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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 led 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.

References:

1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders: DSM-5TM. 5th ed. Washington D.C.: American Psychiatric Publishing; 2013.
2. Yehuda R, Hoge CW, McFarlane AC, et al. Post-traumatic stress disorder. *Nat Rev Dis Prim.* 2015;1(1):15057. doi:10.1038/nrdp.2015.57
3. Suomi A, Evans L, Rodgers B, Taplin S, Cowlshaw S. Couple and family therapies for post-traumatic stress disorder (PTSD). *Cochrane Database Syst Rev.* 2019;2019(12). doi:10.1002/14651858.CD011257.pub2
4. Priebe K, Kleindienst N, Schropp A, et al. Defining the index trauma in post-traumatic stress disorder patients with multiple trauma exposure: impact on severity scores and treatment effects of using worst single incident versus multiple traumatic events. *Eur J Psychotraumatol.* 2018;9(1). doi:10.1080/20008198.2018.1486124
5. Lancaster C, Teeters J, Gros D, Back S. Posttraumatic stress disorder: overview of evidence-based assessment and treatment. *J Clin Med.* 2016;5(11):105. doi:10.3390/jcm5110105
6. Spottswood M, Davydow DS, Huang H. The prevalence of posttraumatic stress disorder in primary care: a systematic review. *Harv Rev Psychiatry.* 2017;25(4):159-169. doi:10.1097/HRP.000000000000136
7. Kilpatrick DG, Resnick HS, Milanak ME, Miller MW, Keyes KM, Friedman MJ. National estimates of exposure to traumatic events and PTSD prevalence using DSM-IV and DSM-5 criteria. *J Trauma Stress.* 2013;26(5):537-547. doi:10.1002/jts.21848
8. Lehavot K, Katon JG, Chen JA, Fortney JC, Simpson TL. Post-traumatic stress disorder by gender and veteran status. *Am J Prev Med.* 2018;54(1):e1-e9. doi:10.1016/j.amepre.2017.09.008
9. US Census Bureau. National Population by Characteristics: 2020-2022. US Census Bureau. Published 2022. Accessed September 6, 2023. www.census.gov/data/tables/time-series/demo/popest/2020s-national-detail.html
10. Data on file (Prevalence Estimate).
11. U.S. Department of Veterans Affairs. VA/DoD Clinical Practice Guideline for the Management of Posttraumatic Stress Disorder and Acute Stress Disorder. Version 4.0. Published 2023. Accessed September 6, 2023. www.healthquality.va.gov/guidelines/MH/ptsd/VA-DoD-CPG-PTSDFull-CPG.pdf
12. Koenen KC, Ratanatharathorn A, Ng L, et al. Posttraumatic stress disorder in the World Mental Health Surveys. *Psychol Med.* 2017;47(13):2260-2274. doi:10.1017/S0033291717000708
13. Davis LL, Schein J, Cloutier M, et al. The economic burden of posttraumatic stress disorder in the United States from a societal perspective. *J Clin Psychiatry.* 2022;83(3). doi:10.4088/JCP.21m14116
14. United Nations, Department of Economic and Social Affairs PD. World Population Prospects 2019: Highlights. Published 2019. Accessed September 6, 2023. population.un.org/wpp/Publications/Files/WPP2019_Highlights.pdf
15. Kessler RC, Chiu WT, Demler O, Walters EE. Prevalence, severity, and comorbidity of 12-Month DSM-IV Disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry.* 2005;62(6):617-627. doi:10.1001/archpsyc.62.6.617
16. Liu H, Petukhova M V., Sampson NA, et al. Association of DSM-IV posttraumatic stress disorder with traumatic experience type and history in the World Health Organization World Mental Health Surveys. *JAMA Psychiatry.* 2017;74(3):270. doi:10.1001/jamapsychiatry.2016.3783
17. Luz MP, Coutinho ESF, Berger W, et al. Conditional risk for posttraumatic stress disorder in an epidemiological study of a Brazilian urban population. *J Psychiatr Res.* 2016;72:51-57. doi:10.1016/j.jpsychires.2015.10.011
18. Tortella-Feliu M, Fullana MA, Pérez-Vigil A, et al. Risk factors for posttraumatic stress disorder: an umbrella review of systematic reviews and meta-analyses. *Neurosci Biobehav Rev.* 2019;107:154-165. doi:10.1016/j.neubiorev.2019.09.013
19. Kessler RC, Aguilar-Gaxiola S, Alonso J, et al. Trauma and PTSD in the WHO World Mental Health Surveys. *Eur J*

