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PTSD Unmet Needs: A Lens on Burden, Impact, and Treatment Challenges

Announcer:
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This medical industry feature, titled "PTSD Unmet Needs: A Lens on Burden, Impact, and Treatment Challenges," is sponsored by Otsuka.

Here's your host, Dr. Charles Turck.

Dr. Turck:
This is ReachMD, and I'm Dr. Charles Turck. Joining me today to discuss the disease burden, identify unmet needs, and review clinical challenges in post-traumatic stress disorder, or PTSD, is Dr. John Krystal. He is the Chair of Psychiatry at Yale School of Medicine.

Dr. Krystal, welcome to the program.

Dr. Krystal:
Thank you for having me.

Dr. Turck:
To start off our discussion, Dr. Krystal, can you explain what PTSD is, and who typically develops PTSD?

Dr. Krystal:
Allow me to start with a brief definition of PTSD, which is a psychiatric disorder that may occur in people who've experienced or witnessed a traumatic event, series of events, or set of circumstances, defined as the index trauma.[1–4] PTSD affects mental, physical, social, and spiritual well-being and it can be life-threatening.[1-3]

It's important to note that PTSD is one of the most common mental health disorders in the US.[5,6] About 13 million adults in the US, or about 4.9 percent of the population, will experience PTSD during a given year. This is estimated based on a published secondary analysis of PTSD prevalence from a National Epidemiology Survey conducted from 2012 to 2013 along with US Census Bureau data from 2022.[7–11] And seven to eight out of every 100 people in the US will experience PTSD at some point in their lives.[7,8,11,12]

There's a general misconception that PTSD occurs mainly in the male military population. However, the incidence of PTSD is actually two times higher in women than men, and females in the civilian population experience PTSD for a longer duration than do males.[1,7,13] It's also important to note that over 80 percent of PTSD patients are in the general population instead of the military population.[13–15] The typical onset for PTSD is in young and middle adulthood, with 23 years being the median age of onset among US adults.[15]

Now the risk of developing PTSD varies widely depending on the index trauma type.[16–19] In the World Health Organization, or WHO, World Mental Health Survey analysis of over 50,000 traumatic events, the highest proportion of PTSD cases were related to the unexpected death of a loved one, at about 31 percent, and directly witnessing death or serious injury, around 24 percent.[19]

Other trauma types with increased risk of developing PTSD include sexual relationship and interpersonal violence, child abuse, and life-threatening illness or injury.[20] The presence of certain demographic and behavioral health factors are also associated with an increased risk of PTSD, including diagnosed mental illness, race and ethnicity—as Black individuals are at an increased risk of developing PTSD

compared to White, Hispanic, or Asian individuals—divorced status, substance use disorders, including drug and alcohol use, and LGBTQ plus orientation.[20–22]

Dr. Turck:
Now let's explore the broader picture. Dr. Krystal, could you share your insights on the overall impact and burden of PTSD?

Dr. Krystal:
Of course. To start, we should understand that there are four *core* symptom clusters of PTSD tied to the diagnostic criteria in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition—commonly referred to as the DSM-5.[1,23] And we'll talk more about these in just a minute. These include intrusion or re-experiencing, avoidance, negative cognition and mood, and alterations in arousal and reactivity.[23] As a result, PTSD is associated with a high impact on the individual and can impair function across a range of different domains, including interpersonal, occupational, and social functions.[24]

Symptoms of PTSD can make interacting with friends and family difficult. It can also undermine social support networks.[2,24,25] In terms of occupational burden, based on the 2005 Survey of Healthcare Experiences of Patients data, 78 percent of the civilian and 81 percent of the military populations with PTSD are unemployed in the US, and the likelihood of unemployment increases with symptom severity.[26-29] PTSD can also contribute to homelessness and interactions with the criminal justice system.[2,30,31]

Dr. Turck:
You mentioned the DSM-5 criteria for PTSD; could you take us through these in context of the diagnostic process?

Dr. Krystal:
By expanding on the core symptom clusters of PTSD, the DSM-5 establishes criteria for the diagnosis of PTSD, starting with exposure to the index trauma event.[1,23]

Next, intrusion symptoms include the re-experiencing of the trauma, and can include recurrent distressing dreams, memories, or flashbacks.[1,23] Third, avoidance is the persistent effort to prevent distressing memories, thoughts, or feelings, which may include avoiding any triggers that can be reminders of the trauma.[1,23]

For these parameters, one or more symptom from both intrusion and avoidance meets these criteria.[1,23] Now the DSM-5 requires at least two symptoms of negative cognition and mood for a diagnosis of PTSD. These can include persistent negative emotions, such as anger, fear, guilt, or shame, or on the other hand, feelings of detachment, estrangement, or the inability to feel a positive emotion. Cognition surrounding the trauma can become distorted or affect the ability to remember an important facet of the trauma.[1,23]

