Clinical staging: a heuristic model for psychiatry and youth mental health

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ABSTRACT

- Diagnosis in psychiatry continues to struggle to fulfil its key purposes, namely to guide treatment and to predict outcome. A clinical staging model, widely used in clinical medicine, could improve the utility of diagnosis in psychiatry, especially in young people with emerging disorders.
- Clinical staging has immediate potential to improve the logic and timing of interventions in psychiatry, as it does in many complex and potentially serious medical disorders. Interventions could be evaluated in terms of their ability to prevent or delay progression from earlier to later stages of a disorder, and selected by consumers and clinicians on the basis of clear-cut risk–benefit criteria. This would ensure that, as treatments are offered earlier, they remain safe, acceptable and affordable, and potentially more effective.
- Biological variables and a range of candidate risk and protective factors could be studied within and across stages, and their role, specificity and centrality in risk, onset and progression of disorders clarified. In this way, a clinicopathological framework could be progressively constructed.
- Clinical staging, with restructuring across and within diagnostic boundaries and explicit operational criteria for extent and progression of disorder, should be actively explored in psychiatry as a heuristic strategy for developing and evaluating earlier, safer, and more effective clinical interventions, and for clarifying the biological basis of psychiatric disorders. Young people with emerging mental and substance use disorders could be the main beneficiaries.

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Diagnosis is central to quality medical care,[1] yet in psychiatry it still struggles to fulfil its key purposes of guiding treatment selection and predicting outcome. This has been concealed by the apparent success of global efforts to construct internationally agreed, operationally defined criteria for psychiatric disorders, which have undoubtedly improved the reliability but not the validity of diagnosis.[2] Unfortunately, this process has done little more than create a spurious precision, which does not extend far beyond the research setting. Virtually none of the available pharmacological and psychosocial treatments have real specificity for current operationally defined disorders, which, similarly, lack predictive validity.

Our official diagnostic systems have also impeded the search for neurobiological and psychosocial risk factors. The *Diagnostic and statistical manual of mental disorders* (4th ed) and *The international classification of diseases* (10th revision) are characterised by artificial divisions based on cross-sectional symptom sets, which are infused and confused with course-of-illness variables. Early clinical features are not differentiated from those that become apparent as a disorder persists. Diagnostic concepts are typically derived from samples of patients with chronic illness in tertiary care settings, where the impression of stability and validity is enhanced. Such diagnoses make more sense in those settings and can be best viewed as stable outcome variables rather than useful tools for guiding early intervention or treatment of people with less severe illness.

Understanding of this is crucial in youth mental health where new and evolving syndromal patterns are the norm. Comorbidity and polypharmacy are potent reflections of the practical weakness of our current diagnostic concepts. Psychosocial treatments appropriately focus on broader personal and social needs and hence range freely across the diagnostic landscape. If diagnosis is the art of "carving nature at its joints",[3] then everyday clinical experiences and a logjam of research findings suggest that, in young people with emerging mental health disorders, we are reliably cutting through bone.

How can we reform and refine diagnosis so that treatments can be selected in a safer, more effective manner; prognosis can be more accurately assessed; and the confusing array of biological disturbances condensed into something resembling a clinicopathological framework? Clinical staging, a deceptively simple and practical tool found useful in other areas of medicine, may provide a way forward.[4,5]

What is clinical staging?

Clinical staging is, simply, a more refined form of diagnosis. Its value is recognised in the treatment of malignancies, where quality of life and survival rely on the earliest possible delivery of effective interventions. However, it also has applicability in diseases as diverse as osteomyelitis, sarcoidosis, autoimmune diseases and idiopathic myelofibrosis.[6-8] Clinical staging differs from conventional diagnostic practice in that it not only defines the extent of progression of a disorder at a particular point in time, but also where a person lies currently along the continuum of the course of an illness. The differentiation of early and milder clinical phenomena from those that accompany illness extension, progression and chronicity, lies at the heart of the concept, which therefore makes it potentially useful in young people. It enables the clinician to select treatments relevant to earlier stages of an illness, and assumes that such interventions will be both more effective and less harmful than treatments delivered later in the course.[4]

