Sarra Nazem: Thanks so much everyone for joining the webinar today. I'm so grateful to have an opportunity to have to talk about insomnia, suicide prevention, and technology for the next hour.

Before we get started, I wanted to provide the disclaimer that today's presentation is definitely based on work supported, in part, by the VA and the Department of Defense, but does not necessarily represent the view of the VA or the US government.

I'd also like to acknowledge the funding and support behind much of the work I'll present on today, which included my Department of Defense Military Suicide Research Consortium Grant and the Rocky Mountain MIRECC where I worked from 2013 to 2020.

So, here's an overview for the next 45 minutes to hour together; I wanted to just start with a very brief introduction and background about insomnia, as I'm assuming most folks are familiar with that content. And then we'll review the evidence base supporting insomnia as an empirical suicide risk factor; we'll discuss the potential mechanisms whereby insomnia may increase risk for suicide; we'll then briefly pivot to discuss cognitive behavioral therapy for insomnia to set the stage for me to then describe my current research, which has investigated the efficacy of a computerized cognitive behavioral therapy for insomnia. And then we should have some time for some Q&A too.

So, let's go ahead and get started with a little bit of background on insomnia. So, sleep has definitely become a societal and research hot topic. So, for example, if you google, like I did, "I can't sleep," over two billion hits come up; that number is so large, I had to double-check myself to verify the zeros because I wasn't quite sure. We know that the internet is saturated with tips, and techniques, and approaches to improving sleep; and wearable technologies have intensified intrigue around sleep with people now having access to sleep data in ways that were historically only available in specialty medical settings.

In addition to just general interest about sleep, it's suspected that more than 30 million people in the US are believed to have some kind of sleep disorder; these sleep disorders can affect things like our health, relationships, and work, giving us our initial window into thinking about why sleep matters to both clinical and research endeavors, and suicide prevention.

As many of you likely know, insomnia refers to a dissatisfaction with sleep quality or quantity, which involves difficulties with initiating sleep, maintaining sleep, which can include frequent awakenings, or trouble falling back asleep, or early morning awakening with an inability to return to sleep.

In the US general population, it's suspected that about one-third of adults report insomnia symptoms. When we think about insomnia as a diagnosis, however, which would involve clinically significant distress or impairment with frequent-- which is defined as more than three nights a week--and a chronic course, which is more than three months, it's estimated that somewhere between 6 to 10 percent of those that have symptoms would actually meet diagnostic criteria for insomnia.

In addition to insomnia being distressing and impairing in and of itself, it's also true that insomnia is a partner in crime with many other medical and psychological disorders. Impaired sleep is often a symptom of other diagnoses, and we often see clinically, comorbidity, where insomnia disorder is present along with another disorder.

So, taking a look at the US general population again, it's estimated that somewhere between 40 to 50 percent of individuals present with a comorbid mental health disorder when they also have insomnia disorder, which is, of course, a really high, kind of strikingly high rate here. We also know that this kind of comorbidity exists in veteran populations too. For the sake of time, I'll only highlight two common disorders we see in the veteran population as a mini window into the common comorbidity we see in veterans with insomnia symptoms.

So, first, veterans with mild TBI, it's estimated that somewhere between 40 to 65 percent of veterans with mild TBI report symptoms of insomnia; when we take a look at veterans with PTSD, we see that anywhere between 44 to 90 percent, which is a strikingly large range of veterans with PTSD also report difficulties falling asleep or staying asleep. Now that we have had just a very quick--and that was really quick--but a basic overview on insomnia, its prevalence, and its comorbidity, what I wanted to do next is take a look at what we know about insomnia as it relates to suicide risk.

So, empirical data has consistently demonstrated that insomnia is an empirical risk factor for suicidal ideation and self-directed violence. To help us evaluate the evidence base, though, I'm going to introduce my friend, Puzzle Panda, who is a well-known scientist that engages in healthy scientific skepticism to help us break this down. So, as we go ahead and break this down, Puzzle Panda's first question might be, "Well, in what samples have we found empirical data?" So, what we can see is that data supports this association across samples including community-based, college, as well as clinical samples.

Good Panda scientists will then come back and ask, "Well, using what methodology?" Again, we see support across various methodological designs including cross-sectional prospective and longitudinal. And then Puzzle Panda might ask, "Well, what about its systematic reviews or

meta-analyses that can account for study bias?" So, she's really sharp and on her game today; and we can let Puzzle Panda again know that this association has maintained a meta-analysis that can account for study biases.

