NIGHTWARE

Value Dossier

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A Patient's Story

Not actual patient. Model is for illustrative purpose only.

JEN'S STORY IS REAL, BUT WE'VE CHANGED HER NAME FOR THIS STORY TO PROTECT HER PRIVACY

Jen is a mother of a school-age boy; a wife; and an Air Force veteran. Her husband also served in the Air Force. Shortly after her husband returned from deployment in Afghanistan, Jen started having frequent nightmares. Her nightmares were filled with scenes of military plane crashes involving her husband, family, and friends. In other disturbing dreams she was overcome by fear that because she had forgotten her flight book, her aircraft crashed and everyone on her flight team was killed.

The nightmares made Jen sweat through her pajamas and sheets multiple times each night. She slept on separate sheets so she could easily switch them out and not wake her husband. Her heart would race and it was difficult to calm down after waking up – the images and feelings the nightmares brought on continued to haunt her even when she was awake. Soon the nightmares were so persistent that Jen spent many nights lying on the tile floor in the bathroom trying to cool down and calm herself so she wouldn't wake her family.

Lying there alone she felt desperate for help.

After a night of nightmares, Jen found it hard to get through the workday. She felt exhausted and foggy-headed all day. As an engineer, her inability to think clearly was frustrating and she began to second-guess her work. The anxiety she felt about new assignments and projects was overwhelming. As a manager, she noticed herself becoming increasingly agitated and disconnected from her team and anxious about upcoming meetings and presentations. She didn't have the energy to engage socially with colleagues. It took all her energy to show up and participate in regular interactions. After particularly difficult nights with multiple nightmares, Jen would have no choice but to call in sick the following day and try to recover and get some rest. She missed work more frequently and her performance declined. She feared that her supervisor and others were noticing her inability to function and she worried this would affect how people viewed her ability to lead her team and take on new responsibilities.

At home, Jen seemed distant and stressed. She was less patient with their son and lacked the energy to participate in day-to-day activities. Putting her son to bed brought anxiety as Jen feared she would fall asleep reading to him and he would witness her nightmares. Jen's husband took on more childcare responsibilities as Jen spiraled further into isolation, depression and anxiety.

Jen was under the care of a psychiatrist for depression and anxiety but Jen never mentioned her nightmares to her doctor because she didn't think they could be treated. Jen returned to her doctor several times noting that her depression and anxiety were not improving. In fact, she felt that in many parts of her life things were getting worse. Her provider prescribed a number of different pharmaceutical sleep aids, but none of them were well tolerated or seemed to help Jen. With each pharmaceutical she tried and failed, Jen felt more hopeless about getting better sleep and being able to show up at work and for her family.

Jen also sought the care of her primary care physician for physical ailments that suddenly were showing up, such as muscle tension; wrist and hand pain; and weight gain. Tests showed no underlying condition that could be causing these symptoms. Without a diagnosis to point to and because nothing she tried helped her get better sleep, Jen felt like her world was spiraling out of control.

JEN ISN'T AN ABNORMAL PATIENT. LIKE SO MANY OTHERS, SHE HAS STRUGGLED CONTINUALLY WITH NIGHTMARES. BUT WHAT IF THERE WAS A POSSIBLE SOLUTION?

EXECUTIVE SUMMARY

Nightmare Disorder and PTSD-Associated Nightmares are Prevalent and Serious

Nightmares that are frequent and disturbing are common. Two large population-based studies put the number of people with frequent, disturbing nightmares at around 2–8% of the population.[4,5] Nightmares associated with post-traumatic stress disorder (PTSD) are also common. Around 50% of patients with PTSD experience chronic frequent, disturbing nightmares.[16–18] Approximately 8% of women and 4% of men in civilian population in United States[6], and approximately 8% of the military and veteran populations have PTSD[7–15] , resulting in over 10 million people suffering from debilitating nightmares.

Frequent, severe nightmares are linked to several psychiatric problems, most notably mood disorders, sleep-disordered breathing, and daytime dysfunctional behaviors.[1–3] These issues result in people with dramatically higher utilization of the healthcare system including prescription drugs, the emergency department and institutional mental health services, ultimately manifesting in healthcare costs that are ~5x that of the general population. Importantly, frequent dysfunctional nightmares are a known independent risk factor for suicide attempts and suicide[1] and impose a staggering indirect cost of $43B in the military population and $189B in the civilian population due to productivity loss, unemployment and premature mortality, more than all other mental health conditions except major depression.[60]

New Therapeutics Approaches are (desperately?/sorely?) Needed

The most recent DoD/VA clinical practice guideline on PTSD management did not recommend any particular treatment for nightmares but acknowledged that an effective treatment was badly needed.[26] Pharmaceuticals and psychotherapy are the primary treatment options available to treat nightmare disorder and nightmares associated with PTSD. Prazosin, a drug with an indication for hypertension and used off-label to treat nightmare disorder, is the most widely prescribed. Despite extensive clinical study, including by well conducted RCTs, Prazosin has not conclusively been shown to be more effective than a placebo.[19-25].

Imagery Rehearsal Therapy (IRT) has very weak evidence of efficacy, and other forms of psychotherapy are even more poorly supported.[26] The one randomized trial of IRT that used a placebo control did not demonstrate IRT's effectiveness, while other trials of IRT suffered from the usage of wait-list control group that limit the strength of the evidence of efficacy[29-35]. Furthermore, the high-quality randomized trial saw very high discontinuation rates in the IRT treatment arm, evidence of the burden psychotherapy places on patients.

Given the lack of compelling evidence, the American Academy of Sleep Medicine (AASM) released a position paper on nightmare treatment in 2018 with IRT weakly recommeneded as the best available treatment option and no position taken on prazosin.[27] Due to poor treatment options, patients are at high risk for psychotropic medication polypharmacy, which is itself independently associated with overdose and suicide-related behavior, and many patients self-medicate with alcohol or other drugs leading to more than 20% of patients with concurrent Substance Use Disorder.[28, 61] Non-pharmacologic interventions are sorely needed and are especially sought by members of the military, many of whom prefer to avoid dependency on medications.

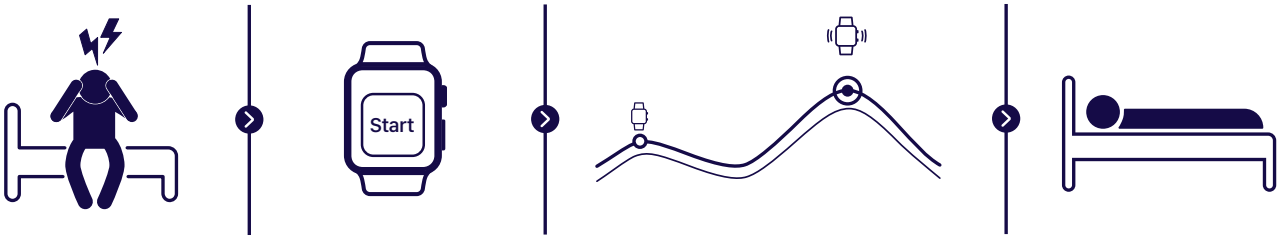
NightWare Offers A Solution to Sleep Disturbance Related to Nightmare Disorder or PTSD-Related Nightmares

NightWare is a digital therapeutic solution that reduces sleep disturbance in patients with nightmare disorder or nightmares related to PTSD. Because of the need for an effective treatment for nightmares, NightWare received breakthrough status from the FDA in April 2019, was FDA cleared in November 2020 as a class II medical device, and is the first and only FDA-cleared digital therapeutic shown to improve sleep in patients with nightmare disorder or PTSD-related nightmares.

Using artificial intelligence and biosensors, NightWare continually evaluates user's stress index by tracking heart rate accelerometer, and gyroscope data to determine if they are having a nightmare. This information is monitored in real time to determine when an intervention to disrupt a nightmare is needed. NightWare then provides short vibrations of varying intensity and patterns that the software has determined will best interrupt nightmares and improve sleep. This simple, low risk intervention offers a new therapeutic approach to doctors and patients who seek more effective options with fewer side effects and lower barriers to adherence.

FIGURE A

How NightWare Works



Patient with nightmares experiencing poor quality of sleep and distress

Prescribed NightWare which delivers therapy through Apple Watch application

Patient data collected and evaluated to create custom sleep profile that provides interventions to interrupt nightmares

Patient gets better quality of sleep

Evidence of NightWare's Safety and Effectiveness Is Compelling

NightWare's safety and efficacy is supported by two clinical trials, including a double-blind, sham controlled, randomized clinical trial (RCT), as well as Real World evidence generated through usage of NightWare by over 1,000 patients prescribed NightWare as part of normal clinical practice.

