aps ASSOCIATION FOR PSYCHOLOGICAL SCIENCE

Psychological Science in the Public Interest
2017, Vol. 18(2) 72–145

DOI: 10.1177/1529100617727266
www.psychologicalscience.org/PSPI
SAGE

Three Approaches to Understanding and Classifying Mental Disorder: *ICD-11*, *DSM-5*, and the National Institute of Mental Health's Research Domain Criteria (RDoC)

Lee Anna Clark[1], Bruce Cuthbert[2], Roberto Lewis-Fernández[3], William E. Narrow[4], and Geoffrey M. Reed[5,6]

[1]Department of Psychology, University of Notre Dame; [2]Research Domain Criteria Unit, National Institute of Mental Health; [3]Department of Psychiatry, Columbia University, New York State Psychiatric Institute; [4]Department of Psychiatry and Behavioral Sciences, University of New Mexico School of Medicine; [5]Department of Mental Health and Substance Abuse, World Health Organization; and [6]Global Mental Health Program, Columbia University Medical Center

Abstract

The diagnosis of mental disorder initially appears relatively straightforward: Patients present with symptoms or visible signs of illness; health professionals make diagnoses based primarily on these symptoms and signs; and they prescribe medication, psychotherapy, or both, accordingly. However, despite a dramatic expansion of knowledge about mental disorders during the past half century, understanding of their components and processes remains rudimentary. We provide histories and descriptions of three systems with different purposes relevant to understanding and classifying mental disorder. Two major diagnostic manuals—the *International Classification of Diseases* and the *Diagnostic and Statistical Manual of Mental Disorders*—provide classification systems relevant to public health, clinical diagnosis, service provision, and specific research applications, the former internationally and the latter primarily for the United States. In contrast, the National Institute of Mental Health's Research Domain Criteria provides a framework that emphasizes integration of basic behavioral and neuroscience research to deepen the understanding of mental disorder. We identify four key issues that present challenges to understanding and classifying mental disorder: *etiology*, including the multiple causality of mental disorder; whether the relevant phenomena are discrete *categories* or *dimensions; thresholds*, which set the boundaries between disorder and nondisorder; and *comorbidity*, the fact that individuals with mental illness often meet diagnostic requirements for multiple conditions. We discuss how the three systems' approaches to these key issues correspond or diverge as a result of their different histories, purposes, and constituencies. Although the systems have varying degrees of overlap and distinguishing features, they share the goal of reducing the burden of suffering due to mental disorder.

Keywords

diagnosis, classification, mental disorder, *International Classification of Diseases,* ICD*, Diagnostic and Statistical Manual of Mental Disorders,* DSM, Research Domain Criteria, RDoC

What we call a beginning is often the end
and to make an end is to make a beginning.
The end is where we start from. . . .
We shall not cease from exploration
And the end of all our exploring
Will be to arrive where we started
And know the place for the first time.

—T. S. Eliot (1942)

Though no man can draw a stroke between the confines of day and night, yet light and darkness are upon the whole tolerably distinguishable.

—Edmund Burke (1770/1913, p.43)

Corresponding Author:
Lee Anna Clark, Department of Psychology, University of Notre Dame, Notre Dame, IN 46556
E-mail: la.clark@nd.edu

The classification of mental disorders has its roots in antiquity. Like most natural phenomena in early human history, mental illness was often attributed to supernatural origins (e.g., demonic possession), although psychosocial causes such as traumatic stress also were posited. Perhaps the earliest natural-science theory of mental illness was Galen's typology, in the 2nd century A.D., of four categories of temperament—choleric, sanguine, melancholic, and phlegmatic—based on Hippocrates's theory, dating to the 5th or 4th century B.C., that health required a balance among the body's purported "four humors": yellow bile, blood, black bile, and phlegm. Each temperament had an associated pathology, which was the result of excess in one of those humors. Today, scientific theories on the biological bases of mental illness[1] reference brain structures and various biological processes rather than the four humors; supernatural causes are absent from professional nosologies (although nonscientific ideas about mental illness are still prominent worldwide); and we know considerably more about psychosocial influences. Yet our understanding of exactly how multiple factors influence the development and course of most common mental disorders is still incomplete. As a result, our major classification systems are based almost exclusively on observable behaviors (signs) and self-reported feelings and thoughts (symptoms) rather than on their underlying causal mechanisms. Categories and the classification systems that are organized around them are important because they help us to make sense of complex observations, but we seem to have reached the limits of understanding mental disorder through outwardly observable signs and internally experienced symptoms alone.

This article discusses the approaches to describing and classifying mental disorders taken by three key organizations: the World Health Organization (WHO),[2] which is in the process of developing the 11th revision of the *International Classification of Diseases (*ICD*)*, scheduled to be released for use by WHO member states in 2018; the American Psychiatric Association (APA), which published the 5th edition of its *Diagnostic and Statistical Manual of Mental Disorders (*DSM*)* in 2013; and the U.S. National Institute of Mental Health (NIMH), which launched its Research Domain Criteria (RDoC)[3] project in 2009. The approaches taken by these three organizations in understanding and classifying mental disorder have both points of overlap and clear differences, owing to their distinct institutional goals and the distinct purposes of their systems. Most notably, the RDoC project does not provide a classification system intended for immediate clinical use. We include it because of its potential for increasing our understanding of mental illness and, consequently, improving mental-disorder classification. At times these three organizations have worked closely together, and at other times they have worked quite independently.

Our goal in this article is to lead readers to a more extensive understanding of psychopathology by describing the aims and purposes of these different approaches and the way in which each addresses four major challenges in defining, diagnosing, and furthering knowledge about mental disorders. We first briefly introduce these four major challenges and then describe each of the three organizations just mentioned, including their relevant history, their similarities and differences, and their general approaches to diagnosing, classifying, and understanding mental disorder. Next, we discuss in more depth the four fundamental, interrelated issues that complicate efforts to understand and classify psychopathology and explore how the approaches taken by the three institutions, informed by their varying perspectives, grapple with these issues. Finally, we offer a set of considerations to facilitate the related goals of (a) improving classification of mental illness, (b) advancing clinicians' ability to identify and treat the diverse manifestations of psychopathology, and (c) deepening knowledge of how mental disorders develop, are maintained, and can be ameliorated. To facilitate the reading this lengthy article, we have provided a glossary of abbreviations/acronyms (see Appendix 1). To highlight our "take-home messages," we provide an executive summary with key conclusions and action items (see Box 1).

Four Key Issues

In our discussions leading up to the writing of this article, we found ourselves returning time and again to four major issues that pose challenges for mental-disorder classification. Thus, the core of this article is organized around these issues. We introduce them briefly here and discuss each of them in more depth later.

Etiology

The alluring possibility of finding *the* cause of various mental disorders has given rise to vigorous nature-versus-nurture debates about whether the single or predominant cause of mental illness is biological or sociocultural/interpersonal, hopeful searches for "*the* gene" responsible for specific mental disorders, and many theories about how parenting, trauma, or some

BOX 1. Executive Summary

Four Key Issues

Etiology (pp. 99–103; summary begins on p. 103)

- Mental disorder develops as the result of the influence of multiple factors—"from neurons to neighborhoods"—and no one level of analysis has causal primacy over the other.
- Ultimately, to understand mental illness in all its complexity, we must discover how all its causal forces—from individuals' genes to their social cultures—interact over time.

Categories and Dimensions (pp. 104–111; summary on p. 111)

- Given its multidimensional complexity, mental-disorder categorization is necessary for human understanding and communication and for clinical decision making.
- Despite the necessity of mental-disorder categorization, we must resist the lure of reification and the illusion of distinct disorders.

Thresholds in Mental Disorder (pp. 111–119; summary on p. 119)

- Setting thresholds is an aspect of categorization and is necessary for clinical decision making.
- Unless further research proves otherwise, all thresholds in mental illness should be regarded as arbitrary.

Comorbidity (pp. 119–126; summary begins on p. 126)

- The rampant comorbidity of current mental-disorder diagnoses is artifactual but not random.
- Comorbidity is an indicator of an imperfect classification system; available steps should be taken to reduce it and clinically viable approaches sought to manage it.

Future Directions

For basic researchers (pp. 128–129)

- Regardless of your particular research focus, always keep in mind the goal of understanding how all the causal forces of mental illness interact over time.

For clinical researchers (pp. 129–130)

- Work toward discerning the most important dimensions of the psychopathology you study from the perspectives of understanding, preventing, and treating mental disorder.
- Develop reliable, valid, and clinically useful assessment measures for these dimensions.
- Work toward developing useful cut points in these measures for multiple clinical decision-making purposes.

For clinicians (p. 130)

- Acknowledge the limitations of current diagnostic classification systems and seek out approaches to assessment and treatment that transcend them.
- Stay abreast of research that furthers understanding of the processes that engender and maintain psychopathology and work to apply it in your practice.
- Advocate for "de-reification" of mental disorders in regulatory, legislative, and legal processes (e.g., by supporting diagnostic flexibility for insurance reimbursement purposes).

For clinical and research organizations (p. 130)

- Educate members about the limitations of current diagnostic classification systems, the use of dimensional assessments of psychopathology in clinical practice, and the value of thinking transdiagnostically when assessing and treating individuals with mental illness.
- Work toward broadening the focus of your society, its journals, and its internal organization to incorporate transdiagnostic, dimensional approaches to psychopathology

For universities and institutes (p. 130)

- Serve as an authority in educating researchers, clinicians, and the public about the dimensional nature of psychopathology.
- Take the lead in developing and disseminating transdiagnostic and dimensional approaches to preventing, assessing, and treating psychopathology.
- Consider how your institution's organizational structure may contribute to narrow diagnostic thinking rather than broader transdiagnostic, dimensional approaches to mental illness.

For the media, the lay public, the groups above, and everyone else (p. 131)

- Recognize that mental disorders are not distinct conditions that someone "has"; rather, they are complex, multidimensional phenomena with multiple causal strands.
- Note that organizations that address issues related to mental illness have a common, long-term goal: To prevent, limit, and/or ameliorate the development and severity of mental illness. Even so, these organizations have distinct purposes, strengths, limitations. and, therefore, short-term goals; nevertheless, they should be considered complementary, not competing.

other factor is "*the* cause" of specific mental disorders. Perhaps because classification of mental disorders in ICD and DSM is tied historically to classification of general medical disorders—many of which do have clear primary causal agents—or because those manuals list distinct mental disorders that correspond to clinically identifiable syndromes in patient populations, their classification systems have sometimes been interpreted as representing the views that (a) mental disorders are distinct diseases with defined boundaries in

the same way that cancer and malaria are distinct diseases; (b) the causes of different mental disorders are similarly clear-cut; and (c) the proper classification—and, by extension, treatment—of mental illness will be clear once we discover "*the* fundamental cause" of each disorder.

In contrast to these simplistic views, research has shown that psychopathology generally arises from multiple biological, behavioral, psychosocial, and cultural factors, all interacting in complex ways and filtered through an individual's lifetime of experience. Research also has shown that the outcomes of these factors and their interactions are *not* clearly definable, distinct diseases, but are instead complex and variable combinations of psychological problems.

Understanding the specifics of these various influences and how they interact to result in the full panoply of psychopathology is a daunting task. The NIMH's RDoC project was initiated specifically to take on this task, but reaching that elusive goal lies somewhere in the future. Another important goal is determining the extent to which mental-illness classification systems can—or even should—be based on or reflect those illnesses' complex etiologies. But even supposing that we had full etiological information, "translating" it to be useful to clinicians in daily practice would itself be a formidable task.

Categories and dimensions

Mental disorder is not an all-or-none phenomenon. Rather, it is continuously graded in severity, from its absence to severe psychopathology. The degree of severity of mental illness is one of its most important aspects, and its dimensional nature is not a problem from a conceptual perspective. For example, it is fully understood that such categories as infant, toddler, child, and so on represent semiarbitrary but useful divisions along the continuum of age. Likewise, we divide the continuum of intellectual ability into semiarbitrary but useful categories, ranging from severe intellectual disability to genius, for various purposes.

However, the dimensionality of mental disorders presents problems in another respect, both conceptually and in practice. In classical categorical systems, each entity is distinct and appears only once in a clearly defined place. With a few exceptions, ICD and DSM are such classical categorical systems. That is, both classify mental disorders as if they were distinct entities, even while acknowledging that people diagnosed with different disorders often have various characteristics in common. Moreover, they do so despite the fact that we know that mental disorders are not distinct disorders but complex combinations of psychological problems, which themselves are dimensional. Clearly, reconciling the complex, multidimensional nature of mental illness with the structure of these classification systems is a major challenge.

Thresholds

Dividing continua into categories is not only commonplace; it is essential for reducing complex information to a level that people can process. However, setting thresholds for mental-disorder classification is difficult for several reasons. First, the very definition of mental disorder remains a subject of debate, an issue that we discuss more fully later. Second, the multidimensional nature of mental illness necessitates that thresholds be set for each component dimension. For example, major depressive disorder (MDD) has dimensions that are emotional (e.g., depressed mood), behavioral (e.g., psychomotor agitation or retardation), cognitive (e.g., difficulty concentrating), and physical (e.g., disrupted sleep). Determining whether individuals are suffering from MDD involves determining whether their difficulties are sufficiently intense and/or persistent (i.e., "above threshold") to be considered disordered on enough of these dimensions to meet the disorder's diagnostic criteria. Many nonmental medical disorders are similarly multidimensional, but their diagnosis often involves the use of objective, quantifiable criteria, such as blood tests, whereas determinations regarding psychological signs and symptoms are based primarily on individuals' self-reports combined with clinicians' experience and judgment. Third, thresholds for classifying mental illness are highly consequential given the many social ramifications of mental-disorder diagnoses. Importantly, the social ramifications may be either negative (e.g., stigma) or positive (e.g., eligibility for services or third-party reimbursement for services).

Comorbidity

Typically, we think of individuals with mental illness as having a particular disorder, and we would like to believe that each disorder is distinct from all others. However, individuals diagnosed with one mental disorder have substantially increased odds of meeting the criteria for at least one other disorder, and many individuals can meet the diagnostic criteria for three or more disorders (Kessler et al., 1994).

This is related to the problem, just described, of applying classical categorical systems to multidimensional phenomena. For example, there are a limited number of robust personality-trait dimensions (e.g., agreeableness vs. antagonism; Markon, Krueger, & Watson, 2005) that are present in all people to greater or lesser degrees. Traits have pathological variants at their extremes, which are a large part of what is being captured with diagnoses

of personality disorder (PD; Tyrer, Reed, & Crawford, 2015). People with severe PD often can be diagnosed with three or more PD categories, because severe PD tends to reflect multiple pathological traits and some traits are indicative of more than one PD diagnosis. For instance, in the DSM, the trait of suspiciousness characterizes both paranoid and schizotypal PDs; thus, paranoid and schizotypal PD "comorbidity" is more accurately described as an artifact stemming from the mismatch between the nature of PD and the structure of the categorical classification system, rather than as analogous to a person's having both a stomach virus and arthritis.

Other examples of the artifactual nature of comorbidity occur commonly among clinical syndromes such as depression, anxiety, and substance use disorders, as well as between clinical syndromes and PD (L. A. Clark, 2005). When the fact that mental disorders commonly co-occur first became widely known in the early 1980s, it was called "comorbidity," which denotes the simultaneous co-occurrence of two distinct disorders (e.g., a stomach virus and arthritis). By the time it was realized that co-occurring mental disorders were rarely distinct, the term *comorbidity* had come to be used so frequently that it stuck, to the point that even authors who have roundly criticized its use (e.g., Lilienfeld, Waldman, & Israel, 1994) continue to use it (e.g., Lilienfeld, 2003; Waldman & Lilienfeld, 2001). In this article as well, we often use the term *comorbidity* as a synonym for coexistence and co-occurrence.

A significant challenge for both the ICD and DSM classification systems is finding ways to reduce artifactual comorbidity in order to represent disorders in a way that is more in keeping with the logic of classification, scientifically more accurate, and clinically more useful. Comorbidity is less of an issue for RDoC, which explicitly focuses on the complex overlapping multidimensionality of mental illness. Indeed, it is hoped that research generated by the RDoC project will inform future revisions of classification systems regarding how they might better characterize this multidimensionality.

Three Current Approaches to Classification of Mental Disorder

We now present a historical overview of the ICD and DSM classification systems to provide a contextual framework for the rest of the article.

Precursors to and early histories of ICD *and* DSM

The ICD's historical lineage traces back to the 19th century (e.g., Farr, 1839) and substantially predates the founding of the WHO (1992a).[4] The first version of ICD had its proximate origin at the first International Statistical Congress, held in 1853 in Brussels, when William Farr of the United Kingdom and Marc d'Espine of Switzerland were asked to prepare an internationally applicable, uniform classification of causes of death. The resulting classification organized diseases by anatomical site and provided the conceptual basis for the subsequent *International List of Causes of Death*, which was adopted by the Institute of International Statistics (1900). Thereafter, revision meetings were convened by the French government approximately every decade until the 1938 conference, which produced the fifth revision of the mortality classification. At that point, there was growing recognition of the need to integrate work on the classification of morbidity (i.e., causes of illness) with that of mortality (WHO, 1992a). Subsequently, the U.S. Committee on Joint Causes of Death, which included representatives of the APA, together with representatives of the governments of Canada and the United Kingdom and of the Health Section of the League of Nations, proposed such an integrated classification, the *Statistical Classification of Diseases, Injuries and Causes of Death* (U.S. Public Health Service, Division of Public Health Methods, 1944). The resulting classification was tested in field trials in the United States, the United Kingdom, and Canada and was modified on the basis of additional international input.

WHO was founded immediately following World War II as a specialized agency of the United Nations. Among the responsibilities it was assigned were establishing and revising international nomenclatures of diseases, causes of death, and public-health practices, as well as standardizing diagnostic procedures. Thus, preparation of the sixth revision of the *International List of Causes of Death* and establishment of the *International Lists of Causes of Morbidity* were assigned to the Interim Commission of WHO in 1946 at the International Health Conference in the United States. The commission undertook an international review process and a revision of the 1944 classification mentioned above.

The resulting classification system, the *International Classification of Diseases, Injuries, and Causes of Death*, came to be known as *ICD-6* (WHO, 1949). This version was the first to use the ICD title, to integrate mortality and morbidity, and, most importantly for our purposes, to include a classification of mental disorders. It was circulated for comment to national governments and was formally approved in 1948 by WHO's governing body, the World Health Assembly.[5] By international treaty, WHO's member states agree to use ICD as a framework for reporting health information so that the data will be internationally comparable. Thus, the importance and impact of ICD arises from its function

as a global common language for defining and communicating about diseases and health conditions. Moreover, because WHO's ultimate objective is "the attainment by all peoples of the highest possible level of health" (WHO, 2014, p. 2), a public-health focus has been fundamental to the goals and internal organization of ICD revisions since *ICD-6*.

In the United States, efforts to classify and count cases of mental disorders separately from national classifications of causes of mortality had been ongoing since at least 1840, when the U.S. Census started to collect information on "idiocy/insanity," which was later expanded to include other, more specific categories (e.g., mania, melancholia, paresis, and epilepsy). Beginning in the late 19th century, other mental-disorder classification systems were used to document the diagnoses of the large populations in psychiatric hospitals. The APA, which was then known as the American Medico-Psychological Association, became involved in this process in 1917.[6] Subsequent U.S. classification systems of mental disorders included the *Statistical Manual for the Use of Institutions of the Insane* (American Medico-Psychological Association, 1918), which evolved by its 10th edition (APA, 1942) into the *Statistical Manual for the Use of Hospitals of Mental Diseases*. Because such an institutionally focused classification did not suit its needs, the U.S. Army developed its own mental-disorder classification system, "Medical 203," during World War II. This system was later modified for use by the Veterans Administration as the "Nomenclature of Psychiatric Disorders and Reactions" in 1947 (Cooper & Blashfield, 2016). The first version of the DSM (APA, 1952) was heavily influenced by both of these classification systems (APA, 2015), as well as by the *ICD-6*, to which APA's representatives had contributed. Thus, with the publication of the first DSM edition of (*DSM-I*), the histories of DSM and ICD became intertwined.

Overlapping history of mental disorder classification: DSM-I *to* DSM-III-R *and* ICD-6 *to* ICD-9

In *ICD-6*, a chapter titled "Mental, Psychoneurotic, and Personality Disorders" included 26 categories, which were grouped into three broad clusters: psychoses, psychoneurotic disorders, and disorders of character, behavior, and intelligence. The *ICD-6* included only category names and code numbers (for use across multiple languages), with a hierarchical organization indicating subcategories of the 26 categories (e.g., Code 300, Schizophrenia, had six subcategories, such as 300.0, Simple Type), along with lists of terms regarding concepts that were to be included and excluded from each category. Other than inclusion and exclusion terms, no definitions or diagnostic guidance were provided.

DSM-I also was organized into three broad groups of disorders, but they were different from those in the *ICD-6*: disorders with an organic basis, subdivided into acute and chronic forms; disorders without an identified organic basis, subdivided into psychotic disorders, psychophysiological disorders, psychoneurotic disorders, PDs, and transient situational PDs; and mental retardation (an outdated term for what are most commonly referred to currently as intellectual disabilities).[7] To increase the clinical utility of the classification system, brief definitions were provided for most categories. Despite their inclusion of "mental retardation," it is noteworthy that the early versions of these systems provided little coverage of child and adolescent disorders.

The ICD classification of mental disorders did not change from *ICD-6* to *ICD-7*, other than to amend errors and inconsistencies. Although most of *ICD-6* and *ICD-7* was well received and widely adopted around the world, the mental-disorder classification was adopted by only a very small number of countries (Fulford & Sartorius, 2009). A report commissioned by WHO to determine why this was the case emphasized the need to separate theoretical constructs from descriptive (i.e., sign- and symptom-based) statements that provided a suitable basis for scientific classification (Stengel, 1959).

Over the next decade, there was substantial collaboration between WHO and APA in developing the mental-disorder classifications in *ICD-8* (WHO, 1967) and *DSM-II* (APA, 1968). As described in *DSM-II*,

> This second edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-II) reflects the growth of the concept that the people of all nations live in one world. With the increasing success of the World Health Organization in promoting its uniform International Classification of Diseases, already used in many countries, the time came for psychiatrists of the United States to collaborate in preparing and using the new Eighth Revision of that classification (ICD-8) as approved by the WHO in 1966, to become effective in 1968. The rapid integration of psychiatry with the rest of medicine also helped create a need to have psychiatric nomenclature and classifications closely integrated with those of other medical practitioners. In the United States such classification has for some years followed closely the *International Classification of Diseases*. (p. vii)

Consequently, *DSM-II* and the mental-disorders chapter of *ICD-8* were nearly identical, using the same three broad categories: psychoses; neuroses, PDs, and other

nonpsychotic mental disorders; and "mental retardation." The terminology, numerical coding system, and order of categories and even subcategories were also largely consistent between the two systems, with a few exceptions and minor variations in category order and specific subcategories (Blashfield, Keeley, Flanagan, & Miles, 2014). One difference carried over from previous versions was that *ICD-8* provided only category names, code numbers, a hierarchical organization of categories, and inclusion and exclusion terms, whereas the *DSM-II* also provided brief definitions for most categories. In retrospect, it is clear that *ICD-8* and *DSM-II* represented the high-water mark of harmonization between the two systems and that both WHO and APA have a legitimate historical claim to the intellectual foundations of modern classifications of mental disorders.

Following the approval of *ICD-8*, WHO decided that additional guidance was needed for meaningful application of its categories in clinical settings and published a glossary of terms (WHO, 1974) that provided definitions for most *ICD-8* mental-disorder categories as well as other key diagnostic concepts. As stated in the glossary's introduction,

> guidance to the [mental-disorders chapter] of *ICD-8* has been added in the form of a glossary because it has become increasingly obvious that many key psychiatric terms are acquiring different meanings in different countries . . . [and] unless some attempt is made to encourage uniformity of usage of descriptive and diagnostic terms, very little meaning can be attributed to the diagnostic side of statistics of mental illness based on ICD and in many other ways communication between psychiatrists will become increasingly difficult. (p. 12)

This WHO statement about the purpose of the glossary makes clear that *ICD-8* was intended not only to serve as a statistical classification system but also to provide information that would be useful in assigning diagnoses in clinical settings, which then would provide the data to be aggregated for statistical reporting. The statement also acknowledges the need for standardization of terms and concepts at a time when diagnostic practice across (and even within) countries was fragmented by idiosyncratic definitions.

The glossary was developed through an international consensus process and adopted a descriptive, operational approach rather than being based on theoretical constructs. Fulford and Sartorius (2009) provided a detailed account of its development, stating that it "became the first predominantly symptom-based modern classification of mental disorders" (p. 30), from which "current descriptive international classifications of mental disorders, the ICD and DSM, are ultimately derived" (p. 37). The glossary's material was largely incorporated into the *ICD-9* (WHO, 1979) chapter on mental disorders, which is the only *ICD-9* chapter with operational definitions for each category, and was readily adopted by nearly all WHO member states.

Parallel to these international efforts at standardization were two noteworthy developments in the United States. First, E. Robins and Guze (1970) published a seminal article proposing a set of principles by which to establish the validity of clinical syndromes (e.g., distinctiveness from other disorders, a common clinical course, genetic aggregation), illustrating them using schizophrenia. Woodruff, Goodwin, and Guze (1974) then applied those principles to 12 diagnostic categories. Second, on the basis of this theoretical perspective, academic departments of psychiatry developed specific diagnostic criterion sets to standardize case identification for research studies, the results of which could be used to improve and establish the criteria's validity. The first such set was the "Feighner criteria" developed at Washington University (Feighner et al., 1972), followed by the Research Diagnostic Criteria (RDC) developed at Columbia University (Spitzer, Endicott, & Robins, 1978). These efforts culminated in the *DSM-III* (APA, 1980), in which the descriptive approach to psychiatric diagnosis was much more fully realized than in any previous mental-health classification system.

Specifically, in *DSM-III*, each mental disorder was operationally defined by a specific list of observable signs (e.g., weight loss of at least 25% of original body weight; defaults on debts or other financial responsibilities) and patient-reported symptoms (e.g., hallucinations, loss of appetite); and by several types of specific thresholds for determining a disorder's presence, including (a) number of signs and symptoms (e.g., "at least four of the following criteria"), (b) duration and course (e.g., "disturbance of at least 2 weeks"; "deterioration from a previous level of functioning in such areas as work, social relations and self-care"; "onset before age 15"), and (c) exclusion criteria, which stipulated, for example, that the signs and symptoms were not due to the effects of a substance or a general medical condition, in which case a different disorder would be diagnosed.

It was intended that the information needed to make a diagnosis could be elicited by any well-trained mental-health professional regardless of theoretical orientation. Further, it was expected that the operationalized definitions would increase interrater reliability, resulting in improved communication among clinicians and more rigorous research standards. Given how radically different *DSM-III* was from previous editions and

from *ICD-9*, it was accepted surprisingly quickly by clinicians across mental-health disciplines. Medical insurance companies in the United States readily adopted *DSM-III* because its specific definitions could easily be incorporated into the "medical necessity" criteria required for patients' reimbursement for care. The specificity also facilitated the development of standardized interviews—for example, the Diagnostic Interview Schedule (L. N. Robins, Helzer, Croughan, & Ratcliff, 1981), a highly structured interview designed for administration by lay interviewers, which was used in large-scale community epidemiological studies such as the NIMH Epidemiologic Catchment Area program (ECA; Regier et al., 1984); and the Structured Clinical Interview for *DSM-III* (SCID; Spitzer, Williams, Gibbon, & First, 1992), which was widely used to specify patient populations in clinical research.

DSM-III diagnoses quickly became the standard for research funded by U.S. federal agencies, particularly NIMH, and for use in testing new drugs for approval and regulation by the U.S. Food and Drug Administration. Starting in the early 1980s, research based on *DSM-III* diagnoses led to a proliferation of new findings on multiple aspects of mental disorders including prevalence, course of illness, genetics, and many others. In addition to providing considerable evidence supporting the new approach to diagnosis, this research also revealed a number of inconsistencies and unclear or invalid criteria in the manual, so work on a fairly extensive revision began within a few years, resulting in the publication of the volume's revised third edition, the *DSM-III-R* (APA, 1987).

One of the primary changes from *DSM-III* to *DSM-III-R* was the removal of many hierarchical exclusion rules, which proscribed the diagnosis of certain disorders if they were considered to be "due to" other specific disorders. We discuss this change in more detail in a later section, "Comorbidity." The revision also reflected developers' great efforts to review the substantial body of research that had been generated in the few years since the publication of *DSM-III*. An annotated bibliography of "all the data available to the APA's Work Group to Review *DSM-III*" (Skodol & Spitzer, 1987, p. xi) included 2,010 citations. Although the application of Robins' and Guze's principles to determine diagnostic validity was a major theoretical aspiration for *DSM-III* and *DSM-III-R*, field trials of diagnostic criteria conducted before the release of each DSM edition, and using increasingly rigorous methods, focused on the more attainable goals of examining reliability and clinical utility. Over the course of this article, we raise the question of whether the Robins and Guze principles are even theoretically applicable to mental disorder.

DSM-IV *and* ICD-10

The development of *DSM-III* and *DSM-III-R* involved almost no international participation and little direct collaboration with WHO, although the DSM gained substantial international influence as a result of its resounding professional and commercial success worldwide (Blashfield et al., 2014). In contrast, there was considerable collaboration between the developers of *ICD-10* and *DSM-IV* (APA, 1994, 2000). In 1978, WHO and the U.S. Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA) entered into a long-term collaboration with the goal of improving international diagnostic classification of mental and substance use disorders (WHO & U.S. ADAMHA, 1985). One outcome of this collaboration was the creation of major epidemiological and clinical diagnostic instruments (e.g., the Composite International Diagnostic Interview: L. N. Robins et al., 1988); another was a systematic examination of cross-national diagnostic traditions and approaches. The resulting collaboration among WHO, ADAMHA, and APA over the next 16 years was instrumental in the development and harmonization of *DSM-IV* and *ICD-10*. As a result of this collaboration and of the increasing dominance of the descriptive model for classifying psychopathology, *ICD-10* and *DSM-IV* were conceptually very similar, though they still had important differences (First, 2009).

DSM-IV was a comprehensive update of *DSM-III-R* that used available research findings as the basis for changes, including structured literature reviews, reanalyses of existing data sets, and field trials (Widiger & Clark, 2000). The level of evidence required to make changes in *DSM-IV* was set quite high, however, such that Allen Frances, who chaired the revision, wrote, "the major innovation of *DSM-IV* will not be in its having surprising new content but rather will reside in the systematic and explicit method by which *DSM-IV* will be constructed and documented" (Frances, Widiger, & Pincus, 1989, p. 375). The emphasis on making changes only on the basis of solid research findings was new for DSM; *DSM-III* had little relevant research to draw upon, so its diagnostic criteria were developed largely through expert consensus, whereas the research base for changes in *DSM-III-R*—given the short time span between the two editions—was neither comprehensive nor well established.

Because of the diversity of WHO's constituencies, *ICD-10* (WHO, 1992a), which remains the current classification system, was published in several different versions to meet a range of needs. The version that WHO member states use as the basis for reporting health statistics is called the *International Statistical Classification of Diseases and Related Health Problems*.

This statistical version lists all health conditions and is intended for use by "coders or clerical workers and also serves as a reference point for compatibility with other classifications" (WHO, 1992b, p. 1). As in *ICD-9*, the "Mental and Behavioural Disorders" chapter is the only one in the *ICD-10* statistical classification with glossary definitions for each condition.

WHO recognized that these definitions did not provide sufficient information for reliable implementation in clinical settings and stated directly that the statistical version of the classification was "not recommended for use by mental health professionals" (WHO, 1992b, p. 1). For that purpose, WHO developed the *ICD-10 Classification of Mental and Behavioural Disorders: Clinical Descriptions and Diagnostic Guidelines* (*CDDG*; WHO, 1992b), "intended for general clinical, educational, and service use" (p. 1). The *CDDG* describes the main clinical and associated features of each mental-disorder category, followed by more operationalized diagnostic guidelines to assist clinicians in making diagnoses. The *CDDG* differs from DSM in offering more flexible guidance—that is, rather than listing specific criteria based on precise duration requirements and symptom counts, the *CDDG* provides more prototypic conceptualizations (see the example of social phobia in Appendix 2). This format is based partly on the need for globally applicable guidance that allows for cultural variation and clinical judgment in response to very different infrastructures and levels of available resources in health settings around the world (see First, Reed, Hyman, & Saxena, 2015, for a description of the development of the *CDDG*).

WHO (1993) also published the *ICD-10 Classification of Mental and Behavioural Disorders: Diagnostic Criteria for Research* (*DCR-10*), which contained specific, operationalized diagnostic criteria highly similar to those in *DSM-IV* (again, see the example in Appendix 2). This similarity was explicitly permitted by a joint WHO-APA agreement allowing each organization to use the other's material. Nonetheless, there are important differences between *ICD-10 DCR* and *DSM-IV*. In a detailed comparison, First (2009) reported that "of the 176 diagnostic categories shared by the two systems, only one, transient tic disorder, is identical," (p. 382) although he judged the differences between criterion sets to be conceptually based in only 21% of them.

Finally, WHO published a version of the *ICD-10* "Mental and Behavioural Disorders" chapter for use in global primary-care settings (WHO, 1996). That volume contains only 26 disorder categories; it excludes conditions that are rare in primary-care settings—for example, obsessive-compulsive disorder (OCD)—and combines disorders with similar management needs at the primary-care level (e.g., acute psychotic disorders). This version is meant to provide adequate coverage of the most prevalent conditions, those accounting for the highest disease burden, and those most commonly presenting in primary-care settings. For each category, information on typical presenting complaints, key diagnostic features, and important differential diagnoses is provided. Also included are management guidelines for each disorder, designed for implementation by nonspecialized health professionals in primary-care settings around the world. Management guidelines are important because referral to more specialized care is not an option in much of the world, and there is little point in identifying conditions with no options for treatment.

Use of ICD *and* DSM

Many—perhaps most—psychopathology researchers use the DSM's specific, operational criteria, whereas those of the *ICD-10 DCR* were never widely adopted in research. In everyday practice (and, therefore, also in research that utilizes patients' chart diagnoses), use of the *ICD-10 CDDG* is far more common. Moreover, practicing clinicians, including those who chart patients' diagnoses in hospitals or outpatient settings, seldom adhere strictly to the specific DSM diagnostic criteria and even more rarely use structured interviews for diagnosis. Initially, when *DSM-III* and *DSM-III-R* were introduced, the criteria for most diagnoses were necessarily based on clinical judgment because they had "not yet been fully validated" (APA, 1980, p. 8; APA, 1987, p. xxiv). By contrast, the *DSM-IV* and *DSM-5* explicitly acknowledged the role of clinical judgment not only in the criteria's original creation but also in their clinical application: "Diagnostic criteria are offered as guidelines for making diagnoses, and their use should be informed by clinical judgment" (APA, 2013, p. 21).

Most U.S. mental health professionals, and perhaps the lay public as well, likely imagine that DSM is the mental-disorder classification system that is used most widely throughout the world, but this is not the case. A survey of nearly 5,000 international psychiatrists in 44 countries (Reed, Correia, Esparza, Saxena, & Maj, 2011) found that for 70% of respondents, *ICD-10* was the classification system used most in daily clinical work (likely in part because the governments of those respondents' countries require its use for administrative and billing purposes; Maj, 2014); only 23% reported that they primarily used *DSM-IV*. Use of *ICD-10* was particularly predominant in Europe, whereas *DSM-IV* use was nearly universal in the United States and common in several other countries that participated in the survey (e.g., Argentina, Australia, Kenya, Turkey). The few respondents who reported most commonly using a classification system other than *ICD-10* or *DSM-IV*

generally used either *ICD-9* or a country-level or regional adaptation of *ICD-10* (e.g., *The Chinese Classification of Mental Disorders*: Chen, 2002; *The Cuban Glossary of Psychiatry*: Otero-Ojeda, 1998).

***How countries use* ICD.** As noted, WHO member states are responsible for reporting health statistics based on ICD to WHO (e.g., causes of mortality and morbidity, prevalence). An example of how these national health statistics are used is the ongoing Global Burden of Disease (GBD) study. The most recent wave of this study showed that mental and behavioral disorders account for 6.6% of total global disease burden as measured by disability-adjusted life years (GBD 2015 DALYs and HALE Collaborators, 2016), which represent a combination of prevalence, premature mortality, and disability. Vigo, Thornicroft, and Atun (2016) argued that the 6.6% total is an underestimate because the study attributes many outcomes of mental and behavioral disorders to other causes, and that the true percentage is closer to 13.0%. The GBD study also showed that mental and behavioral disorders account for an even larger percentage (18.9%) of global disability and that the top 20 causes of global disability include anxiety disorders, schizophrenia, autism spectrum disorder (ASD), and substance use disorders, as well as other mental and behavioral disorders (GBD 2015 Disease and Injury Incidence and Prevalence Collaborators, 2016).

Over the past several decades, governments of WHO member states have increasingly integrated ICD into clinical processes and policies related to health care coverage and reimbursement, social services, and disability benefits (International Advisory Group for the Revision of *ICD-10* Mental and Behavioural Disorders [IAG], 2011). In most countries, provision of medical services other than routine examinations or preventive services is contingent on a qualifying diagnosis. Thus, diagnoses are used to facilitate access to appropriate health care, and the lack of a qualifying ICD diagnosis is used (often appropriately, but sometimes inappropriately) to deny services. This integration of ICD with clinical processes has increased as a result of more intensive administrative management of health services, the development and integration of electronic-information infrastructure for health care (e.g., electronic health records), automated treatment algorithms and care pathways, and increased implementation of standards of care and "evidence-based clinical guidelines," most of which are based on diagnostic categories (e.g., National Institute for Health and Care Excellence, U.K., 2015). The match between diagnosis and services received is also used to evaluate treatment delivery and outcomes. Likewise, national and private health-insurance policies often use ICD (again, in both appropriate and inappropriate ways) to define the scope of practice and reimbursement policies for specific groups of health professionals.

These applications of ICD in health care systems are governed by national and local laws and regulations as well as by health-system policies and are not directly determined by WHO. However, many countries, including the United States, legally require the use of ICD (or national modifications of it) for the collection and reporting of diagnostic information as a part of health encounters. Country-level modifications usually include additional codes for hospital records, but they may also involve the addition or, less commonly, the deletion of diagnostic categories or subtypes. Changes in ICD, therefore, have major implications for national and health-system policies and processes and may require legislative or regulatory changes. As a result, WHO member states view themselves as major stakeholders in ICD revisions.

Use of* ICD *in the United States. The U.S. government has published ICD adaptations as frameworks for government morbidity and mortality statistics beginning with *ICD-7*. The National Center for Health Statistics and the Centers for Medicare and Medicaid Services are currently responsible for developing and maintaining the adaptations, which contain additional information to facilitate indexing by hospitals and to enable the coding of morbidity and utilization data from patient records. These U.S. adaptations of ICD, called "Clinical Modifications" (CMs), initially had little direct relevance to U.S. health professionals. However, they became substantially more important when federal regulations required health professionals to use *ICD-CM* codes on Medicare claims and, after the passage of the Health Insurance Portability and Accountability Act (HIPAA) in 1996, on all electronic transactions for billing and reimbursement (U.S. Centers for Medicare and Medicaid Services, 2015). Effective October 1, 2015, 25 years after the approval of *ICD-10* by the World Health Assembly, the U.S. government began requiring U.S. health professionals and health systems to use a new CM, *ICD-10-CM* (U.S. National Center for Health Statistics, 2015). The overlapping time frames of *DSM-5*, the U.S. *ICD-10-CM*, and WHO's forthcoming *ICD-11* have created substantial confusion among U.S. health professionals.

An obvious question is why the U.S. would require this expensive and time-consuming transition to *ICD-10* just before the completion of *ICD-11*. Not surprisingly, the answer is complex. The *ICD-10-CM* had been under development for years and was intended for substantially earlier implementation, but objections from health systems, health insurers, and professional associations (e.g., the American Medical Association) regarding expense and burdensome administrative requirements

delayed implementation to the point that many suggested that the United States skip implementation of *ICD-10* and move directly to *ICD-11* (Natale, 2014; Sullivan, 2012). However, the U.S. Department of Health and Human Services argued that, first, the *ICD-10-CM* implementation was urgently needed to correct many *ICD-9-CM* deficiencies, and second, the development of a U.S. *ICD-11-CM* would require several additional years after the *ICD-11's* approval by the World Health Assembly and its initial release, which is expected in 2018. Congress eventually passed legislation requiring *ICD-10-CM* implementation.

When the United States will move to *ICD-11* remains to be seen. On the one hand, those who resisted *ICD-10-CM* almost certainly will resist a subsequent change. On the other hand, implementing *ICD-11* after its completion and approval would be consistent with the United States' responsibilities as a WHO member state and with the country's leadership role in many WHO activities, including key aspects of *ICD-11*'s development. The U.S. government has already modified *ICD-10-CM* to make its categories and terminology more compatible with their *DSM-5* counterparts. Some of these changes effectively move *ICD-10-CM* closer to *ICD-11.* However, a piecemeal process may result in a patchwork classification system that is far from ideal, as demonstrated in past efforts to update *ICD-9-CM* to accommodate the categories and terms of *DSM-IV*, so it would be better if a full update were made sooner rather than later.

Thus far, we have introduced the major concepts that we address in this article and provided a historical context for the remainder of the article by reviewing the development of ICD and DSM. We now turn to describing the current (or, in the case of ICD, impending) instantiations of the three descriptive systems of psychopathology that are our primary focus.

ICD-11

Since its initial publication, *ICD-10* (WHO, 1992a) has been updated regularly through a formal intergovernmental process. For example, new categories have been added for emerging disease entities (e.g., severe acute respiratory syndrome) and emerging disease characteristics (e.g., resistance to antimicrobial and antineoplastic drugs). However, the current 25-year period is the longest in ICD history without a major revision. Responsibility for coordinating the revision activities related to Chapter V, "Mental, Behavioural, and Neurodevelopmental Disorders," was assigned to WHO's Department of Mental Health and Substance Abuse, which appointed its international advisory group in 2006 for consultation throughout the revision process. This group made recommendations about early decisions and helped to articulate general principles that would govern the chapter's development (IAG, 2011). The department views its mandate for developing *ICD-11* Chapter V as a pragmatic one that relates to two fundamental questions:

1. Given the best evidence available, which mental and behavioral disorder categories and related health conditions does the world's global health authority consider important for its member states to track as a basis for both health reporting and structuring clinical care; and
2. How should those categories be defined and operationalized?