So, for example, even after accounting for comorbidity, there's about a two times increased risk for suicidal ideation, attempt and death in those with insomnia. Based on what I described earlier, it's important to also determine whether findings hold when we examine individuals with comorbid psychiatric diagnoses such as depression, PTSD, or mild TBI and insomnia. Data suggests that these individuals are more likely to endure suicidal ideation and engage in self-directed violence at a 2.66x risk compared to individuals with psychiatric disorders and no insomnia-related symptoms or diagnoses. I do want to note here that additional research is necessary to determine the direct and indirect ways that insomnia confers risk for suicide; I encourage you all to check out Todd Bishop's recent work to learn a bit more about these important future directions.

Finally, the last bullet on the slide, we know that persistent symptoms of insomnia are associated with increased odds of depression and suicidal ideation, suggesting the need for early identification and treatment to reduce future negative outcomes such as self-directed violence.

Although the empirical base is constantly growing and advancing due to improved methodological approaches, in sum, what we know is that there's robust data to support that insomnia is indirectly a associated with suicide risk, and some evidence to support that there may be a direct and independent association as well. The important takeaway is that insomnia is linked with suicide risk in many ways, implicating it as a key empirical suicide risk factor.

It's also important to examine whether these findings hold in-service member and veteran populations as well. This is critical as these two populations are often characterized by complicated medical and mental health comorbidity; and, of course, are at greater risk for suicide compared to the general population.

Empirical support for insomnia as a robust independent risk factor holds when examining military populations. So, for example, in one study, even after controlling for depression, hopelessness PTSD diagnosis, anxiety symptoms, and drug and alcohol use, insomnia still conferred unique variants when explaining suicide risk. Those of you that are on the up and up in the suicide research world know that these same variables that are listed here on the slide that I just read out are independent risk factors for suicide, demonstrating again the potency of insomnia in this association.

Insomnia symptoms at baseline have also been found to independently predict suicide attempts one month later; this was found in a model that also included key suicide risk factors.

And then finally, as depicted here in the last set of bullets, Wil Pigeon and colleagues have also found that VA-utilizing veterans with sleep disturbances including insomnia died sooner by suicide after their last VA visit compared to veterans without sleep disturbances. This model did account for psychiatric and substance abuse comorbidity as well. This 100-day difference you see on this slide translates to sleep disturbances predicting a 57 percent loss in survival time, again, an important clinical takeaway for us.

When we work with individuals clinically and they report sleep disturbances like insomnia, we need to be assessing for and thinking about suicide risk.

At this point, I hope I've provided some robust support that chronic sleep difficulties, including insomnia, is a significant public health and clinical problem affecting our patients and also our research participants. What I'd like to do next is visually depict what I just reviewed to drive home the fact that insomnia confers risk for suicide in multiple ways across the suicide risk spectrum.

So, if we imagine this hypothetical line depicting a continuum of risk for suicide, we know that there are many risk factors that are associated with this risk. What I'm going to do next is show all the ways that insomnia will confer risk along this hypothetical continuum of risk.

First, insomnia may proceed or confer additional risk of subsequent psychiatric symptoms; we also know that insomnia can exacerbate psychiatric symptoms and diagnoses, including key suicide risk factors. Of course, really good VA clinicians will utilize evidence-based therapies or EBTs to reduce risk for suicide but we also know that insomnia often impedes the ability to meaningfully participate in our evidence-based therapies; and even after successful delivery of evidence-based therapy, poor sleep remains at clinical levels and can continue to adversely impact functioning. And, as I mentioned before, there's some evidence to support that insomnia is also an evidence-based independent and direct risk factor for suicide.

The next logical question then is why? Understanding what drives this relation is not only mechanistically important to the science of suicidology, but also clinically informative to our interventions as clinicians. Over the next few slides, I'm going to highlight several potential mechanisms whereby insomnia may increase risk for suicide.

Note that some of the science behind this work has begun but much more is necessary to move us forward.

First, insomnia may cause impairment of stress appraisal processes, coping mechanisms, or interrupt the consolidation of emotional memory processing. Those of you familiar with emotion regulation will, of course, recognize that these are key mechanisms that can increase susceptibility to psychiatric disorders and risk for self-directed violence by impairing emotion regulation and emotional processing abilities.

There's also evidence to suggest that nocturnal wakefulness may be an underlying mechanism associated with increased suicide risk. Perlis and colleagues did some great pioneering work in this space by conducting an analysis that accounted for the proportion of the population awake at each clock hour, and found that although the largest number of suicides occurred during the day, typically peaks at noon, when the proportion of people awake at each hour is taken into account, a disproportionate number of suicides occur at night.