A single-arm open-label pilot study[37] of NightWare in 9 subjects was conducted in 2018 to provide preliminary evidence of safety and efficacy and support the design of follow-up studies. Encouragingly **large, clinically significant 6-point improvements in the Pittsburgh Sleep Quality Index (PSQI) and Patient Health Questionnaire 9 (PHQ-9), well-validated measures of sleep quality and depressive symptoms, were observed in the study**. Importantly, these improvements in sleep quality and depressive symptoms were quickly realized; the improvements were seen within two weeks of use.

Following the strong results of the pilot trial, a 240 patient, multi-site RCT was launched in the Veterans Affairs Health Care System to strengthen the evidence of the safety and efficacy of the NightWare digital therapeutic system. While the trial is on-going, a published, peer-reviewed interim analysis conducted to support FDA clearnance[36] **demonstrated the active treatment group experienced a clinically significant improvement in sleep quality.** Comparisons between NightWare and Sham showed NightWare had a positive impact on 7 of the 8 efficacy outcomes measures, with most nearing statistical significance despite only ~33% of the planned 240 patents included in the interim analysis. Once the study reaches full enrollment of 240 patients it's anticipated that the primary endpoint and many of the secondary endpoints will reach statistical significance.

Beyond increasing sleep quality, evaluation of the Trauma Related Nightmare Scale question responses shows evidence of an increase in sleep duration. Study subjects treated with NightWare reported **an increase in sleep duration of 54 minutes per night**, while those treated with a sham device reported an increase of 18 minutes per night. Compared to sham treatment, NightWare increased the odds of sleep quantity improvement 3.1-fold.

NightWare's use in normal clinical practice, outside of the controlled, clinical trial environment, is also providing evidence of strong device usage patterns, improved sleep quality, strong provider adoption and satisfaction, and treatment efficacy even when used in combination with other therapies. NightWare has been prescribed more than 1,000 times in the DoD by over 225 clinicians. **80% of patients surveyed stated NightWare was working well, with 20% stating NightWare delivered life-changing treatment.** Impressively, patients are highly adherent to the therapy, with **patients choosing to use NightWare on more than 60% of nights**. Collectively, this real world evidence demonstrates patients and clinicians continue trust NightWare to deliver treatment outcomes and fewer follow-up appointments with NightWare.

Finally, the cost of NightWare treatment is expected to be offset by direct cost savings after 1 year and thereafter generate a net savings of ~$7k per year as people are no longer dependent on multiple medications with side-effects, require constant trips to receive mental health services and in-patient treatment, and struggle to manage other health issues due to uncontrolled nightmare and PTSD symptoms.

Patients and Clinicians Deserve the Chance to Use NightWare

NNightmares and PTSD-related nightmares continue to be problems for millions of American civilians and military members. The current treatment paradigms are insufficient to address the issue and new approaches are desperately needed. NightWare offers a unique solution that has been demonstrated to be safe and effective through well-controlled experimentation and in real-world scenarios. No civilian, veteran, or active-duty military member should have to live another day hoping for a better treatment.

PART 1:

NIGHTMARES AND THE IMPACT ON PATIENTS

The Impact of Nightmares

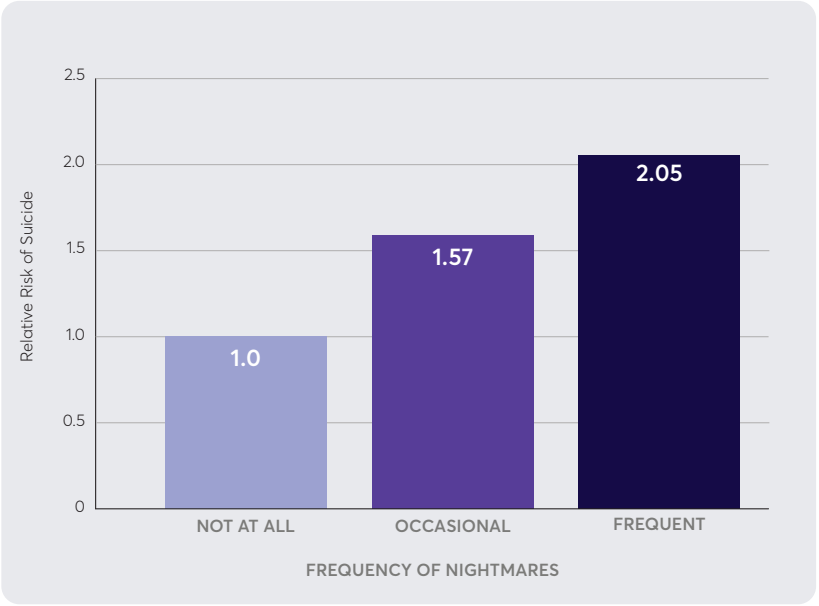
Frequent nightmares disrupt sleep and often lead to chronic sleep deprivation. This sleep deprivation is associated with considerable social, financial, and health-related costs.[39] Sleep deprivation and sleep fragmentation related to nightmares are associated with cognitive performance deficits, a decreased positive mood, impaired learning, and attention deficits. A study by Li et al[3] demonstrated that insomnia symptoms, sleep-disordered breathing symptoms, and consequences of low-quality sleep—daytime fatigue and sleepiness, morning headache, and difficulty getting up in the morning—are well-correlated with increased nightmare frequency. This study found that insomnia correlated most strongly with nightmares. Psychiatric disorders, especially mood disorders, are also associated with frequent nightmares in multiple studies.[39–41] In insomnia patients, chronic recurrent nightmares are present in approximately 18% of these patients, and the nightmares caused significant problems with daytime functioning.[42]

Suicide and Nightmares

Suicide is the 10th leading cause of death from all causes in the United States. Approximately 48,000 people die by suicide in the United States alone.[43] The suicide rate in the U.S. Armed Forces has been rising in recent years, and in 2008, the military's suicide rate surpassed that of the general population.[44] The suicide rate in 2016 for veterans was roughly double that of the non-veteran U.S. population.[45] Frequent nightmares have been demonstrated to be an independent risk factor for repeated suicide attempts.[1] Other research demonstrates this clear association between suicidality and nightmares.[46–48] Depressed patients with nightmares have been found to be more suicidal than those without nightmares.[49-50] Tanskanen and colleagues conducted a large, prospective population-based study to evaluate the risk of suicide among adults with nightmares over a 20-year period. They found those with frequent nightmares at baseline were 57% more likely to die by suicide than those without nightmares (Figure B). These studies, taken together, demonstrate that nightmares are a unique predictor of suicidal ideation, suicide attempts, and completed suicide.

FIGURE B

Suicide Risk and Nightmare Frequency



Adapted from Tanskanen et al. Nightmares as predictors of suicide. Sleep 2001.

PART 2:
CURRENT TREATMENTS FOR NIGHTMARES AND NIGHTMARE DISORDER

An Effective Treatment for Sleep Disturbance Related to Nightmare Disorder and PTSD-Associated Nightmares Is An Unmet Need

Nightmares that are frequent and disturbing are common. Although dysfunctional nightmares are most common in PTSD, they are also seen in patients with mood and anxiety disorders. Nightmares are more common in patients with other sleep problems. In one study, 18.3% of patient with insomnia reported frequent distressing nightmares.[42] This study found that frequent nightmares are strongly associated with problems such as daytime sleepiness, mood problems, and deficits in concentration, attention, and memory.

It is widely recognized the dysfunctional nightmares that disrupt sleep are a major problem for some patients, especially those with PTSD.[13–15] Some patients respond to the current treatments, but the research on these treatments is contradictory. Prazosin, a quinazoline approved for the treatment of hypertension, was used in 6 small studies for the treatment of nightmares conducted from 2003 to 2014.[19-24] These studies appeared to show that prazosin is more effective than placebo in the treatment of PTSD-associated nightmares; however, prazosin had not been FDA approved for the treatment of nightmares. In 2018, a very large, well-designed multi-center trial in the VA hospital system failed to show any benefit of prazosin over placebo.[25] The experience of many clinicians is that while a subset of patients respond to prazosin or psychotherapy, for many patients, these treatments are ineffective.

