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Concerns Over Divergent Approaches in the Diagnostics of Posttraumatic Stress Disorder

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ABSTRACT

Since the inception of posttraumatic stress disorder (PTSD) in the *Diagnostic and Statistical Manual of Mental Disorders,* third edition (*DSM-III*), there has been an ongoing polemic debate about the veracity, assessment, neurobiology, and longitudinal course of the disorder. As a consequence, its clinical utility has been the subject of a significant amount of conflicting opinion due to the competing interests involving clinicians, insurance companies, victim's groups, and governments. This article reviews some of the current divergent approaches in the diagnosis of PTSD, including the debate on the condition itself, claims that it is overdiagnosed, the usefulness of the "A" criterion, equivalence of cluster criteria, the role of combat and civilian PTSD, the role of biomarkers, incongruences in diagnostic practice, and the need for a consistent approach that ensures diagnostic congruence. Critical drivers of divergent diagnostic systems are that they should not produce significantly different rates or produce high levels of discordance. However, one of the concerns is that the anticipated *International Statistical Classification of Diseases and Related Health Problems*, eleventh edition (*ICD-11*) has moved away from this primary aim and taken a markedly divergent approach that is incompatible with the advancement of consensus within this critical field. This article explores some of the primary arguments and evidence cited for this approach in *ICD-11* and recent changes in *DSM-5*. **[*Psychiatr Ann*. 2016;46(9):498-509.]**

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There is no diagnosis in psychiatry that is subject to such legal and statutory scrutiny as posttraumatic stress disorder (PTSD). Since its inclusion in the *Diagnostic and Statistical Manual of Mental Disorders*, third edition (*DSM-III*),[1] there has been an ongoing debate about the veracity, the neurobiology, and legal status of the disorder.[2-6] As a consequence, the clinical utility of the definition has been subject to competing interests from insurance companies, victim's groups, and policy makers. Also, there is no other mental health diagnosis in which the causation is directly linked to the diagnosis; a status that has particular ramifications in compensation settings.[7] Forty years after the Vietnam war, the prevalence of PTSD in Vietnam veterans has been estimated to range from 4.5% to 11.2% depending on the instrument used.[8] A larger number of Vietnam era veterans have sought care for PTSD during the more recent wars in Iraq and Afghanistan, presumably a consequence of transitions in their life associated with aging. Within the Veterans Health Administration, Vietnam era veterans need to be diagnosed with "conversion" to PTSD to be eligible for receipt of disability compensation.[9] This places particular obligation on the scientific community to ensure that the diagnostic criteria are based upon a valid, replicable, and consistent synthesis of the scientific literature.[10]

For 35 years, PTSD was defined as an anxiety disorder. Several changes have been implemented and are proposed for implementation in the two leading classification systems for mental health disorders, the *DSM-5*[11] and the *International Statistical Classification of Diseases and Related Health Problems,* eleventh edition (*ICD-11*).[12] Contrary to the recommendations by some experts,[13] a specific posttraumatic stress spectrum disorders section was not accepted in *DSM-5,*[11] and PTSD was instead lumped into a "trauma and stressor" disorder chapter with conditions that lack a neurobiological relationship to PTSD, including the catch-all diagnosis of "exclusion, adjustment disorder." In *DSM-5,*[11] the "A" criterion remains a prerequisite for the diagnosis, but has been dramatically changed with the addition of specific descriptors of the qualifying events; for example, from global to specific descriptors of the qualifying events (ie, explicitly included sexual violence). A different approach for definition of the disorder has been proposed by the *ICD-11*[12] working group of the World Health Organization (WHO). Although the WHO workgroup also moved PTSD out of the anxiety spectrum section and labeled PTSD among the "disorders associated with stress," the traumatic requirements are different. Even if it is recognized that symptoms must have developed after exposure to an event of an extremely threatening or horrific nature, the diagnosis is mainly based on symptom presentation rather than on determination of whether or not the event constitutes an eligible traumatic stressor. The historic and pivotal aspect of PTSD, which is exposure to a severe traumatic event, is stringently defined in *DSM-5*[11] but essentially left to individual clinicians to define in *ICD-11*.[12] This has implications for treatment and legal/disability evaluations. It is notable that some of the committee members who advocated for the *DSM-5*[11] definition were also on the *IDC-11*[12] committee supporting this contradictory approach, which may have far-reaching consequences in our view.