The diagnosis also requires at least two symptoms that reflect marked alterations in arousal and reactivity, which may present as hypervigilance, an exaggerated startle response, sleep disturbances, self-destructive behavior, or irritability and aggression.[1,23]

Finally, the remaining criteria focus on symptoms. These require that the symptoms are of at least one month duration, they cause clinically significant distress or impairment, and they're not attributable to a substance or other medical condition.[1,23]

Dr. Turck:
And with that in mind, can you share your thoughts on the clinical burden of PTSD and current unmet needs?

Dr. Krystal:
Yes – we now know that PTSD is often underdiagnosed or misdiagnosed as another mental health condition.[19,32]

Critically, less than 50 percent of people who meet the criteria for PTSD are correctly diagnosed in primary and secondary care settings, resulting in delay of appropriate treatment while patients continue to experience symptoms.[32-34] In fact, data show that patients unfortunately experience a remarkably protracted time from index trauma to PTSD diagnosis of 8.7 years on average.[35]

One factor contributing to under- or misdiagnosis is PTSD-related stigma, which has a negative impact on patient outcomes in addition to creating a significant barrier to treatment-seeking and engagement. Individuals with PTSD may avoid treatment due to perceived shame or the fear of being discriminated against or negatively judged.[35–40]

This may contribute to underdiagnosis, which has lead to undertreatment and potential adverse outcomes, including , including increased risk for long-term PTSD, disruptions to daily life, deterioration of family and social relationships, risk of isolation and distress, poor quality of life, suicide attempts, and increased risk of mortality.[41-47]

Thus, early diagnosis and intervention are necessary to minimize the long-term outcomes associated with PTSD.[23]

PTSD is also associated with an increased risk of suicidal ideation, attempted suicide, and completed suicide. Specifically, civilians who develop PTSD are at an increased risk of attempted suicide, at a relative risk of 2.7, compared to individuals who have never experienced a traumatic event.[48-51]

Additionally, PTSD is often linked with medical comorbidities. And insomnia is a common comorbidity in individuals with PTSD, up to 87 percent of people suffering from PTSD reported sleep disturbance.[52-54] And looking at cardiovascular disease, a positive screening for PTSD was significantly correlated with newly self-reported heart disease.[55]

Of key importance, PTSD is associated with an increased risk of mortality, including cardiovascular, external-cause, as well as all-cause mortality.[56-59]

In addition to medical comorbidities, PTSD often presents with other psychiatric comorbidities. As demonstrated by National Surveys data, about 80 to 90 percent of patients with PTSD meet criteria for at least one other psychiatric disorder.[60-62] The most common psychiatric comorbidities include affective disorders, such as depression, approximately fifty percent of people with PTSD also had comorbid major depressive disorder.[61-63] In addition, individuals with PTSD have 2.4 to 7.1 higher odds of having an anxiety disorder, with the majority comprising of phobias and generalized anxiety disorder.[63]

Lastly, substance use disorder is common in individuals with PTSD, with an estimated prevalence around 46 percent.[64-66]

Dr. Turck:
For those just tuning in, you're listening to ReachMD.

I'm Dr. Charles Turck, and today I'm speaking with Dr. John Krystal about the burden, impact, and treatment challenges of PTSD.

Dr. Krystal, now that we've discussed the clinical burden of PTSD, I'd like to set our focus on treatment. Can you walk us through the current treatment landscape for PTSD.

Dr. Krystal:
Psychotherapy's demonstrated clinical benefits for PTSD include reduced symptom severity and improved remission rates.[2,68,70]

That being said, in order to utilize psychotherapy effectively, several considerations must be made for the individual patient, including treatment cost, resource availability, and patient preference and comorbidities.[71] Notably, despite psychotherapy's clinical benefits, over 60 percent of patients don't meet improvement criteria after psychotherapy, which implies that further intervention is necessary for many patients.[72]

In clinical practice, the efficacy of psychotherapy may be limited due to a combination of high demand, limited resources, visit frequency needs, healthcare provider expertise, and access in rural areas.[71-73]

In addition, some of the patient barriers include a perceived lack of usefulness, significant comorbidities, and a preference for drug treatment.[71,72,74] As a result, it's important that we individualize treatment care plans based on patient and clinical factors.[71,73] So looking next at medication management of PTSD, early and effective pharmacotherapy has been shown to improve symptoms, reduce disability, and improve long-term outcomes.[75-77] However, there are only two FDA-approved medications for PTSD, both being SSRIs.[78,79]