The experience of many clinicians is that while a subset of patients respond to prazosin or psychotherapy, for many patients, these treatments are ineffective.

It should be noted that there are some significant safety and adverse effect concerns with prazosin use. The FDA label for Prazosin for the treatment of hypertension carries a bolded warning for syncope occasionally associated with tachycardia and a Warning for priapism, and a precaution for intraoperative floppy iris syndrome. The most common adverse reaction to prazosin include dizziness, headache, drowsiness, lack of energy, weakness, palpitations and nausea. Additionally, many patients with nightmare disorders take multiple medications, and the risk of polypharmacy adverse effects is increased in these situations.[28]

The medical research on Imagery Rehearsal Therapy (IRT) and other forms of psychotherapy for nightmares is contradictory. Most of the studies of IRT used wait-list control groups,[29–33] which effectively eliminates any placebo effect of treatment. Higher quality studies demonstrated no benefit of IRT over a credible placebo.[34,35] In one of the high-quality trials, there were very high discontinuation rates in the IRT treatment.[35] Other treatments, including medications and psychotherapy methods, have been used to treat Nightmare Disorder and PTSD-associated nightmares. The evidence for these treatments is even more sparse than for prazosin and IRT, and none of these treatments are recommended in clinical practice guidelines .[26, 27]

Nightmare disorder is also underdiagnosed. Zadra and Donderi found a much higher incidence of nightmares and "bad dreams" (defined as disturbing dreams that did not cause an awakening) in patients keeping daily logs rather than recall over longer periods.[40] In one study of active duty military members, only 3.9% of the study population reported nightmares as the reason for sleep evaluation, yet 31.2% of these patients had clinically significant nightmares.[52]

Although Nightmare Disorder can be present along with other mental health disorders, it most often is noticed clinically in patients with PTSD. Piertrzak et al[6] provide the best prevalence data on PTSD, with 8% of women and 4% of men having a PTSD diagnosis. Estimates of PTSD prevalence in military populations vary from 4–17%, with the best estimates being around 8%.[6–12] Approximately 72% of patients newly diagnosed with PTSD complain of frequent, disturbing nightmares, and about 50% of patients with PTSD still complain about these nightmares 6 months after diagnosis.[13–15] These nightmares disrupt patient's sleep, and by disrupting sleep, they decrease patients' focus, attention, and cognitive abilities. This inadequate and poor-quality sleep can impair the patient's ability to participate in psychotherapy to treat PTSD, and impair their ability to function well in their families and society.

> *Approximately 72% of patients newly diagnosed with PTSD complain of frequent, disturbing nightmares, and about 50% of patients with PTSD still complain about these nightmares 6 months after diagnosis.[13–15]*

Current Guidelines Have Weak or No Recommendations for the Treatment of Nightmares

There are two current guidelines for the treatment of nightmares. First, the DoD/VA clinical practice guideline on PTSD management, published in 2017, did not recommend any particular treatment for nightmares.[26] In light of the limited data on the effectiveness of prazosin, the guideline did not recommend its use. The authors felt that data were lacking regarding psychotherapies, including IRT, and did not recommend any of them.

Second, the American Academy of Sleep Medicine (AASM) released a position paper on nightmare treatment in 2018.[27] Imagery Rehearsal Therapy was weakly recommended as the best available treatment. The AASM paper did not recommend for or against the use of prazosin. Multiple anti-psychotics, antidepressants, and other medications were mentioned as possible treatments, but the position paper noted that none of these choices had evidence to support their use. Both guidelines lamented the lack of proven treatments for nightmare disorders, and put out a call for new and more effective treatments for nightmares.

> *"For nightmares associated with PTSD, there is insufficient evidence to recommend for or against the use of prazosin as mono- or augmentation therapy."*
>
> VA/DOD CLINICAL PRACTICE GUIDELINE FOR THE MANAGEMENT OF POSTTRAUMATIC STRESS DISORDER AND ACUTE STRESS DISORDER, 2017

NightWare is not a standalone therapy for PTSD. The device should be used in conjunction with prescribed medications for PTSD and other recommended therapies for PTSD-associated nightmares and nightmare disorder.

PART 3:
NIGHTWARE BACKGROUND

NightWare Description and Indication

NightWare is a digital therapeutic system that temporarily reduces sleep disturbance related to nightmares. NightWare provides customized medical treatment for dysfunctional nightmares and is the only FDA-cleared treatment for this disorder.

The NightWare digital therapeutic is indicated to provide vibrotactile feedback on an Apple Watch based on an analysis of heart rate and motion during sleep for the temporary reduction of sleep disturbance related to nightmares in adults 22 years or older who suffer from nightmare disorder or have nightmares from post-traumatic stress disorder (PTSD). It is intended for home use.

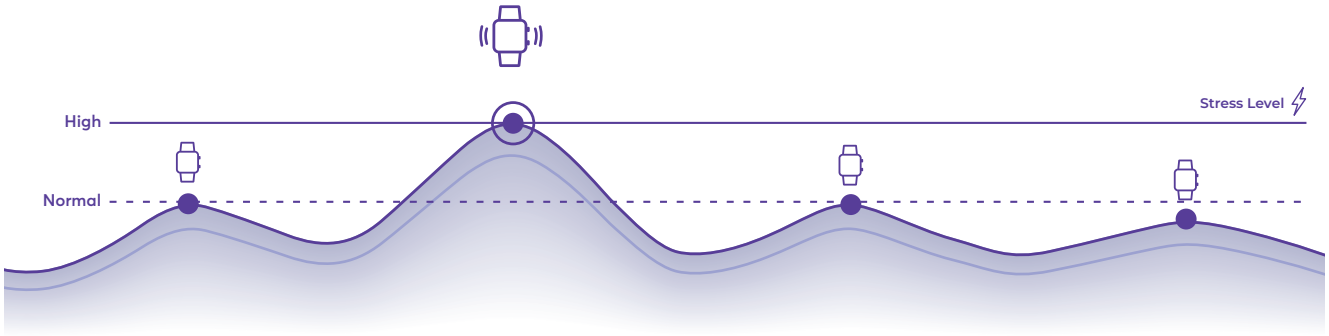
NightWare Specifications

NightWare consists of a backbone of cloud-based artificial intelligence and delivers its intervention through the Apple Watch and an iPhone®. The phone and watch are secured and only function to deliver the NightWare therapy. The phone is necessary for connecting to data servers.

Using artificial intelligence, NightWare first learns the patient's physiologic patterns over a period of 2–20 hours. After this learning period, NightWare will continually evaluate the user's stress index*by tracking heart rate and movement data obtained from an Apple Watch. NightWare uses a combination of the patient's heart rate, accelerometer, and gyroscope data to determine when a patient has a high stress index. As the patient's stress index changes, the device can update the information that it has, and new "set points" for the patient's stress index can be determined. In this way, NightWare is continually updating its information about a particular patient. Artificial Intelligence is needed for this application because the data is highly granular and continual evaluation is required to make the individualized decision to intervene in sleep.

