

# Posttraumatic Stress Disorder and Benzodiazepines: A Myth Agreed Upon

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Recognizing that benzodiazepines have definite abuse and dependence potential, they possibly treat PTSD-associated anxiety and insomnia better than any other class of drugs. This author challenges the fact that they are so persistently viewed through a negative lens.

**N**apoleon Bonaparte, best known for being a warrior, was an effective propagandist. Reports from the field during his first campaign in Italy were crafted with the goal of spreading his grandeur and concealing his ruthlessness. “Even when I am gone,” he said, “I shall remain in people’s minds the star of their rights, my name will be the war cry of their efforts, the motto of their hopes.”<sup>1</sup> The French general summed it up with, “History is a myth that men have agreed upon.” This might be said of benzodiazepines as well.

Benzodiazepines are highly effective, safe, and versatile medications that are FDA approved to treat insomnia, muscle spasm, seizures, agitation, alcohol withdrawal, and in particular, anxiety. They are unrivaled in their overall effectiveness and safety for these conditions. Yet there has been an unremitting drumbeat of negativity about this class of medication that has succeeded in fostering its disapprobation or complete absence from the most highly respected clinical guidelines for posttraumatic

stress disorder (PTSD), acute stress reaction (ASR), and acute stress disorder (ASD).<sup>2-8</sup> This would seem to reflect the negative and avoidant manner in which benzodiazepines historically have been treated, and continue to be treated relative to PTSD.

It is useful to review the history of this class of medication to understand where this negativity came from, and why it has flourished. In addition to this brief review, this article compares and contrasts the clinical guidelines regarding the prescription of benzodiazepines for patients with PTSD diagnoses from 4 national and international groups and their 3 updates. The evidence on which the guidelines are based is examined, with the goal of encouraging clinicians to avoid reflexively embracing the published guidelines, and to give thoughtful consideration to this class of medication for appropriate patients with PTSD diagnoses when there is a clear indication for them.

## A BRIEF HISTORY OF BENZODIAZEPINES

The first benzodiazepine, chlordi-azepoxide, synthesized in 1955, showed strong sedative, anticonvulsant, and muscle relaxant effects, and was marketed in 1960. Diazepam was marketed in 1963.<sup>9</sup> It became

the top-selling pharmaceutical in the United States from 1969 to 1982, with peak sales in 1978 of 2.3 billion tablets.<sup>10</sup> The risk of dependence with benzodiazepines became evident in the 1980s, and the drug class was subsequently responsible for the largest-ever class-action lawsuit against drug manufacturers in the United Kingdom. The court case against the drug manufacturers never reached a verdict—but it did lead to changes in the British law, making class-action law suits more difficult to effect.

In 1983, as a resident fellow in forensic psychiatry at the Federal Correctional Institution in Butner, North Carolina, I discovered that benzodiazepines were almost entirely proscribed in penal systems nationwide. The relatively uncommon dependence and abuse issues were just beginning to come into focus at that time, and the concern was raised that we were creating a nation of addicts, rather than asking how or why the population became so anxiety-ridden. My research resulted in a publication of recommended guidelines for benzodiazepine use in correctional facilities.<sup>11</sup> Little has changed since that time, which becomes apparent when evaluating the details of the research supporting recent national and international practice guidelines.

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## THE GUIDELINES

In reviewing these guidelines and analyzing the references listed to support their recommendations, a repetition of many of the same studies cited is found. That is not necessarily a problem, but many of these papers are quite dated and many draw their conclusions from very small sample sizes. Even in studies with larger sample sizes, positive results often are overlooked, ignored, or reported in a dismissive manner.

