

## Transdiagnostic psychiatry: premature closure on a crucial pathway to clinical utility for psychiatric diagnosis

There is no doubt that psychiatric diagnosis faces a crisis and needs a new way forward which is grounded in clinical utility<sup>1-3</sup>. We have proposed a transdiagnostic approach built upon a clinical staging framework<sup>3,4</sup>, which, while reflecting strongly the dimensional nature of the clinical phenotypes, retains a categorical or syndromal approach and many of the existing concepts, such as depression and psychosis. This is a heuristic strategy which seeks to pave the way to improved clinical utility. Transdiagnostic clinical staging is a relatively recent proposal and data is accumulating which will test its validity.

Fusar-Poli et al<sup>5</sup> create the impression that they are addressing this question in the introduction to their recent systematic review of transdiagnostic research. However, it soon becomes clear that their expedition has captured research which is of quite a different nature and has little bearing on the higher order challenge facing psychiatry. Conceptually, they have ignored most of the literature on contemporary transdiagnostic thinking and new nosological approaches (e.g., clinical staging, Hierarchical Taxonomy of Psychopathology (HiTOP), network theory, p factor). The one exception is the Research Domain Criteria (RDoC) project, which, while transcending DSM categories for research purposes, is fully dimensional and does not claim to provide any usable framework for clinical purposes.

The authors characterize the origins of transdiagnostic approaches in an idiosyncratic manner. Their gold standard definition is drawn from a reference in the cognitive behavioral therapy (CBT) field<sup>6</sup>, and the search they conducted yielded material largely from the CBT space. The critique in their discussion focuses strongly on dimensional vs. traditional categorical approaches, rather than acknowledging that transdiagnostic categorical approaches which respect dimensionality might be possible. It becomes apparent that, despite their claim to be relevant to the wider issues in nosology and diagnosis, they are really talking about the psychotherapy field, providing a critique of recent trends. Hence, their comments about rediscovery versus true innovation are arguably correct in that context.

The authors acknowledge that the quality of the studies they accessed was low, that one fifth were not even transdiagnostic at all, and that only 3 of the 111 studies included met their gold standard definition. Their search, which put undue emphasis on article titles, actually captured only a limited number of relevant studies. It is premature to conduct such reviews with such narrow search terms and confused focus, and we suggest that the field would benefit more from high quality knowledge-generating research aimed at developing and evaluating emerging approaches.

Some form of transdiagnostic paradigm is clearly required, and perhaps Fusar-Poli et al were motivated to stimulate a renewed effort to develop one. However, there is also a risk that their review might dampen enthusiasm for the great challenge

of creating and testing a simpler, more useful approach to diagnosis and understanding the process of disorder onset and evolution. Our traditional diagnostic systems are categorical and siloed, consisting of polythetic operational definitions of clinical phenotypes. They have not worked for patients, clinicians or researchers. Boundaries between syndromes and phenotypes are not clear, as the authors correctly point out, and comorbidity is the rule rather than the exception. Syndromes are not discrete disease entities, and we know that dimensionality underlies most of these phenotypes, even though a dimensional approach is too unwieldy for clinical care, and that distress, impairment and need for care are not limited to the full threshold versions of these phenotypes.

This means that some version of a transdiagnostic approach is going to be necessary. The dynamics of early psychopathology are complex, and emerging microphenotypes ebb, flow, and evolve through many patterns, which do not follow rigid train tracks to discrete macrophenotypes such as schizophrenia or bipolar disorder. Ubiquitous comorbidity and heterotypic evolution of syndromes over stages of illness underline the flaws of current diagnostic systems<sup>7</sup>. The reification of these late macrophenotypes has led to a spurious certainty about the indications, specificity and timing of drug therapies (less so psychosocial therapies), with risks of premature treatment, overtreatment, undertreatment, and mismatched treatment.

Emerging psychopathology is a mixture of anxiety, affective dysregulation, aberrant salience, cognitive impairment, and motivational changes that dynamically influence one another over time, creating a range of clinical patterns. Despite this complexity and dimensionality, treatment decisions are largely binary, and clinicians need useful categories for guiding these decisions<sup>8</sup>. This is why clinical staging has emerged as a potentially useful model.

Clinical staging has been adapted from mainstream health care as a framework to facilitate early intervention, enhancing prediction and personalization of care through profiling within stages, and guiding research<sup>9</sup>. It has particular value when applied in the *early stages* of illness, where it supports the proportional yet proactive treatment of young people experiencing distress, a need for care, and an unstable and fluctuating collection of microphenotypes which nevertheless connotes substantial risk of suicidal behaviour and functional impairment.

Some authors have attempted to mould the staging idea to the procrustean silos of existing late macrophenotypes. However, the essential feature of the model is that it is transdiagnostic. This does not mean that late macrophenotypes such as mania, psychosis and anorexia cannot be accommodated as they differentiate out and stabilize. The specificity of treatment approaches or otherwise can be examined and the spurious

precision of the licensing of medications and other therapies replaced by a more flexible and accurate evidence-based approach as in mainstream health care.