These guiding questions have had a major effect on the development process of *ICD-11* chapter on mental disorders and on decisions about the nature of the diagnostic guidance to be provided by WHO.

WHO public-health priorities for mental and behavioral disorders. The priorities of WHO's Department of Mental Health and Substance Abuse in developing the *ICD-11* classification of mental and behavioral disorders are rooted in WHO's public-health mission and objectives. The department has long been concerned about an unacceptable global "mental health gap" (WHO, 2008). Despite the major contribution of mental disorders to global disease burden and disability, treatment for them remains unavailable or woefully inadequate in most of the world. The 2004 World Mental Health Survey found that in low- and middle-income countries, less than 25% of individuals with serious mental illness (e.g., schizophrenia, bipolar disorder, MDD) had received any treatment in the past year, and even in high-income countries (e.g., the U.S., Western European countries), the proportion was only a third to a half (World Health Organization World Mental Health Survey Consortium, 2004). In that same year, Kohn, Saxena, Levav, and Saraceno (2004) estimated that the global treatment gap between those who needed treatment for mental disorder and those who received it ranged from 32% to 78%, depending on the disorder.

Moreover, it is well established that people with serious mental illness have a much higher prevalence of nonmental health conditions (e.g., cardiovascular, metabolic, and respiratory diseases; De Hert, Correll, et al., 2011; Svendsen, Singer, Foti, & Mauer, 2006), which contributes to disproportionately higher rates of mortality and a substantially reduced life expectancy (Cuijpers & Smit, 2002; Thornicroft, 2011, 2013; Walker, McGee, & Druss, 2015). There may be direct relations between mental disorders and specific health conditions, such as cardiovascular disease (e.g., Davidson, 2012; Scott et al., 2013). However, paradoxically, a possible indirect relation is that traditional institutional treatment for

mental disorders may aggravate modifiable risk factors such as smoking and obesity (Shin et al., 2012), which are the greatest contributors to poor physical health and excess mortality among people with mental disorders (e.g., Cerimele & Katon, 2013; de Leon & Diaz, 2005; Scott & Happell, 2011). In addition, common pharmacological treatments for mental disorders may have side effects that are damaging to overall health (Correll, 2007).

Major contributors to the mental-health treatment gap are specific patient, provider, treatment, and system factors that act as barriers to the recognition and management of physical diseases in people with mental disorder (De Hert, Cohen, et al., 2011). System factors include deficient resources in mental-health-care systems, issues of stigma, inadequate prevention programming, and lack of parity in health financing, including through insurance coverage (Saxena, Thornicroft, Knapp, & Whiteford, 2007). Not surprisingly, the greatest health disparities are found among underserved population groups, such as African Americans in the United States, who face increased morbidity as a result of their minority status when they experience mental disorder (Carliner et al., 2014; Das-Munchi et al., 2016; Mookhoek, deVries, Hovens, Bouwers, & Loone, 2001; Stecker, Fortney, Steffick, & Prajapati, 2006; Voruganti et al., 2007). Thornicroft (2011) has suggested that physical-health disparities among people with mental disorder contravene international conventions regarding the "right to health."

Another contributing factor to the mental-health treatment gap is the absence of specialized expertise and qualified mental-health service providers in most parts of the world. Data from WHO's *Mental Health Atlas* (WHO, 2011) indicate that high-income countries are reasonably well supplied with mental-health professionals, with nearly 44 for every 100,000 people. But less than 20% of the world's population lives in these countries (World Bank, 2015). In upper-middle-income countries (e.g., Brazil, China, Mexico), which represent about 33% of the world's population, there are fewer than one-third as many mental health professionals—less than 14 for every 100,000 people. Lower-middle-income countries (e.g., India, Indonesia, Nigeria), which represent about 39% of the world's population, have fewer than four mental-health professionals for every 100,000 people and, on average, nearly three of these are nurses. In low-income countries including much of sub-Saharan Africa, which represent 9% of the world's population, mental-health professionals are essentially nonexistent. Simply put, these statistics mean that most people with mental disorder in the world are unlikely to see a mental-health professional at any time in their lives.

Clearly, the current status of health care provided to people with mental disorder around the world is an urgent public-health priority. To begin to address this situation, the World Health Assembly approved the global "Mental Health Action Plan 2013–2020" (WHO, 2013a). The action plan and accompanying resolution represented a formal recognition by WHO member states of the importance of mental health and committed them to specific and measurable actions to improve mental health, including increasing service coverage for people with severe mental illness by 20%. The plan further moved away from "a wholly medical model to address income generation and education opportunities, housing and social services, and other social determinants of mental health" (Saxena, Funk, & Chisholm, 2013, p. 1971).

The *ICD-11* classification of mental and behavioral disorders serves as a primary means for identifying individuals in need of services. As such, it is integrally connected to the WHO's "Mental Health Action Plan," which supports WHO's Department of Mental Health and Substance Abuse's overarching goal for revising the classification: that *ICD-11* provide a better tool for helping clinicians to identify not only the people in need of mental-health services but also the treatments and management strategies most likely to be effective, with the ultimate goal of helping WHO member states reduce the disease burden associated with mental disorder.

Another WHO product that is integrally related to the action plan is the Mental Health Gap Action Programme's "mhGAP Intervention Guide for Mental, Neurological, and Substance Use Disorders in Non-Specialized Health Settings," now in its second edition (WHO, 2016a). This document includes evidence-based treatment guidelines designed to be implemented in primary-care settings in low- and middle-income countries for "priority" mental disorders, which are defined on the basis of disease burden, prevalence, and the extent to which evidence-based treatments can be implemented in such settings. Designed to be consistent with the *ICD-11*, the intervention guide provides guidance for a range of conditions including depression, psychoses, child and adolescent mental and behavioral disorders, dementia, disorders due to substance use, and self-harm and suicide, as well as guidance on more broadly targeted psychosocial interventions. WHO has also developed similar guidelines for conditions specifically related to stress (e.g., posttraumatic stress disorder, or PTSD; WHO, 2013b).

Development of* ICD-11 *mental and behavioral disorders. The public-health aims described above have substantially influenced the methods and priorities of the developers of *ICD-11*. To be a better tool for reducing the

disease burden of mental disorders, the new system will need to be useful and usable throughout the world at the points where people with mental-health needs are most likely to come into contact with opportunities for care. For this reason, WHO is particularly focused on issues of clinical utility and global applicability in developing the revision (Reed et al., 2013).

Clinical utility. The IAG (2011) and others (Reed, 2010) have noted that the current revision is unlikely to yield major improvements in the validity of ICD mental-disorder categories, as also was the case for *DSM-5* (Hyman, 2007, 2010). Importantly, however, they have pointed out that major problems with the clinical utility of the ICD's mental-disorder classifications can and should be addressed. To guide the revision and field testing for it, WHO provided a definition of clinical utility (Reed, 2010; Reed et al., 2013), based on earlier definitions (e.g., First et al., 2004), that refers to the extent to which a mental-disorder classification or diagnostic category (a) facilitates communication among users; (b) facilitates conceptualization and understanding of the entity or entities classified; (c) can be implemented easily and accurately by relevant health professionals (e.g., because the categories fit patients well, the system is easy to understand and use, or clinicians can easily reach a diagnostic conclusion); and (d) helps health professionals to select treatments and manage clinical conditions. Reed and colleagues (2013) pointed out that if implementing the *ICD-11* mental-disorder classification was difficult or cumbersome, then clinical practice would be guided by concepts other than the *ICD-11*'s standardized, operationally defined categories; in turn, wide use of nonstandard concepts would undermine improvement in practice and the assessment of outcomes, and would not generate valid data for health programs and policies or for global health statistics.

Thus, not surprisingly, most of the proposed changes in *ICD-11*, particularly in the *ICD-11 CDDG*, are intended to enhance the categories' clinical utility. First and colleagues (2015) provided an overview of the proposed structure and content of the *ICD-11 CDDG* for use by mental-health professionals in clinical settings. For each condition, the guidelines include a list of "essential features," which are the "symptoms or characteristics that a clinician could reasonably expect to find in all cases of the disorder" (First et al., 2015, p. 85). Although these lists superficially resemble diagnostic criteria, they are written in more flexible language (e.g., "minimum duration is about 2 weeks" in ICD vs. "symptoms have been present during the same 2-week period" in DSM) to allow greater scope for the exercise of clinical judgment in determining the diagnosis that best fits each patient, an approach that international users of both ICD and DSM overwhelmingly prefer to a strict criteria-based approach (Evans et al., 2013; Reed et al., 2011). Arbitrary cutoffs and precise requirements related to symptom counts and duration are generally avoided unless these have been empirically established across countries and cultures or there is another compelling reason to include them. The more flexible language of the *ICD-11* diagnostic guidelines is intended to increase clinical utility by allowing for cultural variations in presentation as well as contextual and health-system factors that may affect diagnostic practice. (See First et al., 2015, for an example of the proposed *CDDG* version of the diagnostic guidelines for PTSD.)

One of WHO's core conclusions related to clinical utility is that a single version of the classification (e.g., the *CDDG*) cannot possibly meet the needs of all global settings, as was found to be the case for *ICD-10*. Thus, a primary-care version of the classification is being developed simultaneously. Its content and format are driven by similar clinical-utility considerations but are modified for use by health professionals in primary-care settings, with particular attention to low- and middle-income countries (Goldberg, Prisciandaro, & Williams, 2012).

WHO's Department of Mental Health and Substance Abuse has developed a systematic program of field studies specifically focused on the clinical utility of the proposed diagnostic guidelines for *ICD-11*'s "Mental, Behavioural, and Neurodevelopmental Disorders" chapter (Keeley et al., 2016). This program of work contrasts with studies of previous classifications, which have focused on reliability. Specifically, the WHO field-studies program represents an integrated and complementary set of field-study strategies, including (a) large international surveys of health professionals, (b) formative field studies examining how clinicians conceptualize relations among mental disorders and how mental disorders should be classified to correspond best to clinical practice, (c) studies using experimental methodologies based on standardized case material in the form of vignettes to evaluate the specific impact of proposed changes on the consistency and accuracy of clinicians' diagnostic decision making, and (d) field studies of the guidelines in the global clinical settings in which they ultimately will be implemented. These studies are being conducted in both specialty mental-health and primary-care settings, and their results already are being used to improve the structure and content of *ICD-11* diagnostic guidelines (see Keeley et al., 2016, for examples).

Global applicability. Global applicability is related to clinical utility, but it also explicitly involves the extent to which a classification is useful in different regions and countries, languages, cultural contexts, and settings with

dramatically different levels of resources. Given the role and constituencies of WHO, the goal of global applicability has guided WHO's policies and methods for developing *ICD-11* in several important ways. First, the IAG and all working groups for *ICD-11* mental and behavioral disorders include representatives from all WHO global regions. Second, professional surveys (Evans et al., 2013; Reed et al., 2011) and formative studies to inform early decisions about the structure of the classification (Reed et al., 2013; Roberts et al., 2012) were conducted in multiple languages and with broadly international groups of participants. Third, diagnostic guidelines for the *ICD-11 CDDG* will include a specific section on cultural issues related to the clinical presentation and diagnosis of each condition (see First et al., 2015, for an example). Fourth, initial field testing of the proposed *ICD-11* diagnostic guidelines is being conducted via the Global Clinical Practice Network (GCPN; Reed et al., 2015), an international network of more than 14,000 mental-health and primary-care professionals from more than 150 countries. (See Evans et al., 2015, and Keeley et al., 2016, for detailed descriptions of the methodology of GCPN studies.) Field testing using standardized case material with the GCPN is currently taking place in six languages: Chinese, English, French, Japanese, Russian, and Spanish. The final phase of field testing—the application of *ICD-11* diagnostic guidelines to real patients in the clinical settings in which they receive care—emphasizes the participation of large middle-income countries (e.g., Brazil, China, India, Mexico, Nigeria), which represent nearly 50% of the world's population. WHO's field-testing program was designed specifically to examine linguistic and regional differences in the accuracy, consistency, and clinical utility of the *ICD-11* diagnostic guidelines to maximize their global applicability before the revision is finalized.

DSM-5

DSM-5 reflects the product of well over a decade of development and over 3 decades of research since *DSM-III*. Initial hopes that the rapidly increasing research base in biological psychiatry would contribute in a major way to the revision of the classification were dispelled in the early phases of the process. Thus, the focus was shifted toward incorporating important developments in other research areas (e.g., clinical, psychopathological, epidemiological, gender related, cultural, and developmental) to produce a manual that would be a useful, more research-based upgrade to *DSM-IV*.

Rationale for the* DSM-5 *revision. Since the release of *DSM-III* in 1980, several problems with its diagnostic system (which for the most part also apply to the ICD classification; Sturt, 1981) had become evident. It also gradually became clear that the rapid and widespread adoption of *DSM-III* and its successors as the standard for funding federal grants, drug trials, and reimbursement for mental-health services had had several negative effects. One effect was reification of DSM categories and criteria as a direct reflection of the true nature of psychopathology, and a second was their almost exclusive use in research evaluating treatment efficacy, which we discuss further below. The rapid pace of mental-health research in the 1990s and increasing concerns about correcting the DSM's perceived deficiencies led to a meeting of the leadership of APA and NIMH in 1999 to discuss the possible next steps for DSM. This meeting set the *DSM-5* development process into motion.

Epidemiologic studies, starting with the Epidemiologic Catchment Area program (Boyd et al., 1984) and, later, the National Comorbidity Survey (Kessler, 1994) and its replication (Kessler & Merikangas, 2004), revealed high rates of comorbidity among DSM disorders, especially when diagnostic-hierarchy requirements (in which Disorder X could not be diagnosed if it was "due to" Diagnosis Y) were ignored. Some comorbidity patterns were expected on the basis of presumed etiologic mechanisms and clinical observation; for example, various anxiety disorders were found to be comorbid with each other, perhaps as the result of a hypothesized common underlying dimension of sensitivity and hyperreactivity to threat stimuli (e.g., T. A. Brown & Barlow, 1992). However, much of the comorbidity was unexpected or nonspecific—for example, 56% of National Comorbidity Survey respondents with at least one mental disorder had two or more (Kessler et al., 1994), and anxiety disorders were comorbid not only with each other but also with various depressive (L. A. Clark & Watson, 1991) and alcohol-use disorders (Kushner, Sher, & Beitman, 1990). Although diagnostic hierarchies were largely discontinued in *DSM-III-R*, concerns about the validity of DSM's categorical diagnostic boundaries persisted for other reasons.

One particular issue is the specificity with which diagnoses direct treatments—a major rationale for any diagnostic system. For example, emerging research evidence strongly suggested that the targets of psychopharmacologic treatments did not fit neatly into specific DSM categories. New antidepressants, such as selective serotonin reuptake inhibitors (e.g., fluoxetine, better known as Prozac) and second-generation antipsychotic medications, were introduced in the 1980s and 1990s. As these therapies were subjected to further investigation, results showed that "antidepressants" were effective in the treatment of many disorders beyond depression, such as eating disorders and anxiety disorders. Likewise, several of the second-generation antipsychotic medications were found to be effective alone

or as adjunctive treatments for nonpsychotic mood disorders.

Concurrently, psychotherapy research led to the introduction of "manualized" treatments—in particular, cognitive-behavioral and interpersonal therapies—that were standardized and could be disseminated for clinical and research purposes. Cognitive-behavioral therapy, originally developed to treat depression, has since been used successfully in a very wide range of mental disorders, including anxiety, obsessive-compulsive disorder, eating disorders, PDs, and substance use disorders (e.g., see https://www.div12.org/psychological-treatments/treatments/). In sum, the nonspecificity of both pharmacological and psychosocial treatments called into question the specificity of the DSM disorders and their purported underlying mechanisms. Major questions were raised about the boundary between MDD and generalized anxiety disorder (GAD), and those among schizophrenia, bipolar disorder, MDD, and schizoaffective disorder, as well as between and among other pairs and groups of often co-occurring disorders (e.g., L. A. Clark, Watson, & Reynolds, 1995).

Similarly, another negative effect of the rapid and widespread adoption of the diagnostic categories of *DSM-III* and its successors was their almost exclusive use in research evaluating treatment efficacy, with the highest level of evidence seen as that coming from randomized controlled trials testing the effects of specific treatments in patient populations defined by specific DSM categories. Initially, *DSM-III* was heralded as providing an empirical basis for mental-disorder treatments. However, as evidence of the nonspecificity of both pharmacological and psychosocial treatments accrued, the nearly exclusive reliance on DSM diagnoses in treatment research was criticized for limiting the ability of such research to cut across category boundaries (Cuthbert & Insel, 2013; Hyman, 2010). It also systematically disadvantaged treatments with broad effects by requiring repetitive demonstrations of their efficacy in specific, narrowly defined patient populations, despite the fact that most treatments' mechanisms of action are likely the same across many disorders (Tucker & Reed, 2008).

The requirement of repetitive demonstrations presented a particular barrier for psychological treatments (e.g., cognitive-behavioral therapy) as opposed to pharmacological ones, given that psychological treatments generally lack the financial backing of organized commercial interests that would support treatment trials with large samples (Tanenbaum, 2005). Compared with trials of psychological treatments, large-scale drug trials can be completed in relatively short time frames, because any licensed physician can prescribe a medication and "treatment sessions" can be brief and intermittent. Thus, the labor costs of pharmacological treatment trials are relatively low, and such studies are readily funded by pharmaceutical companies, which stand to profit considerably if a trial supports a drug's efficacy. In contrast, training clinicians to administer a psychological treatment with a high level of reliability is time-consuming, and treatment sessions typically require a commitment of an hour or two weekly, so the labor costs are high and there are few to no financial incentives for companies to fund such studies.

To the extent that people tend to believe that response to a pharmacological agent means that a disorder has a biological cause, this situation also contributed to a self-perpetuating emphasis on biological causality. Although it is reasonable to assume that a complete and accurate understanding of biological causality will be important to developing more effective treatment strategies for mental and behavioral disorders, an overemphasis on biological causality runs counter to increasing evidence regarding the multicausal nature of mental illness.

The growth in epidemiological studies worldwide since 1994 (Kessler, 1999) also revealed substantially more cross-national epidemiological variation in *DSM-IV* disorder prevalence than expected. For example, social anxiety disorder showed a 34-fold variation in prevalence between the country with the highest prevalence and the country with the lowest prevalence despite use of the same instrument (the Composite International Diagnostic Interview for *DSM-IV*) and the same time frame of measurement (12 months; for other examples, see Hinton & Lewis-Fernández, 2011, and Lewis-Fernández et al., 2010). These findings raised the question of whether the diagnostic criteria underlying the epidemiological instruments were overly specific and thus could fail to identify different cultural expressions of the same disorders (Lewis-Fernández et al., 2010). It is always possible, of course, that the prevalence of particular disorders is highly variable or that lack of familiarity with the disorders resulting from lower access to mental health care and information in some settings leads to lower endorsement of symptoms. The APA's *DSM-5* Task Force opted to revise disorder criteria if the cross-cultural data warranted it. For example, one criterion for the diagnosis of social anxiety disorder, fear of negative evaluation, was broadened to include alternative presentations that are typical in Asia. A separate section, "Culture-Related Diagnostic Issues," was added to most *DSM-5* disorders to facilitate cross-cultural application of the nosology.

Some questions about the underlying mechanisms of DSM disorders were prompted by the inability to find laboratory markers or tests for the vast majority of disorders. A few initially promising tests were found

subsequently to be of little or no practical value for clinical practice. Currently, narcolepsy is the only mental condition that has a biomarker (hypocretin deficiency) as a criterion, although robust biomarkers for various causes of neurocognitive disorder have been found (e.g., Alzheimer's disease) or are likely to be found in the relatively near future (e.g., prion disease) and may be added as criteria in future versions of the DSM.

Generally, the search for indicators of the construct validity of diagnoses as outlined in E. Robins and Guze's (1970) classic article has been frustrating. Initially promising findings, such as a gene mutation associated with *DSM-III* bipolar disorder (Egeland et al., 1987), were later disproved (Ginns et al., 1992), deflating the optimism that we might soon find "the gene for" various mental illnesses (Kendler, 2005, p. 1243). Endophenotypes—measurable, typically biological, characteristics "along the pathway" between genes and clinical disorders—were the next object of enthusiasm (e.g., Gottesman & Gould, 2003, p. 636), as it was hoped that they would "more clearly reflect the impact of specific genes" (Patrick, 2014, p. 1333). However, endophenotypes are proving to be no simpler genetically than the clinical phenotypes with which they are associated (Iacono, Vaidyanathan, Vrieze, & Malone, 2014).

Nonetheless, the processes of seeking specific genetic influences and examining why early findings were disproved have led to more sophisticated research designs, technologies, and statistical methods. These improved research methods, in turn, have led to findings that reveal significant genetic overlap among many *DSM-IV* diagnoses and may "provide valuable insights into the psychological and neural mechanisms" that give rise to psychopathology (Iacono et al., 2014, p. 1339)—a hope that is the foundation of NIMH's RDoC project. For example, researchers recently found significant variation in a particular cluster of genes that they were able to link both to a specific immune-system function—synaptic pruning—and to schizophrenia (Sekar et al., 2016). Related findings in the study showed that variation in the function's expression affected mouse brains in a way that was consistent with observed characteristics in schizophrenia, indicating a potential neural mechanism contributing to the disorder's development.

The limitations of *DSM-IV* diagnostic categories were also seen in clinical use. One of the most striking manifestations was the high rate of nonspecific diagnoses used in general clinical practice, expressed as disorders "not otherwise specified" (NOS). Certain NOS diagnoses were used particularly frequently, including NOS variants of PD (Verheul & Widiger, 2004), eating disorder (Smink, van Hoeken, & Hoek, 2013), dissociative disorder (Johnson, Cohen, Kasen, & Brook, 2006), and pervasive developmental disorder (Lauritsen, Mortensen, & Pedersen, 2004 The use of NOS diagnoses was acceptable for cases in which (a) a named syndrome was not classified in the DSM (e.g., a diagnosis of eating disorder NOS for cases of binge eating disorder); (b) a broad diagnosis could be made, but diagnostic criteria were not met for any specific diagnosis (e.g., PD-NOS); or (c) insufficient information was available for a specific diagnosis (e.g., a diagnosis of psychotic disorder NOS as a placeholder until general medical and substance-related causes could be ruled out). Although such usage was permitted, the high use of NOS categories indicated problems in diagnostic coverage (e.g., should binge eating disorder be added to the classification?) or criteria (e.g., is there a more useful way to describe the PDs and pervasive developmental disorders seen in clinical practice?).

Clinicians were also given limited ability to document clinically significant symptoms that occurred outside the criteria of the patient's primary diagnoses. For example, anxiety symptoms are frequently seen in patients with MDD and are associated with poorer outcomes (Walker & Druss, 2015). However, there was no way to acknowledge these symptoms if they did not meet criteria for a specified anxiety disorder, despite their clear clinical effect. Likewise, sleep difficulty is a frequent experience of persons with a wide range of mental disorders and often is treated, despite being a symptom of only a few diagnoses (e.g., GAD, bipolar disorder, and MDD) outside sleep disorders themselves. The limited availability of ways to document these commonly associated symptoms hindered the overall ability of practitioners using *DSM-IV* to describe the diversity of patient presentations, to justify treatment decisions, and to follow important treatment outcomes.

DSM-5: *Process and outcome.* The overall consensus of the *DSM-5* developers was that despite acknowledged advantages, the specificity of DSM diagnostic criteria was starting to hinder progress in the search for underlying mechanisms of mental disorders, and the criteria were not describing the clinical realities experienced by patients and treated by clinicians. Initially, it was thought that knowledge generated since the development of *DSM-IV* might be useful in improving the validity of DSM disorders—particularly, that findings in genetic epidemiology, molecular genetics, and functional and structural imaging might help the manual move toward a more etiologically based classification. Accordingly, dimensional models of diagnosis, a topic of interest that was abandoned as premature for *DSM-IV* development, was resurrected in early *DSM-5* discussions (Kupfer, First, & Regier, 2002), and *DSM-5* development started with commitments to examine research evidence from multiple

scientific fields and an openness to complementary and alternative classifications systems (e.g., the Spectrum Project; Maser & Patterson, 2002).

The revision of *DSM-IV* was undertaken with several guiding principles. First, as with *ICD-11*, the highest priority in modifying *DSM-IV* was to optimize clinical utility. Second, revisions were to be guided by research evidence. A 5-year, NIH-funded series of research-planning conferences was held before the appointment of the *DSM-5* Task Force to synthesize research evidence in important areas and to identify gaps in research. Third, it was felt that continuity with *DSM-IV* should be maintained in *DSM-5* to prevent upheaval in the field, although there were no a priori constraints on the degree of change that could be made between *DSM-IV* and *DSM-5* if the supporting research evidence was strong.

After the planning conferences, the *DSM-5* Task Force, work groups, and cross-cutting study groups met for approximately 5 years. Proposals for changes were reviewed for the strength of their supporting research evidence and, when indicated, for their clinical, public health, and forensic implications. They also were reviewed by the APA Assembly and, finally, by the APA Board of Trustees, the two governing bodies of the APA. The Assembly's members are selected by geographically based psychiatric societies across the United States, its territories, and Canada, with additional members representing various constituencies (e.g., early-career psychiatrists, underrepresented minority groups); approved allied organizations also sit on the Assembly. The group acts in an advisory capacity to the Board of Trustees, representing the needs of its constituents. The Board of Trustees is composed of officers elected by the APA general membership, representatives elected by members in geographic areas, a limited number of past presidents, and additional members representing the Assembly and various other constituencies. The Board of Trustees is responsible for determining APA's priorities, policies, and budgets. The leadership and members of the APA Assembly and Board of Trustees tend to reflect the diverse membership of the organization and include researchers, academicians, and full-time clinicians in a range of practice settings. However, participation of the general membership in electing officers has been less than representative (e.g., fewer than 15% of members cast a vote for President-Elect of the Board of Trustees in 2016).

In the end, this process resulted in a revised manual that was considerably more conservative than had been envisioned more than 10 years earlier. The consensus from the early research-conference series was that, in general, current neuroscience findings would not be translatable to clinically useful diagnostic criteria, a conclusion that shut down hopes for a "paradigm shift" toward more etiologically based diagnostic criteria. Dimensional assessment measures of symptom and diagnostic severity and of disability were recommended by the *DSM-5* Task Force for clinical use but were rejected by the Board of Trustees because of a lack of evidence on their utility in improving patient care and outcomes. The *DSM-5* Personality and PD Work Group's proposal of a radically different method to diagnose PDs, a hybrid categorical-dimensional model, was also rejected, largely because the Board of Trustees was not convinced that its clinical utility had been sufficiently well established despite many iterations in its development to maximize usability and its acceptable performance in the *DSM-5* field trials.

***Notable changes in* DSM-5.** In the end, the changes in *DSM-5* were relatively conservative. Nonetheless, many evidence-based innovations were introduced that were expected to lay the groundwork for future diagnostic improvements. We discuss those involving reorganization, introduction of the spectrum concept, elimination of the multiaxial system of diagnosis, and emphasis on developmental, gender-related, and cultural aspects of mental disorder.

Reorganization. First, in collaboration with WHO, as part of an effort to maximize the structural similarity of the *DSM-5* and *ICD-11*, the chapter structure of *DSM-5* was altered and many disorders were regrouped. Several new chapter groupings were introduced—for example, "Obsessive-Compulsive and Related Disorders" (OCRDs) and "Trauma- and Stressor-Related Disorders" (see Phillips et al., 2010, and Friedman, Resick, Bryant, & Brewin, 2011, respectively, for literature reviews that supported these organizational changes). These chapters mostly included diagnoses that had been classified in *DSM-IV* as anxiety disorders, but they also included disorders that previously had been grouped elsewhere or that were new in *DSM-5*. For example, two disorders classified as OCRDs were body dysmorphic disorder, which was classified as a somatoform disorder in *DSM-IV*, and the newly created hoarding disorder (see Phillips & Stein, 2015, for an overview of the OCRDs). Some broad disorder groupings were subdivided. For example, the *DSM-IV* "Mood Disorders" chapter was split into two separate chapters, "Depressive Disorders" and "Bipolar Disorders," largely on the basis of a literature review (Goldberg, Andrews, & Hobbs, 2009) that considered 11 diagnostic validators.

Further, reflecting a more conscious developmental perspective that most mental disorders begin early in life, the former chapter of "Disorders Usually First Diagnosed in Infancy, Childhood, or Adolescence" was deleted. Most of its disorders were placed in a chapter for neurodevelopmental disorders, and the rest were

distributed to other chapters depending on their primary symptoms. For example, disorders from the deleted chapter's section "Feeding and Eating Disorders of Infancy or Early Childhood" were placed in *DSM-5*'s "Feeding and Eating Disorders" chapter (formerly simply "Eating Disorders" in *DSM-IV*), and separation anxiety disorder was placed in the "Anxiety Disorders" chapter.

The sequence of chapters also was changed so that related groups of disorders would be located near each other. For example, on the basis of epidemiological and neurobiological evidence of their relatedness, the "Neurodevelopmental Disorders," "Schizophrenia Spectrum and Other Psychotic Disorders," "Bipolar Disorders," and "Depressive Disorders" chapters were placed in sequence. Likewise, the sequence of chapters including "Depressive Disorders," "Anxiety Disorders," "OCRDs," "Trauma- and Stressor-Related Disorders," "Dissociative Disorders," and "Somatic Symptom and Related Disorders" reflects a growing recognition of the relatedness of many of these disorders. The next series of chapters all contain disorders with prominent physical manifestations, such as "Feeding and Eating Disorders," "Elimination Disorders," "Sleep-Wake Disorders," and "Sexual Dysfunctions." Clinical considerations and the well-justified objections of advocacy groups led to the separation of gender dysphoria from sexual dysfunctions and paraphilic disorders, so these disorder groups are now in three separate chapters, with the "Gender Dysphoria" chapter preceded by the "Sexual Dysfunctions" chapter and followed by the "Paraphilic Disorders" chapter, which is the last chapter before chapters describing miscellaneous mental disorders, medication-induced conditions (e.g., tardive dyskinesia), and any other conditions that may be a focus of clinical attention.

Introduction of spectra. Another set of changes related to the "spectrum" concept (Cassano et al., 1997; see also Maser & Akiskal, 2002, and the articles that follow in the same issue for a set of papers related to diagnostic spectra). A well-accepted change was the use of the term "schizophrenia spectrum" as a chapter title. This term, in use in the research community for years, reflects the genetic and neurobiological relations among schizophrenia, schizoaffective disorder, and schizotypal PD. Although shared underlying vulnerabilities have also been suggested among the schizophrenia-spectrum disorders, bipolar disorder, and MDD with psychotic features, it was felt that further research was needed before combining these disorders into one chapter. Their relations were instead represented by a contiguous sequencing of the respective chapters.

The autism spectrum was also a frequently used concept by scientific, clinical, and lay groups to describe the group of *DSM-IV* pervasive developmental disorders that included autistic disorder, Rett syndrome, childhood disintegrative disorder, Asperger disorder, and the widely used pervasive developmental disorder not otherwise specified (PDD-NOS). The separation of these various conditions into distinct diagnoses was not well supported by the research literature, which suggested that they represented a single underlying disorder with varying degrees of impairment in the domains of social communication and restrictive, repetitive behaviors (Lord & Jones, 2012). Nonetheless, the proposal to combine these diagnoses formally into a single entity, ASD, with the ability to specify severity of impairment in the two domains, was met with resistance from various parent and patient groups as well as some clinical researchers. Among the concerns raised was that the symptoms presented by some patients might not meet the revised diagnostic criteria, which could cause them to lose access to services. This concern was addressed with a "grandfathering" stipulation that individuals who had received a well-established diagnosis of autistic disorder, Asperger's disorder, or PDD-NOS before the release of *DSM-5* should receive a diagnosis of ASD. To address concerns that individuals with marked deficits in social communication alone would no longer receive a diagnosis of Asperger's disorder, which would grant them eligibility for services, the suggestion was made to evaluate such individuals for social (pragmatic) communication disorder, a new disorder in *DSM-5*. Concerns that the ASD diagnosis would stigmatize relatively high-functioning individuals with a *DSM-IV* diagnosis of Asperger's disorder were considered but ultimately not acted upon, because the clinical and research benefits of recognizing the underlying commonalities of all individuals with ASD across the severity spectrum were predicted to overcome the potential effects of stigma.

Another prominent example of the use of the spectrum concept in *DSM-5* was in the substance use disorders. The work group studying these disorders was confronted with several problems in the long-standing convention of separating abuse and dependence. This separation was based on assumptions that evidence suggested were not true, namely that abuse was both a less severe condition than and a precursor to dependence. Further, the validity of the abuse-dependence distinction was questioned in studies examining the underlying factor structure of the substance use disorders. The work group's review of published evidence and its own secondary data analyses of a diverse group of clinical and epidemiological data sets confirmed that abuse was not necessarily a precursor to dependence. Moreover, results of item-response-theory-based analyses of the data sets showed that symptoms of abuse were not necessarily less severe than those of dependence and

that there was no clear delimitation of the two disorders—in fact, their symptoms were intermixed when listed by increasing severity (Hasin et al., 2013). Therefore, separate substance-abuse and -dependence diagnoses were eliminated in *DSM-5*. Instead, their symptoms were combined into a single list, with one symptom dropped (the abuse-specific symptom of legal problems) and one added (craving). Substantial empirical data indicated that a threshold of two symptoms was sufficient to diagnose the new *DSM-5* disorder, named simply substance use disorder (SUD). The work group held that this unitary disorder could be described usefully across a spectrum of severity, with two to three symptoms (of 11) designated as mild SUD, four to five symptoms as moderate, and six or more as severe SUD.

Elimination of multiaxial diagnosis. *DSM-III* had introduced a multiaxial diagnostic system, which required five distinct assessments for a complete diagnosis. Each axis was designed to provide specific information about an individual's signs and symptoms; psychological, physical, psychosocial, or environmental context; or functioning: Axis I, clinical syndromes; Axis II, PD and "mental retardation"; Axis III, general medical conditions; Axis IV, psychosocial and environmental problems; and Axis V, Global Assessment of Functioning. Eliminating this system reflected both a desire to diagnose psychopathology in a manner consistent with the medical diagnosis of nonmental health conditions, which lacks this multiaxial structure, and a recognition that elements of the multiaxial system had outlived their usefulness. More specifically, Axis II had been created to highlight the importance of PD and what we now call intellectual disability in the overall assessment of patients. In practice, it also was being used by payers to exclude treatment of PD from reimbursement, presumably because disorders placed on Axis II were interpreted as less severe than the "major" mental disorders on Axis I. The increase of knowledge about both groups of Axis II disorders, treatment development, and the formation of advocacy groups for patients with these disorders also contributed to the lessening need for their segregation on a separate axis.

Regarding Axis III, which was designed to document general medical conditions relevant to understanding or managing individuals' mental disorders, users of *DSM-5* are advised simply to list them as such. Axis IV was viewed as a useful teaching tool but was seldom used in practice, at least by psychiatrists (Probst, 2014), and had limited reliability. In *DSM-5*, the chapter "Other Conditions That May Be a Focus of Clinical Attention" lists, describes, and provides codes for relevant psychosocial and environmental factors. They are to be included in the medical record if they are a reason for the current visit; help to explain the need for a test, procedure, or treatment; or provide information about circumstances that may affect patient care. Finally, Axis V's Global Assessment of Functioning was problematic for several reasons, especially inadequate interrater reliability and the ambiguity of scores due to the assessment's confounding of disability with symptom severity.

Attention to developmental, gender-related, and cultural aspects of disorder. *DSM-5* greatly increased the emphasis on the developmental, gender-related, and cultural aspects of diagnostic criteria and textual descriptions of individual disorders (Alarcón et al., 2002; Narrow, First, Sirovatka, & Regier, 2007). *DSM-III* and *DSM-III-R* included only brief reports of age of onset and sex ratio for many disorders. For most disorders, *DSM-IV* added a separate section on "Specific Culture, Age, and Gender Features" that contained information on how disorder onset, prevalence, and symptom presentations change over the course of development and vary depending on cultural characteristics and gender. *DSM-5* expanded this focus, creating three new sections on "Development and Course," "Culture-Related Diagnostic Issues," and "Gender-Related Diagnostic Issues" for nearly every disorder. Each section provided a summary of research findings that would help guide the diagnostic process, such as how individuals with anorexia nervosa may present without an associated fear of weight gain in certain cultural contexts, particularly in Asia (Becker, Thomas, & Pike, 2009), or that females with attention-deficit/hyperactivity disorder (ADHD) are more likely than males to present primarily with inattentive features (Biederman et al., 1999).

In a few cases, developmental considerations led to the stipulation of distinct criteria for younger age groups, such as simplified PTSD criteria for children 6 years old and younger (Scheeringa, Zeanah, & Cohen, 2011), differences in the required number of ADHD criteria for younger children versus older adolescents and adults (Wakschlag, Leventhal, Thomas, & Pine, 2007), or differences in how long the symptoms of separation anxiety disorder were required to be present. In essence, the continuity between youth and adult forms of psychopathology was expressed by describing two versions of the disorder in a single category. Finally, as in *ICD-11*, disorder groupings were ordered in *DSM-5* so as to correspond logically to developmental psychopathology. For example, neurodevelopmental disorders that manifest early in life were placed first, and neurocognitive disorders that are most relevant in later life were placed near the end.

This greater focus on developmental, gender-related, and cultural aspects of diagnosis was intended to highlight how an individual's specific symptom presentation is

partly related to a set of contextual factors. It was hoped that this information would counter the reification that often accompanies diagnostic practice and that suggests erroneously that disorders exist as independent entities irrespective of social and life-span considerations.

Section III. Emerging measures and models. Each iteration of DSM has a different organization, and *DSM-5* parted notably from its predecessors by introducing a hierarchical structure. Following its introductory material, *DSM-5* was divided into three sections plus an appendix, each of which was composed of multiple chapters. Sections I, II, and the appendix each had counterparts in previous DSMs (e.g., chapters in the main Section II contained the diagnostic criteria, codes, and accompanying text). In contrast, Section III is entirely new in *DSM-5* and contains several innovations intended to aid clinical decision making, increase sensitivity to the cultural context of mental disorder, introduce a dimensional approach to PD diagnosis, and propose criteria for a number of clinical conditions for which there were insufficient data for inclusion as "official" diagnoses in Section II.

Assessment measures. The WHO Disability Assessment Schedule 2.0 was recommended by the *DSM-5* Task Force as an alternative to the Global Assessment of Functioning, but it was not approved by the APA Board of Trustees, pending further data on its utility in improving patient care and outcomes. Likewise, the APA Board of Trustees did not approve the many patient-reported dimensional assessment measures that the *DSM-5* Task Force recommended for clinical use. Specifically, a number of cross-cutting symptom measures with follow-up questions to probe domains that screening identified as relevant were compiled to provide a comprehensive overview of commonly seen psychiatric symptoms that could guide psychiatric assessment and treatment, and highlight potentially overlooked problems. For many disorders, diagnostic severity measures that focus on syndromes and were designed primarily for administration after a diagnosis had been made also were recommended. Both of these types of measures are discussed in a later section. It is notable that *DSM-5* does not include a quality-of-life measure, which may be considered an oversight due to the relatively low level of patient involvement in the overall *DSM-5* development process. Future testing of the *DSM-5*'s assessment measures should involve patients and their families to ensure that the measures are comprehensive and include domains that are important to them and not just to clinicians. If the published measures are found to be lacking in this regard, they should be supplemented.

Another assessment measure in Section III is the Cultural Formulation Interview (CFI; Lewis-Fernández, Aggarwal, Hinton, Hinton, & Kirmayer, 2016). The CFI converts the *DSM-IV* Outline for Cultural Formulation (OCF) into a set of standard questions and explicit instructions that can be used easily by busy clinicians. The main goal of the OCF in *DSM-IV* was to help clinicians identify how culture and context affect patients in ways that are relevant to diagnosis and treatment (Mezzich, Caracci, Fabrega, & Kirmayer, 2009). The CFI operationalizes the OCF framework as three sets of semistructured questionnaires: a core 16-item interview that can be used during a routine initial evaluation with any patient by any clinician in any setting; the CFI–Informant version of the assessment, which is used to gather information from close associates of the patient (e.g., family members); and 12 supplementary modules that expand on these basic assessments if a comprehensive cultural assessment is needed (these supplementary modules are available through the APA Web site at http://www.psychiatry.org/psychiatrists/practice/dsm/dsm-5/online-assessment-measures). The core interview aims to enhance the person-centeredness of an evaluation by grounding it from the outset in the patient's own experience of illness (Lewis-Fernández & Aggarwal, 2013).

The CFI was included in *DSM-5* because culture affects every aspect of clinical care, including patients' and families' concepts of illness, the patterning of symptoms, help-seeking choices and treatment expectations, and even the models that clinicians use to interpret and understand symptoms in terms of psychiatric diagnoses (Lewis-Fernández et al., 2016). All individuals, not only nondominant groups such as racial/ethnic minorities, are influenced by their cultural backgrounds and people draw upon different aspects of their backgrounds at different times. To emphasize these issues and help guide implementation of the CFI, "culture" was defined in the instructions in a way that would apply to all people—as "the values, orientations, knowledge, and practices that individuals derive from membership in diverse social groups," "aspects of the person's background that may affect his or her perspective," and "the influence of family, friends, and other community members" (APA, 2013, p. 750). The CFI was included in Section III to help clinicians include basic information on the social context of individuals and their networks in diagnostic assessments, thereby helping to reduce misdiagnosis, to calibrate the assessment of severity, and to facilitate patients' engagement in treatment (Adeponle, Thombs, Groleau, Jarvis, & Kirmayer, 2012; Aggarwal, Nicasio, DeSilva, Boiler, & Lewis-Fernández, 2015).

Alternative *DSM-5* model for personality disorders. The APA Board of Trustees retained the *DSM-IV*

system for personality diagnosis in the main Section II and placed the Alternative *DSM-5* Model for Personality Disorders (AMPD) developed by the Personality and PD Work Group in Section III "to preserve continuity with current clinical practice, while also introducing a new approach that aims to address numerous shortcomings of the current approach" (APA, 2013, p. 761). The two main criteria of the AMPD are "impairments in personality *functioning* and pathological personality *traits*" (APA, 2013, p. 761; emphasis in original). The first criterion represents the core dysfunction of PD and consists of impairment in self-functioning (defined as problems in identity, self-direction, or both) or in interpersonal functioning (defined as problems in empathy, intimacy, or both). The second criterion describes the way in which personality impairment is expressed, operationalized as any one or more of 25 specific traits (e.g., submissiveness, manipulativeness) or the five broad domains in which they are organized: negative affectivity, detachment, antagonism, disinhibition, and psychoticism. Both personality functioning and traits are dimensional, and the model provides guidelines to help clinicians and researchers determine whether a given criterion is above threshold for impairment, in the case of functioning, or pathology, in the case of traits.

