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Prevention of Post Intensive Care Syndrome-Family with Sensation Awareness Focused Training Intervention: A Randomized Controlled Trial Pilot Study

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Prevention of Post Intensive Care Syndrome-Family with Sensation Awareness Focused Training Intervention: A Randomized Controlled Trial Pilot Study

by

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DEDICATION

To my loving husband Paul Cairns, a strong and gentle soul who taught me to believe all is possible. To my late brother Aaron Miller, an honorable man whose sacrifice for our country led me to Accelerated Resolution Therapy and Sensation Awareness Focused Training. To my loving parents Eddie and Avis Miller, their pain and loss led me to Post Intensive Care Syndrome-Family. To my aunt Earlene Searcy, for loving me unconditionally. To my late grandmother Bonnie Sherrill, a great role model. To my late best friend Jerry Tiblier, an evolved soul and guardian angel. To my beloved nephew Seth Miller and his beautiful family, who make my heart smile. Lastly, to the rest of my friends and family who have supported me throughout this all-consuming journey – my love to everyone!

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LIST OF ABBREVIATIONS

Abbreviation:	Explanation:
APA	American Psychiatric Association
ART	Accelerated Resolution Therapy
ASD	Acute Stress Disorder
COPE	Creating Opportunities for Parent Empowerment
EMDR	Eye Movement Desensitization and Reprocessing
HADS	Hospital Anxiety and Depression Scale
ICU	Intensive Care Unit
IES	Impact of Event Scale
NIH	National Institutes of Health
PI	Principal Investigator
PICS	Post Intensive Care Syndrome
PICS-F	Post Intensive Care Syndrome-Family
PSS	Perceived Stress Scale
PTSD	Posttraumatic Stress Disorder
RCT	Randomized Controlled Trial
SĀF-T	Sensation Awareness Focused Training
SAMHSA	Substance Abuse and Mental Health Services Administration
SCCM	Society of Critical Care Medicine

ABSTRACT

Post Intensive Care Syndrome-Family (PICS-F) refers to acute and chronic psychological effects of critical illness on family members of patients in intensive care units (ICU). Evidence about the increase and persistence of PICS-F warrants the need for prevention interventions. This study evaluated the feasibility of providing Sensation Awareness Focused Training (SĀF-T) during the ICU stay for spouses of mechanically ventilated patients. Methods: A randomized controlled trial of SĀF-T versus a control group was conducted (n=10) to assess safety, acceptability, feasibility, and effect size of the intervention on PICS-F symptoms. Symptoms assessed as outcome measures included stress, anxiety, depression, posttraumatic stress disorder, and sleep efficiency. Those randomly assigned to SĀF-T received one session daily over 3-days in the ICU. Repeated measures (day 1, day 3, day 30, and day 90) of PICS-F symptoms in both groups were analyzed. Results: Mean age was 58 ± 12 years; 70% were female. Feasibility success criteria were met in weekly recruitment (8 ± 3.5), enrollment rate (67%), SĀF-T acceptability (100% of doses received, no adverse events) with significantly lower post SĀF-T stress levels (p<.05) compared to pre SĀF-T stress levels, ActiWatch acceptability rate (90% agreed to wear, no adverse events) with no significant difference in sleep efficiency between groups (p>.05), and repeated measures completion rate (>90%). Conclusions: This study provided guidance for modifications to protocol outcome measures and evidence of a large effect size, which will inform a larger clinical trial to assess the effectiveness of the SĀF-T intervention in reducing PICS-F.

CHAPTER ONE:

BACKGROUND

Post Intensive Care Syndrome

More than 5.7 million patients are admitted to intensive care units (ICU) each year in the United States (Society of Critical Care Medicine [SCCM], 2015). Surviving critical illness is a turning point in the lives of patients (ICU survivors) and their families. SCCM (2013) identified a cluster of complications from experiencing critical care that occur in both ICU survivors and their family members, as Post Intensive Care Syndrome (PICS) with an added "F" to represent presence in family (PICS-F). PICS is defined as new or worsening impairment in physical (ICU-acquired neuromuscular weakness), cognitive (thinking and judgement), or mental health status arising after critical illness and persisting beyond discharge from the acute care setting. PICS-F refers to acute and chronic psychological effects of critical illness on family members of the patient and includes symptoms that are experienced by family members during the critical illness, as well as those that occur following ICU discharge or death of a loved one in the ICU (Rawal et al., 2017). In the context of the study, family is defined by the patient, as related or unrelated individuals who provide support and with whom the patient has a significant relationship (Davidson et al., 2017). Spouse is defined by the patient as the individual with whom the patient has a significant intimate relationship.

PICS conditions convey substantial burden including decreased quality of life and significant physical, cognitive, and psychological impairment. Specifically, PICS conditions

include ICU-acquired weakness; problems with executive function, memory, and attention; ongoing anxiety, depression, and posttraumatic stress disorder (PTSD). These symptoms may occur in a variety of combinations. Furthermore, Figure 1 exhibits how PICS conditions vary among ICU survivors and their family members.

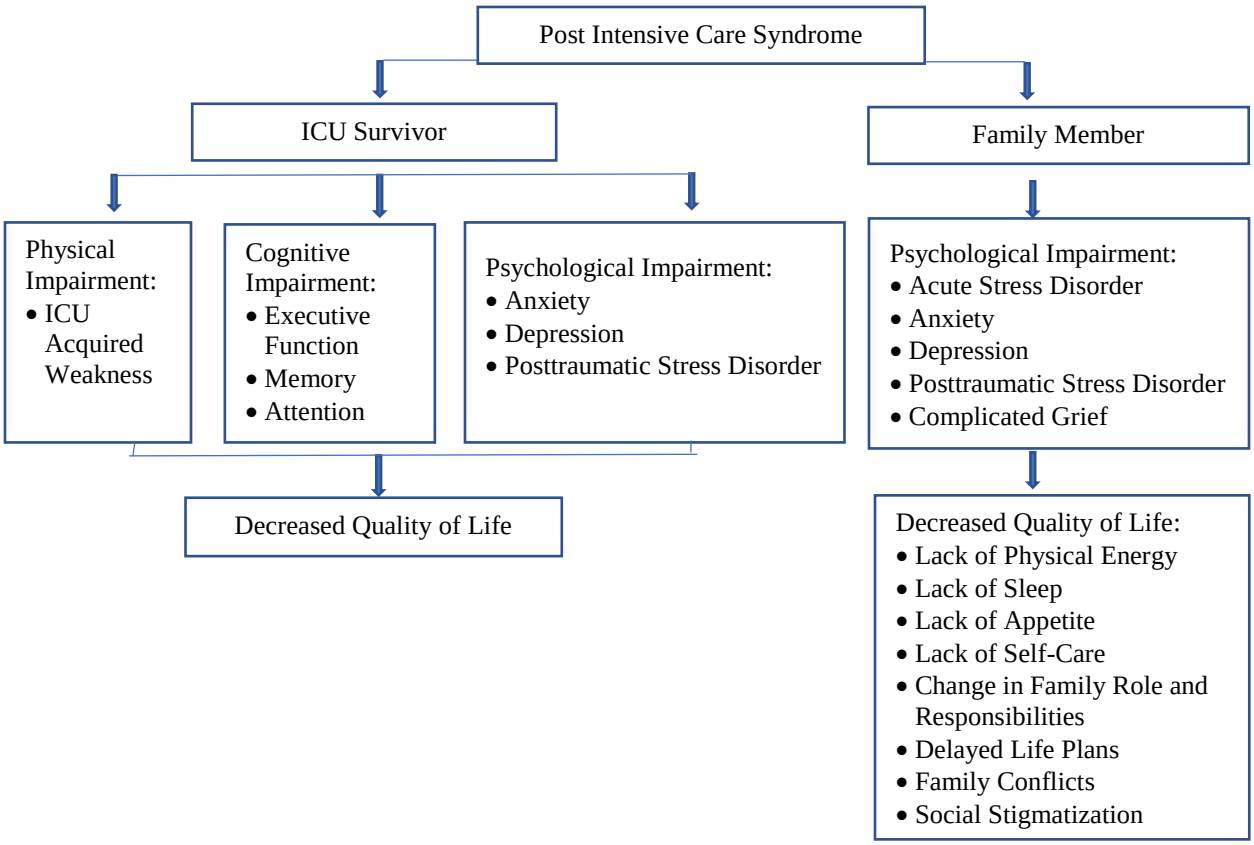

Figure 1. Post Intensive Care Syndrome (PICS) Model in ICU survivors and family members.

PICS physical and cognitive impairments are prevalent among ICU survivors as critical illness sequelae. PICS psychological impairments are prevalent in both ICU survivors and their family members (PICS-F) suggesting an association with the ICU experience. Psychological impairment is greater and persists longer in family members than in ICU survivors (Fumis, Ranzani, Martins, & Schettino, 2015). One rationale for greater prevalence in family members is that they are acutely aware of and witnessing the events their loved one is going through with a sense of forced helplessness. A rationale for longer persistence is that many family members

experience the incumbrance of informal caregiver for long road of recovery for the ICU survivor, which can have physiological and social consequences (i.e., lack of physical energy, lack of sleep, lack of appetite, lack of self-care, change in family role and responsibilities, delayed life plans, family conflicts, and social stigmatization). PICS is now being recognized as a public health burden due to the associated neuropsychological and functional disability, however, the psychological impact on family members (PICS-F) are usually under-recognized and interventions targeted on symptoms of PICS-F are lacking.

Post Intensive Care Syndrome-Family

Family members suffer a great deal when a loved one is admitted to the ICU. Inside the crowded, beeping, blinking, alarming ICU room, normal sleep is disrupted. Sleep disturbances are reported as one of the top stressors during the ICU stay by family members (Netzer & Sullivan, 2014; Novaes et al., 1999; Verceles et al., 2014). Since many ICU patients are not cognitively intact as a result of acute illness and accompanying medical treatments, family members of ICU patients are often asked to make health decisions for their loved one. Family members in the role of surrogate health decision-maker are often burdened with the responsibility of making the "right" decisions for patients. The uncertainty and life-threatening nature of critical illness, combined with the burden of surrogate health decision-making and the added stress of sleep disturbances elicit a state of psychological distress in family members during the ICU stay. Increased distress in family members during the ICU stay may increase risk of PICS-F.

The psychological impact of PICS-F in family members include ongoing stress, anxiety, depression, and posttraumatic stress disorder (PTSD). Pochard et al. (2005) reported spouses of critically ill patients were more likely to suffer from depressive symptoms compared to all other

family members. The researchers confirmed that symptoms of anxiety and depression were found in 73.4% of spouses and 35.3 % of family members respectively. These results are consistent with other researchers indicating that as many as two thirds of family members have symptoms of anxiety while the patient is in the ICU (Azoulay et al., 2005). In addition to depression and anxiety, Paparrigopoulos and colleagues (2006) reported that during the first week of critical illness, a majority (81%) of family members had a quantity of symptoms which placed them at risk for PTSD. Azoulay and colleagues (2005) reported more than a third of family members are at risk for PTSD at three months. Anderson and colleagues (2008) found that almost half (49%) of family members reported PTSD six months after the ICU survivors' hospital discharge.

Problem Statement

Critical illness is a family crisis. Spouses of critically ill patients are often sleep deprived and fearful of surrogate decision-making due to the difficulty in the "uncertainty of not knowing" (Almerud, Alapack, Fridlund, & Ekebergh, 2007). Evidence in the literature suggest higher stress levels experienced in the ICU increase risk for PICS-F in family members (Anderson, Arnold, Angus, & Bryce, 2009; Azoulay et al., 2005; Gries et al., 2010; Heyland et al., 2003; Kentish-Barnes, Lemiale, Chaize, Pochard, & Azoulay, 2009; Kross et al., 2011; Lefkowitz, Baxt, & Evans, 2010; Miles, Holditch-Davis, Schwartz, & Scher, 2007; Siegel, Hayes, Vanderwerker, Loseth, & Prigerson, 2008). To date, the focus of PICS-F research has been on description, detection, and estimation of prevalence. There is limited evidence regarding management of distress during the ICU stay for family members who are at the highest-risk for developing PICS-F (i.e., spouses and surrogate health decision-makers). Emerging evidence about the increase and persistence of psychological symptoms among family members of ICU survivors

warrants the need for interventions to prevent PICS-F. Thus, effective, easy to implement, innovative interventions specifically targeting the management of distress for family members during the ICU stay are needed.

Sensation Awareness Focused Training (SĀF-T) Intervention

The approach for the study focuses on prevention of PICS-F using an innovative rapid stress-reduction intervention called Sensation Awareness Focused Training (SĀF-T). SĀF-T is adapted from Accelerated Resolution Therapy (ART) for psychological trauma and depression prevention. Laney Rosenzweig at the Rosenzweig Center for Rapid Recovery developed ART and SĀF-T. SĀF-T utilizes eye movements to rapidly eliminate negative biological sensations of stress. SĀF-T is designed to elicit a calming response; interrupt negative thoughts, negative feelings, and negative behaviors; and ultimately serve as a self-management stress reduction method for individuals. This study is the first to examine the effects of SĀF-T in family members of ICU patients.

Purpose of the Study

The purpose of this study is to assess the safety, acceptability, and feasibility of SĀF-T in a small sample of subjects in preparation for a larger study of the intervention's effectiveness. The pilot study is a small-scale, stand-alone version of a larger future randomized controlled trial (RCT) of the intervention. Pilot data will not be pooled with the future study to ensure key features that were not possible in the pilot study are preserved (e.g., blinding in RCTs). The pilot study carefully examines safety, intervention acceptability, protocol feasibility, and subject adherence. The study provides important data to determine sample size required for the larger RCT. This study is not powered to detect meaningful differences in clinically important

endpoints, and hypothesis testing will be reserved for the larger study. Feasibility aims, objectives and success criteria are utilized to determine overall evidence of feasibility for the future RCT. The purpose of the future RCT will be to investigate the impact of SĀF-T to reduce stress in spouses of critically ill, mechanically ventilated patients during the ICU hospitalization, which may reduce their likelihood of PICS-F. The primary aim will be to test the effect of SĀF-T on PICS-F among spouses of critically ill, mechanically ventilated patients. A prospective, RCT will be used to assess the effectiveness of the intervention in the larger future study.

Primary Aim

Assess feasibility and estimate effect size of the 3-day SĀF-T intervention on PICS-F (symptoms of stress, anxiety, depression, and PTSD) for spouses of mechanically ventilated patients admitted to the ICU who are acting as the surrogate decision-maker for the patient.

Objective 1

Determine enrollment rate of subjects along with identification of any barriers to consent for planning timeline of the future RCT.

Success criteria 1. a) At least 4 subjects per week can be recruited; b) at least 50% of all eligible subjects can be enrolled; and c) at least 60% of all recruited subjects completed both follow-up measures.

Objective 2

Determine acceptability of providing SĀF-T to subjects during the ICU stay.

Success criteria 2. a) At least 90% of recruited subjects randomized to intervention group received 2 of the 3 scheduled doses of SĀF-T in the ICU; and b) >90% of subjects received SĀF-T without adverse events (e.g., increased stress on post-SĀF-T assessment).

Objective 3

Evaluate selection of most appropriate primary outcome measures.

Success criteria 3. Measures with highest reliability (Cronbach's alpha), more clinical relevance, and least influenced by factors other than the intervention are the primary outcome measures to move forward to the future RCT.

Objective 4

Estimate effect size of SĀF-T on primary outcome measures to calculate sample size for the larger future study.

Success criteria 4. a) Large estimated effect size (>0.5) with 95% confidence intervals for SĀF-T on outcome measures study day 1 (pre-SĀF-T in intervention group) and study day 3 (post-SĀF-T for intervention group) and sustained over time (study day 1 to study day 30, and study day 1 to study day 90) are the primary outcome variable targets for the future study, b) small and medium estimated effect size (<0.5) with 95% confidence intervals for SĀF-T on outcome measures are possible secondary outcomes for a future RCT of SAT-T effectiveness.

Secondary Aim

Explore sleep in spouses during the ICU stay.

Objective 5

Test wrist actigraphy data collection on subjects during the ICU stay.

Success criteria 5. a) At least 90% of recruited subjects wore ActiWatch during the ICU stay; and b) >90% of recruited subjects who wore the ActiWatch did not experience adverse events (e.g., skin irritation).

Significance and Innovation

The study is significant because SĀF-T may provide benefit through reducing symptoms of PICS-F in spouses of critically ill, mechanically ventilated patients during and after the ICU stay. High stress levels in spouses during the ICU stay can have a significant impact on their psychological wellbeing. Findings gained from this study provide preliminary data to determine feasibility of SĀF-T in the ICU setting and estimate effect size for a larger future study. Additionally, if proven to be effective, SĀF-T represents a widely available, low cost, simple to implement, non-pharmacologic intervention that can be used by nurses and other clinicians to aid in reducing symptoms of PICS-F. The study is consistent with the National Institute of Nursing Research strategic plan to advance management of symptoms during chronic and critical illness and promote family-centered care. The study is innovative as the first to assess feasibility of SĀF-T among spouses of critically ill, mechanically ventilated patients.

CHAPTER TWO:

LITERATURE REVIEW

The chapter includes a review of the literature relevant to ICU experiences of family members and development of PICS-F, as well as intervention outcomes that led to the scientific premise for the study. ICU experiences of family members found in the literature that are strongly associated with PICS-F include surrogate health decision-making and sleep disturbances. Evidence found in the literature on prevalence of PICS-F conditions, along with the psychological, physiological, and social consequences are discussed. Also included in this chapter are the interventions to date for PICS-F and the theoretical basis for the SĀF-T intervention.

