

636,120 Ways to Have Posttraumatic Stress Disorder

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Abstract

In an attempt to capture the variety of symptoms that emerge following traumatic stress, the revision of posttraumatic stress disorder (PTSD) criteria in the 5th edition of the *Diagnostic and Statistical Manual of Mental Disorders (DSM–5)* has expanded to include additional symptom presentations. One consequence of this expansion is that it increases the amorphous nature of the classification. Using a binomial equation to elucidate possible symptom combinations, we demonstrate that the *DSM–IV* criteria listed for PTSD have a high level of symptom profile heterogeneity (79,794 combinations); the changes result in an eightfold expansion in the *DSM–5*, to 636,120 combinations. In this article, we use the example of PTSD to discuss the limitations of *DSM*-based diagnostic entities for classification in research by elucidating inherent flaws that are either specific artifacts from the history of the *DSM* or intrinsic to the underlying logic of the *DSM*'s method of classification. We discuss new directions in research that can provide better information regarding both clinical and nonclinical behavioral heterogeneity in response to potentially traumatic and common stressful life events. These empirical alternatives to an a priori classification system hold promise for answering questions about why diversity occurs in response to stressors.

Keywords

posttraumatic stress disorder (PTSD), diagnosis, *DSM–5*, heterogeneity, combinatorics, latent growth mixture modeling

Diagnostic categories are commonly used for research and treatment of mental illness. These categories allow clinicians and researchers to identify those who have a disorder on the basis of a clear set of symptoms and symptom categories. By accurately defining symptom requirements for the illness, researchers and clinicians can identify predictors and correlates of specific mental illnesses and subsequently develop and apply more targeted treatments. Abstractly, this approach seems simple and clear, achieving the ongoing goal of the *Diagnostic and Statistical Manual of Mental Disorders (DSM)* framework to create well-defined, nonobscure diagnoses to aid in research and treatment (Spitzer, Endicott, & Robins, 1978). However, upon closer scrutiny, we find that many of the diagnostic classifications are not simple or specific. Individuals with the same diagnosis can have remarkably distinct symptom presentations. This calls the use of *DSM* diagnoses as research and treatment tools into question.

This article describes the current diagnostic system, which often relies on identifying combinations of subsets of symptoms, or criteria, to define diagnoses. We describe

the initial and evolving role the *DSM* has played as a research tool. We first examine the history of the *DSM* and the posttraumatic stress disorder (PTSD) diagnosis. We discuss how attempts to clearly define diagnostic entities led to built-in measurement issues that limit the utility of diagnoses for research or the evaluation of treatment effects. We focus on the underlying mathematical foundations of this scheme to demonstrate that as the *DSM* moves through permutations, the diagnostic criteria rarely become clarified and in some cases become increasingly obscured as the diagnosis expands to encompass more heterogeneous presentations. Finally, we discuss recent developments that have emerged as a potentially more robust method for identifying meaningful clinical outcomes without reliance on *DSM* diagnoses.

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We focus primarily on PTSD because it is a good example of how many factors, both historical and mathematical, have led to a nondescript classification. To demonstrate this point, we show how the PTSD diagnosis has expanded to encompass increasing numbers of populations and presentations, leading to increasing underlying heterogeneity in the diagnosis. Next, we discuss empirical efforts to clarify the *DSM* PTSD diagnosis, the current findings related to PTSD, and the limitations of these efforts in the light of the measurement problems intrinsic to the diagnosis. Finally, we discuss the relevance of the issues highlighted by the problems with diagnosis in nonclinical contexts where researchers are interested in identifying discrete populations on the basis of behavioral characteristics.

A Brief History of *DSM* Diagnoses as a Measurement Tool

Despite their use in medical, psychological, and sociological research, *DSM* diagnoses were not initially intended or designed to explore basic science hypotheses (Kraemer, 2007). Some of the confusion with regard to their intended use may come from the word “statistical” in the *DSM* title. This term was initially in reference to the new ability to count the number of individuals meeting a specific diagnosis in mental hospitals and in the general population, not as an allusion to the diagnosis's value as a statistical variable (Kraemer, 2007). However, the initial iterations of the *DSM* (*DSM-I* and *DSM-II*) were heavily criticized as being overly broad, vague, and theoretically driven. In particular, these diagnostic classifications were ineffective at differentiating mental disorders and those who were sick from those who were healthy (M. Wilson, 1993), making them inadequate for the purpose for which they were designed.

Beginning with the *DSM-III*, a concerted effort was made to create a system where the diagnosis was defined only in terms of observable symptoms to combat previous criticisms. The primary goal was to create a classification system that was highly reliable, meaning that any clinician observing the same patient independently would reach the same diagnosis. Vague terms, such as “neurosis” and “psychosis,” were removed in favor of specific, observable, symptom-based criteria for each diagnosis (Spitzer, Endicott, & Robins, 1975). An explicit assumption was made that the validity of diagnoses would follow from the establishment of reliability and that clear diagnostic criteria could be used as a foundation for clinical research by relating these classifications to genetics and psychobiology (Spitzer et al., 1978). The *DSM* task force, a select group of clinicians, administrators, and researchers, was formed with the goal of creating a diagnostic manual that defined diagnoses only in terms of reliably observable symptoms based on “the

best available evidence” with clearly defined cutoffs separating normality from pathology (Galatzer-Levy & Galatzer-Levy, 2007; M. Wilson, 1993). Common symptoms were left out if clinicians were not reliable in recording them. For example, “blunted affect,” a commonly observed symptom of schizophrenia where the individual displays a limited emotional range, was not included in the diagnosis because clinicians were unreliable in observing it (Spitzer et al., 1978).