In addition, the AMPD describes six specific PD types (of the 10 in Section II, the main section of *DSM-5*) —antisocial, avoidant, borderline, narcissistic, obsessive-compulsive, and schizotypal—using particularized versions of the four subareas of personality impairment (i.e., identity, self-direction, empathy, and intimacy) and specific sets of traits. For example, the avoidant PD type is characterized by anxiousness and at least two of three other specific traits: withdrawal, anhedonia, and intimacy avoidance. These six PDs were chosen for inclusion because each had a considerable empirical and clinical literature, whereas the other four did not. Moreover, the remaining PDs (paranoid, schizoid, histrionic, and dependent) could be characterized very simply using one or two of the AMPD's specific traits. For example, submissiveness and insecure attachment together form dependent PD.

The AMPD also includes a "PD-trait specified" diagnosis, which the text states can be used "when a personality disorder is considered present, but the criteria for a specific disorder are not" (APA, 2013, p. 761). It also has the potential to describe any combination of personality impairment and pathological traits (even when the criteria for a specific disorder are met), and preliminary evidence suggests that an expanded definition of "PD-trait specified" would provide both comparable coverage of the PD domain and greater specificity and flexibility in describing individuals' personality pathology (L. A. Clark et al., 2015), as well as eliminate within-PD comorbidity by allowing for a single diagnosis, albeit one with myriad trait manifestations.

The AMPD is broadly congruent with what is proposed for PD diagnosis in *ICD-11*, as described further in a later section, "Categories and Dimensions."

Conditions for further study. The final chapter in Section III contains criterion sets and supporting text for eight syndromes, disorders, or conditions that were proposed for *DSM-5* but judged by the Task Force to have insufficient empirical evidence to warrant their inclusion in the main Section II (e.g., attenuated psychosis syndrome, internet gaming disorder, and nonsuicidal self-injury). They were included in Section III to facilitate research that will provide data for their consideration in a future DSM version.

Basic similarities and differences of ICD-11 *and* DSM-5

Structural similarities. Of the various criticisms of *DSM-IV* that were considered by *DSM-5*'s developers, virtually all apply to *ICD-10* and are being considered in *ICD-11*'s development as well. *ICD-11*'s developers have had the advantage of being able to consider both the initial *DSM-5* proposals and its final published version, as well as the evidence used to support changes from *DSM-IV* to *DSM-5*. As with the *DSM-5*, the development of *ICD-11* has involved a model of working groups, but these groups were required to be globally representative and multidisciplinary and typically included one or more members from parallel *DSM-5* work group to facilitate harmonization of the proposals. Therefore, in many instances, changes proposed for *ICD-11* have been similar to those made in *DSM-5*.

The overall architecture of *DSM-5* and the proposed "Mental, Behavioural, and Neurodevelopmental Disorders" chapter of *ICD-11*—that is, the broad groupings they contain and the order of those groupings—were the subject of a series of meetings between representatives of APA and WHO; the documents' similarity is a tangible result of these harmonization efforts. For example, the new *DSM-5* groupings of "Obsessive-Compulsive and Related Disorders" and "Disorders Specifically Associated with Stress" (in *ICD-11*) or "Trauma- and Stressor-Related Disorders" (in *DSM-5*) are part of a broader grouping in *ICD-10* that includes anxiety disorders. Some proposed *ICD-11* groupings have names slightly different from those of their *DSM-5* counterparts, but they are conceptually similar. Further, the integration of forms of disorders that are seen as continuous across youth and adult psychopathology has been accomplished in both classifications. Diagnostic-hierarchy requirements were eliminated in a previous version of the *DSM* and have been eliminated in the proposed *ICD-11*, although in a few specific instances, disorders that should not be simultaneously diagnosed are explicitly noted. Conversely, ICD has never had a multiaxial system, so this change in *DSM-5* made it more similar to *ICD-11*.

In some cases, the combination of substantive structural changes from *ICD-10* to *ICD-11* and related changes from *DSM-IV* to *DSM-5* increased the similarity between the manuals. For example, the *ICD-10* classification of sleep disorders reflects an inaccurate mind-body dualism: Ostensibly "nonorganic" sleep disorders were in the chapter on "Mental and Behavioural Disorders," whereas ostensibly "organic" sleep disorders were included in such chapters as "Diseases of the Nervous System" or "Diseases of the Respiratory System." In contrast, a new and separate chapter has been proposed for *ICD-11* that includes all sleep-wake disorders. Likewise, sexual dysfunctions that were divided in *ICD-10* into "nonorganic" and "organic" forms are combined in a new *ICD-11* chapter called "Conditions Related to Sexual Health." Parallel changes in *DSM-5*—the elimination of *DSM-IV*'s primary/secondary and organic/nonorganic distinctions in both of these disorder groups—were less obvious but effectively rendered the two manuals more similar.

Structural differences. *ICD-10*'s gender identity disorders have been substantially reformulated, renamed "gender incongruence" (Reed et al., 2016), and moved out of the mental disorders chapter.[8] The *ICD-11* Working Group deemed this a substantial improvement over the current classification of categories related to transgender identity as mental disorders. Impulse control disorders and disruptive behaviour and dissocial disorders are grouped in their own separate chapters in *ICD-11* but are combined in *DSM-5*. PDs are placed earlier in the proposed *ICD-11* classification structure than in *DSM-5* (where they are one of the last chapters) to reflect their more developmental sequence. Finally, mental and behavioral syndromes due to particular types of diseases or disorders are organized differently in *ICD-11* than in *DSM-5* because of differences in the way that the two classifications handle primary and secondary disorders.

Several categories have been recommended for inclusion in the *ICD-11* that were considered but not included in the *DSM-5*, such as olfactory reference disorder (Stein et al., 2016), complex PTSD, and prolonged grief disorder (Maercker et al., 2013). Conversely, *DSM-5* contains several categories that have not been recommended for inclusion in *ICD-11*, such as disruptive mood dysregulation disorder (Evans et al., 2017). *ICD-11* has retained *ICD-10*'s separate categories for harmful use of substances and substance dependence in order to reflect the public-health importance of harmful use, particularly for population-based prevention programs and early clinical interventions, such as in primary-care settings (Poznyak, Reed, & Clark, 2011).

Shared unintended consequences of classifying mental disorder. The origins of ICD and DSM as public-health-focused classification systems account for some of the characteristics that have contributed to subsequent problems in classifying mental disorders. We discuss these problems more fully in our four main topic sections, but it is fitting to describe the characteristics themselves here, in the context of the systems' descriptions. Specifically, a main characteristic of both ICD and DSM is that they are classic hierarchical categorical systems, such as Carl Linnaeus's biological classification set forth almost 3 centuries ago.[9] Hierarchical categorical classification systems are exhaustive, their elements are mutually exclusive, and lower levels of the structure are related systematically to specific higher levels. Every entity is distinct, must be classified in one and only one place in the system, and is more closely related to its near-neighbor entities than to those in more distant "branches." The ICD and DSM systems are intended to have these qualities but, importantly, as applied to diseases, disorders, or health conditions—that is, unlike the biological classification of living beings, these systems categorize not people with disorders but rather the disorders that people may develop. (In ICD, these disorders include all health conditions, whereas DSM is confined to mental disorders.)

Several characteristics of both ICD and DSM that stem largely from these structural requirements have received criticism. First, disorders can be represented in one and only one place, but the basis for assigning certain disorders to particular places in either system is arbitrary and not fully consistent with all available evidence. For example, in both systems, major depression and GAD are classified in different places, even though they are highly comorbid and the genetic contribution to these disorders is essentially identical (Kendler, 1996, p. 68). Both *DSM-5* and *ICD-11* modified this structural requirement and cross-listed a few disorders so that the systems would better reflect the complexity of mental-disorder diagnosis. For example, *DSM-5* placed schizotypal PD and antisocial PD with the other PDs; moreover, it also placed schizotypal PD with other schizophrenia-spectrum disorders and antisocial PD with its required childhood precursor, conduct disorder. Similarly, *ICD-11* classified Tourette syndrome both in the chapter "Diseases of the Nervous System," with other tic disorders, and with the "Obsessive-Compulsive and Related Disorders," because of comorbidity and shared familiality.

Second, categorical systems are ideal when the entities being classified are taxa (i.e., unique, nonoverlapping kinds), which, for the most part, mental disorders clearly are not (Haslam, Holland, & Kuppens, 2012). Such systems can classify dimension-based entities only by imposing cut points, which may be relatively arbitrary. This is not particularly problematic in the case of "simple" health conditions that are based on one or two dimensions, such as obesity or blood pressure, because

it is easy to understand, for example, that a person with a body mass index (BMI) of 29.9 will be classified as "overweight" and one with a BMI of 30.0 will be classified as "obese" for practical reasons, not because these two BMIs are fundamentally distinct. However, classifying nontaxonic, multidimensional phenomena such as mental disorders, which can overlap in myriad ways, is not straightforward.

Third, because each disorder must be classified in one and only one place, there is a tendency to make each entity as distinct as possible, resulting in highly—indeed, overly—specified categories. This issue is manifested in several ways, each of which has associated problems that are among the core criticisms of ICD and DSM. For example, major depression can present with marked anxiety, psychotic features, or both, so to keep these three disorder presentations distinct, a comprehensive categorical system must do one or more of the following:

1. Specify exclusion rules (e.g., exclude a diagnosis of GAD if a person meets the criteria for major depression); this choice comes at the expense of incompletely capturing the clinical picture of many individuals.
2. Create either specified intermediate categories (e.g., "mixed anxiety–depressive disorder" and "schizoaffective disorder") or use disorder specifiers (e.g., "major depression with psychotic features"). This tactic is problematic because such disorders also have to be classified in one and only one place, but placement near one disorder imposes a distance from the other, violating the hierarchical organizational principle according to which entities should be closely related to their near neighbors but not to those in more distant "branches" of the system. For instance, schizoaffective disorder is placed with schizophrenia-spectrum disorders, so it cannot also be placed with mood disorders; conversely, major depression with psychotic features is placed with the mood disorders, so it cannot placed with other psychotic disorders. This approach also results in the proliferation of diagnostic categories, because every important overlap between dimensions then requires the creation of specific diagnostic label.
3. Define disorders' criteria specifically but permit multiple comorbidities (i.e., allow a person to meet the criteria for major depression, an anxiety disorder, and a psychotic disorder). Resulting diagnoses may misleadingly suggest that the individual has three disorders rather than a single, complex mental disorder. We discuss these issues further in our sections on "Multidimensionality" and "Comorbidity."
4. Define disorders overly specifically, with the result that many individuals' conditions fall into "wastebasket" categories, such as "other depressive episodes" (*ICD-10*), "depressive disorder, unspecified" (*ICD-10* and *ICD-11*), "depressive disorder, NOS" (*DSM-IV*), or "other specified depressive disorder" (*DSM-5*). Research literature reviews and meta-analyses have shown that in some domains of psychopathology, a greater percentage of individuals are more accurately characterized as having these types of diagnoses than meet the criteria for any specific disorder in the domain (e.g., Thomas, Vartanian, & Brownell, 2009, for eating disorder; Verheul & Widiger, 2004, for PD).

In addition to these various problems, an overarching unintended consequence of overspecification is that it contributes to the reification of disorders. That is, when disorders are highly specified, a natural assumption is that there is an empirical basis for the precision with which they are defined, so they come to be regarded as representing real and distinct natural phenomena. In turn, thinking about mental disorder in this way obscures the arbitrary nature of and lack of scientific evidence for many distinctions among categories or between disorder and health, as well as inhibits inquiry into their interrelationships and common substrates.

In summary, despite the many changes and improvements in *ICD-11* and *DSM-5* from their predecessors and the various differences between them, they both remain categorical classification systems that are fundamentally descriptive in nature, based primarily on self-reported symptoms, clinically observed signs, and a few tests (e.g., of intellectual functioning). In contrast, the perspective adopted by NIMH for its RDoC project, to which we turn next, diverges markedly from the conventions developed by ICD and DSM.

NIMH's RDoC project

Context and background of the RDoC project. As discussed, the *DSM-5* developers' hope for a more neuroscience-based manual was quickly dashed by the facts that research findings indicated that biological factors not only cut across multiple disorders but also varied within disorders (Hyman, 2007) and there was insufficient research to support an alternative, empirically based organization. In no small part this was because, since the early 1980s, NIMH and other funding agencies had virtually mandated the use of DSM or ICD diagnostic categories. Thus, although the criterion-based approach of

DSM-III and *ICD-9* led to voluminous research and important scientific advances that ultimately made RDoC's alternative approach possible, this very research also showed that the two classifications' methods and overreliance on narrow, symptom-based categories ran counter to the study of mental disorder with full consideration of its multiple interacting etiologies (L. A. Clark & Watson, 1991; Hyman, 2010; Kapur, Phillips, & Insel, 2012; Owen, 2014; Sharma, Markon, & Clark, 2014).

The RDoC project was initiated in early 2009 in response to this changing landscape, including feedback received in late 2008 from researchers in the field as NIMH prepared its new strategic plan. An experimental approach was deemed necessary, given the still-nascent state of the science of mental disorder and the conceptual and empirical constraints of research based on current classifications. It was apparent that if developments in basic and translational science were to be applied to the science of mental disorder, a long-term approach would be needed. Such an approach would need to examine psychopathology with reference to behavioral and brain mechanisms rather than in terms of existing disorder categories. It was not that decades (or, indeed, centuries) of clinical observation and research should be discarded wholesale, but rather that an alternative research framework was needed to understand more fully the basic mechanisms that are disrupted in mental disorders.

The RDoC project thus was developed to respond to both of the difficulties that the groups revising *DSM-5* encountered: the hitherto predominant reliance on the DSM and ICD diagnostic categories to guide research on the causes and mechanisms of disorder, and the lack of a clear alternative in the face of the failure of this research to support existing diagnostic systems. Accordingly, RDoC differs from the DSM and ICD in two important ways. First, it is based upon a fundamentally different approach to dimensionality, one more in line with *DSM-5*'s AMPD than with current diagnostic procedures; the bulk of this section elaborates RDoC's dimensional approach. Second, the RDoC project was not intended for practical clinical use in the near future. Rather, it provides a framework for research. It does not formally incorporate any current ICD or DSM disorders and, in fact, does not define mental disorder or any specific disorders. It was thought that such a radical departure was needed to create a research framework that could address the problems discussed above in trying to understand, diagnose, and treat mental disorder.

It is important to contextualize the RDoC project not only within the "political" domain of institutional taxonomies but also in response to prior and ongoing intellectual advances, particularly those in developmental psychopathology. Many behavioral and psychological problems in children and adolescents reflect early stages in the development of later psychopathology, yet there is reluctance to label still-maturing individuals as having a mental disorder. Taken together, these points may explain why reification of mental disorder in younger age groups (as opposed to in adults) developed more slowly and less strongly. Accordingly, the work of developmental psychopathologists was a rich intellectual source for many aspects of the RDoC project. For example, as early as the mid-1960s, Achenbach (1966) had proposed that psychopathology has a hierarchical structure; moreover, such concepts as equifinality (the idea that diverse developmental pathways can lead to the same or similar outcomes) and multifinality (the idea that a given risk factor may result in different outcomes depending on the environment) had been used for several decades to understand the development of psychopathology as an outcome of person-environment interactions (e.g., Cicchetti & Rogosch, 1996; Sroufe & Rutter, 1984).

What is new about RDoC is the idea that to understand mental illness in all its complexity, the field needs a research framework that accommodates the study of all causal factors together. Although it is of course impossible to incorporate all factors in any given study, what the RDoC project hopes to do is break researchers away from studying a few relevant factors in isolation—that is, without consideration of how they fit together with all the other relevant factors. Similarly, given the work of developmental psychopathologists, by the time the RDoC project was being designed, almost all mental illness had come to be regarded as neurodevelopmental—as being affected by, and also affecting, neural structures and processes throughout development. The RDoC perspective, therefore, is that it is vital to incorporate a neurodevelopmental aspect in research programs, and yet the problems delineated above (e.g., overspecification and comorbidity) indicate that current disorder criteria miss or insufficiently reflect fundamental mechanisms that are important in the development and maintenance of mental illness. Until recently, it was difficult to investigate what these mechanisms might be. Now, new methods in neuroimaging, behavioral neuroscience, psychometric analyses of behavior, and for examining the effects of various events and social contexts upon behavior and the brain are transforming our understanding of normal and abnormal functioning.

These considerations provide important contexts for the RDoC project, which shares with DSM and ICD the quest for optimal classification—identifying the appropriate groupings and/or dimensions for study and, ultimately, for treatment. However, rather than continuing the research tradition of seeking deeper understanding of the mental disorders in our current classification systems, the RDoC project is intended to provide a

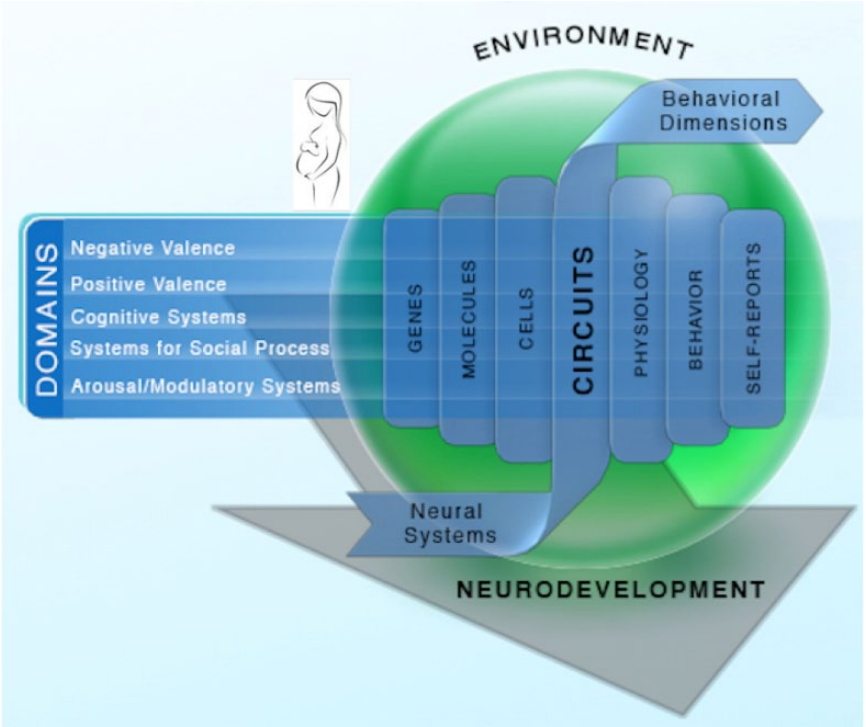

Fig. 1. The framework of the National Institutes of Mental Health's Research Domain Criteria. This figure depicts the five-by-seven RDoC matrix and its environmental and neurodevelopmental contexts.

research framework that will deepen our understanding of the neurological, biological, psychological, social, and cultural structures and processes that underlie mental illness broadly speaking. In turn, this information can guide the evolution of the classification of mental illness into more valid groupings and dimensions, much as Linnaeus's two-kingdom system of plants and animals has evolved into a six-kingdom system. The hope is that this approach also will facilitate development of improved methods for preventing and treating mental illness. Rather than a wholesale overturn of current diagnostic systems, RDoC is intended to provide an alternative perspective that eventually will inform the field as to which aspects of current approaches should be retained or minimally modified, and which should be replaced or greatly revised. Importantly, the current RDoC scheme is considered "Version 1.0" and is explicitly intended to evolve as research progresses.

The RDoC framework is intended to facilitate the study of brain-behavior relations across developmental and environmental contexts. In recent decades, research has increasingly specified major functional aspects of behavior and mental operations—fear, executive functioning, and social attachment—and the neural systems that implement them. Given this trend, a research framework with a dual emphasis on brain and behavior seemed the most promising point of departure for an experimental program. However, there is no claim that the RDoC framework has "got it right." Both the specific aspects of a neural-circuit-based framework and its overall organizational scheme are likely to change—perhaps dramatically—as research in this new direction accumulates.

RDoC's four major components. The RDoC research framework, depicted in Figure 1, has four major components intended to provide guidance for clinical research. Two components—neurodevelopmental and environmental factors—provide the broad context for the framework as a whole. The other two—functional domains and their units of analysis—form the "RDoC matrix," which is situated in the context of the neurodevelopmental and environmental components. Although RDoC's contextual components have not received as much attention as its matrix, they are essential aspects to consider in programs of research. That is neurodevelopment's inclusion in the research framework does not mean that every study must include a longitudinal component, but investigators are encouraged to address potential antecedent or consequent aspects of development and to relate their results to these associated data. In turn, environmental factors are intended to encompass the totality of external

influences—both the effects of the broader environmental context, such as culture, family, class, and other social groupings and hierarchies, and also the effects of particular events, such as accidents and traumatic experiences. Environment also interacts significantly with neurodevelopmental processes, and its effects may differ by the age at which events occur or milieus are experienced. Thus, these two components constitute the broad—and indispensable—contexts that must be considered in studying one or more aspects of behavior.

Within this essential context, RDoC calls for studying psychopathology with respect to basic functional dimensions, organized into five major domains. For example, in the domain of "negative valence systems," dimensions such as the fear system perform the biological function of enabling the organism to respond to aversive or threatening stimuli and contexts. These functional dimensions are conceived in terms of the continuous span of functioning from the normal, adaptive range to increasing degrees of abnormality in each system (e.g., mild fear to full-blown panic). They are assessed by measurements taken across several units of analysis, which range from measures of genetics and neural-circuit activation to measures of overt behavior and self-report assessments. The goal of studying these various units of analysis is not to explain behavior or cognitive activity in terms of molecular or cellular processes (i.e., reductionism), but rather to understand more thoroughly the relations among the different activities of various systems. The five domains and their seven units of analysis, which together form the RDoC matrix, are currently the most fully articulated aspects of the RDoC project, but it is important to remember that the matrix must be considered within the essential frame of the neurodevelopmental-environmental context.

RDoC-based research projects that are focused on further articulating the matrix explore psychopathology through the study of one or more functional dimensions, which are hypothesized to be related to specific kinds of symptoms that typically cut across two or more ICD or DSM disorders. For example, anxiety symptoms are hypothesized to be related to impairment in the dimension that has the function of responding to potential threat, whereas impaired social functioning and problems with concentration are hypothesized to be related to functional dimensions in the domains of, respectively, social processes and cognitive systems. Because cross-cutting symptoms such as anxiety, impaired social functioning, and concentration problems appear to be a major reason for much of the comorbidity that is particularly problematic in research studies, RDoC is agnostic to current diagnostic categories. RDoC's vision for the matrix is to generate a research literature regarding relations among physiological, behavioral, cognitive, and symptomatic measures that can inform future versions of ICD and DSM, with a particular potential to incorporate biological and/or psychometrically advanced measures of behavior and cognition into a precise diagnostic assessment that points to more tailored treatments. Again, however, we must not lose sight of the fact that this research literature will be incomplete until it is understood in its neurodevelopmental-environmental context.

The RDoC matrix. The way in which the four major RDoC components just described are developed relates to RDoC's role as a framework for research. The five major domains of functioning comprise the "rows" of the two-dimensional RDoC matrix:

1. Negative valence: systems that enable response to aversive stimuli or contexts (e.g., threat, loss, aggression due to frustration);
2. Positive valence: systems that mediate reward-related activity (e.g., approach motivation, reward responsiveness);
3. Cognitive systems, such as attention, perception, and memory;
4. Social processes, such as affiliation and attachment, facial expressions and other social communication, and perception and understanding of the self and others; and
5. Arousal and modulatory systems, such as circadian rhythms, sleep-wakefulness, and brain-stem activation and arousal systems.

Each of these five domains contains three to six specific dimensions, termed *constructs* (the customary term in psychology for a functional element of behavior or cognition). For instance, the cognitive-systems domain contains constructs for attention, perception (visual, auditory, etc.), working memory (the short-term storage of relevant information—e.g., remembering a phone number long enough to dial it), declarative memory (memory for general and personal facts and events), language behavior, and cognitive control (the ability to focus on goals and to inhibit unwanted behavior).

The constructs are the heart of the RDoC system, and each was defined in a series of workshops (one per domain) by subject-matter experts using three criteria: first, evidence for the validity of the construct as an affective, behavioral, and/or cognitive dimension; second, an implementing neural system or circuit; and third, a presumed relation to one or more specific symptoms or other aspects of psychopathology. For instance, fear is a classic psychological construct that

has been measured in many ways (e.g., with self-reports, observations of behavior, and physiological assessments); has a neural circuit that has been well delineated over the past 30 years, involving (at a minimum) a potential-threat-recognition signal, a memory component, and an interpretation of the signal's meaning, which originate in the amygdala, hippocampus, and cortex, respectively (e.g., LeDoux & Pine, 2016); and is clearly important for fear-relevant behavior in many anxiety and posttraumatic disorders (Lang, Davis, & Öhman, 2000).

The units of analysis represented by the seven columns of the RDoC matrix denote measures of genes, molecules, cells, neural-circuit activity, physiology (e.g., heart rate or cortisol level), behavior (quantitative ratings of either spontaneous behavior or behavior in laboratory tasks), and self-reports (including clinician-rated interviews). The aim is that experimental studies will use measures from several of these columns to study the constructs in an integrative way, relating the measurements to each other to achieve a more in-depth understanding of the particular dimensions being studied. In addition, there is an eighth column termed "paradigms" (not shown in the figure) to reflect the fact that many measures in the other columns are gathered in the context of particular tasks or self-report assessment instruments.

As mentioned, the constructs and units of analysis are to be examined within the critical frame of neurodevelopment and environment influences, both of which interact with the constructs and the units of analysis. The overall intent of RDoC is to increase attention to neurodevelopmental and environmental effects and to free investigators from having to use descriptively oriented ICD/DSM categories, encouraging them instead to focus on basic mechanisms that are more relevant to etiology. However, the RDoC matrix does not explicitly delineate specific elements for the neurodevelopmental and environmental components in the way that the domains/constructs and the units of analysis are specified. Although this was intended to provide investigators with maximum flexibility in creating research designs that pursue the particular questions of their research, the lack of specification has been interpreted by many researchers as indicating less NIMH interest in these components; accordingly, NIMH is considering providing guidelines that may prove useful to investigators and that will rectify the false impression that the contextual components may be ignored.

Basic differences between RDoC and the* ICD-11 *and* DSM-5 *frameworks. It is important to examine differences between RDoC and current approaches to mental-disorder classification, as well as the implications of shifting to an alternative framework. First, in *ICD-11* and *DSM-5*, mental disorders are characterized primarily by a description of current symptoms and associated features, such as age of onset, duration, and course. In contrast, as an experimental framework that is intended to generate new research hypotheses and data, RDoC is not bound by the need to produce a clinically usable document. Rather, it can temporarily set aside the premises of the classical approach to diagnosis to try to address the limitations of this approach for mental illness that research has revealed. In essence, RDoC inverts the usual paradigm for understanding mental illness. Its emphasis starts with elucidating basic dimensions of behavior and cognitive/affective processing together with the neural systems that play a major role in implementing them, and then considers psychopathology in terms of abnormalities of various degrees in these systems.

The goal is not to explain current syndromes in terms of these dimensions; rather, it is to characterize the kinds of symptoms or disabilities that result from abnormality in a given dimension or interacting set of dimensions, such as the effects of fear upon cognitive processes, in their neurodevelopmental and environmental contexts. The approach is fully and explicitly dimensional—not simply across the severity range of a diagnosed disorder but across the entire span of normal to abnormal functioning. This approach is currently recognized in the diagnosis of some domains of mental disorder, such as intellectual functioning and PD, and the cross-cutting symptom assessments in *DSM-5*'s Section III, but not in most others.

Second, although DSM and ICD still use a classical approach, clinicians and researchers today do tend to accept that the causes of mental disorder are multifactorial in nature, and yet etiological considerations are typically not a major focus in either diagnosis or treatment formulation. In contrast, RDoC is specifically focused on etiology: A major goal of RDoC is to foster research that elaborates the complex interactions among genetic vulnerability, perturbations in neurodevelopment, and bidirectional influences with various facets of the environment (broadly conceived), the effects of which also depend upon the time or times at which they occur. Similarly, RDoC encourages investigators to acquire data across multiple units of analysis (biological, cognitive-behavioral, self-reported) and to examine the results in a multivariate way (e.g., with computational modeling; Marquand, Rezek, Buitelaar, & Beckmann, 2016). The aim is to develop an integrated understanding of causal and other relations among neural systems, psychological operations, and relevant symptoms or impaired functioning. The long-term goal is not to pursue a reductionist model that explains all phenomena in terms of neural activity but rather to

arrive eventually at a more sophisticated account of how symptoms of psychopathology relate to quantifiable measures in other domains.

Finally, although—to their developers' credit—*ICD-11* and *DSM-5* have begun to include information concerning developmental and environmental factors, these are ancillary to their main purpose, whereas RDoC explicitly encourages theoretical models that include neurodevelopmental and environmental components. From an RDoC perspective, the first aim is to develop a comprehensive literature about the convergent and interacting roles of neurodevelopment and the environment as well as their relations with biological, psychological, and social variables in the onset and course of impairment in various functional domains. At that point, we will be in a stronger empirical position to discuss more abstract questions such as how best to define mental illness and to classify mental disorder. Thus, for the present, the RDoC approach sets aside issues related to definition and classification, as well as how best to describe patients' current status in the context of their development and past and current environments. It is anticipated that RDoC will be able to offer relevant data to address these issues as it accrues information that can guide and be incorporated into future iterations of ICD and DSM.

Four Key Issues in Considering Classifications of Mental Disorder

We turn now to discussion of the four key issues we described briefly in the beginning of this article. For each issue, we start with a general introduction and then discuss how each of the three systems—*ICD-11, DSM-5*, and RDoC—addresses the topic.

Etiology

It is now well established that mental disorder has diverse causal factors. Individuals' genetic composition plays a role that varies by the type of psychopathology—for example, the cluster of conditions collectively called schizophrenia has a substantial genetic loading (Light et al., 2014; Tsuang, Glatt, & Faraone, 2003), whereas the heritability of much psychopathology that is grounded in emotion, such as unipolar depression and GAD, is considerably lower (Rutter, 2002). Life history is also very important. Even genetically identical twins may not be concordant for a given mental disorder because of differences in, for example, life stressors (Pitman et al., 2012). The timing and circumstances of life events also matter: Losing a parent is a key risk factor for depression when the loss occurs at an early age (Bifulco, Harris, & Brown, 1992; G. W. Brown, Harris, & Copeland, 1977), but not when it occurs later in life.

Individuals' social position often plays a substantial role by aiding or hindering their access to key goods and services, including health-promoting resources, or, conversely, channeling individuals toward illness-producing life circumstances (Metzl & Hansen, 2014). MDD, for example, is much more common among people of lower socioeconomic status (Lorant et al., 2003), and changes in socioeconomic status can prompt changes in depression (Lorant et al., 2007). Moreover, changes in social position can have serious consequences related to mental disorder. For example, although overall mortality rates in affluent countries worldwide fell from 2000 to 2015, those of less-educated, middle-aged non-Hispanic Whites in the United States increased, primarily because of increases in drug- and alcohol-related problems and in suicides (Case & Deaton, 2015). The authors hypothesized that the observed increases were related to economic insecurity among members of this demographic group in the context of rising income inequality in the United States. Finally, the meaning of events and expectations of mental illness within a culture also influence the risk and form of psychopathology (Kleinman, 1977). Among Tibetan refugees, for example, having experienced torture was no more likely to be associated with mental illness than witnessing the intentional destruction of religious symbols (Sachs, Rosenfeld, Lhewa, Rasmussen, & Keller, 2008).

The multicausality of mental illness means that disorders do not have a single origin. As a general principle, for example, genetics has no more causal primacy than people's experiences or the totality of their environments. Rather, those who suffer from mental illness are at the nexus of multiple forces—contributions not only from their biology and personal life history but also from factors that transcend them as individuals, such as social structures and cultural systems. The influence of these various forces on individuals' health and well-being is constantly in flux, given that individuals, families, and societies not only "inherit" them, both biologically and socioculturally, but also reconfigure and recreate them in different ways throughout their lives.

Biologically, even at the molecular level, the study of epigenetics—changes in gene expression without change in the DNA template—has shown that environmental factors shape the very chemistry and function of genes (Beauchaine & McNulty, 2013; Bogdan, Hyde, & Hariri, 2013; Halldorsdottir & Binder, 2017; Nigg, 2016). Mental processes—such as how we interpret and make sense of the events in our lives, including internal events—have important effects on our physical and mental health. These mental processes occur with varying

degrees of conscious awareness, from deliberate attempts to rethink aspects of our lives, as in psychotherapy, to gradual changes in the way we think about things in everyday life. Social forces also continually evolve. Thus, individuals' risk factors for psychopathology are not static but are contingent on multiple interrelations among diverse causal factors that themselves are in flux (Rutter, 2012; Turecki, Ota, Belangero, Jackowski, & Kaufman, 2014).

For many years, a *diathesis–stress framework* was the dominant model for understanding the interplay between individuals' genetic/biological factors and other, primarily environmental, forces that resulted in psychopathology (e.g., Ingram & Luxton, 2005; Rende & Plomin, 1992). According to this model, the onset of psychopathology was related to the interaction between a person's underlying vulnerability (diathesis) and the degree of disruption produced by a disturbing event or condition (stress). The vulnerability factor could be a specific gene or set of genes, a temperamental variable, or even an event or set of events (e.g., certain early-life experiences, such as the death of a parent, appear to increase vulnerability for later depression). However, recent developmental psychopathology research has shown that many genes previously thought to be risk factors are better conceptualized as "plasticity genes" (Belsky, Jonassaint, Pluess, Brummett, & Williams, 2009). That is, certain variants of these genes are more reactive than other variants, not only to adverse environmental effects but also to supportive or even simply benign environments. As a result, depending on whether their experiences are adverse or are supportive or benign, individuals with such gene variants have either worse or actually better outcomes, respectively, than those who have less reactive variants of the same genes. This new framework is known as the *differential-susceptibility hypothesis*. Much more knowledge than we currently have is needed to determine the relative contributions of each type of factor (i.e., genetics, individual life history, social structure, and cultural systems) to the onset and form of mental illness and, more importantly, how these factors interact to result in psychopathology.

The fact that we do not fully understand the causes of most mental disorders is sometimes used to question the entire diagnostic enterprise, even though mental disorders are not different from many medical conditions (e.g., hypertension, migraine, myocardial infarction) whose risk factors are well established but whose cause at the individual level can rarely be determined with certainty. Moreover, currently available treatment strategies for mental disorders are often connected only loosely to their proposed causes.

For example, intellectual disability can be caused by a wide variety of infections, chromosomal abnormalities, environmental insults, metabolic diseases, nutritional deficiencies, toxins, or traumatic injuries. In most cases, the specific cause is never clearly identified. Prevention or reversal of these cases would obviously require their specific identification, but the fact that we cannot currently offer cures for them does not suggest that etiological research on intellectual ability is unimportant. Of equal importance, the fact that the cause of a particular case of intellectual disability is unknown does not mean that the disability itself cannot be validly and reliably assessed or that there are not effective and cost-effective interventions that could enhance the individual's functioning, autonomy, and quality of life. These assessment and intervention strategies are generally unrelated to the cause of the disability. Likewise, the fact that cognitive-behavioral therapy is an effective treatment for a variety of mental and behavioral disorders does not mean that the maladaptive thought patterns targeted by such therapy constitute the cause of these disorders; for example, contrary to the cognitive model of depression (D. A. Clark, Beck, & Alford, 1999), which posits that depressive affect arises, at least in part, from maladaptive cognitions, there is evidence that cognitive change does not mediate symptom change in major depression (Vittengl, Clark, Thase, & Jarrett, 2014).

Thus, the significance of the multicausality of mental disorders is not that it marks a point of difference between mental disorders and many other health conditions. Rather, it is important to raise issues of multicausality because of continuing concerns that biological causes and treatments for mental disorders receive disproportionate attention and resources, whereas psychological, social, and cultural factors are relatively unaddressed, despite compelling evidence for their importance. Therefore, the multicausality issue in relation to mental-disorder classification might be reframed as being about the ways in which these classifications offer systematic opportunities to note and record the influences of psycho-socio-cultural factors, thereby providing a basis for more research into them and for the development of additional assessment and intervention strategies. The three institutions discussed in this article tackle the problem of etiology in different ways; however, the efforts to harmonize DSM and ICD that have occurred since *DSM-III* have resulted in quite similar approaches to etiology, so we first discuss their shared aspects.

Shared aspects of* ICD-11 *and* DSM-5 *with regard to etiology. Both the third and fourth editions of the DSM and the eighth through tenth editions of the ICD included a few disorders for which evidence of a psychological causation was required. For example, conversion disorder was based on the psychoanalytic concept of defense mechanisms and involved the expression of unconscious

psychological conflicts as somatic symptoms (e.g., paralysis). The *DSM-IV* required that "psychological factors are judged to be associated with the symptom or deficit because the initiation or exacerbation of the symptom or deficit is preceded by conflicts or other stressors" (APA, 2000, p. 492), whereas *ICD-10* was even more direct, requiring for a definitive diagnosis of dissociative (conversion) disorders "evidence for psychological causation, in the form of clear association in time with stressful events and problems or disturbed relationships (even if denied by the individual)" (WHO, 1992b, p. 123). This criterion for conversion disorder was rewritten in *DSM-5* to eliminate one of the last remaining vestiges of "purely" psychologically defined etiology, now requiring simply that "clinical findings provide evidence of incompatibility between the symptom and recognized neurological or medical conditions" (APA, 2013, p. 318). Similar changes are proposed for *ICD-11*.

In addition, in recent versions of ICD and *DSM-III* to *-IV*, environmental causation in the form of exposure to one or more stressful life circumstances or traumatic events is a required part of several diagnoses (e.g., PTSD, acute stress disorder). Both *ICD-11* and *DSM-5* have taken this criterion a step further and include a new section devoted to disorders specifically related to stress (trauma- and stressor-related disorders), which also includes adjustment disorder, reactive attachment disorder, and disinhibited social engagement disorder and, in *ICD-11*, complex PTSD and prolonged grief disorder. Exposure to a traumatic event or a stressor is a diagnostic requirement for these disorders and therefore a necessary element in their etiology. However, how the stress or trauma fits into a larger etiological framework that includes both pathophysiological processes and cultural factors requires further investigation, as do relations among the various disorders specifically associated with stress, and even certain disorders for which stress is not a diagnostic requirement but that have overlapping phenomenology (e.g., mood and anxiety disorders). In contrast to the relatively few diagnoses that include explicit psychological or environmental etiologies, *ICD-11* and *DSM-5* contain multiple examples of etiological thinking based on biological causation. The specific ways in which these are organized are somewhat different in the two manuals, so we discuss them separately below.

Another proposed revision for *ICD-11* is elimination of the problematic organic/psychogenic dichotomy for sexual dysfunctions, which partly involved moving these to a separate chapter on "Conditions Related to Sexual Health." *DSM-5* made similar changes within the limits of the fact that it remains a classification of mental disorders. Each classification implemented an approach that recognizes the potential role of many factors in contributing to the development and maintenance of sexual dysfunctions. Likewise, *ICD-11* and *DSM-5* share an emphasis on the importance of illicit substances, prescribed medications, and general medical conditions in the causation of mental disorders, and practitioners should consider these factors as causes before making a definitive diagnosis and commencing treatment, because substance intoxication and withdrawal, adverse reactions to medication, and general medical conditions can result in symptoms indistinguishable from those of "primary" mental disorders.

***Etiological issues in* ICD-11.** For the most part, the organization of ICD across all health conditions is not based on etiology. Rather, most of its chapters are organized according to organ systems (e.g., diseases of the circulatory system, diseases of the respiratory system) or their most characteristic symptoms (e.g., sleep-wake disorders, mental and behavioral disorders). Some chapters have multiple organization schemes. For example, the "Infectious Diseases" chapter contains groupings of disease categories based on the types of organisms that cause them (e.g., bacteria, viruses, fungi), their mode of transmission (e.g., predominantly sexually transmitted infections), the organ system they primarily affect (e.g., viral infections of the central nervous system), or their presenting symptoms (e.g., viral infections characterized by skin and mucous-membrane lesions).

Many diseases and health conditions in ICD are characterized, like mental and behavioral disorders, by multiple, interacting causes (e.g., acute myocardial infarction, type 2 diabetes mellitus). Where they are placed in ICD may reflect only one of those causal factors or another organizing principle that is considered to be clinically important. For example, diabetic retinopathy is classified with other forms of retinopathy under diseases of the visual system, even though it is known to be a consequence of diabetes mellitus, which is classified under endocrine, nutritional, and metabolic diseases. In fact, type 2 diabetes itself, even though insulin resistance is essential in its etiology, has treatment ramifications that resemble those of cardiovascular disease. Given our considerable knowledge of the mechanisms or pathophysiology of many of these disorders, however, their placement causes little to no difficulty in ICD. In contrast, even though we understand that mental processes and mental events all have substrates in the brain, the chapters on "Mental, Behavioural, and Neurodevelopmental Disorders" and "Diseases of the Nervous System" are separate in ICD, likely for two main reasons: First, brain substrates are only one aspect of the etiology and phenomenology of these disorders, which primarily involve impairments in the higher order functions of cognition, emotion, and behavior and are influenced by interpersonal, social, and cultural factors; and second, our understanding of their causal mechanisms is still rudimentary.

Further, the "Mental and Behavioural Disorders" chapter in *ICD-10* is one of those with multiple organization schemes. Whereas some groupings are based on causation (e.g., mental and behavioral disorders due to psychoactive substance use), most are based on similarity of symptoms and evidence of shared validators such as familiality (the tendency for mental disorders to run in families) and temperamental antecedents. Thus, mood disorders form one grouping, whereas schizophrenia, schizotypal, and delusional disorders constitute another. Still others are now seen as unhelpful conglomerations of entities based on outdated theoretical perspectives and will be reorganized in *ICD-11*. For example, *ICD-10*'s grouping of neurotic, stress-related, and somatoform disorders is proposed in *ICD-11* to be reorganized into several narrower groupings, none of which is referred to as "neurotic."

