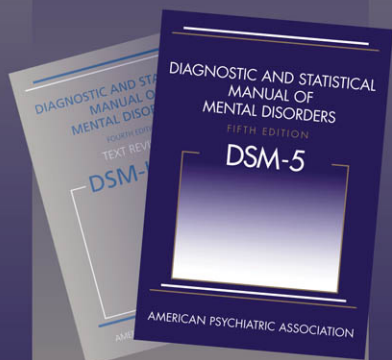


THE CONCEPTUAL EVOLUTION OF DSM-5



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William E. Narrow, M.D., M.P.H.
Emily A. Kuhl, Ph.D.
David J. Kupfer, M.D.

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Washington, DC
London, England

Note: The authors have worked to ensure that all information in this book is accurate at the time of publication and consistent with general psychiatric and medical standards, and that information concerning drug dosages, schedules, and routes of administration is accurate at the time of publication and consistent with standards set by the U.S. Food and Drug Administration and the general medical community. As medical research and practice continue to advance, however, therapeutic standards may change. Moreover, specific situations may require a specific therapeutic response not included in this book. For these reasons and because human and mechanical errors sometimes occur, we recommend that readers follow the advice of physicians directly involved in their care or the care of a member of their family.

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Introduction

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Over the past 30 years, there has been a continuous testing of multiple hypotheses that are inherent in the *Diagnostic and Statistical Manual of Mental Disorders*, from the third edition (DSM-III; American Psychiatric Association 1980) to the fourth (DSM-IV; American Psychiatric Association 1994). Although DSM-III was the first official classification from the American Psychiatric Association (APA) to embrace these hypotheses, their intellectual origin is more properly attributed to Eli Robins and Samuel Guze's landmark 1970 article on the establishment of diagnostic validity in psychiatric illness (Robins and Guze 1970) and the subsequent 1972 release of the St. Louis "Feighner diagnostic criteria" (Feighner et al. 1972). These formed the basis for the 1978 Research Diagnostic Criteria (Spitzer et al. 1978), which were used in the longitudinal collaborative study on the psychobiology of depression supported by the National Institute of Mental Health (Rice et al. 2005) and ultimately were the prototypical diagnoses adopted in DSM-III in 1980.

The expectation of Robins and Guze (1970) was that each clinical syndrome described in the Feighner criteria, Research Diagnostic Criteria, and DSM-III would ultimately be validated by its separation from other disorders, common clinical course, genetic aggregation in families, and further differentiation by future laboratory tests—which would now include anatomical and functional imaging, molecular genetics, pathophysiological variations, and neuropsychological testing.

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To the original validators Kendler (1990) added differential response to treatment, which could include both pharmacological and psychotherapeutic interventions.

After almost 40 years of testing these hypotheses, we are impressed by the remarkable advances in research and clinical practice that were facilitated by having explicit diagnostic criteria that produced greater reliability in diagnosis across clinicians and research investigators in many countries. The benefit of using explicit criteria to increase reliability in the absence of etiological understanding was an outcome predicted by the British psychiatrist Ervin Stengel (1959). However, as these criteria have been tested in multiple epidemiological, clinical, and genetic studies through slightly revised DSM-III-R (American Psychiatric Association 1987), DSM-IV, and DSM-IV-TR (American Psychiatric Association 2000) editions, the lack of clear separation of these syndromes became apparent from the high levels of comorbidity that were reported (Boyd et al. 1984; Regier et al. 1990). A particularly clear discussion of the inability to identify “zones of rarity” between mental disorders was presented by Kendell and Jablensky (2003). In addition, treatment response became less specific as selective serotonin reuptake inhibitors were found to be effective for a wide range of anxiety, mood, and eating disorders and atypical antipsychotics received indications for schizophrenia, bipolar disorder, and treatment-resistant major depression.

More recently, it was found that a majority of patients with entry diagnoses of major depression in the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study had significant anxiety symptoms, and this subgroup had a more severe clinical course and was less responsive to available treatments (Howland et al. 2009). The lack of clear separation between current disorders defined by DSM-IV-TR was clearly illustrated in a survey of primary care patients (Lowe et al. 2008), which found that among individuals with the most severe ratings of depression, anxiety, or somatization, more than one-half in each syndrome group also had at least one, if not both, of the other two disorders. Furthermore, the combined influence of the three syndromes on functional impairment was far more significant than any of their individual effects. Likewise, we have come to understand that we are unlikely to find single gene underpinnings for most mental disorders, which are more likely to have polygenetic vulnerabilities interacting with epigenetic factors (that switch genes on and off) and environmental exposures to produce disorders.

In retrospect, it is interesting that there was such a strict separation of mood, anxiety, psychotic, somatic, substance use, and personality disorder symptoms for the original Feighner diagnoses (Regier et al. 2005). It is clear that an hierarchy was present that tended to suppress the significance of lower-order symptoms in the syndrome definitions in order to achieve such pure types. This hier-

archical arrangement of disorders was implicit in the Kraepelinean classification tradition of ranking organic mental disorders, nuclear schizophrenia, manic-depressive illness, and neurotic illnesses from higher- to lower-order conditions (Surtees and Kendell 1979). It was followed by an explicit statement of Jaspers (1963): “The principle of medical diagnosis is that all the disease-phenomena should be characterized within a single diagnosis...in any one person” (p. 611). Although the idea of a strict hierarchy, in which the presence of any disorder could cause manifestations of disorders lower in the hierarchy, was explicitly abandoned for DSM-III-R after publication and review (Regier 1987) of the article by Boyd et al. (1984), the strict separation of symptoms and disorder types has persisted through DSM-IV-TR. Some remnants of the hierarchy persist in a few areas, such as the diagnosis of autistic disorder (299.00), in which there is still an explicit exclusion of a diagnosis of attention-deficit/hyperactivity disorder (ADHD) if autistic disorder is present. The practical effect of this exclusion is that insurance reimbursement is often denied for co-occurring symptoms of ADHD in the presence of a diagnosis of autism. To support this strict separation, we now have a plethora of comorbidity—because patients do not usually have only mood, somatic, or anxiety symptoms but tend to come with a mix from multiple symptom groups. Hence, we have heterogeneous conditions within single diagnostic groups, a remarkably high rate in specialty mental health settings of “not otherwise specified” diagnoses that do not quite fit the existing criteria, as well as high rates of “subsyndromal” mixed anxiety-mood-somatic disorders in primary care settings.

How then are we to update our classification to recognize the most prominent syndromes that are actually present in nature, rather than in the heuristic and anachronistic pure types of previous scientific eras? A serious consideration from the aforementioned study by Lowe et al. (2008) is that some patients with clinically significant distress and impairment might have only a few symptoms from mood, anxiety, and somatic diagnostic criteria sets that do not qualify for a formal diagnosis in any one disorder, although the aggregate burden requires a not-otherwise-specified diagnosis and treatment. A more important clinical consideration is that the clinical course and treatment response for anxious depression, posttraumatic stress disorder with depression, and other mixed disorders cannot be predicted from clinical trials of medications or psychosocial interventions that are based on outcomes with patient groups selected for pure categorical disorders or that contain an unknown heterogeneous mix of comorbid conditions. In addition, supraordinate dimensional measures may provide better phenotypic expressions for linkage to illness susceptibility substrates identified by neuroimaging and genetic studies. Common genetic determinants of schizophrenia and bipolar disorder have resulted in calls for a reappraisal of

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