Conceptual Framework

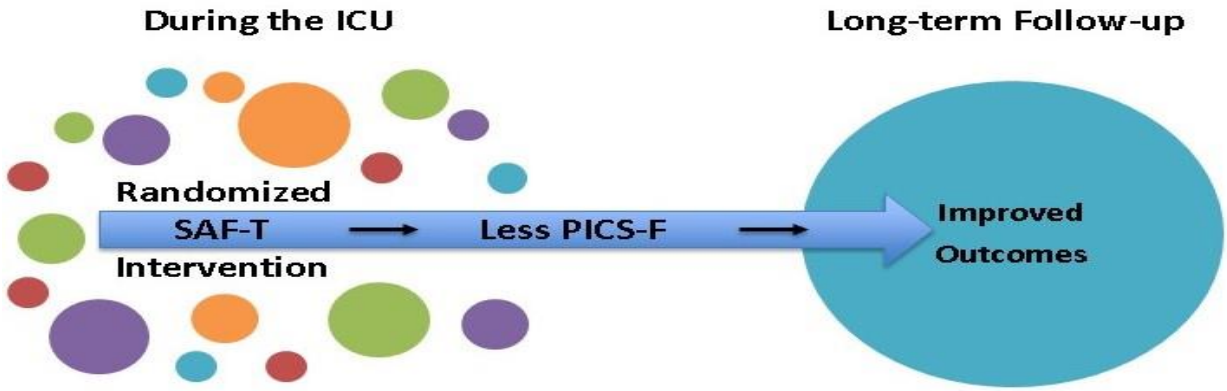

Figure 2. Conceptual SĀF-T (Sensation Awareness Focused Training) to prevent PICS-F (Post Intensive Care-Family) model.

The conceptual frame work presented in Figure 2 represents a family-centered intervention, which may reduce risk of PICS-F in family members of patients admitted to ICU. The conceptual framework guided the following review of the literature.

Surrogate Health Decision-Making

Amid the perceived chaos of an ICU admission and stay, family members are often asked to make decisions that center around the life and death of their loved ones. Pochard and colleagues (2005) found that 73% of hospitalized patients required surrogate health decision-making most commonly from a family member. Surrogate health decision-making is even higher in critically ill, mechanically ventilated patients, who are typically sedated. Family members are fearful of surrogate health decision-making due to the difficulty in the "uncertainty of not knowing" (Almerud, Alapack, Fridlund, & Ekebergh, 2007). Surrogate health decision-making can have adverse psychological outcomes for family members that last long after the ICU stay (Azoulay et al., 2005; Hickman, Daly, Douglas, & Clochesy, 2010; Petrinec, Mazanec, Burant, Hoffer, & Daly, 2015; Sullivan et al., 2012).

Sleep Disturbances

Inside the crowded, beeping, blinking, alarming ICU room, normal sleep is disrupted and concerns about the patient may make sleep difficult when the family member is not at the hospital. Family members report sleep disturbances as one of the top stressors during the ICU stay (Netzer & Sullivan, 2014; Novaes et al., 1999; Verceles et al., 2014). Sleep adequacy is defined as a combination of three factors: latency (the time it takes to fall asleep), efficiency ([time spent sleeping ÷ total time in bed] × 100), and duration of sleep (Morin & Espi, 2003). According to the American Academy of Sleep Medicine (2000) for adequate sleep, persons should fall asleep within 15 minutes, stay asleep for at least 85% of the time they are in bed, and have a total sleep time of no less than 7 hours. Reasons reported by family members for sleep disturbances include environmental noise, anxiety, tension, and fear (Day, Haj-Bakri, Lubchansky, & Mehta, 2013). Sleep disturbances may play a role in the development of PICS-F

(Davidson, Jones, & Bienvenu, 2012; Verceles et al., 2014). Although anxiety, tension, and fear are to be expected when a family member is critically ill, acknowledging these feelings and practicing stress-reducing techniques can reduce the impact these feelings have on sleep (Chesson et al., 1999). Therefore, management of stress in family members throughout the daytime may improve nighttime sleep and reduce risk of PICS-F.

Post Intensive Care Syndrome –Family (PICS-F)

There is strong evidence that family distress in response to critical illness is prevalent during the ICU stay and does not disappear after ICU discharge or death of the patient. The Society of Critical Care Medicine (2013) identified a cluster of complications that occur in family members from exposure to critical care as post intensive care syndrome-family (PICS-F). PICS-F conditions include acute stress disorder (ASD), anxiety, depression, posttraumatic stress disorder (PTSD), and complicated grief. In review of the literature, a sample of 34 studies related to PICS-F conditions were identified from around the world. These studies include 5,571 subjects from 23 (68%) prevalence studies and 11 (32%) intervention studies. A literature search flow diagram (See Figure 3) and summarization table of these studies (See Table 1) can be found at the end of this chapter.

Acute Stress Disorder (ASD)

ASD is the development of severe anxiety and dissociative symptoms within 3 days to a maximum of 4 weeks of event exposure (American Psychiatric Association [APA], 2013). Data suggest approximately 30% of parents of critically ill children experience symptoms of ASD (Lefkowitz, Baxt, & Evans, 2010; Shaw, Bernard, Deblois, Ikuta, Ginzburg, & Koopman, 2009). Two prevalence studies on ASD were limited to parents of critically ill children and did not use

the same measurement instruments. The results of these studies conflicted on the prevalence of ASD by sex of the parent. Shaw and colleagues (2009) found in their baseline measures (*n*=40) during the first few weeks of ICU admission, 44% of mothers (*n*=11) were classified as meeting the symptom criterion for ASD, while none of the fathers (*n*=0) met this criterion, suggesting ASD was associated with the female sex. However, at follow-up measures (*n*=18, 45% retention rate) 4-months post-birth of their premature infant, 33% of fathers (*n*=2) and 9% of mothers (*n*=1) met criterion for PTSD (Shaw et al., 2009). Lefkowitz and colleagues (2010) discovered from their study (*n*=127) that 35% of mothers (*n*=30) and 24% of fathers (*n*=10) met ASD diagnostic criterion during the ICU, and 15% of mothers (*n*=9) and 8% of fathers (*n*=2) met PTSD diagnostic criterion 1-month later (Lefkowitz et al., 2010). The conflicting prevalence of ASD in the male sex is most likely contributed to the differences in sample size and instruments used to assess ASD. Currently, there is a gap in the literature on the prevalence of ASD in family members of adult critically ill patients, as well as intervention studies for ASD.

Ongoing Anxiety

Anxiety disorder is disproportionate anxiety and worry that remains present for at least 6-months, with a minimum of three additional symptoms (i.e., restless, on edge, fatigue, trouble concentrating, irritable, tight muscles, and sleep difficulty) (American Psychiatric Association [APA], 2013). Data suggest up to 44% of family members of critically ill patients experience symptoms of anxiety (Fotiou et al., 2016; Melnyk, Crean, Feinstein, & Fairbanks, 2008; Zelkowitz et al., 2011). Three randomized intervention studies on anxiety were limited to parents of critically ill children (Fotiou et al., 2016; Melnyk et al., 2008; Zelkowitz et al., 2011). The same instrument was used to measure anxiety (State Trait Anxiety Index) at 2 to 3-months post-ICU experience. Fotiou et al. (2016) used three relaxation techniques (deep breathing, guided

imagery, and progressive muscle relaxation) as an intervention and the control group received general information about infants. Both intervention and control groups (*n*=59) experienced a decrease in anxiety at 3-months post-ICU experience, with no significant difference between groups (Fotiou et al., 2016). Data suggest the effect of the intervention (relaxation techniques) was better with higher baseline anxiety scores (Fotiou et al., 2016). Zelkowitz et al. (2011) compared two educational programs, CUES versus CARE, as interventions to reduce anxiety in mothers (*n*=121). More than half of the mothers experienced anxiety scores in the clinical range at baseline. Both groups reported fewer symptoms of anxiety post-intervention, with no significant difference between the two groups (Zelkowitz et al., 2011). Melnyk and colleagues (2008) conducted a secondary analysis on the Creating Opportunities for Parent Empowerment (COPE) intervention for mothers (*n*=246). Mothers experienced a decrease in anxiety at 2-months post ICU experience. Maternal anxiety was only related to beliefs during the ICU and not related post hospital (Melnyk et al., 2008). Data from all three studies suggest anxiety in parents of neonate ICU survivors decreases over time, without a significant difference among education and relaxation interventions (Fotiou et al., 2016; Melnyk et al., 2008; Zelkowitz et al., 2011).

Depression

Episodes of depression can be mild, moderate, or severe. Depressive episodes may include sadness, loss of joy, low energy, a decrease in self-esteem, guilt, pessimistic thoughts, disrupted sleep, lack of appetite, and suicidal thoughts (APA, 2013). Data suggest up to 36% of family members of critically ill patients experience symptoms of depression (Choi et al., 2014; Davydow, Hough, Langa, & Iwashyna, 2012; Lemaile et al., 2010; Miles, Holditch-Davis, Schwartz, & Scher, 2007; Mulder, Carter, Frampton, & Darlow, 2014; Pinelli et al., 2008). There were 6 prevalence studies on depression in family members of ICU patients. Of these, 3 studies

recruited family of adult ICU patients, and 3 studies recruited parents of children in the ICUs. Choi and colleagues (2014) completed a secondary analysis in family members (*n*=47) of adult ICU survivors. Measures of depression associated with fatigue were collected at three different time points post-ICU experience (≤ 2-weeks, 2-months, & 4-months). Mean depression scores remained substantial during each time point, and more so in the presence of clinically significant fatigue (Choi et al., 2014). Davydow and colleagues (2012) prospectively examined spouses (*n*=865) of sepsis survivors. Measures of depression were assessed at an average of 1.1-years post-ICU experience. Approximately 34% of wives experienced substantial depressive symptoms, while 25% of husbands experienced substantial depressive symptoms (Davydow et al., 2012). Lemaile and colleagues (2010) followed-up with family (*n*=284) of adult ICU patients. Measures were obtained on their mental health and quality of life at 3-months following their ICU experience. Approximately 36% of family members were taking medications for anxiety and depression. Factors that influenced mental health scores include admission for shock, end-of-life decisions, age, female sex, adult child, lower income, chronic disease, newly prescribed psychotropic medications, and perceived conflicts with ICU staff (Lemaile et al., 2010). Overall, a range of 25% to 36% of family members of adult patients experienced symptoms of depression from 2-months to over 1-year post-ICU experience (Choi et al., 2014; Davydow et al., 2012; Lemaile et al., 2010). Although the event of admitting a child to the ICU may be particularly stressful, Mulder and colleagues (2014) did not find any difference in psychological distress or depression after 2-years in parents whose infants were admitted to an ICU compared with control parents (Mulder et al., 2014). Pinelli and colleagues (2008) observed depression scores in mothers of sick newborns in the ICU. Depression scores in mothers ranged from 12% to 16% and in fathers from 7% to 12% at 3-months and 12-months post-ICU

experience respectively (Pinelli et al., 2008). Miles and colleagues (2007) observed similar results. Depression scores tapered down to a range of 12% to 21% at 6-months and 27-months post-ICU experience in mothers of sick newborns (Miles et al., 2007). Over the long term, data suggest depression is less prevalent in parents of sick newborns, ranging from 7% to 21% (Miles et al., 2007; Mulder et al., 2014; Pinelli et al., 2008) when compared to family members of critically ill adults, ranging from 25% to 36% prevalence (Choi et al., 2014, Davydow et al., 2012; Lemaile et al., 2010).

Posttraumatic Stress Disorder (PTSD)

PTSD can be subclinical, in which the criteria are almost, but not fully met, or meets all eight criteria for a clinical diagnosis. The eight criteria for PTSD include: experiencing a traumatic event, re-experiencing the traumatic event, avoidance, negative alterations in cognitions, alterations in arousal and reactivity, duration of symptoms is >1-month, clinically significant distress, or impairment in functioning, and unrelated to other medical conditions or substances (APA, 2013). Of note, ASD, anxiety, and depression may be secondary to PTSD (Azoulay et al., 2005). Data suggest up to 75% of family members of critically ill patients experience symptoms of PTSD (Azoulay et al., 2005; van den Born-van Zanten, Dongelmans, Dettling-Ihnenfeldt, Vink, & van der Schaaf, 2016; Bronner, Knoester, Bos, Last, & Grootenhuis, 2008; Colville, Cream, & Kerry, 2010; Feeley et al., 2011; Fumis, Ranzani, Martins, & Schettino, 2015; Garrouste-Orgeas et al., 2012; Jones, Bäckman, & Griffiths, 2012; Kross et al., 2011; McAdam, Fontaine, White, Dracup, & Puntillo, 2012; de Miranda et al., 2011; Petrinec, Mazanec, Burant, Hoffer, & Daly, 2015; Rosendahl, Brunkhorst, Jaenichen, & Strauss, 2013; Wolters et al., 2014). There were 14 studies with PTSD as the primary focus. Of these, there were 11 prevalence studies, and 3 intervention studies. The 11 prevalence studies included

family members of both critically ill children and adults. PTSD was assessed as early as 1-month up to 55-months post-ICU experience. The range of PTSD prevalence was 21% to 75% of family members (Azoulay et al., 2005; van den Born-van Zanten et al., 2016; Bronner et al., 2008; Feeley et al., 2011; Fumis et al., 2015; Kross et al., 2011; McAdam et al., 2012; de Miranda et al., 2011; Petrinec et al., 2015; Rosendahl et al., 2013; Wolters et al., 2014). Risk factors included spouses (Fumis et al., 2015; Rosendahl et al., 2013), surrogate decision-makers (Azoulay et al., 2005; McAdam et al., 2012; de Miranda et al., 2011; Petrinec et al., 2015), incomplete information provided in the ICU (Azoulay et al., 2005), present at the time of death (Kross et al., 2011), and peritraumatic dissociation (de Miranda et al., 2011). Three intervention studies use augmented communication strategies as interventions for PTSD. Two studies augmented communication with ICU diaries (Garrouste-Orgeas et al., 2012; Jones et al., 2012). A third study augmented communication with follow-up outpatient clinic visits (Colville et al., 2010). Data suggest ICU diaries may significantly affect symptoms of PTSD at 3-months and 12-months post-ICU experience (Garrouste-Orgeas et al., 2012; Jones et al., 2012). No significant difference was found in offering parents of PICU survivors a follow-up clinic appointment (Colville et al., 2010).

Complicated Grief

Complicated grief is a proposed disorder in psychiatry for those who are significantly impaired by grief symptoms for at least 1-month beyond 6-months of bereavement (APA, 2013). Data suggest the prevalence of complicated grief may be as high as 52% in family members of patients who die in the ICU (Anderson et al., 2008; Gries et al., 2010; Kentish-Barnes et al., 2017; Meert et al., 2011; Siegel et al., 2008). There were nine studies on complicated grief. Of these, there were five prevalence studies, and four intervention studies. The five prevalence

studies include family members of both children and adults who died in the ICU (Anderson et al., 2008; Gries et al., 2010; Kentish-Barnes et al., 2017; Meert et al., 2011; Siegel et al., 2008). Risk factors associated with complicated grief include female sex (Gries et al., 2010; Kentish-Barnes et al., 2017), spousal role (Siegel et al., 2008), being the biological parent with no other children (Meert et al., 2011), patient refusal of treatment (Kentish-Barnes et al., 2017), patient died while intubated (Kentish-Barnes et al., 2017), discordance with surrogate health decision-making (Gries et al., 2010), patient illness < 5-years (Gries et al., 2010; Siegel et al., 2008), lower education level (Anderson et al., 2008), experiencing additional stressors after the loss such as living alone (Kentish-Barnes et al., 2017; Siegel et al., 2008), present at time of death (Kentish-Barnes et al., 2017), did not get a chance to say goodbye (Kentish-Barnes et al., 2017), poor communication with ICU staff or amongst relatives (Kentish-Barnes et al., 2017), history of psychiatric treatment (Gries et al., 2010), and presence of PTSD (Anderson et al., 2008). The four randomized intervention studies utilized education and communication strategies as interventions for complicated grief. The education intervention was a randomized controlled trial that invited family members (n=58) to remain present at the bedside during brain death evaluation (Tawil et al., 2014). There was no difference in the psychological well-being between the intervention and control groups at 1-month and 3-months. Data suggests family presence during brain death evaluation is feasible and safe (Tawil et al., 2014). The communication intervention consisted of detailed guidelines to follow during the end-of-life conference with family members, at which time they received a brochure on bereavement (Lautrette et al., 2007). There was a significant difference ($p < .05$) of fewer symptoms of complicated grief in the intervention group compared with the control group. Another communication intervention consisted of a nurse or social worker trained in the role of communication facilitator (Curtis et

al., 2013). There was no significant difference in the psychological well-being of family members between the intervention and control groups. Lastly, a communication intervention in the form of a condolence letter by the ICU team was sent to family members at 15-days post death. The condolence letter failed to alleviate grief symptoms and may have worsened depression and PTSD-related symptoms (Kentish-Barnes et al., 2017). The evidence from these intervention studies suggests additional procedural education and enhanced communication in the ICU may lessen the burden of bereavement for family members.

Physiological and Social Consequences of PICS-F

PICS after ICU discharge does not only affect the patient, but also reduces the physical, mental, social, and financial position of their family members. Physiological consequences of PICS-F include lack of physical energy, lack of sleep, lack of appetite, and lack of self-care (Wolters et al., 2014). Social consequences of PICS-F include interruptions in routine, role, and responsibilities of the family; delayed life plans; family conflicts; and stigmatization (Wolters et al., 2014). Studies report that almost 50% of family members, who were employed at study enrollment, reduced their work hours, quit their job, or were fired in order to provide informal care (Douglas, Daly, O'Toole, & Hickman, 2010; Swoboda et al., 2002). Swoboda and colleagues (2002) found that 38% of family members reported it was somewhat difficult to pay for basic needs such as food, housing, medical care, and heating. PICS-F also interferes with family members' ability to perform care, and ICU survivors require care long after hospital discharge (Johansson, Fridlund, & Hildingh, 2004; Scott & Arslanian-Engoren, 2002).