FIGURE C

How NightWare Treatment Produces A Better Night's Sleep



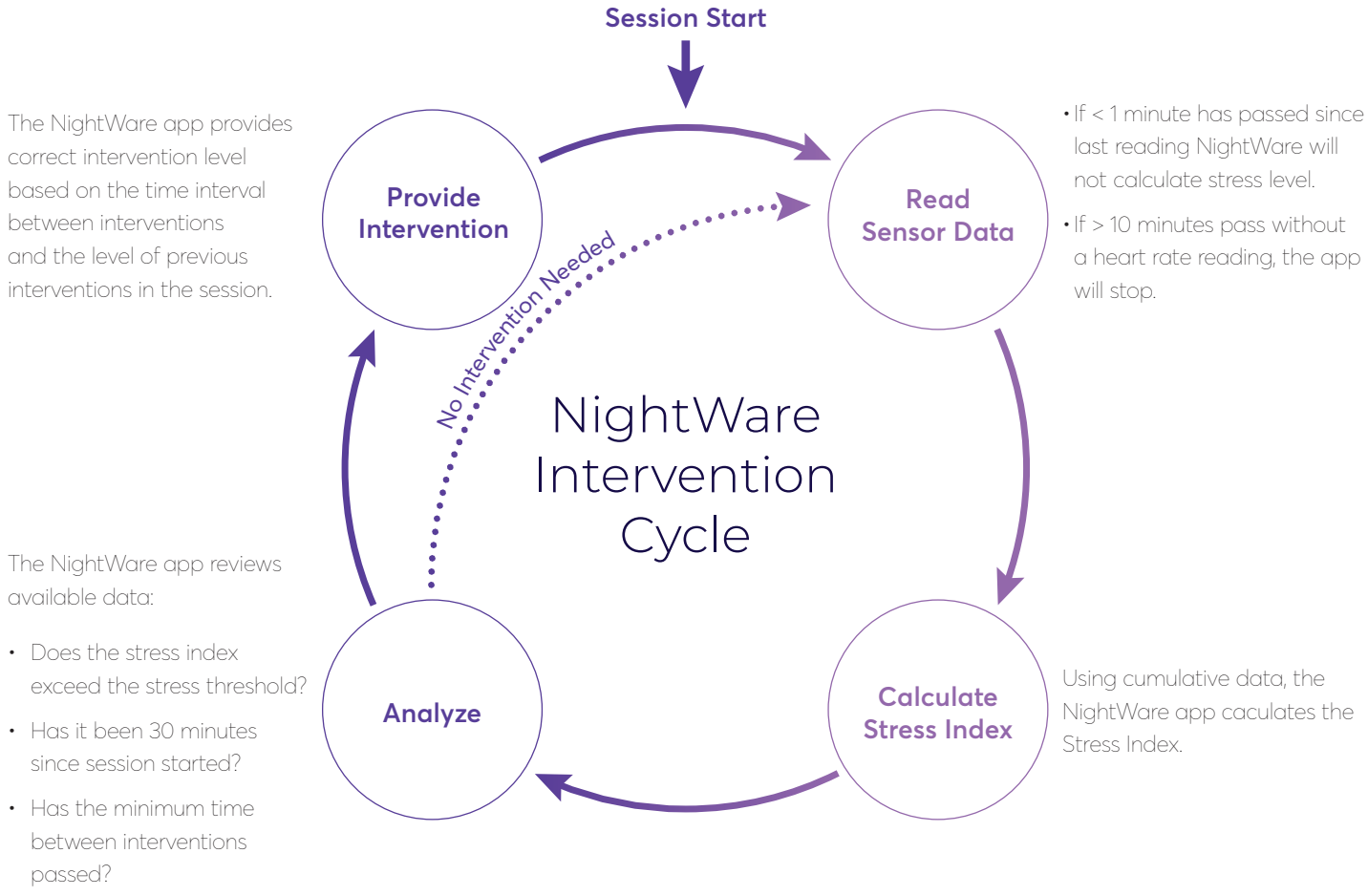
* Stress index is a device-specific measurement and does not represent a clinically validated measure of stress.

When NightWare detects an increased stress index past the intervention level for a patient, a series of customized vibrations interrupt the nightmare. There are 3 intervention levels of increasing intensity and 9 vibration patterns that NightWare can apply. The minimum time between interventions can also vary from 1–5 minutes, depending on the individual patient. Based on the response to the interventions in the past, NightWare will increase, maintain, or decrease the intervention level. In the clinical studies of NightWare, these interventions did not awaken patients, but rather, they interrupted nightmares and improved sleep. NightWare is personalized treatment for nightmares.

> *NightWare continuously monitors sleep and provides personalized interventions to improve sleep in patients with dysfunctional nightmares.*

FIGURE D

Continuous Monitoring and Intervention



PART 4:

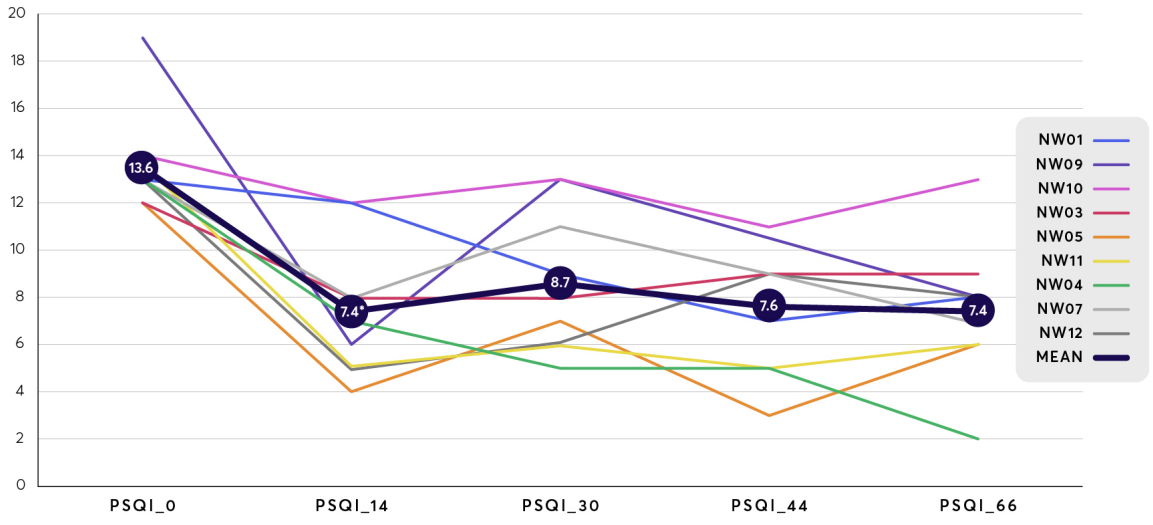
CLINICAL EVIDENCE OF NIGHTWARE'S SAFETY & EFFICACY

NightWare Pilot Study Shows Strong Effect on Sleep Quality

In a single-arm open-label pilot study of NightWare in 9 subjects[37] to explore the effects of NightWare on sleep quality, there was a large effect size of a 6-point improvement in the Pittsburgh Sleep Quality Index (PSQI), a well-validated measure of sleep quality [Figure E].[54, 55] The Patient Health Questionnaire 9 (PHQ-9), a standard questionnaire to measure the severity of depressive symptoms, demonstrated a 6-point improvement [Figure F]. The large effect size for these measures was considered impressive and suggested tangible improvement in sleep quality for patients with frequent nightmares. Importantly, these improvements in sleep quality and depressive symptoms were quickly realized; the improvements were seen within just two weeks of use. No safety concerns were noted in this trial. Based on these results, a large randomized controlled trial was initiated.

FIGURE E

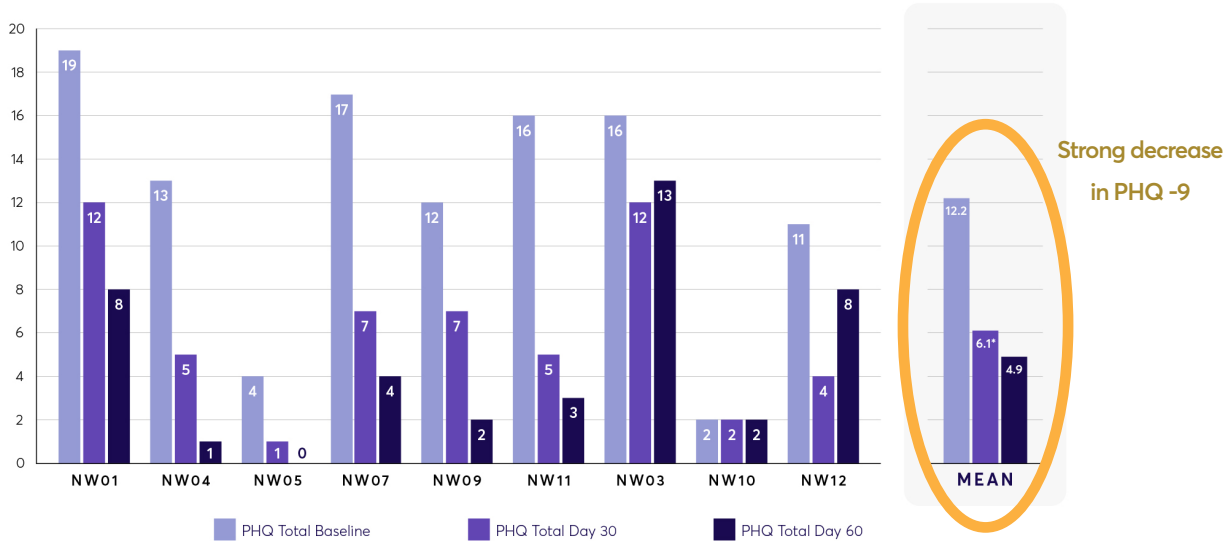
Total PSQI at Biweekly Assessments



*While there was a 3.2 range in the PSQI for NightWare and the Sham was 2.2, there was no statistical significance between the two. The PSQI-A was also not statistically significant.