We replicated their methodology in a veteran sample and also found that the peak of veteran suicides fell between the hours of 10 AM and noon; but after accounting for the population awake, the peak proportion of suicide shifted to the early morning hours between midnight and 3 AM.

So, why might this be? First, we know that nocturnal wakefulness and sleep loss impairs top-down regulatory systems observed by both reduced functional activity in the prefrontal cortex and by impairment in executive functioning. This can further exacerbate emotion regulation difficulties, which we know are a key prospective mechanism from the previous slide; and then taking it one step, further impairment in these domains may increase impulsivity and decrease problem-solving abilities, which may be particularly dangerous factors during nocturnal time periods where social support and coping mechanisms may be harder to engage.

Finally, in an area where I'm definitely not an expert but is worth noting, we know that physiological and biological processes such as inflammation, abnormal serotonergic pathways, and agitation are also three examples of long-term as well as acute risk factors for self-directed violence which are affected by sleep disturbances.

Future research is necessary to ascertain the temporal element of all of these mechanistic pathways that I briefly highlighted, specifically whether acute insomnia versus chronic insomnia and how that confers risk in differential and clinically meaningful ways.

So, given these shared pathways of susceptibility, I strongly believe that treatment for insomnia is essential to reduce suicide risk, and therefore may be an especially promising approach to decreasing mechanistic processes that confer risk for suicide. In addition to improving insomnia-specific outcomes, sleep interventions therefore, are critical to suicide prevention approaches.

So, what I want to do is just highlight the many different ways that insomnia treatment is relevant to suicide prevention. But before I go there, just a quick overview on suicide prevention strategies.

So, those of you that are familiar with public health models know that suicide prevention strategies can target a range of populations, starting with Universal, which is targeting an entire population; Selective, which is targeting subgroups of the population that are determined to be at increased risk for suicide; and then Indicated populations, so those that are at highest risk.

What's notable is that insomnia interventions can be utilized across the entire range of prevention approaches, and this is notable because, first, we continue to face difficulty, both as clinicians and as researchers, at predicting who will fall into the indicated population. Furthermore, if we concentrate too heavily on indicated populations, that precludes the opportunity for us to prevent the initial development of mechanisms that underlie heightened risk for self-directed violence.

So, I argue by focusing in on insomnia, we can extend the range of our interventions to approach in both downstream and upstream waves; this is especially essential to suicide prevention as this ultimately means that we can target larger and larger cohorts to have the greatest potential impact on the overall rates of suicide.

So, now, that we've made the case that insomnia is prevalent and bad and it's associated with suicide risk empirically, likely due to important shared important shared mechanisms, the next question is what can we do about it? And that's where cognitive behavioral therapy for insomnia, or CBT-I, for short comes in.

CBT-I works by targeting maladaptive behaviors and dysfunctional thoughts that are believed to perpetuate sleep problems. In 2005, the National Institutes of Health State of the Science Conference on insomnia identified CBT-I as a first-line treatment, given that CBT-I was found to be as effective as prescription medications for the short-term treatment of insomnia. As such, I'm going to award a star for this finding.

Moreover, researchers have found that the effects of CBT-I last longer than those seen with sleep medications, so we're going to award a second star. We also know that reducing use of medications is critical, especially within specific veteran cohorts, as there's increasing data to suggest that over-reliance on benzodiazepines and opioids in these populations, and evidence that rates of suicidal ideation may be elevated in individuals that report insomnia and take medication hypnotics. So, I'm going to award a third star in favor of CBT-I.

Aside from my informal star awarding, which likely does not have the rigor that Puzzle Panda and you all might be looking for, it is true that researchers and clinicians typically regard CBT-I as the best treatment for insomnia, both for short and long-term gains, especially when considering the side effects and potential risk for drug interactions that may come with insomnia medication use. In terms of the evidence space behind CBT-I, it's quite robust; as I mentioned before, it's typically the treatment of choice; empirical data suggests that somewhere between 70 to 80 percent of individuals will obtain benefit from CBT-I, which those of you that are familiar from psychotherapy research know that those are really, really high rates. We also find large effect sizes in advocacy and effectiveness studies; and as I'll talk about a little bit later, there are also sustained gains. So, oftentimes, people have their gains out to at least one year out.

