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SLEEP DISORDERS (P GEHRMAN, SECTION EDITOR)

Management of Post-Traumatic Nightmares: a Review of Pharmacologic and Nonpharmacologic Treatments Since 2013

Scott H. Waltman[1] · David Shearer[2] · Bret A. Moore[1]

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Abstract

Purpose of Review Post-traumatic nightmares (PTN) are a common and enduring problem for individuals with post-traumatic stress disorder (PTSD) and other clinical presentations. PTN cause significant distress, are associated with large costs, and are an independent risk factor for suicide. Pharmacological and non-pharmacological treatment options for PTN exist. A previous review in this journal demonstrated that Prazosin, an alpha blocker, was a preferred pharmacological treatment for PTN and imagery rescripting therapy (IRT) was a preferred non-pharmacological treatment. Since that time, new and important research findings create the need for an updated review.

Recent Findings Based on the results of a recent study in the New England Journal of Medicine, Prazosin has been downgraded by both the American Academy of Sleep Medicine (AASM) and the Veterans Health Administration/Department of Defense (VA/DoD) for PTN. In Canada, Nabilone, a synthetic cannabinoid, appears to be promising. Few recent studies have been published on non-pharmacological interventions for PTN; however, recent data is available with regard to using IRT on an inpatient setting, with German combat veterans, and through the use of virtual technology. Recent evidence supports the use of exposure, relaxation, and rescripting therapy (ERRT) with children and individuals with comorbid bipolar disorder and PTN.

Summary Prazosin is no longer considered a first-line pharmacological intervention for PTN by AASM and VA/DoD. However, in the absence of a suitable alternative, it will likely remain the preferred option of prescribers. IRT and ERRT remain preferred non-pharmacological treatments of PTN. Combining cognitive behavior therapy for insomnia (CBT-I) with IRT or ERRT may lead to improved outcomes.

Keywords Nightmares · Trauma · Traumatic · PTSD · Trauma nightmare · Prazosin · Imagery rehearsal therapy

Introduction

Efforts to treat and understand distressing and peculiar dreams are as old as psychiatry itself [1–2]. Freud's seminal text that coined the term "psychoanalysis" was on the interpretation of dreams [2]. According to Freud, dreams were a path to accessing the unconscious mind, and content that was judged by the mind as being unacceptable might later emerge in the dream state [1, 2]. Nightmares are different from bad dreams. Nightmares are dreams that induce fear and typically awake the dreamer from rapid-eye movement (REM) sleep [3]. The treatment of nightmares has advanced since the days of Freud [1]. Post-traumatic nightmares (PTN), also called trauma-related nightmares, are recognized as being a distinct phenomenon from non-trauma-based nightmares; PTN nightmares are a re-experiencing of previous traumas that happened in real life [1, 4, 5]. PTN are typically diagnosed as being part of the reliving/intrusive symptoms of post-traumatic stress disorder

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✉ Scott H. Waltman
scott.h.waltman.civ@mail.mil

[1] Warrior Resiliency Program, Regional Health Command–Central, 7800 IH-10 West, Suite 300, San Antonio, TX 78230, USA

[2] Department of Family Medicine, Madigan Army Medical Center, Tacoma, WA 98431, USA

(PTSD; APA, 2013) or as nightmare disorder [6]—though PTN can occur in the absence of these diagnoses [7, 8]. PTN can also persist in individuals who have already undergone evidence-based treatment for PTSD [9]. In fact, PTN occur in 70–90% of individuals who have PTSD [7, 10, 11••], and one study found that 15–35% of individuals with PTSD who responded to evidence-based psychotherapies for PTSD had residual nightmares [12]. The exact prevalence of PTN is unclear, as research shows it is often under-reported by patients and perhaps under-recognized by clinicians [7, 13].

