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Research planning for the future of psychiatric diagnosis

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Abstract

More than 10 years prior to the anticipated 2013 publication of DSM-5, processes were set in motion to assess the research and clinical issues that would best inform future diagnostic classification of mental disorders. These efforts intended to identify the clinical and research needs within various populations, examine the current state of the science to determine the empirical evidence for improving criteria within and across disorders, and stimulate research in areas that could potentially provide evidence for change. In the second phase of the revision process, the American Psychiatric Institute for Research and Education (APIRE) recently completed the 5-year international series of 13 diagnostic conferences convened by APA/APIRE in collaboration with the World Health Organization and the National Institutes of Health (NIH), under a cooperative grant funded by the NIH. From these conferences, the DSM-5 Task Force and Work Groups have developed plans for potential revisions for DSM-5, including the incorporation of dimensional approaches within and across diagnostic groups to clarify heterogeneity, improve diagnostic validity, and enhance clinical case conceptualization. Use of dimensions for measurement-based care has been shown to be feasible in psychiatric and primary care settings and may inform monitoring of disorder threshold, severity, and treatment outcomes. The integration of dimensions with diagnostic categories represents an exciting and potentially transformative approach for DSM-5 to simultaneously address DSM-IV's clinical short-comings and create novel pathways for research in neurobiology, genetics, and psychiatric epidemiology.

Keywords

DSM-5; ICD-11; Psychiatric nosology; Classification of psychiatric disorders

The release of the fifth edition of the Diagnostic and Statistical Manual for Mental Disorders (DSM-5) may well mark the advent of a modified approach to psychiatric diagnostic and classification.Despite its advances in clinical utility and reliability, the fourth edition of DSM (DSM-IV [3]) drew criticism that diagnostic validity had become mired in numerous extraneous factors, including excessive comorbidities, overreliance on the "Not Otherwise Specified" category, vague operationalization of the clinical significance criterion, lack of treatment specificity, and under-evaluation of genetic and biomedical outcomes in psychiatric research and epidemiology. Consequently, among the DSM-5 revision experts now faced with assessing the current state of the science, validity and dimensional

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classification have moved to the forefront of DSM-5's purview. The neo-Kraeplinian use of explicit diagnostic criteria in DSM-III, reflecting a phenomenological rather than etiological assumption, represented a vast departure from the psychodynamic schemata embraced by DSM-I and DSM-II, but the question of where the field of psychiatry will land as we move beyond this approach is still unclear. What is clear is that DSM-5 will need to represent, at the very least a reevaluation of the implicit hierarchical structure of DSM-IV and ICD-10 that has a strict separation of psychosis, mood, anxiety, somatic, and personality disorder syndromes and an absence of any dimensional components in diagnostic criteria.

1. Planning for DSM-5

As the American Psychiatric Institute for Research and Education (APIRE)–an affiliated corporation of the APA–began the formal planning process for DSM-5 in 1999, it soon became evident that greater attention would need to be given to crosscutting issues relevant to all diagnostic categories, such as age- and gender-related features of disorders, diagnosis across the developmental lifespan, assessment of impairment and disability, and cultural expressions of disorders. The mass acceleration of advances in neuroscience and genetics during the 1990s, appropriately proclaimed the "Decade of the Brain", also needed to be reflected in our understanding of lab science and neurobiological underpinnings of mental disease. In an effort to summarize the gaps in the current nosology and to discuss how these issues may potentially be adopted in DSM-5, APIRE, under direction of the author (D.A.R.), collaborated with the National Institute for Mental Health (NIMH) to develop a series of white papers, later published by APA in two volumes, A Research Agenda for DSM-5 [16] and Age and Gender Considerations in Psychiatric Diagnosis: A Research Agenda for DSM-5 [20].