When we think about CBT-I in relation to suicide risk, what's critical is that CBT-I components such as sleep restriction and cognitive restructuring directly target those theorized mediators and mechanisms underlying the association that we discussed between insomnia, and suicidal ideation, and self-directed violence. In support of this proposition, CBT-I has actually been found to be associated with decreases in suicidal ideation, so using longitudinal data from over 400 veterans, every seven-point decrease in the Insomnia Severity Index achieved during CBT-I was associated with the 65 percent reduction in odds of suicidal ideation. CBT-I also leads to benefits beyond insomnia symptom reduction including improvement in overall well-being and reduction of depressive symptoms.

What's important is that because CBT-I can rapidly and significantly improve insomnia symptoms, as well as comorbid symptoms like suicidal ideation and depression, CBT-I is an especially promising candidate for use in suicide prevention approaches.

However, there are unfortunately several barriers that veterans, as well as non-veterans, face when attempting to access care for insomnia. These barriers include scheduling and travel demands, stigma, having enough trained evidence-based therapists to meet treatment demand, which can lead to delays before having the opportunity to receive an evidence-

based treatment. Dominant models of delivering treatments like face-to-face interactions are incapable of meeting treatment demands of all those that seek care. This seems obvious now due to the pandemic; but when we pitched the grant I'm about to discuss, there was still some reluctance and hesitancy for how to best incorporate technology to meet treatment demands. But what we know is that leveraging technology to meet treatment demands is consistent with service delivery models based upon step care principles.

So, as depicted here in this triangle on the slide, stepped care principles argue that the least complex and most successful intervention from which treatment benefit is likely to be provided up front to a large number of people by utilizing self-administered approaches. This means that the greatest number of individuals here depicted at the bottom of the pyramid who need treatment can receive treatment without long waits or significant hardships.

One way to accomplish that goal is to utilize computerized cognitive behavioral therapies that provide the opportunity to engage in an evidence-based therapy via the computer or the internet. Computerized CBTs are low-cost, they're scalable, adaptive, and effective, so they would allow the VA to offer access to evidence-based care 24/7. I don't have time to go into this today, but I do want to note that computerized CBT-Is have comparable effects when compared to face-to-face CBT-I or other types of CBT, with effect sizes ranging from 0.2 to over 1.

Again, after experiencing kind of one and a half years of this pandemic, it seems obvious that we would rely on and need technology to help us in healthcare. What's exciting is that we designed and executed the study that I'm about to describe during a time when we could have never expected how important and how quickly we would need to integrate technological solutions in our healthcare system.

Back in 2017, the DoD funded us to embark in the first study examining a computerized CBT-I called Sleep Healthy Using the Internet, or SHUTi, for short, in a veteran population.

The leading example of a computerized CBT for insomnia at the time was SHUTi. and as depicted here in this table, there's been a general consensus on the importance of empirically examining SHUTi. So, small-scale studies initially in select populations demonstrated feasibility and efficacy of the intervention; larger studies then examine issues of cost in SHUTi as a prevention tool for major depressive disorder; no RCT, however, had examined the efficacy of SHUTi for military or veteran populations; further, no studies had examined suicide specific outcomes.

There is skepticism that a technology-based solution would not potentially work as well for non-civilian populations.

A little bit about SHUTi. It's based upon face-to-face CBT-I, which consists of six cores that allow for movement through the intervention based on a time and event-based schedule. Content is individually tailored and includes interactive elements that have been found to be associated with greater treatment engagement and adherence. During the RCT, the commercial company that held a license for SHUTi, which is BeHealth Solutions, was acquired by Pear Therapeutics, who have now received FDA approval and transitioned the intervention to be mobile-based, and it's now called Somryst; so, just a heads-up in case you wanted to check it out after this webinar, that the product no longer exists as SHUTi, but is now called Somryst and is provided by Pear Therapeutics.

So, despite the strong background identifying insomnia as an evidence-based risk factor for suicide, the depth and breadth of support for CBT-I, including its association with reducing suicide risk and mounting evidence supporting the use of computerized CPTs, especially for treatment of insomnia; as I mentioned, no RCT prior to ours had examined SHUTi in military personnel or veterans.

So, our aim for this particular grant was to determine the efficacy of SHUTi, specifically among OEF/OIF/OND veterans using a two-group, the SHUTi versus the educational website control for timepoint longitudinal RCT design.

Our primary and second year secondary outcomes involved examination of insomnia symptom severity, as well as physical and mental health functioning; our exploratory analyses included evaluation of outcomes like suicide risk, depressive anxiety, and PTSD symptoms.