Trauma-related sleep disorders can be comorbid, and PTN can worsen other sleep problems [7]—possibly because individuals with PTN may avoid sleep to avoid nightmares [13, 14]. An abundance of costs and problems are associated with PTN including: significant distress, functional impairment, decreased productivity, worsened work quality, accidents, litigation, and death—with estimated costs of sleep disturbances being tens of billions of US Dollars [see 15•]. A chief concern is the relation between PTN and risk for suicide [7, 16]. It was previously thought that perhaps the association between PTN and suicide was actually a proxy for the relation between trauma and suicide [16]; recent findings have shown that nightmares are an independent risk factor for suicide [16, 17]. With the rising suicide rate in the USA, addressing risk factors such as nightmares is increasingly urgent [17]. The persistence of chronic nightmares increases risk for suicide [17], and there are some early indications from a case series that treating nightmares may decrease the risk for suicide [18•].

While nightmares are typically considered to only occur in REM sleep [1], studies of military populations with PTN demonstrate that service members will report experiencing PTN during periods of time that polysomnography would indicate as being non-REM sleep [19]. As PTN appear to have some variation from non-trauma-based nightmares, clinical distinctions are warranted. Recently, a new diagnosis of trauma-associated sleep disorder (TSD) has been suggested [20]; this diagnosis is based on the findings that trauma survivors often have disruptive nocturnal behaviors and different sleep disorder symptoms than people who have not experienced major trauma [21]. This may be especially pronounced among military veterans [21]. TSD is theorized to result in decreased inhibition of the amygdala resulting in increased sleep deprivation, perhaps exacerbating other problems like insomnia and obstructive sleep apnea [21]. Symptoms include altered dream content, abnormal vocalizations or motor movements in sleep, autonomic hyperarousal, and REM sleep without atonia present. Some theorists suggest that these sleep disturbances are better understood to be similar to night terrors, or sleep terrors [1], while others suggest that perhaps, "Traumatic nightmares can occur in stages of sleep in which people do not ordinarily dream [4] (p. 39)." Less is known about how to best treat night terrors in adults [22], and they are typically thought to resolve on their own [23]. Post-traumatic night terrors have historically been treated with imipramine [24]; though, there is a dearth of recent literature on the topic.

In her seminal text on trauma and recovery, Herman [4] explained, "Just as traumatic memories are unlike ordinary memories, traumatic dreams are unlike ordinary dreams. In form, these dreams share many of the unusual features of the traumatic memories that occur in waking states. They often include fragments of the traumatic event in extract form, with little or no imaginative elaboration. Identical dreams often occur repeatedly. They are often experienced with terrifying immediacy, as if occurring in the present (p. 39)." As PTN are considered to be a distinct phenomenon, it has been suggested that PTN might need to be treated with methods that differ from those used to treat idiographic nightmares [see 5] that are not trauma-based [1]. Studies comparing treatment outcomes with different types of nightmares are rare; one such study found that patients with nightmare disorder fared better than patients with PTSD and PTN when receiving a frontline psychotherapy for nightmares [25]. Information about the prevalence of PTN in the nightmare disorder group was unavailable; however, presumably, the PTSD group had a higher rate of PTN and perhaps this is indicative of differential treatment outcomes in the treatment of PTN and nightmares that are not trauma-based [see 25].

A few years ago, a review article was published in this journal which detailed relatively recent advances in the treatment of PTN like the use of Prazosin, an alpha-blocker, and imagery rehearsal therapy (IRT), a cognitive-behavioral intervention [15•]. Recent theoretical advances and research findings clarify and extend previous findings such that an updated review is warranted.

A meta-analysis on IRT and Prazosin for the treatment of PTN found that prazosin and IRT had similar outcomes [8]. Further, there were some early indications that IRT outcomes can be enhanced by the addition of cognitive behavior therapy for insomnia (CBT-I) [8]; however, this finding was based on only a handful of studies and the researchers urged caution in interpreting their findings. The benefits of combining CBT-I with cognitive behavioral treatments for PTN (e.g., IRT) have been emphasized by other review articles [see 14, 26].

Pharmacological Treatment Interventions

As PTN have been thought to be a problem of over-activation of central nervous system adrenergic activity during sleep [1, 4], an alpha-blocker like Prazosin (an α1-adrenoreceptor antagonist) has in recent history been an ideal treatment for PTN [9]. The supremacy of Prazosin has been called into question following a recent publication in the New England Journal of Medicine [27••]. This particular study will be discussed in detail below. The findings of that study led to Prazosin for PTN being downgraded to neither recommend for nor recommend against

in the revised Clinical Practice Guidelines for the Management Posttraumatic Stress Disorder from the Department of Veterans Affairs and the Department of Defense [26]. The American Academy of Sleep Medicine (AASM) also recently downgraded recommendations regarding using Prazosin to treat PTN [28]. Their task force noted that many patients do respond well to Prazosin and that despite the downgrade, it remains the first choice for pharmacotherapy of PTN [28].