> *There is no other mental health diagnosis in which the causation is directly linked to the diagnosis.*

In this article, we review some divergent approaches in the diagnosis of PTSD. We focus on the "reality" of the disorder, viewpoints on whether the condition is over or underdiagnosed, the "A" criterion and equivalence of symptom criteria, incongruences in classification, and the need for an accepted process in the diagnosis of PTSD. This article also explores some of the primary arguments and evidence cited for the diagnostic approach in *ICD-11*[12] and similarly reviews changes from previous *DSM* editions in *DSM-5*.[11]

PTSD AS SOCIAL CONSTRUCTION REVISITED

It is unfortunate in our view that the *ICD-11*[12] working group seems to have reintroduced the argument of whether PTSD is a social construction, despite decades of neurobiological research. The field should have moved to a more reasoned consideration of the neurobiological evidence in its reformulation rather than relying on broad sociologic arguments or opinions of experts advocating for particular models of treatment. During the past decades, trauma has been seen as a highly prevalent occurrence, often accompanied by posttraumatic distress, and less commonly followed by a persistent pathological response (ie, PTSD). Yet, there are those who insist that the responses to traumatic events are by definition normal responses that need to be understood solely within a sociopolitical framework, calling PTSD a "social construction."[14] In an article in 2007, Stein et al.[6] argued that PTSD has led to increasing medicalization of the problem, fostering popular acceptance

of the reality of posttraumatic psychiatric sequelae, boosting research into the pathogenesis of the disorder and leading to improved pharmacological and psychological management. Yet, the authors point out that the subjective experience of trauma and subsequent expression of symptoms vary considerably, and caution is needed that not all psychological distress or psychiatric disorders after trauma should be termed PTSD. Their argument is that PTSD is not a valid medical entity, and several articles argue that the language around it should be radically changed. This viewpoint comes up consistently in the popular media and public debates.[15-17]

There are both conceptual and empirical problems with the social construction approach. One problem with the "medicalization" of conditions is that it introduces moral judgment into the medical encounter by implying that the symptoms patients are presenting with are being overly embraced as a medical condition rather than a normal response. There was a time when people with epilepsy were judged to be possessed by the devil and executed. Obesity or addictive disorders have often been viewed as moral failures rather than medical problems involving multiple regulatory systems. The darker side of emphasizing resilience in the face of trauma is the potential for judgment upon those who, by virtue of biological predisposition or other factors, develop PTSD and suffer more from specific traumatic exposures; the implication is that their inability to cope with the "normal" response to trauma involving nightmares, numbing, and irritability are due to a weakness of character rather than exposure to violence and other biological risk factors. Although certainly not all psychological distress or psychiatric disorders after trauma should be termed PTSD, it needs to be emphasized that there is wealth of clinical and neurobiological evidence supporting this condition as formulated in *DSM*, third edition, revised[18] (*DSM-III-R*) and *DSM*, fourth edition[19] (*DSM-IV*) (which were nearly identical definitions). Distress does carry a different meaning than traumatic stress. PTSD is no less "real" than major depressive disorder (MDD) or panic disorder, all of which have well-delineated neurobiological processes. Yet, for whatever reason (perhaps because the etiology of the condition is included in the definition), PTSD is a disorder vulnerable to moral judgment.

There are both conceptual and empirical problems with the social construction approach.

In a letter to the editor we[20] wrote a response regarding "medicalization" of conditions:

> Obesity can be seen as a moral failure or a disorder, as is the case with addiction...Consider the example of cardiac disease. It is clearly influenced by sociopolitical forces that affect diet, exercise, and smoking behaviour. Not everybody who is obese, has high cholesterol, and smokes, has a myocardial infarction. Should we call them "resilient" and encourage others to follow their example?...PTSD, with its clearly defined symptoms, is not a failure of character or resilience, nor is it a social construction. It is part of the human condition.

IS PTSD A REAL DISORDER?