As a result, US guidelines recommend these two SSRIS, as well as off-label use of certain SSRIs and serotonin and norepinephrine reuptake inhibitors, or SNRIs, for the treatment of PTSD.[11,71,80]

Select SSRIs and SNRIs are recommended by guidelines for PTSD treatment.[11,69] However, these agents demonstrate variable efficacy.[76] Reportedly, compared to placebo, patients who receive FDA-approved SSRIs to treat PTSD have less than 40 percent likelihood of an adequate response.[76]

Moreover, analyses prescribing trends in patients with PTSD treated in the Veterans Health Administration found that only 20 percent of patients receive FDA-approved SSRIs.[81]

Dr. Turck:
And as a follow-up, let's take a closer look at the commonly used drugs for PTSD treatment? Can you share some key insights?

Dr. Krystal:
As with any treatment, varied response rates are typical, as each patient responds a bit differently than the next due to patient specific factors.[76] SSRIs and SNRIs, while included in US guideline recommendations, have also shown variable efficacy in the treatment of PTSD.[76,82,83]

As a result, a significant proportion of patients with PTSD continue to have an unmet need for effective, evidence-based treatment, despite being treated with pharmacotherapy.[84]

For example, claims data indicate that almost 70 percent of patients have a pharmacological treatment change after a PTSD diagnosis, with about 60 percent of patients receiving at least two distinct PTSD-related agents within 24 months following diagnosis. And the most commonly reported reason, at approximately 50 percent, for treatment changes is "inadequate [or] suboptimal management of PTSD symptoms with prior treatment."[84]

As a consequence, providers often use off-label and non-evidence–based treatments in attempts to address ongoing PTSD symptoms—although these treatments aren't recommended by guidelines.[81,85-87]

Analyses of prescribing trends in patients with PTSD found that 21 percent receive benzodiazepines and 18 percent receive anxiolytics or sedative hypnotics—classes of medications that may actually contribute to an increased adverse event burden.[2,86] Anxiolytics and benzodiazepines are commonly prescribed to treat sleep disturbance and hyperarousal symptoms, despite the guidelines' strong recommendation *against* the use of benzodiazepines in several published guidelines.[11,88] Adrenergic antagonists are also used for PTSD-related nightmares, although they're not efficacious in treating recurrent distressing dreams or improving sleep quality.[89]

And finally, atypical antipsychotics have been used for treatment augmentation in cases of incomplete response or residual symptoms, though again, guidelines recommend *against* these given weak existing evidence.[85,90]

Dr. Turck:
As we come to the end of today's program, as a specialist in this area, Dr. Krystal, what can you tell us about treatment challenges with the current therapeutic landscape?

Dr. Krystal:
In terms of pharmacotherapy, no new drugs have received approval by the FDA for PTSD treatment in over two decades.[78,79] Limited treatment options have necessitated trial and error polypharmacy with off-label medications for a vast majority of patients to address unresolved PTSD symptoms.[91]

So often, individuals are prescribed an average of 1.6 medications for PTSD with combinations that commonly include SSRIs, anxiolytics, and benzodiazepines to address depression and sleep disturbances.[81,85] Regarding benzodiazepines, there are concerns that the risks may outweigh potential short-term benefits, and could even increase the risk of developing PTSD.[2,88]

What's particularly concerning is that about 20 percent of patients with PTSD self-medicate with drugs or alcohol in an attempt to relieve their symptoms.[65]

Taken together, it's important to understand that patients can experience clinical barriers to effective PTSD management. In a US-based survey, 41.8 percent of patients with PTSD reported an unmet need for treatment, emphasizing disparities in access to care and treatment utilization.[74] Interestingly, 16.4 percent of these individuals didn't want to see a professional, and 25 percent of these individuals didn't believe that treatment would help.[74]

Patients often expressed fear of re-experiencing traumatic events or certain trauma-related memories as a significant trauma-related barrier to mental health service use. Notably, trauma memory re-exposure is one of the techniques used in psychotherapy.[39,40]

In closing, as providers we should continue to emphasize the importance of individualized treatment care plans based on patient and clinical factors.[71,73]

Dr. Turck:

Great way to round out our discussion on this topic.

I want to thank my guest, Dr. John Krystal, for his insights into the burden, unmet needs, and treatment challenges of PTSD.

Dr. Krystal, it was great speaking with you today.

Dr. Krystal:
Thank you. It was my pleasure.

Dr. Turck:
I'm Dr. Charles Turck.

Announcer:
This program was sponsored by Otsuka. If you missed any part of this discussion, visit Medical Industry Features on ReachMD.com where you can Be Part of the Knowledge.

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February 2024 US.UNB.V.23.00027