Prazosin

The treatment of nightmares in PTSD was a more difficult prospect for prescribers before the ascension of prazosin as the treatment of choice. Evidence for the use of prazosin for PTN has accumulated and it has become the go-to treatment for nightmares [e.g., 29–30]. In addition to the moderately-sized RCTs conducted by Raskind et al. and others [31–35], multiple case studies provided additional anecdotal support for prazosin's efficacy in the treatment of PTN [e.g., 36–40].

The absence of a significant difference between prazosin and placebo for PTN in the most recent RCT was all the more surprising given this history [27••]. The multi-site RCT compared prazosin to placebo in 304 military veterans randomly assigned to either placebo or active treatment. At the end of a 10-week trial, there was no significant difference between the placebo and prazosin groups; neither sleep quality nor distressing dreams were improved with prazosin.

Raskind et al. [27••] provided possible explanations for the lack of efficacy of prazosin in this study. The authors posit that a potential reason for the absence of a significant treatment effect might stem from the selection process used to include and exclude participants. Psychosocial instability was an exclusion criteria for participation as was the continued use of trazodone, an α1-adrenoreceptor antagonist. Conceivably, permitting more instability might have introduced greater variance and more opportunity to identify differences between groups. Those excluded from the study due to the ongoing use of trazodone may have removed the very patients most likely to show an effect with an α1-adrenergic blocker. The variability in participants was further reduced by requiring a relatively high frequency and intensity of nightmares for study participation. Alternatively, Ressler [41] considers that the failure of the Raskind et al. [27••] study could indicate that prazosin may only be effective in treating some subtypes of PTN. He goes on to theorize that a more successful utilization of prazosin for PTN may have to await an ability to use biomarkers to target patients with specific adrenergic dysregulation.

Despite this disappointing and unexpected negative finding for prazosin [27••], and the downgraded recommendations by both the AASM [28] and the Department of Veterans Affairs and the Department of Defense [26], prazosin is likely to remain a staple of PTN treatment for the time being. The clinical experience of many prescribers, past evidence in favor of the use of prazosin for PTN, and supporting case studies make its continued use probable in the absence of a better alternative.

Other pharmacologic agents have been investigated in the treatment of PTN for patients with PTSD. Much of this data is composed of case series, chart reviews, cohort studies, and case control studies. In a few cases, more rigorous studies were conducted, but these are few in number. There are several promising agents, but more research is needed. Although much of the research is dated, we review some of the available evidence for these medications below as there are relatively few medications available for mitigating PTN.

Adrenergic Agents

Prazosin is an alpha 1 adrenergic receptor antagonist. Rationally, it makes sense that investigators would consider evaluating the use of other adrenergic agents in the treatment of nightmares, and indeed, several researchers have looked into these medications.

Terazosin, also an alpha 1 adrenergic receptor antagonist, has support from at least two case studies [42, 43]. Another alpha 1 adrenergic receptor antagonist, doxazosin, has limited support in case studies and has received attention as possible alternative to prazosin due to a longer half-life requiring less frequent dosing and relative safety in normotensive populations [44, 45]. Neither terazosin nor doxazosin are considered for use in PTN by AASM [28], but are intriguing targets for further study. Clonidine, an alpha 2 adrenergic agonist, has limited evidence in case studies showing efficacy for nightmares in PTSD [46–48].

Atypical Antipsychotics

There is some compelling, but limited support for the use of atypical antipsychotics to treat nightmares in patients with PTSD. Aripiprazole, risperidone, and olanzapine have been investigated. Aripiprazole is a dopamine partial agonist (DPA) while risperidone and olanzapine are serotonin-dopamine antagonists (SDAs). Case series for olanzapine [49], open label and retrospective chart reviews for risperidone [50–52], and case series for aripiprazole [53] all show some promising utility in PTN. Aripiprazole may be better tolerated than either olanzapine or risperidone which may make it a good candidate for further study.