Interventions for PICS-F

To date, the focus of PICS-F research has been on description, detection, and prevalence using self-report measures. Early psychological screening among family members of the critically ill can identify individuals who may benefit from interventions that prevent further psychological impairment. However, there are limited numbers of interventional studies for PICS-F conditions. The majority of interventions were designed around communication or education in the ICU. Communication interventions consist of providing pro-active end-of-life family conferences with bereavement brochures (Lautrette et al., 2007), utilizing interprofessional communication facilitators (Curtis et al., 2013), palliative care-led meetings for families of patients with chronic critical illness (Carson et al., 2016), implementing ICU diaries (Garrouste-Orgeas et al., 2012; Jones, Bäckman, & Griffiths, 2012), offering follow-up clinic visits (Colville, Cream, & Kerry, 2010), and sending condolence letters (Kentish-Barnes et al., 2017). Among these communication studies, multidisciplinary teams were required to facilitate the meetings with family members. Even though some results are promising with reduced ICU length of stay and increased palliative care consultations, the adherence to early and routine family conferences was usually low and conferences happened late in the disease course. In some of the studies, signals from the qualitative results did not always match the quantitative results, indicating the intervention did not work with signals of harm noted (Carson et al., 2016; Curtis et al., 2013; Kentish-Barnes et al., 2017). Educational interventions include Creating Opportunities for Parent Empowerment (COPE) (Melnyk et al., 2008), infant CUES and CARE programs (Zelkowitz et al., 2011), stress management education with relaxation techniques (Fotiou et al., 2016), and family presence during brain death evaluation with education at the bedside (Tawil et al., 2014). Most of the educational studies are targeted for parents of the

pediatric patient population (Melnyk et al., 2008; Zelkowitz et al., 2011; Fotiou et al., 2016). Few studies that targeted family members of adult ICU patients provided the rigor of randomized controlled trials (Lautrette et al. 2007; Curtis et al. 2013; Jones, Bäckman, & Griffiths, 2012). Thus, low-cost, easy to implement, family-centered interventions need to be developed and rigorously tested with family-centered outcomes to reduce risk of PICS-F.

Sensation Awareness Focused Training Intervention (SĀF-T)

Laney Rosenzweig at the Rosenzweig Center for Rapid Recovery developed SĀF-T. This study is the first randomized controlled trial to use SĀF-T as an intervention. SĀF-T is adapted from Accelerated Resolution Therapy (ART), which combines eye movements used in eye movement desensitization and reprocessing (EMDR) with Gestalt techniques, metaphors, and solution-focused emphasis. The Substance Abuse and Mental Health Services Administration (SAMHSA) designated ART to be an evidence-based treatment for trauma-related disorders, depression, and personal resilience. Studies have reported beneficial clinical effects of ART for treatment of symptoms of PTSD in both civilians and veterans (Kip et al., 2012; Kip et al., 2013). SĀF-T uses an adapted approach from ART to rapidly eliminate negative biological sensations of stress. The SĀF-T intervention takes approximately 15-20 minutes per session. The SĀF-T intervention includes scripted coaching from SĀF-T trained research staff on awareness of biological sensations. Research staff sit across from the subject and ask them to use their eyes to follow hand movements that induce lateral left-right (smooth pursuit) eye movements followed with slow deep breaths. These actions in the SĀF-T intervention shift autonomic balance toward parasympathetic dominance.

The theoretical basis for SĀF-T is psychophysiological. The scripted coaching in SĀF-T engages working memory. Taxing of working memory renders traumatic images less vivid and

emotional (Lee & Cuijpers, 2013; van den Hout, Muris, Salemink, & Kindt, 2001). Therefore, the secondary task of eye movements in SĀF-T reduce vividness and emotionality of mental images through interplay of dual taxation of working memory (Gunter & Bodner, 2008). Thus, the distressing memory that elicits stressful sensations cannot be retrieved completely and in turn lessens the impact of stress induced sensations.

Additionally, episodic memory recall of personal (autobiographical) facts, is facilitated by increased interaction between two cerebral hemispheres. The sequences of left–right bilateral eye movements result in simultaneous activation of both cerebral hemispheres (Christman, Garvey, Proper, & Phaneuf, 2003). Because the majority of eye movements during REM sleep are horizontal (Hansotia, Broste, So, Ruggles, Wall, & Friske, 1990), this evidence suggests that bilateral eye movements are associated with increased interhemispheric interaction and coordination. Facilitating episodic memory increases taxation on working memory, which dampens the vividness and emotionality, thereby diminishes stress induced sensations.

Evidence in the literature also suggests repetitive eye movements may activate the parasympathetic nervous system and relaxation response (Barrowcliff, Gray, MacCulloch, Freeman, & MacCulloch, 2003; Elofsson, von Scheele, Theorell, & Sondergaard, 2008; Obrist, 1981; Stickgold, 2002). Lastly, the mindful deep breathing in SĀF-T relieves stress and anxiety due to its physiological effect on the parasympathetic nervous system (Jerath, Edry, Barnes, & Jerath, 2006). Collectively, dual taxation of working memory, increased interhemispheric interaction, smooth pursuit eye movements, and slow deep breathing shift autonomic balance towards parasympathetic dominance. (Barrowcliff, Gray, MacCulloch, Freeman, & MacCulloch, 2003; Elofsson, von Scheele, Theorell, & Sondergaard, 2008; Jerath, Edry, Barnes, & Jerath, 2006; Obrist, 1981; Stickgold, 2002).

The sympathetic nervous system controls the body's fight or flight response to perceived threats (Science Daily, 2018). Anxiety, tension, and fear are to be expected when a loved one is critically ill; thus, it is likely the autonomic balance of family members shift towards sympathetic dominance during the ICU stay. SĀF-T shifts the autonomic balance back towards parasympathetic dominance. The parasympathetic nervous system controls homeostasis and is responsible for the body's rest and digest function by reducing activity of the brain, the muscles, and the adrenal and thyroid glands (Science Daily, 2018). SĀF-T may enhance rest and sleep through shifting the autonomic balance towards parasympathetic dominance. During rest and restorative sleep, the parasympathetic system renews and heals any damage to the body caused by an over-active sympathetic nervous system (Science Daily, 2018). Autonomic system measures along with sleep/rest actigraphy in family members during the future RCT would be advantageous in assessing the affect SĀF-T may have on the balance between the sympathetic and parasympathetic systems and sleep, which may be important in decreasing risk of PICS-F.

Summary

As demonstrated in the foregoing literature review, exploration of both experimental and non-experimental PICS-F research brings to light the need for new ideas in designing interventions, beyond communication and education protocols, to support family members during and after the critical illness of their loved ones (Turner-Cobb, Smith, Ramchandani, Begen, & Padkin, 2016). The scientific premise for the study is based on the substantial challenge to manage symptoms of stressful events experienced by family members during the ICU stay, and an intriguing, innovative intervention with psychophysiological rationale that supports the SĀF-T protocol as a promising approach to reduce risk of PICS-F. The SĀF-T intervention is an easy to implement, low-cost, non-pharmacological intervention that could be

used to reduce psychological distress in family members of patients admitted to ICU. There is enormous opportunity to rethink and redesign how critical care is provided to include both patients and their family as a unit in need of care for optimal outcomes. This study promotes family-centered care to advance the management of symptoms of stressful events during the ICU experience and improve outcomes post ICU and hospital discharge for both patient and family. Below is a flow diagram of the literature search specific to PICS-F research (See Figure 3). Table 1 presents a summarization of the PICS-F studies by prevalence and interventions.

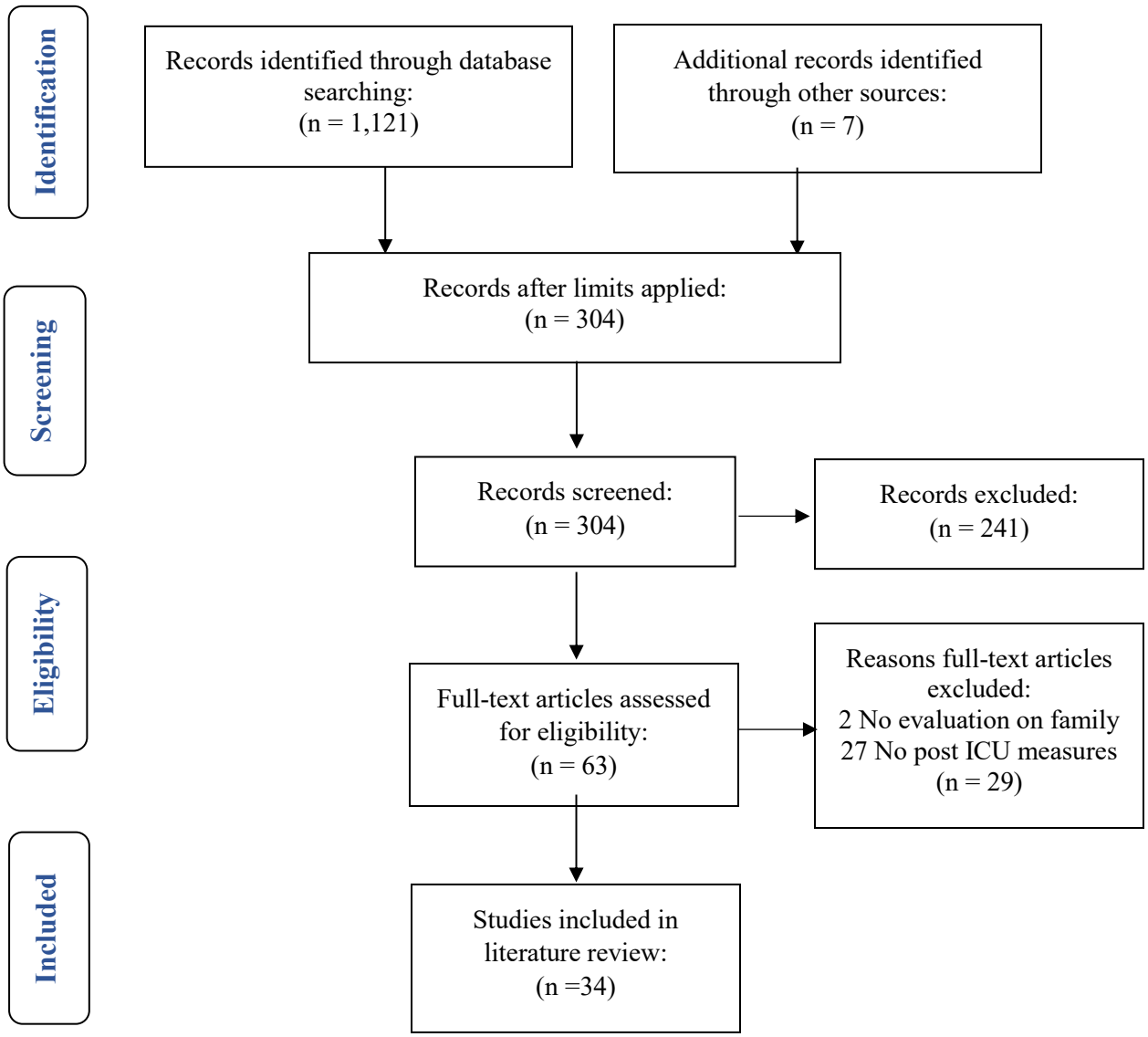

Figure 3. Flow diagram of literature search.

Table 1. Summarization of PICS-F Studies by Prevalence and Interventions

Prevalence Studies		
Author, year, and location	Design, sample size, PICS-F conditions assessed and instruments	Outcomes of PICS-F conditions
Anderson et al., 2008 United States	Prospective longitudinal cohort; N = 50 relatives *PICS-F conditions:* Symptoms of anxiety, depression, PTSD & complicated grief *Instruments:* Hospital Anxiety and Depression (HAD), Impact of Events Scale (IES), Inventory of Complicated Grief (ICG)	Comparing measurements at baseline, 1 month, & 6 months post discharge, symptoms of anxiety and depression diminished over time, but both bereaved and non-bereaved participants had high rates of posttraumatic stress & complicated grief. Prevalence of complicated grief was 46% & PTSD was 35% at 6 months post-ICU experience.
Azoulay et al., 2005 France	Prospective longitudinal cohort; N = 284 relatives *PICS-F conditions:* Symptoms of anxiety, depression & PTSD *Instruments:* HAD, IES & Short Form (SF)-36	At 3 months post discharge, severe post-traumatic stress reaction was associated with increased rates of anxiety and depression and decreased quality of life in family members.
Bronner et al., 2008 Netherlands	Prospective follow-up; N = 144 parents *PICS-F conditions:* Symptoms & diagnosis of PTSD *Instruments:* Social Relationship Satisfaction (SRS)-PTSD	At 3 months & 9 months post discharge, more than three-quarters of the parents experienced persistent symptoms of PTSD. In 15% of mothers and 9.3% of fathers, the full psychiatric diagnosis of PTSD was determined by a psychologist. In six families, both parents had PTSD.
Choi et al., 2014 United States	Secondary analysis of a longitudinal study; N = 47 family caregivers *PICS-F conditions:* Symptoms of depression *Instruments:* Center for Epidemiologic Studies-Depression (CES-D)	Comparing measures at 2 weeks, 2 months & 4 months, caregiver depressive symptoms and health risk behaviors were highly prevalent and correlated with each other while their loved ones were in the ICU. During the initial two months following ICU discharge, close to half of caregivers continued to report high levels of depressive symptoms, greater burden, and more health risk behaviors.
Davydow et al., 2012 United States	Prospective, longitudinal cohort; N = 865 spouses *PICS-F conditions:* Symptoms of depression *Instruments:* CES-D	At 1-year post discharge, each additional impairment of ADLs that a severe sepsis survivor had was associated with a 35% increase in the odds of substantial depressive symptoms in their wife.
Feeley et al., 2011 Canada	Descriptive correlational; N = 21 mothers *PICS-F conditions:* Symptoms of PTSD *Instruments:* (PPQ)	At 6 months post discharge, 23% of mothers scored in the clinical range on a measure of PTSD.
Fumis et al., 2015 Brazil	Prospective study; N = 184 spouses *PICS-F conditions:* Symptoms of anxiety, depression & PTSD *Instruments:* HAD & IES	Comparing measures during ICU, and 1 month & 3 months post discharge, anxiety, depression, and posttraumatic stress symptoms are higher and persist longer in family members than in patients.
Gries et al., 2010 United States	Follow-up survey study; N = 226 family members; *PICS-F conditions:* Depression & PTSD *Instruments:* PCL & PHQ-8	At 6 months post death in the ICU, PTSD and depressive symptoms in family members were 14.0% and 18.4%, respectively.

Table 1 (Continued)

Kross et al., 2011 United States	Cohort follow-up survey associated with a cluster randomized trial; N = 226 family members *PICS-F conditions:* Symptoms of depression & PTSD *Instruments:* PCL, PHQ-8	At 6 months post death in the ICU, Family members of older patients had lower scores for PTSD. Family members that were present at the time of death and family members of patients with early family conferences reported higher symptoms of PTSD. When withdrawal of a ventilator was ordered, family members reported lower symptoms of depression
Lefkowitz et al., 2010 United States	Prospective longitudinal survey; N = 127 parents *PICS-F conditions:* Symptoms of ASD, depression & PTSD *Instruments:* Acute Stress Disorder Scale (ASDS), PCL, & Postpartum Depression Screening Scale (PDSS)	35% of mothers and 24% of fathers met ASD diagnostic criteria during the ICU, and 15% of mothers and 8% of fathers met PTSD diagnostic criteria 1 month later. PTSD symptom severity was correlated with concurrent stressors and family history of anxiety and depression.
Lemiale et al., 2010 France	Multicenter observational study; N = 284 relatives *PICS-F conditions:* Symptoms of anxiety & depression *Instruments:* SF-36 - Mental Component Summary	The SF-36 showed evidence of impaired mental health in relatives of ICU patients 90 days after discharge or death. 35.9% of relatives were taking anxiolytic or antidepressant drugs, and 8.4% were taking psychotropic agents prescribed since the discharge or death of the patient. Among factors independently associated with a worse mental score, 2 were patient-related (admission for shock or implementation of end-of-life decision), 6 were family-related (older age, female gender, child of the patient, low income, chronic disease, and newly prescribed psychotropic medications), and 1 was related to the ICU experience (perceived conflicts between ICU staff and relatives).
McAdam et al., 2012 United States	Longitudinal descriptive study; N = 41 relatives *PICS-F conditions:* Symptoms of anxiety, depression & PTSD *Instruments:* HAD & IES	Even though symptoms (compared during the ICU and at 3 months post discharge) decreased over time, many of the family members scored at or higher than the cut-off levels on the IES-R and the HADS instruments, indicating that the members were still at high risk for PTSD, anxiety, and depression.
Meert et al., 2011 United States	Longitudinal follow-up survey; N = 138 parents *PICS-F conditions:* Symptoms of complicated grief *Instruments:* ICG	ICG scores at 6 months and 18 months represented an improvement. Complicated grief was present in 59% of parents at 6 months and 38% of parents at 18 months.
Miles et al., 2007 United States	Longitudinal descriptive study; N = 102 mothers *PICS-F conditions:* Symptoms of depression *Instruments:* CES-D	Mean depressive symptoms scores on the CES-D during hospitalization were high in 63% of mothers indicating risk of depression. Depressive scores declined over time until 6 months and then were fairly stable.
de Miranda et al., 2011 France	Prospective multicenter study; N = 102 relatives *PICS-F conditions:* Symptoms of anxiety, depression & PTSD *Instruments:* HAD & IES	Symptoms of anxiety and depression prevalence in relatives were 72.2% and 25.7% at intensive care unit discharge and 40.4% and 14.9% on day 90, respectively. PTSD symptoms were found in 29.8% of relatives on day 90.
Mulder et al., 2014 New Zealand	2-year follow-up; N=420 parents *PICS-F conditions: D*epression *Instruments:* EPNDS	There are no significant long-term negative psychological effects on parents whose infants were admitted to a NICU.