FIGURE F

Total PHQ-9 at Monthly Assessments



*While there was a 3.2 range in the PSQI for NightWare and the Sham was 2.2, there was no statistical significance between the two. The PSQI-A was also not statistically significant.

Background on Randomized, Sham-Controlled Trial (Ongoing)

Currently, a double-blind, sham-controlled, randomized controlled trial of NightWare is ongoing. The goal of this trial is to generate definitive evidence of NightWare's safety and efficacy. This is a 30-day trial with a plan for 240 subjects. The inclusion criteria include patients with significant sleep disturbance (a baseline PSQI of 10 or more), repetitive disturbing nightmares, and a PTSD diagnosis. Patients with dream-enacting behavior, DAST-10 score greater than 2 or AUDIT score greater than or equal to 8, and severe depression are excluded. All patients have to be off of prazosin for at least two weeks prior to starting the trial. The primary efficacy measure is a change in the average PSQI score from baseline at the 30-day point in the study. Safety is assessed using the Epworth Sleepiness Scale and adverse events associated with the treatment.

Due to the COVID-19 pandemic, enrollment was put on hold shortly after the trial was initiated with only 65 out of the planned 240 patients enrolled (enrollment has subsequently resumed). While the trial was paused, an interim analysis was conducted to examine if there were any preliminary findings of safety and efficacy that could support FDA review and approval.

Preliminary Data from Ongoing Randomized Sham Controlled Trial

Safety

Safety data from this trial demonstrates that NightWare is safe to use. Thus far in the study, there have not been any adverse events attributable to the use of NightWare. Additionally, the Epworth Sleepiness Index showing an identical small decrease between the active treatment and sham groups (see Table 1 below), demonstrating that usage of the NightWare device does not increase daytime sleepiness.

Efficacy

An interim analysis[36] of the NightWare RCT demonstrated the Active treatment group had clinically significant improvement. Comparisons between NightWare and Sham show NightWare having a positive impact on 7 of the 8 efficacy outcomes measures, with p-values already approaching 0.05 for the PSQI-A and the NightWare Likert Scale and below 0.3 for the PSQI, PHQ-9, PTSD checklist, and TRNS. However, with only 65 of the 240 patients enrolled and analyzed, none of the comparisons of individual outcome measures have yet met the 0.05 threshold of statistical significance.

TABLE 1

Mean (SD) Change Between Baseline and Primary Outcome Visit at 30 Days for Each Outcome Measure by Study Arm.

Baseline Outcome Measure		NightWare (n = 29)	Sham (n = 34)	p-value
PSQI	Pittsburgh Sleep Quality Index	-3.2 (3.7)	-2.2 (2.9)	0.2606
PHQ-9	Patient Health Questionnaire-9	-2 (3.7)	-1 (3.8)	0.2719
PCL	PTSD Checklist	-9.9 (13.4)	-6.5 (9.9)	0.2727
ESS	Epworth Sleepiness Scale	-1.2 (4.1)	-1.2 (3.1)	0.9739
TRNS	Trauma-Related Nightmare Scale	-4.8 (7.3)	-2.7 (4.4)	0.1909
FOS	Functional Outcomes of Sleep Questionnaire	1.4 (2.8)	0.8 (2.3)	0.3683
PSQI-A	Pittsburgh Sleep Quality Index Addendum	-3.3 (4.9)	-1.4 (3.5)	0.0938
VR12	Veterans RAND 12 Item Health Survey	2 (5.8)	1.6 (6.9)	0.8093
NWL	NightWare Likert Scale*	4.5 (4.4)	2.7 (3.8)	0.0910

P-values reflect a two-sample t-test.

*The NightWare Likert Scale is a device-specific, non-validated tool designed to measure changes in sleep quantity, sleep quality, and improvement in nightmares.

In-depth analysis of the Trauma Related Nightmare Scale (TRNS) questionnaire found substantial improvement in reported sleep quantity. Active treatment arm participants reported 54 more minutes of sleep per night during the study, while the Sham treatment arm reported 18 more minutes of sleep per night. The active treatment arm was more than 3.67 times more likely to report increased sleep quantity than the Sham treatment arm (OR: 3.67 [1.3,10]). When adjusted for compliance with treatment, the adjusted odds ratio for increased sleep quantity in the Active treatment arm was 3.12 [1.2, 11], compared to the Sham treatment arm. This improvement in sleep quantity was also seen on a post-hoc analysis of this study data focused on High Usage patients (see following section).

Because under-utilization during the trial may have contributed to an under-estimation of the treatment effect, a post-hoc analysis was done which excluded participants that used NightWare for fewer than 50% of the study nights.

Seventeen participants (9 Active, 8 Sham) were excluded (median usage: Active 33%, Sham 39%). Analysis of the remaining "high usage" subsample (Median usage: Active 74%, Sham 75%) demonstrated statistically significant improvement in the Active group on the primary outcome measure, the PSQI (p=0.016, d=072), and on the NWL (p=0.002, d=0.94). The full results of all outcome measures in the high usage cohorts are listed in Table 2. Of note, the degree of change in the sham condition in the full set and high usage subset was similar, indicating better adherence with the inactive device had little effect in outcomes. The high usage Active treatment group showed greater effectiveness of the treatment in improving sleep quality.

The major effects of treatment were improvement in sleep latency (the time it takes to initially fall asleep) and sleep disturbances in the PSQI. This analysis provides evidence that NightWare users fall asleep faster and have less sleep disturbance when using this treatment, and the effect is greater the more that they use it. This data suggests that the primary effect is reducing autonomic arousals, which allows the patient to fall asleep faster and wake less during sleep. The mechanism of action is thought to be that NightWare disrupts the sleep stage in which distress is present, which stops the stress response to the nightmares, and allows the patient to transition to a more restful state of sleep.

This analysis also found that the high usage Active group used NightWare slept an additional hour each night, while the high usage Sham group did not increase their sleep duration. This subjective increase in sleep quantity is important as there is a large body of evidence demonstrating decreased morbidity and mortality in those sleeping 7 hours per night.[55-59]

This post-hoc analysis provides evidence that NightWare may improve sleep quality in the treatment-adherent population and was published in the Journal of Clinical Sleep Medicine, DOI: 10.5664/jcsm.10338.

TABLE 2

Mean (SD) Change in 'High Usage' Subsample Between Baseline and Primary Outcome Visit at 30 Days for Each Outcome Measure

Baseline Outcome Measure		NightWare (n = 21)	Sham (n = 27)	p-value
PSQI	Pittsburgh Sleep Quality Index	**-4.1 (3.4)**	**-1.9 (2.9)**	*0.016*
PHQ-9	Patient Health Questionnaire-9	**-2.5 (3.0)**	-0.6 (3.9)	0.067
PCL	PTSD Checklist	**-9.9 (14.8)**	**-5.9 (10.3)**	0.264
TRNS	Trauma-Related Nightmare Scale	**-6.1 (8.1)**	**-2.5 (5.1)**	0.063
FOSQ	Functional Outcomes of Sleep Questionnaire	**1.5 (3.0)**	1.0 (2.4)a	0.483
PSQI-A	Pittsburgh Sleep Quality Index Addendum	-1.2 (4.7)	-0.9 (3.1)	0.778
NWL	NightWare Likert Scale	**6.1 (3.9)**	**2.7 (3.5)**	*0.002*

P-values reflect a two-sample t-test.

Values in italic represent significance (P < .05) after correction for multiple comparisons. Values in bold represent significant changes from baseline (1-sample t-test, P < .05).

[a]n = 26 Sham due to missing baseline data.

> *Conclusion: Like many trials of nightmare treatments, there is a strong placebo effect present in this trial. However, based on the interim results, it is expected the primary and many secondary endpoints will be achieved once the trial is complete. Given the lack of FDA-cleared therapies for nightmare disorder or PTSD-related nightmares, the low safety risks for the use of NightWare, and emerging evidence from the trial interim analysis, the data supported FDA clearance.*

PART 5:
REAL WORLD EVIDENCE & USER/PRESCRIBER FEEDBACK

Experience within the Department of Defense (DoD)

Both patients and clinicians at the DoD have had remarkable experiences using and prescribing NightWare. Clinician adoption has been strong, with 225+ unique clinicians prescribing NightWare over 1,000 times across 45+ unique bases since July 2021. Importantly, 98% of prescriptions written have been approved by TRICARE ensuring patients promptly receive treatment and clinicians don't have to worry about delays in treatment and uncertainty about if the device will be covered.