Cyproheptadine

Cyproheptadine is an antihistamine and antiserotonergic medication, sometimes used in cases of serotonin overdose. We are not aware of any recent studies on cyproheptadine for

PTN, but older case series and a retrospective chart review show some possible utility [54–56].

Fluvoxamine

Two small studies show some efficacy for the treatment of PTN with the SSRI fluvoxamine in PTSD, but the data is limited and dated [57, 58].

Gabapentin

Gabapentin, a calcium channel blocker, is FDA approved for seizures, postherpetic neuralgia, and restless leg syndrome. It is often used off label for neuropathic and chronic pain. An intriguing retrospective case series using gabapentin to treat PTN in veteran PTSD patients showed notable improvement for both insomnia and nightmares [59].

Nabilone

Nabilone, a synthetic cannabinoid, was used as an adjunct medication in treatment-resistant nightmares for patients with PTSD in Canada [60]. Almost three quarters of patients in this trial (72%) reported no nightmares or significant reduction in nightmare intensity. A very small RCT investigating the use of nabilone in treating Canadian military personnel with PTSD showed a significant improvement in nightmares for the treatment group vs placebo [61]. Nabilone is not available for prescription in the USA, but this research suggests that cannabinoids may have a roll in the treatment of nightmares.

Topiramate

Topiramate, a sodium channel blocker, has been used for a wide variety of purposes including seizures, migraine prophylaxis, weight management, and others. Some case studies have demonstrated some efficacy for topiramate in treating nightmares in PTSD [62–64]. Two small RCTs showed a nonsignificant, but positive trend, in reducing PTNs using topiramate in civilians with PTSD [65, 66].

Phenelzine

Phenelzine, a monoamine oxidase inhibitor, was examined in a case series of veterans with PTSD that resulted in a significant reduction or cessation of nightmares, and 60% of patients remained fee of nightmares after discontinuing the medication [67]. However, an open-label prospective study of phenelzine in veterans with PTSD did not reach significance in reduction of nightmare severity [68]. Further, in this later study, poor efficacy and notable side effects resulted in a high drop-out rate. Restrictions on diet and risk of drug-drug interactions make phenelzine a less appealing choice in the treatment of PTNs.

Trazodone and Nefazodone

Trazodone, a serotonin 2 antagonist/reuptake inhibitor, is an antidepressant frequently used off label for insomnia. A retrospective cohort study showed some support for trazodone in the treatment of PTN, but side effects were notable [69]. Trazodone's common use as a sleep agent makes it an interesting option for patients with PTSD who often have insomnia as well as nightmares. Nefazodone is a serotonin 2 antagonist/reuptake inhibitor like trazodone. Open label and uncontrolled studies of nefazodone show some efficacy, but due to a documented risk of hepatic failure, it may not be a favored option [70–72].

Tricyclic Antidepressants

A small case series of concentration camp survivors on variable combinations of the tricyclic antidepressants imipramine, doxepin, and amitriptyline showed cessation or improvement in PTN in 80% of the 10 cases reviewed [73]. Some of the patients were also prescribed phenelzine (reviewed above).

Clonazepam, Venlafaxine, Triazolam, and Nitrazepam

Two studies of clonazepam, a benzodiazepine, and venlafaxine, a dual serotonin and norepinephrine reuptake inhibitor have shown no significant differences between treatment and placebo groups [74, 75]. Currently, we believe that there is inadequate information to consider triazolam, nitrazepam, or cortisol as treatment options for PTN in PTSD.

Summary of Pharmacologic Treatment Interventions

As of the writing of this article, there are no recommended first-line pharmacologic interventions for PTN. However, despite the recent negative findings [27••], prazosin is likely to continue to be a first choice for the treatment of nightmares in PTSD given prior research, case evidence, and anecdotal success. For the cases in which an adequate trial of prazosin fails to treat PTN, or is poorly tolerated, providers will have to

consider other less well-studied agents. For conceptual and practical reasons, the present authors are hopeful regarding future research into drugs that moderate activity at adrenergic receptors. While sparse, the research on nabilone, a synthetic cannabinoid, is an intriguing option. However, lack of FDA approval will make this a non-starter in the USA. For providers who need to look beyond prazosin for treatment alternatives, the guidance is not robust [e.g., 28]. When making pharmacologic treatment choices for PTN, providers are encouraged to consider agents that (1) have some level of support for use in PTN, (2) minimize the risk of drug-drug interactions, (3) have fewer risks associated with use (.e.g., consider the risk of liver failure with nefazodone), and (4) may treat multiple symptoms (e.g., trazodone could theoretically treat both insomnia and PTN).