Like *ICD-10, ICD-11* will incorporate the classification of specific causal factors when they are clearly relevant to treatment strategies. For example, separate categories are provided for mental and behavioral syndromes that are symptomatically similar but caused by substances (illicit or prescribed) or an underlying medical condition (e.g., a brain tumor). Delirium is classified according to its etiology because the particular cause of a patient's delirium is a critical factor in the immediately necessary treatment response; likewise with dementia and other neurocognitive disorders, in that etiology guides the prediction of a case's course and outcome and the selection of management strategies.

In some areas, the classification proposed for *ICD-11* goes considerably further than that of *ICD-10* in incorporating etiology. For example, the *ICD-10* classification of sexual dysfunctions relies on an artificial dichotomy between "organic" sexual dysfunctions, classified mostly in the chapter "Diseases of the Genitourinary System," and "nonorganic sexual dysfunctions," classified under mental and behavioral disorders. This mind-body split is not consistent with either current research or best practices, which are based on a view of sexual response as a complex interaction of psychological, interpersonal, social, cultural, physiological, and gender-influenced processes, any or all of which may contribute to the development of sexual dysfunctions. For *ICD-11*, an integrated classification of sexual dysfunctions has been proposed and a system of etiological qualifiers provided because of their relevance to treatment selection (Reed et al., 2016).

Further, as a broad classification of health conditions, ICD encompasses a variety of ways in which causal influences in mental disorders can be recorded. For example, one may note toxic environmental factors using categories from the chapter on "Injury, Poisoning and Certain Other Consequences of External Causes." The chapter "Factors Influencing Health Status and Contact With Health Services" contains a wide range of categories for documenting contributory factors to an individual's illness, including potential health hazards related to socioeconomic and psychosocial circumstances such as education and literacy, unemployment, problems related to the physical environment (e.g., occupational exposure, noise, pollution), the social environment (e.g., acculturation difficulty, social exclusion), housing, and negative events in childhood (WHO, 2016b). Further expansion of these categories has been proposed for *ICD-11* (WHO, 2017). Moreover, *ICD*'s sibling classification, the *International Classification of Functioning, Disability and Health* (WHO, 2001), contains a comprehensive classification of environmental factors that may affect functioning and disability in the context of a given health condition, such as human-made environmental changes, supportive or nonsupportive relationships, and services, systems, and policies. The categories of the two classifications were designed to be used together to provide a more comprehensive picture of individuals' health status and functioning (Reed, Spaulding, & Bufka, 2009).

In sum, WHO classifications offer a relatively comprehensive framework for identifying factors that may contribute to the etiology and expression of mental disorders and other health conditions. These categories could be used as a framework for additional epidemiological and clinical research and further refined on this basis, but national health-data systems and reimbursement policies generally do not facilitate systematic collection and reporting of this type of information (e.g., by reimbursing health professionals to record it as a part of standard health-encounter documentation), so the availability of these data for analysis on a global level is extremely limited. In general, WHO classification systems do not restrict the range of causes and contributory factors that may be considered in conceptualizing mental disorder. Rather, a specific subset of factors is prioritized in allocating resources for public-health data collection, research, and health-service reimbursement. These decisions are most frequently made at the level of national governments.

***Etiological issues in* DSM-5.** By relying on a mix of etiological views that incorporate both biological and psychodynamic factors, pre–*DSM-II* U.S. classification explicitly acknowledged multiple causal factors in the development of mental disorders. A major emphasis in developing *DSM-III* was to be atheoretical with regard to etiology or pathophysiological process unless one or both of these were well established (e.g., in the "Organic Mental Disorders" section for adjustment disorder, which stated "the disturbance is a reaction to psychosocial stress"; APA, 1980, pp. 6–7). This stance was taken partly to shed earlier references to psychodynamic causation, as well as to acknowledge that the cause of most mental disorders was unknown. Moreover, the possibility of

multicausality was acknowledged: "Undoubtedly, with time, some of the disorders of unknown etiology will be found to have specific biological etiologies, others to have specific psychological causes, and still others to result mainly from a particular interplay of psychological, social and biological factors" (APA, 1980, p. 7). Identifying either specific biological causes or a particular interplay of psychological, sociocultural, and biological factors has proved to be difficult, although there are a few disorders in *DSM-5* that have subtypes with specific, identifiable causes (e.g., narcolepsy, major and mild neurocognitive disorders).

Beginning with *DSM-IV*, etiological considerations were introduced into descriptive text sections devoted to risk and prognostic factors and culture- and gender-related issues. The sections on risk and prognostic factors include explicit references to environmental causation when appropriate (e.g., the relevant section on PTSD references the severity of the trauma, personal injury, etc.) but typically indicate more general risk factors (e.g., season of birth and urban rearing in schizophrenia). The culture section includes discussion of the causal contribution of cultural systems. For example, the relevant PTSD section states the following:

> The risk of onset and severity of PTSD may differ across cultural groups as a result of . . . the impact on disorder severity of the meaning attributed to the traumatic event (e.g., inability to perform funerary rites after a mass killing), the ongoing sociocultural context (e.g., residing among unpunished perpetrators in postconflict settings) . . . (APA, 2013, p. 278)

Most such references, however, are purely probabilistic and offer little utility in diagnosing individuals.

In sum, as knowledge on the causes of mental disorders has advanced, *DSM-5* has been able to progress from the atheoretical stance of *DSM-III*. To the extent allowed by current knowledge, it describes biological (e.g., genetics, neurodevelopment) and both general (e.g., culture) and specific (e.g., traumatic events) environmental factors that play a role in the onset and prognosis of mental illness. It also acknowledges the complexity of these causal factors, stating "the range of genetic/environmental interactions over the course of human development affecting cognitive, emotional and behavioral function is virtually limitless" (APA, 2013, p. 19) and cautions that "a diagnosis does not carry any necessary implications regarding the etiology or causes of the individual's mental disorder" (APA, 2013, p. 25).

Etiological issues in RDoC. RDoC is based in etiological thinking. Indeed, a major emphasis of the project is to learn more about the causes and mechanisms of mental illness, ultimately integrating knowledge relating to all four of its components (i.e., functional domains and units of analysis in the contexts of neurodevelopment and all that "the environment" encompasses).

Recent studies on psychosis provide an example of an RDoC-themed approach to identifying and understanding etiological factors in a particular disorder spectrum. Schizophrenia has for some time been recognized as a neurodevelopmental disorder, with the overt symptoms of psychosis being the end state of an extended process (Rapoport, Giedd, & Gogtay, 2012). Various lines of investigation have explored possible avenues to understanding the aberrant development that leads to psychosis. One long-standing hypothesis is that synaptic pruning—the reduction in cortical synapses that occurs as a part of normal development across adolescence (e.g., Feinberg, 1982)—is excessive in schizophrenia, such that there is an aberrant reduction in these synapses. Support for this hypothesis is accumulating: Cannon et al. (2015) found accelerated loss of gray matter in the years leading up to an overt episode of psychosis (i.e., the schizophrenia prodrome) was a critical factor in disease onset, and a genetics study has provided evidence for one mechanism by which this excessive pruning may occur (Sekar et al., 2016).

Although these reports focused on schizophrenia, a recent groundbreaking study suggests a broader and more nuanced picture. The Bipolar and Schizophrenia Network on Intermediate Phenotypes is investigating patients diagnosed with schizophrenia, psychotic bipolar disorder, or schizoaffective disorder, an intermediate category between the other two disorders (Clementz et al., 2016). Rather than comparing the three disorders against one another, the investigators set aside the patients' different diagnoses and sought other measures that could sort them in novel ways. A clustering analysis returned two major factors of "cognitive control" (cognitive and self-regulatory functioning) and "sensorimotor reactivity" (brain activity in response to simple stimuli such as tones and lights). Various combinations of these two factors resulted in three groups, labeled "biotypes," each of which included patients from all three diagnostic groups. The amount of gray-matter loss differed systematically across the three biotypes, but not as a function of their DSM diagnostic categories, and one biotype was associated with increased use of marijuana. Of course, no one study is conclusive, but these data illustrate the potential for biological and behavioral measures to identify intermediate phenotypes more directly related to interacting neurodevelopmental and environmental factors relevant for etiology.

Etiology: summary. As awareness has grown that virtually all mental disorders result from many different factors, ICD and DSM have both acknowledged this complexity

and moved to incorporate etiological factors in the relatively few instances in which they are known. In contrast, RDoC was developed in large part to support research into the etiologies of mental disorder. Its ambitious goal is to understand how functional deviations in various brain and behavioral response systems interact to result in mental disorder, while emphasizing that these processes are developmental rather than static and that they occur in the context of individuals' interpersonal, social, and cultural environments.

Categories and dimensions

Mental disorders are not all-or-none phenomena. First, the overall degree of severity of a person's mental illness is one of its most critical aspects. In fact, recent evidence suggests the existence of a broad, general-psychopathology dimension (e.g., Caspi et al., 2014; Kotov et al., 2017; Laceulle, Vollebergh, & Ormel, 2015) that encompasses a wide range of—or even all—variations of psychopathology, perhaps in a very fundamental way, much as general intelligence is a broad dimension that has multiple interrelated components. (We discuss this further in the section "Comorbidity.") Second, many symptoms of mental disorder overlap with psychological states that are common in the general population (e.g., depressed mood) and range in severity, from relatively rare and circumstantial symptoms in generally healthy individuals to mild, transient disturbance to moderate symptoms that are components or reflections of mental disorder to severe and prolonged distress.

Third, some dimensions reflect bipolarity in which the optimal level is somewhere between opposing pathological extremes. Symptom dimensions best conceptualized as continuous in this manner include

- emotions, many of which have an optimal middle range, such as mood, for which healthy levels generally lie between depressed and elated extremes, and anxiety, which has what is known an "inverse U" relation to performance, such that performance is lower at both the low and the high extremes, whereas moderate levels of anxiety are associated with maximal performance (Yerkes-Dodson law; e.g., Keeley, Zayac, & Correia, 2008);
- cognitions, such as good reality testing versus hallucinations or delusional thought processes; attention control, which can range from distractibility to hyperattentiveness; unwanted intrusive thoughts; dissociation; and impaired intellectual functioning;
- behaviors, such as avoidance of feared objects or situations versus risk taking, and lethargy versus hyperactivity; and
- physical symptoms, such as sleep disturbance, appetite disturbance, and physiological arousal.

Most manifestations of mental disorder can be described along a number of these symptom dimensions. For example, panic disorder involves dimensions of emotional symptoms (i.e., fear) cognitive symptoms (i.e., derealization/depersonalization, fear of losing control or dying); behavioral dimensions (i.e., behavioral change designed to avoid having panic attacks, such as avoidance of unfamiliar situations); and physical symptoms (e.g., palpitations; sweating, trembling, or shaking; chest pain or discomfort; gastrointestinal distress).

In some contexts, the overall degree of severity is the most significant dimension in that it indicates which individuals are in the greatest or most immediate need of treatment. However, knowing only the severity of an individual's mental illness may not be particularly helpful in determining the best type of treatment. In most cases, more specific information is needed, so clinicians typically assess the severity of various symptom dimensions. Given the total number of symptom dimensions, there are too many possible combinations for the human mind to process them all simultaneously. A primary function of any classification system is to aid understanding of complexity by organizing important recurrent patterns into categories. In the case of mental disorder, diagnostic categories are intended to reflect meaningful, recurrent symptom patterns. To be sure, using diagnoses to describe the symptom profiles of individuals with mental illness facilitates assessment and conveys a considerable amount of information succinctly. However, because simplifying complex symptom profiles into diagnoses does not perfectly reflect reality, the reification of diagnostic categories eventually impedes a deeper understanding of them (Hyman, 2010). With the widespread acceptance of *DSM-III*, professionals and lay people alike came to consider and treat mental disorder diagnoses as "true objects in nature" rather than convenient groupings of symptom dimensions.

Fortunately, science is self-correcting in the long run, partly because it typically involves looking at things in more than one way, which is one reason that the hegemony of DSM eventually became problematic. Research into patterns of comorbidity among categorical diagnoses eventually began to suggest the utility of studying more directly the interrelations among symptom dimensions that make up commonly comorbid diagnoses. There has been an upsurge of such research since the turn of this century. Results indicate that current classification systems only partially reflect the empirical relational patterns of symptom dimensions (Markon, 2010), raising the possibility of a more valid approach.

Importantly, both diagnostic comorbidity and symptom dimensions have been shown to have a hierarchical structure, with certain more specific diagnoses or symptom dimensions being related systematically, such that they combine into broader diagnostic categories or symptom dimensions, respectively, similarly to how certain related biological species form broader genuses, related genuses form still broader families, and so on.

Out of 20 symptom dimensions, Markon (2010) found that four broad higher order factors across a wide range of clinical syndromes and PDs captured the covariation among them: an internalizing dimension (e.g., subjective, distressing experiences, such as feelings of depression and somatic symptoms), an externalizing dimension (e.g., observable behaviors that often directly affect others, such as those related to substance use, attention seeking, and aggression), a dimension of thought disorder or cognitive disturbance (e.g., eccentric thought processes, paranoia, cognitive rigidity), and a pathological-introversion dimension composed of such symptom dimensions as social anxiety and unassertiveness/dependency. Moreover, each of the 20 symptom dimensions could be subdivided into component dimensions—smaller clusters within a symptom dimension that are even more highly related. For example, the dimensions of worry, apprehension, and irritability formed the anxiety dimension. Together, the lower order, mid-level, and higher order factors constitute a multilevel dimensional hierarchy (see also Boschloo et al., 2015; Fullana et al., 2010; Watson et al., 2012).

Neither the validity nor the clinical utility of such a wholly symptom-dimension-based approach to understanding psychopathology has been studied as extensively and systematically as those of the current diagnostic systems, but evidence is accruing that the approach has considerable value (e.g., Allardyce, McCreadie, Morrison, & van Os, 2007; Villalta-Gil et al., 2006). For example, a large-scale study in the United Kingdom (Brittain et al., 2013) compared the predictive power of symptom dimensions versus diagnoses for 14 clinical outcomes (e.g., aggressive behavior, relationship problems, self-injury). There was no difference for eight outcomes, and symptom dimensions outpredicted diagnoses for five outcomes (aggressive behavior, nonsuicidal self-injury, problems due to hallucinations or delusions, depressed mood, and activities of daily living). For example, the number of negative symptoms (e.g., restricted or blunted affect, poverty of thought) and disorganization symptoms (e.g., incoherent speech, bizarre behavior) better predicted problems with activities of daily living (e.g., bathing and dressing oneself) than did having a diagnosis of schizophrenia. Diagnoses outpredicted symptoms only for duration of inpatient stay, which may have been due to diagnosis-based hospital administrative processes (i.e., certain diagnoses were allowed longer hospitalization periods than others).

We said earlier that "current classification systems only partially reflect the empirical relational patterns of symptom dimensions." However, they do reflect them to some extent, and they currently represent our best option for clinical use. The three institutions that are our article's focus all recognize and acknowledge the multidimensional nature of mental disorder, but because they are responding to different constituencies with diverse needs and requirements, they take different approaches to address the dimensional aspects of mental disorder.

***Categories and dimensions in* ICD-11.** The dimensional nature of many, perhaps most, phenomena underlying mental disorders has long been clear to careful readers of the scientific literature and observers of clinical phenomenology. However, ICD remains structured as a categorical taxonomic system because this format is necessary for its application as the classification system for global health statistics and, to a large extent, for its use in clinical systems (e.g., in treatment selection and the determination of eligibility for health care services). For this reason, ICD follows particular rules and conventions that have deep historical roots and are well accepted as the basis for classification in other areas of medicine, even though one can point to many aspects of health conditions across diverse areas of medicine that are more accurately and precisely conceptualized as dimensions (e.g., blood pressure).

The *ICD-11* classification of mental and behavioral disorders is required to follow the same set of structural and taxonomic rules as those used in the rest of ICD's classification system. This requirement imposes different and much stricter restrictions on its classification model for mental and behavioral disorders than is the case for RDoC or, theoretically, even for the DSM, the taxonomic focus of which is limited to mental and behavioral disorders. At the same time, WHO's IAG (2011) has pointed out that the inclusion of mental disorders in ICD facilitates coordination with classification of other disorders, including neurological and other medical conditions that are frequently comorbid with mental and behavioral disorders, and facilitates the search for related mechanisms of etiology, pathophysiology, and comorbidity of disease processes. The representation of mental and behavioral disorders alongside other health conditions in the *ICD-11* also provides a solid basis for the parity of the mental health field with the rest of medicine for clinical, administrative, and financial functions in health care.

One way to integrate dimensional constructs into a categorical system is to divide a given dimension into

ordinal subcategories. For instance, *ICD-10* included subcategories corresponding to the severity of a current depressive episode in depressive and bipolar disorders, which have been retained in *ICD-11* with some refinements. Other *ICD-11* diagnoses have subcategories created by imposing clinically important cutoffs on dimensional phenomena, such as dangerously low body weight in anorexia nervosa and extent of functional language impairment in ASD.

Likewise, subcategories of "mental retardation" in *ICD-10* were based on the severity of intellectual impairment: mild, moderate, severe, and profound. Determination of these levels was based primarily on standardized tests of intellectual functioning (i.e., IQ), using cutoffs that were relatively well accepted when *ICD-10* was developed in the late 1980s. The equivalent diagnostic categories in *ICD-11*, now called disorders of intellectual development, provides an example of a second strategy for incorporating dimensional information in a categorical system: being more explicit about the dimensions that clinicians must consider to arrive at a particular diagnostic determination. Specifically, to derive the appropriate severity-based subcategory for a disorder of intellectual development in *ICD-11*, the clinician must make judgments on multiple dimensions, considering both intellectual functioning and adaptive behavior across the domains of conceptual, social, and practical skills.

The proposed changes in the *ICD-11* diagnostic guidelines for paraphilic disorders, called disorders of sexual preference in *ICD-10*, provide another example of categories that incorporate multiple dimensional judgments. In *ICD-10*, the diagnostic guidelines for these disorders often merely described the behaviors they involved. In *ICD-11*, in keeping with the ICD's central function as a global public-health tool that provides the framework for international public-health surveillance and reporting, a distinction has been made between conditions that are relevant to public health and indicate the need for health services and those that involve private behaviors without any appreciable public-health impact and for which treatment is neither indicated nor sought (Krueger et al., 2017). The core proposed diagnostic requirements for a paraphilic disorder in *ICD-11* are, first, a sustained, focused, and intense pattern of sexual arousal—as manifested by persistent sexual thoughts, fantasies, urges, or behaviors—that involves others whose age or status renders them unwilling or unable to consent, and, second, the individual's having acted on these thoughts, fantasies, or urges or having been markedly distressed by them. However, a paraphilic disorder diagnosis may also be assigned when the pattern of sexual arousal is associated with marked distress or significant risk of injury or death, even if it does not focus on nonconsenting individuals. This formulation thus implicitly requires that clinicians who are applying the guidelines assess several components of the diagnosis, each of which can be conceptualized along a dimension—degrees of arousal, consent, action, distress, and harm—to determine whether a diagnosis of a paraphilic disorder is warranted.

More fully dimensional characterizations of disorder entities proposed for *ICD-11* have been made possible by specific structural innovations. (For a description of structural changes from *ICD-10* to *ICD-11*, see First et al., 2015.) One example is the proposal to eliminate specific PDs in *ICD-11* because of well-established problems with their validity and application in clinical systems and to replace these with a dimensional classification (Tyrer et al., 2015). Specifically, the proposed *ICD-11* model contains, first, a set of essential features (i.e., features that must be present to make a diagnosis) that are centered on self- and interpersonal dysfunction. If the essential features are met, then the clinician makes a determination regarding how severe the disturbance is and assigns a diagnosis of mild, moderate, or severe PD. (A subclinical level—personality difficulty—is also included.)

PDs may then be described further through the use of six qualifiers. Five of these are trait-domain qualifiers, which are a set of dimensions that correspond to the underlying structure of the full range of adaptive-to-maladaptive personality traits: negative affectivity (the tendency to experience, and to have difficulty regulating, a wide range of distressing emotions and related cognitions), detachment (the tendency to maintain emotional and interpersonal distance), dissociality (the tendency to disregard social obligations and conventions and the rights and feelings of others), disinhibition (the tendency to act impulsively in response to immediate external or internal stimuli without consideration of longer term consequences), and anankastia (the tendency to maintain a narrow focus on controlling one's own and others' behavior and situations to ensure conformity to one's own "correct" standards). As many of these trait domains may be noted as are judged to be prominent and contributing to the PD and its severity. A borderline qualifier (the last of the six) is also included and may be used if a certain characteristic pattern of maladaptive functioning is evident.

Likewise, the *ICD-10* subtypes of schizophrenia (e.g., paranoid, hebephrenic, catatonic) have been proposed for elimination in *ICD-11* because of their lack of validity. They are to be replaced by a set of symptom ratings that may be applied not only to individuals with schizophrenia but also those with other primary psychotic disorders (Gaebel, 2012). The rated dimensions include positive symptoms (delusions, hallucinations, disorganized thinking and behavior; experiences of passivity

and control); negative symptoms (constricted, blunted, or flat affect; alogia, or paucity of speech; avolition; anhedonia), depressive mood symptoms, manic mood symptoms, psychomotor symptoms, and cognitive symptoms.

These proposals to incorporate more sophisticated dimensional elements in *ICD-11* address a series of specific problems. For disorders of intellectual development, for example, the proposal addresses an inadequate measurement model that takes insufficient account of how people actually function in daily life (Tassé, Luckasson, & Nygren, 2013). For paraphilic disorders, the previous formulation led to overpathologizing private behaviors that lacked clinical relevance or public-health importance (Reed et al., 2016). The classification of specific PDs and subtypes of schizophrenia in *ICD-10* (and similar elements in *DSM-IV*) had produced reified categories commonly seen as unchanging, lifetime diagnoses that identified specific types of people. However, these ideal types were insufficiently informative for effective management of actual patients with personality pathology or schizophrenia, and the proposals for *ICD-11* better represent current scientific evidence regarding the nature of these disorders (Gaebel, 2012; Tyrer et al., 2015).

At the same time, these proposals for dimensional classification are in some ways more complex than the purely categorical approach they are intended to replace, and they may impose increased clinical and administrative burdens on their users, at least initially, when the new system is unfamiliar. After a period of adjustment, however, clinicians may find that, overall, the new system is actually simpler than the one it is replacing. For example, *ICD-10* defines 10 specific personality disorders, whereas the *ICD-11* proposal has only three levels of severity and six optional specifiers, requiring a maximum of nine. Nonetheless, these new proposals have little hope of being adopted and widely implemented in clinical practice unless they provide useful information at the level of clinical encounters that justifies the time and effort that learning the new systems will involve. Moreover, they will be of little use for health statistics or other policy applications based on aggregated patient-encounter data if clinicians cannot apply them consistently (Reed et al., 2013), Whether clinicians can apply these dimensional assessments appropriately and consistently and whether they find that doing so yields clinically important information is currently being tested in field studies that will influence the final form of the *ICD-11* diagnostic guidelines (Keeley et al., 2016).

***Categories and dimensions in* DSM-5.** The limitations of the categorical diagnostic system were clearly recognized by the developers of *DSM-5*. Early in the planning process, it was decided that the categorical system, despite its flaws, had an intrinsic appeal to clinicians—especially psychiatrists, DSM's key target audience—who are trained to determine patients' diagnoses. Nonetheless, the loss of information inherent in categorical diagnoses was seen as a deficit worth ameliorating with supplemental dimensional approaches. Two key candidates for incorporating dimensions into a categorical diagnostic system were diagnostic severity and cross-cutting symptoms.

The *DSM-IV* contained a brief section defining diagnostic severity in its introduction and, like *ICD-10*, provided specific guidance for conduct disorder, MDD, and "mental retardation." The importance of being able to note the severity of individuals' symptoms when making diagnoses is particularly well exemplified by the latter two disorders. Individuals whose MDD is of mild severity compared with those whose symptoms are moderate or severe have been shown to respond differentially to certain treatments (Hollon & Ponniah, 2010). Further, treatment research has long used change in severity (e.g., as measured by the Hamilton Depression Rating Scale; Hamilton, 1960), in addition to the less informative categorical presence or absence of the disorder, to assess outcomes. The severity levels of "mental retardation" have been used widely to gauge the level of support needed for individuals with this diagnosis. Not surprisingly, the service needs of an individual with profound or severe intellectual deficits are considerably more intensive than those of an individual with mild deficits. Thus, diagnostic severity has implications for research, provision of treatment and rehabilitation services, service planning, and resource allocation.

Under the guidance of the Diagnostic Assessment Instruments Study Group, the *DSM-5* work groups were tasked with identifying or developing measures to assess severity of a wider range of diagnoses. In conjunction with the Impairment and Disability Study Group, the members of the former Study Group proposed that these be based on the symptoms of the disorder and not on the extent of disability resulting from those symptoms. Disability—the effect of individuals' symptoms on their ability for self-care and engagement in social and other life activities—was recognized as an important consequence of disorder severity, but a domain to be measured separately. Likewise, the level of distress caused by symptoms was felt to be a consequence of symptom severity and disability, and thus not a suitable indicator of diagnosis-specific severity. The study groups proposed that measurements of severity generally should either take the form of a symptom count, as did the guidelines for assessing severity in *DSM-IV*, or be based on a more fine-grained

assessment of symptom frequency, intensity, and/or duration.

To reduce clinicians' burden, measures were to have a patient-administered format, although it was recognized that clinician-completed measures might be necessary for some disorders and symptoms. To be included, severity measures were to be freely available (i.e., not proprietary), short enough for use in busy clinical settings (containing approximately 10 items at most), and, for clinician-rated measures, able to be used without formal training in their administration. When severity instruments that met these requirements were not already available for a particular diagnosis, a *DSM-5* work group could develop one. Most of the severity measures recommended by the work groups were based on symptom frequency, intensity, or duration; some (e.g., the Patient Health Questionnaire–9; Kroenke, Spitzer, & Williams, 2001) were based directly on the diagnostic criteria for the disorder. Other instruments measured severity as manifested through specific aspects of a disorder, such as BMI for anorexia nervosa. As proposed for *ICD-11*, severity of schizophrenia in *DSM-5* is assessed through several of its associated symptoms, some of which (e.g., impaired cognition, depression, and mania) are not included in the disorder's diagnostic criteria. Finally, because individuals can have clinically significant symptoms that do not meet full diagnostic criteria, the instructions for the diagnosis-specific severity measures indicate that they may be used to assess individuals with such symptoms regardless of whether their symptoms are above threshold for diagnosis.

Soon after the publication of *DSM-III*, it was recognized that rigid diagnostic categories often do not correspond to clinical reality. Rather, patient presentations often include any number of clinically significant symptoms that are not among the criteria of a particular diagnosis. Some of these symptoms (e.g., sleep problems and anxiety) are seen frequently across a wide range of mental disorders. Others (e.g., suicidal ideation, illicit drug use) are less frequent but are of high clinical significance when they do occur. Increasingly, these nondiagnostic, co-occurring symptoms (e.g., presence of anxiety symptoms in MDD or depressive symptoms in schizophrenia) are viewed as important predictors of patients' treatment response and prognosis (Conley, Ascher-Svanum, Zhu, Faries, & Kinon, 2007; Fava et al., 2008).

The *DSM-5* work groups developed measures of many of these nondiagnostic, cross-cutting symptoms for such symptom domains as depression, somatic complaints, and substance use, and they serve two purposes. First, they provide documentation of the presence and severity of extra-diagnostic symptoms to guide clinicians' treatment decisions and allow them to follow patients' outcomes. Second, when administered before a clinical visit (e.g., via patient self-ratings), the measures draw attention to symptoms that might otherwise be missed because they are outside patients' formal diagnoses. The *DSM-5* work groups and study groups provided input as to which cross-cutting symptom domains to include.

For ease of administration, the Diagnostic Assessment Instruments Study Group recommended a two-stage process using patient-rated—or parent-rated, for children—measures. The first stage, Level 1, includes a few screening questions for each symptom domain. For several domains, for example, a score of at least 2 on one 5-point rating scale (i.e., corresponding to at least "mild" severity) indicates the need for a Level 2 assessment. The Level 2 assessments are more complete symptom assessments, which allows them to be used easily to assess outcomes, including change over multiple time points. Table 1 lists the Level 1 cross-cutting symptom domains and the corresponding Level 2 measures for adults, adolescents (ages 11–17), and children (aged 6–17, assessed through parent or guardian reports). Some Level 1 domains do not have associated Level 2 assessments. For these domains, scores above a predetermined threshold are "flags" for the clinician to conduct further individualized follow-up assessments. It is noteworthy that many of the Level 2 measures are relatively pure assessments of clinically important symptoms rather than of diagnostic syndromes, which often include heterogeneous groups of symptoms. As such, they may have use in bridging clinical practice and RDoC research on basic neuroscience and behavioral domains.

The cross-cutting symptom measures were tested in the *DSM-5* field trials and had generally good to excellent test-retest reliabilities in all three age groups (Narrow et al., 2013). Importantly, the diagnostic approach that was tested in the field trials—namely, using dimensional assessments in addition to categorical diagnoses—was well accepted by clinicians. Patients and their parents or guardians found the self-rated dimensional assessments useful for describing their symptoms and helping their clinicians understand their experiences.

The cross-cutting and severity measures, which were mostly self-administered by patients, were intended for use at initial evaluation and at follow-up visits to help both clinicians and patients make treatment decisions and track treatment outcomes, consistent with the contemporary U.S. emphasis on measurement-based care and patient-reported outcome measurement. However, the APA Board of Trustees decided that there was not yet sufficient evidence that use of most of the

Table 1. Cross-Cutting Level 1 and Level 2 Symptom Assessments in the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*

Level 1 domain and patient age group	Level 2 measure
Depression	
Adults	PROMIS Depression—Short Form
Adolescents	PROMIS Depression—Pediatric Item Bank
Children	PROMIS Depression—Parent Item Bank
Anxiety	
Adults	PROMIS Anxiety—Short Form
Adolescents	PROMIS Anxiety—Pediatric Item Bank
Children	PROMIS Anxiety—Parent Item Bank
Anger	
Adults	PROMIS Anger—Short Form
Adolescents	PROMIS Calibrated Anger Measure—Pediatric
Children	PROMIS Calibrated Anger Measure—Parent
Irritability	
Adults	N.A.
Adolescents	Affective Reactivity Index (adapted)[a]
Children	Affective Reactivity Index (adapted)[a]
Inattention	
Adults	N.A.
Adolescents	N.A.
Children	Swanson, Nolan, and Pelham Questionnaire–IV
Mania	
Adults	Altman Self-Rating Mania Scale[b]
Adolescents and children	Altman Self-Rating Mania Scale (adapted)
Somatic Symptoms	
Adults	Patient Health Questionnaire–15 Somatic Symptom Severity Scale[c]
Adolescents and children	
Psychosis	
Adults	None
Adolescents and children	None
Sleep Problems	
Adults	PROMIS: Sleep Disturbance—Short Form
Adolescents and children	PROMIS: Sleep Disturbance—Short Form
Repetitive Thoughts and Behaviors	
Adults	Florida Obsessive-Compulsive Inventory Severity Scale (Part B, adapted)[d]
Adolescents	Children's Florida Obsessive-Compulsive Inventory Severity Scale (Part B, adapted)[e]
Children	N.A.
Substance Use	
Adults	NIDA-Modified Alcohol, Smoking and Substance Involvement Screening Test (adapted)[f]
Adolescents and children	NIDA-Modified Alcohol, Smoking and Substance Involvement Screening Test (adapted)[f]
Suicidal Ideation/Attempts	
Adults	N.A.
Adolescents and children	N.A.
Dissociation	
Adults	N.A.
Memory	
Adults	N.A.
Personality Functioning	
Adults	N.A.

Note: Adolescents are individuals between the ages of 11 and 17. Children are individuals between the ages of 6 and 17. All assessments for children shown in the table are completed by the child's parent or guardian. N.A. = not applicable (i.e., no measure is available for a given age group). NIDA = National Institute on Drug Abuse; PROMIS = Patient Reported Outcomes Measurement Information System (see http://www.nihpromis.org).

[a]Stringaris et al. (2012; http://www.kcl.ac.uk/ioppn/depts/cap/research/moodlab/ari.aspx). [b]Altman, Hedeker, Peterson, and Davis (1997). [c]Kroenke, Spitzer, and Williams (2001). [d]Storch et al. (2007). [e]Storch et al. (2009). [f]National Institute on Drug Abuse (2012).

diagnostic-severity and cross-cutting symptom measures would improve clinical care and patient outcomes to warrant approval for general clinical use. Therefore, the Board of Trustees approved only a few simple scales for assessing severity—such as BMI for anorexia nervosa, symptom counts for substance use disorders, and "setting counts" (indicating whether symptoms were seen in only one, only two, or three or more settings) for oppositional defiant disorder—for inclusion in the main Section II of *DSM-5*. A representative sample of other measures is included in *DSM-5*'s Section III as "emerging measures" needing further testing, and all measures are available online (https://www.psychiatry.org/psychiatrists/practice/dsm/educational-resources/assessment-measures). Clinicians are encouraged to use the measures and report their experiences to the APA to provide evidence of the measures' utility for clinical practice.

Finally, as mentioned previously, the proposed *ICD-11* system for PD is conceptually quite similar to the *DSM-5* AMPD, but there are three notable differences between the ICD and DSM models. First, the *DSM-5* model has greater specification for both functional impairment and for traits, but this has resulted in a model that WHO considered to be too complex for implementation except in research or in the most specialized settings in high-resource countries. Second, the models each have five broad trait domains but share only four: negative affectivity, detachment, disinhibition, and a domain that is called antagonism in *DSM-5* and dissociality in *ICD-11*. Then, each has a fifth trait domain that the other does not: anankastia (a focus on the control and regulation of one's own and others' behavior to ensure conformity to one's high standards) in *ICD-11* and psychoticism (eccentric perceptions, cognitions, beliefs, experiences, and behaviors) in *DSM-5*. This domain is not included in the *ICD-11* proposal because schizotypal disorder is classified as part of the schizophrenia spectrum in ICD, whereas in *DSM-5* schizotypal PD's primary placement is in the PD chapter, and trait psychoticism is needed to characterize this PD. Third, the proposed *ICD-11* model includes a borderline qualifier, in contrast to the six combinations of traits forming specific PDs in *DSM-5*'s AMPD. This is not intended as a claim that the borderline pattern has unique ontological status. Rather, because this has been the most frequently diagnosed *ICD-10* PD, its inclusion is specifically intended to facilitate the transition from a categorical to a dimensional PD model, and to give clinicians tools for documenting the variability in presentation of people who were previously considered to have BPD by also noting the particular trait domain(s) that characterize individuals' PD presentation.

Categories and dimensions in RDoC. The RDoC research framework embodies a fully dimensional approach to mental disorder. This approach does not merely entail assessing severity dimensions of currently recognized disorders (e.g., a dimension of mild to moderate to severe MDD) but rather reflects the view that psychopathology should be studied with respect to the full range of operation of its various constructs, from healthy through severely pathological range.

There are multiple reasons for taking this approach. First, given RDoC's emphasis on etiology, its near-term goal is not to improve current diagnoses or develop an alternative clinical nosology but rather to direct the research community toward a more comprehensive understanding of how a variety of factors intersect over time and across different contexts to yield various types and degrees of psychopathology. It is becoming increasingly clear that most mental and behavioral functions in psychopathology are on continuous dimensions with functioning in the general population rather than qualitatively distinct. The pathological trait criteria of PD provide a clear elaboration of this continuity, as do some criteria of MDD (e.g., diminished interest or pleasure in activities) and GAD (e.g., excessive anxiety and worry; L. A. Clark, 2005) that are related to RDoC constructs. However, similar patterns hold for other mental functions that initially might seem to be more distinct from normality.

For instance, large community studies have shown that hallucinations and delusions are distributed continuously in the population (van Os, Linscott, Myin-Germeys, Delespaul, & Krabbendam, 2009) and that the need for services is more correlated with the extent of these phenomena than with their simple presence versus absence (Kaymaz & van Os, 2010). Research also suggests that genetic loads may be continuous across clinical and nonclinical populations. For instance, parents with a child diagnosed with ASD who had one or more unaffected siblings were asked to report on the psychosocial functioning of all their children, and they reported considerable overlap in the functioning levels of those with and without the disorder. Within the range of overlap, the relation between genetic loading and functioning level was virtually identical in both groups. These data suggest that the same genetic factors are operative in both typically developing and diagnosed children (Robinson et al., 2016).

Second, RDoC's focus on dimensions of mental and behavioral functioning provides a more quantitative basis for prevention research. Scales that have been validated for various mental functions and behaviors can help identify individuals who are beginning to trend toward dysfunction that, if the trend were to

continue, could eventuate in disorder. This approach is directly comparable to approaches in other areas of medicine, such as the measurement of blood sugar, in which progressive divergence from normal levels prompts increasingly aggressive treatment options—from lifestyle changes to medication or other, more intensive interventions. Thus, as with the rest of medicine, assessment of symptom levels across the full normal-to-abnormal spectrum is fundamental to the development of preventive interventions.

An early example of the potential for this approach to mental disorders with respect to cognitive domains is provided by data from the Pennsylvania Neurodevelopmental Cohort study, in which children admitted to a hospital for a variety of reasons were given a large battery of neuroimaging and cognitive tasks and followed for several years. A retrospective analysis of the youths who later developed psychotic symptoms showed that their cognitive functioning fell behind that of typically developing children at about 9 years of age and stayed about 1 year behind normal cognitive development for the rest of the study (Gur et al., 2014). Studies aimed at understanding the nature of such developmental delays, and more precise means of identifying individuals at particular risk for psychosis, could eventually lead to targeted prevention interventions.

Categories and dimensions: summary. Both ICD and DSM, each in its own way, have made modifications to acknowledge the existence of dimensional features that are relevant to mental disorder and to incorporate dimensional features into their diagnostic and classification systems. For example, *DSM-5* incorporated the concept of severity consistently across its classification system and added a set of cross-cutting symptom dimensions that can be used to provide a more complete clinical picture without using additional diagnoses that increase spurious comorbidity. Likewise, the developers of *ICD-11* have taken steps toward abandoning artificial subtypes by, for example, proposing a severity dimension as the primary basis for classifying PD, with trait dimensions as specifiers. They have also proposed to implement a more dimensional system of symptom expression in schizophrenia and other primary psychotic disorders. And yet both systems remain fundamentally categorical for reasons that are germane to the various purposes for which they were developed and still are primarily used: compilation of health statistics, allocation of mental-health resources, clinical communication, and decision making in regulatory, legal, and health-insurance systems, all of which ultimately serve public mental health care needs. Providing a basis for decisions about what constitutes a case of mental disorder is a fundamental requirement of these systems, and such decisions are inevitably categorical.

In contrast, the RDoC system represents a fundamentally different approach to mental illness, with the goal of identifying the basic brain and behavioral processes that, together with sociocultural forces, give rise to multiple dimensions that may become dysfunctional and constitute psychopathology. It seeks deeper understanding of the scientific basis of psychopathology through the integration of biological and behavioral measurements, while also recognizing that these processes are developmental and embedded in interpersonal, social, and cultural contexts. NIMH's overarching goal is to serve the public's mental health care needs; with the RDoC system, it is pursuing this goal with a longer time horizon. Given the complexity of mental illness, the RDoC initiative sets forth a research program that may require many years before its findings materially affect current diagnostic and classification systems.

Thresholds in mental disorder

In the introduction to this article, we noted that setting thresholds in mental disorder is difficult for three reasons: first, the very definition of mental disorder is still being debated; second, mental disorders are multidimensional; and third, thresholds for mental disorder diagnoses carry considerable clinical and social ramifications. Here, we discuss each of these points in more detail.

Definition of mental disorder. How mental disorder is defined is critical for establishing the threshold between health and disorder, and several aspects of this issue warrant discussion. First, current guidance for assigning diagnoses in ICD and DSM is based upon symptoms and signs of psychopathology, representing a descriptive approach to classification. This aspect of diagnostic classification is widely accepted. Further, like physical disorders, mental disorders are diagnosed on the basis of various tests (e.g., chest X-rays, standardized assessments of intellectual functioning) as well as observable signs (e.g., swelling, suicidal gestures) and patient-reported symptoms (e.g., pain, hallucinations). However, there is a general perception that psychological assessments are less reliable and less valid than medical tests, even though there is substantial evidence that this is not necessarily the case (e.g., Kraemer, Kupfer, Clarke, Narrow, & Regier, 2012; Meyer et al., 2001). To be sure, assessing the signs and symptoms of mental disorders requires considerable clinical judgment based on the observation of an individual and on his or her self-reported mood, cognitive and sensory experiences, and behaviors; however, identifying and correctly classifying physical signs and symptoms to diagnose medical illnesses can also rely heavily on clinical judgment. Nonetheless, the availability of objective measures for many physical signs (e.g., assessments of liver

size using CT scans rather than palpations of the abdomen) creates a general—though not fully justified—sense that the diagnosis of general medical problems is more scientifically accurate than that of mental disorders.

Mental-disorder diagnoses generally rely heavily on patients' reports of their own experiences, even though patients' symptoms often affect their ability to report on their experiences. For example, depression affects one's perspective on life events, so depressed people may view mildly negative experiences and events as being far more distressing than do nondepressed individuals; people with anorexia nervosa typically do not perceive how thin they are objectively; individuals with substance use disorders often deny the extent to which their behavior affects others as well as themselves; and so on. Moreover, as previously discussed, many mental-disorder symptoms are common in the general population (e.g., Nuevo et al., 2012) and exist along dimensions that are continuous with normal variation (e.g., Tyrer et al., 2015). These issues complicate the determination of where the threshold lies between the healthy and psychopathological ranges of specific symptom presentations.

The difficulty and inherent arbitrariness of assigning a diagnostic threshold for mental disorders are widely agreed upon and not conceptually controversial. Nonetheless, there is ongoing debate regarding the definition of mental disorder itself. Wakefield (e.g., 1992, 2007) has been a primary proponent of the view that to be labeled a disorder, an abnormal health condition must include an element of "harm" (e.g., personal distress or sociocultural difficulty, impairment, or disadvantage). Others have criticized this view for a number of reasons, including its limited practical utility in clinical decision making (Jablensky, 2007). Moreover, in general medicine, the degree to which signs and symptoms are distressing or impairing typically is considered extrinsic to the diagnostic process per se, although it may play a key role in determining treatment. Down syndrome and cataracts are examples of health conditions that are diagnosed without regard for the presence or amount of distress or psychosocial dysfunction.

