

Emerging Bias in the Treatment of Posttraumatic Stress Disorder

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The article “Declining Benzodiazepine Use in Veterans With Posttraumatic Stress Disorder” by Lund and colleagues¹ comes on the heels of the recent update of the US Department of Veterans Affairs (VA) and Department of Defense (DoD) Clinical Practice Guideline for Management of Post-Traumatic Stress² and the position taken by the National Center for PTSD³ regarding benzodiazepine use. The Guideline was first published in 2004 and updated in 2010. Dr Friedman is the executive director of the National Center for PTSD, the cochair of the workgroup that wrote the Guideline, and one of the authors of the Lund et al article. Therefore, I think that it is fair, that, as I discuss this article, I also discuss the Guideline. The authors cite scarce recent studies to arrive at the conclusion that benzodiazepines have no benefit and may cause harm. In spite of this insufficient evidence, they inform us that the 152,413 veterans (30.6% of 498,081) who are in treatment for post-traumatic stress disorder (PTSD) in the VA and are taking benzodiazepines are receiving inappropriate treatment. In fact, according to the authors, these patients are being given drugs that have no benefit and there are “long-term harms imposed by benzodiazepine use.”^{1(p292)} They fail to present conclusive evidence to support this statement; however, they clearly imply that we are in the midst of a public health crisis as a result of benzodiazepine use. These numbers do not include the many thousands of individuals outside the VA who are being prescribed benzodiazepines for PTSD and other anxiety disorders. While there is some general agreement that benzodiazepines should have only an adjunctive role in PTSD treatment, the authors are overly biased in the negative. Even though the authors say that “determining the impact of the Guideline publication was not an objective of our analysis,”^{1(p295)} this seems to be exactly what this study is about. It takes for granted the conclusion that benzodiazepines are not useful in the treatment of PTSD and in fact can be quite harmful and that the gradual reduction with ultimate elimination of benzodiazepines should be a national goal. They conclude that “minimizing benzodiazepine exposure will remain a vital policy issue for the VA.”^{1(p296)}

In contrast to the National Center for PTSD recommendation, the American Psychiatric Association’s Practice Guideline for the Treatment of Patients With Acute Stress Disorder and Posttraumatic Stress Disorder⁴ takes a more reasoned approach. It addresses the same risks as reported in the National Center for PTSD recommendations, while

including benzodiazepines as a recommendation for reducing anxiety and improving sleep. In addition, it doesn’t describe them as harmful.

Furthermore, a study⁵ of veterans treated by the VA has shown that the rationale for benzodiazepine use is usually PTSD severity and anxiety and that the negative outcomes predicted by the Guideline are not occurring. The authors of the study concluded that “among PTSD patients with comorbid substance abuse, benzodiazepine treatment was not associated with adverse effects on outcome.”^{5(p1)} Those who were treated with benzodiazepines “were more likely to have been previously hospitalized, had more severe PTSD symptoms, and had more anxiety and overall psychiatric symptoms.”^{5(p4)}

Lund and colleagues also state that “[c]urrently, no data support the efficacy of benzodiazepines for the treatment of core PTSD symptoms.”^{1(p292)} They then draw the unfounded conclusion that “benzodiazepines are ineffective for core PTSD symptoms like avoidance or dissociation.”^{1(p292)} It is illogical to conclude that, since there are not enough data, the treatment is ineffective. In addition, this statement focuses on only a subset of symptoms. The article also states that “[b]ecause benzodiazepine discontinuation is often challenging, the least problematic means to curtail use is to avoid these drugs in newly treated, benzodiazepine-naive patients.”^{1(p295)} Discontinuation symptoms may occur in some cases but often are not a problem. All patients do not become tolerant, and some take benzodiazepines for years with continued therapeutic benefit and no problems. Although the authors state that “setting a target goal of zero benzodiazepine use is probably not realistic,”^{1(p295)} it is implicit in the article that zero use should be the goal. Benzodiazepines have been around for at least 50 years and prior to the *DSM* diagnosis of PTSD. Funding for the study of new indications is generally absent for these drugs since they have long had US Food and Drug Administration approval. Conclusions should not be based on a lack of evidence.

The authors claim that reducing anxiety with benzodiazepines will interfere with the psychotherapeutic treatment of PTSD. They bring to our attention that

...growing evidence from animal research has shown that benzodiazepines interfere with the extinction of conditioned fear. Since extinction of conditioned fear is a critical element of prolonged exposure therapy, there is concern that this cornerstone of PTSD treatment may be affected by benzodiazepine use. While this relationship has not been conclusively demonstrated in real-world patients, there is some clinical evidence that benzodiazepines can reduce the effectiveness of prolonged exposure therapy.^{1(p292)}

On the basis of these assumptions, it is concluded that benzodiazepines should not be used. The authors state,

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“[c]linicians and patients will attest that benzodiazepines can bring about rapid, short-term symptomatic relief.”^{1(p292)} This clinical evidence is considered a bad thing, as it may make the patient less inclined to engage in psychotherapy. This philosophy reflects one that has been espoused in years past and states that psychopharmacologic treatment only masks symptoms and suppresses an individual’s ability to make long-term gains.

Alcoholics Anonymous (AA) used to advise our patients that they shouldn’t take any medicines since taking a pill would just lead to another addiction. Alcoholic patients attending AA were forbidden to take antidepressants because they would interfere with recovery. The standard of care now is to treat the comorbid conditions medically to alleviate suffering, which does not interfere with recovery from addiction.