At the close of this initial phase of DSM-5 development, APIRE received a $1.1 million grant from the National Institutes of Health (NIH) to convene a series of international planning conferences. These meetings were designed with three primary goals in mind: to stimulate the empirical research base for future changes in diagnostic classification; to promote international collaboration for cross-talk between DSM-5 and the forthcoming 11th edition of the International Classification of Diseases (ICD-11); and to begin building a consensus about revised criteria, in an effort to maximize clinical and research validity of DSM-5 diagnoses. The conference series, which was jointly sponsored by NIMH, the National Institute on Drug Abuse, the National Institute on Alcohol Abuse and Alcoholism, and the World Health Organization (WHO), organized 13 diagnosis-specific international meetings over the span of 5 years, from 2003–2008. As a result, more than 190 scholarly articles and 13 white paper monographs [4,9–11,14,16,20–22,27,31,32,35] have been published as resource documents for the DSM-5 Task Force and Work Group members. These publications have become integral components to the literature reviews conducted by the DSM-5 Work Groups to assess the current state of the criteria and determine which revisions are warranted. Since one of the aims of the conference series was to provide specific recommendations for how DSM-5 might address gaps in the literature, each monograph provides summary content theorizing how DSM-5 might begin to answer the numerous questions raised throughout the meetings. This has made the monograph series particularly valuable to the revision process.

The importance of the international aspect of the conference series should not be overlooked, as DSM-5 is attempting to move closer to creating a universally-accepted and culturally-sensitive perspective on diagnosis than previously [17]. To that end, the conferences included in sum nearly 400 participants from 39 countries, including 16 developing nations. One of the conferences devoted to implications of psychiatric diagnosis and classification on aspects of public health [28] was specifically structured to solicit input

from international colleagues on global public health needs and how these might be impacted by DSM-5. The proposed harmonization of DSM-5 with ICD-11 is a reflection of the interplay between mental health and more general public health efforts on the world stage. These efforts include WHO's interest in statistics on mortality and morbidity; the translation of psychiatric diagnoses into primary care terminology; economic and socio-demographic implications across the globe; the role of private, public, and consumer stakeholders in psychiatric classification; and the interrelationship between psychiatric diagnosis and various cultural expressions of mental disorders. DSM-5 Task Force members and APIRE representatives are continuing to work closely with the WHO to ensure DSM-5 and ICD-11 provide a common international scientific framework for clinical practice and future research.

2. Dimensions as an avenue to improved validity in DSM-5

As noted above, DSM-IV's improvements were somewhat tempered by concerns about validity, which stemmed partially from DSM-IV's attempts to help rectify the diagnostic rigidity created by the third iteration of DSM (DSM-III [1]). DSM-III introduced a hierarchical classification that eliminated simultaneous diagnoses and gave deference to "higher order" diagnoses, such as organic brain diseases, schizophrenia, bipolar disorder, and major depression. After its release, the inability to co-classify disorders, such as anxiety disorders in patients with schizophrenia, became a particular point of contention [5]. Furthermore, DSM-III's exclusionary rules inhibited accurate identification of clinically comorbid cases, hindering treatment planning. The revised edition of DSM-III (DSM-III-R [2,24]) consequently removed the hierarchical structure, but in doing so, introduced a new diagnostic challenge–comorbidities.

The descriptive and categorical nature of DSM-IV, combined with its comparatively lax approach to inclusion/exclusion criteria, resulted in a dramatic rise in the prevalence of comorbid conditions from DSM-III-R [23]. Using the National Comorbidity Survey Replication (NCS-R) study, 55% of individuals with a psychiatric diagnosis had a single diagnosis, while approximately 22% had two diagnoses and 23% three diagnoses [13]. However, clinicians in routine clinical practice, who do not always strictly adhere to DSM-IV criteria, are typically underreporting comorbidities. In a comparison of 1,000 patients assessed for psychiatric intake [36], wherein half were diagnosed via the DSM-IV Structured Clinical Interview for DSM-IV Axis I Disorders (SCID [8]) and half using an unstructured clinical evaluation, the SCID sample was twice as likely to have two or more diagnoses (OR = 2.1) than the clinical sample. These odds increased exponentially with the number of diagnoses (e.g., three or more diagnoses, OR = 4.9; four or more diagnosis, OR = 16.0), with more than one-third of the SCID group receiving three or more diagnoses. By comparison, less than 10% of the clinical group received the same. Mood, anxiety, eating, somatoform, and impulse control disorders were significantly more frequent in the SCID sample.