So, our RCT was designed to produce data to inform direct application to insomnia as well as important comorbid symptoms like suicidal ideation across the short and long term. So, specifically, the follow-up that we had in this RCT which was out to one year, was a significant strength of the methodological approach.

Today, just for the interest of time, I'm going to focus specifically on the insomnia symptom findings, as well as some of our exploratory findings; but know that there's much more, so let me know if you're interested during the Q&A or even afterwards via email.

So, this is our consort diagram. What I'm going to do is quickly walk through some highlights of our accomplishments as well as our design. So, we began the trial by screening 844 interested veterans; this yielded

289 veterans that were eligible for the study, exceeding our initial target which was 250. After accounting for potential attrition due to lack of interest, timing, and not meeting sleep diary prerequisites that were part of the study design, we needed to randomize 226 participants, and we exceeded that by randomizing 231. We utilized a very conservative attrition estimate of 25 percent, which, in tandem, with our power analysis meant that we needed to have at least 168 participants complete assessment; we exceeded that by 20 with 188 participants completing post.

Similarly, for six months and 12-month follow-up we were aiming for at least 126 participants to complete these follow-up assessments, and we exceeded that again by collecting 164 post-assessments at 6 months, as well as 12 months. So, in summary, just to have in the back of your mind, we're able to meet all of our goals and our RCT were adequately powered and had solid response rates with all of our participants even at the one-year mark with decently low attrition.

This is a high-level demographics table here to give you a quick glimpse of our sample. First and importantly, you can see that randomization worked which is exciting; the researchers in the crowd, you know you can trust this, but you never know until you know, right? So, it came out in the way that you'd expect as there are no differences between the two groups.

On average, our participants were just about 40 years old; three-fourths of them identified as male and white, and a little under one-fifth of the sample identified as Hispanic. Even though this was an OEF, OAF, OND cohort specifically, you can see that the majority of the sample had deployed. We also stratified on the suicide attempt variable which you can see in the last row; and as you can see, 20 percent of the sample reported a past suicide attempt.

When it comes to computerized or technology-based methods for service delivery, the current literature is pretty inconclusive as to how much support is necessary when you use these types of modalities. Before I highlighted our results, I wanted you to know that the methodology we employed utilized a true hands-off engagement during the intervention window. So, in other words, my fantastic research assistants, who are fantastic, were not calling to remind people to complete a core, were not providing motivational interviewing or any kind of support strategies to facilitate behavioral engagement during the intervention window. Instead, we relied solely on the SHUTi program itself which utilized things like email reminders to help promote engagement.

So, the results that I'm about to present then were the outcomes from an intervention that was truly self-administered, so keep that in mind.

To begin, I wanted to first show this line graph which depicts the change in insomnia symptom severity as measured by the Insomnia Severity Index across our four timepoints and by group. I'm going to present the statistical analyses next; but from this graph, you can see that both groups began at moderate levels of insomnia severity, but the SHUTi group moved from this moderate symptom severity to self-threshold symptom severity between baseline and all the follow-up time points; whereas the educational website control participants, on average, did not experience a reduction in insomnia severity.

Importantly, as you can see depicted here in the graph, gains achieved were maintained long term with the SHUTi group remaining stable and their average gains even out to one year.

In our main intent to treat analysis examining the Insomnia Symptom Severity Index, again as measured by the ISI, our models took a look at the change from baseline to Time 2, Time 3--as a reminder, six months; and Time 4, which again, was 12 months. These models account for baseline Insomnia Symptom Severity Index scores and history of suicide attempts. Those of you that are familiar with statistical procedures, I wanted to share that we use the home sequential procedures to adjust P-value thresholds to take into account all nine outcomes, which included our primary and secondary outcomes.

In addition to the parameter estimates that are provided here on the table, we also provide generalized eta and omega squared values, which are effect size estimates that can be compared across studies; and just for your reference, a small effect size is 0.02, medium is 0.06; and large is 0.14.

So, as displayed in the previous graph, SHUTi participants experienced statistically significant pre-to-post decrease in insomnia symptom severity compared to the educational left-side control participants across all timepoints; this was on the cusp of a large effect for Time 2, as well as Time 3; and a medium effect for Time 4. So, in sum, these data supported our hypotheses.

For the sake of time, I'm not going to present in-depth or analyses that utilized a per-protocol analysis, but I did want to share the effect sizes of those analyses to demonstrate that when our participants engaged in four or more of the six SHUTi cores, which is considered the clinically significant dose, and was two-thirds of our sample, the findings that are displayed here in this table were maintained, and we saw stronger effect sizes as you'd expect.

