

Reimagining outcomes requires reimagining mental health conditions

A striking observation in Cuijpers' review of the range of targets and outcomes for psychological therapies is the somewhat sobering statement that "it is still not clear what these [mental] disorders exactly are"¹.

Despite decades of research and billions of dollars spent, a major barrier to understanding the nature, and therefore treatment, of mental health conditions is the dominant approach to classification based on clinical phenotypes leading to binary categories. This approach, despite being the only pragmatic one devised to date, has "limited validity" and "although most research on mental disorders in the past decades has been using the different versions of these systems, they have been widely criticized"¹. Thus, we are still unable to address the seemingly impossible-to-resolve question which has bedeviled psychiatry from its inception: what is a case?

The key reason for the limited validity of the binary classification approach is that "there is evidence that most mental disorders should not be considered as separate entities but rather as consisting of dimensions, on which some people score high and others score low"¹. In short, binary models of mental disorder which classify people into "cases" and "non-cases" are not grounded in empirical observations. Indeed, the content of Cuijpers' paper could just as easily be applied to the full range of psychiatric therapies, including medications. The bottom line is that we need to develop a way of phenotyping mental health conditions using approaches which reflect their true pattern and distribution in the population.

The Lancet Commission on Global Mental Health and Sustainable Development² has endorsed the staging approach to bridge dimensional and binary frameworks to describing mental health conditions. Rather than being static, discrete and stable (implying distinct aetiologies and therapies), these conditions are syndromes which overlap and develop in stages. Our future classifications may well re-

duce the myriad diagnoses to a parsimonious number of dimensions, each of which might be mapped onto a specific brain network or circuit³. People experiencing mental health problems may then be characterized along these dimensions.

Implicit in the staging approach is the notion of a continuum from the complete absence of psychopathology to states where phenomena are mild and often undifferentiated, to states where clusters of phenomena begin to emerge, to an "end-stage" when they become severe and chronic. Across this continuum, there is a high degree of correlation with social functioning, with psychopathology and social functioning interacting in bi-directional pathways across the spectrum of severity.

Relatedly, a basic question is how "deep" should our phenotyping go beyond reported phenomena such as specific symptoms, to cognitive phenotypes such as impulsivity or attentional deficits, or what are the valid clusters of phenomena, and to what extent should these also capture social and somatic phenomena. The alignment of the staging approach with other frameworks, in particular Research Domain Criteria and network theories, is necessary to address these complex questions. As Cuijpers points out, these frameworks emphasize dysfunction of neural circuits as the mechanism for specific domains of psychopathology which can offer novel targets for interventions.

This approach is particularly suited to psychotherapies, as these can be calibrated according to the severity of the symptoms and social impairment⁴. From a clinical and public health perspective, the staging approach points to the opportunity to shift the care of those with mild, early-stage, problems to low-intensity interventions, such as digitally delivered guided self-care and community health worker delivered psychological and social interventions⁵. This is not only an efficient way to reserve expensive mental health specialist services for those individuals who are at the more severe end of the continuum, but it is simul-

taneously also more empowering to the large proportion of individuals with milder conditions who can recover and stay well without the need for a diagnosis through interventions which may be accessed via diverse affordable delivery platforms.

The dimensional approach also offers a mechanistic foundation for the growing body of evidence in support of single element psychotherapeutic interventions, for example behavioural activation for depressive symptoms or exposure for anxiety symptoms. These may be conceptualized as targeting the specific brain networks or circuits which are associated with these experiences (and which, as our ability to map and image the connectome improves, may offer novel targets for interventions). While some of these elements may themselves be transdiagnostic, reflecting how diverse brain regions influence one another through networks, multiple elements could be clubbed together into a single transdiagnostic protocol which can be tailored to target specific psychopathologies across a diverse range of mental health conditions.

What, then, might be the most appropriate outcome? Cuijpers argues: "if we do not yet really know what these disorders are and how they should be defined, what should be the targets of treatments and how can we measure their outcomes?"¹. Indeed! While I completely agree that there need not be one outcome which is prioritized by all stakeholders, I believe that the distress experienced by the person receiving the mental health intervention must take precedence.

If that is the case, what then should this look like? Dimensional measures of general psychopathology which were once widely used (e.g., the General Health Questionnaire or the Self-Reporting Questionnaire) might return into vogue. Domain specific dimensional measures, such as the Patient Health Questionnaire - 9 (PHQ-9) for depressive symptoms, are already the most frequently reported outcomes. In essence, we do not need to define our "target" group on the basis of their baseline

“diagnosis” relying on current classification systems.

