <sup>a</sup>	
	Skin-related Illness <sup>a</sup>	
	Blood-related Illness <sup>a</sup>	
	Allergic Illness <sup>a</sup>	
	Cancer or Tumour-related Illness <sup>a</sup>	
	Renal or Urinary Illness <sup>a</sup>	
	Ophthalmic Illness <sup>a</sup>	
	Hearing-related Illness <sup>a</sup>	
Personal Mental Illness History	Any Childhood Disorder	0.54
	Childhood ASD	0.90
	Childhood ADHD	0.59
	Childhood Anxiety Disorder	0.19
	Other Childhood Neurodevelopmental Disorder	0.18
	Childhood Depression <sup>a</sup>	
	Childhood Behavioural or Conduct Disorder <sup>a</sup>	
	Childhood OCD <sup>a</sup>	
	Other Childhood Disorder <sup>a</sup>	
Family History of Mental Illness	Any Family History of Mental Illness	0.54
	Family History of Bipolar Disorder	0.92
	Family History of Psychotic Disorder	0.57
	Family History of Depressive Disorder	0.50
	Family History of Anxiety Disorder	0.69
	Family History of Alcohol Use Disorder	0.76
	Family History of Substance Use Disorder	0.63
	Family History of Suicide <sup>a</sup>	
Treatment Utilisation	Psychological Therapy	0.25
	Any Psychiatric Medication	0.84
	Antidepressants	0.82
	Antipsychotics	0.82
	Stimulants	0.73
	Mood Stabilisers	0.68
	Any Hospitalisation	0.62
	Hospitalisation due to Severity	0.46
	Hospitalisation due to Suicidality	0.46

ICC = inter-class correlation coefficient; OCD = Obsessive Compulsive Disorder; ASD = Autism Spectrum Disorder; ADHD = Attention Deficit Hyperactivity Disorder; SOFAS = Social and Occupational Functioning Assessment Scale; NEET = Not in Education Employment or Training. <sup>a</sup> Unable to assess inter-rater reliability due to low prevalence.

**Appendix C Full- and Sub-threshold Diagnoses in the *Optymise* Cohort at Baseline**

Diagnostic Category	Diagnosis	Full -threshold		Sub-threshold	
		N	% of sample	N	% of sample
<b>Depressive Disorder</b>					
	Major depressive disorder	820	29.6%	390	14.1%
	Persistent depressive disorder (dysthymia)	49	1.8%	27	1.0%
	Substance/medication-induced depressive disorder	0	0%	3	0.1%
	Depressive disorder due to another medical condition	1	<.1%	6	0.2%
	Other specified depressive disorder	3	0.1%	10	0.4%
	Unspecified depressive disorder	102	3.7%	558	20.2%
<b>Anxiety Disorder</b>					
	Agoraphobia	18	0.7%	8	0.3%
	Generalised anxiety disorder	289	10.4%	203	7.3%
	Panic disorder	29	1.0%	22	0.8%
	Social anxiety	271	9.8%	214	7.7%
	Specific phobia	3	0.1%	3	0.1%
	Substance/medication-induced anxiety disorder	0	0%	1	<0.1%
	Anxiety disorder due to another medical condition	0	0%	1	<0.1%
	Unspecified anxiety disorder	136	4.9%	525	19.0%
<b>Bipolar or Related Disorder</b>					
	Bipolar I	37	1.3%	0	0%
	Bipolar II	54	2.0%	79	2.9%
	Cyclothymic disorder	1	<0.1%	16	0.6%
	Substance/medication-induced bipolar	0	0%	2	0.1%
	Bipolar due to another medical condition	0	0%	0	0%
	Other specified bipolar or related disorder	2	0.1%	1	<0.1%
	Unspecified bipolar or related disorder	29	1.1%	67	2.4%
<b>Schizophrenia Spectrum or Other Psychotic Disorder</b>					
	Brief psychotic disorder	20	0.7%	7	0.3%
	Schizophreniform disorder	11	0.4%	5	0.2%
	Schizophrenia	48	1.7%	13	0.5%
	Schizoaffective disorder	20	0.7%	12	0.4%
	Substance/medication-induced psychotic disorder	25	0.9%	9	0.3%
	Psychotic disorder due to another medical condition	0	0%	0	0%
	Other specified schizophrenia spectrum or other psychotic disorder	2	0.1%	6	0.2%
	Unspecified schizophrenia spectrum or other psychotic disorder	12	0.4%	65	2.3%

<b>Neurodevelopmental Disorder</b>				
Intellectual disability	2	0.1%	16	0.6%
Global developmental delay	3	0.1%	2	0.1%
Autism spectrum disorder	84	3.0%	34	1.2%
Attention-deficit/hyperactivity disorder	156	5.6%	83	3.0%
Other specified neurodevelopmental disorder	14	0.5%	15	0.5%
Unspecified neurodevelopmental disorder	1	<0.1%	11	0.4%
<b>Disruptive, Impulse-control, or Conduct Disorder</b>				
Conduct disorder	9	0.3%	14	0.5%
Oppositional defiant disorder	27	1.0%	35	1.3%
Intermittent explosive disorder	0	0%	1	<0.1%
Other specified disruptive, impulse-control, or conduct disorder	0	0%	11	0.4%
Unspecified disruptive, impulse-control, or conduct disorder	10	0.4%	93	3.4%
<b>Trauma- or Stressor-related Disorder</b>				
Posttraumatic stress disorder	37	1.3%	58	2.1%
Acute stress disorder	1	<0.1%	4	0.1%
Adjustment disorder	14	0.5%	44	1.6%
Other specified trauma- or stressor-related disorder	4	0.1%	6	0.2%
Unspecified trauma- or stressor-related disorder	9	0.3%	49	1.8%
<b>Substance-related or Addictive Disorder</b>				
Alcohol use disorder	59	2.1%	45	1.6%
Substance use disorder	136	4.9%	94	3.4%
Other substance-related or addictive disorder	2	0.1%	1	<0.1%
<b>Obsessive-compulsive or Related Disorder</b>				
Obsessive-compulsive disorder	56	2.0%	52	1.9%
Substance/medication-induced obsessive compulsive or related disorder	0	0%	0	0%
Obsessive-compulsive or related disorder due to another medical condition	1	<0.1%	1	<0.1%
Other specified obsessive-compulsive and related disorder	0	0%	11	0.4%
Unspecified obsessive-compulsive and related disorder	1	0.04%	19	0.73%
<b>Eating Disorder</b>				
Anorexia nervosa	11	0.4%	6	0.2%
Bulimia	16	0.6%	6	0.2%
Binge eating disorder	0	0%	8	0.3%
Other specified eating disorder	2	0.1%	0	0%
Unspecified eating disorder	18	0.7%	70	2.5%

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Personality Disorder				
Antisocial personality disorder	0	0%	1	<0.1%
Avoidant personality disorder	0	0%	4	0.1%
Borderline personality disorder	28	1.0%	44	1.6%
Narcissistic personality disorder	0	0%	0	0%
Schizotypal personality disorder	1	<0.1%	2	0.1%
Other specified personality disorder	0	0%	5	0.2%
Unspecified personality disorder	0	0%	8	0.3%

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Other Disorder (thresholds not specified)				
Gender dysphoria			41	1.5%
Somatic disorder			36	1.3%
Dissociative disorder			6	0.2%
Sleep-wake disorder			32	1.2%

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