So, I just put these up the effect sizes for that protocol analysis. So, you can see when you compare these side by side, these effect sizes suggest

that for those that engage in more of the intervention, they will likely have an even greater impact on their immediate as well as long-term insomnia symptom severity. So, we saw that initial kind of concept of a large effect definitely moved to a large effect at Time 2; medium to large effect at Time 3 as well as Time 4.

Statistical significance aside, as a clinician, I find it important to examine the clinical significance of these results. These graphs here up on the slide depict the proportion of each group by insomnia symptom severity category across our four timepoints. So, starting in the upper left-hand corner at Time 1, we see a similar distribution and insomnia severity between the two groups with 65 percent of the SHUTi sample and 64 percent of the educational control sample reporting clinically significant insomnia.

At Time 2, what's exciting is that we see a greater percentage of shadow participants moving into the no clinically-significant symptoms, which is depicted here in this dark navy-blue area, and this is 31 percent of the SHUTi sample versus 4 percent of the educational control group. This points to the quick and immediate gains during the intervention window that some of our SHUTi participants experienced. Relatedly, we see a reduction of only 33 percent of the SHUTi sample now endorsing clinically significant insomnia versus 50 percent in educational website control.

Moving down to Time 3, we saw maintenance and some increased gain of SHUTi superiority and the no clinically significant symptom category, which at Time 3, was 38 percent of the SHUTi group versus 7 percent of educational group. Again, we see 38 percent of the educational control sample; at Time 3, we're still endorsing clinically significant insomnia compared to only 27 percent of the SHUTi sample.

And then, finally, at Time 4, we see continued maintenance again with 41 percent of the SHUTi sample, and that no clinically significant insomnia category versus 13 percent; and then similar to six months, the proportion that endorsed clinically significant symptoms stayed nearly equivalent in favor of SHUTi with 27 percent versus 41 percent.

I want to feature this clinical significance piece in two other ways. The first is taking a look at the literature including previous SHUTi trials, treatment responders have been defined as those who experience a reduction of more than seven points on the ISI. So, as you'll recall, this aligns with the seven-point increments that designate levels of insomnia severity that we just took a look at in a couple of different graphs. So, the findings displayed on this graph support that SHUTi participants experience clinically significant changes when compared to educational control participants, with a much larger proportion of SHUTi participants

achieving the definition of treatment responders at each of the three timepoints compared to educational control participants.

To say it another way, this means that SHUTi participants experience meaningful changes in their insomnia severity, not just two to three-point decreases on the ISI, which could be statistically significant but perhaps, not as clinically meaningful.

Next. Again, in the literature, there have been a couple of different cutoffs utilized to indicate insomnia remittance as assessed by the ISI. Using perhaps the most stringent definition, which defines insomnia as a score of seven or less in the ISI, we found that participants randomized to SHUTi were more likely to achieve this definition than the educational control participants at each of the subsequent time points. Time 2 is 30 percent is versus 40 percent; Time 3, 37 percent versus 7 percent; and then Time 4, 40 percent versus 13 percent. Again, we see stability of the finding across the one-year time frame.

Sleep diary findings, which are presented here for pre to post, were also all in favor of the SHUTi group. Notably, you can see that the educational control participants did improve in some of these indices, indicating that they may have benefited from the educational information provided and/or the mere tracking of sleep data, which some argue can be an intervention in and of itself, may have been helpful. Starting off on the upper left-hand side with the side and the sleep onset latency, or, SOL, we found statistically significant differences between pre and post, with SHUTi participants having an average mean decrease of 30 minutes in their sleep onset latency compared to educational control participants; this was a small to medium effect.

Next, taking a look at Week After Sleep onset, which includes Early Morning Awakenings, or WASO-EMA, SHUTi participants, on average, their Week After Sleep Onset decreased by 25 minutes compared to educational website control; this is a small effect.

Left-hand side, time in bed. About a half-hour change in SHUTi participants for their time and bed was observed with relatively no change in the educational website control group, and this is a medium-to-large effect. For those of you that do CBT-I, you know that this is exciting, the idea that sort of time and bad reduced for our participants with all the other data, means that they're gaining back a half-hour of their life to do something else, and so that's always exciting to see.

And then finally for sleep efficiency, we observed about a 10 percent average improvement for SHUTi participants; notably, we see that the educational website control group also improves sleep efficiency, so this difference was just a small effect.

Again, I'll note that the findings were similar for that for protocol analysis, which took a look at only SHUTi participants that completed four or more cores. The same pattern of findings, but, again, incrementally stronger effect sizes.