In response to high rates of comorbidities, particularly in primary care settings, the DSM-5 revision experts are proposing the use of dimensional assessments to clarify heterogeneity within and across disorders and to aid clinicians in systematically assessing a wide range of symptoms that may inform diagnosis and treatment planning and monitoring. This includes measurement of symptoms that cut across most patient populations, such as mood, anxiety, sleep functioning, suicidal ideation, cognition, and psychosis. These cross-cutting assessments provide a more thorough conceptualization of diagnosis that mirrors general medicine's "review of systems" and calls attention to symptoms of clinical importance that might otherwise be overlooked. Endorsement of any of these cross-cutting dimensions would lead to administration of a second tier of assessments that further delineate symptoms

and assess thresholds for a possible comorbid diagnosis, such as administration of the Generalized Anxiety Disorder-7 [30] upon endorsement of the anxiety questions.

Yet another level of cross-cutting assessments should prompt the clinician to consider symptoms of disorders specifically related to the primary diagnosis. This could include, for example, the assessment of impulsivity in children with oppositional-defiant disorder or substance use in adults with personality disorders. Finally, dimensional assessments will involve the measurement of disorder severity, which is not clearly operationalized in DSM-IV and, as a result, is currently underutilized despite the fact that severity offers important information about clinical course and magnitude of change over time. Severity measures will likely be criteria-specific and may be operationalized differently across disorders. For instance, simple symptom counts may be appropriate for substance use disorders, while severity of major depression can be assessed directly as a component of the Nine-Item Patient Health Questionnaire.

The cumulative effect of comorbid psychiatric diagnoses on prognosis includes poorer response to treatment [34], presumably due in part to ineffective interventions and/or inaccurate diagnosis. Cross-cutting and severity dimensions would help enhance diagnostic assessment, specify treatment, and reduce the likelihood that busy clinicians in general medical settings will overlook or misdiagnose patients. While DSM-5 will still support a binary decision-making process, the inclusion of dimensional assessments gives clinicians the tools to better conceptualize, treat, and monitor patients.

Although the allowance of greater diagnostic information can enrich the clinical picture and aid practitioners in treatment and planning, the absence of treatment information from clinical trials on “comorbid” disorders leads to confusion and potentially misleading extrapolations for treatment studies of “pure” disorders. The role of dimensions in reducing excessive comorbidities is appealing, in part because of benefits to improving diagnostic validity [6,14,33]. The clinical realities of patient care confirm that diagnoses are not neatly compartmentalized into hierarchies or categories, making the integration of dimensions a seemingly intuitive operation. Using the strict DSM-III-R and DSM-IV categorical criteria, some mild disorders carry a significant risk for poor outcomes, including hospitalization, suicide attempt, and disability [12,19]. Dimensions may allow clinicians and researchers to better identify more specific diagnostic thresholds [25] and address the nuances of psychiatric disorders, such as individual differences in symptomotology, onset, course, severity, and treatment response–as well as comorbid conditions. Culture, like gender and age/development, is a source of variability that is not well-accounted for in DSM-IV. Dimensions may also facilitate research in developing sociocultural symptom profiles, providing an empirical framework for identifying culture-based subtypes, specifiers, and culture-bound syndromes. Expanding the research base in culture and psychiatry will inform subsequent revisions to DSM and allow clinicians to better contextualize disorders from a sociocultural perspective. All of these help to better reflect the true heterogeneous nature of currently defined mental disorders and may provide a much-needed transition to identifying more homogeneous and valid diagnostic distinctions and categories [14].

At the present time, the DSM-5 Task Force is actively reviewing results from epidemiological and clinical research studies to improve the validity of our diagnostic categories. Lee Robins has offered a useful perspective on the manner in which testing of previous versions of the diagnostic criteria can lead to a better understanding of how people actually experience a wide range of symptoms that express the underlying pathophysiology of mental disorders in nature [26]. Examples of this research include the identification of underlying factors that may support and partially explain apparent comorbidities could also inform classification. Krueger and Markon’s [15] meta-analysis of five large-scale,

population-based epidemiological studies (n = 23,557), supported a two-item superordinate spectrum of internalizing and externalizing disorders among 11 diagnoses. Slade and Watson [29], fitting both DSM-IV and ICD-10 disorders of unipolar mood, anxiety disorders, and substance dependence, replicated the same superordinate characterization of internalizing-distress, internalizing-fear, and externalizing spectra. Taken together, these studies provide support for the possible common etiology of co-occurring syndromes as they are currently defined and speak to the presence of latent umbrella pathophysiologies. The natural inference is that the boundaries between currently defined disorders are not nearly as distinct as once thought, but this raises the question of how DSM-5 revisions can go about transitioning from concept to reality.