Table 1 (Continued)

Pinelli et al., 2008 Canada	Correlational longitudinal study; N = 152 parents *PICS-F conditions:* Depression *Instruments:* CES-D	Although the frequency of depression decreases after the first 3 months for most parents, 20% of parents continue to report depression over the next 9 months.
Petrinec et al., 2015 United States	Single-group descriptive longitudinal correlational study; N = 77 family members *PICS-F conditions:* PTSD *Instruments:* PTSS & IES	Avoidant and Problem-Focused coping strategy use is a significant predictor of posttraumatic stress symptom severity 60 days after hospitalization in family decision makers of ICU patients
Rosendahl et al., 2013 Germany	Prospective study; N = 55 spouses *PICS-F conditions:* Symptoms of anxiety, depression & PTSD *Instruments:* HAD & PTSS	Interventions to treat posttraumatic stress symptoms after critical illness to improve mental health-related quality of life should consider spouses at 55 months.
Shaw et al., 2009 United States	Longitudinal follow-up survey; N = 40 & 18 parents *PICS-F conditions:* ASD, anxiety, depression & PTSD *Instruments:* Parental Stressor Scale: Neonatal Intensive Care Unit (PSS:NICU) and Stanford Acute Stress Reaction Questionnaire (SASRQ) Davidson Trauma Scale, Beck Depression Inventory-II, & Symptom Check List-90-R	At 2-4 weeks following ICU admission, 28% of parents had ASD from the stress of having an infant hospitalized in the ICU; 44% of mothers were classified as meeting the symptom criteria for ASD, although none of the fathers did. At 4 months post birth of their premature infant, 33% of fathers, and 9% of mothers met criteria for PTSD.
Siegel et al., 2008 United States	Cross-sectional survey cohort; N = 41 next of kin *PICS-F conditions:* Criteria for anxiety, depression, & complicated grief *Instruments:* ICG & clinical interview by a psychologist	Following 3-12 months post death in the ICU, 34% next of kin met criteria for at least one psychiatric illness: 27% had major depressive disorder, 10% had generalized anxiety disorder, 10% had panic disorder, & 5% had complicated grief disorder.
Van den Born–Van Zanten et al., 2016 Netherlands	Questionnaire cohort; N=94 relatives *PICS-F conditions:* PTSD *Instruments:* Trauma Screening Questionnaire (TSQ)	At 3 months post discharge, PTSD-related symptoms were seen in 21% of the caregivers. This study shows that relatives of ICU survivors could experience strain 3 months after hospital discharge and are at risk of developing PTSD-related symptoms.
Wolters et al., 2014 Netherlands	Descriptive cohort follow-up; N = 88 relatives *PICS-F conditions:* Symptoms of PTSD *Instruments:* TSQ	Family completed the TSQ in 59 cases, of whom 15% were likely to suffer from PTSD. These findings support the presence of PICS in family members at 3 months.
Intervention Studies		
Author, year, and location	Design, sample size, PICS-F conditions assessed and instruments	Outcomes of PICS-F conditions
Carson et al., 2016 United States	Multicenter RCT with family surrogate decision-makers – at least 2 palliative care-led family meetings; N= 365family members *PICS-F conditions:* Symptoms of anxiety, depression & PTSD *Instruments*: HADS & IES	At 3 months, there was no significant difference in anxiety and depression symptoms between groups. PTSD symptoms were higher in the intervention group. Use of palliative care-led informational and emotional support meetings compared with usual care did not reduce anxiety or depression symptoms and may have increased posttraumatic stress disorder symptoms.

Table 1 (Continued)

Colville et al., 2010 United Kingdom	RCT with PICU Follow-up Clinic visit 2 months post discharge intervention; N = 105 parents *PICS-F conditions:* Symptoms of anxiety, depression & PTSD *Instruments:* PSS:PICU, IES, HAD	No significant difference with intervention. Parents with higher baseline stress reported lower rates of post-traumatic stress (25% vs. 57%) and depression (19% vs. 52%) at 5 months post PICU discharge if they had been offered an appointment than if they had not.
Curtis et al., 2013 United States	Clustered randomized trial of a communication facilitator intervention; N = 268 family members *PICS-F conditions:* Symptoms of anxiety, depression & PTSD *Instruments:* PHQ-9, PCL & Generalized Anxiety Disorder (GAD)-7	There were no significant differences in psychological symptoms at 3 months or anxiety or PTSD at 6 months. The intervention was associated with decreased depressive symptoms at 6 months.
Fotiou et al., 2016 Greece	RCT with 3 relaxation technique (DB, GI & PMR) interventions; N=59 parents *PICS-F conditions:* anxiety *Instruments:* PSS, STAI & Salivary Cortisol	Three months after discharge, both groups showed reduced levels of anxiety, more so in the IG, but without a statistically significant difference as a total.
Garrouste-Orgeas et al., 2012 France	Prospective open study comparing a diary period and the pre-diary and post diary periods; N = 143 relatives *PICS-F conditions:* Symptoms of anxiety, depression & PTSD *Instruments:* HAD & IES	The intensive care unit diary significantly affected posttraumatic stress–related symptoms in relatives 12 months after intensive care unit discharge. Prevention Intervention: ICU Diary
Jones et al., 2012 United Kingdom	Prospective experiment with ICU Diary intervention; N = 30 relatives *PICS-F conditions:* Symptoms of PTSD *Instruments:* PTSS	Family members of patients who received their diary at 1 month had lower levels of symptoms related to PTSD at the 3-month follow-up than did the control family members. Prevention Intervention: ICU Diary
Kentish-Barnes et al., 2017 France	Multicenter RCT; N = 242 relatives *PICS-F conditions:* Symptoms of anxiety, depression, PTSD & complicated grief *Instruments:* HAD, IES & ICG	Telephone interviews at 1-month & 6-months. In relatives of patients who died in the ICU, a condolence letter failed to alleviate grief symptoms and may have worsened depression and PTSD-related symptoms at 6-months.
Lautrette et al., 2007 France	Prospective RCT with End-of-Life Conference and Brochure intervention; N = 126 family members *PICS-F conditions:* Symptoms of anxiety, depression & PTSD *Instruments:* HAD & IES	On day 90, the 56 participants in the intervention group who responded to the telephone interview had a significantly lower median IES score than the 52 participants in the control group (27 vs. 39, P = 0.02) and a lower prevalence of PTSD-related symptoms (45% vs. 69%, P = 0.01). The median HADS score was also lower in the intervention group (11, vs. 17 in the control group; P = 0.004), and symptoms of both anxiety and depression were less prevalent (anxiety, 45% vs. 67%; P = 0.02; depression, 29% vs. 56%; P = 0.003).
Melnyk et al., 2008 United States	RCT with COPE intervention; N = 246 mothers *PICS-F conditions:* Symptoms of anxiety & depression *Instruments:* PSS, STAI, BDI	Participation in COPE was both directly and indirectly related to mothers' decreased post hospital depression and anxiety.

Table 1 (Continued)

Tawil et al., 2014 United States	RCT with being present during Brain Death Evaluation intervention; N = 58 family members *PICS-F conditions:* PTSD *Instruments:* IES	Family presence during brain death evaluation improves understanding of brain death with no apparent adverse impact on psychological well-being.
Zelkowitz et al., 2011 Canada	RCT with educational CUES & CARE intervention; N = 121 mothers; *PICS-F conditions:* Symptoms of anxiety, depression & PTSD *Instruments:* STAI, Perinatal PTSD, Global Rating Scales of Mother-Infant Interaction, Edinburgh Postnatal Depression Scale	The groups did not differ in levels of anxiety, depression, and symptoms of posttraumatic stress.

CHAPTER THREE:

METHODS

This chapter presents the study methods. It is organized by design, setting, population, sample size, measures, procedures, and data analysis plan. The chapter ends with feasibility aims, objectives, and success criteria and study flow chart (See Figure 4).

Design

The primary aim of this study was to assess the feasibility and estimate effect size of the 3-day SĀF-T intervention on PICS-F (including stress, anxiety, depression, and PTSD) in spouses of mechanically ventilated patients admitted to the ICU, who are acting as surrogate health decision-makers for the ICU patient. A secondary aim of the study was to explore sleep in spouses during the ICU stay. A prospective, randomized controlled trial design accomplished the specific aims.

Setting

Spouses of critically ill, mechanically ventilated patients participated in the study at a level I trauma center with 225 critical care beds.

Sample

The target sample size of 10 subjects was a reasonable representative of the target population for the pilot study (Thabane et al., 2010). After consent, eligible subjects were randomly assigned to one of two groups (*n*=5 intervention group, *n*=5 control group). Subjects in

the intervention group received the SĀF-T intervention once a day over 3-days during the ICU stay. Subjects in the control group did not receive the SĀF-T intervention. Usual care by the healthcare team was provided to both groups (intervention and control), which included orientation to ICU patient room and ICU waiting room, use of bathroom and shower in patient's room, review of ICU visiting policy with contact information, optional guest food tray, other onsite locations to acquire food and beverages, clean towels, warm blankets, and resources for spiritual support. Subjects in both groups met all eligibility and exclusion criteria. Eligibility criteria included: spouses of patients intubated and admitted within 36 hours to the adult ICUs, who were expected to remain in the ICU at least 36 hours, spouse was aged 18 years or older, and understood English. Exclusion criteria included: anticipation by the clinical provider of imminent patient death, spouse was under the age of 18 years old, did not understand English, or was actively being treated for a PICS condition (stress, anxiety, depression, or PTSD).

Sample Size Justification

The sample size of 10 subjects was designed to represent the target population, assess feasibility, and estimate effect size of SĀF-T to conduct *a priori* power analysis for a future RCT investigating SĀF-T effectiveness. The sample size (n=10) was not powered to examine effectiveness of the SĀF-T intervention.

Measures

Measures of key variables collected from subjects are outlined in Table 2.

Table 2. Key Variables, Measures, and Data Collection Time Points

Concept	Measures	Data Collection Time Points: Study Day 1	Study Day 3	Study Day 30	Study Day 90
PICS-F -Symptoms of Anxiety -Symptoms of Depression	Hospital Anxiety and Depression Scale (HADS)	*	*	*	*
-Symptoms of PTSD	Impact Event Scale (IES)	*	*	*	*
-Stress	Perceived Stress Scale (PSS)	*	*	*	*
PICS-F	NIH Toolbox Emotional Battery	*	*	*	*
Sleep/Rest	Actigraphy Sleep Efficiency (continuous over 3-days in ICU)	*	*		
SĀF-T Intervention	Stress Visual Analog Scale (daily over 3-days in ICU)	*	*		
Demographic Characteristics	Age, race, ethnicity, sex, level of education, & distance of hospital commute	*			

The instruments used to collect data were selected from the literature most commonly referenced to measure symptoms of PICS-F conditions (stress, anxiety, depression, and PTSD). This study is the first to measure wrist actigraphy and the NIH Toolbox Emotional Battery and administer SĀF-T in this population.

Hospital Anxiety and Depression Scale (HADS)

HADS (Zigmond & Snaith, 1983) was used to measure anxiety and depression. HADS has been successfully used to measure symptoms of anxiety and depression in the general population and in family members of ICU patients (Anderson et al., 2008; Azoulay et al., 2005; Fumis et al., 2015; Jones et al., 2004; Kentish-Barnes et al., 2017; Lemiale et al., 2010; McAdams et al., 2012; Wolters et al., 2014). It is a 14-item self-report measure divided into 2 subscales (HADS-A & HADS-D) of 7 questions with 4 response options for each question (weighted 0-3). Total score range for each subscale is 0-21. Score categories for each subscale:

0-7 = normal, 8-10 = mild, 11-14 = moderate, and 15-21 = severe. Cronbach's alpha coefficient of internal consistency for HADS-A from .68 to .93 (mean .83), and for HADS-D from .67 to .90 (mean .82). Optimal balance between sensitivity and specificity for HADS as a screening instrument was achieved most frequently at a cutpoint score of 8 for HADS-A and HADS-D.

Impact of Event Scale (IES)

IES is one of the earliest self-report measures of posttraumatic disturbance (Horowitz, et al 1979). The IES is the most commonly used instrument to measure symptoms of PTSD in PICS-F research (Davidson, Jones, & Bienvenu, 2012). The IES has been widely used for many years and found reliable across a broad range of traumatic events **(**Sundin & Horowitz, 2003; Azoulay et al., 2005; Fumis et al., 2015; Jones et al., 2004; Kentish-Barnes et al., 2017; McAdams et al., 2012; Petrinec et al., 2015). The IES is not a tool for diagnosing PTSD, but instead detects symptoms indicating a risk of PTSD. Each of the 15 items were scored on a 6-point scale rated from 0 to 5, so that the total score can range from 0 to 75 (Horowitz, Wilner, & Alvarez, 1979). Higher scores indicate more severe post-traumatic stress symptoms. Score categories include 0-8 = subclinical range, 9-25 = mild range, 26-43 = moderate range, 44-75 = severe range. A correlation of 0.42 ($p< 0.01$) scale scores indicates that the two subsets are associated, but do not measure identical dimensions; test-retest reliability of 0.87 for the total stress scores, 0.89 for the intrusion subscale, and 0.79 for the avoidance subscale.

Perceived Stress Scale (PSS)

Symptoms of stress were quantified using Cohen's et al. (1983) PSS, which is a 10-item measure with a total score range of 0-40. Response options include 0 = never, 1 = almost never, 2 = sometimes, 3 = fairly often, 4 = very often. It is intended to capture the degree to which

persons perceive situations in their life as excessively stressful relative to their ability to cope. Cronbach's alpha is >.70 in multiple studies.

Actigraphy Sleep Efficiency

A wrist ActiWatch (ActiWatch Spectrum, Philips Respironics, Bend, OR) was placed on the subject during study enrollment and activity and ambient light levels were measured continuously over a 3-day period. The AcitWatch is a small, lightweight, limb-worn activity and light-monitoring device that provides sleep/rest actigraphy based on sleep algorithms. Polysomnography is the gold standard measurement of sleep but not feasible in the setting of the SĀF-T study. Actigraphy is frequently used as a measure of sleep/rest in clinical research. The accuracy of actigraphy (0.863), sensitivity (0.965), and specificity (0.329) are weakly correlated with polysomnography (Gironda, Lloyd, Clark, & Walker, 2007; Tonetti, Pasquini, Fabbri, Belluzzi, & Natale, 2008).

National Institutes of Health (NIH) Toolbox Emotional Battery

The NIH Toolbox Emotional Battery (version 1.11) testing was used to measure the full spectrum of emotional health. The battery is made up of four subdomains including Negative Affect, Psychological Well-Being, Stress and Self-Efficacy, and Social Relationships (Salsman, Butt, Pilkonis, Cyranowski, Zill, Hendrie, Cella, et al., 2013). The subdomain stress and self-efficacy focus on individual perceptions about the nature of events and their relationship to the perceived coping resources of the individual. In general, psychological stress occurs when and individual perceives that the environmental or internal demands that are personally meaningful exceed adaptive capacity (Cohen, Kessler, & Gordon,1997). The subscale perceived stress is defined by the individual's perceptions about the nature of events and relationship to their values

and coping resources (Salsman et al., 2013). The subscale self-efficacy is described as a person's belief in their capacity to manage functioning and have control over meaningful events (Bandura, 1997). Life satisfaction subscale is the cognitive evaluation of life experiences (Salsman et al., 2013). This measure is concerned with whether or not people like their lives. The subscale fear affect includes feelings of fearfulness, panic, and anxious misery (Salsman et al., 2013). While fear somatic arousal subscale reflects autonomic arousal to perceptions of threat (Salsman et al., 2013). The subscale sadness is distinguished by low levels of positive affect and comprised of symptoms that are primarily affective (poor mood) and cognitive (negative perceptions of self, the world, and the future) indicators of depression (Salsman et al., 2013). Each subscale associated with a specific subdomain has been calibrated and validated through expert panels and factor analyses. The principal investigator attended the 3-day inaugural training by NIH in Washington, D.C. on all domains in addition to the new 2-day training at Northwestern University for the iPad application.

Procedures

Approval and Registration

University of South Florida Institutional Review Board granted approval for the study (Pro00026246). The study is registered in ClinicalTrials.gov (NCT03129204).

Screening, Recruitment, and Informed Consent

The Principal Investigator (PI) made daily rounds to the adult ICUs and spoke with charge nurses regarding availability of spouses of patients intubated and admitted within the last 36 hours and expected to stay in the ICU for at least 36 hours. Permission was obtained from the bedside ICU nurse for the PI to approach the potential subject with an invitation to enroll in the

study. The potential subject was provided with an oral explanation of the nature of the study, as well as study information in writing. The information included all elements required for informed consent, pertinent contact information, and information about withdrawal from the study. Written consent was obtained from subjects for study participation.

Group Assignment

A block design randomized assignment (randomizer.org) was used to determine group assignment (intervention or control) for subjects. Following signed consent, each subject had an equal chance of receiving the intervention with the opening of a sealed, opaque envelope to obtain the group assignment. Usual care by the healthcare team was provided to both groups (intervention and control), which included orientation to ICU patient room and ICU waiting room, use of bathroom and shower in patient's room, review of ICU visiting policy with contact information, optional guest food tray, other onsite locations to acquire food and beverages, clean towels, warm blankets, and resources for spiritual support.

Description of Intervention

The SĀF-T intervention takes approximately 15-20 minutes to deliver each day, over a 3-day period. The SĀF-T intervention includes coaching from SĀF-T trained research staff (for this study, the PI) on awareness of biological sensations associated with events in the ICU that are perceived stressful. The PI sat across from the subject and asked them to use their eyes to follow hand movements that induce lateral left-right (smooth pursuit) eye movements, followed with deep breaths. To monitor the safety of subjects in the intervention group, immediately before and after (pretest/posttest) each SĀF-T intervention, the subject was asked based on a visual analog scale of 1-10 (1 being a low amount and 10 being a high amount) to rate the

amount of stress they were currently sensing throughout their body. An increased stress level post SĀF-T intervention would be documented an adverse event. Two consecutive adverse events of increased stress levels post SĀF-T intervention would be considered a signal of harm and the subject would be withdrawn from the study.

Data Collection

The collection of primary outcome measures from each subject took approximately 30 minutes during each of the four-time points for both groups: study day 1 (prior to SĀF-T for intervention group), study day 3 (following SĀF-T for the intervention group), study day 30 (1-month), and study day 90 (3-months). Post ICU follow-up data was collected by telephone interview on or within 48 hours of study day 30 and study day 90. The ActiWatch placed on the subject's wrist at the time of study enrollment (study day 1) collected continuous activity and light data over a 3-day period (study day 3).