Non-pharmacological Treatment Interventions for PTN

Preferred nonpharmacological treatments for trauma-related sleep disturbances are typically cognitive and behavioral [11••]. Regarding PTN, IRT has been the most prolifically studied and disseminated treatment [1, 15•]. Similar treatments like exposure, relaxation, and rescripting therapy (ERRT) have also been found to be effective [15•]. A lingering question in the literature has been raised regarding how nonpharmacological treatments for nightmares work [15•, 76]. A recent systemic review applied the qualitative method of thematic analysis of the extant literature to clarify potential mechanisms of actions [77]. Notably, this investigation did not gather new data or have a methodology that allowed for conclusions about causality or mechanisms of action—rather it is a synthesis of the extant thinking about how nonpharmacological treatment for nightmares might work. It was observed that the various research-supported protocols for treatment nightmares contained similar elements. Six potential mechanisms of action were identified: increased sense of mastery over the nightmares, emotional processing, modification of nightmare-related beliefs, restoration of sleep functions, decreased arousal, and prevention of avoidance. The theorists posited that emotional processing was the main mechanism by which psychotherapy for nightmares worked. Their model is pending empirical validation.

Imagery Rehearsal Therapy

Imagery rehearsal therapy (IRT) is a time-limited, cognitive-behavioral intervention that has shown to be effective for PTN in a number of randomized clinical trials, open-label trials, and case studies [15•]. Although the focus on specific interventional aspects of IRT differs between clinicians and researchers, the earliest and most studied version of IRT is one that minimizes exposure to the traumatic content associated with the nightmare(s) addressed in treatment. Traditional versions of IRT consist of several main components. First, the patient is educated about sleep, nightmares, and sound sleep practices that promote efficient and restorative sleep. Second, the patient is asked to choose a nightmare that he or she would like to eradicate. Third, the patient changes the nightmare narrative in a way that is no longer distressing. And finally, the patient rehearses the new dream narrative during wakefulness [76, 78]. However, as noted above, there are multiple variations on the intervention as a standard manualized protocol has not been widely accepted. Therefore, it is difficult to truly discern the active components of IRT.

One of the most recent studies of IRT involved adult psychiatric patients on an inpatient ward. Controlling for cognitive impairment and psychosis, 20 patients with a variety of chronic and treatment-resistant psychiatric conditions were treated with IRT in a group format over a period of 3 weeks. Although the nightmares in this study were associated with diverse psychopathology and not necessarily trauma-related, results revealed significant reduction in the number of nightmares experienced as well as reduction in the intensity of residual nightmares. Interestingly, patients showed reductions in symptomology in a variety of clinical areas to include suicidal ideation. This supports the notion that there is indeed a connection between nightmares and suicide [18•].

A similar inpatient study was conducted in which ten sessions of IRT were provided to 14 German soldiers suffering from combat-related nightmares and PTSD. The soldiers were assessed prior to the intervention and 2 weeks and 3 months post-intervention on indices of sleep quality, nightmares, depression, and other trauma symptoms. The frequency of nightmares was reduced 2 weeks following treatment and maintained for the full 3 months. Reductions in general sleep disturbances, depression, and trauma were also noted [79].

Researchers from the United Kingdom reported on a case series of six patients with psychosis and comorbid nightmares, although not necessarily trauma-related. Five of the six patients completed a minimum of four sessions of IRT. Nightmare, sleep quality, psychotic, and mood-related measures were completed prior to treatment and immediately afterwards. Although nightmare frequency was unchanged, participants reported reductions in nightmare vividness and intensity. Although this is a small case series, this study indicates that IRT may be well-tolerated and suited for patients suffering from psychosis [80].