Abstract debates about defining mental disorder aside, *ICD-11* and *DSM-5* still must meet their users' need to decide such things as who should be counted as having a particular disorder in national health statistics and who should be eligible to receive and be covered financially for a particular type of heath service. In fact, determining "caseness"—whether or not a person has a particular condition—explicitly involves setting a threshold between disorder and nondisorder, and is perhaps the most fundamental requirement of these systems. Consistent with Wakefield's view, classifications of mental disorder that are intended to guide determinations of eligibility for services or treatment decisions often have attempted to resolve the difficulties inherent in setting diagnostic thresholds by requiring that symptoms and signs be associated with clinically significant distress or impaired psychosocial functioning, a solution typically referred to, especially in relation to DSM, as the *clinical significance criterion* (note that this criterion implicitly acknowledges the presence of these symptoms and signs in the general population and their continuity with normal variation). We discuss the somewhat different stances that *ICD-11* and *DSM-5* have taken regarding this issue in their respective sections below.

As for RDoC, it is just as agnostic to defining mental disorder as it is to current diagnostic categories. By providing a framework for the exploration of functional processes that extend from the healthy to the pathological range, it aims to provide empirical data for establishing caseness in the long term rather than positing thresholds at this time.

Multidimensionality. There are a few mental disorders that essentially consist of a unidimensional symptom, such as trichotillomania, the primary symptom of which is recurrent pulling out of one's hair, resulting in hair loss, despite repeated attempts to decrease or stop. However, as discussed, most mental disorders are multidimensional, composed of multiple emotional, cognitive, and behavioral dimensions, many of which are shared across disorders, although some are unique. Further, disorder severity is an overarching dimension common to all disorders, although how it is manifested depends on individuals' particular problems. To diagnose a mental disorder, therefore, one must determine what kind, what combination(s), and "how much" of different aspects of a patient's clinical presentation are needed to constitute a particular disorder. Because most individuals with mental illness show a mix of symptoms, multiple thresholds typically need to be considered in the diagnostic process. To diagnose individuals with both mood disturbance and psychotic cognitions, for example, it is necessary to determine the sequence, relative duration, and severity of these two types of symptoms before choosing a diagnosis from among schizophrenia, mood disorder with psychotic features, or schizoaffective disorder. Again, in their respective sections below, we discuss the somewhat (but not radically) different approaches of *ICD-11* and *DSM-5* to dealing with specific aspects of mental disorders' multidimensionality.

Consequences of thresholds. Important boundaries in everyday life are often somewhat arbitrary—for instance, the boundaries between states, countries, and time zones; between ages at which people are and are not of legal drinking age or eligible for Medicare; between tax brackets,

and so forth. This arbitrariness (or semiarbitrariness) is widely recognized, and although we may not like a particular threshold and may even fight to change it, we generally accept the idea that thresholds are pragmatically necessary. In the case of mental disorder also, establishing thresholds between health and disorder is accepted as pragmatically necessary, particularly when a major reason for doing so is to identify those individuals who should receive mental-health services in the context of health systems with limited resources. However, regardless of their necessity, setting thresholds for mental disorder is highly consequential for multiple reasons. First, where thresholds are placed affects clinicians' and researchers' conceptualization of the relevant phenomena, clinical care, and knowledge generation. "Misplaced" boundaries may even interfere with optimal clinical care and research efforts.

Second, threshold placement is highly consequential because of the many social ramifications of a mental-disorder diagnosis. Diagnoses in general have consequences that are both positive (e.g., access to and payment for treatment; the right to "reasonable accommodations" under the Americans with Disabilities Act) and negative (e.g., social stigma; loss of ability to perform certain occupations). For example, children and adolescents with ASD are eligible to receive certain educational accommodations in the United States (Carter, Skimkets, & Bornemann, 2014; Corrigan, Druss, & Perlick, 2014), but many individuals who had been diagnosed with Asperger's disorder and their families were strongly opposed to the *DSM-5*'s inclusion of that disorder in the autism spectrum, at least partly because of the stigma associated with autism.

Third, diagnostic thresholds may also be highly consequential in forensic settings—for example, insofar as they may be used to establish "diminished capacity," which affects culpability for crimes; ineligibility for the death penalty as a result of intellectual disability; or need for civil commitment because of the high risk of reoffending associated with certain forms of mental disorder. Diagnostic thresholds also are a foundational aspect of epidemiology, with estimates of the incidence and prevalence of specific mental disorders used as a basis for policy and planning. Thus, from a public-health perspective, major changes in thresholds (e.g., via revision of a diagnostic manual) have considerable implications for policy and resource allocation because they affect prevalence estimates. For example, diagnostic thresholds are used to determine eligibility and reimbursement for health services, as well as for social and educational programs. If changing the diagnostic threshold for a particular disorder were to raise prevalence estimates from 5% to 25%, either considerably more resources would need to be directed toward its treatment or the level of severity required for service eligibility would need to be raised. Public-health agencies are also concerned about the continuity of data. Continuous use of the same thresholds facilitates interpretation of changes in prevalence estimates over time—for instance, assessments of the effectiveness of public-health campaigns to reduce teenage drug use that are based on changes in the prevalence of substance-use disorder among young adults.

Health professionals use either explicit or implicit thresholds to decide whether to assign a particular diagnosis or apply a particular treatment. Some treatments are relatively benign and unlikely to have negative side effects, such as cognitive-behavior therapy for anxiety disorders. Other treatments may have potentially dangerous side effects, necessitating the patient's full understanding of their risks and benefits, such as second-generation antipsychotic medications administered to adults with schizophrenia. The consequences of false positives (diagnoses assigned when a mental disorder is not actually present, which increase when lower thresholds are used) and false negatives (diagnoses not assigned when a disorder actually is present, which increase when higher thresholds are used) vary widely according to the specific circumstances surrounding particular diagnostic decisions.

We next discuss the different approaches that our three focal institutions take to setting mental-disorder thresholds, particularly with respect to the definition of mental disorder, its multidimensionality, and the consequential nature of mental-disorder diagnoses.

***Threshold issues in* ICD-11.** The *CDDG* for *ICD-10* mental and behavioral disorders define a mental disorder as "a clinically recognizable set of symptoms or behaviors associated in most cases with distress and with interference with personal functions" (WHO, 1992b, p. 11). "Clinically recognizable" is a critical phase in this definition because it is not difficult to think of sets of symptoms or behaviors that typically are associated with distress or interfere with personal functioning but are not considered mental disorders (e.g., bereavement following the death of a loved one or anxiety following a job loss). After considerable discussion, the IAG (2011) recommended retaining this definition for *ICD-11*, favoring its simplicity over the more complex definition used in *DSM-IV* (discussed in the Threshold Issues in *DSM-5* section), which was generally intended to encompass the same range of conditions.

This *ICD-10* and *ICD-11* definition is conceptually similar to the one subsequently adopted for *DSM-5* (APA, 2013), but the *DSM-5* definition is more elaborately worded and mentions exemptions for culturally approved responses to a common stressor or loss (e.g., bereavement) and social deviation. In the *ICD-11*, these

exemptions are made clear in the context of diagnostic guidelines for specific relevant disorders (e.g., bereavement reactions should not be mistaken for depression; sexual behaviors should not be diagnosed as paraphilic disorders solely because they are socially stigmatized) but are not mentioned in the overall definition of mental disorder. The difficulty inherent in distinguishing mental disorder from normal variation on the basis of symptoms and behaviors alone was described in the previous section, "Categories and Dimensions." With most conditions, there simply is no clear line that separates the two, so any threshold is to some extent arbitrary. Moreover, different thresholds may be appropriate for different purposes or in different settings. For example, in primary-care settings in developing countries, the diagnosis of depression may focus on identification of those cases with the most severe symptoms and greatest functional impairment (WHO, 2016c).

General approach. The *ICD-11*'s *CDDG* for mental and behavioral disorders is intended primarily for use by mental-health professionals in a wide range of settings around the world. WHO's IAG (2011) explicitly noted that diagnostic classification is only a part of patient assessment, stating that "the focus of the ICD is on the classification of *disorders* and not the assessment and treatment of *people*, who are frequently characterized by multiple disorders and diverse needs" (p. 91). Various additional factors must be considered in making decisions about patient care, such as associated disability, severity, risk of harm to self or others, exacerbating psychosocial factors, level of social support, and cultural factors, as well as the relative effectiveness of locally available treatments. Information about risk factors and protective factors may also be important in formulating population-based strategies.

Thus, rather than attempting to establish discrete, specific cutoffs through the use of criteria, the *CDDG* describes the essential features of each disorder, providing explicit guidance about the symptoms and/or characteristics that clinicians can reasonably expect to find in all cases of the disorder (First et al., 2015). This diagnostic approach is intended to enable more flexible application of clinical judgment and allow for cultural variation in symptom presentation. Although the *ICD-11*'s lists of essential features superficially resemble diagnostic criteria in their overall format, they generally do not contain the precise symptom counts, duration thresholds, or polythetic sets of items (stipulating that, e.g., a patient must have three of a list of four symptoms) that characterize the diagnostic criterion sets in *DSM-5* (First et al., 2015). Whereas DSM diagnoses generally attempt to set a precise threshold for every disorder to be applied across all settings, the *ICD-11 CDDG* uses more flexible language in an effort to conform to the way clinicians typically make psychiatric diagnosis—that is, by exercising clinical judgment regarding the context and consequences of the specific decision that is being made. The aim of the *ICD-11 CDDG* is to help clinicians identify the diagnostic formulation that is most likely to be useful in making treatment and management decisions.

This also is the goal of the proposed primary-care version of the *ICD-11*, which consists of 27 mental disorders judged to be clinically important in primary-care settings—both those that are commonly seen in such settings and less common but more severe mental disorders that are important to recognize in these settings. In this version of the classification, disorders are described in a way that reflects primary-care presentations to facilitate their identification by primary-care professionals. For most disorders, they identify a subset of the cases that would be identified by the application of the complete *CDDG* (Goldberg et al., 2016).

Need for fully specified thresholds. The approach to thresholds taken in ICD-11's *CDDG* and its primary-care version is consistent with WHO's goal of improving the identification of people with mental-health needs who currently, at a global level, are unlikely to receive appropriate care and even less likely to see a psychiatrist in their lives. This approach also is consistent with WHO's goal of reducing global disease burden, but it will not work for all purposes. For example, the *CDDG* could not be used as a basis for defining patient groups for research purposes that are homogeneous with respect to highly specified operational criteria, specifically because of its flexibility and the need for clinical judgment in its application. For studies in which this is important, a more fully operationalized adaptation of the guidelines would be needed, as had been provided for *ICD-10* by the Diagnostic Criteria for Research (WHO, 1993). To create an analogous version for the *ICD-11*, decisions would need to be made for every disorder about what specific number of which symptoms must be present over a specified period of time to warrant an individual's inclusion in an experimental group for the purpose of a particular study. These requirements will likely vary across studies (a point that echoes the RDoC rationale). However, to the extent that they may have some uniformity, a structured interview for identifying more specifically defined research groups for a range of diagnoses is currently being developed.

Likewise, the *CDDG* is not intended for application to the general population in nonclinical settings by lay interviewers as a part of epidemiological studies. This is not only because its administration requires

the exercise of clinical judgment, but also because it implicitly uses clinical populations in mental-health settings as its standard of comparison. In contrast, epidemiological studies may require the use of stricter or otherwise modified thresholds based on the psychometrics of particular cutoffs in relation to the community-level prevalence of particular symptoms (Finn, 1982; Kendler, Gallagher, Abelson, & Kessler, 1996; Vilagut, Forero, Barbaglia, & Aloso, 2016).

Functional impairment and distress. Compared with *ICD-10, DSM-IV* invoked the clinical significance criterion as a basis for distinguishing disorder from nondisorder in mental-disorder classification much more often. In fact, the criterion represented the most important source of differences between the two manuals (First, 2009). Per the clinical significance criterion, a person whose symptoms cause either distress or difficulty with functioning socially or in some other important way could be judged to have a mental disorder, whereas another person with the same symptoms who is not bothered or functionally impaired by them would not receive a diagnosis. The more frequent use of an explicit distress- and impairment-based criterion in DSM compared with ICD may be due to the DSM's emphasis on specified criteria to set thresholds for disorder; ICD's more general descriptions of disorder may allow clinicians greater flexibility in determining whether a disorder is actually present.

In practice, the distress component of the clinical significance criterion is typically easy to satisfy, given that various forms of psychological distress (e.g., anxiety) are themselves symptoms of many mental disorders and that individuals' requests for mental-health services are generally taken as direct evidence of their distress or their concern about the effects of their current mental health on their functioning. There even are a number of categories in which distress is a central component of the clinical phenomenology of the disorder. For example, most of the criteria for PTSD involve distress or avoidance of things that cause distress. Therefore, the distress criterion has practical implications that are especially relevant in epidemiological research among individuals who are not seeking mental health services, in that it provides a way to avoid assigning a diagnosis to individuals in the community whose symptoms are similar to those of individuals presenting in clinical settings but who deny being distressed by those symptoms. Whether one considers such cases to be false negatives (i.e., they actually should be assigned the diagnosis) or true negatives (i.e., not assigning the diagnosis is the correct decision) depends upon the purpose and goals of the assessment.

The issues related to functional impairment are even more complex. Recall that the definition of mental disorder in the *ICD-10 CDDG*, proposed for retention in the *ICD-11*, refers to functional impairment but does not require it. In fact, the *ICD-10 CDDG* states as a general principle that interference with the performance of social roles (e.g., at home or at work) should not be used as a diagnostic guideline. The major problem with functional impairment as a diagnostic requirement is that it is more properly conceptualized as an outcome of a mental disorder or other health condition, and conflating the disorder itself with its consequences creates a variety of problems—for example, in evaluating the effectiveness of treatments.

Üstün and Kennedy (2009) took an extreme position on this, insisting on a complete separation of functioning and disability from diagnostic thresholds or ratings of disorder severity. However, IAG (2011) noted that this ideal would be impossible to implement in *ICD-11* given the current state of science and clinical practice, because of the lack of direct, objective disease indicators for a wide range of mental disorders, as well as their continuity with normal variations in behavior. The advisory group recommended that the *ICD-11* avoid incorporating functional impairment as a part of diagnostic guidelines whenever possible and, for categories in which inclusion of functional impairment in the diagnostic guidelines is needed, set a clearly identifiable threshold between disorder and nondisorder.

The *ICD-11* approach reflects the perspective that if a disorder can be described adequately on the basis of its symptoms alone, without reference to distress or impairment, then it is more parsimonious to consider distress or impairment as consequences of the disorder, and, accordingly, these elements need not—indeed, should not—be included in its diagnostic criteria. The question in ICD is not whether disorders are associated with distress or impairment, because typically they are, but rather whether including distress or impairment as a diagnostic criterion alters what constitutes a "case" of a particular disorder. The development of assessments that conceptualize distress and functioning as outcomes rather than as inherent features of disorder is an area for future work (Robles et al., 2016).

Threshold issues in DSM-5

Thresholds in the definition of mental disorder. Beginning with *DSM-III*, the threshold between normality and disorder in the DSM has been based largely on specific symptoms, requiring either all or a subset of symptoms for diagnosis. In *DSM-III* and *DSM-III-R*, the specific number of symptoms required (e.g., five of nine for MDD; four of 13 for panic disorder) was typically based on clinical heuristics given the absence of clear research evidence. More recently, some diagnostic criteria have been established using a more substantial research base (e.g., for alcohol and other substance use disorders; Hasin

et al., 2013; Kerridge, Saha, Gmel, & Rehm, 2013). However, WHO has questioned the clinical and public-health utility of this approach (Poznyak et al., 2011), and some research findings challenge whether the current thresholds (e.g., two of 11 symptoms for alcohol use disorder) are optimal or too low (e.g., Mewton, Slade, McBride, Grove, & Teesson, 2011).

Diagnostic criteria for many disorders in *DSM-III* and *DSM-III-R* made implicit or explicit reference to clinical significance, but the assumption was that "careful specification of symptom criteria for each disorder would suffice in establishing a disorder threshold" (Narrow, Kuhl, & Regier, 2009, p. 88). However, unexpectedly high rates of mental disorders were found in general population surveys. Therefore, to reduce the concern that the manual overdiagnosed mental disorders, *DSM-IV* introduced the clinical significance criterion, which was typically worded ". . . causes clinically significant distress or impairment in social, occupational, or other important areas of functioning." The stated rationale for its inclusion was that it "helps establish the threshold for the diagnosis of a disorder in those situations in which the symptomatic presentation by itself (particularly in its milder forms) is not inherently pathological and may be encountered in individuals for whom a diagnosis of 'mental disorder' would be inappropriate" (APA, 2000, p. 8). The criterion's addition did reduce the rates of mental disorder in community surveys (Narrow, Rae, Robins, & Regier, 2002), but a number of problems remained (Narrow et al., 2009).

First, what constituted clinically significant distress or impairment was not defined, and *DSM-IV* simply acknowledged that "assessing whether the criterion is met . . . is an inherently difficult clinical judgment" (APA, 2000, p. 8). A second problem was that the scale in *DSM-IV* for assessing functioning, the Global Assessment of Functioning, intermingled symptom severity, social functioning, and assessments of dangerousness rather than considering these elements separately. Moreover, many "symptoms" in the diagnostic criteria themselves refer to psychosocial impairment (e.g., "often has difficulty organizing tasks and activities" is listed as a symptom of ADHD rather than a consequence of the disorder).

In part because of the goal of "harmonizing" the ICD and DSM systems, it was widely debated whether the clinical significance criterion should be eliminated in *DSM-5*. Wakefield (2007) continued to advocate for the importance of retaining it, whereas Üstün and Kennedy (2009) argued that *DSM-5* should adopt WHO's position that disorders (defined by symptoms and signs) and their resulting disability should be assessed separately, although they should be considered together to determine caseness (WHO, 2001). Hyman (2010) expressed the concern that if the definition of mental disorder includes the criterion that the symptoms must cause clinically significant impairment or distress, "it denies an appropriate clinical status to early or milder symptom presentations . . . [and] illogically confounds a severity measure with a symptom list" (pp. 164–165).

We currently have little understanding of how disability and distress arise in individuals with mental disorder, including the roles of individual symptoms, environmental factors, and other intrinsic factors not directly related to specific symptom criteria. Further, the measurement or specification of the core symptoms of many disorders is lacking. For example, many of the criteria for ADHD reflect consequences of inattention, hyperactivity, and impulsivity (e.g., "makes careless mistakes") rather than direct measures of these domains because either there currently is no reliable and valid means of directly assessing the core symptoms or the assessments are not feasible in routine clinical practice. As another example, the frequency, intensity, and duration of schizophrenia symptoms (delusions, hallucinations, disorganized speech, grossly disorganized or catatonic behavior, negative symptoms) have not been precisely specified; *DSM-5* also requires a marked decline in "level of functioning in one or more major areas, such as work, interpersonal relations, or self-care" (APA, 2013, p. 99) for diagnosis.

Use of the clinical significance criterion means that a patient's report of significant distress or significantly affected daily functioning becomes the de facto threshold of many, if not most, mental disorders. Nonetheless, there was considerable resistance from the *DSM-5* work groups to remove the criterion. A frequent concern was that without it, there would be inadequate thresholds between mild forms of the disorder and nondisorder, leading to overdiagnosis of mental disorders and, consequently, increased public perception that the *DSM-5* pathologizes the emotional ups and downs of everyday life (e.g., Horwitz & Wakefield, 2007). In part, the clinical significance criterion was deemed important because of the DSM developers' commitment to a criterion-based diagnostic approach that has been regarded as useful in increasing reliability. Reliability, in turn, was considered important for not only clinical but also practical reasons, such as those relating to forensic settings, reimbursement, and research. The ICD *CDDG's* use of more prototypic conceptualizations to define disorders may allow clinicians greater flexibility in determining whether the disorder is present without an explicit clinical significance criterion. Thus, the uses of the classification systems also have a role in shaping them.

Ultimately, *DSM-5* implemented a compromise. The definition of mental disorder used in *DSM-III* through

DSM-IV-TR was modified to emphasize that disorders reflect dysfunctional mental processes and are "*usually associated with* significant distress or disability in social, occupational, or other important activities" (APA, 2013, p. 20; emphasis added), substituting "are usually associated with" for *DSM-IV*'s "causes." Effectively, this brings the *DSM-5*'s definition more in line with the definition used in *ICD-10* and the forthcoming *ICD-11*. Moreover, individual work groups were allowed to decide whether to retain or remove the clinical significance criterion. Whereas some did opt to eliminate it, most disorders in *DSM-5* retain the criterion. Therefore, *ICD-11* and *DSM-5* have approached this same issue from opposite directions, with *ICD-11* including an impairment requirement only when it is deemed necessary and *DSM-5* eliminating it when possible. As a result, the two systems have become more similar, although not identical, in the way that they describe distress and disability as required features for particular diagnoses.

Thresholds and multidimensionality. The multidimensionality of mental disorder is reflected in some *DSM-5* diagnoses' use of subcriteria. For example, the multidimensionality of ADHD is apparent in its very name, which conveys its two primary criteria, each of which has nine subcriteria, with a diagnostic threshold of six items (five for those over the age of 17). Thus, a child or adolescent might receive an ADHD diagnosis by having six or more inattentive symptoms (but fewer than six hyperactive/impulsive symptoms), six or more hyperactive/impulsive symptoms (but fewer than six inattentive symptoms), or six or more symptoms of each type. It also is important to note that the nine criteria on each list are not fully independent from one another but are intended to represent possible behavioral manifestations of an underlying dimension. The two types of symptoms commonly co-occur and may shift over time within individuals; thus, including them in a single diagnostic criterion set is intended to avoid comorbid diagnoses and unhelpful diagnostic changes over time for patients.

In some cases, criteria have different numbers of subcriteria and thresholds. For example, a diagnosis of PTSD in adults requires the following:

1. One or more of five intrusion symptoms (e.g., nightmares, flashbacks),
2. One or both cognitive or behavioral avoidance symptoms,
3. Two or more of seven possible alterations in cognitions (e.g., memory loss) or mood (e.g., anhedonia), and
4. Two or more of six arousal symptoms (e.g., sleep disturbance) or reactivity symptoms (e.g., exaggerated startle response).

This level of diagnostic flexibility has both benefits and costs: It accommodates a wide variety of symptom presentations, but it does so at the associated cost of increasing within-diagnosis heterogeneity and both frequency and variation in overlap with other diagnoses. Again using PTSD as an example, Galatzer-Levy and Bryant (2013) calculated that there were 636,120 ways to meet *DSM-5* criteria for PTSD. Moreover, Gallagher and Brown (2015) found that depending on which particular PTSD criteria individuals met, they were more likely also to meet criteria for a depressive disorder, an anxiety disorder, or both. In sum, as a result of the multidimensionality of PTSD and the use of specific thresholds for each of its dimensions, patients diagnosed with PTSD can present with a great variety of symptoms and patterns of comorbidity.

Partly in response to this problem, *ICD-11* has proposed a narrower operationalization of PTSD characterized by the required presence of three core symptoms (Maercker et al., 2013), which is being tested in a variety of studies (e.g., Danzi & La Greca, 2016; Hansen, Hyland, Armour, Shevlin, & Elklit, 2015). Whether or not the *ICD-11* proposal will ultimately help to reduce diagnostic heterogeneity for PTSD, within-category heterogeneity that results from disorders' multidimensionality remains a significant challenge for classification systems to address.

Consequences of thresholds. It is widely acknowledged that specific *DSM-5* thresholds are often somewhat arbitrary and should be viewed with some flexibility in their application. For example, an individual whose symptoms do not fully meet the criteria for a diagnosis at a given time may nonetheless have a need for treatment, either to prevent the development of a more severe condition or to address urgent symptoms such as suicidal thinking. Of importance to research on the causes of mental disorders, individuals who are "subthreshold" for a disorder may possess genetic and neurophysiological characteristics similar to those of individuals (e.g., family members) whose presentations are at or above a diagnostic threshold. The DSM has long attempted to accommodate subthreshold presentations through the use of NOS diagnoses in *DSM-III, DSM-III-R*, and *DSM-IV*, which became "other specified" and "unspecified" diagnoses in *DSM-5*. It also is widely acknowledged, albeit tacitly, that higher or lower diagnostic thresholds are needed for specific purposes (e.g., administrative, forensic, treatment related). Moreover, the scientific argument that different diagnostic thresholds may need to be specified based on the setting in which they are used has some empirical grounding (Finn, 1982).

However, because of the complexity of implementation, the reification of existing thresholds by U.S.

regulatory and research-funding agencies, and concerns about a breakdown in the "common language" that the DSM has promoted for decades, implementing different thresholds did not gain much traction and was not seriously considered in *DSM-5*'s development. This marks a contrast between that manual and the ICD, in which thresholds differ among the *CDDG*, the primary-care version, and the Diagnostic Criteria for Research. As with previous editions of the DSM, the *DSM-5* work groups instead implemented a single cut point for each diagnosis based on their evaluation of the available evidence.

The evolution of more reliable diagnostic systems via specific-criterion approaches was the basis for an explosion of knowledge about psychopathology in the years following *DSM-III*'s publication. Nonetheless, the near-ubiquitous use of the DSM's specific criteria and thresholds limited the types of research questions asked. Of course, researchers could measure and analyze additional relevant dimensions, but as long as there was an expectation that DSM diagnoses would be used in NIMH-funded research, alternative approaches were constrained. Thus, the use not only of the DSM's specific criteria but also its semiarbitrary thresholds had a huge influence on psychopathology research—for both good and ill.

In addition, the DSM is used in psychopathology training of mental-health professionals across many disciplines, most research establishing empirically based treatments is conducted using specific DSM diagnoses, and the manual is used widely in administrative and billing systems in the United States and some other countries (e.g., The Netherlands). As a result, DSM thresholds have had a strong influence on clinicians' approach to patients and their treatment, although many clinicians find the highly specified thresholds of DSM diagnoses clinically limiting and have developed ways to use the manual flexibly—for example, they may use diagnoses for administrative purposes but implement treatment on the basis of individual patients' symptom profiles. Nonetheless, there still is widespread acceptance among clinicians of DSM disorders as nonarbitrary (i.e., real or valid), at least quasi-discrete natural entities.

With both the research and clinical communities using the DSM system and its specific thresholds, the lay public has also widely embraced it, in large part because it provides reassuring clarity that the problems with which they or their loved ones suffer are "real" disorders and not "all in their heads," and because researched treatments are available for many disorders. The media have also increasingly featured articles and news pieces about specific DSM diagnoses, further cementing the erroneous view that they are discrete, natural entities with nonarbitrary boundaries that are the same all over the world. Such articles ignore the fact that the vast majority of *DSM-5*–based research has been conducted in English-speaking countries or Western Europe. In contrast, we believe that advancing the more nuanced view that *DSM-5*'s diagnostic thresholds are semiarbitrary will foster public understanding of mental disorders and help reduce the stigma that follows upon the false belief that there is a clear line between those with mental disorders and "the rest of us." This perspective is conceptually consistent with that taken by *ICD-11*.

Threshold issues in RDoC. The RDoC approach to thresholds follows directly from a consideration of their consequences. As noted, the necessity of organizing research designs around DSM or ICD categories has constrained the kinds of research that can be conducted, particularly with respect to individuals with symptoms that fall below current thresholds for diagnosis. There certainly is clinical utility in setting at least some thresholds, but the problem for researchers is to determine the particular kinds of criteria to use for setting thresholds (e.g., various symptoms or types of functioning) and where to set thresholds to facilitate empirically based decisions (e.g., whether to treat, hospitalize, or prescribe medication). These types of research questions constitute a critical part of the RDoC framework. An important aim is to support research that will provide systematic information about the range of mental functioning and distress from typical levels through various levels of impairment, and about asymptomatic risk states indexed by biomarkers that may precede symptoms, such as cortical thinning (e.g., Cannon et al., 2015). Relevant findings could be used to inform future revisions of the DSM and ICD on how and where to set treatment thresholds, including whether to establish more than one treatment range (e.g., mild, moderate, severe) and offer different treatment recommendations for each range.

This aim of RDoC has two implications for research. First, the emphasis upon particular functional constructs (e.g., fear, cognitive functioning) that can be measured by various means across different RDoC units (e.g., physiological responses, observed behaviors, subjective reports) is intended to lay the groundwork for a strongly quantitative, psychometrically sound approach to assessment. Second, taking a dimensional approach will often necessitate research designs that involve an examination of psychopathology based upon continuous rather than categorical variables. For instance, rather than a design that involves patients with two subcategories of major depression (e.g., mild and severe) and controls, an RDoC design might include research participants with a range of mood or anxiety

symptoms (including those with minimal or no symptoms) to explore how changes in neural reward-system activity relate to reward-related behavior in a laboratory setting, or to the correlation between reward-related behavior and cognitive performance or clinical mood states. Thus, at the current time, RDoC does not have a strong position about thresholds as they apply to contemporary clinical practice. However, a major aim of RDoC is to promote a research literature that will help clinicians in the future provide more sensitive assessments that, in turn, will lead to improved ways to determine thresholds (or ranges) for empirically based diagnosis, prevention, and treatment interventions.

Threshold issues: summary. Once again, we see that the public-health and clinical-use purposes shared by ICD and DSM have led them to adopt similar—although not identical—approaches to defining and using thresholds in mental-disorder diagnosis, whereas RDoC can take a more flexible approach. That is, RDoC-based research can either set one or more thresholds if doing so is important for a particular research purpose, or not address threshold issues if they are not relevant for research purposes or applications in clinical settings or health policy. A long-term RDoC goal is to provide information that will facilitate setting thresholds in diagnostic systems of mental disorder. This goal includes providing for the possibility that various thresholds will be needed for different purposes. To analogize from general medicine, research has informed the setting of various thresholds for the treatment of blood pressure and obesity (i.e., at lower levels, diet and exercise may be sufficient, whereas higher levels may require more "aggressive" treatment). However, at present, reasoned clinical judgment is still required in most circumstances.

Comorbidity

For a person to have two or more disorders at the same time—that is, coexisting or comorbid disorders—is not conceptually problematic. Examples in physical medicine abound: A person with carpal tunnel syndrome may also have the flu, and another with a herniated disk may also have appendicitis. In such cases, the two disorders have distinct signs, symptoms, and etiologies and can be considered random co-occurrences. Comorbid disorders also may be linked while still being clearly distinct; such phenomena are often said to be "complications of" or "secondary to" the disorder that was present first. Again using examples from physical medicine, kidney disease is a common complication of diabetes, and ear infections are a common complication of measles, but each represents a distinct health condition with a distinct treatment.

The comorbidity seen in mental illness was initially presumed to follow one or the other of these medical models, particularly the complication model. However, beginning around 1990, and based on the widespread use of *DSM-III* and *DSM-III-R* in research, a plethora of findings revealed that comorbidity in mental disorders is the rule rather than the exception, that pure and uncomplicated symptom presentations are relatively rare, and that some putatively distinct disorders may be better described as different aspects of a single disorder, or as having shared risk factors. An example of putative comorbidity involves individuals with "double depression" (Keller & Shapiro, 1982): recurrent major depressive episodes that punctuate sustained depressive symptoms that are significant but below the diagnostic threshold for a major depressive episode. It seems unlikely that such individuals have two distinct mood disorders, but capturing this presentation in ICD requires two diagnoses: recurrent depressive disorder and dysthymic disorder (further discussed in the following section, "Comorbidity Issues in *ICD-11*"). The DSM's approach is even more complex, involving the use of two diagnoses to cover the major depressive episode and the persistent depressive disorder, plus additional specifiers for the persistent depressive disorder.

Research on rampant comorbidity also revealed that much mental-disorder comorbidity was not due to random co-occurrence. Rather, there were systematic patterns to comorbidity. To date, analyses of almost a dozen distinct data sets with a combined sample size of almost 100,000 individuals between the ages of 6 and 65 have converged to indicate that DSM and ICD mental-disorder diagnoses can be organized hierarchically (see Kotov et al., 2017, for a synthesis of this literature). This structure of these mental-disorder diagnoses has a broad, very general factor of psychopathology at its apex (as mentioned briefly in the section "Categories and Dimensions"), followed by at least three broad dimensions of disorders at the next level, which correspond to three of the four dimensions of symptoms identified by Markon (2010): internalizing disorders, in which individuals' subjective experience of distress is a major component (e.g., depressive disorders, GAD); externalizing disorders, in which the primary manifestations are typically observable behaviors (e.g., alcohol and drug dependence, conduct disorder); and thought disorders or cognitive disturbance (e.g., schizophrenia-spectrum disorders, psychotic mood disorders).

Like Markon's symptom-level dimensions, each higher level dimension divides into smaller dimensions that are based on subsets of disorders that more frequently co-occur, which yields lower levels of the hierarchy. For instance, the broad internalizing dimension

divides into two more specific dimensions (Krueger, 1999; Slade & Watson, 2006; Vollebergh et al., 2001; Watson, 2005): one, typically labeled "distress" or "anxious misery," includes depressive disorders and GAD; the other, labeled "fear," includes panic disorder and phobias. Genetic research has indicated that the comorbidity of particular disorders (e.g., MDD and GAD) may be explained entirely by shared genes and that differences between them may be due to individuals' unique life experiences (see Mineka, Watson, & Clark, 1998, for review) and broad sociocultural trends. As discussed in the section "Etiology," however, we lack a detailed explanation of how mental disorder arises from these various factors.

Research also has revealed a strong correlation between comorbidity and severity, such that the likelihood of comorbidity is substantially higher when illness is more severe (L. A. Clark et al., 1995). The general psychopathology dimension at the apex of diagnostic structural analyses, dubbed the p factor (analogous to the g factor of general intelligence; Caspi et al., 2014), provides a possible explanation for this finding. If all mental disorders share a common dimension, then it makes sense that that the stronger this general factor is in an individual, the more ways in which it will be manifested, and the more severe these various manifestations will be. Of the three second-level dimensions of psychopathology, the p factor related most strongly to thought disorder and cognitive disturbance; importantly, it also was associated with increased impairment in daily functioning, greater familiality, worse developmental histories, and more compromised early-life brain function, consistent with its being a general dimension that marks severity.

Evidence of such supraordinate dimensions—the p factor and of its subordinate internalizing, externalizing, and thought-disorder/cognitive-disturbance factors—has many implications for understanding, classifying, treating, and perhaps even preventing mental illness. For example, the p factor's association with both compromised early-life brain function and thought disorder/ cognitive disturbance suggests that the level of functioning of certain of one's basic brain processes may affect one's level of susceptibility to a wide variety of mental illness. Thus, it may be more fruitful to search for common causes of all or major groups of mental illness than to use E. Robins and Guze's (1970) principles for establishing the validity of distinct clinical syndromes. The unified protocol for transdiagnostic treatment of emotional disorders (Barlow et al., 2011) illustrates this notion, emphasizing the commonalities in phenomenology, risk factors, and treatment response across a wide range of disorders, including all anxiety and mood disorders as well as PDs and many somatoform and dissociative disorders. This treatment is receiving increasing research support for its short- and long-term efficacy in reducing symptoms and distress and for increasing quality of life (e.g., Bullis, Fortune, Farchione, & Barlow, 2014; Gallagher, Sauer-Zavala, et al., 2013; Lopez et al., 2014).

Neuroticism/negative affectivity is central in Barlow's unified protocol, and Lahey (2009) noted that this personality trait "is a robust correlate and predictor of many different mental and physical disorders [and] of the quality and longevity of our lives" (p. 241). He further went on to say that "knowing why neuroticism predicts such a wide variety of seemingly diverse outcomes should lead to improved understanding of commonalities among those outcomes and improved strategies for preventing them" (p. 241). Despite their breadth, neither Barlow's unified protocol nor neuroticism/negative affectivity encompasses all of psychopathology, so additional research is needed to determine, for example, whether other commonalities (e.g., dysfunction in certain basic brain processes) have implications for an even wider range of psychopathology or whether a different set of brain processes has implications for the treatment of another subset of mental disorders.

In sum, data on comorbidity clearly indicate that very detailed, operational definitions of mental disorders, such as those in recent versions of the DSM, are overly specific. Of course, those data also indicate that current classification systems do at least partially reflect empirical patterns. If they did not, research would not have revealed a hierarchical structure; rather, it would have found that all symptoms and disorders were equally interrelated. As with other issues, and again because they have diverse purposes and constituencies, the three institutions discussed in this article tackle these challenges of comorbidity in different ways, which we now explore.

***Comorbidity issues in* ICD-11.** As mentioned earlier, the first version of ICD to include a classification of mental disorders—the *ICD-6*, approved by the World Health Assembly in 1948—grouped mental disorders into three classes: psychoses, psychoneurotic disorders, and disorders of character, behavior, and intelligence. Psychoses were characterized by gross distortions of emotional and mental functioning, such as delusions and hallucinations, and corresponded to conditions viewed as constituting "insanity" or "madness." Psychotic conditions included severe mental disorders such as schizophrenia, manic-depressive reaction, and involutional melancholia (a very severe form of depression) and could be caused by organic processes (e.g., as in dementia) or by substances such as alcohol or cocaine. Psychoneurotic disorders

were viewed as milder mental disorders characterized by symptoms such as anxiety, depressed mood, or somatization that did not involve major distortions in perceptions and experience of reality. Neurotic symptoms could occur in the context of psychoses, in which case they were considered to represent lesser manifestations of the more severe underlying disorder and not independent phenomena. In contrast, symptoms such as delusions, hallucinations, and other gross distortions of mental functioning were not characteristic of psychoneurotic disorders. In other words, these phenomena were viewed as hierarchical: A person with a psychotic disorder could not also be diagnosed as having a neurotic disorder. The third group of disorders, however, which included alcohol or other drug addiction, "mental deficiency" (disorders of intellectual development in *ICD-11*), and PD, corresponded to entities that were independent of the psychotic/neurotic axis and could coexist with other forms of mental disorder. By the time *ICD-8* was approved in 1965, substance-related disorders and PDs had been moved to an expanded neurotic-disorders grouping, with only "mental retardation" remaining in the third grouping. In *ICD-9*, approved in 1975, a distinction was made between organic psychotic disorders (those due to dementia, substance use, or delirium) and psychoses due to primary mental disorders, but the broad *ICD-8* groupings were otherwise preserved. Throughout this time, the idea that symptoms of milder disorders were entirely attributable to more serious disorders and, therefore, diagnostically irrelevant remained the dominant view. Comorbidity was not a major issue for the field.

A major explosion in diagnostic classes—from four to 10—occurred with *ICD-10*, approved in 1990. Even so, some of *ICD-10*'s diagnostic classes represented clinically unhelpful conglomerations of disparate phenomena, made necessary by the limitations imposed by *ICD-10*'s categorical system. For example, the section "Behavioural syndromes associated with physiological disturbances and physical factors" included eating disorders, sleep disorders, and sexual dysfunctions, which have very little overlap in terms of signs, symptoms, etiology, or treatment. A hierarchical model of mental disorders was much more difficult to conceptualize in the context of this expanded array of options.

To preserve aspects of the hierarchical model, the *ICD-10 CDDG* contains many rules that were intended to assist clinicians in making choices among diagnoses, to reduce comorbidity rates, and to maximize parsimony in accounting for presenting symptoms. For example, per the *ICD-10 CDDG*, for patients presenting with symptoms of both depressive and anxiety disorders, depressive diagnoses should be given diagnostic primacy over anxiety diagnoses if the depression preceded the onset of the anxiety. Likewise, GAD should not be diagnosed in the presence of a depressive episode, a phobic anxiety disorder, panic disorder, or obsessive-compulsive disorder. (These hierarchical rules are akin those implemented in *DSM-III* for similar reasons.)

Other diagnostic formulations conveyed a theoretical position about relations between sets of symptoms. For example, the *ICD-10 CDDG* indicated that agoraphobia and panic disorder should not be diagnosed together. Rather, agoraphobia included the qualifiers with or without panic disorder. Several new "combination" categories, such as schizoaffective disorder and mixed anxiety and depressive disorders, were introduced to avoid forcing a diagnostic choice for or assigning multiple diagnoses to a single presentation. Sometimes these decision rules or diagnostic conventions were tied to explicit clinical rationales (Maj, 2005), but usually they were theoretically based and lacked specific empirical support. These rules were also sometimes difficult to follow and logically inconsistent (Kogan et al., 2016), and they were increasingly ignored over time. Moreover, they came to be seen as conceptually incompatible with a criterion-based approach to classification. If disorders were determined by the presence of a particular number of specified symptoms, and this was a valid way of defining them, why would they not be considered present because of the contemporaneous presence of another condition? (*DSM-III*'s hierarchical rules were largely abandoned in *DSM-III-R* for similar reasons.)

These and other factors (which primarily involved health conditions other than mental disorders) contributed to the use of multiple diagnostic codes to describe complex clinical presentations, which is now the globally dominant ICD (and DSM) convention in diagnostic coding and reporting. Contemporaneously, a model in *ICD-10* for identifying primary and related disorders was universally unpopular and largely ignored, and has been abandoned in *ICD-11*. Therefore, the assignment of multiple diagnoses is often the best way to capture the complexity of clinical presentations and may be viewed in part as a marker of disorders' severity. We mentioned earlier the problem of "double depression," the combined diagnosis of recurrent depressive disorder and dysthymic disorder in *ICD-10*. The *ICD-11* Working Group on Mood and Anxiety Disorders considered alternative ways to address this issue but ultimately chose to leave the two codes as they were, concluding that the assignment of two codes was the most accurate way of describing this clinical presentation even though the working group did not consider individuals with both diagnoses to have two independent mood disorders.

Some psychopathology researchers are intellectually offended by the inelegance of a two-code approach to

what they view as a single mood disorder, but the fact is that at the level of brain mechanisms, we actually do not know whether the chronic state and the periodic episodes of exacerbated symptoms represent two processes or one. Still, a conceptual and scientific problem is introduced when these two codes are interpreted as representing separate, objective disease entities rather than as capturing a particular presentation, especially when mental-health policies and research policies are structured on this basis (van Os, 2016). At a pragmatic level, an individual whose condition is characterized by both of these diagnoses is likely to require different, more complex, or more intensive interventions than an individual whose condition is described by either diagnosis alone.