The *DSM* as it appears now typically offers diagnostic categories that are made up of what are termed “criteria.” These are symptom clusters that are heuristically grouped together. Each diagnosis has one or several criteria, each of which contains either one or several possible symptoms. If the criterion has more than one possible symptom, there is often a rule that in order for said criterion to be met, a certain number of those symptoms must be present. For the overall diagnosis to be given, a specified number of criteria must also be met.

A Brief History of the PTSD Diagnosis

PTSD was first defined in the *DSM-III* (American Psychiatric Association, 1980) following intense political pressure placed on the mental health field to recognize the psychological effects of war that were observed among Vietnam veterans as well as concentration camp survivors (Helzer, Robins, & McEvoy, 1987). The diagnosis of PTSD was proposed to recognize that persistent psychological reactions to horrific events represented an illness requiring care and treatment, not cowardice or the manifestation of a previous psychiatric illness, such as depression, hysteria, or psychosis. The recognition of this unique disorder laid the groundwork for governments to provide specific mental health services to veterans who had previously been ignored, court-martialed, or sent away to mental hospitals for generic treatments (Gersons & Carlier, 1992).

PTSD was defined in the *DSM-III* to include a total minimum of 4 of a possible 12 symptoms from three symptom criteria. The event itself had to be one that was outside of normal human experience and would be considered distressing to almost anyone. Consistent with other *DSM-III* diagnoses, the PTSD diagnosis was meant primarily for differential diagnosis (i.e., differentiating the disorder from other disorders). The diagnosis was intended to identify severe and persistent fear responses and was not meant as an exhaustive list of possible symptoms of any posttraumatic condition (J. P. Wilson, 1994).

Along with the rest of the *DSM*, PTSD was further codified following a series of criticisms of the manual, leading to the revised *DSM-III* (*DSM-III-R*; American Psychiatric Association, 1987; M. Wilson, 1993). The *DSM-III-R* expanded the total potential symptoms from 12 to 17 in response to criticism that the previous criteria were

narrowly focused on responses observed in Vietnam veterans and Holocaust survivors and needed to better recognize responses of survivors of other events, such as natural disasters (Helzer et al., 1987; McFarlane, 1988). The *DSM-III-R* maintained the *DSM-III*'s criterion defining a traumatic event. Further, the diagnosis required a minimum number of symptoms from each of the three other criteria: (a) reexperiencing symptoms, such as intrusive thoughts or images of the event or "flashbacks," where the individual feels as if he or she is back at the event; (b) avoidance and numbing symptoms, such as efforts to avoid activities or situations associated with the traumatic event or diminished interest in activities overall; and (c) arousal symptoms, such as difficulty falling or staying asleep or irritability or outbursts of anger (for complete symptom listing for each criterion, see American Psychiatric Association, 1987). Symptoms were chosen and heuristically grouped together by the *DSM* task force on the basis of "best available evidence" consistent with the *DSM* scheme (J. P. Wilson, 1994; M. Wilson, 1993). As such, individuals were required to display a minimum of 6 of 17 total possible symptoms distributed across the three criteria. These symptoms were required to be sustained for at least 1 month, and, it is important to note, any combination of symptoms would suffice as long as the required symptom count was met or exceeded to meet each criterion.

Only a few alterations were made to the PTSD diagnosis for the *DSM-IV*. The definition of a traumatic event was expanded to be more inclusive and now encompassed experiencing, witnessing, or being otherwise confronted with any event that involves actual or threatened physical harm to self or others, and some symptoms switched criteria (American Psychiatric Association, 1994). With *DSM-5*, a new criterion has been introduced of *alterations in mood and cognition*, which includes new symptoms of various states (e.g., guilt, shame, mistrust). These have been added, in part, because they are commonly reported in PTSD presentations in military, emergency responder, and interpersonal violence populations. Conceptually, this addition represents an extension from the traditional fear response focus of PTSD to encompass other affective responses. This expansion has resulted in the *DSM-5* work group defining PTSD by four criteria and requiring a minimum of 8 of 19 possible total symptoms. It is important to note that PTSD, along with many *DSM* diagnoses, requires meeting a final criterion that the symptoms cause significant distress or impairment.