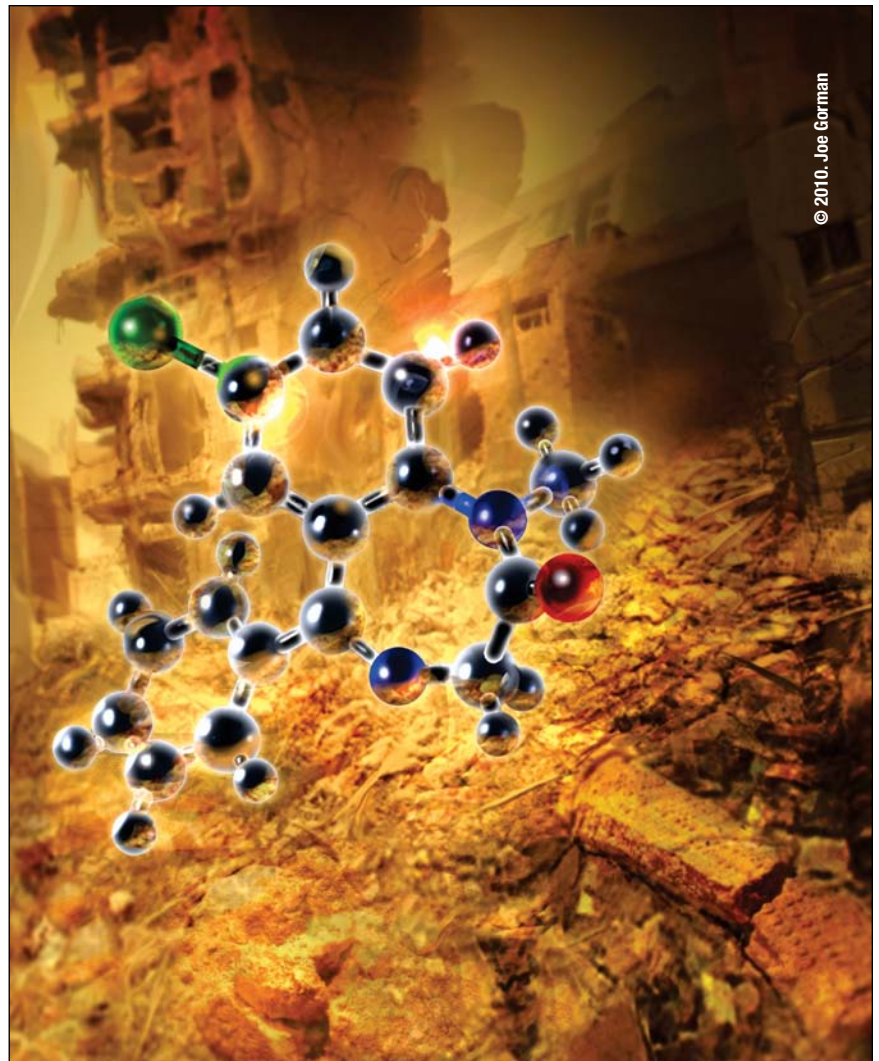
Guideline conclusions and recommendations of the following organizations or consensus groups are presented: the American Psychiatric Association (APA), the VA and DoD, the International Consensus Group on Depression and Anxiety (ICGDA), and the National Institute for Clinical Excellence (NICE). This is followed by an examination of the articles cited to support the recommendations.

### APA guidelines

The 2004 APA guidelines for PTSD and ASD have a relatively simple coding system, classifying drugs in 1 of 3 categories: recommended “with substantial clinical confidence,” “with moderate clinical confidence,” or “on the basis of individual circumstances.”<sup>2</sup> Benzodiazepines are in the third category and are described as:

...useful in reducing anxiety and improving sleep.... However, clinical observations include the possibility of dependence, increased incidence of PTSD after early treatment with these medications, or worsening of PTSD symptoms after withdrawal of these medications.<sup>2</sup>

Four references (Mellman and colleagues [2002],<sup>12</sup> Gelpin and colleagues,<sup>13</sup> Risse and colleagues,<sup>14</sup> and Kosten and colleagues<sup>15</sup>) are cited to support the above statement. In a later section, titled, “Review and Synthesis of Available Evidence,”



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the authors conclude that benzodiazepines “cannot be recommended as monotherapy for PTSD patients, despite their proven efficacy in generalized anxiety disorder,” and, “Despite widespread use in treatment of PTSD, their utility in PTSD has not been adequately evaluated.” Two additional references (Braun and colleagues<sup>16</sup> and Mellman and colleagues [1998]<sup>17</sup>) are cited.