- Psychotraumatol.* 2017;8(sup5). doi:10.1080/20008198.2017.1353383
20. Data on file (Prevalence and Risk Factors of Post-Traumatic Stress Disorder in the United States).
 21. Schein J, Houle C, Urganus A, et al. Prevalence of post-traumatic stress disorder in the United States: a systematic literature review. *Curr Med Res Opin.* 2021;37(12):2151-2161. doi:10.1080/03007995.2021.1978417
 22. Roberts AL, Austin SB, Corliss HL, Vandermorris AK, Koenen KC. Pervasive trauma exposure among US sexual orientation minority adults and risk of posttraumatic stress disorder. *Am J Public Health.* 2010;100(12):2433-2441. doi:10.2105/AJPH.2009.168971
 23. Mann SK, Marwaha R. Posttraumatic Stress Disorder. StatPearls. [Updated 2023 Jan 30]. Accessed November 3, 2023. www.ncbi.nlm.nih.gov/books/NBK559129/
 24. Rodriguez P, Holowka DW, Marx BP. Assessment of posttraumatic stress disorder-related functional impairment: a review. *J Rehabil Res Dev.* 2012;49(5):649-666. doi:10.1682/JRRD.2011.09.0162
 25. Koven S. Veteran Treatments: PTSD Interventions. *Healthcare.* 2018;6(3):94. doi:10.3390/healthcare6030094
 26. Zivin K, Bohnert AS, Mezuk B, et al. Employment status of patients in the VA health system: implications for mental health services. *Psychiatr Serv.* 2011;62(1):35-38. doi:10.1176/ps.62.1.pss6201_0035
 27. Savoca E, Rosenheck R. The civilian labor market experiences of Vietnam-era veterans: the influence of psychiatric disorders. *J Ment Health Policy Econ.* 2000;3(4):199-207. doi:10.1002/mhp.102
 28. Horn SR, DeWilde K, Feder A, et al. Severity of post traumatic stress disorder and its impact on employment status. Poster presented at: 167th American Psychiatric Association Annual Meeting; May, 2014; New York, NY.
 29. Smith MW, Schnurr PP, Rosenheck RA. Employment outcomes and PTSD symptom severity. *Ment Health Serv Res.* 2005;7(2):89-101. doi:10.1007/s11020-005-3780-2
 30. Ayano G, Solomon M, Tsegay L, Yohannes K, Abraha M. A systematic review and meta-analysis of the prevalence of post-traumatic stress disorder among homeless people. *Psychiatr Q.* 2020;91(4):949-963. doi:10.1007/s11126-020-09746-1
 31. Jäggi LJ, Mezuk B, Watkins DC, Jackson JS. The relationship between trauma, arrest, and incarceration history among Black Americans. *Soc Ment Health.* 2016;6(3):187-206. doi:10.1177/2156869316641730
 32. Greene T, Neria Y, Gross R. Prevalence, detection and correlates of PTSD in the primary care setting: a systematic review. *J Clin Psychol Med Settings.* 2016;23(2):160-180. doi:10.1007/s10880-016-9449-8
 33. Liebschutz J, Saitz R, Brower V, et al. PTSD in Urban Primary Care: High Prevalence and Low Physician Recognition. *J Gen Intern Med.* 2007;22(6):719-726. doi:10.1007/s11606-007-0161-0
 34. Zammit S, Lewis C, Dawson S, et al. Undetected Post-Traumatic Stress Disorder in Secondary-Care Mental Health Services: Systematic Review. *Br J Psychiatry.* 2018;212(1):11-18. doi:10.1192/bjp.2017.8
 35. Davis L, Aggarwal J, Urganus A, Gagnon-Sanschagrín P, Maitland J. Patient Journey of Civilian Adults Treated for Post-Traumatic Stress Disorder - A Chart Review Study. Poster presented at: Annual Meeting of the American Society of Clinical Psychopharmacology (ASCP); May 30-Jun 2, 2023. Published online 2023.