A Brief History of Epidemiological Research Into PTSD

Though the modern *DSM* project, beginning with *DSM-III*, focused exclusively on diagnoses based on

observable symptoms with the goal of creating "the best possible classification system based on the latest available knowledge" (M. Wilson, 1993), it remains unclear whether existing empirical knowledge at that time was a firm enough foundation to build from, at least in the case of PTSD. Differentiating disorders from each other and differentiating normality from pathology on the basis of symptom presentation is central to the *DSM* endeavor. However, PTSD encompasses a number of common stress symptoms that may typically occur in the general population. A number of PTSD symptoms have been shown to emerge in response to minor oral surgery (de Jongh et al., 2008), routine childbirth (Olde, Hart, Kleber, & Son, 2006), and bad movies (Lees-Haley, Price, Williams, & Betz, 2001). These findings make sense if we consider that many of the symptoms of PTSD, such as nightmares and sleep disturbances, represent common nondescript stress symptoms (Bonanno, Galea, Bucciarelli, & Vlahov, 2006).

Sorting out the distribution of symptoms that is common in nonpathological populations from that of pathological populations is essential if decisions are to be made about which symptoms or what level of symptoms signal pathology. The first epidemiological studies of trauma-exposed populations meant to assess rates of clinical outcomes, to our knowledge, were the National Vietnam Veterans Readjustment Study (Kulka et al., 1990), commissioned by Congress; the Vietnam Experience Study, conducted by the Centers for Disease Control (Centers for Disease Control Vietnam Experience Study Group, 1988); and the Epidemiologic Catchment Area Survey of Detroit-area youth (Breslau, Davis, Andreski, & Peterson, 1991); all of these were conducted after the establishment of the *DSM-III-R* PTSD criteria. As such, the *DSM* committee had limited empirical data to differentiate abnormal from common stress response symptoms. Salient general stress features may have been chosen because they were commonly observed, not because they were shown to separate normal from pathological populations. This concern is reflected in suggestions that future *DSM* and other diagnostic systems identify and focus on rare rather than common symptoms of posttraumatic stress (McNally, 2009).

Attempts to Improve the Diagnosis by Empirically Identifying the Structure of PTSD

Though criteria and symptoms have always ultimately been decided by a *DSM* committee of experts who define the diagnosis (Buckley, Blanchard, & Hickling, 1998), attempts have been made over the years to put this practice on stronger empirical footing. To this end, numerous factor analytic studies have been conducted to empirically identify the correct criteria and symptoms of PTSD

by determining what symptoms hang together into common factors along with the number of common factors. Factor analyses have revealed two- (Buckley et al., 1998; Taylor, Kuch, Koch, Crockett, & Passey, 1998), three- (Larsson, 2005), and four-factor solutions (Asmundson et al., 2000; King, Leskin, King, & Weathers, 1998; Palmieri & Fitzgerald, 2005; Simms, Watson, & Doebbeling, 2002). The symptoms within a factor often vary across these studies even if the number of factors does not. The *DSM-5* work group has come out in favor of four criteria based in part on these factor analytic studies (APA, 2013). The reason for the different factor solutions remains unknown. However, recent findings indicate that the factor structure of PTSD, including the number of factors and symptoms that comprise them, is population dependent (Shevlin & Elklit, 2012). Furthermore, a number of these factor analytic studies have shown that the factors are highly correlated, often at or exceeding a correlation of .90, bringing their uniqueness as separate diagnostic criteria into question. Taken together, these findings may indicate that the theoretically driven *DSM* model for PTSD—one that conceptualizes separate symptom criteria representing different aspects of the disorder—may not best fit the data. Additionally, defining a specific structure for PTSD on the basis of factor analyses may introduce measurement error, as there is evidence that it is not generalizable.

A second limitation of this approach is that it does not provide information about the relationship between symptoms and a dependent outcome, such as level of functioning, well-being, or distress. Factor analysis can provide information only about the underlying relationship between the variables that are in the model. Without prior information from population-based research that has identified symptoms associated with negative outcomes, factor analysis is limited because it may retain features that are strongly related to one another but have limited explanatory or predictive validity as related to clinically meaningful outcomes. As discussed above, that kind of data was missing when symptoms were selected. Further, features that are strongly related to clinically meaningful outcomes but not to other features may be excluded in a factor analysis if the goal is to identify a finite number of factors and the items that fall into those factors.

Hidden Heterogeneity in the *DSM* and PTSD

Factor analysis has been used to refine the symptom criteria. However, defining the presence or absence of a mental illness on the basis of symptoms above a cutoff on multiple criteria remains problematic regardless of how the criteria are identified or validated. Defining a

mental illness on the basis of a set of logical rules comes with a built-in limitation for validity that stands in contrast to the hopes that validity would naturally flow from reliability. The *DSM* strives to create a set of rules that accurately discriminates cases of the disorder from non-cases. However, it has been proven that any logical systems that derive definitions from a set of axioms (rules) are, by definition, incomplete ones (Gödel, 1992). The only formal logical way around this is to have an infinite number of axioms that deterministically describe all possible outcomes, past, present, and future. (The exception to this occurs only when the axiom is trivially defined; Gödel, 1992.) Gödel's proofs concern the limitations of mathematical axioms for proving all mathematical results, and as a result, the relationship between his proofs and *DSM* diagnoses may not be apparent. However, the *DSM* is a mathematical model of mental illness that utilizes a series of logical statements to define discrete disorders, and as such, it suffers from the limitations of the modeling approach it uses. A complete set of rules that define mental illness a priori is not achievable according to Gödel's proofs. It is important to stress that attempts to identify a set of rules a priori can lead to high levels of complexity without getting closer to the goal of achieving a consistently applicable definition.