### APA guideline watch

The March 2009 update to the APA guidelines for PTSD does not mention benzodiazepines.<sup>3</sup>

### VA/DoD guidelines

In the 175-page, jointly published VA and DoD guidelines for PTSD, a third derivative disorder is added: ASR.<sup>4</sup> The recommendations regarding benzodiazepines in this lengthy document are both copious and abstruse (Figure). The legends may serve an academic interest, but they offer little practical help to the clinician in the decision-making process. For example, for ASR, benzodiazepines are placed in the “Some benefit” category, with the recommendation “insufficient evidence to recommend for or against—the clinician will use clinical

| Quality of evidence | Net effect of the intervention |          |       |                  |
|---------------------|--------------------------------|----------|-------|------------------|
|                     | Substantial                    | Moderate | Small | Zero or negative |
| Good                | A                              | B        | C     | D                |
| Fair                | B                              | B        | C     | D                |
| Poor                | I                              | I        | I     | I                |

**Quality of evidence**  
**I** At least 1 properly done randomized controlled trial  
**II-1** Well-designed controlled trial without randomization  
**II-2** Well-designed cohort or case-control analytic study  
**II-3** Multiple time-series, dramatic results of uncontrolled experiment  
**III** Opinion of respected authorities, case reports, and expert committees

**Overall quality**  
**Good:** High grade evidence (I or II-1) directly linked to health outcome  
**Fair:** High grade evidence (I or II-1) linked to intermediate outcome or moderate grade evidence (II-2 or II-3) directly linked to health outcome  
**Poor:** Level III evidence or no linkage of evidence to health outcome

**Net effect of the intervention**  
**Substantial:** More than a small relative impact on a frequent condition with a substantial burden of suffering; or a large impact on an infrequent condition with a significant impact on the individual patient level  
**Moderate:** A small relative impact on a frequent condition with a substantial burden of suffering; or a moderate impact on an infrequent condition with a significant impact on the individual patient level  
**Small:** A negligible relative impact on a frequent condition with a substantial burden of suffering; or a small impact on an infrequent condition with a significant impact on the individual patient level  
**Zero or negative:** Negative impact on patients; or no relative impact on either a frequent condition with a substantial burden of suffering; or An infrequent condition with a significant impact on the individual patient level

**Rating scheme for the strength of the recommendations**  
**A** A strong recommendation that the intervention is always indicated and acceptable  
**B** A recommendation that the intervention may be useful/effective  
**C** A recommendation that the intervention may be considered  
**D** A recommendation that a procedure may be considered not useful/effective, or may be harmful  
**I** Insufficient evidence to recommend for or against—the clinician will use clinical judgment

Figure. Quality of evidence, overall quality, net effect of the intervention, and rating scheme for the strength of the recommendations made in the VA/DoD Clinical Practice Guidelines for the Management of Post-traumatic Stress.<sup>4</sup>

judgment.” For ASD, benzodiazepines are listed in the “unknown” benefit category. While short-term use of benzodiazepines (less than 10 days) is recommended for acute symptom management in patients with ASR and

ASD, it is discouraged for longer use in those disorders. Finally, for PTSD, the VA/DoD guidelines are unequivocal, stating not only that there is “no benefit” but also warning of potential “harm” if they are used.<sup>4</sup>

References cited to support the VA/DoD recommendations and non-recommendations are Gelpin and colleagues,<sup>13</sup> Risse and colleagues,<sup>14</sup> and Kosten and colleagues<sup>15</sup> (the same as in the APA guidelines) and

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1 additional reference (Viola and colleagues<sup>18</sup>).

### Consensus statement on PTSD from the ICGDA

Regarding benzodiazepines, this group states the following:

No studies support the efficacy of benzodiazepines in PTSD. On the contrary, some evidence suggests that the clinical condition of patients with PTSD deteriorates when they are treated with benzodiazepines, with impairment of learning in a clinical situation and disturbing withdrawal symptoms.<sup>5</sup>

There are 15 references listed at the end of this consensus statement, but none are designated in the body of the paper to support the above statement.