Data Analysis Plan

IBM SPSS software, version 24 was used to assure data integrity. A review of statistical power, test assumptions, missing data, and measurement tools provided confidence in the results of parametric statistical procedures (Bannon, 2013). Due to the small sample size (n=10), statistical power is insufficient (<.80) to examine all relationships between variables and detect all significant effects. Demographic and clinical characteristics of the study sample were described by means and standard deviations for continuous variables and percentages for categorical variables. Since our sample size is small, it was difficult to verify the sample characteristics were normally distributed. Therefore, distributions of these characteristics were compared by random assignment by use of Fisher's exact test and Mann-Whitney U test.

Given that the repeated dependent variables (*n*=38) stress, anxiety, depression, PTSD, and emotional health are continuous, five principal assumptions (normal distribution, multicollinearity, homoscedasticity, linearity, and no undue influence of outlier scores) were examined before general linear models were used in analysis (Bannon, 2013). Scores of primary outcome measures were approximately normally distributed. Both skewness and kurtosis were less than twice the standard error of each measure (Bannon, 2013). No problems of multicollinearity (correlation coefficient >.90) were detected among predictor variables. Homoscedasticity was supported through Levene's test of homogeneity (p>.05). Linearity between the predictor variables and dependent variables were met. There were no outlier scores impacting normality, thus there was no undue influence of outliers on study results. There were no missing data through study day 1(pre-SĀF-T for intervention group) and study day 3 (post-SĀF-T for intervention group) outcome measures. However, one subject was lost due to attrition for post-ICU follow-up measures (study day 30 and study day 90). This subject's spouse died during the ICU stay and did not return either of the two voicemails to schedule follow-up measures.

SAS version 9.4 was used for Repeated Measures Mixed Effects Models. Specification of the linear mixed model was with maximum likelihood estimation and two categorical variables. The model equation was that each outcome measure mean score was being evaluated in relation to group assignment, assessment period (study day 1 to study day 3, study day 1 to study day 30, and study day 1 to study day 90), and group assignment "x" assessment period for rate of change by group over time. The specification that this was a repeated measures analysis was by the subject ID number indicating how the data were repeated and using an unstructured covariance matrix. The variable Group was the main effect term and compared mean scores between the

SĀF-T and control groups across all time points, including study day 1. The variable Assessment Period was the time variable scored as study day 1, study day 3, study day 30, and study day 90, and evaluated whether the outcome measure scores changed over time. The variable Rate of Change (Group "x" Assessment Period) evaluated whether the rate of change in outcome measure scores over time differed by random assignment, which is a comparison of the slopes for the SĀF-T and control groups. Consequences of significant differences in Rate of Change ($p<0.05$) are not the scores as much as what they imply about the process underlying the scores, which is of most relevance.

Primary Aim

Assess feasibility and estimate effect size of the 3-day SĀF-T intervention on PICS-F (symptoms of stress, anxiety, depression, and PTSD) for spouses of mechanically ventilated patients admitted to the ICU, for whom the spouse is the surrogate health decision-maker.

Objective 1

Determine enrollment rate of subjects along with identification of any barriers to consent for planning timeline of future RCT.

Success criteria 1. a) At least 4 subjects per week can be recruited; b) at least 50% of all eligible subjects can be enrolled; and c) at least 60% of all recruited subjects completed both follow-up measures.

Analysis plan. Descriptive statistics for sample demographic and clinical characteristics were determined as means and standard deviations for continuous variables and as frequencies and percentages for categorical variables. Distributions of these characteristics were compared by random assignment by use of Fisher's exact test and Mann-Whitney U-test. Weekly

recruitment rate, enrollment rate, and measures completion rate were calculated as frequencies and percentages.

Objective 2

Determine acceptability of providing SĀF-T to subjects during the ICU stay.

Success criteria 2. a) At least 90% of recruited subjects randomized to intervention group received 2 of the 3 scheduled doses of SĀF-T in the ICU; and b) >90% of subjects received SĀF-T without adverse events (e.g., increased stress on post-SĀF-T assessment).

Analysis plan. Descriptive statistics for intervention were calculated as means and standard deviations. Wilcoxon Signed Rank Test was used to detect statistical significance of change in pre-SĀF-T and post-SĀF-T stress visual analog scale scores. Received doses and adverse events were calculated in frequencies and percentages.

Objective 3

Evaluate selection of most appropriate primary outcome measures.

Success criteria 3. Measures with highest reliability (Cronbach's alpha), more clinical relevance, and least influenced by factors other than the intervention are the primary outcome measures to move forward to the future RCT.

Analysis plan. Reliability of the study data by instrument were determined with Cronbach's alpha. Significance of SĀF-T on outcome measures were evaluated with *p*-values by Group, Assessment Period, and Rate of Change by group over time using constructed repeated measures general linear mixed models.

Objective 4

Estimate effect size of SĀF-T on primary outcome measures to calculate sample size for the larger future study.

Success criteria 4. a) Large estimated effect size (>0.5) with 95% confidence intervals for SĀF-T on outcome measures study day 1 (pre-SĀF-T for intervention group) and study day 3 (post-SĀF-T for intervention group) and sustained over time (study day 1 to study day 30, and study day 1 to study day 90) are the primary outcome variable targets for the future study, b) small to medium estimated effect size (<0.5) with 95% confidence intervals for SĀF-T on outcome measures are possible secondary outcomes for the future RCT of SAT-T effectiveness.

Analysis plan. Means and standard deviations, effect size, and 95% confidence intervals were determined for outcome measures by group over time.

Secondary Aim

Explore sleep in spouses during the ICU stay.

Objective 5

Test wrist actigraphy data collection on subjects during the ICU stay.

Success criteria 5. a) At least 90% of recruited subjects wore ActiWatch during the ICU stay; and b) >90% of recruited subjects who wore the ActiWatch did not experience adverse events (e.g., skin irritation).

Analysis plan. Descriptive statistics (means and standard deviations) for actigraphy sleep efficiency were determined by group. Mann-Whitney U-test was used to detect differences in actigraphy sleep efficiency by group. Agreed to wear ActiWatch and adverse events were calculated in frequencies and percentages.

Study Evaluation

Evidence of the overall study outcome is evaluated with the following options:

- Stop – future larger RCT of SĀF-T is not feasible;
- Continue but modify protocol – larger RCT is feasible with modifications;
- Continue without modifications, but monitor closely – RCT is feasible with close monitoring; or
- Continue without modifications – RCT is feasible as is.

The study flow chart (See Figure 4) presents a visual overview of the feasibility objectives paired with study processes and includes success criteria.

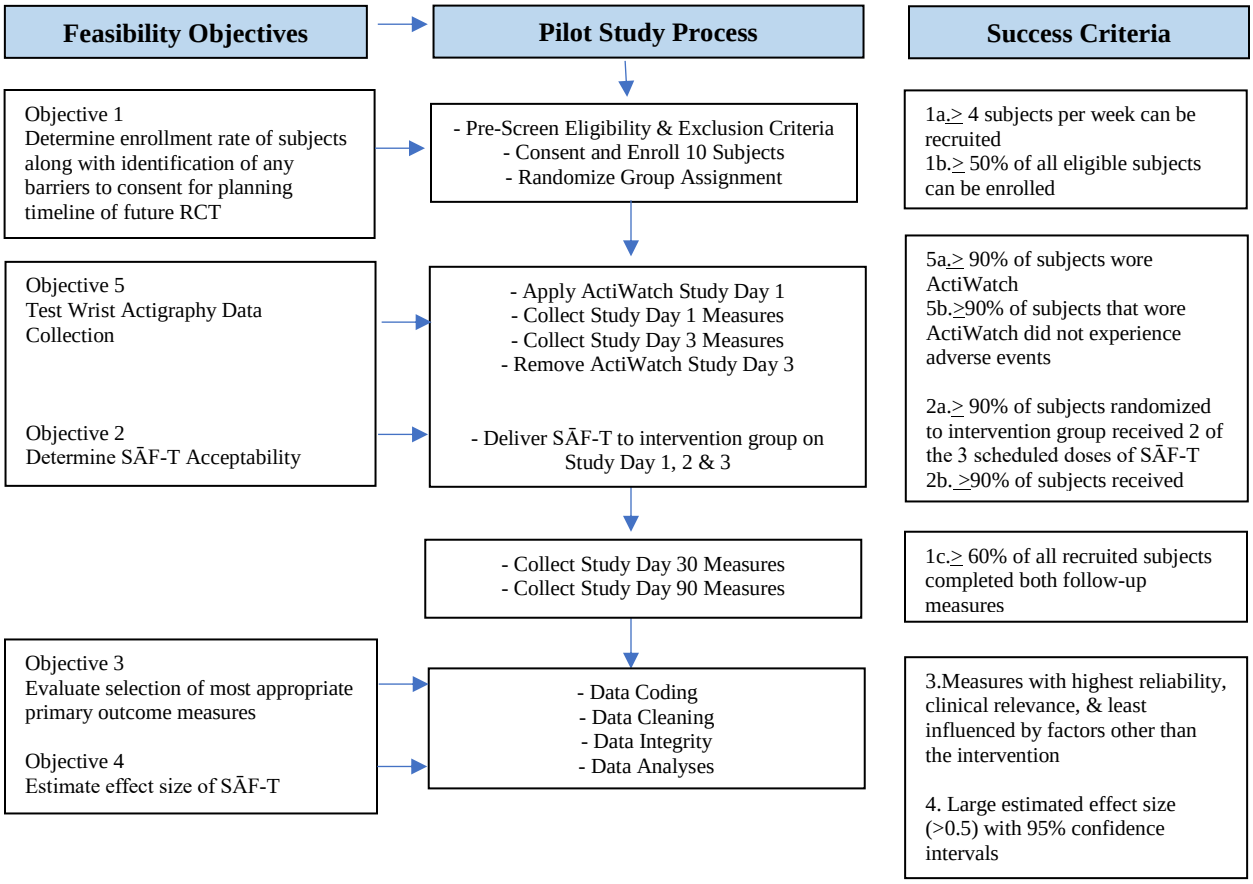

Figure 4. Study flow chart with feasibility objectives and success criteria.

CHAPTER FOUR:

RESULTS

This chapter presents the results of the study. The chapter begins with the sample, including the flow of trial progress by group with a consort diagram, followed by a description of the trial population with demographic characteristics and baseline clinical characteristics.

Sample

A total of 15 spouses were assessed for trial eligibility, of whom, 10 (66.7%) were eligible and enrolled. Of the 5 subjects randomly assigned to the SĀF-T intervention (50% of the sample), 5 (100%) received all interventions, which was1 SĀF-T intervention each day over a 3-day period in the ICU environment. Of the 5 subjects assigned to the control group, 5 (100%) received usual care each day over a 3-day period in the ICU environment. Considering both groups, 10 of 10 subjects (100%) completed study day 1 and study day 3 assessments. Of these, 9 (90%) provided follow-up data at study day 30 and study day 90 (See Figure 5).

Demographic Characteristics

The mean age of the study sample was 57.7 ± 11.9 years, 70% were female, 70% were White, and 30% were of Hispanic ethnicity (See Table 3). The mean distance of hospital commute was 70.7 ± 57.3 miles. The mean level of education was 12.8 ± 1.9 years. Overall, the two groups were well balanced on demographic characteristics except for age. The mean age for the SĀF-T group was 64.6 ± 9.4 and 50.8 ± 10.7 for the control group. The distribution for age in the two groups differed significantly (U=3, $p<0.05$).

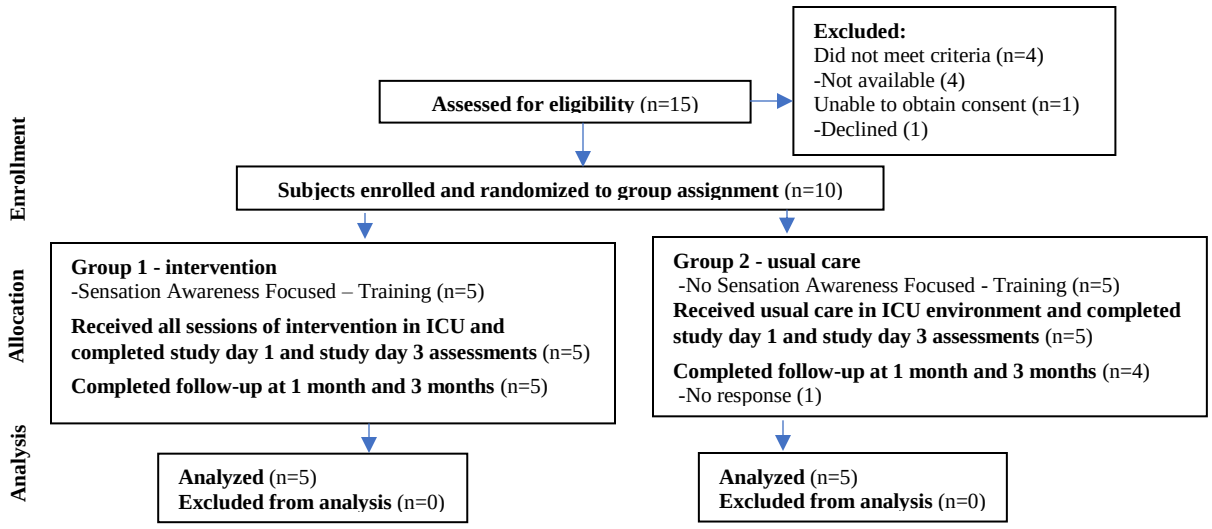

Figure 5. Consort diagram of trial population with enrollment, allocation, and analysis.

Table 3. Demographic Characteristics by Random Assignment

Characteristic	All (*n*=10)	SĀF-T (*n*=5)	Control (*n*=5)	*p*-Value
Race *n* (%):				0.17
White	7 (70.0)	2 (40.0)	5 (100)	
Black	3 (30.0)	3 (60.0)	0 (00.0)	
Ethnicity *n* (%):				1.0
Non-Hispanic	7 (70.0)	4 (80.0)	3 (60.0)	
Hispanic	3 (30.0)	1 (20.0)	2 (40.0)	
Sex *n* (%):				1.0
Male	3 (30.0)	2 (40.0)	1 (20.0)	
Female	7 (70.0)	3 (60.0)	4 (80.0)	
Age in years, mean (SD)	57.7 (11.94)	64.6 (09.37)	50.8 (10.66)	0.05
Distance of hospital commute in miles, mean(SD)	70.7 (57.33)	100 (68.59)	41.4 (23.31)	0.08
Level of education in years, mean (SD)	12.8 (1.93)	12.4 (00.89)	13.2 (02.68)	0.72

Note: Fisher's Exact test and Mann-Whitney U-test for distribution significance by group ($p<0.05$).

Baseline Measures

Baseline (study day 1, pre-SĀF-T for the intervention group) data for PICS-F measures are presented in Table 4. The mean PSS score was 16.9 ± 4.20, 90% had a PSS score of ≥14.7, the suggested cutpoint mean score on the norm table (Cohen, Kamarck, & Mermelstein, 1983). In addition, 80% of the sample scored within the abnormal range (11-21) and 20% of the sample scored within the borderline abnormal range (8-10) on the HADS anxiety subscale; while 100% of the sample scored within the normal range (0-7) on the HADS depression subscale (Zigmond

& Snaith, 1983). The mean IES score was 26.9 ± 6.03, 80% had a IES score ≥ 26, the suggested cutpoint for symptoms of PTSD (Horowitz, Wilner, & Alvarez, 1979). Additional emotional health affect subscales of the NIH Toolbox Emotional Battery were evaluated by converting the raw score of each measure to an uncorrected standard score (T-Score), utilizing a normative mean of 50 (Salsman et al., 2013). At baseline, 100% of the sample fell within the T-Score range of 40–60 on all 17 subscales. Scores more than one standard deviation (10) below the mean (T≤40) suggest "low" levels of the affect measured and scores more than one standard deviation (10) above the mean (T≥60) suggest "high" levels of the affect measured.

Overall, the two groups were balanced in the following baseline measures (study day 1, pre-SĀF-T for the intervention group): PSS, HADS anxiety, HADS depression, PTSD, positive affect, general life satisfaction-B, friendship, loneliness, self-efficacy, perceived stress, fear affect, sadness, and anger physical aggression. The SĀF-T intervention group, compared to the control group, presented with statistically significant more perceived rejection (U=0, p=0.01), more perceived hostility (U=1, p=0.01), higher anger affect (U-0, p=0.01), and an increased amount of anger hostility (U=2.5, p=0.02).

Lastly, compared to the control group, the SĀF-T intervention group presented at baseline (study day 1, pre-SĀF-T for the intervention group) with statistically significant lower amount of general life satisfaction-A (U=0.5, p=0.01), lower amount of meaning and purpose (U=0, p=0.01), not as much emotional support (U=0.5, p=0.01), a lesser amount of instrumental support (U=0, p=0.01), and a lower amount of fear somatic arousal (U=0, p=0.01).