While staging links treatment selection and prediction, its role in the former is more crucial than in the latter, particularly as early successful treatment may change the prognosis and thus prevent progression to subsequent stages or, even better, result in remission and cure. Our current categories exist in a kind of no man's land, disconnected from the underlying substrates of the disorders, but imposing artificial boundaries without utility. In addition to guiding treatment selection, a staging framework, which moves beyond the current diagnostic silos to encompass a broader range of clinical phenotypes, yet which introduces subtypes along a longitudinal dimension, has the potential to organise endophenotypic data in a more coherent and mutually validating fashion. However, diagnostic progress in psychiatry represents a major global challenge, and we regard our proposed staging model as heuristic and complementary at this point. Its value will ultimately be determined by its utility.

Clinical staging model framework for psychotic and severe mood disorders*†

Stage	Definition	Target populations and referral sources	Potential interventions
0	Increased risk of psychotic or severe mood disorder No symptoms currently	• First-degree teenage relatives of probands	• Improved mental health literacy • Family education, drug education • Brief cognitive skills training
1a	Mild or non-specific symptoms (including neurocognitive deficits) of psychosis or severe mood disorder. Mild functional change or decline	• Screening of teenage populations • *Referral by:* primary care physicians; school counsellors	• Formal mental health literacy • Family psychoeducation, formal CBT • Active substance misuse reduction
1b	Ultra high risk: moderate but subthreshold symptoms, with moderate neurocognitive changes and functional decline to caseness (GAF, < 70)	• *Referral by:* educational agencies; primary care physicians; emergency departments; welfare agencies	• Family psychoeducation, formal CBT • Active substance misuse reduction • Omega-3 fatty acids • Atypical antipsychotic agents • Antidepressant agents or mood stabilisers
2	First episode of psychotic or severe mood disorder Full threshold disorder with moderate to severe symptoms, neurocognitive deficits and functional decline (GAF, 30–50)	• *Referral by:* primary care physicians; emergency departments; welfare agencies; specialist care agencies; drug and alcohol services	• Family psychoeducation, formal CBT • Active substance misuse reduction • Atypical antipsychotic agents • Antidepressant agents or mood stabilisers • Vocational rehabilitation
3a	Incomplete remission from first episode of care Patient's management could be linked or fast-tracked to Stage 4	• Primary and specialist care services	• As for Stage 2, but with additional emphasis on medical and psychosocial strategies to achieve full remission
3b	Recurrence or relapse of psychotic or mood disorder, which stabilises with treatment at a GAF level, or with residual symptoms or neurocognition below the best level achieved after remission from the first episode	• Primary and specialist care services	• As for Stage 3a, but with additional emphasis on relapse prevention and strategies to detect "early warning signs"
3c	Multiple relapses, provided worsening in clinical extent and impact of illness is objectively present	• Specialist care services	• As for Stage 3b, but with emphasis on long-term stabilisation
4	Severe, persistent ***or*** unremitting illness, as judged by symptoms, neurocognition, and disability criteria Patient's management could be fast-tracked to this stage at first presentation, based on specific clinical and functional criteria (from Stage 2), or because of failure to respond to treatment (from Stage 3a)	• Specialised care services	• As for Stage 3c, but with emphasis on clozapine, other tertiary treatments, and social participation despite ongoing disability

* This table has been reproduced in a modified form with the permission of the *Australian and New Zealand Journal of Psychiatry.* It was originally published in McGorry et al (2006).[5] † The model is bidirectional, so that disorders may not only progress, but also recede and remit fully, often on a sustained and long-term basis, under the influence of biological, environmental, and therapeutic variables.
CBT = cognitive behaviour therapy. GAF = global assessment of functioning (scale, 0–100). ◆

What kinds of disorders lend themselves to a clinical staging model?