Next, I'm showing some graphs here depicting our exploratory Intent to Treat analyses. Starting with the Back Depression Inventory in the upper left, we see our best outcomes where SHUTi participants, on average, move from moderate depressive symptoms at baseline to minimal depressive symptoms, and we saw significant differences in SHUTi participants for baseline to six months and baseline to 12 months.

For the Beck Anxiety Inventory, we see minimal change for both groups who, on average, started the intervention with mild anxiety symptoms. So, just from a statistical standpoint, it's going to be hard to pick up an effect here with most participants having mild symptoms. We did find a significant difference in SHUTi participants for baseline to 12 months only.

On the bottom left-hand side, the Adult Suicidal Ideation Questionnaire, evidence of a pre- to post-intervention difference for SHUTi participants; however, ASIQ scores did not differ at the follow-up time points.

And then on the PCL, so measuring PTSD symptoms, researchers and clinicians suggest that a five-point change on the PCL is the minimum threshold for determining whether an individual has responded, with 10 being a clinically meaningful change. We observe that SHUTi participants roughly achieved that change in their baseline from two, six, and 12 months.

Notably, when we zoom out and take a look at these graphs, one thing that we've really observed is that for the most part, comorbidity did not decrease until our longer-term follow-up time points, with the exception of suicidal ideation, suggesting that, at least for our sample, veterans may have needed additional time beyond the nine-week intervention window to see the impact on comorbid symptoms.

Finally, again, that presented here I wanted to mention that when we examined these analyses using the per protocol approach, findings were very similar. We did see larger effect sizes for depression, picked up a pre-to-post difference for anxiety, and a 12-month difference for the ASIQ. This may suggest that when SHUTi participants receive the clinically adequate dose, they may be more likely to experience reductions in depressive symptoms, have improvements in immediate anxiety, and longer-term changes in suicidal ideation.

So, in short, our RCT supports the use of a computerized CBT-I for OEF/OIF/OND veterans; that the data that we have dispels some of the concern that, I think, this type of intervention wouldn't be associated with improved outcomes, and a population often characterized as dissimilar due to their complex comorbidity and presentation compared to civilian samples. Our RCT also supports that insomnia interventions delivered via technology are efficacious and reducing insomnia symptoms severity and comorbid symptoms, and this is the case even when using an intervention that did not involve clinician support or engagement during the actual intervention.

We found that our outcomes are even more pronounced when individuals engaged in the intervention to receive an adequate dose, which makes sense; our data also support that insomnia interventions are associated with depressive symptom reduction, as has been seen in the literature for non-technology delivered CBT-I.

Not presented here today, but I did want to note that our data only partially supported our hypotheses that participants randomized to SHUTi would report improvement in physical and mental health functioning compared to participants who are randomized to educational website control. We plan to look into these results a bit further to ascertain if there are participant characteristics driving the differences. I'm sure that those of you that have attempted to assess general mental and physical health functioning studies can attest to the fact that these are challenging constructs to measure, as the factors that can contribute to these metrics are multi-determined. So, for example, factors like pain, social support, physical abilities, just to name a few, can influence these indices. So, it's a tricky construct to assess for, but an important one.

So, our major takeaway was that our hypothesis was confirmed, specifically that technology-based delivery of CBT-I mitigated insomnia severely in a population characterized by complicated comorbidity. So, the next steps involve examining the timing of insomnia interventions for veteran and military populations; there are so many questions around implementation that stems from this work and other important work being done in the field. So, self-administered options are available, do we offer that just upfront to people; do we offer that combined with in-person treatment, something different? How do we go about that?

And another important question that remains is whether there are specific profiles that are most associated gains? This is something that our group plans to do with our data.

I think in this future work, some thoughts that come to mind are needing to examine, in our data, as well as in other studies, who doesn't improve and why? And so, clearly, there was a portion of our sample that didn't

improve. So, was this due to lack of engagement; was it due to the intervention; was it due to comorbidity something else. We also had incredible interest in the study, but another important question is which of our veterans are not interested in self-administered approaches and why and how can we learn from that to inform our implementation approaches. And then, again, we have low attrition and the most commonly endorsed reason for termination in our RCT was lack of time; but again, how can we utilize this information and these data to inform treatment planning and share decision-making with our veterans when we utilize technology and our clinical practice?