Past and current authors, in their review of sources of dissonance that influence diagnostic categories and how this affects the clinician-patient relationship, point out that medicine (and by extension psychiatry) is imbedded within a societal context of social, cultural, and economic influences that can vary over time and that contribute to the disease definitions, as well as society's response to that disease.[21,22] Controversies about the validity of PTSD, past and current, flow in part from such attitudes, as well as the high societal valence on opposing sides that accompanied the process of redefinition of trauma-related mental disturbance from a personal or moral failing to that of a psychiatric diagnosis.[23,24] In contrast to advocates for PTSD as a separate and valid psychiatric diagnostic category, the most ardent skeptics have expressed views that the diagnosis *per se* is a medicalization of a normal reaction; a cultural construct tied to the insurance and pharmaceutical industries that reflects health care system constraints necessary to permit reimbursement of services. Others have focused on failures of the *DSM* diagnostic criteria, which have fostered a "top-down," reductionist approach of questionnaires and symptom probes rather than a "bottom-up" assessment of the patient's full biography, accounting for prior mental health problems, personality, environment, and current mental state;thus moving the mental health field away from, and not toward, comprehending responses to trauma.[25,26] Changes in PTSD diagnostic criteria in *DSM-5*[11] (which in our opinion are the most significant changes since *DSM-III-R*[18]), continue to result in high PTSD and MDD co-occurrence; there has been no change in the finding that approximately half of people with PTSD also meet diagnostic criteria for MDD (see Flory and Yehuda[27] for review). Whether this co-occurrence represents a common underlying

PTSD-MDD construct as advocated by Elhai et al.[28] is the product of poorly specific diagnostic criteria, or has biological validity perhaps representing a distinct depressive PTSD phenotype remains in dispute and under active investigation.[27-30] Whether PTSD diagnosis accuracy and validity are best served by a broad or narrow diagnostic criteria expressed in the latest revisions of the definition are consequential conceptual disagreements with important clinical and legal implications that are now being played out in reality via discontinuity in diagnostic criteria in *DSM-5*[11] versus *ICD-11*.[12,25,31-32]

In the decades after its introduction, PTSD has been validated by a flurry of cross-sectional and longitudinal research studies that provided clear clinical, epidemiological, and biological marker correlates comparable to other mental disorders. Although this has not provided objective laboratory-based diagnostics (a problem that is not unique to PTSD and is also seen in schizophrenia or a neurological disorder like multiple sclerosis), the research has led to effective treatments based on sound theoretical underpinnings, as well as greater understanding of intrinsic vulnerabilities and risk factors. After 4 decades of research, we feel it is justified to say that PTSD is not fabricated or invented but a disorder of the human condition.

Although psychiatry in general has moved away from a factor analytical approach of disorders (eg, schizophrenia or MDD), for PTSD a four-factor model has gradually become the standard view of the disorder. In *DSM-5,*[11] it consists of re-experiencing, effortful avoidance, negative mood or cognitive symptoms, and hyperarousal. However, *ICD-11*[12] decided to retain a three-factor structure. Furthermore, the considerable changes in symptom wording and clustering in both definitions do not appear to provide any improvements clinically ensuring that the complex array of trauma-related emotions associated with military settings, disasters, or early-life trauma (single of repetitive) are adequately captured in the definition. Several studies are linking PTSD to shame, dissociation, depression, substance abuse, and suicidality. In a biologic framework, PTSD has been viewed as a disorder of traumatic stress exposure, a memory disorder,[33,34] and more recently as a disorder of emotional regulation.[35,36] Current focus is on the interplay between cognition and emotion,[37] and moral issues such as guilt are now new drivers of treatment decisions.[38] Significant advancements in research on PTSD-related biologic abnormalities across multiple biologic systems and modalities have been made.[39-43] From these studies it can be concluded that PTSD is a heterogeneous disorder in which several neurobiological systems interplay. A number of different theoretical models have been used to guide treatment approaches.[27,44,45]

IS PTSD OVERDIAGNOSED?

A further troubling argument, in our view, being posited by the *ICD-11*[12] WHO working group is that PTSD is overused in the absence of objective evidence. Overdiagnosis of PTSD was one of the arguments that will have the effect in the formulation of *ICD-11*[12] in reducing its prevalence.[46] In making this argument, the authors reference a discussion in an article by Stein et al.[6] from 2007 that this overdiagnosis has led to the "medicalization of human suffering." However, this argument was based on an opinion rather than an objective examination of clinical evidence.[47-49] Furthermore, the *ICD-11*[12] committee has questioned the "high rates of these diagnoses in populations experiencing natural or man-made disasters," despite the fact that rates in many disasters remain relatively low.[50-52]