The *ICD-11 CDDG*, therefore, adopted a relatively pragmatic approach to the issue of comorbidity that views the assignment of multiple diagnostic codes as sometimes necessary to describe complex clinical conditions accurately, but does not intend this as a scientific statement about the independence of reified co-occurring disease entities. This partly explains why the term "co-occurrence" rather than "comorbidity" is used in the *ICD-11*. The proposed *ICD-11 CDDG* does specify some exclusion rules, but many fewer than were in *ICD-10*, and those that are included tend to be based on explicit overlap of diagnostic features rather than on theoretical considerations. For example, the proposed diagnostic guidelines for adjustment disorder note that it is common for episodes of other mental disorders to be triggered or exacerbated by stressful life experiences and that a diagnosis of adjustment disorder should not be assigned if the symptoms are sufficiently severe or specific to meet the diagnostic requirements for another mental disorder, such as PTSD or a depressive or anxiety disorder. Likewise, the guidelines state that developmental language disorder with impairment of pragmatic language should not be diagnosed in the presence of ASD. This is because the pragmatic language impairment can be considered part of the characterization of ASD in the context of ASD's broader pattern of symptoms.

The proposed *ICD-11* diagnostic guidelines contain a section called "Boundary With Other Disorders" for each category (First et al., 2015) that describes the basis on which a given condition should be distinguished from common differential diagnoses and the circumstances under which it may be appropriate to assign co-occurring diagnoses. Sometimes, this decision is based on the clinical utility of an additional diagnosis in the context of a particular case and explicitly left to the judgment of the clinician. For example, the diagnostic guidelines for stereotyped movement disorders indicate that although repetitive and stereotyped motor movements can be a characteristic feature of ASD, assignment of both diagnoses may be warranted if the stereotyped motor movements constitute a separate focus of clinical attention (e.g., because of the potential for self-injury). Likewise, the diagnostic guidelines for complex PTSD acknowledge that characteristic symptoms of that disorder related to affect dysregulation, distorted view of the self, and difficulties in sustaining relationships may be similar to those observed in some individuals with PD. When individuals meet the diagnostic requirements for both disorders, decisions about whether to assign both diagnoses should be based on considerations of clinical utility.

At the same time, the developers of the *ICD-11 CDDG* have taken specific steps to reduce problematic artifactual comorbidity. One example is in the classification of PDs, described previously. Comorbidity among supposedly distinct PDs and, conversely, the high frequency of such diagnoses as "other specific PD" and "PD, unspecified" in previous ICD versions were glaring problems—first, because a clear majority of individuals diagnosed with PD either meet criteria for two or more PDs or do not meet the criteria for any one, specific PD (thus meeting the criteria for one of the above nonspecific alternatives), and second, because individuals have only one personality,[10] so PD comorbidity does not make conceptual sense. In addition, there is strong evidence that there is a general factor in PD (e.g., Sharp et al., 2015; Trull, Vergés, Wood, & Sher, 2013; Wright, Hopwood, Skodol, & Morey, 2016) and that the most important element in PD is its severity (e.g., Tyrer et al., 2011; Tyrer et al., 2015).

As described earlier in the section "Categories and Dimensions in *ICD-11*," the *ICD-11* proposal for PD reflects this evidence by offering a single PD diagnosis divided into three subcategories marked by different levels of severity, plus a subthreshold category termed "personality difficulty." This approach is fundamentally different from that of the *ICD-10*, which listed eight specific PDs, plus "other specific PD" and "PD, unspecified." As also described previously, the proposed restructuring allows any of the *ICD-11* diagnoses to be characterized further as prominently featuring one or more of five personality-trait dimensions, as well as providing a borderline qualifier. This formulation facilitates diagnosis of all individuals with personality pathology and allows clinicians to describe the nature of that pathology either quite simply (e.g., as "moderate PD") or in considerable detail, using whatever combination of prominent trait dimensions and/or the borderline qualifier best characterizes the person.

Across the *ICD-11*, additional features are being built into the classification, particularly for use with electronic coding applications. These features are intended

to enable conceptual relations between different parts of the classification with the goal of reducing the proliferation of additional codes and artifactual comorbidity. The first of these is *multiple parenting*, which allows a particular code or set of codes to appear in more than one place. For example, the diagnostic entities that represent the various etiologies for dementia are listed in both the "Diseases of the Nervous System" chapter and the "Mental and Behavioural Disorders" chapter, with the same code in both chapters. This obviates the need to create a partially redundant set of codes to represent the psychiatric or behavioral aspects of dementia while conveying that dementia is a legitimate part of the scope of practice of mental-health professionals. A second feature is *cluster coding*, which allows codes from different parts of the *ICD-11*, such as codes representing the multiple manifestations of conditions such as diabetes mellitus in different body systems, to be linked so that they are understood as being different aspects of the same underlying condition in a particular individual. Although we have not progressed to this point in our understanding of mental disorders, eventually it should be possible to link codes that represent the symptomatic manifestations of an underlying causal factor such as substance abuse or of a more general dimension such as externalizing or negative affectivity.

***Comorbidity issues in* DSM-5.** As mentioned previously, around the time *DSM-III* was published, comorbid mental disorders were typically thought to be "ordered," such that one was a complication of the other. On the basis of available information and clinical judgment, decisions were made in *DSM-III* regarding which disorders were more likely to be complications of others. The final criterion for approximately 60% of disorders in *DSM-III* was "Not due to another mental disorder, such as . . ." (Boyd et al., 1984), followed by a list of disorders that presumably might be the "primary" disorder of which the disorder being considered was a complication. For example, a criterion of GAD was "Not due to another mental disorder, such as a Depressive Disorder or Schizophrenia" (APA, 1980, p. 233). The manual offered neither a rationale to justify these hierarchical exclusion criteria nor guidance as to how to apply them, stating only that the phrase meant that the diagnosis was not to be given "if the characteristic symptoms are caused by [the other] disorder" (APA, 1980, p. 32).

However, clinicians and researchers alike found it difficult to determine whether one disorder was "due to" another, and not long after the release of *DSM-III*, researchers began to publish the results of studies that ignored the exclusion criteria and revealed widespread comorbidity (e.g., Boyd et al., 1984). Many exclusion criteria were eliminated in *DSM-III-R* (APA, 1987), thus permitting more comorbid diagnoses, and an explosion of research on comorbidity followed. Whereas from 1980 to 1989, 110 articles and books with "comorbidity" as a keyword were published, in the ensuing two decades, the corresponding figures were 3,808 and 14,057, respectively (values based on a PsycINFO search conducted November 9, 2017).

This research belied the notion that DSM disorders were distinct entities, and the challenge of comorbidity is frankly acknowledged in *DSM-5*:

> Because the previous DSM approach considered each diagnosis as categorically separate from health and from other diagnoses, it did not capture the widespread sharing of symptoms and risk factors across many disorders that is apparent in studies of comorbidity. Earlier editions of DSM focused on excluding false-positive results from diagnoses; thus, its categories were overly narrow. . . . Indeed, the once plausible goal of identifying homogeneous populations for treatment and research resulted in narrow diagnostic categories that did not capture clinical reality. . . . The historical aspiration of achieving diagnostic homogeneity by progressive subtyping within disorder categories no longer is sensible. (APA, 2013, p. 12)

At the same time, the *DSM-5* Task Force aimed "to better fill the need of clinicians, patients, families, and researchers for a clear and concise description of each mental disorder organized by explicit diagnostic criteria" (APA, 2013, p. 5) and recognized that "it is premature scientifically to propose alternative definitions for most disorders" (p. 13). Nonetheless, the Task Force strongly endorsed efforts to reduce diagnostic comorbidity through several lines of investigation. The first was the recognition of cross-cutting symptoms—frequently occurring, frequently treated symptoms (e.g., sleep problems, anxiety). Their assessment was an alternative to assigning multiple comorbid diagnoses for treatment planning, justification of treatment to payers, and outcome tracking. Cross-cutting symptoms that need treatment but are clearly subordinate to a primary diagnosis can be documented without the need to make a comorbid diagnosis, which previously had often been a NOS diagnosis. For example, a clinician could add insomnia of moderate severity to the problem list for a patient with schizophrenia without needing to justify the treatment of insomnia with a diagnosis of insomnia disorder, other specified insomnia disorder, or unspecified insomnia disorder.

Another major step taken by the *DSM-5* Task Force in relation to comorbidity was to re-examine how

disorders were grouped into chapters. The chapter structure of earlier versions of the DSM was based primarily on clinical phenomena: Disorders with primary symptoms relating to mood, anxiety, and psychosis each had their own respective chapters. This symptom-based structure made sense when research findings were scarce, and it became ingrained in the provision of clinical services and in research. For example, on the basis of the diagnoses contained in the *DSM-III* and *-IV* "Anxiety Disorders" chapter, anxiety clinics might have included patients with obsessive-compulsive disorder, the primary symptoms of which are quite distinct from those of other anxiety disorders, but not patients with sexual aversion disorder, even though they exhibit significant underlying phobic and panic symptoms associated with anxiety disorders (Brotto, 2010).

Although these kinds of groupings made some sense for the provision of targeted treatment services, the *DSM-5* Task Force was faced with emerging evidence that the existing symptom-based chapter structure was not entirely valid. The Diagnostic Spectra Study Group was formed to take a closer look at how the *DSM-IV* chapter structure might be revised to reflect not only symptom similarity but also related etiologies or pathophysiology. Revising the *DSM-IV* chapter structure in this way was felt to be an initial step in correcting errors in the boundaries between disorders. With disorders grouped together more accurately, artificial comorbidities resulting from erroneous, overly fine-grained splitting of disorders might eventually be corrected with ongoing research. This study group worked closely with developers of *ICD-11* to ensure cross-national harmonization of the two systems' chapter structures.

The Diagnostic Spectra Study Group selected 11 validators to investigate relations between disorders. Following E. Robins and Guze (1970), they reasoned that disorders could be considered closely related to the extent that their validators showed the same patterns. The specific presumptive criteria for grouping disorders were (a) high rates of comorbidity among disorders as currently defined, (b) familiality, (c) shared genetic and/or environmental risk factors, (d) shared temperamental antecedents, (e) shared cognitive and emotional processing abnormalities, (f) shared neural substrates, and (g) shared biomarkers. Symptom similarity, the course of illness, and treatment response were also included as potential validators, but they alone could not be used to determine relatedness.

Some of the potential new diagnostic groups targeted for study were a group for OCRDs (e.g., Tourette syndrome), and two new groups formed largely from the current group of mood disorders: specifically, a group of unipolar depressive disorders and GAD, which would reflect the anxious-misery dimension mentioned previously, and a second group for bipolar disorders. It was thought that if OCD and GAD were assigned to new groups, then remaining anxiety disorders (e.g., panic disorder, phobic disorders, and PTSD and related disorders) might be grouped as fear-related anxiety disorders on the basis of their underlying neurocircuitry. The study group also suggested that schizophrenia and related disorders such as schizotypal PD be examined for similarities with each other, as well as with bipolar disorders. The pervasive developmental disorders were seen as ripe for reexamination, particularly given that autistic disorder and Asperger's disorder were listed as two distinct disorders despite their many shared characteristics and validators, and that pervasive developmental disorder NOS was used frequently in clinical settings, suggesting the possibility of better specification with this broad domain. Addictive disorders, for which there was evidence of shared neurocircuitry, were another suggested grouping. Pathological gambling, an established DSM disorder with ties to substance use disorders, and various less established conditions, such as internet gaming addiction, were potential new additions to this group.

In the final, published version of *DSM-5*, several of these options were implemented on the basis of a close examination of the 11 validators. For example, the various pervasive developmental disorders were combined into a single diagnosis, ASD, for which clinicians could specify the severity of symptoms in two domains: social communication and restricted, repetitive behaviors. Gambling disorder was included in the newly conceptualized chapter "Substance-Related and Addictive Disorders," which encouraged research on other nonsubstance-related "behavioral addictions," such as severe overengagement in internet gaming. The OCRDs were given a chapter of their own, separate from anxiety disorders, that included such disorders as trichotillomania and body dysmorphic disorder, which previously had appeared in other chapters on the basis of their symptom presentation rather than their underlying characteristics.

Other possibilities ultimately were rejected: Tourette syndrome and other tic disorders were placed in the "Neurodevelopmental Disorders" chapter rather than with OCRDs, a separate "Trauma and Stress-Related Disorders" chapter (which included, e.g., PTSD) was added, and GAD was kept with the anxiety disorders. The reasons for these decisions varied. For example, it was argued that the data were not sufficiently strong to consider tic disorders as OCRDs (Phillips & Stein, 2015; Phillips et al., 2010); PTSD was not categorized with the anxiety disorders because, as currently defined, it is much more complex; and the decision not to classify GAD with MDD and related disorders was made in

large part because the forces of tradition and shared phenomenology were stronger than those of comorbidity and genetics.

A third major effort to reduce artificial comorbidity in DSM diagnoses focused on implementing a dimensional model for PD. As in prior versions of the ICD, PD comorbidity and the high frequency of PD-NOS diagnoses were major problems in *DSM-III* through *DSM-IV*. A trait-dimensional PD model was considered briefly for *DSM-IV* but was deemed premature. Nonetheless, *DSM-IV* included a brief section, "Dimensional Models for Personality Disorder," that listed a number of existing trait models with varying numbers of dimensions, acknowledging that they "had much in common and together appear to cover the important areas of personality dysfunction" (APA, 2000, p. 690). Importantly, between the publication of *DSM-IV* and the beginning of the *DSM-5* revision, research had shown that the large majority of what had been considered competing models of normal- and maladaptive-range personality could be integrated into a single hierarchical model, in which the dimensions of the five-factor model of personality (e.g., Benet-Martínez & John, 1998; McCrae & Costa, 1987) formed the most differentiated level (Markon et al., 2005). (Even more differentiated levels—usually called "facets"—of the five major trait domains exist, but their integration across various personality models is incomplete.) Because all personality configurations can be described using this hierarchical trait model, its implementation in *DSM-5* was considered an important step in solving the artificial comorbidity problem in the PD domain. This integrated five-factor model is the starting point for the trait aspect of both the AMPD and the *ICD-11* PD proposal so, as described earlier, they are largely similar.

Arguably, a trait model alone is insufficient for PD diagnosis because even extreme traits may be adaptive in certain environments (Livesley & Jang, 2005). This consideration was the basis for the *DSM-5* Personality and PD Work Group's proposal that impairment in personality functioning be the first criterion for a PD diagnosis—specifically, individuals met this criterion if they were rated at or above a threshold of 2 on a 0-to-4 severity dimension of personality functioning, with 0 representing healthy functioning, 1 denoting subthreshold personality problems, and 2 through 4 representing moderate, severe, and extreme impairment, respectively. Note that these severity levels are conceptually quite similar to *ICD-11*'s no PD, personality difficulty, and mild, moderate, and severe PD, despite differences in their labels and in the particulars of how they are specified.

Finally, as described earlier in "Alternative Model for Personality Disorders," the AMPD includes six specific configurations of personality impairment plus pathological trait dimensions, which has the unfortunate consequence of retaining the problem of comorbidity. For example, a person could have severe personality impairment and exhibit a combination of pathological traits that warrants diagnosis of both antisocial and narcissistic PD. Comorbid PD diagnoses could be avoided entirely by expanding the definition of PD–trait specified (L. A. Clark et al., 2015), but the *DSM-5* Task Force felt that specific PD configurations would help clinicians transition from traditional categories to a more fully dimensional system in the future. As noted earlier, the APA Board of Trustees went even further and rejected the AMPD for placement in *DSM-5*'s main Section II, placing it instead in Section III, "Emerging Models and Measures."

One of the findings of the voluminous research into mental-disorder comorbidity is that there is as much overlap between clinical syndromes and PDs as there is among clinical syndromes or among PDs (L. A. Clark, 2005). Moreover, evidence indicates that common personality traits, which range from healthy to pathological, underlie both types of disorders and thus provide at least a partial explanation for both types of overlap. We mentioned earlier that comorbidity of MDD and GAD can be explained entirely by shared genes; importantly, the trait of negative affectivity (also known as neuroticism) also shares a significant portion of these common genes (Kendler, Gardner, Gatz, & Pedersen, 2007). Other research indicates that common personality traits link social anxiety disorder and avoidant PD (Watson, Clark, & Carey, 1988; Wilberg, Urnes, Friis, Pedersen, & Karterud, 1999), schizophrenia and schizotypal PD (e.g., Picchioni et al., 2010), and various externalizing disorders (e.g., substance-use disorders and antisocial PD; Ruiz, Pincus, & Schinka, 2008). The extent of overlap between personality and both PD and clinical syndromes is such that personality is most likely an underlying cause of comorbidity (L. A. Clark, 2005). That is, different personality traits are risk factors for—or confer differential susceptibility to—specific subsets of mental disorders (Hettema, Neale, Myers, Prescott, & Kendler, 2006; Khan, Jacobson, Gardner, Prescott, & Kendler, 2005; Tackett, Waldman, Van Hulle, & Lahey, 2011).

Comparisons of* ICD-11 *and* DSM-5 *with regard to comorbidity. The more specified criterion-based approach of DSM and the less specified diagnostic-guidelines approach of ICD each have strengths and weaknesses with regard to reflecting comorbidity data. If *DSM-5* criteria are strictly applied (e.g., by using a structured interview), comorbidity is higher than when a less structured approach is used. This is because practicing clinicians tend to focus on the most prominent or problematic aspects of the symptom picture and tend not to document all possible comorbid disorders in an individual (Wilk et al., 2006). In this

sense, diagnostic practice is more consistent with the less highly specified *ICD-11*. Such an approach has the obvious advantage of addressing patients' most prominent problems first, but it is disadvantageous if clinically important comorbidities are overlooked (e.g., a pattern of unexpected panic attacks in the context of social anxiety disorder). The *DSM-5* cross-cutting dimensions were developed in part to help draw attention to such overlooked conditions in diagnostic evaluations. Similar psychological and behavioral symptoms are also available for coding in the *ICD-11* chapter on symptoms, signs, and clinical findings not elsewhere classified.

Both *DSM-5* and *ICD-11* have hierarchical categorical structures that place more specific disorders in broader groupings—for instance, placing specific phobia, social anxiety disorder, and panic disorder in a grouping of anxiety and fear-related disorders. The structure of *ICD-11* can be utilized for particular purposes (e.g., in primary-care settings) with more general diagnostic guidelines for the higher order categories. Specifically, *ICD-11* has "parent" categories higher in the structure that subsume "child" categories lower in the structure. For example, the *ICD-11* primary-care version facilitates use of less specific, higher order codes, whereas the version for specialist mental-health settings provides codes at a greater level of specification. *DSM-5* is organized such that only what corresponds to the lower level of *ICD-11* diagnoses can be used; if revisions to the *DSM-5* were to follow *ICD-11*, they would require a more explicitly articulated hierarchical structure than *DSM-5* now has.

Overall, there is substantial conceptual similarity in the *ICD-11* and *DSM-5* approaches to comorbidity. Nonetheless, in practical terms, the more highly specified criteria in *DSM-5* can exacerbate the tendency for individuals to meet the requirements of multiple diagnoses.

Comorbidity issues in RDoC. As might be anticipated, RDoC is much more aligned with structural approaches to psychopathology than with the approaches of the two clinical manuals. Observed patterns of covariation in structural analyses of DSM disorders (e.g., Krueger, 1999; Watson, 2005) contributed to the outlines of RDoC domains, such as Negative Valence and Positive Valence. At a more detailed level, the RDoC construct of Acute Threat ("Fear") is well aligned with the fear-disorders factor of structural psychopathology models, whereas the construct of Potential Threat ("Anxiety") bears similarity to the distress and anxious-misery disorders. If an individual has dysfunction in, for example, the fear circuit—perhaps as a result of hyperreactivity or deficient emotion regulation—it is not unlikely for that individual to present with a range of symptoms that meet criteria for multiple ICD/DSM anxiety disorders, such as specific phobia, social phobia, or panic disorder.

Another aspect of psychopathology concerns the externalizing construct, which has largely been related to the ability to exert control over behavior. Deficient inhibitory control, commonly called impulsivity, is linked to substance use disorders, ADHD, borderline PD, antisocial PD/psychopathy, childhood behavior disorders (e.g., conduct disorder), binge eating, risky sexual behaviors, excessive gambling, and criminal behavior. Thus, if individuals are pathologically low in their ability to inhibit behavior, that tendency will likely be observed in multiple spheres of behavior and may lead to a number of different "comorbid" ICD or DSM diagnoses.

An example of this kind of transdiagnostic, construct-based approach is provided by a study of children diagnosed with ADHD that included measurement of temperament factors (Karalunas et al., 2014). A clustering statistic was used to divide the children into three groups on the basis of parents' reports of their child's temperament. One group had only mild symptoms of ADHD and essentially normal temperament. The other two groups had equal scores on measures of attention problems, reflecting greater impairment, but they differed in that one group was characterized as having an extraverted temperament, characterized by high activity level and high levels of positive emotions such as elation and excitement, whereas the other group was characterized as having an irritable temperament, high levels of negative emotions such as anger, and difficulty returning to baseline when upset, agitated, or sad.

Although the authors did not report comorbid diagnoses, the irritable group would be expected to include children who met the criteria for such diagnoses as conduct disorder and oppositional-defiant disorder (Evans et al., 2017), whereas extreme cases in the extraverted group might have met the criteria for a diagnosis of bipolar disorder (e.g., Masi et al., 2006). Clearly, these data suggest that observed symptomatic comorbidities may emerge as a result of relations among multiple temperamental factors, which can be studied systematically. On the basis of their findings, the authors suggested that "a biologically informed temperament-based typology . . . provides a superior description of heterogeneity in the ADHD population than does any current clinical nosologic criteria" (Karalunas et al., 2014, p. E1). Results such as these are promising for pursuing a nosology based on the underlying dimensions of psychopathology.

Comorbidity: summary. As we have seen with the other key issues discussed, the approaches that the three institutions take to addressing comorbidity are aligned

with their basic purposes—WHO and APA to provide information for public-health statistics and clinical care, and NIMH to increase understanding of the mechanisms and processes through which mental disorders arise. Because the ICD and DSM classification systems are necessarily based on extant knowledge, they must acknowledge the comorbidity implied by this knowledge, even if that means giving a patient multiple diagnoses to provide a complete clinical picture. To their credit, the developers of each classification have taken steps to reduce artifactual comorbidity that unnecessarily complicates rather than clarifies patients' mental-health conditions. Insofar as ICD and DSM differ, they do so in ways that are consistent with their different histories and responsive to their different constituents and purposes. In particular, ICD must have utility in a much wider range of socioeconomic and cultural environments than DSM. In contrast, inherent in RDoC's goal to extend current knowledge is the challenge of discovering the complex causes that create the phenomenon known as comorbidity. It is hoped that the knowledge gained from RDoC-based research eventually will provide information that will be useful in improving future diagnostic and classification systems.

Summary, Conclusions, and Future Directions

At the outset of this article, we said that we would extract from our deliberations a set of considerations intended to facilitate the related goals of improving classification of mental illness, advancing clinicians' ability to identify and treat the diverse manifestations of psychopathology, and deepening knowledge of how mental disorders develop, are maintained, and can be ameliorated. In this concluding section, we first summarize the historical context and current status of the understanding of mental disorder and then offer a road map for future research directions that will facilitate these goals.

Historical context and current status

Recognition of phenomena we now call collectively mental illness, as well as efforts to understand and categorize its various manifestations, date back over 2,500 years, but the modern era of the study of mental illness began less than 250 years ago. Early modern classification systems were developed primarily for governments' and hospitals' statistical and record-keeping purposes, but by the mid-20th century, these purposes had expanded to include a wide range of public-health concerns. The two major clinical nosologies that emerged from this process, ICD and DSM, share many features (e.g., a categorical structure) that respond to the purposes for which they were developed and are primarily used, which include compilation of health statistics, allocation of mental-health resources, clinical communication, and decision making in regulatory, legal, and health-insurance systems, all ultimately in service of public mental-health-care needs. Yet ICD and DSM also have idiosyncratic differences, which stem from their distinct histories, developmental processes, and primary constituencies.

For example, WHO has prioritized the local applicability of ICD in very diverse global environments, resulting in specific nosologies for distinct uses and settings (e.g., statistical reporting, primary care, research, and clinical and educational practice), and the use of prototypical descriptions of disorders rather than lists of criteria, to facilitate accommodation of both cultural variations in phenomenology and contextual and health-system factors that may affect diagnostic practice. In contrast, APA has made a strong commitment to using a single classification system for all purposes, anchored by criterial definitions of mental disorders. This facilitates reliability across time points and individuals making diagnoses, with the associated benefit of clear communication to all constituents of a single set of standardized descriptions of mental illness. However, this approach also can reduce the flexible application of definitions of disorders in diverse sociocultural and clinical settings, resulting in potential misdiagnosis. As discussed, each approach promotes certain goals as well as creating particular constraints.

RDoC, in turn, has emerged from this history of nosological developments; it attempts to overcome some of their constraints by taking a novel approach to the study of the basic brain and behavioral processes that in specific environmental contexts give rise to the full range of healthy to psychopathological experience. In doing so, however, RDoC postpones its clinical and health-systems applicability until these fundamental processes have been elucidated.

We have described how the trajectory of nosological development in psychiatry across the 20th century has spanned a diversity of approaches, illustrated in the histories of the three institutions we have described. Earlier in the century, the prevailing clinical focus was not on diagnostic categories but on more narrative case formulations grounded in various theoretical models. Beginning around 1970, concerted efforts were made to describe mental disorders on the basis of observable and patient-reported phenomena, without regard to theories of how they developed. The underlying assumption in this shift was that mental disorders were discrete entities that could be reliably diagnosed for research and clinical purposes, and that these descriptive definitions would stimulate research on the validity of the mental disorders and their diagnoses. At the time,

the prevailing understanding was that mental disorders operated on a diathesis-stress model—that is, that they resulted from certain genetic diatheses interacting with sufficient, and in some cases specific, environmental stressors. These various forces gave rise to the highly specified criterion sets of *DSM-III*, which further intensified research to clarify both the classification of mental disorders and the factors that engendered them. Within 30 years, this research had revealed a more complex picture, indicating that, rather than discrete entities with single causes such as specific gene mutation, mental disorders are multidimensional phenomena that emerge from a combination of general, overlapping, and only partially determinative genetic causes interacting in complex ways with individuals' personal, social, and cultural context and experiences.

ICD-11 *and* DSM-5. In response to this body of research, *DSM-5* and *ICD-11*

- were restructured so that the classification systems' organizations would align better with the empirical structure of psychopathology;
- introduced diagnoses that combined disorders that formerly had been considered distinct into single spectra (e.g., PD in *ICD-11*, ASD in both systems);
- provided various "extra-diagnostic" ways to capture patients' complex symptom presentations (e.g., identification of specific functional problems as well as associated symptoms in *ICD-11* and cross-cutting symptom dimensions in *DSM-5*);
- addressed the underlying continuity of symptom and disorder dimensions, from healthy to severely pathological, in various ways (e.g., *ICD-11*'s category of personality difficulty, which captures subthreshold conditions that nevertheless affect functioning; *DSM-5*'s diagnostic severity measures); and
- described in more detail the ways in which developmental, gender-related, and sociocultural processes affect the onset and form of mental illness (e.g., *ICD-11*'s and *DSM-5*'s sections on culture-related issues and *DSM-5*'s Cultural Formulation Interview in Section III).

Effort also was expended to harmonize the two systems. This was most successfully achieved in relation to the overall structure of both systems, although some substantive differences remain. The level of responsiveness to research-based findings in the development of both the *ICD-11* and the *DSM-5* clearly indicates that both systems are intended to be research-based and iterative in terms of their processes for defining psychopathological conditions and the diagnoses that result from applying those definitions. It remains to be seen whether these processes will produce greater convergence or greater divergence in the future.

Of course, both classification systems also continue to provide a defined set of traditional mental disorders that together form a vitally important framework for clinical use in diagnosing individuals with mental disorder; that help patients and their families make sense of their distressing experiences by providing both names for—and, more importantly, an organized corpus of information about—their condition; and that are intended to provide the most useful information available for essential clinical, public-health, and statistical record-keeping purposes.

RDoC. In contrast, the NIMH developed the RDoC as a new framework for psychopathology research. This framework is fundamentally multidimensional, focused on discovering causal mechanisms, and centered on brain circuitry and brain/cognitive functions. From this center, it extends both "down" to genes/molecules and "up" to macro-level behavior and self-reports, and is contextualized in terms of both individuals' development and their sociocultural environments. Finally, it is agnostic as to the nature and form of the resultant psychopathology, neither rejecting nor embracing the diagnostic entities of current categorical systems. The hope for this initiative is that it will lead to a better understanding of "basic dimensions of functioning underlying the full range of human behavior from normal to abnormal" (https://www.nimh.nih.gov/research-priorities/rdoc/index.shtml) and that from this understanding will emerge a more valid system of mental-disorder classification.

Future directions

For basic researchers. The RDoC framework is preliminary—an initial set of hypotheses that need to be tested and refined. Considerable research is needed both to test the validity of specific implications of RDoC as it currently is formulated and to develop and test alternative hypotheses that no doubt will lead to changes in RDoC. Neuroscience certainly holds great promise for increasing our understanding of psychopathology, but the embeddedness of brain processes in sociocultural contexts must not be minimized (Gallagher, Hutto, Slaby, & Cole, 2013). Mental health and illness are inherently multilevel, multicausal phenomena that require integrated frameworks linking different levels of research—for example, psychophysiological, sociophysiological, and psychosocial (Paris & Kirmayer, 2016). Through epigenetic and other mechanisms, brain function is remodeled to

adapt to particular social circumstances; emergent properties of neurobiological structures can lead to healthy adaptation or pathology across different environments; and self-reflection, narrative interpretation of experience, and patterns of interaction with others (called the *interactome* after the connectome, which maps brain interconnections) can affect the form, onset, and course of disorder (Berrios & Marková, 2015; Kirmayer & Crafa, 2014; Lilienfeld, 2014; Meloni, 2014; Paris & Kirmayer, 2016; van Os, Lataster, Delespaul, Wichers, & Myin-Germeys, 2014). As work on RDoC proceeds, it will necessarily focus on these consequences of multicausality. Thus, we need basic researchers studying both sociocultural processes and brain circuitry, as well as their interaction. Acquisition of basic knowledge about genomics, environmental effects, neurodevelopmental trajectories, neurocircuitry and its processes is critical; however, for RDoC to achieve its purpose, we also need to devise new research strategies to examine how multiple factors—"from neurons to neighborhoods"—simultaneously and interactively affect the development of psychological health and psychopathology.

In particular, phylogenetically older brain circuits that mediate basic emotional and cognitive processes (e.g., in the midbrain and limbic system) interact with newer brain systems that mediate interpretive and context-dependent processes (e.g., in the cerebral cortices). This fundamental interactivity means that the symptoms that constitute multiple mental disorders (e.g., alterations in sleep, appetite, attention, and perception) are determined in part by individuals' interpretations of their experiences. It is possible, for example, to develop an illness from the meaning ascribed to emotional experiences. PTSD, for example, may emerge as a result of witnessing the accidental death of a loved one, and major depression from the loss of a parent in childhood (Bifulco, Brown, & Harris, 1987). In such cases, it is typically the closeness of the patient's interpersonal relationship with the person that modulates the pathological effect. Because interpretation is always mediated by the sociocultural contexts and meaning traditions in which the person is immersed, the study of brain processes needs to take into account the interpretive contexts and cognitive-emotional assumptions in which research assessments are embedded.

Most comorbidity is likely due to shared, "transdiagnostic" mechanisms, so we need to identify those mechanisms and determine both the extent to which they account for similarities in the relevant syndromes and what variance remains unexplained. Phrased differently, we need studies that cut across current diagnostic categories within a multidimensional perspective, as well as research to identify both the general and specific mechanisms of current treatments, asking not only what works or whether Treatment X works but, even more importantly, how treatments work. Clearly, fulfilling the promise of RDoC is a complex endeavor that will take time as well as considerable resources and effort.

For clinical researchers. In the relative short term—that is, largely on the basis of current knowledge—a set of clinically relevant dimensions is needed to supplement current classification systems. Attempts to introduce dimensions into the *DSM-5* diagnostic framework met political and professional opposition. Such resistance has also begun to emerge in relation to *ICD-11* and may be stimulated by initial attempts at implementation. Reasons for this resistance, such as clinicians' unfamiliarity with or lack of knowledge about specific dimensional approaches, can be addressed largely through education, but the lack of established thresholds that would allow for specific decisions based on dimensional information needs to be rectified by clinical research. Beneficial directions would include (a) identifying the most useful dimensions and appropriate cut points for aspects of care that require categorical decisions—from "purely practical" issues, such as defining caseness for administrative purposes (e.g., billing, insurance coverage, and disability determination), to treatment decisions, such as whether to hospitalize patients or treat them on an outpatient basis—and (b) identifying the most useful dimensions for aspects of care that are more variable, such as types of treatment and their respective durations. These dimensions may be fairly directly tied to current diagnoses (e.g., subthreshold vs. mild, moderate, and severe levels of syndromes such as depressive illnesses), may be symptom based (e.g., subclinical vs. mild, moderate, and severe levels of specific symptoms, such as anhedonia or behavioral avoidance), or may reflect functional processes (e.g., dimensions of different types of cognitive processes that cut across current disorders).

There has been considerable progress in the development of dimensional self- and other- (e.g., parent-) report instruments with strong convergent and discriminant validity (Kotov et al., 2017, provide a broad, albeit not comprehensive, list), but few of these have been disseminated into wide clinical use. Most were developed for research and lack validated cut points for clinical use. The *DSM-5* dimensional assessment measures themselves have not undergone rigorous research scrutiny beyond the *DSM-5* field trials to determine how they may be most useful clinically. The research literature has been accruing since the publication of these measures in 2013, but slowly, because it is difficult to obtain funding for this type of practical, applied clinical research.

Measures also are needed that do not depend on self- or other-reports for patients, from those based in behavioral tasks to biological assessments across many levels—from physiology to molecular genetics. Successful examples of behavioral measures do exist (e.g., measures of intelligence and neuropsychological assessments), but most other behavioral measures have been developed for research use, and their clinical utility has not been established. Finally, how best to measure "the environment" and "development" for integrated, multilevel research has proved quite challenging and remains largely unresolved. It is important to note that the brevity of this paragraph belies the complexity and difficulty of these tasks.

Looking toward the more distant future, it will not be sufficient simply to accrue more fundamental knowledge about genomics, environmental effects, neurodevelopmental trajectories, and processes related to neurocircuitry, as discussed above. In addition, we will need to determine how to use this knowledge in complex, real-world situations—that is, how to translate basic research findings into practical methods for assessment and treatment that can be implemented in clinical settings. Even if we came to understand a great deal more than we currently do about psychopathological processes and mechanisms of change, to be most helpful in determining, for example, which of several treatments would be most beneficial for a particular patient, we would need treatment trials to test hypotheses about how these processes and mechanisms are linked to each other and to manifestations of mental disorder.

We also would need practically feasible, reliable, and valid assessment methods for patients' psychopathology that are based on research findings but do not necessarily require clinicians to understand the underlying mechanisms in detail. (Analogously, physicians who treat cancer do not necessarily understand the complex cellular processes that give rise to malignant tumors, but as long as the nature of the tumor is diagnosed reliably and validly, they know what treatment options are most likely to be beneficial.) Finally, at the clinic or population level, we also would need to determine which implementation strategies best facilitate the uptake, fidelity, and sustainability of the range of interventions developed for particular disorders. This seemingly late stage is in fact crucially informative at the onset of the intervention-development process (Carroll & Rounsaville, 2003). From a public-health perspective, novel interventions or high-resource assessment methods (e.g., neuroimaging) that can be used with only a minority of the population are no more than minimally effective. Thus, as our basic knowledge increases, there will be considerable applied work yet to do.

For clinicians. It is difficult to overstate that strong forces are operating to maintain current diagnostic practices and classification systems, or to overemphasize how difficult changing them will be. The current categorical diagnostic system is entrenched not only in research but also in drug-approval, legal, insurance-reimbursement, and health-service delivery systems, such that clinicians cannot avoid using it. However, on a practical level, most clinicians implicitly recognize the limitations of diagnostic categories in treating their patients, so after making diagnoses for administrative purposes, clinicians often select treatments on the basis of their patients' most prominent symptoms, including symptoms that are not listed in the criteria of the recorded diagnoses.

For clinical and research organizations. It is important that clinicians and the organizations that represent and serve them—APA and WHO, along with local psychiatric and psychological associations worldwide—continue to evolve in the way they approach their classification efforts. This includes acknowledging the limitations of current diagnostic and classification systems, supporting RDoC and other research efforts that will clarify the diagnostic issues we have described, and advocating for appropriate steps to "de-reify" mental disorders in regulatory, legislative, and legal processes. Organizations representing clinicians also play a key role in disseminating new clinical directions to their members, and this dissemination must include education about the use of dimensional assessments of psychopathology in clinical practice and the value of thinking transdiagnostically when considering treatments. To their credit, many clinicians already have embraced these principles.

For universities and institutes. As systemic changes are made to incorporate the dimensionality of psychopathology into classification systems, scholarly organizations should be in the vanguard of reflecting these changes, and universities should be in the vanguard of training professionals to use dimensional systems. Currently, the field is organized in ways that reflect the extant diagnostic systems. For example, many scholarly organizations reflect the current categorical system of disorders (e.g., the Eating Disorders Research Society, the International Society for the Study of Personality Disorders), as do a panoply of journals covering specific categories of disorders (e.g., the *Journal of Depression and Therapy, Alcoholism and Drug Addiction; Autism Research*) and many academic medical centers in which clinical services are organized around diagnostic categories (e.g., clinics for mood disorders, substance use disorders, and eating disorders). Concerning the last case, clinical research is typically carried out only with the patients in these clinics, with little crossover. Such a narrow approach to research inhibits its study of the points of overlap and distinction among these diagnostic groupings. The landscape is changing,

however. A PsycINFO search found two articles with the term "transdiagnostic" anywhere in the record before 2000; it found 89 in the first decade of the 21st century and, in the current decade, 1,200 already have been published. Moreover, the electronic marketplace, being nimbler than print-based publishers, is already leading the way: Journals such *Ecological Psychology* show up in our browsers when we go online to learn about the most recent scientific work.

For the media, the lay public, the groups above, and everyone else. As we worked together over many months to develop this article, we found ourselves coming back time and again to the four key issues that all three systems must and do address in various ways. In the first part of the article, therefore, we described the three systems to provide the historical and contemporary contexts within which they address these issues: etiology, categories and dimensions, thresholds, and comorbidity. We then provided in-depth discussion of each key issue, first from a general perspective and then from the perspective of each institution and its corresponding system of describing mental disorder.

As we discussed and wrote about these key issues, we gradually arrived at what we agreed was our most fundamental "take-home message": The way one approaches the entire topic of mental disorder and, consequently, the way one grapples with, and tentatively resolves, these key issues depend largely, if not entirely, upon the purposes for which one is doing so. Put simply, the three approaches to mental illness that are this article's focus each have both strengths and limitations and should be considered complementary rather than competing.

We further thought that the media and, more generally, the public may have viewed the purpose of diagnosis and classification of mental disorder to be only, or at least primarily, to provide descriptions of a set of well-defined disorders to guide clinicians in determining which of these disorders each patient "has." We wish to broaden this view to encompass awareness that, first, although we know far more about mental disorders that we did a half century ago, they still are not fully understood; second, even describing mental disorder is a complex task, to say nothing of understanding how various factors combine to cause its many manifestations; and third, again, the various ways to think about mental disorder described in this article are each important for their own purposes. These purposes include describing mental disorders on the basis of the best available evidence for use by patients, their families, and their clinicians and for various governmental functions, as well as furthering the understanding of the causes of mental illness and ways to ameliorate it, and, ultimately, prevent its development or minimize its severity.

At the very beginning of this article, we provide two quotes, each of which is an analogy for aspects of our message. One, by Edmund Burke, reminds us that although both processes and dimensions are continuous and without clear boundaries, we nonetheless can distinguish and categorize them. The other, by T. S. Eliot, suggests that as we deepen our understanding of mental disorder, we will not gain knowledge that is altogether unrecognizable; rather, we will gain a new and clear perspective on what we now only dimly understand. It is our hope that the approaches to mental disorder taken by the three systems described in this article eventually will arrive at the same clear point of understanding. That day may yet be a long way off, but it is the goal toward which we strive.

Appendix 1: Glossary of Acronyms and Terminology

ADAMHA: Alcohol, Drug Abuse, and Mental Health Administration
ADHD: attention-deficit/hyperactivity disorder
AMPD: Alternative *DSM-5* Model for Personality Disorders
APA: American Psychiatric Association
ASD: autism spectrum disorder
BMI: body mass index
CDDG: *Clinical Descriptions and Diagnostic Guidelines*
CFI: Cultural Formulation Interview
CM: Clinical Modification
Clinical and associated features: Clinical features are the symptoms and signs that are common to a diagnosis and collectively constitute its diagnostic criteria; associated features are symptoms and signs that are often seen in patients with a disorder but that do not contribute to its diagnosis.
Clinical syndrome: A commonly co-occurring set of clinical signs and symptoms that collectively represent a recognizable clinical entity; the term encompasses officially recognized disorders but also includes common clinical entities that are not associated with an official diagnosis. The term is most typically used in contrast to personality disorder.
DCR: Diagnostic Criteria for Research
DSM: *Diagnostic and Statistical Manual of Mental Disorders* (subsequent numbers indicate editions; "R" indicates a revision)
General medical disorders: Conditions that are listed in ICD outside the "Mental, Behavioural, and Neurodevelopmental Disorders" chapter.
GAD: generalized anxiety disorder
GBD: Global Burden of Disease
GCPN: Global Clinical Practice Network

ICD: International Classification of Diseases (subsequent numbers indicate editions)
MDD: major depressive disorder
mhGAP: Mental Health Gap Action Programme
NIH: National Institutes of Health
NIMH: National Institute of Mental Health
NOS: not otherwise specified
OCF: Outline for Cultural Formulation
OCRDs: obsessive-compulsive and related disorders
PD: personality disorder
PTSD: posttraumatic stress disorder
RDoC: Research Domain Criteria
SUD: substance use disorder
WHO: World Health Organization

Appendix 2: Diagnostic Criteria for Social Phobia/Social Anxiety Disorder

ICD-10: Clinical Description and Diagnostic Guidelines

Clinical Description and Diagnostic Guidelines for Social Phobias, *International Classification of Diseases and Related Health Problems, Tenth Revision* (World Health Organization, 1992b, pp. 113–114).