Table 4. Baseline Measures by Random Assignment

Measure	All (n=10)	SĀF-T (n=5)	Control (n=5)	p-Value
PSS, mean (SD)	16.9 (4.20)	18.2 (2.39)	15.6 (5.46)	0.35
HADS -Anxiety, mean (SD)	12.6 (2.67)	13.0 (1.22)	12.2 (3.77)	0.45
HADS -Depression, mean (SD)	4.9 (2.18)	6.2 (2.05)	3.6 (1.52)	0.09
IES (PTSD)	26.9 (6.03)	30.4 (3.05)	23.4 (6.47)	0.07

Table 4 (Continued)

Measure	All (*n*=10)	SĀF-T (*n*=5)	Control (*n*=5)	*p*-Value
NIH Toolbox - Emotional Battery, mean (SD)				
-Positive Affect	49.9 (12.40)	47.8 (11.65)	52.0 (14.11)	0.35
-General Life Satisfaction	29.2 (7.93)	24.6 (9.40)	33.8 (0.45)	0.01
-Meaning & Purpose	30.8 (4.13)	27.6 (3.58)	34.0(0.00)	0.01
-Emotional Support	33.7 (6.80)	28.6(5.98)	38.8 (1.79)	0.01
-Instrumental Support	33.8 (6.41)	28.0 (2.74)	39.6 (0.89)	0.01
-Friendship	33.2 (5.71)	32.8 (7.73)	33.6 (3.65)	1.00
-Loneliness	7.7 (4.11)	9.0 (5.48)	6.4 (1.95)	0.64
-Perceived Rejection	13.2 (5.43)	17.0 (5.48)	9.4 (0.55)	0.01
-Perceived Hostility	11.1 (3.07)	13.0 (3.46)	9.2 (0.45)	0.01
-Self-Efficacy	30.9 (6.19)	27.4 (4.67)	34.4 (5.81)	0.07
-Perceived Stress	27.2 (3.39)	28.4 (2.30)	26.0 (5.05)	0.34
-Fear Affect	17.6 (4.79)	20.8 (1.10)	14.4 (4.98)	0.11
-Fear Somatic Arousal	9.7 (2.31)	8.8 (1.64)	10.6 (2.70)	0.01
-Sadness	13.4 (3.86)	15.0 (5.10)	11.8 (1.10)	0.50
-Anger Affect	10.9 (2.73)	13.0 (2.35)	8.8 (0.45)	0.01
-Anger Hostility	6.8 (2.94)	8.6 (3.36)	5.0 (0.00)	0.02
-Anger Physical Aggression	8.3 (2.21)	8.8 (3.03)	7.8 (1.10)	1.00

Note: Mann-Whitney U-test to determine distribution significance by group ($p<0.05$). PSS (Perceived Stress Scale), HADS (Hospital Anxiety & Depression Scale), IES (Impact of Event Scale).

Primary Aim

Assess feasibility and estimate effect size of the 3-day SĀF-T intervention on PICS-F (symptoms of stress, anxiety, depression, and PTSD) for spouses of mechanically ventilated patients admitted to the ICU who are acting as the surrogate decision-maker for the patient.

Objective 1

Determine enrollment rate of subjects along with identification of any barriers to consent for planning timeline of future RCT.

Success Criteria 1. a) 4 subjects per week can be recruited; b) at least 50% of all eligible subjects can be enrolled; and c) at least 60% of all recruited subjects completed follow-up measures.

The mean weekly recruitment of subjects was 7.5, which is well above the success criteria of 4 subjects per week. The mean enrollment rate was 67%, exceeding the success criteria of a minimum 50% enrollment rate (See Figure 6). All 10 (100%) subjects completed study day 1 (pretest) and study day 3 (posttest) assessments during the ICU stay, and 9 (90%) subjects completed the follow-up measures at study day 30 and study day 90 (See Figure 7). The success criteria of at least 60% completed measures rate was achieved.

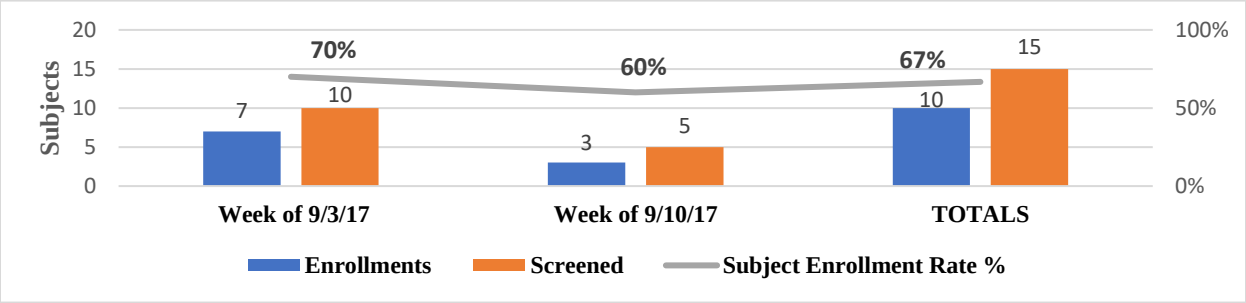

Figure 6. Weekly recruitment and subject enrollment rate meet feasibility success criteria.

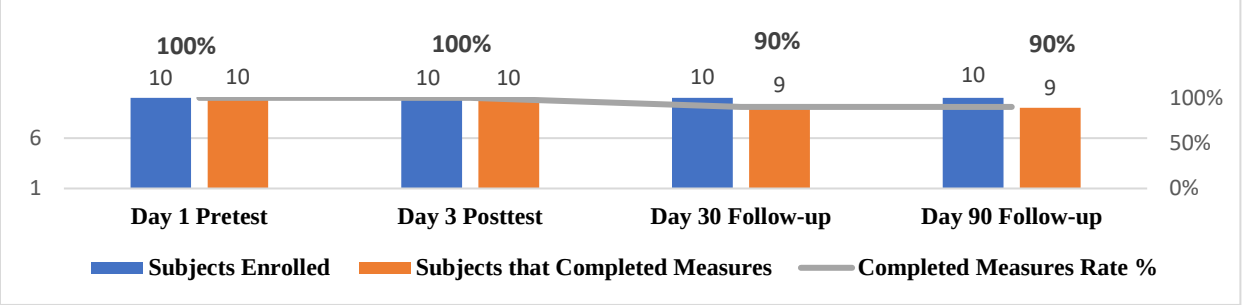

Figure 7. Outcome measures completion rate meet feasibility success criteria.

Objective 2

Determine acceptability of providing SĀF-T to subjects during the ICU stay.

Success Criteria 2. a) At least 90% of recruited subjects randomized to intervention group received 2 of the 3 scheduled doses of SĀF-T in the ICU; and b) >90% of subjects received SĀF-T without adverse events (e.g., increased stress on post-SĀF-T assessment).

Among the 5 recruited subjects randomized to receive SĀF-T, 5 (100%) underwent all 3 sessions, for a total of 15 (100%) sessions, which exceeds the success criteria. The mean individual SĀF-T session time was 12.3 ± 1.05 minutes. The combined total mean SĀF-T session time was 37 ± 3.16 minutes (See Table 5). The pre SĀF-T stress mean visual analog score was 6.3 ± 1.29 and the post SĀF-T stress mean visual analog score was 3.8 ± 0.56 with a mean difference of 2.53 ± 0.36. A Wilcoxon-Signed Rank Test indicated the post SĀF-T stress visual analog scores were statistically significantly lower than the pre SĀF-T stress visual analog scores (Z = -3.47, p=0.01). There were no adverse events reported (See Figure 8). The SĀF-T intervention met all acceptability criteria.

Table 5. Descriptive Statistics for Sensation Awareness Focused Training (SĀF-T) Intervention

				Stress Visual Analog Scale Score Range 1-10 (*n*=15)		
SĀF-T Group (*n*=5)	Number of SĀF-T Sessions	Combined SĀF-T Sessions Total Time (minutes)	Daily SĀF-T Session Time Mean (SD)	Pre SĀF-T Mean (SD)	Post SĀF-T Mean (SD)	Change in Pre-SĀF-T & Post SĀF-T Stress Scores
1	3	32.0	10.7 (1.15)	5.3 (0.58)	3.3 (0.58)	2.00
2	3	36.0	12.0 (2.00)	6.0 (1.00)	4.0 (0.00)	2.00
3	3	40.0	13.3 (2.89)	7.3 (2.08)	4.0 (1.00)	3.33
4	3	38.0	12.7 (1.15)	6.3 (0.58)	4.0 (0.00)	2.33
5	3	39.0	13.0 (2.65)	6.7 (1.53)	3.7 (0.58)	3.00
Overall mean, (SD)	3 (0)	37.0 (3.16)	12.3 (1.05)	6.3 (1.29)	3.8 (0.56)	*p*=0.01

Note: Wilcoxon Signed Rank Test for significance in change of pre-SĀF-T/post-SĀF-T scores (p<0.05).

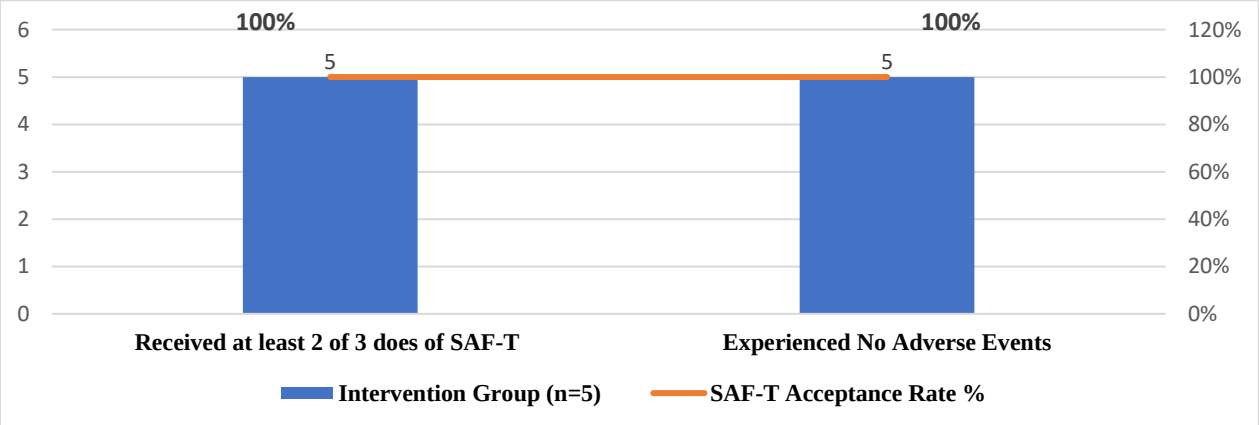

Figure 8. SĀF-T (Sensation Awareness Focused Training) intervention was acceptable.

Objective 3

Evaluate selection of most appropriate primary outcome measures.

Success Criteria 3. Measures with highest reliability (Cronbach's alpha), more clinical relevance, and least influenced by factors other than the intervention are the primary outcome measures to move forward to the future RCT.

Cronbach's alpha for the study with the Perceived Stress Scale (.65) and NIH Toolbox Emotional Battery subscale perceived stress (.66) suggests approximately equivalent reliability (See Table 6). To include both measures for the larger study may add unnecessary subject burden and data redundancy. The comparison of Cronbach's alpha for the HADS subscale anxiety (.61) and NIH Toolbox Emotional Battery subscale fear affect (.78) suggests greater reliability in the study using the NIH Toolbox. Cronbach's alpha for data collected in the study using the HADS subscale depression (.16) was not reliable. Depression is captured in the NIH Toolbox Emotional Battery with the subscale sadness and Cronbach's alpha (.90) suggests this data collected during the study has high reliability. Comparison of Cronbach's alpha for IES (.57) symptoms of PTSD and the NIH Toolbox Emotional Battery subscales fear affect (.78), fear somatic arousal (.53), sadness (.90), anger affect (.79), anger hostility (.90), anger physical aggression (.78), perceived stress (.66), and self-efficacy (.94) suggest higher reliability in the data collected during the study using the NIH Toolbox.

The NIH Toolbox Emotional Battery is made up of four subdomains (Negative Affect, Psychological Well-Being, Stress and Self-Efficacy, and Social Relationships) that are clinically relevant to health outcomes. The PSS and HADS instruments did not demonstrate added clinical relevance to be recommended for inclusion in the larger study. However, an instrument, other than the IES (due to study Cronbach's alpha <.70), that is specific to assess symptoms of PTSD

in the main study is needed. This is the first study to utilize SĀF-T as an intervention for PICS-F. Mediators and moderators that effect SĀF-T are not known. The broadness of measurements in the NIH Toolbox Emotional Battery is advantageous with a wide variety of common metrics for use in the main study.

Table 6. Reliability of Study Outcome Measures (n=38)

Outcome Measure	Instrument	Cronbach's Alpha
-Symptoms of Stress	Perceived Stress Scale (PSS)	.65
-Symptoms of Anxiety	Hospital Anxiety and Depression Scale	.61
-Symptoms of Depression	(HADS)	.16
-Symptoms of PTSD	Impact Event Scale (IES)	.57
-Positive Affect	NIH Toolbox Emotional Battery	.95
-General Life Satisfaction		.97
-Meaning & Purpose		.93
-Emotional Support		.97
-Instrumental Support		.98
-Friendship		.92
-Loneliness		.97
-Loneliness		.97
-Perceived Rejection		.96
-Perceived Hostility		.87
-Self-Efficacy		.94
-Perceived Stress		.66
-Fear Affect		.78
-Fear Somatic Arousal		.53
-Sadness		.90
-Anger Affect		.79
-Anger Hostility		.90
-Anger Physical Aggression		.78

Among the 5 subjects randomly assigned to SĀF-T compared to the control group, the mean scores were statistically significant in general life satisfaction (p=0.04), meaning and purpose (p=0.01), emotional support (p=0.01), perceived rejection (p=0.03), self-efficacy (p=0.01), fear affect (p=0.01), fear somatic arousal (p=0.01), sadness (p=0.01), and anger affect (p=0.01). The change in mean scores by assessment period were statistically significant in PSS (p=0.01), HADS anxiety (p=0.04), IES PTSD (p=0.01), meaning and purpose (p=0.01), emotional support (p=0.01), self-efficacy (p=0.01), and perceived stress (p=0.01). The rate of

change in scores between the SĀF-T group and control group were statistically significant in PSS (p=0.01), IES PTSD (p=0.03), general life satisfaction (p=0.01), perceived rejection (p=0.01), self-efficacy (p=0.01), perceived stress (p=0.02), fear affect (p=0.03), fear somatic arousal (p=0.01), and sadness (p=0.03).

There was insufficient data variability in the sample for the mixed model to converge in the outcome variables depression, instrumental support, friendship, loneliness, perceived hostility, anger hostility, and anger physical aggression.

Table 7. Repeated Measures Mixed Model on Outcome Measures

Outcome Measure	*n*	Group *p*-Value	Assessment Period *p*-Value	Rate of Change *p*-Value
Perceived Stress Scale	38	0.21	0.01	0.01
-Anxiety	38	0.42	0.04	0.06
Impact of Event Scale (PTSD)	38	0.28	0.01	0.03
-Positive Affect	38	0.53	0.15	0.33
-General Life Satisfaction	38	0.04	0.54	0.01
-Meaning & Purpose	38	0.01	0.01	0.16
-Emotional Support	38	0.01	0.01	0.06
-Perceived Rejection	38	0.03	0.26	0.01
-Self-Efficacy	38	0.01	0.01	0.01
-Perceived Stress	38	0.65	0.01	0.02
-Fear Affect	38	0.01	0.75	0.03
-Fear Somatic Arousal	38	0.01	0.13	0.01
-Sadness	38	0.01	0.75	0.03
-Anger Affect	38	0.01	0.08	0.98

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The following Figures 9-17 illustrate a comparison of slopes by group over time with significant differences in rate of change (p<0.05). At study day 1, subjects randomly assigned to SĀF-T perceived more stress than the control group. Mean scores within each group significantly changed over time (p=0.01). Perceived stress increased during the ICU stay for the control group and decreased in the group that received SĀF-T each day for 3-days in the ICU. The rate of change in the PSS and NIH Toolbox Emotion Battery subscale perceived stress (a comparison of the slopes between the SĀF-T group and control group over time) were statistically significant (PSS, p=0.01; perceived stress, p=0.02) (See Figures 9 & 10).

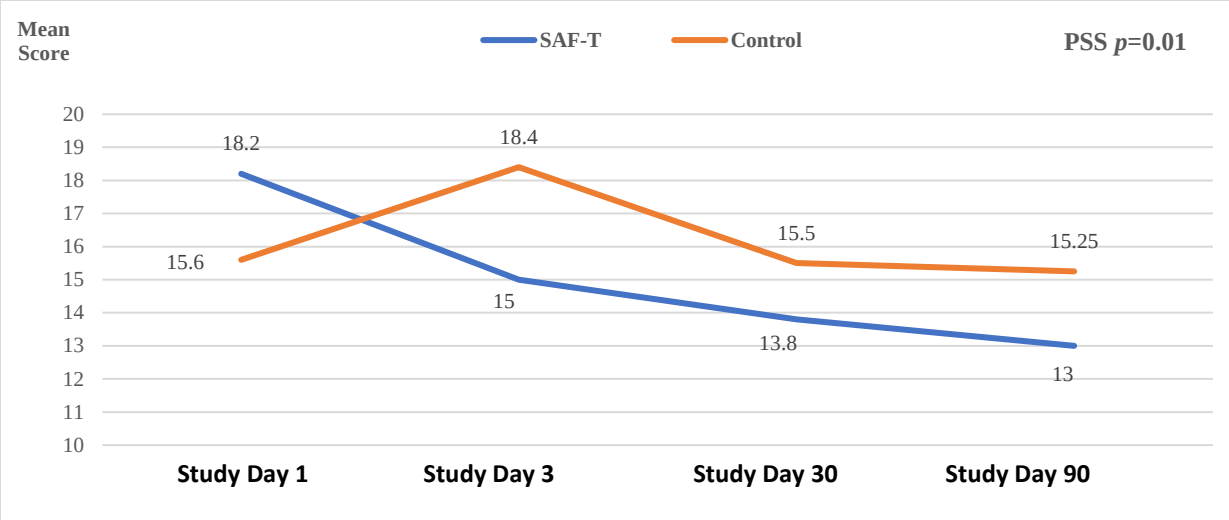

Figure 9. Rate of change in Perceived Stress Scale was statistically significant in repeated measures mixed model.