We still need to figure out what constitutes a meaningful change in scores and we might have to stick with relatively arbitrary clinical indices such as response (for example, the 50% reduction in scores often used in depression trials) which are also used for other dimensional health conditions (such as hypertension), or we could calibrate a meaningful change in scores against patient-defined global ratings to generate a “minimal clinically important difference”⁶. Outcomes may, in turn, vary across the severity dimension of the psychopathology; for example, the primary domain of concern may be symptom experience at one stage, but may shift to social functioning at another.

Another implication of adopting di-

mensional approaches is that new kinds of outcomes, amenable to remote monitoring, may become a reality, for example real-time passive assessment of digital behavioural markers. In this context, outcome assessments are not only useful as end-points to evaluate the effectiveness of psychotherapy, but also as dynamic decision points for guiding treatment choices which can allocate more intensive interventions as per patient trajectories, for example to distinguish early responders to low-intensity interventions from those who need more intensive treatments.

In short, reimagining outcomes and targets must require a reimagining of the nature of mental health conditions. We must invest in clinical research paradigms which adopt novel, dimensional, approaches to characterizing these conditions, offering

new approaches to defining targets and outcomes. The current system which has been the foundation of psychiatric research, and which historically was envisioned to lead to an elucidation of etiology, mechanisms and therapeutics, has brought us to a dead-end.

Vikram Patel

Department of Global Health and Social Medicine, Harvard Medical School, Boston, MA, USA

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Therapeutic change processes link and clarify targets and outcomes

The dominance of the latent disease model of the DSM and ICD has led to an over-emphasis on symptom reduction as the primary target and outcome of psychotherapeutic interventions, as Cuijpers¹ points out.

Clients, employers, funders and the public at large did not demand the narrowing of focus that has accompanied psychiatric nosology. As Cuijpers¹ correctly notes, there are other targets and outcomes that might be far more important, such as improvement in quality of life or life functioning, or economic outcomes. To those we might add prosocial and physical health variables, such as reductions in interpersonal violence or life-style related physical diseases.

Cuijpers¹ concludes that the greatest weight should be given to patients when determining the priorities for the targets and outcomes of psychotherapies. We agree. But, if we are to consider a broader range of intervention outcomes, it will be all the more important to clarify how to move empirically from individual characteristics to individual goals by learning more about the “set of theory-based, dynamic, progressive, and multilevel changes that occur in predictable empirically

established sequences oriented toward the desirable outcomes”². In other words, we will need to understand therapeutic change processes and link them to effective intervention kernels.

The core question in modern intervention science is “What core biopsychosocial processes should be targeted with this client given this goal in this situation, and how can they most efficiently and effectively be changed?”². In that context, we are concerned with Cuijpers’ dismissal of processes of change and other theory-driven “intermediate outcomes”. Without a process focus, broadening our outcome perspective could result in even more technological proliferation and confusion than we have now.

Based on studies of mediation, Cuijpers concludes that “there is no evidence” that it is helpful to target processes of change. We disagree. Mediation is only one approach, and the traditional approach to studying mediation is flawed in many ways. Processes of change are idiographic by their nature³, and thus the statistical assumptions built into classical mediation analysis are universally violated.

Classical mediation focuses on a few processes, assumed to be related to out-

comes linearly, unchanging across time, without any feedback loops or recursive processes. Such highly implausible assumptions form the basis of demands to prove that there have been no violations of temporality between mediators and outcomes, to show a dose-response effect, or to prove that no third variable can be involved. In some areas (e.g., third variables) there is no agreed upon way to meet these requirements, and in others (e.g., temporality) little can be recommended beyond guesswork.

Nevertheless, it is supposedly scientifically conservative to prohibit publication of mediational results unless these methodological requirements are met. The result is a domain of ignorance at the core of psychotherapy research that has been to some degree artificially produced. Psychotherapy is rarely – if ever – a paucivariate, linear, continuous and unidirectional event. Instead, psychotherapy typically changes many interconnected variables that form a dynamic system in a non-linear, bidirectional, dynamic and complex manner. This is best studied by adopting a dynamic systems and complex network approach⁴. Linear regression models of a few variables are simply inadequate.