In addition, there have been well-known, prestigious institutions that, in the past, advocated⁶ against the use of psychotropic medicines, as they were believed to interfere with the emotional response that was necessary to fully benefit from therapy. This philosophy of providing only the preferred psychotherapy of the day to the exclusion of psychotropic medications was deployed in even the most severe cases in inpatient settings. Proponents of this philosophy believed that clinicians had to get to the core of the psychological trauma in therapy, unhampered by medications that were both unnecessary and potentially damaging to the therapeutic process. This conflict came to climax in the *Osheroff v Chestnut Lodge Hospital* (1984) lawsuit, which finally ended this practice. Most studies have supported the combined use of medicines and psychotherapy, and this approach has become the standard of practice. The view that the use of benzodiazepines, which rapidly reduce anxiety, interferes with the success of psychotherapy for PTSD harkens back to that philosophy discredited years ago. There should be convincing evidence that this is the case before making such strong recommendations, lest we end up with another landmark legal case.

A related issue, not specifically addressed by Lund and colleagues but a theme in the Guideline, is the endorsement of PTSD therapies for which there is very little evidence of their efficacy. Eye movement and desensitization reprocessing is one such therapy. Eye movement and desensitization reprocessing combines exposure therapy with eye movements. The Guideline shows that eye movement and desensitization reprocessing has approximately equivalent benefit as exposure therapy without the unnecessary theatrics of therapist-guided eye movements.^{2(p129–130)} Other attempts were made in the past to use training eye movements as a treatment for psychiatric disorders such as attention-deficit/hyperactivity disorder, but no evidence has been found to support this practice. As expected, by combining a known therapy (exposure therapy) with a benign activity (eye movements), one gets the same results as the known therapy alone. By including this in a professional publication suggests that eye movement therapy has scientific merit. This has not been shown and eye movement and desensitization reprocessing should not have been given a positive endorsement.

Another example from the Guideline is the inclusion of acupuncture for the treatment of PTSD. Once again, little evidence exists that supports its effectiveness. In fact, the American Medical Association Council of Scientific Affairs on Alternative Medicine found “no evidence exists that acupuncture affects the course of any disease.”⁷ Studies that have compared sham acupuncture to real acupuncture have shown no benefit.⁸ The Guideline supports the finding that acupuncture may be helpful for the management of PTSD despite this limited evidence.

The authors seem to hold the “medical model” to a different standard than that of “evidence-based psychotherapy” or other psychosocial treatments. This results in recommendations that psychotherapy is the treatment of choice with medication necessary only as an adjunct. Bringing a new drug to market requires rigorous testing, costing millions of dollars in order to demonstrate that it is a safe and effective treatment. In contrast, there is really no similar requirement that exists in order to bring to market a new psychosocial intervention. Furthermore, the problem with psychotherapy research is the lack of blinded, placebo-controlled conditions. In addition, there is the potential for a learned response to the rating instruments as opposed to a true treatment effect, since the rating instruments are subjective and so similar in content to the therapeutic interventions. To put it another way, are the patients just being taught how to respond to the rating instruments? This creates a disparity in the standards being used that makes a comparison of these 2 forms of treatment problematic. There has been a consensus in the field that these 2 models are not mutually exclusive but rather complementary.

In “Declining Benzodiazepine Use in Veterans With Posttraumatic Stress Disorder,”¹ Lund and colleagues present some unfounded conclusions regarding the lack of efficacy and the dangers of benzodiazepines in the treatment of PTSD. These conclusions have serious implications for psychiatrists as well as for persons suffering from PTSD. A bias exists toward the use of psychosocial treatment as opposed to psychopharmacologic treatments of PTSD. I have described a historical precedent for this dynamic, which has been a recurring theme in the mental health field over the years.

A companion article authored by the same group, “Prescribing Trends in Veterans With Posttraumatic Stress Disorder,”⁹ is a more balanced review of their analysis of prescribing trends in the VA. Yet, this begets the question, Why look at prescribing patterns? These data may have pharmacoeconomic value for the VA, but they provide little insight into our understanding of what treatments are effective. The authors’ comments, such as, “We observed clinically relevant changes in prescribing across nearly every therapeutic class,”^{9(p300)} seem to suggest they believe the data do provide some insight. How did they determine that these prescribing changes were clinically relevant? Was the clinical outcome better? Where are the data for this observation? The authors do acknowledge at the end the limitations of inferring anything from the data given our lack of information about these patients. To name a few of the confounding

variables: Did the patients actually have PTSD? Were the medicines in the record specifically prescribed *for* PTSD? Did the patients take them? What comorbid conditions did they have? and What other treatments did they receive?

The 2008 Institute of Medicine report "Treatment of PTSD: An Assessment of the Evidence"¹⁰ found that investigator independence was a problem area not only for drug studies, due to pharmaceutical company funding, but also for psychotherapy research. Psychotherapy studies were often conducted by individuals who developed the techniques being studied and thereby had a vested interest in the outcome. In addition, some studies did not include a blind or independent assessment of outcomes. The answer to this question will await an objective diagnostic test for PTSD. The Institute of Medicine found, just as they did for benzodiazepines, that the evidence is inadequate to determine efficacy of eye movement and desensitization reprocessing or any other psychotherapy except exposure therapy.

These studies tend to obscure the *real* need, which is for more research that is methodologically sound and has improved internal validity and investigator independence, as suggested in the Institute of Medicine report.¹⁰ Most of the research published to date is inadequate to make final conclusions regarding which treatments are effective for PTSD. The VA/DoD Clinical Practice Guideline for Management of Post-Traumatic Stress is a useful tool for clinicians who want to know the full range of treatments available for PTSD, but it should reflect more accurately, particularly in the way it addresses benzodiazepines, the state of our knowledge. Unfortunately, it is likely that some patients who have been successfully treated and are stable on their current medical regimen will be forced to change as a result of the very strong

language used in the Guideline and that this will result in an exacerbation of their symptoms.

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