 36. Benfer N, Howell MK, Lucksted A, Romero EG, Drapalski AL. Self-stigma and PTSD: conceptualization and implications for research and treatment. *Psychiatr Serv.* 2023;74(10):1081-1083. doi:10.1176/appi.ps.20220397
 37. Bonfils KA, Lysaker PH, Yanos PT, et al. Self-stigma in PTSD: prevalence and correlates. *Psychiatry Res.* 2018;265:7-12. doi:10.1016/j.psychres.2018.04.004
 38. Hoge CW, Castro CA, Messer SC, McGurk D, Cotting DI, Koffman RL. Combat duty in Iraq and Afghanistan, mental health problems, and barriers to care. *N Engl J Med.* 2004;351(1):13-22. doi:10.1056/NEJMoa040603
 39. Kantor V, Knefel M, Lueger-Schuster B. Perceived barriers and facilitators of mental health service utilization in adult trauma survivors: a systematic review. *Clin Psychol Rev.* 2017;52:52-68. doi:10.1016/j.cpr.2016.12.001
 40. Kazlauskas E. Challenges for providing health care in traumatized populations: barriers for PTSD treatments and the need for new developments. *Glob Health Action.* 2017;10(1):1322399. doi:10.1080/16549716.2017.1322399
 41. Gagnon-Sanschagrín P, Schein J, Urganus A, et al. Identifying individuals with undiagnosed post-traumatic stress disorder in a large United States civilian population – a machine learning approach. *BMC Psychiatry.* 2022;22(1):630. doi:10.1186/s12888-022-04267-6
 42. Wimalawansa S. Post-traumatic stress disorder: an under-diagnosed and under-treated entity. *Compr Res J Med Med Sci.* 2013;1:1-12.
 43. Goenjian AK, Walling D, Steinberg AM, Karayan I, Najarian LM, Pynoos R. A prospective study of posttraumatic stress and depressive reactions among treated and untreated adolescents 5 years after a catastrophic disaster. *Am J Psychiatry.* 2005;162(12):2302-2308. doi:10.1176/appi.ajp.162.12.2302
 44. Priebe S, Matanov A, Janković Gavrilović J, et al. Consequences of untreated posttraumatic stress disorder following war in former Yugoslavia: morbidity, subjective quality of life, and care costs. *Croat Med J.* 2009;50(5):465-475.

- doi:10.3325/cmj.2009.50.465
45. Ellis J, Zaretsky A. Assessment and Management of Posttraumatic Stress Disorder. *Continuum (Minneapolis, Minn)*. 2018;24(3):873-892. doi:10.1212/CON.0000000000000610
 46. Smith BA. Impact of veteran status and timing of PTSD diagnosis on criminal justice outcomes. *Healthcare (Basel)*. 2018;6(3):80. doi:10.3390/healthcare6030080
 47. Cooper J, Metcalf O, Phelps A. PTSD--an update for general practitioners. *Aust Fam Physician*. 2014;43(11):754-757.
 48. Nepon J, Belik SL, Bolton J, Sareen J. The relationship between anxiety disorders and suicide attempts: findings from the National Epidemiologic Survey on Alcohol and Related Conditions. *Depress Anxiety*. 2010;27(9):791-798. doi:10.1002/da.20674
 49. Wilcox HC, Storr CL, Breslau N. Posttraumatic stress disorder and suicide attempts in a community sample of urban american young adults. *Arch Gen Psychiatry*. 2009;66(3):305-311. doi:10.1001/archgenpsychiatry.2008.557
 50. Cogle JR, Keough ME, Riccardi CJ, Sachs-Ericsson N. Anxiety disorders and suicidality in the National Comorbidity Survey-Replication. *J Psychiatr Res*. 2009;43(9):825-829. doi:10.1016/j.jpsychires.2008.12.004
 51. Conner KR, Bossarte RM, He H, et al. Posttraumatic stress disorder and suicide in 5.9 million individuals receiving care in the veterans health administration health system. *J Affect Disord*. 2014;166:1-5. doi:10.1016/j.jad.2014.04.067
 52. Schoenfeld FB, DeViva JC, Manber R. Treatment of sleep disturbances in posttraumatic stress disorder: a review. *J Rehabil Res Dev*. 2012;49(5):729. doi:10.1682/JRRD.2011.09.0164
 53. Lies J, Jones L, Ho R. The management of post-traumatic stress disorder and associated pain and sleep disturbance in refugees. *BJPsych Adv*. 2019;25(3):196-206. doi:10.1192/bja.2019.7
 54. Maher MJ, Rego SA, Asnis GM. Sleep disturbances in patients with post-traumatic stress disorder. *CNS Drugs*. 2006;20(7):567-590. doi:10.2165/00023210-200620070-00003