For example, imagine we wanted to develop an algorithm that differentiates baseball fans from all other people. We could do this easily by giving a trivial definition (i.e., baseball fans are those who say they are fans of baseball). If we wanted to be able to pick them out solely on the basis of a set of features without people telling us whether they are fans, we could make a set of rules in the same manner as the *DSM*, such that baseball fans are those who attend games. However, two types of people attend games: those who are fans and those who are not. There are an infinite number of reasons nonfans would attend games (e.g., they are going with a friend). Ultimately, the rule is ineffective for defining fans because sometimes it will be accurate and other times it will not be. If more rules are added, our definition of a fan could be more exact, but the same problem would persist. For example, we can make a second rule that a baseball fan is defined as one who attends baseball games and watches games on television. This will capture more true fans but leaves out people who either attend games or watch them on television—any number of which could also be true fans. Conversely, we could state that a fan is someone who watches games on television or goes to games. However, the same problem persists that although we are capturing true fans and true nonfans, we are also defining people as fans who are not and defining people as nonfans who are. Further, the definition of a fan has become more diffuse as “fan” could be indicative of different behaviors.

In the case of many *DSM* diagnoses, logical “and/or” rules are often used in an attempt to create a complete definition of the disorder. Continuing with the baseball fan analogy, if we decided our definition was too narrow, we could expand it by using such “and/or” rules. However, the same fundamental problem remains that our definitions capture some fans and some nonfans, but they also identify some nonfans as fans and some fans as nonfans. “Or” rules are common in the *DSM*. When such rules are used, the definition becomes less exact and more heterogeneous. Being a fan encompasses an increasingly heterogeneous set of descriptors as more “or” rules are applied.

This can be demonstrated mathematically using psychiatric diagnoses, many of which are structured in the same manner as our definition of baseball fans. When thinking about psychiatric diagnosis, these issues have real-life implications for research and treatment. Just as true fans may be misclassified by our rules because they do not display the right combination of characteristics, so too do *DSM* diagnoses leave out individuals because they lack the “correct” combination of symptoms or include people for whom such a diagnosis is inappropriate. Further, as the definition becomes more heterogeneous, so does the population that it defines. In the case of fans, using the rules we described comes with the assumption that those who go to games are the same population as those who watch games on television. Similarly, with *DSM* diagnoses, one must assume that individuals with different symptom presentations have the same underlying mental illness.

Analysis of Heterogeneity in Psychiatric Diagnosis

Calculating heterogeneity

To elucidate the heterogeneity within psychiatric diagnoses, we used an n choose k binomial equation with replacement (Equation 1). This equation provides a method for identifying the number of possible combinations of a set of objects. The equation is calculated as follows: $n!$, which is the total number of possible symptoms (n) multiplied by $n - 1$, $n - 2$, . . . until 1 is reached. For example, if I had four objects, I would multiply $4 * 3 * 2 * 1$. This value is divided by $k!$, multiplied by $(n - k)!$. If we wanted to know how many ways we can pick three out of our four objects, $n = 4$ and $k = 3$. As such, we would calculate: $4! / 3! * (4 - 3)!$

$$\prod_{n=i} \left[\sum \binom{n}{k} \right], \text{ where } \binom{n}{k} = n! / k!(n - k)! \quad (1)$$

where N is the number of symptoms per symptom cluster and K represents all possible number of symptoms needed to satisfy or exceed the diagnosis.

There are different ways this can be calculated. We will provide an example where we are drawing all combinations of three of four different colored balls (red, green, blue, yellow) from a bag to determine how many different color combinations are possible. Because we want to know how many different combinations of three of the four balls there were, we would draw three, then put them back and draw again. We would keep drawing until we had pulled all combinations of three of four colored balls. This is known as drawing with replacement. There are four combinations of three out of four balls (red, green, blue; red green, yellow; red, blue, yellow; green, blue, yellow). The way we identify the possible combinations of colored balls is the same way we can identify the possible combinations of symptoms in a criterion. For example, one individual with PTSD could present with difficulty concentrating and hypervigilance, whereas another individual could present with difficulty concentrating and exaggerated startle response. As such, there are multiple combinations that involve the same symptoms, and the *DSM* follows drawing with replacement rules. It is important to note that the *DSM* requires at least a specified number of symptoms. If we stated that we want to know all combinations of at least three of four colored balls, we would also include a fifth combination (red, green, blue, yellow). As such, there are five combinations of at least three of four colored balls.

Diagnostic criteria that are conditional for the diagnosis to be reached, such as PTSD Criterion A (exposure to a traumatic event), do not factor into the above equation because they represent conditions under which the diagnosis is applicable and do not add diversity to the diagnosis. Finally, if a diagnosis has multiple symptom criteria that must be met, the n choose k equation would be calculated for each criterion, and the number of combinations for each criterion are multiplied by each other. For example, to calculate all possible combinations of PTSD presentations, the n choose k equation is applied to each criterion (reexperiencing, avoidance, arousal), and then the number of symptom combinations from each criterion are multiplied.