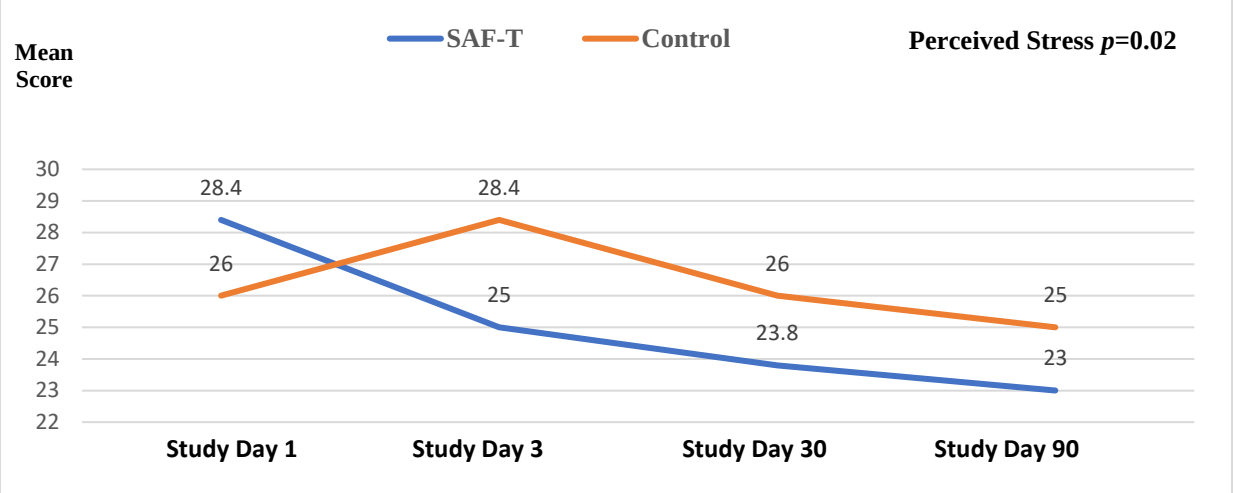

Figure 10. Rate of change in NIH Toolbox Emotional Battery subscale perceived stress was statistically significant in repeated measures mixed model.

At study day 1, subjects randomly assigned to the control group had significantly more self-efficacy than subjects assigned to the SĀF-T group (p=0.01). Mean scores within each group significantly changed over time (p=0.01). Self-efficacy decreased during the ICU stay for the control group and gradually increased over time in the SĀF-T group. The rate of change in self-efficacy (a comparison of the slopes between the SĀF-T group and control group over time), was statistically significant (p=0.01) (See Figure 11).

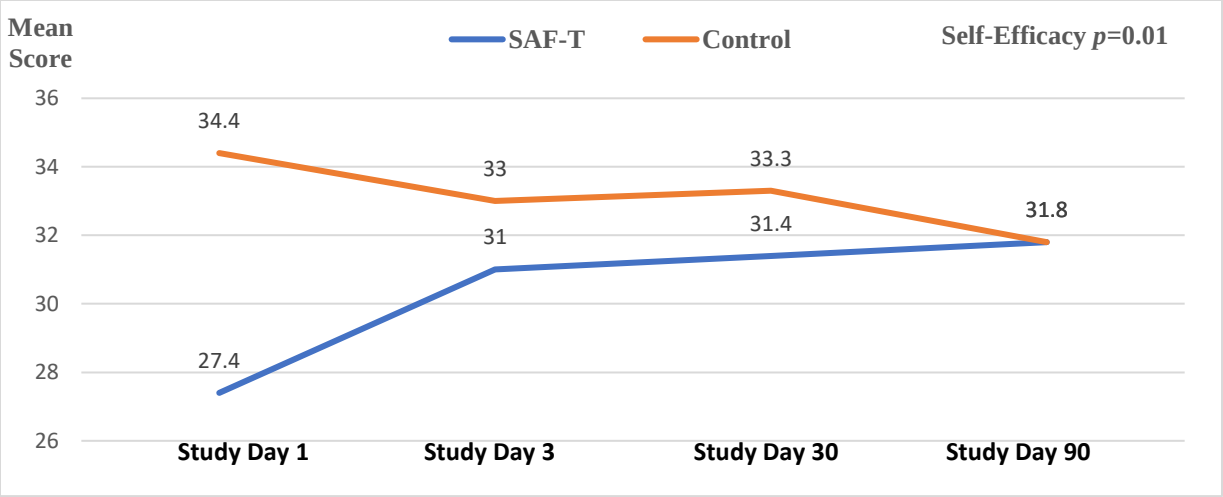

Figure 11. Rate of change in NIH Toolbox Emotional Battery subscale self-efficacy was statistically significant in repeated measures mixed model.

At study day 1, subjects randomly assigned to the SĀF-T group had more symptoms of PTSD than subjects randomly assigned to the control group (See Figure 12). Symptoms of PTSD within each group significantly changed over time (p=0.01). Symptoms of PTSD continuously decreased over time for the SĀF-T group. In the control group, symptoms of PTSD increased during the ICU stay, decreased at study day 30, and increased again at study day 90. The rate of change in symptoms of PTSD (a comparison of the slopes between the SĀF-T group and control group over time), was statistically significant (p=0.03).

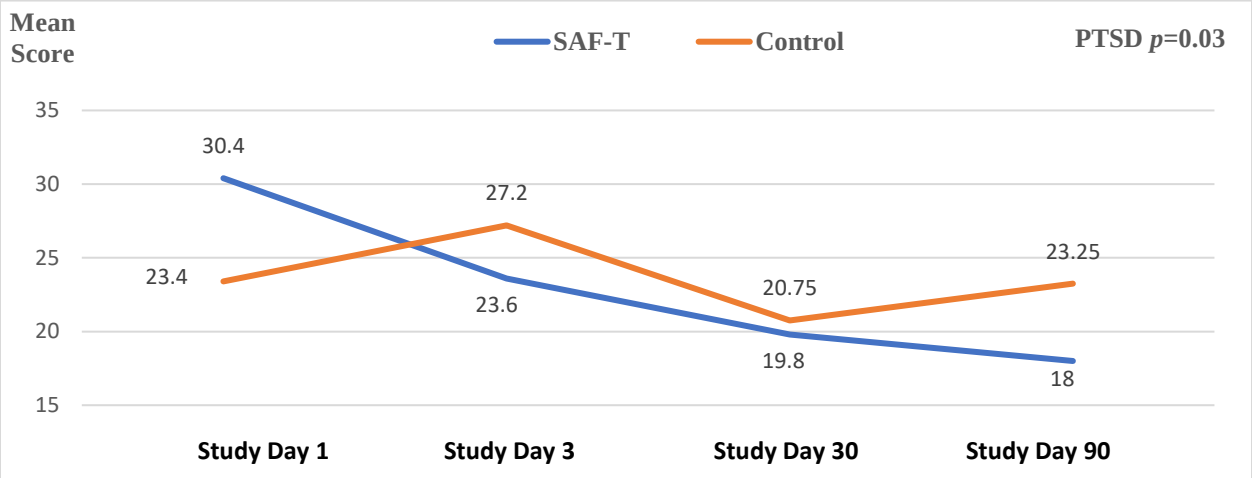

Figure 12. Rate of change in Impact of Event Scale (PTSD) was statistically significant in repeated measures mixed model.

At study day 1 and across all time points, subjects randomly assigned to SĀF-T liked their lives significantly more than the control group (p=0.04). The mean scores within each group remained consistent and did not significantly change over time. In Figure 13, the rate of change (a comparison of the slopes between the SĀF-T group and control group over time) was statistically significant (p=0.01).

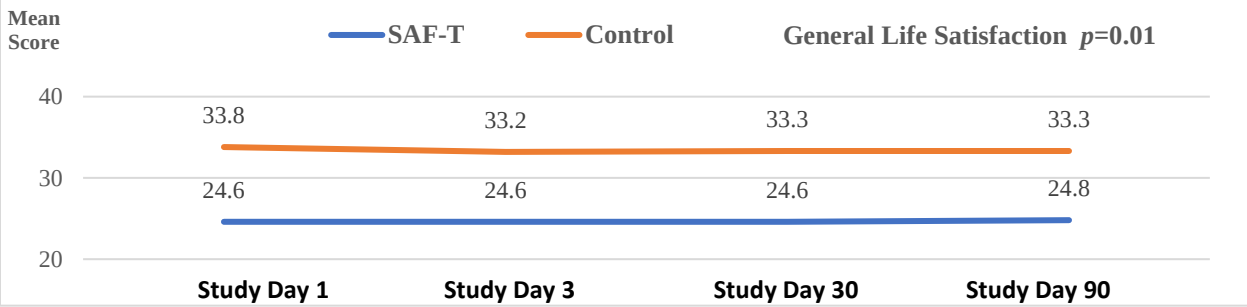

Figure 13. Rate of change in NIH Toolbox Emotional Battery subscale general life satisfaction was statistically significant in repeated measures mixed model.

At study day 1, subjects randomly assigned to SĀF-T perceived significantly more rejection than the control group (p=0.03). Over time, mean perceived rejection scores within the SĀF-T group were trending downward. The mean perceived rejection scores for the control group were trending upward during the ICU stay and over time at study day 30 and began trending downward at study day 90 (See Figure 14). The rate of change (a comparison of the slopes between the SĀF-T group and control group over time), was statistically significant (p=0.01).

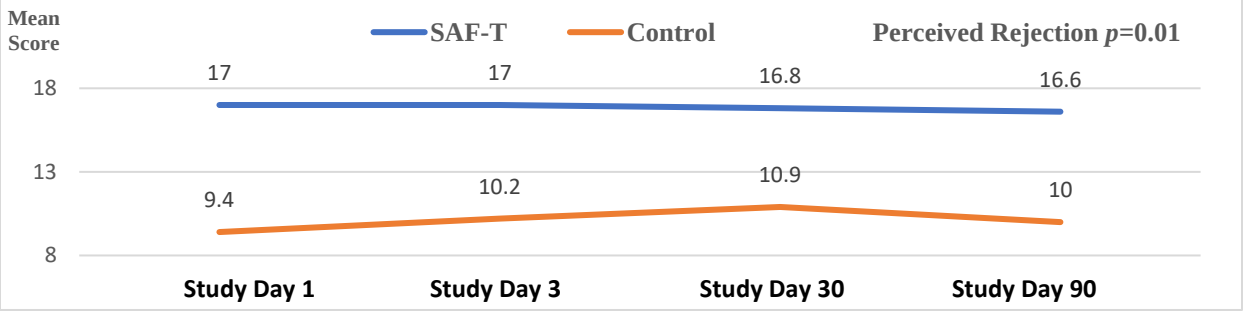

Figure 14. Rate of change in NIH Toolbox Emotional Battery subscale perceived rejection was statistically significant in repeated measures mixed model.

At study day 1, subjects randomly assigned to SĀF-T had significantly more feelings of fearfulness than the control group (p=0.01). Fear affect continuously decreased over time in the SĀF-T group. Fear affect increased during the ICU stay in the control group and decreased at study day 30. The mean scores within each group did not significantly change over time. In Figure 15, the rate of change (a comparison of the slopes between the SĀF-T group and control group over time), was statistically significant (p=0.03).

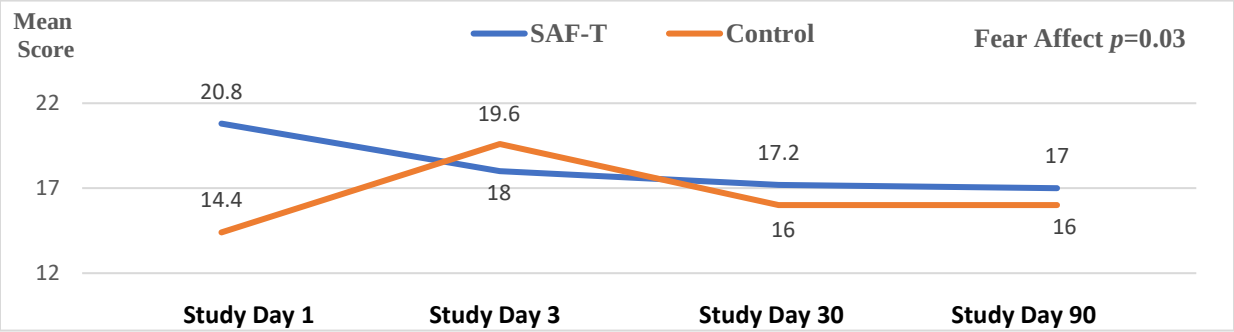

Figure 15. Rate of change in NIH Toolbox Emotional Battery subscale fear affect was statistically significant in repeated measures mixed model.

At study day 1, subjects randomly assigned to SĀF-T had significantly less somatic arousal than the control group (p=0.01). Somatic arousal continuously decreased over time in the SĀF-T group. In the control group, somatic arousal increased during the ICU stay and decreased over time at study day 30 and study day 90. The mean scores within each group did not significantly change over time. In Figure 16, the rate of change (a comparison of the slopes between the SĀF-T group and control group over time), was statistically significant (p=0.01).

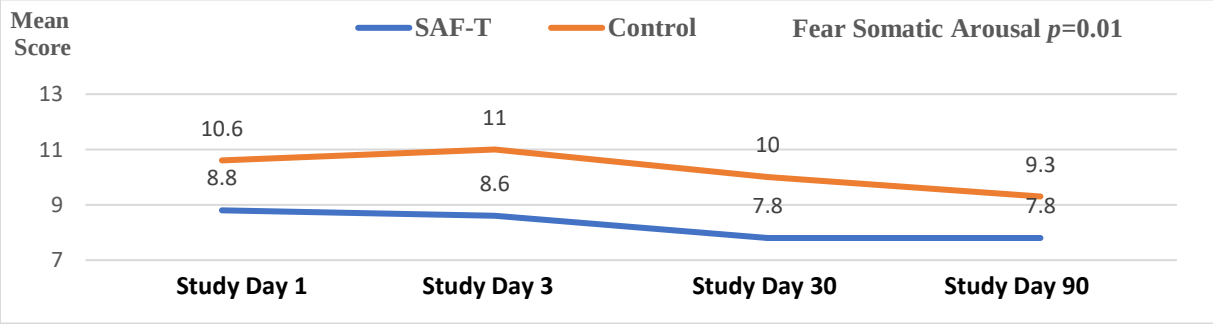

Figure 16. Rate of change in NIH Toolbox Emotional Battery subscale fear somatic arousal was statistically significant in repeated measures mixed model.

At study day 1, subjects randomly assigned to SĀF-T were significantly sadder than the control group (p=0.01). Sadness continuously decreased over time in the SĀF-T group. Sadness increased during the ICU stay in the control group, decreased at study day 30, and returned to baseline at study day 90. The mean scores within each group did not significantly change over time. In Figure 17, the rate of change (a comparison of the slopes between the SĀF-T group and control group over time), was statistically significant (p=0.03).

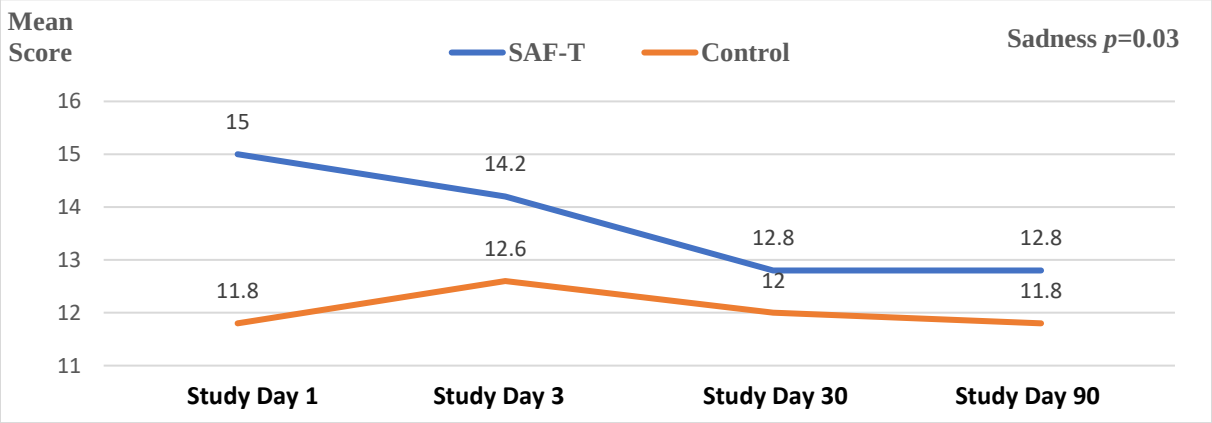

Figure 17. Rate of change in NIH Toolbox Emotional Battery subscale sadness was statistically significant in repeated measures mixed model.

Objective 4

Estimate effect size of SĀF-T on primary outcome measures to calculate sample size for the larger future study.

Success criteria 4. a) Large estimated effect size (>0.5) with 95% confidence intervals for SĀF-T on outcome measures study day 1 (pre-SĀF-T in intervention group) and study day 3 (post-SĀF-T for intervention group) and sustained over time (study day 1 to study day 30, and study day 1 to study day 90) are the primary outcome variable targets for the future study, b) small to medium estimated effect size (<0.5) with 95% confidence intervals for SĀF-T on outcome measures are possible secondary outcomes for a future RCT of SAT-T effectiveness.

The 5 (100%) subjects assigned to SĀF-T completed all 3 sessions (per study protocol). Large estimated effect size among the 5 randomly assigned to SĀF-T compared to the 5 randomly assigned to the control group occurred in the mean study day 1 (pre-SĀF-T for the intervention group) to study day 3 (post-SĀF-T for the intervention group) change in the following outcome measures: fear affect, perceived hostility, PTSD, anxiety, PSS, perceived stress, anger affect, self-efficacy, positive affect, and general life satisfaction (See Table 7). Due to the large estimated effect size, they will serve as primary outcome variable targets for the future RCT.