 55. Jordan HT, Stellman SD, Morabia A, et al. Cardiovascular disease hospitalizations in relation to exposure to the September 11, 2001 World Trade Center disaster and posttraumatic stress disorder. *J Am Heart Assoc*. 2013;2(5). doi:10.1161/JAHA.113.000431
 56. Boscarino JA. Posttraumatic stress disorder and mortality among U.S. Army veterans 30 years after military service. *Ann Epidemiol*. 2006;16(4):248-256. doi:10.1016/j.annepidem.2005.03.009
 57. Boscarino JA. External-cause mortality after psychologic trauma: the effects of stress exposure and predisposition. *Compr Psychiatry*. 2006;47(6):503-514. doi:10.1016/j.comppsy.2006.02.006
 58. Boscarino JA. A prospective study of PTSD and early-age heart disease mortality among vietnam veterans: implications for surveillance and prevention. *Psychosom Med*. 2008;70(6):668-676. doi:10.1097/PSY.0b013e31817bccaf
 59. Lohr JB, Palmer BW, Eidt CA, et al. Is post-traumatic stress disorder associated with premature senescence? A review of the literature. *Am J Geriatr Psychiatry*. 2015;23(7):709-725. doi:10.1016/j.jagp.2015.04.001
 60. Flory JD, Yehuda R. Comorbidity between post-traumatic stress disorder and major depressive disorder: alternative explanations and treatment considerations. *Dialogues Clin Neurosci*. 2015;17(2):141-150. doi:10.31887/DCNS.2015.17.2/jflory
 61. Rytwinski NK, Scur MD, Feeny NC, Youngstrom EA. The co-occurrence of major depressive disorder among individuals with posttraumatic stress disorder: a meta-analysis. *J Trauma Stress*. 2013;26(3):299-309. doi:10.1002/jts.21814
 62. Kessler RC, Sonnega A, Bromet E, Hughes M, C.B. N. Posttraumatic stress disorder in the national comorbidity survey. *Arch Gen Psychiatry*. 1995;52(12):1048-1060. doi:10.1001/archpsyc.1995.03950240066012
 63. Brady KT, Killeen TK, Brewerton T, Lucerini S. Comorbidity of psychiatric disorders and posttraumatic stress disorder. *J Clin Psychiatry*. 2000;61 Suppl 7:22-32.
 64. McCauley JL, Killeen T, Gros DF, Brady KT, Back SE. Posttraumatic stress disorder and co-occurring substance use disorders: advances in assessment and treatment. *Clin Psychol Sci Pract*. 2012;19(3):283-304. doi:10.1111/cpsp.12006
 65. Leeies M, Pagura J, Sareen J, Bolton JM. The use of alcohol and drugs to self-medicate symptoms of posttraumatic stress disorder. *Depress Anxiety*. 2010;27(8):731-736. doi:10.1002/da.20677
 66. Lortye SA, Will JP, Marquenie LA, Goudriaan AE, Arntz A, de Waal MM. Treating posttraumatic stress disorder in substance use disorder patients with co-occurring posttraumatic stress disorder: study protocol for a randomized controlled trial to compare the effectiveness of different types and timings of treatment. *BMC Psychiatry*. 2021;21(1):442. doi:10.1186/s12888-021-03366-0
 67. International Society for Traumatic Stress Studies. ISTSS PTSD Prevention and Treatment Guidelines: Methodology and Recommendations. 2018. Accessed November 3, 2023. istss.org/getattachment/Treating-Trauma/New-ISTSS-Prevention-and-Treatment-Guidelines/ISTSS_PreventionTreatmentGuidelines_FNL.pdf.aspx.
 68. Lee DJ, Schnitzlein CW, Wolf JP, Vythilingam M, Rasmusson AM, Hoge CW. Psychotherapy versus pharmacotherapy for posttraumatic stress disorder: systemic review and meta-analysis to determine first-line treatments. *Depress Anxiety*. 2016;33(9):792-806. doi:10.1002/da.22511
 69. Guideline Development Panel for the Treatment of PTSD in Adults, American Psychological Association. Clinical Practice

- Guideline for the Treatment of Posttraumatic Stress Disorder (PTSD) in Adults. 2017. Accessed November 2, 2023. www.apa.org/ptsd-guideline/ptsd.pdf
70. Mavranouzouli I, Megnin-Viggars O, Daly C, et al. Psychological treatments for post-traumatic stress disorder in adults: a network meta-analysis. *Psychol Med*. 2020;50(4):542-555. doi:10.1017/S0033291720000070
 71. Martin A, Naunton M, Kosari S, Peterson G, Thomas J, Christenson JK. Treatment guidelines for PTSD: a systematic review. *J Clin Med*. 2021;10(18):4175. doi:10.3390/jcm10184175