### Consensus statement update on PTSD from the ICGDA

In their 2004 update to their 2000 consensus statement, the ICGDA says benzodiazepines “are not effective for PTSD.”<sup>7</sup> For sleep difficulty, the group cautioned against using traditional benzodiazepines “because of associated withdrawal symptoms, lack of efficacy in the treatment of depression and PTSD, and interactions with alcohol.” No other reference is cited.

### NICE guidelines

Located in London, England, NICE also has published a set of guidelines for PTSD treatment.<sup>8</sup> Under the heading of “Pharmacological and physical interventions for PTSD,” this 176-page text does not include a section on benzodiazepines, anxiolytics, sedatives, or hypnotics. Benzodiazepines are mentioned only indirectly, as part of a study conducted by Hamner and colleagues, of combat veteran patients who had risperidone added to their previously prescribed medications, some of which were benzodiazepines.<sup>19</sup> Also, under the heading of

“Current clinical practice,” it is noted that, “Mellman et al (2003) point out that the use of [benzodiazepines] is likely not to conform to international guidelines.”<sup>8</sup>

### EXAMINATION OF REFERENCES CITED IN THE GUIDELINES

#### APA guidelines

The APA guidelines<sup>2</sup> cite 6 references<sup>12–17</sup> in support of their conclusions and recommendations. These references were published between 1990 and 2002.

In the first study referenced, Mellman and colleagues (2002) evaluated 22 participants (14 men and 8 women) reporting PTSD symptoms as a result of non-combat related accidents or assaults.<sup>12</sup> The treatment group was given temazepam for 7 days (at a 30-mg dosage for the first 5 days and at a 15-mg dosage for the last 2 days); the control group was given a placebo. There was significant improvement in sleep duration in the temazepam group during the treatment, but no difference in sleep duration 1 week after the medication was discontinued. There also was no difference in core PTSD symptoms (intrusive thoughts/re-experiencing, emotional numbing, hyperarousal, and avoidance) at the end of the 6-week study. The authors did find, however, a correlation between reduced awakenings and improvement in PTSD symptoms. Based on this finding, they suggested the “possibility of a role for other interventions for reducing sleep disruption,” dismissing further consideration of the benzodiazepine that produced the good results.

In the second study referenced, Gelpin and colleagues evaluated 162 patients who had experienced a trauma, 13 of whom reported “excessive distress” (including panic anxiety,

agitation, or persistent insomnia) 1 week after the trauma. These 13 patients were prescribed clonazepam or alprazolam.<sup>13</sup> The control, or non-treatment, group was made up of 13 other trauma survivors, matched by gender and score on the Impact of Event Scale, which measures intrusion/avoidance. Importantly, however, the control group was not matched for State-Trait Anxiety Inventory or Beck Depression Inventory scores, which were significantly (10%) higher to begin with in the benzodiazepine group. Not surprisingly, given the higher severity of symptoms in the benzodiazepine group, the control group fared better at the 6-month follow-up. The authors say the study was “obviously limited by the lack of random assignment to groups and the small sample size.” Moreover, they state:

Given the current design, one cannot rule out the possibility that benzodiazepines did have a beneficial effect on those trauma survivors who were clinically identified as highly distressed. Accordingly, these subjects could have been worse without treatment.<sup>13</sup>

The third reference was published in 1990.<sup>14</sup> In this study, Risse and colleagues state, “Worsening of symptoms with benzodiazepine discontinuation has also been reported.”<sup>14</sup> The authors analyzed data from more than 500 patients with combat-induced PTSD. Of these patients, 116 (23%) received treatment with alprazolam 2 mg/day to 9 mg/day for 1 to 5 years. Seventy-nine patients undertook a withdrawal regimen—34 of whom reported some mild clinical withdrawal symptoms and 8 of whom had severe withdrawal reactions (including anxiety, sleep disturbance, rage, hyperalertness, nightmares, or intrusive thoughts). Six of the 8 reported homicidal ide-



ation. All 8 had a history of alcohol abuse or substance abuse and several had violent histories (including having taken part in torture and killings in combat situations). Although the study authors conclude, "All eight patients demonstrated severe reactions associated with discontinuation of alprazolam after long-term use," they do say there is the possibility that "the severe discomfort caused by alprazolam withdrawal worsened a preexisting condition." They recommend considering the longer-acting benzodiazepine chlordiazepoxide as a substitute for alprazolam, noting chlordiazepoxide's less-severe withdrawal symptoms.