FIGURE G

Prescription Metrics within the Department of Defense

1000+	225+	45+	98%
Devices Prescribed since July 2021	DoD Prescribers	DoD Bases	TRICARE Approval Rate

Additionally, 50% of prescribers have written a prescription in the past 3 months and 73% have written a prescription in the past 6 months, demonstrating clinicians continue to believe NightWare to be a helpful tool in treating their patients.

Examples of Prescriber Feedback:

Allows for **customizable treatment plan** *for each indivudual*

Helps deliver a **holistic treatment expereince**

Is a **valuable resource** *to track patient progress and make informed decisions*

Able to **reduce drug prescription and need for office visits** *while maintianing optimal care*

Experience in the DoD has also shown NightWare is delivering value to the vast majority of patients treated in a Real World situation, with 80% of patients stating NightWare improved their sleep quality and 20% stating NightWare delivered life-changing treatment.

4 out of 5 patients report improved sleep quality

1 out of 5 patients report a life-changing expereince

Efficacy appears strong with concurrent usage of prazosin

A DoD physician, Dr. Andre Liem, conducted a case series study in 2022 in which he reviewed the impact of NightWare on 14 consecutive patients prescribed the NightWare therapy. Of the 14, 11 used the device more than 7 days and were included in the analysis. At baseline, patients included in the analysis had a mean CGI Severity score of 4.63 which indicates moderate to severe nightmares and daytime dysfunction. Treatment with NightWare dramatically improved the CGI score, reflecting a reduction in nightmares and daytime dysfunction.

FIGURE H

Case Series Results from Dr. Liem (2022)

	N	CGI severity (mean)	CGI change
Total cohort	11	4.63	2.09
NightWare only	5	4.60	2.20

Importantly, of the 14 patients studied six were taking prazosin at doses between 1-8mg. Prazosin is a commonly prescribed pharmacologic agent used off-label to treat patients with nightmares associated with PTSD. NightWare was still shown to be effective in this population. This is the first study reporting on the effectiveness of NightWare used with prazosin.

Quality Assurance Evaluations from Portal Data

In January of 2022, NightWare conducted a quality assurance evaluation of data captured by the device and stored in the NightWare portal. This evaluation consisted of 56 commercial NightWare users in the DoD, which focused on evaluating compliance and overall sleep duration. Compliance rate was calculated according to the following:

- Calculate the total number of days within study interval (A)
- If a patient uses the device at least 1 over the 24-hour period, the rate is counted as "1" for that date. Any usage below 1 hour was not counted and excluded from the analysis. NW doesn't intervene for the first 30 minutes of each session.
- Calculate the total number of this rate across study interval (B).
- Compliance rate = A/B x100

Based on these calculations, this population was compliant with the device 69.4% of the treatment course time. Furthermore, when patients used the device for at least 30 days, the compliance rate increased to 73.9%. Usage duration was also calculated by averaging the duration of sleep sessions, excluding sessions that are under 1 hour, from each patient. The average time of use for the time of use for the overall population was 6.4 hours per night, and for those using the device for at least 30 days the average use was 6.6 hours per night.

FIGURE I

Compliance data from Patient Portal

	Entire cohort (n = 56)	30+ days of use (n = 26)
Compliance Rate	69.4%	73.9%
St. Dev.	21%	16.3%
95% Confidence	69.4 +/- 5.5%	73.9 +/- 0.6%

FIGURE J

Use Duration data from Patient Portal

	Entire cohort (n = 56)	30+ days of use (n = 26)
Average Use (hours)	6.4	6.6
St. Dev.	1.26	1.5
95% Confidence	6.3 +/- 0.6	6.6 +/- 0.6

Another quality assurance evaluation of 66 commercial NightWare users from three different prescribers was completed in July 2023. This evaluation again was performed using NightWare Portal data. Compliances rate and usage duration were similar to the analysis that was done in January 2022 in a different set of commercial NightWare users.

Collectively, this real-world monitoring data demonstrates patients consistently use NightWare long after their prescription date for the majority, if not the entirely of the night. This pattern of utilization strongly suggests patients find value in NightWare.

PART 6:
ECONOMIC IMPACT OF NIGHTWARE USAGE

Changing the Paradigm of Standard of Care Utilization

People suffering from PTSD have substantially different patterns of healthcare utilization compared to the general population. To illustrate the dramatic difference, NightWare conducted an analysis on claims data representing a cross-section sample of the general population (Medicare, Medicaid, commercially insured). The steps to conduct this analysis were as follows:

Step 1: Select Cohorts

- PTSD cohort: patients with a PTSD diagnosis in position 1–4 on a medical claim during analysis year. Note: PTSD diagnosis was used as a proxy for Nightmares associated with PTSD to ensure enough claims were available to make an accurate and significant comparison. 80% of patients with PTSD have comorbid nightmares.
- General population: all insured people during analysis year

Step 2: Compile Medical and Pharmacy Claims Data for Each Cohort

Step 3: Aggregate and Group Claims Together

- Total spend = insurer liability + member liability + other insurer liability
- Utilization codes used to categorize spend by type of service

Results of the analysis demonstrate that these patients visit the Emergency Department 3x more frequently, have 19x more outpatient mental health visits, and require Institutional Mental Health care at a rate of 25x that of the general population. Unsurprisingly, the cost of healthcare for these people was almost $25k per year, about 5 times higher than the average person in the general population. Not only is the increasing utilization costly to the healthcare payors, patients bear the significant burden of frequent trips to healthcare facilities to receive care. By more effectively treating a key aspect of PTSD, and doing so at home, NightWare aims to disrupt the costly and burdensome experiences associated with the disorder and its treatment.

FIGURE K

Site of Care Utilization Pattterns in Patients with PTSD vs. General Population

FIGURE L

Healthcare Spending in Patients with PTSD and the General Population

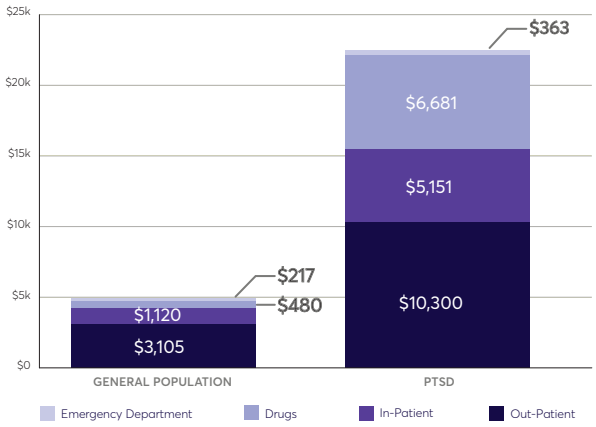


TABLE 3

Comparison of Spending by Service Category

	PTSD	General Pop	Relative Spend
In-patient	$5,151	$1,120	4.6X
E.D.	$363	$217	1.7X
Out-Patient	$10,300	$3,105	3.3X
Drugs	$6,681	$480	13.9X
Total	$22,495	$4,923	4.6X

Beyond the direct impacts of PTSD observed in claims data, recent research published in the Journal of Clinical Psychology[60] estimated the economic burden of posttraumatic stress disorder (PTSD) in the United States civilian and military populations from a societal perspective. Economic costs were estimated to be a staggering $43B in the military population and $189B in the civilian population, more than all other mental health conditions except major depression. The researchers conclude: "Increased awareness of PTSD, development of more effective therapies, and expansion of evidence-based interventions may be warranted to reduce the large clinical and economic burden of PTSD."