Capitalizing on the expansion of technology in the remediation of psychiatric disorders, researchers from Germany studied the delivery of IRT virtually. A total of 127 patients reporting trauma and non-trauma-related nightmares were randomly assigned to 1 of 2 IRT Internet-based groups (guided IRT; unguided IRT) or to 1 of 2 active control groups

(frequency control group; narrative control group). Results revealed that IRT produced greater reductions in nightmare frequency and distress as compared to the frequency control condition. Although no change in nightmare frequency was noted when compared to the narrative control group, nightmare distress was reduced [81].

IRT has also shown promise as an adjunctive treatment with evidence-based interventions for insomnia. A 2013 study revealed that American combat veterans who served in Iraq and/or Afghanistan showed significant improvement in insomnia, nightmares, and other PTSD symptoms when IRT was utilized along with cognitive behavioral treatment for insomnia (CBT-I) [82].

Exposure, Relaxation, and Rescripting Therapy

Exposure, relaxation, and rescripting therapy (ERRT) is a short-term cognitive-behavioral intervention, which unlike IRT, includes intentional exposure to the content of the nightmare. ERRT involves several components to include psychoeducation about sleep, nightmares, and trauma, interventions focused on improving sleep practices, exposure, and nightmare rescripting. As noted in the predecessor of this article, there is scientific support for the use of ERRT [15•]. However, little has been published since the original article.

In a recent study with military veterans, an adapted form for ERRT was used with 19 veterans with previous trauma exposure. Significant improvements were noted in sleep quality, nightmare frequency and severity, depression, and insomnia. Gains were maintained at 2 months [83].

In a case series of seven individuals with comorbid bipolar disorder and PTN, a modified form of ERRT was tested for acceptability and efficacy. Participants attended 5 weeks of nightmare treatment and were assessed prior to the intervention and directly after treatment with a 3-month follow-up assessment. Variables assessed included nightmare frequency, severity, and related symptoms. Significant gains were noted in all areas. In fact, six of the seven participants reported an absence of nightmares at the 3-month follow-up period [84].

A 2013 case series of two children with trauma-related nightmares revealed that after ERRT was used, the children showed reductions in nightmare frequency and improved sleep. Reports from the children's parents also revealed less behavioral problems following treatment. This was the first study to look at ERRT with children [85].

The most notable study in recent years on ERRT is one in which researchers used a dismantling protocol that assessed the intervention by creating two conditions: ERRT with exposure and rescripting and ERRT without exposure and rescripting. Over 6 months with 70 participants, results indicated that both groups offered significant relief from nightmares. Interestingly, exposure and rescripting did not appear to add any additional benefit over psychoeducation, relaxation training, and the promotion of good sleep practices [86].

Combined Treatment

No trials or combined studies of pharmacological and nonpharmacological treatments for PTN were identified for inclusion in this review. See previous review article for a summary of the evidence base for combined treatment of PTN [15•].

Conclusion and Future Directions

A key conclusion is to emphasize the recommendations from the AASM; currently, evidence on what works for treating PTN would suggest that nonpharmacological therapies (e.g., IRT and ERRT) are the preferred treatment for PTN [28], and there is some evidence that combining CBT-I with these treatments may enhance outcomes [8]. Pharmacological treatments are often more readily available or may be the patients' preference. While prazosin may be the first choice among prescribers for the treatment of PTN [28], recommendations regarding the use of prazosin were downgraded by both the VA/DOD [26] and the AASM [28]. In the absence of a good alternative, this will probably remain the preferred option for prescribers. It has been suggested that one future line of research is to seek to identify the types of patients who will respond well to prazosin [28, 41].

Another question that needs to be addressed in the literature is whether there is a meaningful difference between nontraumatic nightmares and PTN. If so, should this be reflected in the diagnostic manual? When diagnosing nightmare disorder, should there be a trauma-specific specifier? Mysliwiec et al. [20] and Rachakonda et al. [21] called for a distinct diagnosis of TSD; however, the evidence to support that exact diagnosis is still lacking. Findings from studies that suggest differences in treatment outcome from PTN and idiographic nightmares would support the assertion that PTN nightmares are a different phenomenon, which is potentially more difficult to treat [25]. Future research should seek to clarify whether the type of nightmare acts as a mediating or moderating variable for treatment outcomes, to help clarify the issue.