3. What can we learn from measurement-based care?

Development of a taxonomy that incorporates dimensional concepts into a categorical diagnostic system may be facilitated by examining the efficacy and implementation of dimensional measures into routine clinical practice. The Nine-Item Patient Health Questionnaire (PHQ-9) is a self-report instrument derived from DSM-IV major depressive episode criteria. Its structure simple, brief, understandable, and has been frequently used in primary care settings for screening and follow-up assessment. Each symptom is rated on four levels of severity and frequency (“not at all”, “several days”, “more than half the days” and “nearly every day”) over a period of 2 weeks. Scores are subtotaled by severity/frequency and summed to yield an overall score. Threshold for severity is operationalized at the mild (5–9), moderate (10–14), moderately severe (15–19), and severe (≥ 20) levels. In measuring treatment response, a decrease in baseline score of at least 5 points at 4–6 weeks after treatment initiation is considered a clinically significant response. A 50% reduction in total score, or achieving a total score less than 10, is considered indicative of treatment responsiveness. A score of less than 5 is considered indicative of depression remission.

The National Depression Management Leadership Initiative was a year-long collaborative effort between the American Academy of Family Physicians, the American College of Physicians, and APIRE to empirically examine the clinical utility and impact of the PHQ-9 [7]. The study sought to pilot test strategies to optimize use of the assessment in primary care and psychiatric treatment settings for improving clinical management of depressed patients. A total of 16 primary care and 17 psychiatric practices participated in the study. A little more than 40% of the sample had comorbid disorders, typically that of anxiety, a second mood, or substance use disorder. All of the psychiatric practices in question adopted routine use of the PHQ-9 for symptom assessment and treatment monitoring. A majority of the psychiatrists said that the PHQ-9 was “extremely helpful” or “very helpful” in diagnosing depression, determining severity, monitoring response to and tailoring treatment, monitoring risk of suicide, and improving therapeutic alliance. Nearly all of the psychiatrists (93%) endorsed its utility in making treatment decisions, with use of the PHQ-9 leading to a change in treatment regimen in 40% of the visits in which it was used. In the remaining 60% of visits, the PHQ-9 helped confirm treatment decisions. Treatment changes as a result of PHQ-9 outcomes included changing the dose of antidepressant (44% of cases), adding another medication to treat depression (26%), initiating or increasing psychotherapy (16%), switching antidepressants (12%), initiating antidepressants (10%), making additional suicide risk assessments (3%), reassessing the depression diagnosis (1%), and making a mental health consultation or referral (1%).

Results from this initiative provide persuasive evidence to suggest that implementation of measurement-based care in clinical practice is not only feasible and acceptable, but that it can bring about meaningful change to how clinicians approach patient care. Further, measurement-base care’s ability to track and tailor treatment response and decision-making

may help optimize symptom relief and quality of life, despite the heterogeneous and complex nature of depression. Recently, the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study [34] evaluated use of a depression treatment algorithm and severity measures to assess symptoms and guide treatments. Results suggest that use of measurement-based care altered clinicians' treatment decisions, which may have contributed to better-than-expected response and remission rates (47% and 28%, respectively) at 12 weeks. Use of the PHQ-9 and other measurement-based care tools, including the Quick Inventory of Depressive Symptomology, can be integrated into clinical settings as a standardized measurement of outcomes. If busy clinicians can successfully implement dimensional assessments into routine patient practice and produce improved outcomes, it's hard to argue against considering extending that same approach to diagnosis.

4. Conclusion: on the road to DSM-5

It has been said that change is inevitable, but growth is optional. How DSM-5 may evolve beyond its predecessors is an unanswerable question at this time, but improving the diagnosis and care of our patients isn't merely an option; it's a necessity. While the importance of research and epidemiological advances are unarguable, any reorganization must err on the side of clinical utility. The addition of dimensions to DSM-5 represents a new and exciting opportunity to refine our nosology into one that is even more authoritative, valid, and useful than currently. The notion of dimensional diagnoses in DSM has long-been discussed, and results from the DSM-5 field trials, which began in 2010, will provide important information about the practicality and feasibility of transitioning from ideology to real-world implementation. The experts committed to DSM-5 are working to ensure that the future of psychiatric diagnoses balances scientific rigor with clinical pragmatism. And in doing so, they seek to make the inevitability of change synonymous with the inevitability of progress.

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