PERSPECTIVE

The next stage for diagnosis: validity through utility

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Since the advent of descriptive psychiatry over two centuries ago, attempts to validate psychiatric diagnosis have been an ongoing source of controversy and disillusionment. The publication of DSM-III in 1980 certainly represented a watershed in its appropriate bid to enhance reliability, but it is apparent that, despite the huge effort and expense devoted to its successors, we have hit a wall in terms of validity and utility.

A succession of authors have described this failure (e.g., 1,2). The apparently new controversies which flared around the DSM-5 were really at the margins and the more fundamental criticisms were revivals of earlier debates about validity and utility, fueled by a solid dose of ideology, polemic and vested interest.

The field trials for DSM-5 indicate that even acceptable reliability remains elusive in clinical practice; for example, the key diagnosis of major depression achieved a very modest kappa value of 0.28 (3). Many of the growing number of diagnostic categories not only have poor reliability, but more importantly, limited validity. Furthermore, most fail to acknowledge the critical differences in clinical presentations associated with the age of onset of illness, the stage of illness, or its course (2,4).

Most criteria sets reinforce categories that have been derived almost exclusively from observations of people with late stage illness. Inevitably, these categories map poorly onto earlier, often less specific clinical presentations, which means that they hamper efforts to intervene early in the course of illness, where pre-emptive interventions are at a premium. Hence, the problem in most parts of the world is not that milder illnesses are being overtreated or inappropriately medicated (though this admittedly does happen to a proportion of people in some developed countries, such as the USA, where treatment has been reduced by a combination of limitations in mindset and health financing to mere prescribing). Rather, and more seriously, the earlier, and milder, stages of ultimately serious illnesses are routinely locked out of care of any kind until they demonstrate a severity and chronicity that certainly rules out any risk of overtreatment, yet at the same time inevitably and dramatically reduces the chances of response to treatment and recovery.

This conceptually and practically restricts psychiatry to a form of palliative care, which reinforces an unfair and false public perception of relative therapeutic impotence. The neglect and consequent underfunding of mental health care in every country is the key to this, but the lack of a diagnostic approach which allows for the early clinical stages of illness to be recognized and treated as well as the later stages is also to blame. The end result is that mental health has not seen the improvements in mortality and morbidity that have occurred in cancer and cardiovascular medicine in recent decades (5).

New research, only recently possible, is essential to determine the effectiveness and safety of such early treatment. Early treatment, as an antidote to therapeutic nihilism and the "soft bigotry of low expectations" must be carefully studied and debated as in cancer and other areas of health care, free of the polemic that too often plagues mental health from within and without.

Diagnosis is classification with utility (6). Diagnosis aims to characterize clinical phenotypes in a shorthand way that helps to distinguish those who are ill and in need of care from those who are not, and to enhance the selection of treatment and prediction of outcome. Utility in medicine is the ultimate test, but much of current psychiatric diagnosis has low clinical utility. Furthermore, our current classification systems presuppose the existence of multiple, independent and parallel pathways each leading to distinct diagnoses – an assumption that is out of keeping with contemporary family, genetic and neurobiological risk factor studies (7-9). A fundamental change is required.

The mental disorders are not static, sharply defined illnesses with separate etiologies and courses, but rather syndromes that overlap and develop in stages (10). Mental ill-health has to start somewhere. However, as critics are keen to point out, it is difficult prospectively to distinguish this from what passes for "normality" or "the human condition". It is certainly easier to recognize this distinction in retrospect from the vantage point of clear-cut and severe mental illness.

Most people experience the onset of mental health as intensifying and persistent emotional distress linked with problems with relationships and/or achievement. Eaton (11) has described how symptoms arise either from intensification of subjective experiences or behaviours that have been present for some time or from acquisition of new experiences or behaviours, or most commonly a combination of both. Daily human experience involves periodic and sometimes intense and mercurial changes in affect and salience in response to the social environment. When these become more prominent, they can be discerned as subclinical "microphenotypes", which wax and wane, interact sequentially or become confluent, and may mature or stabilize towards pure or hybrid "macrophenotypes" (12).

This process is undeniably fluid and dimensional, and several dimensions of psychopathology can be readily

identified, such as aberrant salience and affective dysregulation (13). While categories could be arbitrarily imposed within these dimensions, the concept of the syndrome, where various symptoms cohere in an increasingly strong and predictable manner, as well as impact on each other over time, is essential to mapping early clinical phenotypes (1,14).