Contrary to the viewpoint that PTSD is overdiagnosed, there is extensive evidence showing that the majority of people who are in need of treatment for debilitating symptoms do not receive the care they need.[53-59] Furthermore, there are a range of reports demonstrating that clinicians frequently do not fully document the patient's symptoms and that PTSD is frequently not considered in many clinical settings.[60] The published literature has examined the identification in a number of different settings and health systems,[61-66] including following natural disasters and terrorist attacks where low rates of diagnosis were inconsistent with other population epidemiological studies. This was noted, for example, after the 2005 London terrorist bombings when a screening program was put in place to provide treatment to those directly affected.[67] The clinical records in these settings did not identify the history of trauma exposure nor the symptoms of PTSD, and instead focused on documenting nonspecific symptoms of anxiety, depression, or medically unexplained symptoms. Hence, as seems likely in these cases, the rates of diagnosis of PTSD in many clinical settings underestimate the prevalence of the disorder.[62] For example Liebschutz et al.[65] found that in one clinical setting, 23% of patients were identified as having PTSD when only 11% were noted to have this diagnosis in the clinical record.

To argue that PTSD is overdiagnosed is contrary to a review of the evidence by the Institute of Medicine committee considering possible early interventions that recommended screening for PTSD to improve the rates of case identification, which are important to early intervention.[68] This recommendation is based on the recognition of the importance of early diagnosis and its role in secondary prevention.

Although opinion has its place, it is not a replacement for systematic analysis of the published clinical literature. We feel the *ICD-11* criteria[12] have been based on opinions and arguments that are not supported by a

substantial body of the scientific literature. This issue of overdiagnosis needs to be part of an open debate and raises major questions about the validity of actions to limit the scope of the population captured by the diagnosis. In fact, the confusion created by the varying prevalence rates of PTSD using *DSM-IV*,[19] *DSM-5*,[11] *ICD-10,*[69] and *ICD-11*[12] have led a number of senior researchers in the field to recommend the use of all systems in research publications.[70] Although this may seem like a logical compromise considering the divergent viewpoints, such a decision will lead to an approximate doubling of prevalence and does not really have a basis in scientific evidence. Further advances in the scientific investigation of PTSD depend on consensus definitions based on careful examination of the literature, particularly focused on the clinical utility of the definition.

THE USEFULNESS OF THE "A" CRITERION

Antecedent Events

It is difficult to understand how two committees came to such fundamentally different conclusions on the relevance of antecedent events in the diagnosis of the disorder. PTSD is atypical in that, unlike other psychiatric diagnoses, it requires an antecedent causal event, an emotional trauma that precipitates a symptom profile, defined variably in successive versions of *DSM* PTSD diagnostic criteria since 1980. As a consequence of the category "A" criterion, the PTSD diagnosis is held to a high burden of proof compared to other mental health diagnoses (ie, evidence of a clear link between a precipitating stressor and resultant signs and symptoms defined by currently existing *DSM* symptom criteria).[71] Notably, successive versions of *DSM*, from *DSM-III*[1] to the current version *DSM-5*,[11] have progressively refined criterion "A" due to the recognition of the prevalence of these events in epidemiological studies and the need for more precise definition. However, conceptual theory (fear learning) and clinical treatment place the antecedent (criterion "A" event) as a central component of PTSD diagnosis; for prolonged exposure therapy, successful elucidation of the event, within context, is essential for development of a treatment narrative. Clinically, antecedents and the context within which the named criterion "A" event takes place are highly relevant; emotional or sensory aspects of a singular event can override an arousal system held in check during previous events. Interim studies, exhaustively reviewed by Rosen and Lilienfeld,[72] appear to indicate the (1) nonspecificity of criterion "A," (2) endorsement of PTSD symptoms without clear presence of criterion "A," (3) lack of a monotonic relationship between stressor magnitude and clinical status, and (4) lack of evidence that criterion "A" events is the uniformly most potent contributor to PTSD outcome. All are cited as evidence for doubt regarding the diagnostic validity of PTSD.[72,73] However, not systematically addressed are possible inherent limitations in this body of research; in particular, time and resource constraints that may have limited collection of antecedent history and context information, which ultimately affected the outcomes cited. To fully understand the salience of any event and its intimate relationship to specific PTSD symptoms, the event cannot be decontextualized nor can antecedent events that served as set points both from a biological (eg, concomitant traumatic brain injury)[74,75] as well as a psychological perspective cannot be ignored without losing information regarding the link between the precipitating stressor and resultant PTSD signs and symptoms.

The field of PTSD research has created a complexity that other mental health criteria do not confront.

Equivalence of the B, C, and D Cluster Criteria

In contrast to other psychiatric diagnoses, the field of PTSD research has placed unusual reliance on separating the diagnostic subcategories of PTSD. As a consequence, it introduced a divergence of logic in diagnostic practice in PTSD compared to MDD or schizophrenia. *ICD-11*[12] has used one solution and *DSM-5*[11] has used another, which highlights the lack of consensus to this approach.

