STUDY TITLE: Messy Memories: A Mobile Application Exposure Therapy Intervention to Reduce Psychological Distress and Improve Health Behaviors Following Critical Illness

IRB NUMBER: AAAU1653

NCT NUMBER: NCT05849454

PRINCIPAL INVESTIGATOR: Nadia Liyanage-Don, MD, MS

1. Study Purpose and Rationale

Although posttraumatic stress disorder (PTSD) has traditionally been associated with military combat, sexual assault, or natural disasters, a growing body of literature suggests that it also frequently develops in response to life-threatening medical events, particularly those requiring critical care.[1,2] Critical illness can be an incredibly traumatic experience, often involving treatment in the intensive care unit (ICU), intubation or other invasive medical procedures, altered levels of consciousness, inability to communicate, sensory and sleep deprivation, physical pain, and delirium.[3,4] The cumulative physical and psychological stress associated with critical illness can be severe enough to induce clinically-significant symptoms of PTSD,[5,6] hallmarks of which include intrusive thoughts, persistent re-experiencing of the traumatic event, negative alterations in mood and cognition, increased arousal or hypervigilance, and avoidance of trauma-related stimuli.[7] Up to 63% of critical illness survivors report subsequent PTSD symptoms, which are associated with physical disability, functional impairment, poor health-related quality of life, and diminished life course opportunities.[8-12] Furthermore, patients with medically-related PTSD are more likely to engage in unhealthy behaviors, such as tobacco use,[13,14] sedentary lifestyle,[15,16] poor diet,[16] and medication nonadherence.[17-20]

There are multiple existing treatment modalities for PTSD, including pharmacotherapy, cognitive behavioral therapy, interpersonal therapy, stress inoculation training, and relaxation techniques.[21] However, exposure therapy (ET) is considered the gold standard PTSD treatment,[22] supported by decades of research and recommended in the practice guidelines of organizations such as the Institute of Medicine[23] and the National Institute for Clinical Excellence.[24] Based on emotional processing theory, ET involves habituation, extinction, and modification of the pathological elements of a theoretical fear structure.[25,26] Patients are repeatedly exposed to trauma-related stimuli in a safe clinical environment, leading to habituation of maladaptive emotional responses to the traumatic event and an increased sense of control and self-competence. In turn, this reduces avoidance of trauma-related stimuli, resulting in even more spontaneous exposure to such stimuli and further reduction in PTSD symptoms.[27,28] ET is highly effective for improving PTSD triggered by various forms of trauma, including combat, noncombat, and sexual trauma.[29-32] ET also significantly reduces symptoms that often co-occur with PTSD, such as depression, anxiety, guilt, and anger.[33,34] Several recent large-scale reviews and meta-analyses have confirmed that ET is both safe and effective for improving PTSD symptoms in various patient populations, including those with complex medical comorbidities.[35-37]

Less is known about the role of ET for reducing PTSD symptoms after life-threatening medical events. In a study of patients with PTSD related to hematopoietic stem cell transplantation for hematologic or lymphoid malignancy, exposure-based therapy led to a significant reduction in PTSD symptoms and lower odds of PTSD diagnosis at 12 months compared to an assessment-only control.[38] Among patients with HIV-induced PTSD symptoms, those enrolled in a biweekly ET program experienced a greater decrease in PTSD symptoms both immediately post-intervention and at 3-month follow-up compared to those enrolled in a waitlist control.[39] A study of patients with PTSD symptoms due to a cardiovascular event (e.g., myocardial infarction, coronary artery bypass graft, stroke) showed that ET was associated with an improvement in

PTSD symptoms compared to an education-only control group, though the study was underpowered to reach statistical significance.[40] To our knowledge, there have been no studies exploring the safety, efficacy, or acceptability of ET for treating PTSD specifically induced by critical illness requiring intensive care unit (ICU) treatment. Furthermore, even when PTSD treatments are available and offered, patients often face considerable barriers to accessing such treatments, including financial constraints, availability of mental health providers, travel time or distance, lack of transportation, concerns about privacy, and perceived stigma.[41-44] The avoidant behavior typical of PTSD makes it even more challenging for patients to seek, accept, or engage in effective treatment.[45]