The fourth study cited was published in 2000,<sup>15</sup> and it is larger than any of the others cited in support of the APA guidelines' recommendations. In this study, Kosten and colleagues examined 541 veteran patients with PTSD at baseline for comorbid substance use disorder and benzodiazepine use. A total of 370 patients were available for 1-year follow-up. In half of the 370 patients, comorbid substance use disorder was diagnosed; yet the study concluded that treatment with benzodiazepines was not associated with adverse effects on outcome. This would seem to contradict not only the concern regarding addictive potential so often mentioned along with benzodiazepines but also the generally unchallenged admonition to avoid prescribing benzodiazepines to patients with comorbid substance abuse diagnoses. Specifically, the study authors conclude:

- Benzodiazepine use had no significant impact on clinical outcome in either substance abusers or non-abusers,
- Substance abusers [who were treated with benzodiazepines] had significant reductions in both alco-

hol problems and violence, and

- Violence showed no significant time interactions with benzodiazepine use.

Ultimately, in addition to bringing into sharp question the common practice of forswearing benzodiazepine use in the substance-abusing patient population, the authors conclude, "[T]he therapeutic role of chronic benzodiazepines in PTSD is not clear."

The fifth study cited<sup>16</sup> in the APA guidelines is under the "Review and Synthesis of Available Evidence" section and is distinguished as "the only pertinent randomized, controlled trial" of benzodiazepines in patients with PTSD. Similar to the study by Risse and colleagues, this double-blind crossover trial, by Braun and colleagues, was published in 1990 and the authors studied alprazolam only. Data were from 10 participants with PTSD who completed 5 weeks of alprazolam treatment and 5 weeks of placebo treatment. The authors concluded that their study was "necessarily limited by the small number of subjects and the relatively large number of dropouts," as well as by the fact that theirs was a "treatment-refractory group with a long duration of illness" previously treated unsuccessfully by a number of antidepressants. These drawbacks notwithstanding, the results showed a "significant advantage for alprazolam over placebo" to treat PTSD-related anxiety, according to the Hamilton Anxiety Rating Scale (HAM-A). In addition, 4 of the 6 patients who responded best to alprazolam showed a greater-than-20% improvement on both the HAM-A and the PTSD Scale (which measures intrusion/avoidance).

In the final study cited,<sup>17</sup> Mellman and colleagues (1998) followed a total of 4 men within 1 to 3 weeks of a traumatic experience and hy-

pothesized that "consolidating sleep would be beneficial during the acute aftermath of trauma." In fact, that is exactly what they found. Temazepam was prescribed for 1 week, and the results revealed that, for all 4 patients, "improved sleep continued 1 week after the 7-day course of temazepam had been discontinued, and PTSD symptom severity was reduced." The APA guidelines conclude, "Although [the study] suggested improvement, positive long-term outcome data have not been reported, and a controlled study did not show advantage over placebo." Given the exceedingly small size of this study (n = 4), its singular treatment (temazepam alone), and its short duration (1 to 3 weeks), it would have been reasonable to disregard it altogether, especially for the purposes of establishing guidelines of such major importance. Nevertheless, in spite of the positive results it yielded both for sleep and reduction of PTSD symptoms, it is referenced in support of eschewing the class of benzodiazepines as monotherapy for PTSD.