The field of PTSD research has created a complexity that other mental health criteria do not confront. The Cluster "B" criterion (re-experiencing of the trauma event), has consistently been a factor component in best-fit PTSD symptom models, and is perhaps the primary, or pathognomonic symptom of the disorder, in contrast with "C" (avoidance) and "D" (hyperarousal) criteria, which have overlap with those of other disorders. As such, re-experiencing symptoms has consistently been included in successive *DSM* iterations of diagnostic criteria, with little change.[72,76] Of putative PTSD diagnostic criteria, to our knowledge, only Cluster "B" has been linked to a biological marker, the activity of dopamine beta hydroxylase (DBH), the final enzyme in norepinephrine biosynthesis, which catalyzes the oxidative hydroxylation of dopamine to norepinephrine in the noradrenergic nerve endings of the central and peripheral nervous systems.[77] A

first genome-wide association study on plasma DBH (pDHB) activity[78] recently identified the *DBH* gene as the principal locus determining pDBH levels in both European and Native American populations, explaining 57% of the variability. Using a mendelian randomization approach, Mustapic et al.[78,79] and Hammer and Gold[80] proceeded to further investigate a potential causal effect of the pDBH on PTSD diagnosis, showing pDBH to be a causal component in the development of PTSD re-experiencing (Cluster B) symptoms, although these findings will need to be confirmed in larger studies

INCONGRUENCES IN CLASSIFICATION: *DSM* AND *ICD*

Fluctuations in *DSM* Criteria

The field of PTSD appears puzzled and confused to allow such significant fluctuations in diagnostic criteria from *DSM-IV*[19] to *DSM-5*[11] as well as *ICD-10*[69] and *ICD-11*.[12] Changes were made in classification, trauma definition, inclusion of symptoms, change of clusters, as well as the introduction of subtypes.[81] If it were for the advancement of science, the implications for epidemiological, biological, genetic, and treatment studies would be welcomed.[82] In the absence of clarity in the changes from *DSM-IV*[19] to *DSM-5*,[11] a group of authors has recently advocated adhering to *DSM-IV*[19] criteria.[83] The shift in *DSM-5*[11] as well as in *ICD-11*[12] foregoes the research of 3 decades of neurobiological research that underpins the reactions to traumatic stress. Current proposals in *ICD-11*[12] as well as the changes in *DSM-5*[11] from previous editions also have the potential to lead to a major disjunction of knowledge and disruption of the application of the existing guidelines, with a downstream flow of consequences for clinical practice.

DSM-5[11] departed from a principle that held all previous *DSM* editions closer to clinically observable and reportable symptoms, namely avoiding the use of theoretical constructs as descriptors. This is how *DSM-III*[1] dealt with the previous combat neurosis, by leaving aside conflict theory and motivational assumptions and focusing on more reliably observable, reportable, and eventually quantifiable manifestations, such as "intrusive recollections," "difficulties falling asleep," or having/not having nightmares. Compare these manifestations with Kardiner's[84] main features of combat neurosis: "fixation on the trauma, typical dream life and contraction of general level of functioning." *DSM-5*[11] has reverted to using abstractions as descriptors (abstractions such as "persistent negative beliefs and expectations" or "persistent distorted cognition") and relying on observers' inference about abnormality or distortion of patients' state of mind. Yet, changing phenomenal descriptors such as "nightmares" to "recurrent thoughts" or abandoning the term "re-experiencing" in preference for "intrusion" to accommodate prevalence rates for different versions in classification systems could discount fundamental neurobiological correlates related to these specific symptoms.[85] Dramatic redefining of criteria not backed by solidified research eradicates the contribution of a carefully amassed body of peer-reviewed research.

The fact that many of these abstractions reflect cognitive theory is less material than the fact that they imbue observations and thus add to confusion. In a sense, borrowing from cognitive theory is borrowing from what many professionals learn and believe in now—the exact equivalence of what psychodynamic theory was in the "traumatic neurosis" era. By doing so, *DSM-5*[11] departs from what is reliably observable and reportable into what it assumes might be happening at a wider emotional or cognitive level. It thereby creates suppositions that are less specific, not amenable to direct observation, and that recreate the type of ambiguity that successive editions since *DSM-II*[86] tried to eliminate.[87] Furthermore, the inter-rater reliability of the clinical rating of negative cognitions has not been adequately explored and is likely to be subject to significant variations based on the sociopolitical context of the patient and clinician alike (eg, the reality of the perception of danger and threat is critically dependent on context and experience).