Diagnostic permutations in various disorders

We applied the above calculation to PTSD, social phobia, specific phobia, obsessive-compulsive disorder, panic disorder, and major depressive episode in terms of the *DSM-III-R*, *DSM-IV*, and *DSM-5* criteria, where applicable.

Multiple disorders were examined because diagnoses vary in the number of criteria and symptoms. By examining these disorders side by side and over time, it becomes clearer how heterogeneity increases as a function of symptoms and criteria. (For full symptom criteria for PTSD and other disorders from the *DSM-III* to the *DSM-5*, see American Psychiatric Association, 1980, 1987, 1994, 2013.) For clarity, the criteria for each diagnosis from *DSM-III-R* to the revisions in *DSM-5* are presented in Table 1. Though this exercise could be conducted with any diagnoses, we chose Axis 1 anxiety and mood disorders, as these may share some common underlying causes with PTSD (Cox, Clara, & Enns, 2002). The same binomial equation without replacement was also conducted to demonstrate the number of ways to meet requirements for each diagnosis. Finally, all ways to have symptoms in each criterion without meeting the requirements were calculated. This provides information about the number of presentations that are left out of the diagnosis, because this too is affected as the diagnosis changes (see Table 2).

PTSD. For the *DSM-III-R*, we found that the number of PTSD combinations is equal to the product of 15 possible combinations of reexperiencing symptoms, 99 possible combinations of avoidance–numbing symptoms, and 57 possible combinations of hyperarousal symptoms, resulting in 84,645 presentations. For the *DSM-IV*, we found that the product of 31 possible combinations of intrusion symptoms, 99 possible combinations of avoidance–numbing symptoms, and 26 possible combinations of hyperarousal symptoms resulted in a total of 79,794 presentations. For the *DSM-5*, we found that the product of 31 possible combinations of intrusion symptoms, 3 possible combinations of avoidance symptoms, 120 possible combinations of cognitive–mood symptoms, and 57 possible combinations of hyperarousal symptoms produces 636,120 possible presentations.

Major depressive episode. Using the same binomial equation to analyze major depressive episode, we found that the combination of depressed mood along with all combinations of four or more of the remaining symptoms,

Table 1. Diagnostic Criteria From *DSM-III-R*, *DSM-IV*, and *DSM-5* for PTSD and Major Depressive Episode and Select Anxiety Disorders

Disorder	<i>DSM-III-R</i>	<i>DSM-IV</i>	<i>DSM-5</i>
PTSD	2 conditional criteria 1 of 4 reexperiencing symptoms 3 of 7 avoidance/numbing symptoms 2 of 6 hyperarousal symptoms	4 conditional criteria 1 of 5 reexperiencing symptoms 3 of 7 avoidance/numbing symptoms 2 of 5 hyperarousal symptoms	4 conditional criteria 1 of 5 reexperiencing symptoms 1 of 2 avoidance symptoms 2 of 7 negative alterations in cognition symptoms 2 of 6 hyperarousal symptoms
MDE	4 conditional criteria 5 of 9 symptoms, with at least 1 being depressed mood or loss of interest or pleasure	Unchanged from prior edition	Unchanged from prior edition
Specific phobia	6 conditional criteria	7 conditional criteria	Unchanged from prior edition
Social phobia	7 conditional criteria	8 conditional criteria	10 conditional criteria
OCD	1 conditional criteria 4 of 4 obsession symptoms and/or 3 of 3 compulsion symptoms	4 conditional criteria 4 of 4 obsession symptoms and/or 2 of 2 compulsion symptoms	3 conditional criteria 2 of 2 obsession symptoms and/or 2 of 2 compulsion symptoms
Panic	4 conditional criteria Panic attack criteria defined as 4 of 13 symptoms	3 conditional criteria Panic attack criteria defined as 4 of 13 symptoms, with 1 of 3 accompanying symptoms	2 conditional criteria Panic attack criteria defined as 4 of 13 symptoms, with 1 of 2 accompanying symptoms

Note: *Conditional criteria* refer to diagnosis specific criteria that are invariant and must be endorsed to meet the overall criteria. For example, Criterion E for PTSD, which requires that the duration of the symptoms last more than 1 month, is a conditional criterion because it does not present with variations for diagnosis, and if it is not met, the diagnosis cannot be assigned. PTSD = posttraumatic stress disorder; *DSM-III-R* = *Diagnostic and Statistical Manual of Mental Disorders* (3rd edition, revised); *DSM-IV* = *DSM* (4th edition); *DSM-5* = *DSM* (5th edition); MDE = major depressive episode; OCD = obsessive–compulsive disorder.