### VA/DoD guidelines

The VA/DoD guidelines<sup>4</sup> cite 4 of the same references as the 2004 APA guidelines (Gelpin and colleagues,<sup>13</sup> Risse and colleagues,<sup>14</sup> Kosten and colleagues,<sup>15</sup> and Mellman and colleagues [1998]<sup>17</sup>). The 1 additional reference discussed was published in 1997<sup>18</sup> and is very problematic. In this study, Viola and colleagues retrospectively analyzed data from patients treated at Tripler Army Medical Center, Honolulu, Hawaii, over a 6-year period. The abstract states:

Between 1990 and 1996, 632 patients, the vast majority of whom suffered from combat-related PTSD, were treated. Historically, many PTSD patients were treated with benzodiazepines, often in high dos-

ages. The risks attendant to benzodiazepine management of PTSD, coupled with poor clinical outcome, prompted the staff to explore treatment alternatives.<sup>18</sup>

This is the only mention of benzodiazepines in the entire article. No data, no studies, and no references are cited anywhere in the article to support the statements in the abstract. Yet this article is referenced in the VA/DoD guidelines as support for recommending against the use of benzodiazepines in patients with PTSD.

### Consensus statement on PTSD from the ICGDA

As previously mentioned, the ICGDA's consensus statement on PTSD<sup>5</sup> lists 15 references at the end of the article but none is annotated to support the negative comments regarding benzodiazepine use in the article. Interestingly, though, a textbook on guidelines for traumatic stress, published at the same time as this consensus statement and edited by one of the consensus authors,<sup>6</sup> is much more positive and even-handed in its 2 short paragraphs that mention benzodiazepines. Regarding open trials with alprazolam and clonazepam, the textbook authors state, "patients reported reduced insomnia, anxiety, and irritability, but no improvement in re-experiencing, avoidant, or numbing symptoms." The second paragraph refers to a study<sup>17</sup> that found "pharmacotherapy specifically targeting disrupted sleep was associated with marked reduction in PTSD symptoms." A coeditor of the textbook, from the National Center for PTSD in White River Junction, Vermont, suggested in his own paper<sup>20</sup> 3 possible clinical indications for clonazepam: (1) in patients with ASRs; (2) episodically in chronic PTSD when extreme anxiety interferes with the patient's

participation in treatment; and (3) in carefully selected patients with comorbid alcohol or substance abuse.

### Consensus statement update on PTSD from the ICGDA

The ICGDA's consensus statement update on PTSD<sup>7</sup> cites a single reference (Braun and colleagues<sup>16</sup>) in support of their rejection of benzodiazepines, the same one cited in other guidelines. As previously discussed, the reference is limited in both size (n = 10) and scope (the authors studied only alprazolam), is 2 decades old, and actually showed positive results for PTSD-related anxiety and intrusion/avoidance.

### NICE guidelines

Although the NICE guidelines<sup>8</sup> mention that the clinical practice of prescribing benzodiazepines does not conform to international guidelines, the results of the prescribing patterns study they reference<sup>21</sup> can be interpreted to suggest that clinicians either are not reading or are dismissing the guidelines that go against the grain of their experience and observations. In the prescribing patterns study, the authors analyzed the number of prescription claims Medicaid paid for PTSD during 1 month in the state of New Hampshire. In this community-based nonveteran sample, made up of mostly (88%) women, 41% of 165 patients with PTSD (without comorbid depression) were prescribed benzodiazepines. Perhaps this high percentage of benzodiazepine prescriptions suggests that clinicians are following their own experience and choosing not to withhold a generally very beneficial and helpful medication for their patients.

### RECENT LITERATURE

Recent medical literature carries on the historical tendency to eschew

benzodiazepine use in general and for PTSD treatment in particular.

In a 2009 comprehensive review of meta-analyses and treatment guidelines relative to benzodiazepines for PTSD, Stein and colleagues state, "[D]ifferent from data emerging from the treatment of a range of other anxiety disorders, data from trials of benzodiazepines in PTSD were not persuasive."<sup>22</sup> Again, we find only 1 reference for the statement—the same 1990 randomized controlled trial by Braun and colleagues<sup>16</sup> cited in several of the guidelines that actually showed positive results for anxiety symptoms and intrusion/avoidance.