A disorder which is potentially severe and *tends* to or *may* progress if untreated is likely to be most appropriate for staging. The existence of even a substantial proportion of self-limiting and benign cases does not present a problem for the model, provided there is also a chronic and severe subset. Treatment, and particularly early treatment, should also demonstrably increase the chances of cure or, at least, of reducing mortality and disability. This includes many or most psychiatric disorders, including psychotic disorders[9] and, specifically, schizophrenia,[10] but also mood, anxiety, eating, personality and substance use disorders.

How do we define the stages of a disorder?

In other medical conditions, clinical stages are defined by the extent and progression of the illness and its biological impact on the patient, which in turn must correlate with prognosis. This approach usually depends on a capacity to define pathologically, as well as clinically, the limits or extent of the disease process. In clinical psychiatry, this could involve not only a cross-sectional clinical definition, but a wider biopsychosocial definition of extent or progression. Therefore, in addition to the severity, persistence and recurrence of symptoms, biological changes (eg, hippocampal volume loss) and the social impact of a disorder (eg, the effect on social relationships and employment) could also be drawn into the definition. Ultimately, something approaching a clinicopathological model could emerge. The Box gives an initial flavour of how such a heuristic model could be formulated, with a focus on psychotic and mood disorders in the first instance. Other syndromal domains could be addressed in parallel or incorporated where appropriate.

What are the potential benefits of staging?

On the clinical side, defining discrete stages according to progression of disease creates a framework for the evaluation of interven-

tions oriented towards prevention. The key positive health outcomes are prevention of progression to more advanced stages, or regression to an earlier stage, including full and sustained remission. This requires an accurate understanding of those broad social, biological, and personal risk and protective factors that influence progression from one stage to the next. Furthermore, we need to know the relative potency of these risk factors and which of them may be responsive to current interventions. While some factors may operate across several or all stage transitions, others may be stage-specific; for example, substance misuse or stress may be especially harmful in triggering the onset of the first episode of an illness, yet be less toxic subsequently (or vice versa). Gene–environment interactions almost certainly underpin and mediate these transitions, where environmental variables, such as substance misuse, psychosocial stressors, cognitive style, medication adherence, and social isolation, may interact with genetic and other biological risk factors.[11-13]

From an aetiological perspective, over a century of research with the traditional diagnostic categories of psychosis and severe mood disorders has failed to relate these flawed concepts to any discrete pathophysiological conditions.[14,15] This is despite consistent, spirited, yet largely rhetorical, defence, particularly of the schizophrenia concept.[16] The strategy of determining "endophenotypes" is the latest conceptual step aiming to solve this conundrum, but this is essentially a stepping-stone concept for linking clinical states with biological deviations that fall short of disorder status.[17] Its success depends on the validity or centrality of the endophenotypes, an elusive precondition for nosological progress. A clinical staging model, which allows the relationship of biological markers to stage of disorder to be mapped, may help to validate the boundaries of current or newly defined clinical entities, distinguish core biological processes from epiphenomena and sequelae, and enable existing knowledge to be better represented and understood.

As the articles in this Supplement attest, the clinical staging concept may have much to offer psychiatry, and in particular youth mental health, where the clinical landscape is in dynamic flux. We are already able to see that improved outcomes based on a staging approach are more readily achievable, not only in psychotic disorders (McGorry et al, *page S8*), but potentially in severe mood disorders (Allen et al, *page S15* and Berk et al *page S11*), personality disorders (Chanen et al, *page S18*), and substance use disorders (Lubman et al, *page S22*). Furthermore, by identifying those with an ultra high risk of developing a severe mental disorder, it has been possible to reduce the rate of transition from a functionally impaired prodromal state to a full-blown disorder (Yung et al, *page S43*).

Nonetheless, the staging concept in psychiatry must be explored in a scientific manner in settings with the capacity to blend quality treatment with clinical and biological research. Such settings and facilities are likely to be increasingly common in Australia over the next few years, as a result of the current momentum surrounding reform in youth mental health.

Competing interests

Christos Pantelis receives support to attend meetings as well as speaker fees. He is also on various advisory boards. However, none of these relate to the material in this article.

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