Table 2. Number of Heterogeneous Symptom Combinations to Meet or Not Meet *DSM* Criteria for Six Diagnoses

Disorder	<i>DSM-III-R</i>	<i>DSM-IV</i>	<i>DSM-5</i>
Posttraumatic stress disorder			
Possible combinations	84,645	79,794	636,120
Minimum combinations	2,100	1,750	3,150
Excluded presentations	35,370	42,253	107,973
Major depressive episode			
Possible combinations	227	227	227
Minimum combinations	126	126	126
Excluded presentations	154	154	154
Specific phobia			
Possible combinations	1	1	1
Minimum combinations	1	1	1
Excluded presentations	0	0	0
Social phobia			
Possible combinations	1	1	1
Minimum combinations	1	1	1
Excluded presentations	0	0	0
Obsessive-compulsive disorder			
Possible combinations	3	3	3
Minimum combinations	2	2	2
Excluded presentations	0	0	0
Panic disorder			
Possible combinations	7,814	54,698	23,442
Minimum combinations	715	715	715
Excluded presentations	377	377	377

Note: This table presents (a) possible combinations, defined as all possible combinations of symptoms that qualify for the specified diagnosis; (b) minimum combinations, defined as all possible combinations of symptoms that result in the minimum number of symptoms necessary to qualify for each specified diagnosis; and (c) excluded presentations, defined as all combinations of one or more symptoms in all categories that do not meet diagnostic criteria. The number of combinations was calculated using a binomial n choose k without replacement equation.

excluding loss of interest, produces 64 possible combinations, as does the presence of symptom loss of interest excluding depressed mood. If both symptoms are present, all possible combinations of three or more of the remaining seven symptoms produce 99 combinations. The sum of these combinations equals 227.

Select anxiety disorders. Social and specific phobias, which present with only one criterion and symptom, create a fully identified diagnosis. Though obsessive-compulsive disorder changes in the total number of symptoms, the diagnosis consistently comes with only three permutations, as the presence of all obsessive symptoms, the presence of all compulsive symptoms, or the presence of both represents only three possible combinations of symptoms. These three disorders present with very little or no heterogeneity because they are trivially defined (i.e., there is a specific complete description of what it

means to have the disorder). Finally, we observed that panic disorder increased dramatically from the *DSM-III-R*, with 7,814 presentations; to 54,698 in the *DSM-IV* with the addition of a separate criterion; and then reduced dramatically to 23,442 presentations when the number of symptoms in one criterion was reduced in the *DSM-5*.

Consequences of the DSM measurement scheme: PTSD findings are inconsistent and they miss cases

The consequences of the ignored heterogeneity in *DSM* diagnoses are unclear. PTSD presents with a large amount of heterogeneity. Although we cannot determine whether findings in the PTSD literature have been impacted by this heterogeneity, we can examine the consistency of findings and hypothesize that inconsistency may be the result of heterogeneity in the diagnosis.

A number of meta-analyses have been conducted that have identified consistent social, demographic, trauma-related, and biological correlates of PTSD, as well as treatments that are effective for PTSD, but these same analyses have shown that the effect sizes of many of these variables vary dramatically. In one large meta-analysis of risk factors for PTSD, 11 out of the 14 common predictors, including socioeconomic status, age, race, previous trauma, trauma severity, social support, life stress, and intelligence (among others) displayed significant heterogeneity in their effect size; for example, trauma severity accounts for between 0.02% to 58% of the variance (Brewin, Andrews, & Valentine, 2000). Similarly, though no heterogeneity statistic was offered, a second meta-analysis that examined seven pretrauma and peritraumatic (occurring at the time of the trauma) characteristics demonstrated a wide spread in effect sizes across all seven predictors. For example, the strongest predictors of PTSD, peritraumatic emotions and peritraumatic dissociation, demonstrated effect sizes that ranged from .15 to .55 and from .14 to .94, respectively (Ozer, Best, Lipsey, & Weiss, 2003). Similarly, significant levels of heterogeneity are observed in the effect sizes of treatment for PTSD (Bisson, 2007; Bradley, Greene, Russ, Dutra, & Westen, 2005; Sherman, 1998) and structural brain abnormalities associated with PTSD (Karl et al., 2006). The reason for these inconsistencies in findings is not known. However, as all of the above studies depend on measurement precision within the PTSD diagnosis, measurement error in the PTSD diagnosis is worth examination as a potential culprit.

Sampling and measurement error have also been noted as significant problems with the PTSD diagnosis, given that subthreshold presentations of PTSD are often associated with impairment in psychosocial and occupational functioning in the clinical range (Marshall et al., 2001), and help-seeking behavior among such individuals is similar to those who meet full requirements for the diagnosis (Stein, Walker, Hazen, & Forde, 1997). These findings indicate that the combinatorial experiment provided above does not simply represent an academic exercise but in fact has real-life consequences as the diagnosis appears to produce false negatives, missing cases in need of intervention.