The most recent article found at the time of this writing is an expert review of the pharmacotherapy for PTSD.<sup>23</sup> In this review, Alderman and colleagues state, "[T]he use of these agents for the management of PTSD symptoms remains controversial." To support their statement, the authors cite the same articles cited previously in the medical literature (the APA guidelines,<sup>2</sup> the ICGDA consensus statement update,<sup>7</sup> the NICE guidelines,<sup>8</sup> Gelpin and colleagues,<sup>13</sup> Risse and colleagues,<sup>14</sup> and Braun and colleagues<sup>16</sup>).

They do cite a study not previously discussed.<sup>24</sup> In this article, Cates and colleagues analyzed data from 6 patients, aged 31 to 74 years, in whom "Clonazepam therapy resulted in improvements in the frequency of both sleep-onset problems and early-morning awakenings," compared with placebo. Yet the authors conclude that clonazepam's effects "upon sleep-related PTSD symptoms were unimpressive." Although the improvements Cates and colleagues found in difficulty falling and staying asleep were not significant, any positive trend noted is more important because of the fact that there were only 6 study participants.

Alderman and colleagues go on to cite a review by Jacobsen and colleagues<sup>25</sup> regarding prescribing benzodiazepines to patients with substance use disorders: “Patients report that [central nervous system] depressants, such as alcohol, cannabis, opioids, and benzodiazepines acutely improve PTSD symptoms.” The statement is actually based on findings from a longitudinal study, conducted by Bremner and colleagues and published in 1996, in which 61 Vietnam combat veterans with PTSD were interviewed to assess for PTSD symptoms, alcohol abuse, life stressors, and treatment.<sup>26</sup> Benzodiazepines are not given credit by Alderman and colleagues for being not only the safest but also the only legitimate anti-anxiety medication mentioned among that group of substances.

The last reference cited in the review is from a 2003 pharmacologic review of PTSD treatment.<sup>27</sup> In this article, Ahearn and colleagues state, “Despite the frequent use of benzodiazepines in PTSD, randomized placebo-controlled trials do not suggest a role for these medications,” and they cite the same studies discussed earlier in this paper (Gelpin and colleagues,<sup>13</sup> Risse and colleagues,<sup>14</sup> and Braun and colleagues<sup>16</sup>). As mentioned earlier, however, the results of Braun and colleagues support a significant and beneficial role for benzodiazepines to treat intrusion/avoidance and anxiety in PTSD and Gelpin and colleagues surmised a potential beneficial effect of benzodiazepines in “highly distressed” patients with PTSD.

## DISCUSSION

Significant in all of the PTSD guideline documents is their provision of repeated references (or no references at all) to the same studies of benzodiazepines and PTSD. From their cited

references, the 2004 APA guidelines<sup>2</sup> reasonably conclude that benzodiazepines, “May be recommended on the basis of individual circumstances.” Their March 2009 guideline watch<sup>3</sup> makes no mention of benzodiazepines, hypnotics, or sedatives, letting the open-ended recommendation of 2004 stand. The VA/DoD guidelines<sup>4</sup> cite similar references and supply the most copious and confusing recommendations. Piling Pelion onto Ossa, the VA/DoD guidelines add a third disorder, ASR, and then give different recommendations for benzodiazepine use in each of the 3 disorders. The 2000 ICGDA statement<sup>5</sup> cites no references for the consensus group’s comments regarding benzodiazepines, and their 2004 update<sup>7</sup> cites a well-worn reference (Braun and colleagues<sup>16</sup>). The NICE guidelines<sup>8</sup> do not mention benzodiazepines as a potentially therapeutic medication or adjunct; but this is the only set of guidelines that points out the fact that benzodiazepines are prescribed to a sizeable minority of PTSD patients. More recently, 2009 comprehensive reviews<sup>22,23</sup> again reach back to Braun and colleagues.<sup>16</sup>

The 2 most egregious distortions occur in citing Risse and colleagues<sup>14</sup> and Viola and colleagues.<sup>18</sup> The former is repeatedly cited as support for the “worsening symptoms following benzodiazepine discontinuation,” yet the study addresses only alprazolam in only 8 combat veteran patients (out of 116 who took alprazolam) who had histories of violence and substance abuse. Moreover, the fact that the authors recommended considering chlorthalidone as a substitute benzodiazepine was disregarded. The reference to Viola and colleagues cites the negative statements regarding benzodiazepines in the abstract, without noting that there is not a single word or item of data describing

any study in the body of the paper.