I also wanted to share some preliminary data that we took a look at to support the use of computerized CBT-Is in not only universal and selective populations, but indicated populations too. So, to support an NIH submission that is going to examine the advocacy of a mobile CBT-I and a sample of veterans at elevated risk for suicide, we took a subgroup of our participants from this RCT, which were 50, who had reported moderate to severe ISI scores, as well as moderate to high suicide ideation scores, to determine whether SHUTi was efficacious in reducing insomnia symptom severity and suicide ideation in this higher risk group.

So, what we found first is that participants that receive SHUTi experience a greater reduction in ISI compared to control participants, and this is a large effect size. Further, we also found in the second graph that veterans randomized to receive SHUTi reported a reduction in ideation that was equivalent to a moderate effect size.

And then among those for whom the intervention resulted in a significant ISI reduction, which, this was more than eight points on the ISI, the reduction in suicide ideation was even more pronounced with a robust effect size of nearly 1.
So, obviously, this is just a small mini subsample definitely not powered nor designed to take a look at these kinds of outcomes in this way; but along with the full data I presented on today, I'm hoping that our data, as well as other data in the field, really demonstrate some promising support for the role of insomnia interventions in ongoing suicide prevention efforts, whether that be upstream or downstream.

Alright. So, with that, I'll say thank you and see what kinds of questions we have.

Coordinator: Fantastic. We do have a few pending questions here; I'm just going to start at the top and work my way through. For the audience, if you do have any questions, please use that Q&A screen in Webex to submit those questions into us.

The first question that we have here, "If you have this info available, what were the most common reasons why interested veterans were not eligible after the initial screen?"

Sarra Nazem: At a time, years ago, I used to have it memorized; but for the most part--and I can definitely follow up for whoever asked this question too if you want to be in touch--some of it involved people just not meeting diagnostic criteria of insomnia, so that was the biggest one, so people that had insomnia symptoms but didn't have either more than three nights per week or a three-month course so that was the biggest one. Next, I think, was trying to think a little bit of there was some individuals that had medication changes but we were able to kind of get them back in, so I think the next leading one was just kind of lack of interest in people not wanting to basically do the extra requirements that came with the research study to some of the sleep diary pieces, and kind of knowing that. So, the biggest thing was just people not meeting diagnostic criteria.

Coordinator: Thank you. The next question that we have here, "Can or should Somryst be shared as a resource with veterans who receive care at the VA; does it cost the veteran any money?"

Sarra Nazem: Yeah, that's a good question. So, yes, it would cost money. So, this is a commercial product which is one of the limitations for the RCT that we have as it relates to our veteran population. So, a veteran, if interested, could kind of independently pursue purchasing the app and pursuing intervention that way. I would suggest and take a look at some of the VA options that the National Center for PTSD has offered, like Insomnia Coach as a potential VA alternative, that might be a good option as well.

There are also things like CBT-I Coach which typically are done in unison with face-to-face treatment; but Insomnia Coach is another one to take a look at. There's also Path to Better Sleep which is a CBT-I protocol that is web-based and that's another option to check out.

Coordinator: Great. Thank you. And the next question, you may have just covered this here, but very similar to what the information just gave there, "Can you speak to how this intervention is similar or different to Insomnia Coach or Path to Better Sleep?"

Sarra Nazem: Yeah, I'd say that pretty similar; I haven't seen Insomnia Coach to the detail to talk specifically about the ins and outs, but my understanding is designed Insomnia Coach will be very similar to what we used as SHUTi; I think, potentially, Insomnia Coach may be even a better fit since that was tailored and designed for veterans and military personnel.

Path to Better Sleep has a little bit of a different setup when it comes to sleep restriction, based on sort of the nuances there. So, that's one subtle difference in actual intervention; but I'd say that they're all sort of similar in the same kind of area of a menu, if you imagine that, for self-administered approaches, and I think that there is some research going on to examine Path to Better Sleep and Insomnia Coach specifically to demonstrate efficacy and effectiveness.

Coordinator: Thank you. That is all of the questions that we have received in. Dr. Nazem, do you have any closing remarks you'd like to make, and then we can close the session out?

Sarra Nazem: No, just thanks so much for everybody for joining for the webinar; definitely feel free to be in touch if you have any additional questions, especially for the first individual that was looking for specific data on why people weren't interested. I can actually get to that with some fidelity by taking a look at the data that we have.

But I hope that people can use the kind of nine extra minutes to maybe do some self-care or just take a breath. But thank you so much for joining and appreciate all that you are doing for veterans.

Coordinator: Great. Thank you so much, and thank you so much for taking the time to prepare and present the session; we really do appreciate it.