The potential value of such an approach for the redesign of mental health care cannot be overestimated, as we struggle to replace 50-year-old mindsets and work practices with a modern, dynamic 21st century approach.

Patrick D. McGorry, Barnaby Nelson

Orygen, The National Centre of Excellence in Youth Mental Health, Parkville, Australia; Centre for Youth Mental Health, University of Melbourne, Parkville, Australia

1. McGorry P, van Os J. *Lancet* 2013;381:343-5.
2. McGorry P, Nelson B. *JAMA Psychiatry* 2016;73:191-2.

3. McGorry PD, Hartmann JA, Spooner R et al. *World Psychiatry* 2018;17:133-42.
4. McGorry PD, Hickie IB, Yung AR et al. *Aust N Z J Psychiatry* 2006;40:616-22.
5. Fusar-Poli P, Solmi M, Brondino N et al. *World Psychiatry* 2019;18:192-207.
6. Mansell W, Harvey A, Watkins E et al. *J Cogn Psychother* 2009;23:6-19.
7. Plana-Ripoll O, Pedersen CB, Holtz Y et al. *JAMA Psychiatry* 2019;76:259-70.
8. Kendler KS. *World Psychiatry* 2018;17:241-2.
9. McGorry PD, Hickie IB (eds). *Clinical staging in psychiatry: making diagnosis work for research and treatment*. Cambridge: Cambridge University Press (in press).

DOI:10.1002/wps.20679

## Transdiagnostic psychiatry goes above and beyond classification

For the last decade or so I have been involved in developing the science and practice of psychological interventions that apply across psychiatric disorders<sup>1,2</sup>. These developments, known collectively as the transdiagnostic approach, have recently been challenged in this journal within a systematic review<sup>3</sup>. The review extracted research studies that used the term “transdiagnostic” in their title to include a heterogeneous mix of methodologies and samples. The authors report that few studies met the “Mansell criteria”<sup>4</sup> for transdiagnostic research in psychiatry. In particular, the studies were critiqued for their limited use of standardized diagnostic interviews, and the lack of any alternative classification system. Treatment studies in the review generally found that the outcomes of transdiagnostic and disorder-specific interventions were equivalent.

Each of the above points were presented as shortcomings of the transdiagnostic approach. I will explain here the conceptual foundations of the transdiagnostic approach in more depth to challenge that conclusion.

The “Mansell criteria” were initially developed by A. Harvey and colleagues<sup>1</sup> to organize the existing research literature on cognitive and behavioural processes across psychiatric disorders. At the time, that review provided evidence that twelve different processes were shared across multiple (at least four) disorders. In other words, the transdiagnostic basis of psychological processes across psychopathology was already established.

The literature that is relevant to the transdiagnostic approach goes well beyond the articles that use the word “transdiagnostic”. For example, there is a large, replicated literature on “p”, the general psychopathology factor, which rarely uses the term “transdiagnostic”<sup>5</sup>. These studies show that a single factor underlying the diverse symptoms of psychiatric disorders can be identified and predicts a range of medical, health and socioeconomic outcomes. In addition, one could mention the human connectome research: large-scale studies of brain networks have identified the same disrupted neural pathways across different psychiatric disorders. Most recently, a study of 402 patients with a range

of affective and psychotic disorders, matched with 608 healthy controls, identified a single network (across the frontoparietal regions) that was shared across disorders, and its level of disruption scaled with severity<sup>6</sup>.

Earlier critiques of current classification systems have typically attempted to replace them with a new classification system, such as a dimensional system. Yet, the aim of the transdiagnostic approach is different. It is to identify, utilize and test a general theory of psychopathology<sup>4</sup>. This involves trying to understand the shared, overarching processes that cut across the classification system. This scientific approach is analogous to understanding evolution by natural selection as the mechanism of change that accounts for variation in all the living organisms that are classified<sup>7</sup>. Transdiagnostic interventions then aim to harness a general, neurally mediated, change process, regardless of psychiatric diagnosis. Furthermore, most transdiagnostic approaches posit a mechanism that is on a continuum with the general population, so the strict delineation between a clinical diagnosis and a sub-clinical issue is less critical to this field of research<sup>1</sup>.

The most commonly assessed impact of transdiagnostic interventions is still symptom reduction. Yet, symptom relief is only one possible variable to compare and evaluate treatments. Other valuable variables include efficiency, cost-effectiveness, accessibility, and reduction in patient-reported distress. Patients, public, clinicians, service providers and policy makers need to be consulted to determine what is valued. One consequence of this broader perspective is that showing equivalent symptom reduction to a disorder-specific intervention is a particularly positive outcome for transdiagnostic treatments, because by definition they have a reduced need for diagnostic assessment and no requirement for training in multiple diagnostic treatment models<sup>4</sup>. Furthermore, emerging evidence indicates that some transdiagnostic treatments are more efficient, since they may achieve the same reduction in distress through fewer numbers of sessions<sup>8</sup>.

It is commonly held that randomized controlled trials are