Incongruencies in *ICD* and *DSM*

There is a marked incongruence between the *ICD-11*[12] proposed criteria and *DSM-5*[11] (specifically the absence of the criteria related to the negative alterations in cognitions and mood) that were key new inclusions in *DSM-5*,[11] yet absent in the proposed *ICD-11*.[12] For us, this unusual contradiction raises major concerns about the validity of the process behind the establishment of these new proposed criteria, and could impact the credibility of the field of PTSD research. Although these differences occur, it seems to us that the committees do not see the implications (ie, the possible disservice they also might do to the field of psychiatry, putting the field back in time). The following are issues of particular concern.

1. *ICD-11*[12] is trying to cluster PTSD as a disorder specifically associated with stress but not differentiating the effects of traumatic events from day-to-day stressors. *ICD* is moving away from diagnostic criteria and fails to have diagnostic criteria—they are "guidelines" or bullet points followed by paragraphs that expand on these points, differentiated by virtue of avoiding "pseudo-precise" requirements like symptom counts or precise durations.

2. In *ICD-11,*[12] the second core element is avoidance of the intrusions or

situations reminiscent of the traumatic event, which is in contrast to *ICD-10,*[69] in which these were not seen as an essential characteristic of the diagnosis. Another thing *ICD-10*[69] put in was a core element ("conspicuous emotional detachment and numbing of feeling") that is now excluded in *ICD-11*.[12] This shift was made without adequate explanation and discussion of the evidence.

3. *ICD-11*[12] has removed numbing and detachment as a core element, which is a symptom that is frequently seen in military cohorts and emergency service workers, and also in sexual trauma survivors. Because of that, cases will possibly be missed. This is one cluster of symptoms in PTSD for which there is now a well-characterized neurobiology (ie, numbing and detachment), which highlights the problem of moving away from criteria that are tied to neurobiological data. Hence, a central aspect of the demonstrated psychopathology of PTSD has been dropped without addressing this body of work and explaining its exclusion.

4. A further troubling issue of *ICD-11*[12] is the argument that the threshold of PTSD was relatively low. It was argued that the requirement of functional impairment was necessary to differentiate PTSD from "normal reaction to reactions to extreme stressors." This move ignores the now substantial literature on the prevalence of subsyndromal PTSD, and the evidence of the associated disability,[88,89] as well as subsyndromal symptoms that are a significant marker of later risk of full-blown disorder[90] that are associated with a range of neurobiological symptoms that are consistent with PTSD. To this extent, Stein et al.[32] have highlighted how *ICD-11*[12] criteria are now the most stringent, so that only one-third of broadly defined cases met the criteria in all four systems and another one-third in only one system. As a consequence, the authors argued for a broad definition of PTSD defined by any one of the different systems, "to capture all clinically significant cases with PTSD in future studies." Another example of the hazards of the normalization of the symptoms experienced by people exposed to traumatic events is highlighted by a study of the 2005 London bombings.[67] This study recruited participants to receive treatment from a variety of resources, including emergency departments. It highlighted the inadequacy of standardized referral pathways, such as from primary care clinics, due to poor case definition in general practice.[67]

No rationale is given for why many symptoms primarily owned by other diagnoses than PTSD and throughout psychiatry, such as psychosis, panic, or anxiety, exist in multiple illnesses. For example, delusions are not removed as a disorder because they "belong' to another one (eg, from bipolar disorder because they "belong" to schizophrenia). In fact, psychosis is one of the hallmark diagnoses of both mania and schizophrenia. Hence, there is no rationale for the application for a hierarchical allocation of symptoms to other disorders when it comes to PTSD when this is not a consistent convention across all diagnostic categories. If such an approach is to be used in *ICD*, this should not simply be done for PTSD but should be for the entire body of psychopathology. Furthermore, it assumes a logic that is not consistent with the broad literature of comorbidity.