The potential benefits of combining nonpharmacological treatments for insomnia and PTN have been highlighted by several reviews [10, 14, 26]. What is unclear is the optimal ordering for combined treatments [10]. One systematic review noted that psychotherapies for PTSD often improve nightmares but not insomnia and therefore suggested that a preferred ordering of treatment for PTN in populations who also have PTSD might be to first deliver CBT-I to reduce insomnia,

then to provide an evidence-based psychotherapy for PTSD (e.g., cognitive processing therapy). Subsequently, lingering symptoms of PTN could be treated with IRT or ERRT if needed [10]. Theoretically, this is a sound course of action; certainly, future research studies are needed to validate this treatment model. Following a study on the lingering symptoms of PTSD following receipt of empirically supported treatment, Larsen and colleagues suggested that treatments like CBT-I and IRT may be used to address lingering sleep disturbances. Colvonen et al. [10] cited an under-review article of a pilot study by their first author that examined the effects of CBT-I prior to prolonged exposure for PTSD [87]. Examinations of variants of this sequencing may help to clarify the relation between trauma effects and sleep disruption [10].

As nightmares are an independent risk factor for suicide [16], and there are some early indications that treating PTN might help to reduce risk for suicide [see 16, 17, 18•], treating PTN must be considered an important public health priority. While pharmacological interventions might be more readily available for treating PTN, non-pharmacological interventions like IRT and ERRT are currently the preferred treatment for PTN and have the largest evidence base. Consequently, improved dissemination and implementation of IRT and ERRT to front line psychotherapists are needed. Internet-based interventions may be a viable option [81], pending further research.

If dissemination of IRT and ERRT are to be undertook on a large-scale, further process-oriented research on these treatments are needed. As was pointed out above, various IRT protocols exist and ERRT may be just as effective without the exposure component [86]. Previous reviews have demonstrated that the various psychotherapies for nightmares have similar component [77]. It remains unclear how important fidelity to a treatment manual is when treating PTN. Studies on the potential effects of treatment fidelity and competency of IRT and other nonpharmacological treatments for PTN are lacking [8, 88].

Additionally, a new free resource has been developed by the National Center for Telehealth and Technology (now called DHA Connect Health) to facilitate IRT using a smartphone app called DREAM EZ [89]. This innovation remains untested; further process research on whether it helps facilitate treatment processes and further outcome research on whether it enhances treatment outcomes or maintenance of gains is needed.

One clear question remains, how should the scientific community make sense of the recent Raskind et al. [27••] study where prazosin failed to outperform the placebo? It was an exceedingly well-designed study that was multi-site, treatment condition was randomized, and the provider and patients were double-blinded to the treatment condition—it is unlikely that this finding can be attributed to flaws in the study design, though some concerns about a possible range-restriction due to inclusion and exclusion criteria is highlighted above. The VA and DOD taskforce speculated that perhaps the benefits of prazosin could be attributed to placebo effects [26]. Raskind et al. [27••], listed out several other times that treatments that would have been considered frontline treatment produced negative findings in the VA health care system, including: Sertraline for PTSD [90], trauma-focused group psychotherapy for PTSD [91], naltrexone in the treatment of alcohol use disorders [92], and risperidone in the treatment of schizophrenia [93]. This phenomenon is not solely observed in the VA system. In general, declines in treatment effects can be observed over time [see 94–95]. Various reasons have been given for this well-documented phenomenon ranging from researcher allegiance effects to placebo effects [see 94–95]. Well-designed studies conducted by impartial investigators are needed to evaluate the enduring effects of pharmacological and nonpharmacological treatments for PTN.

Compliance with Ethical Standards

Conflict of Interest Scott H. Waltman worked as a consultant and CBT trainer for the Academy of Cognitive Therapy.

David Shearer declares no potential conflicts of interest.

Bret A. Moore reports he is a CME content reviewer for the Neuroscience Education Institute and Series Editor for Routledge Press book series titled "Clinical Topics in Psychology and Psychiatry."

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- •• Of major importance

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