> *Conclusion: PTSD (as a proxy for patients with nightmares associated with PTSD or nightmare disorder) shows a significantly higher spend per patient than the general population of patients. Additionally, it is anticipated that PTSD with nightmares is likely to be higher spend for treatment per patient than PTSD only. The NightWare digital therapeutic is indicated to provide vibrotactile feedback on an Apple Watch based on an analysis of heart rate and motion during sleep for the temporary reduction of sleep disturbance related to nightmares in adults 22 years or older who suffer from nightmare disorder or have nightmares from post-traumatic stress disorder (PTSD).*

NightWare Anticipated To Be ROI Positive Within 1–2 Years of Use

PTSD Patients (a Proxy for Nightmare Disorder Sufferers) Cost ~$22,500 To Treat Annually

- $10,300 in out-patient treatments
- $5,151 in Inpatient treatments
- $6,681 in drug spending
- $363 in ED visits

Estimated Reductions in Spend

- Fewer institutional MH/SUD stays (est. 20%–33%)
- Fewer outpatient visits for MH (est. 10%–20%)
- Deprescription of drug (est. 20%–33%)
- Reduction in pull-thru spending (est. 10%–33%)
- Estimated payback in 2 years at low savings estimates
- Estimated payback in 1 year at high savings estimates

TABLE 4

Annual PTSD Treatment Costs with Estimated NightWare Impact

	Avg. Costs	Low Impact Estimate	Low Range Reduced Costs	High Impact Estimate	High Range Reduced Costs
In-Patient	$5,151	20%	$1,030.20	33%	$1,699.83
E.D.	$363	10%	$36.30	20%	$72.60
Out-Patient	$10,300	20%	$2,060.00	33%	$3,399.00
Drugs	$6,681	10%	$668.10	33%	$2,204.73
Total	**$22,495**	**–**	**$3,795**	**–**	**$7,376**

> *Conclusion: The cost of NightWare will be offset by direct healthcare savings after ~1 year and will generate a 2x ROI after 2 years of use.*

References

1. Sjöström N, Hetta J, Waern M. Persistent nightmares are associated with repeat suicide attempt: a prospective study. Psychiatry Res. 2009;170(2-3):208–211.
2. Kilpatrick D, Resnick H, Freedy J, et al. Posttraumatic stress disorder field trial: Evaluation of PTSD Construct Criteria A through E. In: Widiger T, Frances A, Pincus H, et al., Eds. DSM-IV Sourcebook. Vol 4. Washington, D.C.: American Psychiatric Press; 1994.
3. Li SX, Zhang B, Li AM, Wing YK. Prevalence and correlates of frequent nightmares: a community based 2-phase study. Sleep 2010;33(6):774–780.
4. Sandman N, Valli K, Kronholm E, et al. Nightmares: prevalence among the Finnish general adult population and war veterans during 1972–2007. Sleep 2013;36:1041.
5. Munezawa T, Kaneita Y, Osaki Y, et al. Nightmare and sleep paralysis among Japanese adolescents: a nationwide representative survey. Sleep Med 2011;12:56–64.
6. Pietrzak RH, Goldstein RB, Southwick SM, Grant BF. Prevalence and Axis I comorbidity of full and partial posttraumatic stress disorder in the United States: Results from wave 2 of the National Epidemiologic Survey on Alcohol and Related Conditions. J Anxiety Disord. Apr 2011;25(3):456–465.
7. Gates MA, Holowka DW, Vasterling JJ, Keane TM, Marx BP, Rosen RC. Posttraumatic stress disorder in Veterans and military personnel: Epidemiology, screening, and case recognition. Psychol Serv. Nov 2012;9(4):361–382.
8. Kok BC, Herrell RK, Thomas JL, Hoge CW. Posttraumatic stress disorder associated with combat service in Iraq or Afghanistan: Reconciling prevalence differences between studies. J Nerv Ment Dis. May 2012;200(5):444–450.
9. Ramchand R, Schell TL, Karney BR, Osilla KC, Burns RM, Caldarone LB. Disparate prevalence estimates of PTSD among service members who served in Iraq and Afghanistan: Possible explanations. J Trauma Stress. Feb 2010;23(1):59–68.
10. Richardson LK, Frueh BC, Acierno R. Prevalence estimates of combat-related post-traumatic stress disorder: Critical review. Aust N Z J Psychiatry. Jan 2010;44(1):4–19.
11. Schell TL, Marshall GN. Survey of individuals previously deployed for OEF/OIF. Invisible wounds of war: Psychological and cognitive injuries, their consequences, and services to assist recovery. 2008:87–115.
12. Ramchand R, Rudavsky R, Grant S, Tanielian T, Jaycox L. Prevalence of, risk factors for, and consequences of posttraumatic stress disorder and other mental health problems in military populations deployed to Iraq and Afghanistan. Curr Psychiatry Rep. May 2015;17(5):37.
13. Thomas JL, Wilk JE, Riviere LA, McGurk D, Castro CA, Hoge CW. Prevalence of mental health problems and functional impairment among active component and National Guard soldiers 3 and 12 months following combat in Iraq. Arch Gen Psychiatry. Jun 2010;67(6):614–623.
14. LeardMann CA, Smith TC, Smith B, Wells TS, Ryan MA. Baseline self reported functional health and vulnerability to post-traumatic stress disorder after combat deployment: Prospective US military cohort study. BMJ. Apr 16 2009;338:b1273.
15. Smith TC, Ryan MA, Wingard DL, Slymen DJ, Sallis JF, Kritz-Silverstein D. New onset and persistent symptoms of post-traumatic stress disorder self reported after deployment and combat exposures: Prospective population based US military cohort study. BMJ. Feb 16 2008;336(7640):366–371.
16. Davis JL, Byrd P, Rhudy JL, Wright DC. Characteristics of chronic nightmares in a trauma-exposed treatment-seeking sample. Dreaming 2007;17:187–98.
17. Wittmann L, Schredl M, Kramer M. Dreaming in posttraumatic stress disorder: a critical review of phenomenology, psychophysiology and treatment. Psychother Psychosom 2007;76:25–39.
18. Gehrman PR, Harb GC, Cook JM, et al. Sleep diaries of Vietnam War veterans with chronic PTSD: the relationships among insomnia symptoms, psychosocial stress, and nightmares. Behav Sleep Med 2015;13(3):255–64.
19. Raskind MA, Peskind ER, Kanter ED, et al. Reduction of nightmares and other PTSD symptoms in combat Veterans by prazosin: A placebo-controlled study. Am J Psychiatry. Feb 2003;160(2):371–373.
20. Raskind MA, Peskind ER, Hoff DJ, et al. A parallel group placebo-controlled study of prazosin for trauma nightmares and sleep disturbance in combat Veterans with post-traumatic stress disorder. Biol Psychiatry. Apr 15 2007;61(8):928–934.
21. Taylor FB, Martin P, Thompson C, et al. Prazosin effects on objective sleep measures and clinical symptoms in civilian trauma posttraumatic stress disorder; a placebo-controlled study. Biol Psychiatry. 2008;63(6):629–632.