> Social phobias often start in adolescence and are centered around a fear of scrutiny by other people in comparatively small groups (as opposed to crowds), usually leading to avoidance of social situations. Unlike most other phobias, social phobias are equally common in men and women. They may be discrete (i.e., restricted to eating in public, to public speaking, or to encounters with the opposite sex) or diffuse, involving almost all social situations outside the family circle. A fear of vomiting in public may be important. Direct eye-to-eye confrontation may be particularly stressful in some cultures. Social phobias are usually associated with low self-esteem and fear of criticism. They may present as a complaint of blushing, hand tremor, nausea, or urgency of micturition, the individual sometimes being convinced that one of these secondary manifestations of anxiety is the primary problem; symptoms may progress to panic attacks. Avoidance is often marked, and in extreme cases may result in almost complete social isolation.
>
> Diagnostic guidelines:
>
> All of the following criteria should be fulfilled for a definite diagnosis:
>
> (a) the psychological, behavioural, or autonomic symptoms must be primarily manifestations of anxiety and not secondary to other symptoms such as delusions or obsessional thoughts;
>
> (b) the anxiety must be restricted to or predominate in particular social situations; and
>
> (c) the phobic situation is avoided whenever possible.

ICD-10: Diagnostic Criteria for Research

Diagnostic Criteria for Social Phobias, *The ICD-10 Classification of Mental and Behavioural Disorders: Diagnostic Criteria for Research* (World Health Organization, 1993, pp. 110–111).

> A. Either (1) or (2):
>
> (1) marked fear of being the focus of attention, or fear of behaving in a way that will be embarrassing or humiliating;
>
> (2) marked avoidance of being the focus of attention or situations in which there is fear of behaving in an embarrassing or humiliating way.
>
> These fears are manifested in social situations, such as eating or speaking in public; encountering known individuals in public; or entering or enduring small group situations, such as parties, meetings and classrooms.
>
> B. At least two symptoms of anxiety in the feared situation at some time since the onset of the disorder, as defined in criterion B for F40.0 (Agoraphobia), and in addition one of the following symptoms:
>
> (1) Blushing.
>
> (2) Fear of vomiting.
>
> (3) Urgency or fear of micturition or defecation.
>
> Significant emotional distress due to the symptoms or to the avoidance.
>
> D. Recognition that the symptoms or the avoidance are excessive or unreasonable.
>
> E. Symptoms are restricted to or predominate in the feared situation or when thinking about it.
>
> F. Most commonly used exclusion criteria: Criteria A and B are not due to delusions, hallucinations, or other symptoms of disorders such as organic mental disorders (F0), schizophrenia and related disorders (F20–F29), affective disorders (F30–F39),

or obsessive compulsive disorder (F42), and are not secondary to cultural beliefs.

ICD-11: Essential Features from the Proposed Diagnostic Guidelines (*CDDG*)

Proposed Diagnostic Guidelines for Social Anxiety Disorder, International Classification of Diseases and Related Health Problems, Eleventh Revision (Kogan et al., 2016, p. 1145).

Proposed essential features from diagnostic guidelines for Social Anxiety Disorder:

- Marked and excessive fear or anxiety that occurs consistently in one or more social situations such as social interactions (e.g., having a conversation), doing something while feeling observed (e.g., eating or drinking in the presence of others), or performing in front of others (e.g., giving a speech).
- The individual is concerned that he or she will act in a way, or show anxiety symptoms, that will be negatively evaluated by others (i.e., be humiliating, embarrassing, lead to rejection, or be offensive).
- Relevant social situations are consistently avoided or endured with intense fear or anxiety.
- The symptoms are not transient; that is, they persist for an extended period of time (e.g., at least several months).
- The symptoms are not better accounted for by another Mental and Behavioural Disorder (e.g., Agoraphobia)
- The symptoms are sufficiently severe to result in significant distress about experiencing persistent anxiety symptoms or result in significant impairment in personal, family, social, educational, occupational, or other important areas of functioning.

DSM-IV: Diagnostic Criteria

Diagnostic Criteria for Social Phobia, *DSM-IV* (American Psychiatric Association, 2000, p. 456). Copyright © 2000 American Psychiatric Association.

A. A marked and persistent fear of one or more social or performance situations in which the person is exposed to unfamiliar people or to possible scrutiny by others. The individual fears that he or she will act in a way (or show anxiety symptoms) that will be humiliating or embarrassing.

B. Exposure to the feared social situation almost invariably provokes anxiety, which may take the form of a situationally bound or situationally predisposed Panic Attack.

C. The person recognizes that the fear is excessive or unreasonable. Note: In children, this feature may be absent.

D. The feared social or performance situations are avoided or else are endured with intense anxiety or distress.

E. The avoidance, anxious anticipation, or distress in the feared social or performance situation(s) interferes significantly with the person's normal routine, occupational (academic) functioning, or social activities or relationships, or there is marked distress about having the phobia.

F. In individuals under age 18 years, the duration is at least 6 months.

G. The fear or avoidance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition and is not better accounted for by another mental disorder (e.g., Panic Disorder With or Without Agoraphobia, Separation Anxiety Disorder, Body Dysmorphic Disorder, a Pervasive Developmental Disorder, or Schizoid Personality Disorder).

H. If a general medical condition or another mental disorder is present, the fear in Criterion A is unrelated to it, e.g., the fear is not of Stuttering, trembling in Parkinson's disease, or exhibiting abnormal eating behavior in Anorexia Nervosa or Bulimia Nervosa.

DSM-5: Diagnostic Criteria

Diagnostic Criteria for Social Anxiety Disorder (Social Phobia) *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (American Psychiatric Association, 2013). Copyright © 2013 American Psychiatric Association.

A. Marked fear or anxiety about one or more social situations in which the individual is exposed to possible scrutiny by others. Examples include social interactions (e.g., having a conversation, meeting unfamiliar people), being observed (e.g., eating or drinking), and performing in front of others (e.g., giving a speech).

Note: In children, the anxiety must occur in peer settings and not just during interactions with adults.

B. The individual fears that he or she will act in a way or show anxiety symptoms that will be negatively evaluated (i.e., will be humiliating or embarrassing; will lead to rejection or offend others).

C. The social situations almost always provoke fear or anxiety.

Note: In children, the fear or anxiety may be expressed by crying, tantrums, freezing, clinging, shrinking, or failing to speak in social situations.

D. The social situations are avoided or endured with intense fear or anxiety.

E. The fear or anxiety is out of proportion to the actual threat posed by the social situation and to the sociocultural context.

F. The fear, anxiety, or avoidance is persistent, typically lasting for 6 months or more.

G. The fear, anxiety, or avoidance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

H. The fear, anxiety, or avoidance is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition.

I. The fear, anxiety, or avoidance is not better explained by the symptoms of another mental disorder, such as panic disorder, body dysmorphic disorder, or autism spectrum disorder.

J. If another medical condition (e.g., Parkinson's disease, obesity, disfigurement from burns or injury) is present, the fear, anxiety, or avoidance is clearly unrelated or is excessive.

Author Contributions

L. A. Clark, B. Cuthbert, R. Lewis-Fernández, W. E. Narrow, and G. M. Reed all contributed to the writing of the manuscript and approved the final version for publication. They are listed alphabetically in the byline. L. A. Clark was the lead author.

Acknowledgments

G. M. Reed is a member of the WHO Secretariat, Department of Mental Health and Substance Abuse. However, unless specifically stated, the views expressed in this article are those of the authors and do not represent the official policies or positions of WHO. We acknowledge the generous assistance of Jack Maser for his many contributions to their discussions and his considerable editing of countless versions of the manuscript. We also thank Eloise Clark for her eagle editing eye and comments that helped us to clarify obscure points.

Declaration of Conflicting Interests

The authors declared that they had no conflicts of interest with respect to their authorship or the publication of this article.

Notes

1. Formal uses of the terms *disorder, illness*, and *disease* vary across disciplines and institutions, and there are also variations in how these terms are used and understood by the lay public. With respect to mental disorder, the distinctions among these terms are blurry and not consistently meaningful, even within disciplines. We generally have used these terms in a manner that is consistent with their use in the respective contexts of the three key organizations around which this article is organized. We caution readers not to infer too precise a meaning from the usages of each term. Similarly, we use the terms in both the singular and plural (e.g., *mental disorder* and *mental disorders*), using the former when we focus on the domain as a whole and the latter when we are referencing the set of distinguishable elements that form the domain.
2. All acronyms used in this report can be found in the Glossary on pages 131 and 132.
3. The name is an acknowledgment of the earlier Research Diagnostic Criteria, which provided the foundation for *DSM-III* and spurred efforts to validate mental-disorder definitions on the basis of E. Robins and Guze's (1970) principles.
4. Volume Two of *ICD-10* (WHO, 1992a) contains a detailed historical account of the public-health innovations related to classification that provided the early foundation for the ICD.
5. The World Health Assembly is made up of the ministers of health of all 194 WHO member states (countries), including the United States. The U.S. representative to the World Health Assembly is the Secretary of Health and Human Services.
6. For purposes of historical accuracy, we note that the present American Psychiatric Association was known by several other names from its founding in 1844 until 1921.
7. Throughout the manuscript, when referencing a particular version of ICD or DSM, we use the terms that were used at that time, some of which may now be considered pejorative. The first time we use such terms, we also provide the currently used term, except in cases for which there is no obvious corresponding term (e.g., neuroses); thereafter, we use quotation marks around the term.
8. The *ICD-11* working group did not adopt *DSM-5*'s term, "gender dysphoria," because "dysphoria" refers to a state of unhappiness or psychological distress; using a name that seemed to define distress as the central feature of the diagnosis was seen as inconsistent with the recommendation to remove it from *ICD-11*'s chapter on mental and behavioral disorders (Evans et al., 2017).
9. In 1735, Linnaeus classified living organisms into an arrangement of seven hierarchical layers—kingdoms, phyla, classes, orders, families, genera, and species—laying the groundwork for modern taxonomic systems in biology.
10. Multiple personality disorder, called dissociative identity disorder in the *DSM-5*, is one possible exception.

References

Achenbach, T. M. (1966). The classification of children's psychiatric symptoms: A factor-analytic study. *Psychological Monographs: General and Applied*, *80*(7), 1–37. doi:10.1037/h0093906

Adeponle, A. B., Thombs, B. D., Groleau, D., Jarvis, E., & Kirmayer, L. J. (2013). Using the cultural formulation to resolve uncertainty in diagnoses of psychosis among ethnoculturally diverse patients. *Psychiatric Services*, *63*, 147–153. doi:10.1176/appi.ps.201100280

Aggarwal, N. K., Nicasio, A. V., DeSilva, R., Boiler, M., & Lewis-Fernández, R. (2015). Does the Cultural Formulation Interview for the fifth revision of the diagnostic and statistical manual of mental disorders (DSM-5) affect medical communication? A qualitative exploratory study from the New York site. *Ethnicity and Health*, *20*(1), 1–28. doi:10.1080/13557858.2013.857762

Alarcón, R. D., Alegría, M., Bell, C. C., Boyce, C., Kirmayer, L. J., Lin, K. M., . . . Wisner, L. W. (2002). Beyond the funhouse mirrors: Research agenda on culture and psychiatric diagnosis. In D. J. Kupfer, M. B. First, & D. A. Regier (Eds.), *A research agenda for DSM-V* (pp. 219–281). Washington, DC: American Psychiatric Association.

Allardyce, J., McCreadie, R. G., Morrison, G., & van Os, J. (2007). Do symptom dimensions or categorical diagnoses best discriminate between known risk factors for psychosis? *Social Psychiatry and Psychiatric Epidemiology*, *42*, 429–437. doi:10.1007/s00127-007-0179-y

Altman, E. G., Hedeker, D., Peterson, J. L., & Davis, J. M. (1997). The Altman Self-Rating Mania Scale. *Biological Psychiatry*, *42*, 948–955. doi:10.1016/S0006-3223(96)00548-3

American Medico-Psychological Association. (1918). *Statistical manual for the use of institutions for the insane*. New York, NY: National Committee for Mental Hygiene.

American Psychiatric Association. (1942). *Statistical manual for the use of hospitals for mental diseases*. Utica, NY: State Hospitals Press.

American Psychiatric Association. (1952). *Diagnostic and statistical manual of mental disorders*. Washington, DC: Author.

American Psychiatric Association. (1968). *Diagnostic and statistical manual of mental disorders* (2nd ed.). Washington, DC: Author.

American Psychiatric Association. (1980). *Diagnostic and statistical manual of mental disorders* (3rd ed.). Washington, DC: Author.

American Psychiatric Association. (1987). *Diagnostic and statistical manual of mental disorders* (3rd ed., Rev.). Washington, DC: Author.

American Psychiatric Association. (1994). *Diagnostic and statistical manual of mental disorders* (4th ed.). Washington, DC: Author.

American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders* (4th ed., text rev.). Washington, DC: Author.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Washington, DC: Author.

American Psychiatric Association. (2015). *DSM: History of the manual*. Retrieved from http://www.psychiatry.org/practice/dsm/dsm-history-of-the-manual

Barlow, D. H., Farchione, T. J., Fairholme, C. P., Ellard, K. K., Boisseau, C. L., Allen, L. B., . . . Ehrenreich-May, J. (2011). *Unified protocol for transdiagnostic treatment of emotional disorders: Therapist guide*. New York, NY: Oxford University Press.

Beauchaine, T. P., & McNulty, T. (2013). Comorbidities and continuities as ontogenic processes: Toward a developmental spectrum model of externalizing psychopathology. *Development and Psychopathology*, *25*, 1505–1528. doi:10.1017/S0954579413000746

Becker, A. E., Thomas, J. J., & Pike, K. M. (2009). Should non-fat-phobic anorexia nervosa be included in DSM-V? *International Journal of Eating Disorders*, *42*, 620–635. doi:10.1002/eat.20727

Belsky, J., Jonassaint, C., Pluess, M., Stanton, M., Brummett, B., & Williams, R. (2009). Vulnerability genes or plasticity genes? *Molecular Psychiatry*, *14*, 746–754. doi:10.1038/mp.2009.44

Benet-Martínez, V., & John, O. P. (1998). *Los Cinco Grandes* across cultures and ethnic groups: Multitrait-multimethod analyses of the Big Five in Spanish and English. *Journal of Personality and Social Psychology*, *75*, 729–750. doi:10.1037/0022-3514.75.3.729

Berrios, G. E., & Marková, I. (2015). Toward a new epistemology of psychiatry. In L. J. Kirmayer, R. Lemelson, & C. A. Cummings (Eds.), *Re-visioning psychiatry: Cultural phenomenology, critical neuroscience and global mental health* (pp. 41–64). New York, NY: Cambridge University Press.

Biederman, J., Faraone, S. V., Mick, E., Williamson, S., Wilens, T. E., Spencer, T. J., . . . Zallen, B. (1999). Clinical correlates of ADHD/ADD in females: Findings from a large group of girls ascertained from pediatric and psychiatric referral sources. *Journal of the American Academy of Child and Adolescent Psychiatry*, *38*, 966–975. doi:10.1097/00004583-199908000-00012

Bifulco, A., Harris, T., & Brown, G. W. (1992). Mourning or early inadequate care? Reexamining the relationship of maternal loss in childhood with adult depression and anxiety. *Development and Psychopathology*, *4*, 433–449. doi:10.1017/S0954579400000882

Bifulco, A. T., Brown, G. W., & Harris, T. O. (1987). Childhood loss of parent, lack of adequate parental care and adult depression: A replication. *Journal of Affective Disorders*, *12*, 115–128. doi:10.1016/0165-0327(87)90003-6

Blashfield, R. K., Keeley, J. W., Flanagan, E. H., & Miles, S. R. (2014). The cycle of classification: DSM-I through DSM-5. *Annual Review of Clinical Psychology*, *10*, 25–51. doi:10.1146/annurev-clinpsy-032813-153639

Bogdan, R., Hyde, L. W., & Hariri, A. R. (2013). A neurogenetics approach to understanding individual differences in brain, behavior, and risk for psychopathology. *Molecular Psychiatry*, *18*, 288–299. doi:10.1038/mp.2012.35

Boschloo, L., van Borkulo, C. D., Rhemtulla, M., Keyes, K. M., Borsboom, D., & Schoevers, R. A. (2015). The network structure of symptoms of the Diagnostic and Statistical Manual of Mental Disorders. *PLOS ONE*, *10*(9), Article e0137621. doi:10.1371/journal.pone.0137621

Boyd, J. H., Burke, J. D., Gruenberg, E., Holzer, C. E., Rae, D. S., George, L. K., . . . Nestadt, G. (1984). Exclusion criteria of DSM-III: A study of co-occurrence of hierarchy-free syndromes. *Archives of General Psychiatry*, *41*, 983–989. doi:10.1001/archpsyc.1984.01790210065008

Brittain, P. J., Lobo, S. E. M., Rucker, J., Amarasinghe, M., Anilkumar, A. P. P., Baggaley, M., . . . Schumann, G. (2013). Harnessing clinical psychiatric data with an electronic assessment tool (OPCRIT+): The utility of symptom dimensions. *PLOS ONE*, *8*(3), Article e58790. doi:10/137/journal/pone.0058790

Brotto, L. A. (2010). The DSM diagnostic criteria for sexual aversion disorder. *Archives of Sexual Behavior*, *39*, 271–277. doi:10.1007/s10508-009-9534-2

Brown, G. W., Harris, T., & Copeland, J. R. (1977). Depression and loss. *The British Journal of Psychiatry*, *130*, 1–18. doi:10.1017/S0954579400000882

Brown, T. A., & Barlow, D. H. (1992). Comorbidity among anxiety disorders: Implications for treatment and DSM-IV. *Journal of Consulting and Clinical Psychology*, *60*, 835–844. doi:10.1037/0022-006X.60.6.835

Bullis, J. R., Fortune, M. R., Farchione, T. J., & Barlow, D. H. (2014). A preliminary investigation of the long-term outcome of the unified protocol for transdiagnostic treatment of emotional disorders. *Comprehensive Psychiatry*, *55*, 1920–1927. doi:10.1016/j.comppsych.2014.07.016

Cannon, T. D., Chung, Y., He, G., Sun, D., Jacobson, A., van Erp, T. G. M., . . . Heinssen, R. (2015). Progressive reduction in cortical thickness as psychosis develops: A multisite longitudinal neuroimaging study of youth at elevated clinical risk. *Biological Psychiatry*, *77*, 147–157. doi:10.1016/j.biopsych.2014.05.023

Carliner, H., Collins, P. Y., Cabassa, L. J., McNallen, A., Joestl, S. S., & Lewis-Fernández, R. (2014). Prevalence of cardiovascular risk factors among racial and ethnic minorities with schizophrenia spectrum and bipolar disorders: A critical literature review. *Comprehensive Psychiatry*, *55*, 233–247. doi:10.1016/j.comppsych.2013.09.009

Carroll, K. M., & Rounsaville, B. J. (2003). Bridging the gap: A hybrid model to link efficacy and effectiveness research in substance abuse treatment. *Psychiatric Services*, *54*, 333–339.

Carter, R., Skimkets, R. P., & Bornemann, T. H. (2014). Creating and changing public policy to reduce the stigma of mental illness. *Psychological Science in the Public Interest*, *15*(2), 35–36. doi:10.1177/1529100614546119

Case, A., & Deaton, A. (2015). Rising morbidity and mortality in midlife among white non-Hispanic Americans in the 21st century. *Proceedings of the National Academy of Sciences, USA*, *112*, 15078–15083. doi:10.1073/pnas.1518393112

Caspi, A., Houts, R. M., Belsky, D. W., Goldman-Mellor, S., Harrington, H., Israel, S., . . . Moffitt, T. E. (2014). The p factor: One general psychopathology factor in the structure of psychiatric disorders? *Clinical Psychological Science*, *2*, 119–137. doi:10.1177/2167702613497473

Cassano, G., Michelini, S., Shear, M. K., Coli, E., Maser, J., & Frank, E. (1997). The panic-agoraphobic spectrum: A new approach to the assessment and treatment of subtle symptomatology. *American Journal of Psychiatry*, *154*(6), 27–38.

Cerimele, J. M., & Katon, W. J. (2013). Associations between health risk behaviors and symptoms of schizophrenia and bipolar disorder: A systematic review. *General Hospital Psychiatry*, *35*(1), 16–22. doi:10.1016/j.genhosppsych.2012.08.001

Chen, Y.-F. (2002). Chinese Classification of Mental Disorders (CCMD-3): Towards integration in international classification. *Psychopathology*, *35*(2–3), 171–175. doi:10.1159/000065140

Cicchetti, D., & Rogosch, F. A. (1996). Equifinality and multifinality in developmental psychopathology. *Development and Psychopathology*, *8*, 597–600. doi:10.1017/S0954579400007318

Clark, D. A., Beck, A. T., & Alford, B. A. (1999). *Scientific foundations of cognitive theory of depression*. New York, NY: Wiley.

Clark, L. A. (2005). Temperament as a unifying basis for personality and psychopathology. *Journal of Abnormal Psychology*, *114*, 505–521. doi:10.1037/0021-843X.114.4.505

Clark, L. A., Vanderbleek, E., Shapiro, J., Nuzum, H., Allen, X., Daly, E., . . . Ro, E. (2015). The brave new world of personality disorder-trait specified: Effects of additional definitions on prevalence and comorbidity. *Psychopathology Review*, *2*(1), 52–82. doi:10.5127/pr.036314

Clark, L. A., & Watson, D. (1991). Tripartite model of anxiety and depression: Psychometric evidence and taxonomic implications. *Journal of Abnormal Psychology*, *100*, 316–336. doi:10.1037/0021-843X.100.3.316

Clark, L. A., Watson, D., & Reynolds, S. K. (1995). Diagnosis and classification of psychopathology: Challenges to the current system and future directions. *Annual Review of Psychology*, *46*, 121–153. doi:10.1146/annurev.psych.46.1.121

Clementz, B. A., Sweeney, J. A., Hamm, J. P., Ivleva, E. L., Ethridge, L. E., Pearlson, G. D., . . . Tamminga, C. A. (2016). Identification of distinct psychosis biotypes using brain-based biomarkers. *American Journal of Psychiatry*, *173*, 373–384.

Conley, R. R., Ascher-Svanum, H., Zhu, B., Faries, D. E., & Kinon, B. J. (2007). The burden of depressive symptoms in the long-term treatment of patients with schizophrenia. *Schizophrenia Research*, *90*, 186–197.

Cooper, R., & Blashfield, R. K. (2016). Re-evaluating DSM-I. *Psychological Medicine*, *46*, 449–456. doi:10.1017/S0033291715002093

Correll, C. U. (2007). Acute and long-term adverse effects of antipsychotics. *CNS Spectrums*, *12*(Suppl. 21), 10–14. doi:10.1017/S1092852900015959

Corrigan, P. W., Druss, B. G., & Perlick, D. A. (2014). The impact of mental illness stigma on seeking and participating in mental health care. *Psychological Science in the Public Interest*, *15*(2), 37–70. doi:10.1177/1529100614531398

Cuijpers, P., & Smit, F. (2002). Excess mortality in depression: A meta-analysis of community studies. *Journal of Affective Disorders*, *72*, 227–236. doi:10.1016/S0165-0327(01)00413-X

Cuthbert, B. N., & Insel, T. R. (2013). Toward precision medicine in psychiatry: The NIMH Research Domain Criteria project. In D. S. Charney, P. Sklar, J. D. Buxbaum, & E. J. Nestler (Eds.), *Neurobiology of mental illness* (4th ed., pp. 1076–1088). New York, NY: Oxford University Press.

Danzi, B., & La Greca, A. M. (2016). DSM-IV, DSM-5, and ICD-11: Identifying children with posttraumatic stress disorder after disasters. *Journal of Child Psychology and Psychiatry*. Advance online publication. doi:10.1111/jcpp.12631

Das-Munchi, J., Stewart, R., Morgan, C., Nazroo, J., Thornicroft, G., & Prince, M. (2016). Reviving the "double jeopardy" hypothesis: Physical health inequalities, ethnicity and severe mental illness. *British Journal of Psychiatry*, *209*, 183–185.

Davidson, K. (2012). Depression and coronary heart disease. *ISRN Cardiology*, 2012, Article 743813. doi:10.5402/2012/743813

De Hert, M., Cohen, D., Bobes, J., Cetkovich-Bakmas, M., Leucht, S., Ndetei, D. M., . . . Correll, C. U. (2011). Physical illness in patients with severe mental disorders. II. Barriers to care, monitoring and treatment guidelines, plus recommendations at the system and individual level. *World Psychiatry*, *10*, 138–151. doi:10.1002/j.2051-5545.2011.tb00036.x

De Hert, M., Correll, C. U., Bobes, J., Cetkovich-Bakmas, M., Cohen, D., Asai, I., . . . Leucht, S. (2011). Physical illness in patients with severe mental disorders. I. Prevalence, impact of medications and disparities in health care. *World Psychiatry*, *10*(1), 52–77. doi:10.1002/j.2051-5545.2011.tb00014.x

de Leon, J., & Diaz, F. J. (2005). A meta-analysis of worldwide studies demonstrates an association between schizophrenia and tobacco smoking behaviors. *Schizophrenia Research*, *76*(2–3), 135–157. doi:10.1016/j.schres.2005.02.010

Egeland, J. A., Gerhard, D. S., Pauls, D. L., Sussex, J. N., Kidd, K. K., Allen, C. R., . . . Housman, D. E. (1987). Bipolar affective disorders linked to DNA markers on chromosome 11. *Nature*, *325*, 783–787. doi:10.1038/325783a0

Evans, S. C., Burke, J. D., Roberts, M. C., Fite, P. J., Lochman, J. E., de, la, Peña, F. R., & Reed, G. M. (2017). Irritability in child and adolescent psychopathology: An integrative review for ICD-11. *Clinical Psychology Review*, *53*, 29–45. doi:10.1016/j.cpr.2017.01.004

Evans, S. C., Reed, G. M., Roberts, M. C., Esparza, P., Watts, A. D., Correia, J. M., . . . Saxena, S. (2013). Psychologists' perspectives on the diagnostic classification of mental disorders: Results from the WHO-IUPsyS Global Survey. *International Journal of Psychology*, *48*, 177–193. doi:10.1080/00207594.2013.804189

Evans, S. C., Roberts, M. C., Keeley, J. W., Blossom, J. B., Amaro, C. M., Garcia, A. M., . . . Reed, G. M. (2015). Using vignette methodologies for study clinicians' decision-making: Validity, utility, and application in ICD-11 field studies. *International Journal of Clinical and Health Psychology*, *15*, 160–170. doi:10.1016/j.ijchp.2014.12.001

Farr, W. (1839). *First annual report*. London, England: Registrar General of England and Wales.

Fava, M., Rush, A. J., Alpert, J. E., Balasubramani, G. K., Wisniewski, S. R., Carmin, C. N., . . . Trivedi, M. H. (2008). Difference in treatment outcome in outpatients with anxious versus nonanxious depression: A STAR*D report. *American Journal of Psychiatry*, *165*, 342–351.

Feighner, J. P., Robins, E., Guze, S. B., Woodruff, R. A., Jr., Winokur, G., & Munoz, R. (1972). Diagnostic criteria for use in psychiatric research. *Archives of General Psychiatry*, *26*(1), 57–63. doi:10.1001/archpsyc.1972.01750190059011

Feinberg, I. (1982). Schizophrenia: Caused by a fault in programmed synaptic elimination during adolescence? *Journal of Psychiatric Research*, *17*, 319–334. doi:10.1016/0022-3956(82)90038-3

Finn, S. E. (1982). Base rates, utilities, and DSM-III: Shortcomings of fixed-rule systems of psychodiagnosis. *Journal of Abnormal Psychology*, *91*, 294–302. doi:10.1037/0021-843X.91.4.294

First, M. B. (2009). Harmonization of ICD-11 and DSM-V: Opportunities and challenges. *British Journal of Psychiatry*, *195*, 382–390. doi:10.1192/bjp.bp.108.060822

First, M. B., Pincus, H. A., Levine, J. B., Williams, J. B. W., Ustun, B., & Peele, R. (2004). Clinical utility as a criterion for revising psychiatric diagnoses. *American Journal of Psychiatry*, *161*, 946–954. doi:10.1176/appi.ajp.161.6.946

First, M. B., Reed, G. M., Hyman, S. E., & Saxena, S. (2015). The development of the ICD-11 clinical descriptions and diagnostic guidelines for mental and behavioral disorders. *World Psychiatry*, *14*, 82–90. doi:10.1002/wps.20189

Frances, A. J., Widiger, T. A., & Pincus, H. A. (1989). The development of *DSM-IV*. *Archives of General Psychiatry*, *46*, 373–375. doi:10.1001/archpsyc.1989.01810040079012

Friedman, M. J., Resick, P. A., Bryant, R. A., & Brewin, C. R. (2011). Considering PTSD for DSM-5. *Depression and Anxiety*, *28*, 750–769. doi:10.1002/da.20767

Fulford, K. W. M., & Sartorius, N. (2009). The secret history of ICD and the hidden future of *DSM*. In M. Broome & L. Bortolotti (Eds.), *Psychiatry as cognitive neuroscience: Philosophical perspectives (pp. 29–48)*. Oxford, England: Oxford University Press.

Fullana, M. A., Vilagut, G., Rojas-Farreras, S., Mataix-Cols, D., de Graaf, R., Demyttenaere, K., . . . Alonso, J. (2010). Obsessive–compulsive symptom dimensions in the general population: Results from an epidemiological study in six European countries. *Journal of Affective Disorders*, *124*, 291–299. doi:10.1016/j.jad.2009.11.020

Gaebel, W. (2012). Status of psychotic disorders in *ICD-11*. *Schizophrenia Bulletin*, *38*, 895–898. doi:10.1093/schbul/sbs104

Galatzer-Levy, I., & Bryant, R. A. (2013). 636,120 ways to have posttraumatic stress disorder. *Perspectives on Psychological Science*, *8*, 651–662. doi:10.1177/1745691613504115

Gallagher, M. W., & Brown, T. A. (2015). Bayesian analysis of current and lifetime comorbidity rates of mood and anxiety disorders in individuals with posttraumatic stress disorder. *Journal of Psychopathology and Behavioral Assessment*, *37*, 60–66. doi:10.1007/s10862-014-9436-z

Gallagher, M. W., Sauer-Zavala, S., Boswell, J. F., Carl, J. R., Bullis, J., Farchione, T. J., . . . Barlow, D. H. (2013). The impact of the unified protocol for emotional disorders on quality of life. *International Journal of Cognitive Therapy*, *6*, 57–72. doi:10.1521/ijct.2013.6.1.57

Gallagher, S., Hutto, D. D., Slaby, J., & Cole, J. (2013). The brain as part of an enactive system. *Behavioral & Brain Sciences*, *36*, 421–422. doi:10.1017/S0140525X12002105

GBD 2015 DALYs and HALE Collaborators. (2016). Global, regional, and national disability-adjusted life-years (DALYs) for 315 diseases and injuries and healthy life expectancy (HALE), 1990–2015: A systematic analysis for the Global Burden of Disease Study 2015. *The Lancet*, *388*, 1603–1658. doi:10.1016/S0140-6736(16)31460-X

GBD 2015 Disease and Injury Incidence and Prevalence Collaborators. (2016). Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: A systematic analysis for the Global Burden of Disease Study 2015. *The Lancet*, *388*, 1545–1602. doi:10.1016/S0140-6736(16)31678-6

Ginns, E. I., Egeland, J. A., Allen, C. R., Pauls, D. L., Falls, K., Keith, T. P., & Paul, S. M. (1992). Update on the search for DNA markers linked to manic-depressive illness in the Old Order Amish. *Journal of Psychiatric Research*, *26*, 305–308. doi:10.1016/0022-3956(92)90037-O

Goldberg, D. P., Andrews, G., & Hobbs, M. J. (2009). Where should bipolar disorder appear in the meta-structure? *Psychological Medicine*, *39*, 2071–2081. doi:10.1017/S0033291709990304

Goldberg, D. P., Prisciandaro, J. J., & Williams, P. (2012). The primary health care version of ICD-11: The detection of common mental disorders in general medical settings. *General Hospital Psychiatry*, *34*, 665–670. doi:10.1016/j.genhosppsych.2012.06.006

Goldberg, D. P., Reed, G. M., Robles, R., Bobes, J., Iglesias, C., Fortes, S., & Saxena, S. (2016). Multiple somatic symptoms in primary care: A field study for ICD-11 PHC, WHO's revised classification of mental disorders in primary care. *Journal of Psychosomatic Research*, *91*, 48–54. doi:10.1016/j.jpsychores.2016.10.002

Gordon, J. A. (2016). On being a circuit psychiatrist. *Nature Neuroscience*, *19*, 1385–1386. doi:10.1038/nn.4419

Gottesman, I. I., & Gould, T. D. (2003). The endophenotype concept in psychiatry: Etymology and strategic intentions. *The American Journal of Psychiatry*, *160*, 636–645. doi:10.1176/appi.ajp.160.4.636

Grant, B. F., Stinson, F. S., Dawson, D. A., Chou, S. P., Dufour, M. C., Compton, W., . . . Kaplan, K. (2004). Prevalence and co-occurrence of substance use disorders and independent mood and anxiety disorders: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Archives of General Psychiatry*, *61*, 807–816. doi:10.1001/archpsyc.61.8.807

Gur, R. C., Calkins, M. E., Satterthwaite, T. D., Ruparel, K., Bilker, W. B., Moore, T. M., . . . Gur, R. E. (2014). Neurocognitive growth charting in psychosis spectrum youths. *JAMA Psychiatry*, *71*, 366–374. doi:10.1001/jamapsychiatry.2013.4190

Halldorsdottir, T., & Binder, E. B. (2017). Gene × Environment interactions: From molecular mechanisms to behavior. *Annual Review of Psychology*, *68*, 215–241. doi:10.1146/annurev-psych-010416-044053

Hamilton, M. (1960). A rating scale for depression. *Journal of Neurology, Neurosurgery & Psychiatry*, *23*, 56–62. doi:10.1136/jnnp.23.1.56

Hansen, M., Hyland, P., Armour, C., Shevlin, M., & Elklit, A. (2015). Less is more? Assessing the validity of the ICD-11 model of PTSD across multiple trauma samples. *European Journal of Psychotraumatology*, *6*, 28766. doi:10.3402/ejpt.v6.28766

Hasin, D. S., O'Brien, C. P., Auriacombe, M., Borges, G., Bucholz, K., Budney, A., . . . Grant, B. F. (2013). DSM-5 criteria for substance use disorders: Recommendations and rationale. *The American Journal of Psychiatry*, *170*, 834–851. doi:10.1176/appi.ajp.2013.12060782

Haslam, N., Holland, E., & Kuppens, P. (2012). Categories versus dimensions in personality and psychopathology: A quantitative review of taxometric research. *Psychological Medicine*, *42*, 903–920. doi:10.1017/S0033291711001966

Hettema, J. M., Neale, M. C., Myers, J. M., Prescott, C. A., & Kendler, K. S. (2006). A population-based twin study of the relationship between neuroticism and internalizing disorders. *The American Journal of Psychiatry*, *163*, 857–864. doi:10.1176/appi.ajp.163.5.857

Hinton, D. E., & Lewis-Fernández, R. (2011). The cross-cultural validity of posttraumatic stress disorder: Implications for DSM-5. *Depression and Anxiety*, *28*, 783–801. doi:10.1002/da.20753

Hollon, S. D., & Ponniah, K. (2010). A review of empirically supported psychological therapies for mood disorders in adults. *Depression and Anxiety*, *27*, 891–932. doi:10.1002/da.20741

Horwitz, A. V., & Wakefield, J. C. (2007). *The loss of sadness: How psychiatry transformed normal sorrow into depressive disorder*. New York, NY: Oxford University Press.

Hyman, S. E. (2007). Can neuroscience be integrated into the DSM-V? *Nature Reviews Neuroscience*, *8*, 725–732. doi:10.1038/nrn2218

Hyman, S. E. (2010). The diagnosis of mental disorders: The problem of reification. *Annual Review of Clinical Psychology*, *6*, 155–179. doi:10.1146/annurev.clinpsy.3.022806.091532

Iacono, W. G., Vaidyanathan, U., Vrieze, S. I., & Malone, S. M. (2014). Knowns and unknowns for psychophysiological endophenotypes: Integration and response to commentaries. *Psychophysiology*, *51*, 1339–1347. doi:10.1111/psyp.12358

Ingram, R. E., & Luxton, D. D. (2005). Vulnerability-stress models. In B. L. Hankin & J. R. Z. Abela (Eds.), *Development of psychopathology: A vulnerability-stress perspective* (pp. 32–46). Thousand Oaks, CA: Sage. doi:10.4135/9781452231655.n2

Institute of International Statistics. (1900). International list of causes of death. *Bulletin of the Institute of International Statistics*, *12*, 280.

International Advisory Group for the Revision of ICD-10 Mental and Behavioural Disorders. (2011). A conceptual framework for the revision of the ICD-10 classification of mental and behavioural disorders. *World Psychiatry*, *10*, 86–92. doi:10.1002/j.2051-5545.2011.tb00022.x

Jablensky, A. (2007). Does psychiatry need an overarching concept of "mental disorder"? *World Psychiatry*, *6*, 157–158.

Johnson, J. G., Cohen, P., Kasen, S., & Brook, J. S. (2006). Dissociative disorders among adults in the community, impaired functioning, and axis I and II comorbidity. *Journal of Psychiatric Research*, *40*, 131–140. doi:10.1016/j.jpsychires.2005.03.003

Kapur, S., Phillips, A. G., & Insel, T. R. (2012). Why has it taken so long for biological psychiatry to develop clinical tests and what to do about it? *Molecular Psychiatry*, *17*, 1174–11779. doi:10.1038/mp.2012.105

Karalunas, S. L., Fair, D., Musser, E. D., Aykes, K., Iyer, S. P., & Nigg, J. T. (2014). Subtyping attention-deficit/hyperactivity disorder using temperament dimensions: Toward biologically based nosologic. *JAMA Psychiatry*, *71*, 1015–1024. doi:10.1001/jamapsychiatry.2014.763

Kaymaz, N., & van Os, J. (2010). Extended psychosis phenotype - yes: Single continuum - unlikely. *Psychological Medicine*, *40*, 1963–1966. doi:10.1017/S0033291710000358

Keeley, J. W., Reed, G. M., Roberts, M. C., Evans, S. C., Medina-Mora, M. E., Robles, R., . . . Saxena, S. (2016). Developing a science of clinical utility in diagnostic classification systems: Field study strategies for ICD-11 Mental and Behavioural Disorders. *American Psychologist*, *71*(1), 3–16. doi:10.1037/a0039972

Keeley, J. W., Zayac, R., & Correia, C. (2008). Curvilinear relationships between statistics anxiety and performance among undergraduate students: Evidence for optimal anxiety. *Statistics Education Research Journal*, *7*(1), 4–15.

Keller, M. B., & Shapiro, R. W. (1982). "Double depression": Superimposition of acute depressive episodes on chronic depressive disorders. *The American Journal of Psychiatry*, *139*, 438–442. doi:10.1176/ajp.139.4.438

Kendler, K. S. (1996). Major depression and generalised anxiety disorder same genes, (partly) different environments—Revisited. *British Journal of Psychiatry*, *168*(Suppl. 30), 68–75. doi:10.1001/archpsyc.1992.01820090044008

Kendler, K. S. (2005). "A gene for ": The nature of gene action in psychiatric disorders. *American Journal of Psychiatry*, *162*, 1243–1252.

Kendler, K. S., Gallagher, T. J., Abelson, J. M., & Kessler, R. C. (1996). Lifetime prevalence, demographic risk factors, and diagnostic validity of nonaffective psychosis as assessed in a U.S. community sample. *Archives of General Psychiatry*, *53*, 1022–1031.

Kendler, K. S., Gardner, C. O., Gatz, M., & Pedersen, N. L. (2007). The sources of co-morbidity between major depression and generalized anxiety disorder in a Swedish national twin sample. *Psychological Medicine*, *37*, 453–462. doi:10.1017/S0033291706009135

Kendler, K. S., Prescott, C. A., Myers, J., & Neale, M. C. (2003). The structure of genetic and environmental risk factors for common psychiatric and substance use disorders in men and women. *Archives of General Psychiatry*, *60*, 929–937.

Kerridge, B. T., Saha, T. D., Gmel, G., & Rehm, J. (2013). Taxometric analysis of DSM-IV and DSM-5 alcohol use disorders. *Drug and Alcohol Dependence*, *129*(1–2), 60–69. doi:10.1016/j.drugalcdep.2012.09.010

Kessler, R. (1999). The World Health Organization International Consortium in Psychiatric Epidemiology (ICPE): Initial work and future directions – the NAPE lecture 1998. *Acta Psychiatrica Scandinavica*, *99*, 2–9. doi:10.1111/j.1600-0447.1999.tb05378.x

Kessler, R. C. (1994). The national comorbidity survey of the United States. *International Review of Psychiatry*, *6*, 365–376. doi:10.3109/09540269409023274

Kessler, R. C., McGonagle, K. A., Zhao, S., Nelson, C. B., Hughes, M., Eshleman, S., . . . Kendler, K. S. (1994). Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States: Results from the national comorbidity study. *Archives of General Psychiatry*, *51*, 8–19. doi:10.1001/archpsyc.1994.0395001000800

Kessler, R. C., & Merikangas, K. R. (2004). The national comorbidity survey replication (NCS-R): Background and aims. *International Journal of Methods in Psychiatric Research*, *13*(2), 60–68. doi:10.1002/mpr.166

Khan, A. A., Jacobson, K. C., Gardner, C. O., Prescott, C. A., & Kendler, K. S. (2005). Personality and comorbidity of common psychiatric disorders. *The British Journal of Psychiatry*, *186*, 190–196. doi:10.1192/bjp.186.3.190

Kirmayer, L. J., & Crafa, D. (2014). What kind of science for psychiatry? *Frontiers in Human Neuroscience*, *8*, 435. doi:10.3389/fnhum.2014.00435

Kleinman, A. (1977). Depression, somatization and the "new cross-cultural psychiatry." *Social Science and Medicine*, *11*(1), 3–9. doi:10.1016/0037-7856(77)90138-X

Kogan, C. S., Stein, D. J., Maj, M., First, M. B., Emmelkamp, P. M. G., & Reed, G. M. (2016). The classification of anxiety and fear-related disorders in the ICD-11. *Depression and Anxiety*. Advance online publication. doi:10.1002/da.22530

Kohn, R., Saxena, S., Levav, I., & Saraceno, B. (2004). The treatment gap in mental health care. *Bulletin of the World Health Organization*, *82*, 858–866. doi:10.1590/S0042-96862004001100011

Kotov, R., Krueger, R. F., Watson, D., Achenbach, T. M., Althoff, R. R., Bagby, R. M., . . . Zimmerman, M. (2017). The hierarchical taxonomy of psychopathology (HiTOP): A dimensional alternative to traditional nosologies. *Journal of Abnormal Psychology*, *126*, 454–477. doi:10.1037/abn0000258

Kotov, R., Ruggero, C. J., Krueger, R. G., Watson, D., Yuan, Q., & Zimmerman, M. (2011). New dimensions in the quantitative classification of mental illness. *Archives of General Psychiatry*, *68*, 1003–1011. doi:10.1001/archgenpsychiatry.2011.107

Kraemer, H. C., Kupfer, D. J., Clarke, D. E., Narrow, W. E., & Regier, D. A. (2012). DSM-5: How reliable is reliable enough? *The American Journal of Psychiatry*, *169*(1), 13–15. doi:10.1176/appi.ajp.2011.11010050

Kroenke, K., Spitzer, R. L., & Williams, J. B. (2001). The PHQ-9: Validity of a brief depression severity measure. *Journal of General Internal Medicine*, *16*, 606–613. doi:10.1046/j.1525-1497.2001.016009606.x

Krueger, R. B., Reed, G. M., First, M. B., Marais, A., Kismodi, E., & Briken, P. (2017). Proposals for paraphilic disorders in the International Classification of Disease and related health problems, Eleventh Revision (ICD-11). *Archives of Sexual Behavior*. Advance online publication. doi:10.1007/s10508-017-0944-2.