Table 8. Estimated Effect Size of SĀF-T on Outcome Measures – Study Day 1 to Study Day 3

	SĀF-T Group			Control Group				
Outcome Measure	Day 1	Day 3	Diff	Day 1	Day 3	Diff	Effect Size	95% CI
Perceived Stress	18.2	15.0	-3.2	15.6	18.4	2.8	1.51	0.15 – 2.87
Hospital Anxiety and Depression Scale								
-Anxiety	13.0	10.0	-3.0	12.2	13.8	1.6	1.58	0.20 – 2.96
-Depression	6.2	6.2	0	3.6	4.2	0.6	0.15	-1.00 – 1.30
Impact of Event (PTSD)	30.4	23.6	-6.8	23.4	27.3	3.9	1.94	0.45 – 3.42
NIH Toolbox Emotional Battery								
-Positive Affect	47.8	55.8	-8.0	52.0	50.2	1.8	-0.73	-1.92 – 0.47
-General Life Satisfaction	24.6	24.6	0.0	33.8	33.2	0.6	-0.64	-1.82 – 0.55
-Meaning & Purpose	27.6	27.4	0.2	34.0	33.0	1.0	-0.16	-1.30 – 0.99
-Emotional Support	28.6	29.2	-0.6	38.8	38.8	0.0	-0.21	-1.36 – 0.94
-Instrumental Support	28.0	28.0	0.0	39.6	38.0	1.6	-0.49	-1.66 – 0.68
-Friendship	32.8	32.8	0.0	33.6	33.6	0.0	0.00	-1.14 – 1.14
-Loneliness	9.0	9.0	0.0	6.4	7.8	-1.4	0.32	-0.84 – 1.47
-Perceived Rejection	17.0	17.0	0.0	9.4	10.2	-0.8	0.19	-0.96 – 1.33
-Perceived Hostility	13.0	13.0	0.0	9.2	15.0	-5.8	2.06	0.53 – 3.58
-Self-Efficacy	27.4	31.0	-3.6	34.4	33.0	1.4	-1.03	-2.28 – 0.22
-Perceived Stress	28.4	25.0	3.4	26.0	28.4	-2.4	1.50	0.14 – 2.87
-Fear Affect	20.8	18.0	2.8	14.4	19.6	-5.2	2.16	0.60 – 3.71
-Fear Somatic Arousal	8.8	8.6	0.2	10.6	11.0	-0.4	0.28	-0.87 – 1.44
-Sadness	15.0	14.2	0.8	11.8	12.6	-0.8	0.45	-0.71 – 1.61
-Anger Affect	13.0	11.4	1.6	8.8	9.4	-0.6	1.28	-0.03 – 2.58
-Anger Hostility	8.6	8.6	0.0	5.0	5.0	0.0	0.00	-1.14 – 1.14
-Anger Physical Aggression	8.8	8.8	0.0	7.8	6.8	1.0	-0.45	-1.61 – 0.72

Of the 10 subjects who completed pretest/posttest assessments, 9 (90%) provided follow-up data at study day 30. Among these 9 subjects, 5 were in the SĀF-T group and 4 were in the control group. Large estimated effect size among the 5 randomly assigned to SĀF-T, compared to the control group, occurred in the mean study day 1 to study day 30 change in the following

outcome measures: perceived hostility, PTSD, instrumental support, fear somatic arousal, perceived stress, anger affect, PSS, anxiety, self-efficacy, fear affect, sadness, positive affect, and general life satisfaction (See Table 8). Due to the large estimated effect size, they will serve as primary outcome variable targets for the future RCT.

Table 9. Estimated Effect Size of SĀF-T on Outcome Measures – Study Day 1 to Study Day 30

	SĀF-T Group			Control Group				
Outcome Measure	Day 1	Day 30	Diff	Day 1	Day 30	Diff	Effect Size	95% CI
Perceived Stress Scale	18.2	13.8	-4.4	15.6	15.5	-0.1	1.13	-0.14 – 2.40
Hospital Anxiety and Depression Scale								
-Anxiety	13.0	9.4	-3.6	12.2	10.0	-2.2	0.95	-0.28 – 2.19
-Depression	6.2	5.0	-1.2	3.6	3.5	-0.1	0.47	-0.70 – 1.64
Impact of Event Scale (PTSD)	30.4	19.8	-10.6	23.4	20.8	-2.6	1.39	0.06 – 2.72
NIH Toolbox Emotional Battery								
-Positive Affect	47.8	58.6	-10.8	52.0	55.3	-3.3	-0.57	-1.81 – 0.67
-General Life Satisfaction	18.4	18.8	-0.4	22.0	21.0	1.0	-0.52	-1.75 – 0.71
-Meaning & Purpose	27.6	27.2	0.4	34.0	32.5	1.5	-0.03	-1.24 – 1.17
-Emotional Support	28.6	29.8	-1.2	38.8	39.0	-0.2	-0.47	-1.70 – 0.75
-Instrumental Support	28.0	28.3	-0.3	39.6	37.3	2.3	-1.31	-2.69 – 0.08
-Friendship	32.8	32.8	0.0	33.6	30.8	2.8	-0.44	-1.66 – 0.78
-Loneliness	9.0	9.0	0.0	6.4	5.0	1.4	-0.30	-1.52 – 0.91
-Perceived Rejection	17.0	16.8	0.2	9.4	10.9	-1.5	0.35	-0.87 – 1.56
-Perceived Hostility	13.0	13.0	0.0	9.2	14.8	-5.6	1.93	0.36 – 3.50
-Self-Efficacy	27.4	31.4	-4.0	34.4	33.3	1.1	-0.90	-2.19 – 0.39
-Perceived Stress	28.4	23.8	4.6	26.0	26.0	0.0	1.23	-0.13 – 2.59
-Fear Affect	20.8	17.2	3.6	14.4	16.0	-1.6	0.81	-0.46 – 2.09
-Fear Somatic Arousal	8.8	7.8	1.0	10.6	10.0	0.6	1.30	-0.08 – 2.68
-Sadness	15.0	12.8	2.2	11.8	12.0	-0.2	0.63	-0.62 – 1.88
-Anger Affect	13.0	11.2	1.8	8.8	8.8	0.0	1.14	-0.20 – 2.48
-Anger Hostility	8.6	8.6	0.0	5.0	5.0	0.0	0.09	-1.11 – 1.29
-Anger Physical Aggression	8.8	8.8	0.0	7.8	6.8	1.0	-0.41	-1.63 – 0.81

Of the 10 subjects who completed study day 1 and study day 3 assessments, 9 (90%) provided follow-up data at study day 90. Among the 9 subjects, 5 were in the SĀF-T group and 4 were in the control group. Large estimated effect size among the 5 randomly assigned to SĀF-T compared to the control group occurred in the mean study day 1 to study day 90 change in the following outcome measures: PTSD, perceived hostility, anger affect, instrumental support, PSS, perceived stress, fear affect, anxiety, self-efficacy, fear somatic arousal, sadness, positive affect, and general life satisfaction (See Table 9). Due to the large estimated effect size, they will serve as primary outcome variable targets for the future RCT.

Table 10. Estimated Effect Size of SĀF-T on Outcome Measures - Study Day 1 to Study Day 90

	SĀF-T Group			Control Group				
Outcome Measure	Day 1	Day 90	Diff	Day 1	Day 90	Diff	Effect Size	95% CI
Perceived Stress Scale	18.2	13.0	-5.2	15.6	15.3	-0.3	1.26	-0.04 – 2.56
Hospital Anxiety and Depression Scale								
-Anxiety	13.0	9.2	-3.8	12.2	10.0	-2.2	0.97	-0.27 – 2.21
-Depression	6.2	5.0	-1.2	3.6	3.5	-0.1	0.47	-0.70 – 1.64
Impact of Event Scale (PTSD)	30.4	18.0	-12.4	23.4	23.3	-0.1	1.95	0.46 – 3.45
NIH Toolbox Emotional Battery								
-Positive Affect	47.8	59.2	-11.4	52.0	56.3	-4.3	-0.54	-1.78 – 0.69
-General Life Satisfaction	18.4	18.8	-0.4	22.0	21.0	1.0	-0.52	-1.75 – 0.71
-Meaning & Purpose	27.6	27.2	0.4	34.0	33.0	1.0	0.22	-0.99 – 1.43
-Emotional Support	28.6	30.0	-1.4	38.8	39.0	-0.2	-0.45	-1.68 – 0.77
-Instrumental Support	28.0	28.2	-0.2	39.6	37.3	2.3	-1.31	-2.69 – 0.08
-Friendship	32.8	32.8	0.0	33.6	30.8	2.8	-0.44	-1.66 – 0.78
-Loneliness	9.0	9.0	0.0	6.4	5.0	1.4	-0.30	-1.52 – 0.91
-Perceived Rejection	17.0	16.6	0.4	9.4	10.0	-0.6	0.41	-0.81 – 1.63
-Perceived Hostility	13.0	13.0	0.0	9.2	14.8	-5.6	1.93	0.36 – 3.50
-Self-Efficacy	27.4	31.8	-4.4	34.4	33.3	1.1	-0.96	-2.26 – 0.35
-Perceived Stress	28.4	23.0	5.4	26.0	25.0	1.0	1.13	-0.21 – 2.47
-Fear Affect	20.8	17.0	3.8	14.4	16.0	-1.6	1.02	-0.30 – 2.33
-Fear Somatic Arousal	8.8	7.8	1.0	10.6	9.3	1.3	0.75	-0.52 – 2.01
-Sadness	15.0	12.8	2.2	11.8	11.8	0.0	0.58	-0.66 – 1.82
-Anger Affect	13.0	11.0	2.0	8.8	8.8	0.0	1.35	-0.05 – 2.74
-Anger Hostility	8.6	8.6	0.0	5.0	5.0	0.0	0.09	-1.11 – 1.29
-Anger Physical Aggression	8.8	8.8	0.0	7.8	6.8	1.0	-0.41	-1.63 – 0.81

Secondary Aim

Explore sleep in spouses during the ICU stay.

Objective 5

Test wrist actigraphy data collection on subjects during the ICU stay.

Success Criteria 5. a) At least 90% of recruited subjects wore ActiWatch during the ICU stay; and b) >90% of recruited subjects who wore the ActiWatch did not experience adverse events (e.g., skin irritation).

Among the 10 recruited subjects, 9 (90%) agreed to wear the ActiWatch and of these 9 (100%) did not experience any adverse events from wearing the ActiWatch, which meets the success criteria for ActiWatch acceptance (See Figure 18).

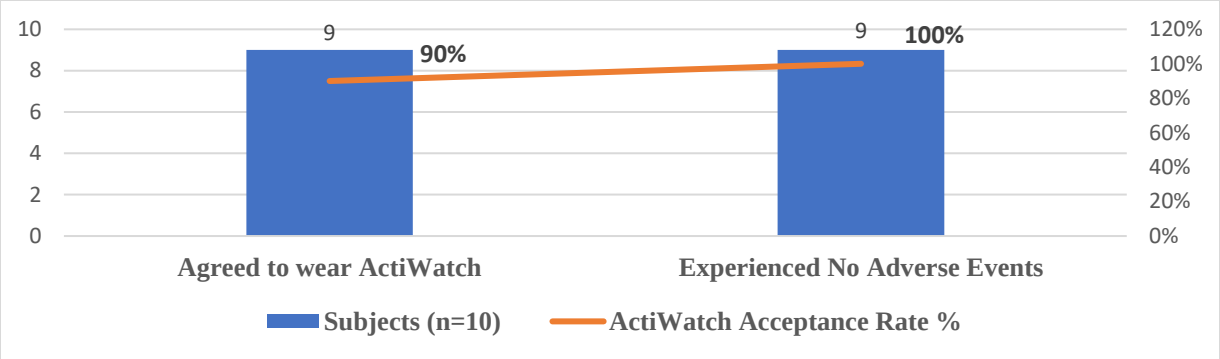

Figure 18. ActiWatch was acceptable and feasible to explore sleep during the ICU stay.

The mean sleep efficiency percentage among the 5 subjects randomly assigned to the SĀF-T group was 70.4 ± 15.24 and among the 4 subjects in the control group was 64 ± 20.59 (See Table 11). A Mann-Whitney U-test suggests the difference of 6.4 ± 4.52 in sleep efficiency percentage between groups was not statistically significant (U=9, p=0.81).

Table 11. Descriptive Statistics for Actigraphy Sleep Efficiency % by Group

Variable	*n*	Mean	SD	Minimum	Maximum	Adverse Events	*p*-Value
Group							0.81
-SĀF-T Group	5	70.4	15.24	54.0	88.0	0	
-Control Group	4	64.0	20.59	40.0	90.0	0	

Note: Mann-Whitney U-test for distribution significance by group ($p<0.05$).

CHAPTER FIVE:

DISCUSSION

The final chapter of this dissertation begins with a summary of the study findings, implications for the main study, and study outcome evaluation. This chapter includes strengths and limitations of the study. Lastly, conclusions of the study are discussed.

Study Findings

The study findings support the primary aim to assess feasibility and estimate effect size of the 3-day SĀF-T intervention on PICS-F (symptoms of stress, anxiety, depression, and PTSD) for spouses of mechanically ventilated patients admitted to the ICU, who are acting as the surrogate decision-maker for the patient; and the secondary aim to explore sleep in spouses during the ICU stay. In this first randomized controlled trial of SĀF-T with a central focus on PICS-F, recruitment and enrollment rates of subjects in the study exceeded the success criteria. Planning the timeline of the larger future study can be completed with a high level of confidence using two subjects per week or eight subjects per month as target enrollment goals. Among those enrolled, it is feasible that approximately 4.8 (60%) subjects per month will complete all repeated outcome measures. Wearing the ActiWatch and administration of SĀF-T during the ICU stay appears to be safe, acceptable, and feasible for subjects. Since the decrease in stress scores following SĀF-T were significant ($p<.05$), it is important in the future study to control subject interaction and incidental sharing of intervention effects, which could have a negative impact in internal validity. Table 12 presents the outcome measures with high reliability

(Cronbach's alpha >.70), large estimated effect size (>.50), and significant rate of change (p<.05) that will serve as primary outcome measures for PICS-F in a future larger RCT to evaluate effectiveness of the intervention.

Table 12. Primary Outcome Measures for PICS-F in Future RCT

Outcome Variable	Cronbach's Alpha	Study Day 1 to Study Day 3 Effect Size	Study Day 1 to Study Day 30 Effect Size	Study Day 1 to Study Day 90 Effect Size	Rate of Change
Self-efficacy	0.94	-1.03	-0.90	-0.96	0.01
General Life Satisfaction	0.97	-0.73	-0.52	-0.52	0.01
Perceived Rejection	0.96	0.19	0.35	0.41	0.01
Fear Somatic Arousal	0.53	0.28	1.30	0.75	0.01
Perceived Stress	0.66	1.50	1.23	1.13	0.02
PTSD	0.57	1.94	1.39	1.95	0.03
Fear Affect	0.78	2.16	0.81	1.02	0.03
Sadness	0.90	0.45	0.63	0.58	0.03
Positive Affect	0.95	-0.73	-0.57	-0.54	0.33
Anger Affect	0.79	1.28	1.14	1.35	0.98
Perceived Hostility	0.87	2.06	1.93	1.93	IDV
Instrumental Support	0.98	-0.49	-1.31	-1.31	IDV

Note: IDV (insufficient data variability) for mixed model.

Similar patterns in the rate of change occurred by group in outcome measures perceived stress, PTSD, fear affect, fear somatic arousal, perceived rejection, and sadness. During the ICU stay, these conditions increased or became worse in the control group and decreased or improved in the SĀF-T group. Consistent with the literature (Salsman et al., 2013), self-efficacy and life satisfaction decreased in the control group as their stress, fear, rejection, and sadness increased. Self-efficacy and life satisfaction in the SĀF-T group increased as their stress, fear, rejection, and sadness decreased.

Due to small effect size, the outcome measures friendship, loneliness, anger hostility, and anger physical aggression will serve as secondary outcome measures in the larger RCT. The PSS is incorporated in the NIH Toolbox Emotion Battery subscale perceived stress. Since Cronbach's alpha was approximately equivalent in study data collected with both instruments, the PSS is redundant will not be used in the larger effectiveness trial. For similar reasons, data collected

during the study using the NIH Toolbox Emotion Battery subscales fear affect and sadness compared with study data collected with HADS appear to be approximately equivalent or superior in reliability. Thus, HADS will not be used in the larger effectiveness trial. The reliability of data collected during the study using the IES for symptoms of PTSD was low (Cronbach's alpha <.70) and did not demonstrate confidence for use in the larger RCT. Evidence in the literature suggest PTSD is the most prevalent condition of PICS-F. Although the NIH Toolbox Emotion Battery has several subscales comparable with symptoms of PTSD (i.e., fear affect, fear somatic arousal, sadness, anger affect, anger hostility, anger physical aggression, perceived stress, and self-efficacy), an additional instrument specific to symptoms of PTSD with sound psychometric properties is recommended for future studies of SĀF-T. Additional areas of measurement to consider for future studies that could be advantageous and are common metrics for the 2017 Family-Centered Care Guidelines include: Family Quality of Life, Family Quality of Dying, Family Burden, and Family Decisional Regret (Davidson et al., 2017).

Study Outcome

Collectively, these findings suggest evidence of SĀF-T feasibility with modifications to protocol outcome measures. The preliminary analyses indicate that additional research about the effectiveness of SĀF-T in reducing PICS-F are warranted. A large effect size can be used in the *a priori* power analysis to calculate the sample size for the future RCT.

Study Strengths and Limitations

Strengths of the study include use of a highly standardized treatment protocol (SĀF-T); randomized controlled trial design; and clear feasibility aims, objectives, and success criteria. Small sample size is both a strength and limitation for the study. The strength of the small

sample size is it allows for optimal focus on feasibility of the study. Limitations of a small sample size include insufficient power to examine all relationships between variables and detect all significant effects (although it is noted that this was not an aim of the study), and inability to assure normal distributions. There are limitations within the use of self-report measures, which can exhibit problems with honesty, introspective ability, accurate understanding, use of rating scales, and response bias. Lastly, a limitation of the pilot study was lack of blinding to the intervention for the research staff. For this reason, unblinded data collected during the pilot study will not be combined with blinded data collected during any future studies.

Conclusions

PICS-F is an emerging, growing problem. Our disproportionately larger aging population is at higher risk for critical care due to age-related trauma and illness. Thus, a growing number of family members will be at the bedside of their aging loved ones and exposed to critical care. Due to advancements in science and technology, the rate of ICU survivorship is increasing, which means an increasing number of family members will become informal caregivers throughout the long recovery process of the ICU survivor. Evidence of feasibility in this small study demonstrates it is possible to redesign critical care to include both patient and their family as a unit in need of care for the best possible outcomes. There is enormous opportunity to work smarter in the delivery of critical care to prevent both PICS and PICS-F. The rigor of randomized controlled trials (RCT) for effective preventative interventions is warranted. Well-designed preliminary studies with clear feasibility aims, objectives, and success criteria are an essential prerequisite to enhance the likelihood of success for full-scale RCT main studies.

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