22. Germain A, Richardson R, Moul DE, et al. Placebo-controlled comparison of prazosin and cognitive- behavioral treatments for sleep disturbances in US military Veterans. J Psychosom Res. Feb 2012;72(2):89–96
23. Raskind MA, Peterson K, Williams T, et al. A trial of prazosin for combat trauma PTSD with nightmares in active-duty soldiers returned from Iraq and Afghanistan. Am J Psychiatry. Sep 2013;170(9):1003–1010.
24. Ahmadpanah M, Sabzeiee P, Hosseini SM, et al. Comparing the effect of prazosin and hydroxyzine on sleep quality in patients suffering from posttraumatic stress disorder. Neuropsychobiology. 2014;69(4):235–242.
25. Raskind MA, Peskind ER, Chow B, Harris C, Davis-Karim A, Holmes HA, et al. Trial of prazosin for post-traumatic stress disorder in military veterans. N Engl J Med. 2018;378(6):507–17.
26. Department of Veterans Affairs, Department of Defense. VA/DoD clinical practice guidelines for the management of posttraumatic stress disorder and acute stress disorder. 2017. https://www.healthquality.va.gov/guidelines/MH/ptsd/VADoDPTSDCPGFinal.pdf Accessed 25 Apr 2020.
27. Morgenthaler TI, Auerbach S, Casey KR, et al. Position Paper for the Treatment of Nightmare Disorder in Adults: An American Academy of Sleep Medicine Position Paper. J Clin Sleep Med. 2018;14(6):1041–1055. Published 2018 Jun 15. doi:10.5664/jcsm.7178
28. Collett GA, Song K, Jaramillo CA, Potter JS, Finley EP, Pugh MJ. Prevalence of Central Nervous System Polypharmacy and Associations with Overdose and Suicide-Related Behaviors in Iraq and Afghanistan War Veterans in VA Care 2010–2011. Drugs Real World Outcomes. 2016 Mar;3(1):45-52. doi: 10.1007/s40801-015-0055-0. PMID: 27747799; PMCID: PMC4819457.
29. Krakow B, Hollifield M, Johnston L, et al. Imagery rehearsal therapy for chronic nightmares in sexual assault survivors with posttraumatic stress disorder: A randomized controlled trial. JAMA. Aug 2001;286(5):537–545.
30. Krakow B, Sandoval D, Schrader R, et al. Treatment of chronic nightmares in adjudicated adolescent girls in a residential facility. J Adolesc Health. Aug 2001;29(2):94–100.
31. Krakow B, Kellner R, Pathak D, Lambert L. Long term reduction of nightmares with imagery rehearsal treatment. Behav Cogn Psychother 1996;24(2):135–148.
32. Krakow B, Kellner R, Neidhardt J, Pathak D, Lambert L. Imagery rehearsal treatment of chronic nightmares: with a thirty month follow-up. J Behav Ther Exp Psychiatry. 1993;24(4):325–330
33. Lancee J, Spoormaker VI, van den Bout J. Cognitive-behavioral self-help treatment for nightmares: a randomized controlled trial. Psychother Psychosom. 2010;79(6):371–377.
34. Thunker J, Pietrowsky R. Effectiveness of a manualized imagery rehearsal therapy for patients suffering from nightmare disorders with and without a comorbidity of depression or PTSD. Behav Res Ther. 2012;50(9):558–564.
35. Cook JM, Harb GC, Gehrman PR, et al. Imagery rehearsal for posttraumatic nightmares: A randomized controlled trial. J Trauma Stress. Oct 2010;23(5):553–563.
36. Davenport ND, Werner JK. A randomized sham-controlled clinical trial of a novel wearable intervention for trauma-related nightmares in military veterans. J Clin Sleep Med. 2022 Oct 28. doi: 10.5664/jcsm.10338. Epub ahead of print. PMID: 36305584.
37. Stephan JT, Davenport N, Evans-Lindquist MK, Hiltner RK, Karlin DR. 1194 An Open-Label Study of Treating Traumatic Nightmares With an Investigational Smartwatch Based System. Sleep. 2020;43(Supplement_1):A457-A457. doi:10.1093/sleep/zsaa056.1188
38. Backhaus J, Junghanns K, Broocks A, Riemann D, Hohagen F. Test-retest reliability and validity of the Pittsburgh Sleep Quality Index in primary insomnia. J Psychosom Res. 2002 Sep;53(3):737–40. doi: 10.1016/s0022-3999(02)00330-6. PMID: 12217446.
39. Goel N, Rao H, Durmer JS, Dinges DF. Neurocognitive consequences of sleep deprivation. Semin Neurol. 2009 Sep;29(4):320-39. doi: 10.1055/s-0029-1237117. Epub 2009 Sep 9. PMID: 19742409; PMCID: PMC3564638.
40. Zadra A, Doneri DC. Nightmares and bad dreams: their prevalence and relationship to well-being. J Abnorm Psychol 2000;109:273–81.
41. Hublin C, Kaprio J, Partinen M, Koskenvuo M. Nightmares: familial aggregation and association with psychiatric disorders in a nationwide twin cohort. Am J Med Genet 1999;88:329–36.
42. Ohayon MM, Moreslli PL, Guilleminault C. Prevalence of nightmares and their relationship to psychopathology and daytime functioning in insomnia subjects. Sleep 1997;20:340–8.
43. Centers for Disease Control and Prevention; National Center for Injury Prevention and Control. Web-based Injury Statistics Query and Reporting System (WISQARS), 2019. Available at https://www.cdc.gov/injury/ wisqars/index.html; accessed March 2, 2020.

44. Schoenbaum M, Kessler RC, Gilman SE, et al: Predictors of suicide and accident death in the Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS): results from the Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS). JAMA Psychiat 2014; 71(5): 493–503. doi: 10.1001/jamapsychiatry.2013.4417.
45. Veterans Affairs National Suicide Data 2005-2016. Office and Mental Health and Suicide Prevention. Available at https://www.mentalhealth.va.gov/docs/data-sheets/OMHSP_National_Suicide_Data_Report_2005-2016_508.pdf#page=4
46. Bernert RA, Joiner TE, Cukrowicz KC, et al. Suicidality and sleep disturbances. Sleep 2005;28(9):1135–41.
47. Cukrowicz KC, Otamendi A, Pinto JV, et al. The impact of insomnia and sleep disturbances on depression and suicidality. Dreaming 2006;16(1):1–10.
48. Nadorff MR, Nazem S, Fiske A. Insomnia symptoms, nightmares, and suicidal ideation in a college student sample. Sleep 2011;34(1):93–8.
49. Ağargün MY, Cilli AS, Kara H, Tarhan N, Kincir F, Oz H. Repetitive and frightening dreams and suicidal behavior in patients with major depression. Compr Psychiatry. 1998 Jul-Aug;39(4):198–202. doi: 10.1016/s0010-440x(98)90060-8. PMID: 9675503.
50. Tanskanen A, Tuomilehto J, Viinamäki H, Vartiainen E, Lehtonen J, Puska P. Nightmares as predictors of suicide. Sleep. 2001 Nov 1;24(7):844–7. PMID: 11683487.
51. Ohayon M, Morselli P, Guilleminault C. Prevalence of nightmares and their relationship to psychopathology and daytime functioning in insomnia subjects. Sleep. 1997;20:340–348.
52. Creamer JL, Brock MS, Matsangas P, Motamedi V, Mysliwiec V. Nightmares in United States Military Personnel With Sleep Disturbances. J Clin Sleep Med. 2018 Mar 15;14(3):419–426. doi: 10.5664/jcsm.6990. PMID: 29510796; PMCID: PMC5837843.
53. NightWare, Inc. (2020). NightWare: Provider Instructions for Use. Hopkins, MN: Author.
54. Buysse DJ, Reynolds CF 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res. 1989 May;28(2):193–213. doi: 10.1016/0165-1781(89)90047-4. PMID: 2748771.
55. Stranges S, Dorn JM, Shipley MJ, Kandala NB, Trevisan M, Miller MA, Donahue RP, Hovey KM, Ferrie JE, Marmot MG, Cappuccio FP. Correlates of short and long sleep duration: a cross-cultural comparison between the United Kingdom and the United States: the Whitehall II Study and the Western New York Health Study. Am J Epidemiol. 2008 Dec 15;168(12):1353-64. doi: 10.1093/aje/kwn337. Epub 2008 Oct 22. PMID: 18945686; PMCID: PMC2727192.
56. Hublin C, Partinen M, Koskenvuo M, Kaprio J. Sleep and mortality: a population-based 22-year follow-up study. Sleep. 2007 Oct;30(10):1245-53. doi: 10.1093/sleep/30.10.1245. PMID: 17969458; PMCID: PMC2266277.
57. Meisinger C, Heier M, Löwel H, Schneider A, Döring A. Sleep duration and sleep complaints and risk of myocardial infarction in middle-aged men and women from the general population: the MONICA/KORA Augsburg cohort study. Sleep. 2007 Sep;30(9):1121-7. doi: 10.1093/sleep/30.9.1121. PMID: 17910384; PMCID: PMC1978404.
58. Nakajima H, Kaneita Y, Yokoyama E, Harano S, Tamaki T, Ibuka E, Kaneko A, Takahashi I, Umeda T, Nakaji S, Ohida T. Association between sleep duration and hemoglobin A1c level. Sleep Med. 2008 Oct;9(7):745-52. doi: 10.1016/j.sleep.2007.07.017. Epub 2007 Oct 24. Erratum in: Sleep Med. 2009 Sep;10(8):937-8. PMID: 17921062.
59. Gangwisch JE, Heymsfield SB, Boden-Albala B, Buijs RM, Kreier F, Pickering TG, Rundle AG, Zammit GK, Malaspina D. Short sleep duration as a risk factor for hypertension: analyses of the first National Health and Nutrition Examination Survey. Hypertension. 2006 May;47(5):833-9. doi: 10.1161/01.HYP.0000217362.34748.e0. Epub 2006 Apr 3. PMID: 16585410.
60. 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):21m14116.
61. National Center for PTSD. https://www.ptsd.va.gov/understand/related/substance_abuse_vet.asp. Accessed 8/7/2023.

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