This process is perhaps best considered in young people as they make the transition through adolescence to independent adulthood, since the incidence of mental illness is highest in young people aged between 12 and 25 years, with 75% of all major mental illnesses having their onset before the age of 25 years (15). The onset of mental illness is difficult to distinguish from the transient and normative changes in affect and behaviour that we all experience, especially in young people, where these experiences can be particularly marked (10).

It is now well-recognized that the major psychiatric disorders are typically preceded by prodromes – subthreshold states or microphenotypes – characterized by a varying blend of non-specific symptomatology, most commonly anxiety and depression, often associated with sustained and significant distress and disability. It is here that the failures of our current diagnostic system are most obvious.

While a proportion of these states will resolve with or without treatment, there is nevertheless a need for at least assessment, time-limited support and care for many, and the risk for persistence or progression in a substantial subset is real. This need for care typically precedes the diagnostic clarity demanded by our current late-stage diagnostic concepts, yet it is these that largely set the threshold at which access to care is offered in our underfunded global mental health care system. What is required is a simpler, more flexible hybrid model that accommodates dimensionality, yet provides a graded categorical framework that facilitates early assessment, tolerates ambiguity, minimizes stigma, and has utility for patients, clinicians and researchers.

The clinical staging model, adapted from general medicine, provides such a framework (2,4). This model sets aside the current diagnostic boundaries to include the full spectrum of disorder, including its continuities with psychopathology in the healthy population, to place a strong diagnostic emphasis on where a person sits in the evolution of the clinical phenotype. Stage is determined on the dimensions of severity of symptoms, distress, disturbances in relationships and functioning, and the persistence of these changes, rather than any specific syndromal content, which can add specificity within a matrix model. It is primarily an agnostic, rather than diagnostic, framework, which recognizes that persistent and multiple microphenotypes of disturbance can justify a need for care on their immediate merits as well as on the basis of the risk for progression to more familiar, specific and stable macrophenotypes; while also acknowledging the need for blending dimensional and categorical models, as was originally hoped for DSM-5.

The staging model ultimately holds out the prospect of a more useful framework for clinicians, in that it acknowledges the "grey zone" of ambiguity between what may simply be transient distress and disturbance, and what may prove to be the onset of a more serious mental illness, as well as the substantial cumulative public health burden of what is currently considered as sub-threshold illness. It provides a more appropriate guide for the choice of therapeutic intervention, by ensuring that the treatments selected are proportional to both the clinical need and the risk of illness progression, while minimizing the risk of overtreatment and consequent unnecessary adverse effects, including that of undertreatment. The "soft entry" aspect also has the welcome effect of dispelling stigma.

These elements deal with many of the fears expressed by critics of "diagnostic inflation". Clinical staging in fact represents diagnostic deflation, in proposing a large reduction of the array of syndromal categories, yet makes no apology for extending the boundaries of mental health care to the earliest point from which benefits can flow safely and without stigma and hence outweigh risks. This goal is especially critical in young people, who bear the major burden of the initial incidence of mental disorders, and thus have the most to lose from late or crude treatment in terms of their developmental trajectories and fulfillment of potential.

Twenty-first century health care places an increasing emphasis on personalized medicine, with the goal of tailoring treatment to the individual. Clinical staging aims to bring us closer to other branches of medicine and pave the way for biosignatures to play a stronger role in individual diagnosis and thus for personalized or stratified medicine in psychiatry (2,14). Over the past two decades, research from areas as diverse as genomics, neurobiology and epidemiology has transformed our thinking on the mental disorders, which we now understand to be disorders of the brain and of development.

These advances have put the concept of pre-emptive psychiatry tantalizingly within reach (16). However, pre-emptive psychiatry requires predictive tools that can be integrated into an appropriate diagnostic framework to assess the risk and course of illness, as well as the response to therapy. The clinical staging model, with its explicit recognition of the evolution of mental disorders from relatively undifferentiated phenotypes to clear syndromes, has heuristic potential in facilitating the integration of our growing understanding of the genetic, biochemical and neurobiological biosignatures of mental illness into our diagnostic framework. This would be a major advance, not only in the quest for personalized medicine, but also for validity in psychiatric diagnosis.

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