There is a clear and present concern regarding benzodiazepines’ potential to cause dependence and addiction. A comprehensive review of benzodiazepines by Longo and colleagues, published in 2000, offered the following: “[Benzodiazepines]... can be addicting. These agents are often taken in combination with other drugs of abuse by patients with addiction disorders.”<sup>28</sup> The authors recommend “caution...when prescribing benzodiazepines to patients with a current or remote history of substance abuse.” They refer to a 1990 report by the APA<sup>29</sup> on benzodiazepine dependence, toxicity, and abuse that indicated:

...11 to 15 percent of the adult population had taken a benzodiazepine one or more times during the preceding year, but only 1 to 2 percent have taken benzodiazepines daily for 12 months or longer.<sup>27</sup>

Although more comprehensive and recent than many of the references cited in the guidelines, Longo and colleagues’ review was not referred to by any of the agencies.

## WHERE DO WE GO FROM HERE?

In the APA guidelines,<sup>2</sup> provider experience, preference in treatment, and clinical judgment prevail. The gingerly manner in which benzodiazepines are recommended in other guidelines tends to disregard the substantial clinical experience that practicing psychiatrists and other clinicians have had for many decades with these medications. Benzodiazepines do not provide a remedy for the core symptoms of PTSD (including nightmares, intrusive thoughts, flashbacks, and avoidance) and these medications should not be considered as a first-line treatment. They rarely turn out to be the most effective monotherapy for patients with

PTSD. In some cases, however, by alleviating the sleep disturbances and anxiety that accompany PTSD, benzodiazepines can facilitate a mitigation of the core symptoms, which may obviate the need for patients to turn to alcohol or illegal substances. In that respect, benzodiazepines can be therapeutic for appropriately identified patients with PTSD.

A negatively-biased framework can deter clinicians from using benzodiazepines altogether for patients who are emotionally traumatized, as they may fear a lack of defense in the event of a lawsuit over an untoward outcome after prescribing or renewing benzodiazepines. Even more problematic, this negativity fosters a tendency to withdraw benzodiazepines for any patient who has a diagnosis of PTSD, no matter how long or how well-stabilized they have been while taking the medication. As noted by Risse and colleagues,<sup>14</sup> withdrawing a benzodiazepine, even on an appropriately cautious schedule, can initiate (or cause a relapse of) severe emotional problems. Several of the available guidelines regarding the use of benzodiazepines actually open clinicians up to increased chances of lawsuits which—whether perceived or verifiable—may cause clinicians to withhold valuable treatment. As a result, an opportunity for a potentially valuable pharmacologic intervention would be missed. All of the PTSD guidelines, with the exception of the APA guidelines, provide little in the way of support. When there is a healthy minority of clinicians who practice differently than the recommendations suggest, it may be reasonable to give more recognition to those standards of practice.

Future studies should move in 2 directions. First, research needs to be more specific in categorizing the diversity of the type of trauma. Com-

bat trauma vs motor vehicle accident trauma vs sexual assault trauma vs natural disaster trauma, even flood disaster trauma vs fire trauma, should be identified and perhaps tested separately. Perhaps age and gender differences also should be tested separately. Second, much larger populations of trauma victims need to be accessed. There are tens of thousands of such victims in all of the above categories across the country, and it would seem feasible to access larger participant groups in order to establish more specific guidelines.

### IN CONCLUSION

Benzodiazepines are among the most widely prescribed medications.<sup>30</sup> For that reason, it behooves the committees responsible for writing guidelines not only to widen the research base on which their recommendations stand, but also to give more weight to the experience of the significant minority of clinicians who continue to prescribe this medication. It is important to recognize benzodiazepines' place in treating—not the diagnosis of PTSD alone, as it is fairly clear that they do not prevent the onset or continuation of the core symptoms—but the anxiety and insomnia that so commonly accompany PTSD. ●

### Author disclosures

*The author reports no actual or potential conflicts of interest with regard to this article.*

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