The concern with *DSM* diagnoses is well understood, and changes are pending. The National Institute of Mental Health (NIMH) recently shifted its focus to the Research Domains Criteria project, which adopts a transdiagnostic approach and focuses on common mechanisms that may underlie disorders (Insel et al., 2010). This focus reflects the concern in the field of the potentially limiting preoccupation with diagnostic categories in conducting psychological and biological research into psychiatric conditions. Specifically, NIMH is moving away from

funding research based on *DSM* diagnoses because of their primary focus on reliability at the expense of validity leading to nonspecific findings. NIMH will refocus its funding efforts around research seeking to understand psychopathology based on alterations in cognition, emotion, and behavior and the underlying biology and neurocircuitry of these domains (Insel, 2013). The heterogeneity found in the PTSD diagnosis exemplifies this problem of primarily using diagnosis as an outcome.

Potential Solutions and Future Directions

Although the *DSM* approach presents with many limitations for identifying populations from a measurement perspective, the field remains interested in identifying and describing normal and pathological populations. The *DSM* diagnostic scheme presents with untenable limitations. The *DSM* defines clinical outcomes a priori. This system often relies on complex sets of rules in an attempt to capture the correct population. However, an unintended consequence of this approach is that the diagnosis encompasses increasingly heterogeneous symptom presentations without addressing the limitations of a priori definitions. Conversely, other traditionally commonly used approaches also have limitations.

Typically, researchers examine population means and infer their clinical meaning on the basis of clinical norms of the measure. If means are charted over time, researchers can make inferences about the course of the disorder or the response to a treatment or life event. However, this approach is unsatisfactory for the reasons that diagnosis is appealing. Diagnosis hopes to provide information about who is doing poorly, and in what ways, and who is doing well, whereas means can reveal only how everyone is doing together.

A second common method for characterizing outcomes, similar to that used in psychiatric diagnosis, is to dichotomize a continuous variable to create two populations on the basis of a cutoff point. This method would reveal heterogeneity and can be used to track the course as one can observe whether individuals change categories over time. However, dichotomizing variables has long been discouraged by methodologists because of evidence that the practice weakens statistical power, increases measurement error, and can lead to falsely significant results (Cohen, 1983), while also artificially separating individuals into two groups when these groups are not naturally occurring (MacCallum, Zhang, Preacher, & Rucker, 2002). Despite these long-standing criticisms, researchers continue to follow this practice because it allows for ease of analysis and aids in interpretation (DeCoster, Iselin, & Gallucci, 2009). New statistical approaches are warranted and necessary.

A number of new methods have emerged that capitalize on computational advances to empirically identify common outcomes. These approaches were out of reach when the *DSM* scheme was first conceived and may provide some viable alternatives for studying outcome heterogeneity in both clinical and nonclinical contexts. We will discuss one method that appears promising, though this description is not meant to be exhaustive.

Relatively new data analytic approaches have recently been used to empirically identify latent (or not directly observable) subpopulations, by identifying finite latent mixture distributions that underlie the observed distribution. This approach can empirically identify distinct populations on the basis of the distribution of their symptoms (or any other outcome measure of interest). It is flexible, as it can be applied to cross-sectional as well as longitudinal data (Muthen, 2000).

An increasing number of studies have utilized cross-sectional latent class analysis to identify distinct populations where it is theoretically relevant to compare populations on the basis of mental health status. For example, researchers have begun to identify latent subpopulations clustered by symptoms and have used those empirically identified subpopulations as outcome variables rather than using *DSM* diagnostic status (Breslau, Reboussin, Anthony, & Storr, 2005; Steenkamp et al., 2012). This approach has also been used to empirically identify subtypes of PTSD that are distinct in their symptom presentation from others with the same diagnostic status (Wolf et al., 2012). Latent class analysis allows the investigator to examine multiple features simultaneously to understand how they commonly cluster together into latent subpopulations. Change in these clusters over time can be examined using methods such as latent transition analysis (Muthen, 2000).

Change over two time points provides limited information. Mixture distributions can be extended longitudinally to identify common populations characterized by their latent symptom course over multiple occasions. A number of recent studies have used approaches such as latent growth mixture modeling and its extensions to identify distinct subpopulations according to longitudinal course following potentially traumatic events. This has been shown to reveal clinically meaningful patterns in multiple domains, including PTSD symptom severity (Berntsen et al., 2012; Bonanno, Mancini, et al., 2012; deRoon-Cassini, 2010; Galatzer-Levy, Madan, Neylan, Henn-Haase, & Marmar, 2011), anxiety and depression symptom severity (Bonanno, Kennedy, Galatzer-Levy, Lude, & Elfström, 2012; Galatzer-Levy & Bonanno, 2012), and general distress that is not diagnosis specific (Galatzer-Levy et al., 2013; Galatzer-Levy, Burton, & Bonanno, 2012).

These studies indicate that there is meaningful heterogeneity in how people respond to significant life stressors and potentially traumatic events. Most cope well with

only a few transient stress symptoms. Some do poorly initially but get better over time, and some suffer chronically with consistently elevated symptom levels. From a research perspective, these distinct outcomes may be influenced and maintained by different factors and may require different forms of remediation. Latent growth mixture modeling and its extensions are relevant to apply in any context where it is not parsimonious to assume one common trajectory across the population (Muthen, 2004), as they allow for the identification of meaningful subpopulations without imposing a set of a priori rules. Further, they account for distributions and measurement error within the identified subpopulations (Muthen, 2004). Using such approaches may significantly reduce measurement error, as clinical outcomes are empirically defined, sidestepping many of the measurement limitations of *DSM* diagnoses. Further, researchers can examine change in any domain that may be affected by significant life events, such as cognitive ability, worldview, emotional valence, or any other theoretically relevant psychological domain. This can provide a broader picture of both adaptive and maladaptive responses to life stressors and may result in the identification of novel treatment targets that are aimed at domains other than symptoms.