Krueger, R. F. (1999). The structure of common mental disorders. *Archives of General Psychiatry*, *56*, 921–926. doi:10.1001/archpsyc.56.10.921

Krueger, R. F., & Markon, K. E. (2006). Reinterpreting comorbidity: A model-based approach to understanding and classifying psychopathology. *Annual Review of Clinical Psychology*, *2*, 111–133. doi:10.1146/annurev.clinpsy.2.022305.095213

Kupfer, D. J., First, M. B., & Regier, D. (Eds.). (2002). *A research agenda for DSM-V*. Arlington, VA: American Psychiatric Association.

Kushner, M. G., Sher, K. J., & Beitman, B. D. (1990). The relation between alcohol problems and the anxiety disorders. *The American Journal of Psychiatry*, *147*, 685–695. doi:10.1176/ajp.147.6.685

Laceulle, O. M., Vollebergh, W. A. M., & Ormel, J. (2015). The structure of psychopathology in adolescence: Replication of a general psychopathology factor in the

trails study. *Clinical Psychological Science*, *3*, 850–860. doi:10.1177/2167702614560750

Lahey, B. B. (2009). Public health significance of neuroticism. *American Psychologist*, *64*, 241–256. doi:10.1037/a0015309

Lahey, B. B., Applegate, B., Hakes, J. K., Zald, D. H., Hariri, A. R., & Rathouz, P. J. (2012). Is there a general factor of prevalent psychopathology during adulthood? *Journal of Abnormal Psychology*, *121*, 971. doi:10.1037/a0028355

Lahey, B. B., Rathouz, P. J., Keenan, K., Stepp, S. D., Loeber, R., & Hipwell, A. E. (2015). Criterion validity of the general factor of psychopathology in a prospective study of girls. *Journal of Child Psychology and Psychiatry*, *56*, 415–422. doi:10.1111/jcpp.12300

Lang, P. J., Davis, M., & Öhman, A. (2000). Fear and anxiety: Animal models and human cognitive psychophysiology. *Journal of Affective Disorders*, *61*, 137–159. doi:10.1016/S0165-0327(00)00343-8

Lauritsen, M. B., Mortensen, P. B., & Pedersen, C. B. (2004). The incidence and prevalence of pervasive developmental disorders: A Danish population-based study. *Psychological Medicine*, *34*, 1339–1346. doi:10.1017/S0033291704002387

LeDoux, J. E., & Pine, D. S. (2016). Using neuroscience to help understand fear and anxiety: A two-system framework. *American Journal of Psychiatry*, *173*, 1083–1093.

Lewis-Fernández, R., & Aggarwal, N. K. (2013). Culture and psychiatric diagnosis. *Advances in Psychosomatic Medicine*, *33*, 15–30. doi:10.1159/000348725

Lewis-Fernández, R., Aggarwal, N. K., Hinton, L., Hinton, D. E., & Kirmayer, L. K. (Eds.). (2016). *The DSM-5 handbook on the Cultural Formulation Interview*. Washington, DC: American Psychiatric Publishing.

Lewis-Fernández, R., Hinton, D. E., Laria, A. J., Patterson, E. H., Hofmann, S. G., Craske, M. G., . . . Liao, B. (2010). Culture and the anxiety disorders: Recommendations for *DSM-V*. *Depression and Anxiety*, *27*, 212–229. doi:10.1002/da.20647

Light, G., Greenwood, T. A., Swerdlow, N. R., Calkins, M. E., Freedman, R., Green, M. F., . . . Braff, D. L. (2014). Comparison of the heritability of schizophrenia and endophenotypes in the COGS-1 family study. *Schizophrenia Bulletin*, *40*, 1404–1411. doi:10.1093/schbul/sbu064

Lilienfeld, S. O. (2003). Comorbidity between and within childhood externalizing and internalizing disorders: Reflections and directions. *Journal of Abnormal Child Psychology*, *31*, 285–291. doi:10.1023/A:1023229529866

Lilienfeld, S. O. (2014). The Research Domain Criteria (RDoC): An analysis of methodological and conceptual challenges. *Behaviour Research & Therapy*, *62*, 129–139. doi:10.1016/j.brat.2014.07.019

Lilienfeld, S. O., Waldman, I. D., & Israel, A. C. (1994). A critical examination of the use of the term and concept of comorbidity in psychopathology research. *Clinical Psychology: Science and Practice*, *1*, 71–83. doi:10.1111/j.1468-2850.1994.tb00007.x

Livesley, J., & Jang, K. L. (2005). Differentiating normal, abnormal, and disordered personality. *European Journal of Personality*, *19*, 257–268. doi:10.1002/per.559

Lopez, M. E., Stoddard, J. A., Noorollah, A., Zerbi, G., Payne, L. A., Hitchcock, C. A., . . . Ray, D. B. (2014). Examining the efficacy of the unified protocol for transdiagnostic treatment of emotional disorders in the treatment of individuals with borderline personality disorder. *Cognitive and Behavioral Practice*, *22*, 522–533. doi:10.1016/j.cbpra.2014.06.006

Lorant, V., Croux, C., Weich, S., Deliège, D., Mackenbach, J., & Ansseau, M. (2007). Depression and socio-economic risk factors: 7-year longitudinal population study. *The British Journal of Psychiatry*, *190*, 293–298. doi:10.1192/bjp.bp.105.020040

Lorant, V., Deliège, D., Eaton, W., Robert, A., Philippot, P., & Ansseau, M. (2003). Socioeconomic inequalities in depression: A meta-analysis. *American Journal of Epidemiology*, *157*, 98–112. doi:10.1093/aje/kwf182

Lord, C., & Jones, R. M. (2012). Annual research review: Re-thinking the classification of autism spectrum disorders. *Journal of Child Psychology and Psychiatry*, *53*, 490–509. doi:10.1111/j.1469-7610.2012.02547.x

Maercker, A., Brewin, C. R., Bryant, R. A., Cloitre, M., van Ommeren, M., Jones, L. M., . . . Reed, G. M. (2013). Diagnosis and classification of disorders specifically associated with stress: Proposals for ICD-11. *World Psychiatry*, *12*, 198–206. doi:10.1002/wps.20057

Maj, M. (2005). 'Psychiatric comorbidity': An artefact of current diagnostic systems? *British Journal of Psychiatry*, *186*, 182–184. doi:10.1192/bjp.186.3.182

Maj, M. (2014). The media campaign on the DSM-5: Recurring comments and lessons for the future of diagnosis in psychiatric practice. *Epidemiology and Psychiatric Sciences*, *24*, 197–202. doi:10.1017/S2045796014000572

Markon, K. E. (2010). Modeling psychopathology structure: A symptom-level analysis of axis I and II disorders. *Psychological Medicine*, *40*, 273–288. doi:10.1017/S0033291709990183

Markon, K. E., Krueger, R. F., & Watson, D. (2005). Delineating the structure of normal and abnormal personality: An integrative hierarchical approach. *Journal of Personality and Social Psychology*, *88*, 139–157. doi:10.1037/0022-3514.88.1.139

Marquand, A. F., Rezek, I., Buitelaar, J., & Beckmann, C. F. (2016). Understanding heterogeneity in clinical cohorts using normative models: Beyond case-control studies. *Biological Psychiatry*, *80*, 552–561. doi:10.1016/j.biopsych.2015.12.023

Maser, J. D., & Akiskal, H. (2002). Preface: Spectrum concepts in major mental disorder. *Psychiatric Clinics of North America*, *25*(4), xi–xiii. doi:10.1016/S0193-953X(02)00034-5

Maser, J. D., & Patterson, T. (2002). Spectrum and nosology: Implications for DSM-V. *Psychiatric Clinics of North America*, *25*, 855–885. doi:10.1016/S0193-953X(02)00022-9

Masi, G., Perugi, G., Toni, C., Millepiedi, S., Mucci, M., Bertini, N., & Pfanner, C. (2006). Attention-deficit hyperactivity disorder—bipolar comorbidity in children and adolescents. *Bipolar Disorders*, *8*, 373–381. doi:10.1111/j.1399-5618.2006.00342.x

McCrae, R. R., & Costa, P. T. (1987). Validation of the five-factor model of personality across instruments and observers. *Journal of Personality and Social Psychology*, *52*(1), 81.

Meloni, M. (2014). The social brain meets the reactive genome: Neuroscience, epigenetics and the new social biology. *Frontiers in Human Neuroscience*, *8*, 309. doi:10.3389/fnhum.2014.00309

Metzl, J. M., & Hansen, H. (2014). Structural competency: Theorizing a new medical engagement with stigma and inequality. *Social Science & Medicine*, *103*, 126–133. doi:10.1016/j.socscimed.2013.06.032

Mewton, L., Slade, T., McBride, O., Grove, R., & Teesson, M. (2011). An evaluation of the proposed DSM-5 alcohol use disorder criteria using Australian national data. *Addiction*, *106*, 941–950. doi:10.1111/j.1360-0443.2010.03340.x

Meyer, G. J., Finn, S. E., Eyde, L. D., Kay, G. G., Moreland, K. L., Dies, R. R., . . . Reed, G. M. (2001). Psychological testing and psychological assessment: A review of evidence and issues. *American Psychologist*, *56*, 128–165. doi:10.1037/0003-066X.56.2.128

Mezzich, J. E., Caracci, G., Fabrega, H., & Kirmayer, L. J. (2009). Cultural formulation guidelines. *Transcultural Psychiatry*, *46*, 383–405. doi:10.1177/1363461509342942

Mineka, S., Watson, D. W., & Clark, L. A. (1998). Psychopathology: Comorbidity of anxiety and unipolar mood disorders. *Annual Review of Psychology*, *49*, 377–412. doi:10.1146/annurev.psych.49.1.377

Mookhoek, E. J., deVries, W. A., Hovens, J. E. J. M., Brouwers, J. R. B. J., & Loonen, A. J. M. (2011). Risk factors for overweight and diabetes mellitus in residential psychiatric patients. *Obesity Facts*, *4*, 341–345. doi:10.1159/000333420

National Institute on Drug Abuse. (2012). Resource guide: Screening for drug use in general medical settings. Retrieved from the NIDA Web site: https://www.drugabuse.gov/publications/resource-guide-screening-drug-use-in-general-medical-settings/nida-quick-screen

Narrow, W. E., Clarke, D. E., Kuramoto, S. J., Kraemer, H. C., Kupfer, D. J., Greiner, L., . . . Regier, D. A. (2013). DSM-5 field trials in the United States and Canada, Part III: Development and reliability testing of a cross-cutting symptom assessment for DSM-5. *American Journal of Psychiatry*, *170*, 71–82. doi:10.1176/appi.ajp.2012.12071000

Narrow, W. E., First, M. B., Sirovatka, P. J., & Regier, D. A. (Eds.). (2007). *Age and gender considerations in psychiatric diagnosis: A research agenda for DSM-V*. Arlington, VA: American Psychiatric Association.

Narrow, W. E., Kuhl, E. A., & Regier, D. A. (2009). DSM-V perspectives on disentangling disability from clinical significance. *World Psychiatry*, *8*, 88–89.

Narrow, W. E., Rae, D. S., Robins, L. N., & Regier, D. A. (2002). Revised prevalence based estimates of mental disorders in the United States: Using a clinical significance criterion to reconcile 2 surveys' estimates. *Archives of General Psychiatry*, *59*, 115–123. doi:10.1001/archpsyc.59.2.115

Natale, C. (2014, April 23). *Is ICD-11 talk just a tactic to stall ICD-10? Government Health IT*. Retrieved from http://www.govhealthit.com/news/ICD-11-advocates-say-skip-ICD-10

National Institute for Health and Care Excellence, U.K. (2015). *Guidance list*. Retrieved from http://www.nice.org.uk/guidance/published?type=cg

Nigg, J. T. (2016). Where do epigenetics and developmental origins take the field of developmental psychopathology? *Journal of Abnormal Child Psychology*, *44*, 405–419. doi:10.1007/s10802-015-0121-9

Nuevo, R., Chatterji, S., Verdes, E., Naidoo, N., Arango, C., & Ayuso-Mateos, J. L. (2012). The continuum of psychotic symptoms in the general population: A cross-national study. *Schizophrenia Bulletin*, *38*, 475–485. doi:10.1093/schbul/sbq099

Ormel, J., Raven, D., van Oort, F., Hartman, C. A., Reijneveld, S. A., Veenstra, R., . . . Oldehinkel, A. J. (2014). Mental health in Dutch adolescents: A TRAILS report on prevalence, severity, age of onset, continuity and co-morbidity of DSM disorders. *Psychological Medicine*, *45*, 345–360. doi:10.1017/S0033291714001469

Otero-Ojeda, A. (1998). *Third Cuban glossary of psychiatry* [Spanish]. Havana, Cuba: Hospital Psiquiátrico de La Habana.

Owen, M. J. (2014). New approaches to psychiatric diagnostic classification. *Neuron*, *84*, 564–571. doi:10.1016/j.neuron.2014.10.028

Paris, J., & Kirmayer, L. J. (2016). The National Institute of Mental Health Research Domain criteria: A bridge too far. *Journal of Nervous and Mental Disease*, *204*, 26–32. doi:10.1097/NMD.0000000000000435

Patrick, C. J. (2014). Genetics, neuroscience, and psychopathology: Clothing the emperor. *Psychophysiology*, *51*, 1333–1334. doi:10.1111/psyp.12356

Phillips, K. A., & Stein, D. J. (2015). Introduction and major changes for the obsessive-compulsive and related disorders in DSM-5. In K. A. Phillips & D. J. Stein (Eds.), *Handbook on obsessive-compulsive and related disorders* (pp. 1–24). Arlington, VA: American Psychiatric Publishing.

Phillips, K. A., Stein, D. J., Rauch, S. L., Hollander, E., Fallon, B. A., Barsky, A., . . . Leckman, J. (2010). Should an obsessive-compulsive spectrum grouping of disorders be included in DSM-V? *Depression and Anxiety*, *27*, 528–555. doi:10.1002/da.20705

Picchioni, M. M., Walshe, M., Toulopoulou, T., McDonald, C., Taylor, M., Waters-Metenier, S., . . . Rijsdijk, F. (2010). Genetic modelling of childhood social development and personality in twins and siblings with schizophrenia. *Psychological Medicine*, *40*, 1305–1316. doi:10.1017/S0033291709991425

Pitman, R. K., Rasmusson, A. M., Koenen, K. C., Shin, L. M., Orr, S. P., Gilbertson, M. W., . . . Liberzon, I. (2012). Biological studies of post-traumatic stress disorder. *Nature Reviews: Neuroscience*, *13*, 769–787. doi:10.1038/nrn3339

Poznyak, V., Reed, G. M., & Clark, N. (2011). Applying an international public health perspective to proposed changes for DSM-V. *Addiction*, *106*, 868–870. doi:10.1111/j.1360-0443.2011.03381.x

Probst, B. (2014). The life and death of axis IV: Caught in the quest for a theory of mental disorder. *Research on Social Work Practice*, *24*, 123–131. doi:10.1177/1049731513491326

Rapoport, J. L., Giedd, J. N., & Gogtay, N. (2012). Neurodevelopmental model of schizophrenia: Update 2012. *Molecular Psychiatry*, *17*, 1228–1238. doi:10.1038/mp.2012.23

Reed, G. M. (2010). Toward ICD-11: Improving the clinical utility of WHO's international classification of mental disorders. *Professional Psychology: Research and Practice*, *41*, 457–464. doi:10.1037/a0021701

Reed, G. M., Correia, J., Esparza, P., Saxena, S., & Maj, M. (2011). The WPA-WHO global survey of psychiatrists' attitudes towards mental disorders classification. *World Psychiatry*, *10*, 118–131. doi:10.1002/j.2051-5545.2011.tb00034.x

Reed, G. M., Drescher, J., Krueger, R. B., Atalla, E., Cochran, S. D., First, M. B., . . . Saxena, S. (2016). Disorders related to sexuality and gender identity in the ICD-11: Revising the ICD-10 classification based on current scientific evidence, best clinical practices, and human rights considerations. *World Psychiatry*, *15*, 205–221.

Reed, G. M., Rebello, T. J., Pike, K. M., Medina-Mora, M. E., Gureje, O., Zhao, M., . . . Saxena, S. (2015). WHO's Global Clinical Practice Network for mental health. *Lancet Psychiatry*, *2*, 379–380. doi:10.1016/S2215-0366(15)00183-2

Reed, G. M., Roberts, M. C., Keeley, J., Hooppell, C., Matsumoto, C., Sharan, P., . . . Medina-Mora, M. E. (2013). Mental health professionals' natural taxonomies of mental disorders: Implications for the clinical utility of the ICD-11 and the DSM-5. *Journal of Clinical Psychology*, *69*, 1191–1212. doi:10.1002/jclp.22031

Reed, G. M., Spaulding, W. D., & Bufka, L. F. (2009). The relevance of the International Classification of Functioning, Disability and Health (ICF) to mental disorders and their treatment. *ALTER: The European Journal of Disability Research*, *3*, 340–359. doi:10.1016/j.alter.2008.11.003

Regier, D. A., Myers, J. K., Kramer, M., Robins, L. N., Blazer, D. G., Hough, R. L., . . . Locke, B. Z. (1984). The NIMH epidemiologic catchment area program: Historical context, major objectives, and study population characteristics. *Archives of General Psychiatry*, *41*, 934–941. doi:10.1001/archpsyc.1984.01790210016003

Rende, R., & Plomin, R. (1992). Diathesis-stress models of psychopathology: A quantitative genetic perspective. *Applied & Preventive Psychology*, *1*, 177–182. doi:10.1016/S0962-1849(05)80123-4

Roberts, M. C., Reed, G. M., Medina-Mora, M. E., Keeley, J. W., Sharan, P., Johnson, D. K., . . . Saxena, S. (2012). A global clinicians' map of mental disorders to improve ICD-11: Analysing meta-structure to enhance clinical utility. *International Review of Psychiatry*, *24*, 578–590. doi:10.3109/09540261.2012.736368

Robins, E., & Guze, S. B. (1970). Establishment of diagnostic validity in psychiatric illness: Its application to schizophrenia. *American Journal of Psychiatry*, *126*, 983–986. doi:10.1176/ajp.126.7.983

Robins, L. N., Helzer, J. E., Croughan, J. L., & Ratcliff, K. S. (1981). National institute of mental health diagnostic interview schedule: Its history, characteristics, and validity. *Archives of General Psychiatry*, *38*, 381–389. doi:10.1001/archpsyc.1981.01780290015001

Robins, L. N., Wing, J., Wittchen, H. U., Helzer, J. E., Babor, T. F., Burke, J., . . . Towle, L. H. (1988). The composite international diagnostic interview: An epidemiologic instrument suitable for use in conjunction with different diagnostic systems and in different cultures. *Archives of General Psychiatry*, *45*, 1069–1077. doi:10.1001/archpsyc.1988.01800360017003

Robinson, E. B., St. Pourcain, B., Anttila, V., Kosmicki, J. A., Bulik-Sullivan, B., Grove, J., . . . Walters, R. (2016). Genetic risk for autism spectrum disorders and neuropsychiatric variation in the general population. *Nature Genetics*, *48*, 552–555. doi:10.1038/ng.3529

Robles, R., Frésan, A., Vega-Ramírez, H., Cruz-Islas, J., Rodríguez-Pérez, V., Domínguez-Martínez, T., . . . Reed, G. M. (2016). Removing transgender identity from the classification of mental disorders: A Mexican field study for ICD-11. *Lancet Psychiatry*, *3*, 850–859. doi:10.1016/S2215-0366(16)30165-1

Ruiz, M. A., Pincus, A. L., & Schinka, J. A. (2008). Externalizing pathology and the Five-Factor Model: A meta-analysis of personality traits associated with antisocial personality disorder, substance use disorder, and their co-occurrence. *Journal of Personality Disorders*, *22*, 365–388. doi:10.1521/pedi.2008.22.4.365

Rutter, M. (2002). The interplay of nature, nurture, and developmental influences: The challenge ahead for mental health. *Archives of General Psychiatry*, *59*, 996–1000. doi:10.1001/archpsyc.59.11.996

Rutter, M. (2012). Gene–environment interdependence. *European Journal of Developmental Psychology*, *9*, 391–412. doi:10.1080/17405629.2012.661174

Sachs, E., Rosenfeld, B., Lhewa, D., Rasmussen, A., & Keller, A. (2008). Entering exile: Trauma, mental health, and coping among Tibetan refugees arriving in Dharamsala, India. *Journal of Traumatic Stress*, *21*, 199–208. doi:10.1002/jts.20324

Saxena, S., Funk, M., & Chisholm, D. (2013). World Health Assembly adopts Comprehensive Mental Health Action Plan 2013–2020. *The Lancet*, *381*, 1970–1971. doi:10.1016/S0140-6736(13)61139-3

Saxena, S., Thornicroft, G., Knapp, M., & Whiteford, H. (2007). Resources for mental health: Scarcity, inequity, and inefficiency. *The Lancet*, *370*, 878–889. doi:10.1016/S0140-6736(07)61239-2

Scheeringa, M. S., Zeanah, C. H., & Cohen, J. A. (2011). PTSD in children and adolescents: Toward in empirically based algorithm. *Depression and Anxiety*, *28*, 770–782. doi:10.1002/da.20736

Scott, D., & Happell, B. (2011). The high prevalence of poor physical health and unhealthy lifestyle behaviours in individuals with severe mental illness. *Issues in Mental Health Nursing*, *32*, 589–597. doi:10.3109/01612840.2011.569846

Scott, K. M., de Jonge, P., Alonso, J., Viana, M. C., Lui, Z., O'Neill, S., . . . Kessler, R. C. (2013). Associations between *DSM-IV* mental disorders and subsequent heart disease onset: Beyond depression. *International Journal of Cardiology*, *168*, 5293–5299. doi:10.1016/j.ijcard.2013.08.012

Sekar, A., Bialas, A. R., de Rivera, H., Davis, A., Hammond, T. R., Kamitaki, N., . . . McCarroll, S. A. (2016). Schizophrenia risk from complex variation of complement component 4. *Nature*, *530*, 177–183. doi:10.1038/nature16549

Sharma, L., Markon, K. E., & Clark, L. A. (2014). Toward a theory of distinct types of "impulsive" behaviors: A meta-analysis of self-report and behavioral measures. *Psychological Bulletin*, *140*, 374–408. doi:10.1037/a0034418

Sharp, C., Wright, A. G. C., Fowler, J. C., Frueh, B. C., Allen, J. G., Oldham, J., . . . Clark, L. A. (2015). The structure of personality pathology: Both general ('g') and specific ('s') factors? *Journal of Abnormal Psychology*, *124*, 387. doi:10.1037/abn0000033

Shin, J. K., Barron, C. T., Chiu, Y. L., Jang, S. H., Touhid, S., & Bang, H. (2012). Weight changes and characteristics of patients associated with weight gain during inpatient psychiatric treatment. *Issues in Mental Health Nursing*, *33*, 505–512. doi:10.3109/01612840.2012.683931

Shin, L. M., & Liberzon, I. (2010). The neurocircuitry of fear, stress, and anxiety disorders. *Neuropsychopharmacology*, *35*, 169–191. doi:10.1038/npp.2009.83

Skodol, A. E., & Spitzer, R. L. (1987). Introduction. In A. E. Skodol & R. L. Spitzer (Eds.), *An annotated bibliography of DSM-III* (pp. xi–xiv). Washington, DC: American Psychiatric Press.

Slade, T., & Watson, D. (2006). The structure of common DSM-IV and ICD-10 mental disorders in the Australian general population. *Psychological Medicine*, *36*, 1593–1600. doi:10.1017/S0033291706008452

Smink, F. R. E., van Hoeken, D., & Hoek, H. W. (2013). Epidemiology, course, and outcome of eating disorders. *Current Opinion in Psychiatry*, *26*, 543–548. doi:10.1097/YCO.0b013e328365a24f

Spitzer, R. L., Endicott, J., & Robins, E. (1978). Research diagnostic criteria: Rationale and reliability. *Archives of General Psychiatry*, *35*, 773–782. doi:10.1001/archpsyc.1978.01770300115013

Spitzer, R. L., Williams, J. B., Gibbon, M., & First, M. B. (1992). The structured clinical interview for DSM-III-R (SCID): I. History, rationale, and description. *Archives of General Psychiatry*, *49*, 8624–8629. doi:10.1001/archpsyc.1992.01820080032005

Spitzer, R. L., & Williams, J. B. W. (1988). The revision of *DSM-III*: Process and changes. In J. E. Mezzich & M. von Cranach (Eds.), *International classification in psychiatry: Unity and diversity* (pp. 263–283). New York, NY: Cambridge University Press.

Sroufe, L. A., & Rutter, M. (1984). The domain of developmental psychopathology. *Child Development*, *55*(1), 17–29. doi:10.2307/1129832

Stecker, T., Fortney, J. C., Steffick, D. E., & Prajapati, S. (2006). The triple threat for chronic disease: Obesity, race, and depression. *Psychosomatics*, *47*, 513–518. doi:10.1176/appi.psy.47.6.513

Stein, D. J., Kogan, C. S., Atmaca, M., Fineberg, N. A., Fontenelle, L. F., Grant, J., . . . Reed, G. M. (2016). The classification of obsessive-compulsive and related disorders in the ICD-11. *Journal of Affective Disorders*, *190*, 663–674. doi:10.1016/j.jad.2015.10.061

Stengel, E. (1959). Classification of mental disorders. *Bulletin of the World Health Organization*, *21*, 601–663.

Storch, E. A., Bagner, D., Merlo, L. J., Shapira, N. A., Geffken, G. R., Murphy, T. K., & Goodman, W. K. (2007). Florida Obsessive-Compulsive Inventory: Development, reliability, and validity. *Journal of Clinical Psychology*, *63*, 851–859. doi:10.1002/jclp.20382

Storch, E. A., Khanna, M., Merlo, L. J., Loew, B. A., Franklin, M., Reid, J. M., . . . Murphy, T. K. (2009). Children's Florida obsessive compulsive inventory: Psychometric properties and feasibility of a self-report measure of obsessive–compulsive symptoms in youth. *Child Psychiatry and Human Development*, *40*(3), 467-483. doi:10.1007/s10578-009-0138-9

Stringaris, A., Goodman, R., Ferdinando, S., Razdan, V., Muhrer, E., Leibenluft, E., & Brotman, A. (2012). The Affective Reactivity Index: A concise irritability scale for clinical and research settings. *Journal of Psychology and Psychiatry*, *53*, 1109–1117.

Sturt, E. (1981). Hierarchical patterns in the distribution of psychiatric symptoms. *Psychological Medicine*, *11*, 783–794. doi:10.1017/S0033291700041283

Sullivan, T. (2012, February 16). Could the U.S. skip ICD-10 and leapfrog directly to ICD-11? *Healthcare Payer News*. Retrieved from http://www.healthcarepayernews.com/content/could-us-skip-ICD-10-and-leapfrog-directly-ICD-11#.VZkeSKZSmXs

Svendsen, D., Singer, P., Foti, M. E., & Mauer, B. (2006). *Morbidity and mortality in people with serious mental illness*. Alexandria, VA: National Association of State Mental Health Program Directors (NASMHPD) Medical Directors Council.

Tackett, J. L., Waldman, I. D., Van Hulle, C. A., & Lahey, B. B. (2011). Shared genetic influences on negative emotionality and major depression/conduct disorder comorbidity. *Journal of the American Academy of Child & Adolescent Psychiatry*, *50*, 818–827. doi:10.1016/j.jaac.2011.05.007

Tanenbaum, S. J. (2005). Evidence-based practice as mental health policy: Three controversies and a caveat. *Health Affairs*, *24*, 163–173. doi:10.1377/hlthaff.24.1.163

Tassé, M. J., Luckasson, R., & Nygren, M. (2013). AAIDD proposed recommendations for ICD-11 and the condition previously known as mental retardation. *Intellectual and Developmental Disabilities*, *51*, 127–131. doi:10.1352/1934-9556-51.2.127

Thomas, J. J., Vartanian, L. R., & Brownell, K. D. (2009). The relationship between eating disorder not otherwise specified (EDNOS) and officially recognized eating disorders: Meta-analysis and implications for DSM. *Psychological Bulletin*, *135*, 407–433. doi:10.1037/a0015326

Thornicroft, G. (2011). Physical health disparities and mental illness: The scandal of premature mortality. *British Journal of Psychiatry*, *199*, 441–442. doi:10.1192/bjp.bp.111.092718

Thornicroft, G. (2013). Premature death among people with mental illness. *British Medical Journal*, *346*, f2969. doi:10.1136/bmj.f2969

Trull, T. J., Vergés, A., Wood, P. K., & Sher, K. J. (2013). The structure of *DSM-IV*-TR personality disorder diagnoses in NESARC: A reanalysis. *Journal of Personality Disorders*, *27*, 727–734. doi:10.1521/pedi_2013_27_107

Tsuang, M. T., Glatt, S. J., & Faraone, S. V. (2003). Genetics and genomics in schizophrenia. *Primary Psychiatry*, *10*, 37–40, 50.

Tucker, J. A., & Reed, G. M. (2008). Evidentiary pluralism as a strategy for research and evidence-based practice in rehabilitation psychology. *Rehabilitation Psychology*, *53*, 269–283. doi:10.1037/a0012963

Turecki, G., Ota, V. K., Belangero, S. I., Jackowski, A., & Kaufman, J. (2014). Early life adversity, genomic plasticity, and psychopathology. *The Lancet Psychiatry*, *1*, 461–466. doi:10.1016/S2215-0366(14)00022-4

Tyrer, P., Crawford, M., Mulder, R., Blashfield, R., Farnam, A., Fossati, A., . . . Reed, G. M. (2011). The rationale for the reclassification of personality disorder in the 11th revision of the international classification of diseases (ICD-11). *Personality and Mental Health*, *5*, 246–259. doi:10.1002/pmh.190

Tyrer, P., Reed, G. M., & Crawford, M. J. (2015). Classification, assessment, prevalence and effect of personality disorder. *The Lancet*, *385*, 717–726. doi:10.1016/S0140-6736(14)61995-4

U.S. Centers for Medicare and Medicaid Services. (2015). *Transaction and code sets standards*. Retrieved from http://www.cms.gov/Regulations-and-Guidance/Administrative-Simplification/HIPAA-ACA/AdoptedStandardsandOperatingRules.html

U.S. National Center for Health Statistics. (2015). *International classification of diseases, 10th revision, clinical modification*. Retrieved from http://www.cdc.gov/nchs/icd/icd10cm.htm

U.S. Public Health Service, Division of Public Health Methods. (1944). *Manual for coding causes of illness according to a diagnosis code for tabulating morbidity statistics* (Miscellaneous Publication No. 32). Washington, DC: Government Publishing Office.

Üstün, B., & Kennedy, C. (2009). What is "functional impairment"? Disentangling disability from clinical significance. *World Psychiatry*, *8*, 82–85. doi:10.1002/j.2051-5545.2009.tb00219.x

van Os, J. (2016). "Schizophrenia" does not exist. *British Medical Journal*, *352*, i375. doi:10.1136/bmj.i375

van Os, J., Lataster, T., Delespaul, P., Wichers, M., & Myin-Germeys, I. (2014). Evidence that a psychopathology interactome has diagnostic value, predicting clinical needs: An experience sampling study. *PLOS ONE*, *9*, e86652. doi:10.1371/journal.pone.0086652

van Os, J., Linscott, R. J., Myin-Germeys, I., Delespaul, P., & Krabbendam, L. (2009). A systematic review and meta-analysis of the psychosis continuum: Evidence for a psychosis proneness–persistence–impairment model of psychotic disorder. *Psychological Medicine*, *39*, 179–195. doi:10.1017/S0033291708003814

Verheul, R., & Widiger, T. A. (2004). A meta-analysis of the prevalence and usage of the personality disorder not otherwise specified (PDNOS) diagnosis. *Journal of Personality Disorders*, *18*, 309–319. doi:10.1521/pedi.18.4.309.40350

Vigo, D., Thornicroft, G., & Atun, R. (2016). Estimating the true global burden of mental illness. *Lancet Psychiatry*, *3*, 171–178. doi:10.1016/S2215-0366(15)00505-2

Vilagut, G., Forero, C. G., Barbaglia, G., & Aloso, J. (2016). Screening for depression in the general population with the Center for Epidemiological Studies Depression (CES-D): A systematic review with meta-analysis. *PLOS ONE*, *11*, e0155431. doi:10.1371/journal.pone.0155431

Villalta-Gil, V., Vilaplana, M., Ochoa, S., Haro, J. M., Dolz, M., Usall, J., & Cervilla, J. (2006). Neurocognitive performance and negative symptoms: Are they equal in explaining disability in schizophrenia outpatients? *Schizophrenia Research*, *87*, 246–253. doi:10.1016/j.schres.2006.06.013

Vittengl, J. R., Clark, L. A., Thase, M. E., & Jarrett, R. B. (2014). Are improvements in cognitive content and depressive symptoms correlates or mediators during acute-phase cognitive therapy for recurrent MDD. *International Journal of Cognitive Therapy*, *7*, 251–271. doi:10.1521/ijct.2014.7.3.251

Vollebergh, W. A. M., Iedema, J., Bijl, R. V., de Graaf, R., Smit, F., & Ormel, J. (2001). The structure and stability of common mental disorders: The NEMESIS Study. *Archives of General Psychiatry*, *586*, 597–603.

Voruganti, L. P., Punthakee, Z., Van Lieshout, R. J., MacCrimmon, D., Parker, G., Awad, A. G., & Gerstein, H. C. (2007). Dysglycemia in a community sample of people treated for schizophrenia: The Diabetes in Schizophrenia in Central-south Ontario (DiSCO) study. *Schizophrenia Research*, *96*, 215–222. doi:10.1016/j.schres.2007.07.016

Wakefield, J. C. (1992). The concept of mental disorder: On the boundary between biological facts and social values. *American Psychologist*, *47*, 373–388. doi:10.1037/0003-066X.47.3.373

Wakefield, J. C. (2007). The concept of mental disorder: Diagnostic implications of the harmful dysfunction analysis. *World Psychiatry*, *6*, 149–156.

Wakschlag, L. S., Leventhal, B. L., Thomas, J., & Pine, D. S. (2007). Disruptive behavior disorders and ADHD in preschool children. In W. E. Narrow, M. B. First, P. J. Sirovatka, & D. A. Regier (Eds.), *Age and gender considerations in psychiatric diagnosis: A research agenda for DSM-V* (pp. 243–257). Arlington, VA: American Psychiatric Association.

Waldman, I. D., & Lilienfeld, S. O. (2001). Applications of taxometric methods to problems of comorbidity: Perspectives and challenges. *Clinical Psychology: Science and Practice*, *8*, 520–527. doi:10.1093/clipsy/8.4.520

Walker, E. R., & Druss, B. G. (2015). Rate and predictors of persistent MDD in a nationally representative sample. *Community Mental Health Journal*, *51*, 701–707. doi:10.1007/s10597-014-9793-9

Walker, E. R., McGee, R. E., & Druss, B. G. (2015). Mortality in mental disorders and global disease burden implications: A systematic review and meta-analysis. *JAMA Psychiatry*, *72*, 334–341. doi:10.1001/jamapsychiatry.2014.2502

Watson, D. (2005). Rethinking the mood and anxiety disorders: A quantitative hierarchical model for DSM-V. *Journal of Abnormal Psychology*, *114*, 522–536. doi:10.1037/0021-843X.114.4.522

Watson, D., Clark, L. A., & Carey, G. (1988). Positive and negative affectivity and their relation to anxiety and depressive disorders. *Journal of Abnormal Psychology*, *97*, 346–353. doi:10.1037/0021-843X.97.3.346

Watson, D., O'Hara, M. W., Naragon-Gainey, K., Koffel, E., Chmielewski, M., Kotov, R., . . . Ruggero, C. J. (2012). Development and validation of new anxiety

and bipolar symptom scales for an expanded version of the IDAS (the IDAS-II). *Assessment*, *19*, 399–420. doi:10.1177/1073191112449857

Widiger, T. A., & Clark, L. A. (2000). Toward DSM-V and the classification of psychopathology. *Psychological Bulletin*, *126*, 946–963. doi:10.1037/0033-2909.126.6.946

Widom, C. (1999). Posttraumatic stress disorder in abused and neglected children grown up. *American Journal of Psychiatry*, *156*, 1223–1229.

Wilberg, T., Urnes, Ø., Friis, S., Pedersen, G., & Karterud, S. (1999). Borderline and avoidant personality disorders and the five-factor model of personality: A comparison between DSM-IV diagnoses and NEO-PI-R. *Journal of Personality Disorders*, *13*, 226–240. doi:10.1521/pedi.1999.13.3.226

Wilk, J. E., West, J. C., Narrow, W. E., Marcus, S., Rubio-Stipec, M., Rae, D. S., . . . Regier, D. A. (2006). Comorbidity patterns in routine psychiatric practice: Is there evidence of under-detection and under-diagnosis? *Comprehensive Psychiatry*, *47*, 258–264. doi:10.1016/j.comppsych.2005.08.007

Woodruff, R. A., Goodwin, D. W., & Guze, S. B. (1974). *Psychiatric diagnosis*. New York, NY: Oxford University Press.

World Health Organization. (1949). *International statistical classification of diseases, injuries, and causes of death, 6th revision*. Geneva, Switzerland: Author.

World Health Organization. (1967). *International statistical classification of diseases, injuries, and causes of death, 8th revision*. Geneva, Switzerland: Author.

World Health Organization. (1974). *Glossary of mental disorders and guide to their classification*. Geneva, Switzerland: Author.

World Health Organization. (1979). *International statistical classification of diseases, injuries, and causes of death, 9th revision*. Geneva, Switzerland: Author.

World Health Organization. (1992a). *International statistical classification of diseases and related health problems, 10th revision*. Geneva, Switzerland: Author.

World Health Organization. (1992b). *The ICD-10 classification of mental and behavioral disorders: Clinical descriptions and diagnostic guidelines*. Geneva, Switzerland: Author.

World Health Organization. (1993). *The ICD-10 classification of mental and behavioural disorders: Diagnostic criteria for research*. Geneva, Switzerland: Author.

World Health Organization. (1996). *Diagnostic and management guidelines for mental disorders in primary care: ICD-10 Chapter V Primary Care Version*. Göttingen, Germany: WHO - Hogrefe and Huber.

World Health Organization. (2001). *International classification of functioning, disability, and health*. Geneva, Switzerland: Author.

World Health Organization. (2008). *mhGAP—Mental Health Gap Action Programme: Scaling up care for mental, neurological, and substance use disorders*. Geneva, Switzerland: Author.

World Health Organization. (2011). *Mental Health Atlas 2011*. Geneva, Switzerland: Author.

World Health Organization. (2013a). *Mental Health Action Plan 2013*-2020. Geneva, Switzerland: Author.

World Health Organization. (2013b). *Assessment and management of conditions specifically related to stress: mhGAP Intervention Guide module*. Geneva, Switzerland: Author.

World Health Organization. (2014). Constitution of the World Health Organization. In *World Health Organization basic documents* (48th ed.). Geneva, Switzerland: Author.

World Health Organization. (2016a). *ICD-11 Beta Draft (Joint Linearization for Mortality and Morbidity Statistics)*. Geneva: Author. Retrieved from http://apps.who.int/classifications/icd11/browse/l-m/en

World Health Organization. (2016b). *International Statistical Classification of Diseases and Related Health Problems, 10th Revision. ICD-10 Version: 2016*. Geneva, Switzerland: Author. Retrieved from http://apps.who.int/classifications/icd10/browse/2016/en

World Health Organization. (2016c). *mhGAP Intervention guide for mental, neurological, and substance use disorders in non-specialized health settings*. Geneva, Switzerland: Author.

World Health Organization & U.S. Alcohol, Drug Abuse, and Mental Health Administration. (1985). *Mental disorders, alcohol, and drug-related problems: International perspectives on their diagnosis and classification*. Oxford, England: Elsevier Science.

World Health Organization World Mental Health Survey Consortium. (2004). Prevalence, severity, and unmet need for treatment of mental disorders in the World Health Organization World Mental Health Surveys. *Journal of the American Medical Association*, *291*, 2581–2590. doi:10.1001/jama.291.21.2581

Wright, A. G. C., Hopwood, C. J., Skodol, A. E., & Morey, L. C. (2016). Longitudinal validation of general and specific structural features of personality pathology. *Journal of Abnormal Psychology*, *125*, 1120. doi:10.1037/abn0000165

Young, G., Lareau, C., & Pierre, B. (2014). One quintillion ways to have PTSD comorbidity: Recommendations for the disordered DSM-5. *Psychological Injury and Law*, *7*(1), 61–74. doi:10.1007/s12207-014-9186-y