5. With *ICD-11,*[12] assuming that the nonspecific symptoms of PTSD are more validly left to belong to other psychiatric disorders rather than to PTSD, it does not address the problem that many cases of other psychiatric disorders, such as depression, may in fact themselves be posttraumatic conditions. Also, in a clinical sample of children and adolescents, the prevalence of PTSD was significantly affected by the use of different diagnostic systems.[91] The use of the criteria proposed for *ICD-11*[12] in a group of children and adolescents exposed to trauma resulted in 27.1% fewer positive cases compared with *ICD-10* and 15.1% fewer positive cases compared with *DSM-IV*.[92]

6. *ICD-11*[12] also introduces the issue of function impairment, suggesting that the absence of this criterion was a major reason for the overdiagnosis in *ICD-11*. Also, the introduction of function impairment again introduces a challenging conundrum in that most other physical diseases do not require impairment to make a diagnosis. Thyrotoxicosis can be diagnosed in the absence of any function impairment. Impairment is dependent on a variety of cultural and environmental factors and, therefore, creates a social context of disease that should not be solely imposed on PTSD in contrast to other psychiatric disorders.

In summary, *ICD-11*[13] authors have constructed a theoretical position that has interfered with the appropriate phenomenological observation that has existed for over 4 decades and are introducing logic that is not applied to other diagnostic categories.

THE ROLE OF DIFFERENCES IN COMBAT AND CIVILIAN PTSD

PTSD has been linked to military service since its origins in *DSM-III*[1] when the American Psychiatric Association, despite the removal of "Gross Stress Reaction" in *DSM-II*,[86] was forced to revisit the potential effects of stress from combat in Vietnam veterans. Interestingly, as the field advances, the modifications attempt to reflect what is seen in soldiers (ie, the removal of the A2 criterion in *DSM-5*[11]). One challenge of traumatology and diagno-

sis is that considerable trauma research and discussion occurs around two groups: soldiers/veterans and victims of violent crime (such as rape). The two groups are quite different, as are the precipitating traumas. Cleary, one group is the victim of violent crime, whereas the others are volunteers who go to war and are to some extent overwhelmed by experiences but would not see themselves as "victims" of combat. Is the gold standard of treatment (ie, prolonged exposure) also based on treatment of rape victims? Does this approach really translate to soldiers with PTSD? Treatment response to both psychotherapy and medication is typically lower in veteran groups than others diagnosed with PTSD.[92] We have argued that given the unique context of warzone engagement, which may include chronic threat, multiple as well as lengthy deployments, and loss, suggests that the disorder is "different" in veterans than in rape victims and not generalizable from civilian trauma exposure.[93]

Part of the difference may be that the stress and fear-based approach to PTSD may be missing a key aspect of veteran's experience, which is the moral injury component of the illness. Quite often, the prevalent feelings such as guilt and shame seem to interfere with recovery in veterans with PTSD but are missing as an element of the diagnosis. Yet, as Hoge et al.[94] points out, 30% of veterans would no longer meet criteria in *DSM-5*[11] because they do not actively avoid (something that soldiers often overcome due to their very nature).

THE USE OF BIOMARKERS IN THE DIAGNOSIS OF PTSD

Although there exists a major body of biological research that has explored PTSD using *DSM-IV*[19] criteria rather than a single biomarker, a range of validated neurobiological correlates have been found. This literature does not appear to have been addressed at all in the development of the *ICD-11*[12] criteria. A major concern regarding divergence in the development of the diagnostic accuracy is that the *ICD-11*[12] criteria do not move the field in a direction that is based on the substantial empirical body of evidence that has been developed over the past decades.

Treatment response to both psychotherapy and medication is typically lower in veteran groups than others.

There are many candidate biomarkers for PTSD built on the biological framework of the disorder. Although there are no established diagnostic biomarkers for PTSD, biological investigations of PTSD have made progress identifying the pathophysiology of PTSD.[41,95,96] Given the biological and clinical complexity of PTSD, it is an accepted reality that no single biomarker of disease will be identified. Rather, investigations will more likely identify or model dynamics of different biomarkers or biosignatures that indicate the presence of clinically significant PTSD symptoms, associate with risk for PTSD after trauma exposure, and predict or identify recovery.[97] Protein, metabolic, as well as genetic and genomic candidate biomarkers are being sought, but none so far has been discovered that shows sufficient sensitivity for PTSD diagnosis as well as specificity (ie, little overlap with other psychiatric diagnoses).[40,98] The most replicated biomarker so far is a hypothalamic-pituitary-adrenal axis finding of low plasma cortisol (especially at the nadir), and increased glucocorticoid receptor sensitivity, a finding opposite that of MDD, despite commonalities that include central nervous system hyperarousal, increased amygdalar reactivity, and diminished parasympathetic outflow.[27,39,99-101] Further potential PTSD biomarkers may be found in imaging, psychological, endocrine, and molecular categories that will be classified into risk, disease, and therapy markers (eg, amygdala dysregulation, hippocampal integrity, fear prediction,[102] hypocorticolaemia, enhanced startle, impairment of cognitive functions, hippocampal integrity) that can create a long-lasting state of physiological reactivity that amplifies and exacerbates the effects of daily life (ie, allostatic load[103]). These factors affect not only individual genes and biomolecules, but also entire biological networks, which in turn increase or decrease the risk of illness or affect illness severity.