 72. Murray H, Kerr A, Warnock-Parkes E, et al. What do others think? The why, when and how of using surveys in CBT. *Cogn Behav Ther*. 2022;15:e42. doi:10.1017/S1754470X22000393
 73. Morland LA, Wells SY, Glassman LH, Greene CJ, Hoffman JE, Rosen CS. Advances in PTSD treatment delivery: review of findings and clinical considerations for the use of telehealth interventions for PTSD. *Curr Treat Options Psychiatry*. 2020;7(3):221-241. doi:10.1007/s40501-020-00215-x
 74. Nobles CJ, Valentine SE, Gerber MW, Shtasel DL, Marques L. Predictors of treatment utilization and unmet treatment need among individuals with posttraumatic stress disorder from a national sample. *Gen Hosp Psychiatry*. 2016;43:38-45. doi:10.1016/j.genhosppsych.2016.09.001
 75. Stein DJ, Ipser JC, Seedat S, Sager C, Amos T. Pharmacotherapy for post traumatic stress disorder (PTSD). *Cochrane Database Syst Rev*. 2006. doi:10.1002/14651858.CD002795.pub2
 76. Williams T, Phillips NJ, Stein DJ, Ipser JC. Pharmacotherapy for post traumatic stress disorder (PTSD). *Cochrane Database Syst Rev*. 2022;2022(3). doi:10.1002/14651858.CD002795.pub3
 77. Davis LL, Frazier EC, Williford RB, Newell JM. Long-term pharmacotherapy for post-traumatic stress disorder. *CNS Drugs*. 2006;20(6):465-476. doi:10.2165/00023210-200620060-00003
 78. GlaxoSmithKline. PAXIL® (paroxetine hydrochloride). Published 2012. Accessed October 10, 2023. www.accessdata.fda.gov/drugsatfda_docs/label/2012/020031s067,020710s031.pdf.
 79. Pfizer. ZOLOFT (sertraline hydrochloride). Published 2016. Accessed October 10, 2023. www.accessdata.fda.gov/drugsatfda_docs/label/2016/019839S74S86S87_20990S35S44S45lbl.pdf.
 80. World Health Organization. Guidelines For The Management Of Conditions Specifically Related To Stress. World Health Organisation. 2013. Accessed September 3, 2023. apps.who.int/iris/bitstream/handle/10665/85119/9789241505406_eng.pdf.
 81. Holder N, Woods A, Neylan TC, et al. Trends in Medication Prescribing in Patients With PTSD From 2009 to 2018. *J Clin Psychiatry*. 2021;82(3). doi:10.4088/JCP.20m13522
 82. Murray H, Grey N, Warnock-Parkes E, et al. Ten misconceptions about trauma-focused CBT for PTSD. *Cogn Behav Therap*. 2022;15:e33. Published 2022 Jul 22. doi:10.1017/S1754470X22000307
 83. Alexander W. Pharmacotherapy for post-traumatic stress disorder in combat veterans: focus on antidepressants and atypical antipsychotic agents. *P T*. 2012;37(1):32-38.
 84. Davis LL, et al. Characteristics and treatment of adult patients with post-traumatic stress disorder – a retrospective claims based analysis. Poster presented at: Psych Congress 2022 Annual Conference; September 17–20, 2022; New Orleans, LA.
 85. Data on file (Treatment Algorithms: Claims Data Analysis in Post-Traumatic Stress Disorder).
 86. Cook JM, Zeber JE, Simiola V, et al. Comparisons between patients diagnosed with PTSD in primary care versus mental health care in five large civilian health care systems. *J Clin Psychol Med Settings*. 2021;28(2):221-228. doi:10.1007/s10880-020-09706-8
 87. Schrader C, Ross A. A Review of PTSD and current treatment strategies. *Mo Med*. 2021;118(6):546-551.
 88. Guina J, Rossetter SR, DeRhodes BJ, Nahhas RW, Welton RS. Benzodiazepines for PTSD. *J Psychiatr Pract*. 2015;21(4):281-303. doi:10.1097/PRA.0000000000000091
 89. Raskind MA, Peskind ER, Chow B, et al. Trial of prazosin for post-traumatic stress disorder in military veterans. *N Engl J Med*. 2018;378(6):507-517. doi:10.1056/NEJMoa1507598
 90. Bajor LA, Balsara C, Osser DN. An evidence-based approach to psychopharmacology for posttraumatic stress disorder (PTSD) - 2022 update. *Psychiatry Res*. 2022;317:114840. doi:10.1016/j.psychres.2022.114840
 91. Krystal JH, Davis LL, Neylan TC, et al. It is time to address the crisis in the pharmacotherapy of posttraumatic stress disorder: a consensus statement of the PTSD Psychopharmacology Working Group. *Biol Psychiatry*. 2017;82(7):e51-e59. doi:10.1016/j.biopsych.2017.03.007

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