Relevance beyond clinical research

The example provided by PTSD is also relevant beyond the scope of clinical research, as it highlights generally important issues in the measurement of behavioral change in response to stressful life events. A number of studies have identified common patterns of adaptation to common stressful life events, examining the course of subjective well-being in response to marriage, divorce, and widowhood (Mancini, Bonanno, & Clark, 2009), unemployment (Galatzer-Levy, Bonanno, & Mancini, 2010), and becoming a parent (Galatzer-Levy, Mazursky, Mancini, & Bonanno, 2011); or focusing on general distress during college (Galatzer-Levy & Bonanno, 2013; Galatzer-Levy et al., 2012). Some of these studies have challenged long-standing findings by identifying errors in estimation on the basis of the use of a single mean trajectory rather than identifying heterogeneous populations. For example, a long-standing body of literature has demonstrated that individuals drop in their level of subjective well-being when they have children and do not recover until their children leave home (Twenge, Campbell, & Foster, 2004). However, when patterns of subjective well-being are examined using a latent growth mixture modeling approach, we find that only a small proportion dip significantly, pulling down the population average. In fact, many new parents increase significantly in their subjective well-being when they become parents (Galatzer-Levy, Mazursky, et al., 2011).

Increasing communication across subdisciplines

The above findings highlight the similarities in the course of the stress responses when measuring outcomes such as subjective well-being or symptoms. An added benefit of new approaches that do not rely on diagnoses is that they can potentially increase the translatability of findings across multiple subdisciplines of psychology. Although few outside of clinical psychology and psychiatry utilize psychiatric diagnoses as an outcome, many fields study behavioral changes in response to common and atypical life stressors, such as how personality changes in response to anxiety-provoking life events (Bolger, 1990); how significant others aid in coping with life-threatening events, such as cancer onset (Bolger, Foster, Vinokur, & Ng, 1996); or how contextual threat cues are encoded into memory, leading to behavior change, in animal models (LeDoux, 2012; Phillips & LeDoux, 1992). It is difficult and often cumbersome to relate these findings to diagnostic entities despite the importance of these bodies of work for understanding clinical outcomes. However, empirical approaches for identifying meaningful subpopulations may be appealing to researchers across disciplines who examine behavioral change. Further, clinical psychology becomes less alienated from other subdisciplines that are studying similar phenomena by examining common outcomes, such as general distress in clinical populations, rather than relying on diagnoses that are rarely used in other research contexts.

Conclusion

This article endeavored to demonstrate the limitations of *DSM* diagnoses from a measurement perspective. We primarily focused on the PTSD diagnosis because it provides an example of the many factors that influenced the *DSM* to create a broad and error-prone diagnostic scheme. We discussed how the desire for a diagnosis to encompass the broad spectrum of posttraumatic presentations led to a diagnosis in *DSM-5* that was complex, even compared with other *DSM* disorders. However, we further discussed that these limitations may be secondary to the primary measurement limitation that results from any attempt to create an algorithm based on a priori rules. As such, the modeling approach of the *DSM* necessarily generates both false positives and false negatives. Finally, we provided some possible solutions focusing on recent research that identifies clinical outcomes empirically rather than a priori and demonstrated how this approach may ultimately provide stronger information about predictors, correlates, and, when relevant, effective treatments related to these outcomes. It also provides an

alternative to single mean trajectory approaches that assume homogeneity even when this is not a parsimonious assumption.

Such an empirical approach for identifying behavioral patterns both in clinical and nonclinical contexts is nascent. A great deal of work is necessary to identify and understand common outcomes of disparate, potentially traumatic, and common stressful life events. However, the lesson learned from the example of PTSD is that empirical findings are only as strong as the clarity of the constructs under study. If the construct is noisy, diffuse, or lacking in validity, it becomes increasingly difficult to study the phenomenon.

Finally, new approaches hold promise for identifying common outcomes that are heuristically meaningful both in clinical and nonclinical contexts. One set of approaches that hold promise is the empirical identification of latent mixture distributions both cross-sectionally and longitudinally. This approach allows for the empirical identification of populations rather than imposing rigid external constraints based on a priori definitions. It also has the added benefit of increasing the translatability of findings across disciplines of psychology, because many subdisciplines study behavioral responses to life stressors, though few outside of clinical fields use psychiatric status as an outcome. The value of these techniques and others will be determined by their empirical utility. Regardless, new approaches that examine the heterogeneity in stress response behavior rather than ignoring it will doubtless lead to stronger and clearer findings by virtue of reducing measurement error and by pursuing both reliability and validity.

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.

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