Although there has been much interest in PTSD biomarkers, there has been far less discussion of their potential clinical applications, and of the social, legal, and ethical implications of such biomarkers. As noted, there is nothing in this domain that passed beyond statistical significance to diagnostic tests. This may be attributable to the heterogeneity of the disorder as well as to the functional relevance of the biomarker. Recently, Schmidt et al.[104] reviewed nongenetic molecular and imaging PTSD risk and resilience markers. A limitation in most biomarker research studies stems in part from not yet being fully able to account for the individual nuances (eg, duration of the disorder, antecedent factors, epigenetic changes).

Hope for further discovery rests along a number of lines of research that include (1) longitudinal studies, which can tease apart preexisting, preexposure risk and resilience traits, as well as persistent biological changes that result from trauma exposure and are a biomarker for PTSD diagnosis; (2) potential diagnostic algorithms

over a number of biological markers that can account for a progressively increasing percentage of the predictability; or (3) challenge tests, such as in the demonstration by Geracioti et al.[105] showing reduced cortisol output under stress in people with PTSD; perhaps a model for challenge tests in psychiatry could be comparable to those that have been so successful in cardiology in predicting disease.

THE WAY AHEAD: NEED FOR AN ACCEPTED PROCESS

One of the most perplexing aspects of the current developments is that the consensus approaches used by the various committees to come to a definition of PTSD appear to be contradictory. Assuming they have a similar process for reviewing the relevant scientific literature, how such divergent conclusions were reached is concerning. This is particularly so, as there is substantial shared authorship of some of the cited articles and committee memberships. This raised concerns about the editorial oversight of the *DMS-5*[11] and *ICD-11*[12] and the apparent failure to resolve quite fundamental differences of approaches implicit in the diagnostic systems. As controversies will certainly remain, we have some recommendations to resolve some of them.

1. The various substantial accumulated body of knowledge aggregated around *DSM* and *ICD* diagnostic criteria means that any diversions should only occur if substantial error or misclassification can be shown to occur as a consequence of the continued use of these criteria. It should be clearly demonstrated that there is a problem to what currently is being used.

2. Literature should not be neglected. In several opinion-based articles we feel that literature is neglected and one-sided approaches emphasized. As research in PTSD has expanded, multiple interpretations of study findings may occur, but never without neglecting published study results that contradict findings or are divergent of common models. Many deliberations of *IDC-11*[12] in regard to stress disorders are disappointing, in our view, due to the simplicity of the arguments provided and the lack of reference to the complex and highly credible literature relevant to the questions at hand. We believe the suggestion that acute stress disorder should be viewed as a reaction falling "in the normal range" is not in keeping with a broad body of research.

There is no empirical support for the notion that PTSD is overdiagnosed.

3. We feel there is a divergence between biological scientists and cognitive theorists in these cases. Our conceptual clinical orientation needs to capture both frames of reference. This is in line with the need for precision psychiatry. Simple reductionist models do not fit with clinical reality, nor do they always adequately address "illness" (ie, the patient's experience of the problem), which implies subjective suffering. Moreover, in a disorder that is as heterogeneous as PTSD, it is important to account for an array of individual differences. If there are 65,000 ways of diagnosing PTSD, there may be an equal number of ways to deliver therapies. As rigorous as scientific approaches need to be, we cannot fit patients into our model. Finally, we are concerned that if a patient does not respond to treatment, then it may be thought that the diagnosis was wrong. This causes error and controversies.

4. It is our belief that the proposed *ICD-11*[12] criteria have been based on political arguments that are not supported by a substantial body of scientific literature. This should be fixed in open debate. Of particular note, it needs to be addressed that there is no empirical support for the notion that PTSD is overdiagnosed.

5. As for depression and other psychiatric diagnoses in PTSD diagnostics, we need to move away from popular misunderstandings and simplifications. Patients have the right to understand upon what their diagnosis is based.[106] For this reason, the medical community has a duty to reach a consensus. Only then can we communicate to the patient a truthful and representative account of medical knowledge.

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