In response to these barriers, novel treatment delivery approaches have been developed in recent years to make therapy for PTSD more accessible and acceptable. Many of these interventions are grounded in ET principles, including a version of PTSD psychotherapy for primary care[46] and strategies to reduce burnout stress in ICU nurses.[47] Preliminary evidence suggests that these brief, flexible, self-directed interventions are effective for treating PTSD and anxiety disorders.[48] Technological solutions, such as clinical videoconferencing and mobile device applications, have also been used to overcome barriers to timely and effective delivery of PTSD care. For example, the smartphone application *PTSD Coach*, which offers psychoeducation about PTSD as well as coping skills based on cognitive behavioral therapy, was found feasible and acceptable when tested in a community sample of trauma survivors.[49] In a subsequent randomized controlled trial, users of the *PTSD Coach* mobile application had a significant decrease in PTSD symptoms compared to a waitlist-control group.[50] A self-directed mobile mindfulness training application initiated in ICU patients following hospital discharge demonstrated feasibility, acceptability, and usability, with similar reductions in psychological distress and physical symptoms compared to either a therapist-led telephone-based mindfulness program or a web-based critical illness education program.[51] Other mobile applications have been developed and tested for treating social anxiety disorder,[52] reducing self-injurious thoughts and behaviors,[53] and lowering alcohol consumption among college students.[54] A variety of mindfulness meditation applications, such as *Headspace* and *Calm*, have also been marketed to the general public with the broader aim of improving mental health and well-being.[55] However, there is currently no mobile application available that directly targets stress-related concerns while following evidence-based ET principles.

The purpose of the proposed pilot study is to conduct preliminary testing of a newly developed mobile application (*Messy Memories*) that specifically targets stress-related concerns to reduce psychological distress and improve health behaviors among survivors of critical illness. The *Messy Memories* app allows the user to self-administer exposure therapy with the goal of reducing psychological distress and ultimately improving health behaviors. The user is asked to document a traumatic or distressing memory (either in writing or via audio recording) and process what it felt like to re-experience the memory. Users can return to their documented memory as often as they like until it becomes easier to re-experience.

The app was initially designed by researchers to target stress-related concerns in frontline healthcare workers after Drs. Sheila Rauch (Emory), Naomi Simon (NYU Langone Health), and Barbara Rothbaum (Emory) created an evidence-informed framework for health system response to a traumatic event based on different levels of intervention (including self-directed intervention). (See https://adaa.org/sites/default/files/PhasedApproachtoCovid-19.ver1.2.pdf for more detail.) This model was presented as a plan for addressing the increasing shortage of mental health resources at a time of increasing need for these resources. Drs. Sheila Rauch and Barbara Rothbaum are renowned experts with decades of experience in the field of PTSD research and treatment (see: Meet the Team | Emory School of Medicine).

The Messy Memories application is a self-directed exposure intervention, and an extension of the framework created by Drs. Rauch, Simon, and Rothbaum. Specifically, the Messy Memories app allows the user to self-administer exposure therapy techniques outside of the traditional psychotherapy context. The Messy Memories app was initially released in a written form for self-help, but with widespread use of smartphones, a mobile application has the potential to further reduce barriers and increase access to care.

The Messy Memories app does not directly request any identifiable information from users. Participants will also be explicitly instructed *not* to provide any identifiable information when utilizing and responding to app prompts. The Messy Memories Study team at CUIMC will not share **any** identifiable subject data with the app developer.

For our study, we will determine the feasibility of enrolling critical illness survivors into the intervention, test the ability of participants to follow the intervention protocol, assess participant satisfaction with the intervention, and measure changes in psychological distress before and after completing the intervention. We note that in order to be eligible, participants will indicate *some* level of psychological distress related to their ICU hospitalization, however the minimum threshold for this level of psychological distress is well below the threshold for PTSD.

Aim 1: Assess the feasibility of recruiting and engaging critical illness survivors in a mobile application-based exposure therapy intervention (*Messy Memories*). **Hypothesis:** The intervention will be feasible based on recruitment, retention, and completion rates of ≥70%.

Aim 2: Assess the acceptability of recruiting and engaging critical illness survivors in a mobile application-based exposure therapy intervention (*Messy Memories*). **Hypothesis:** The intervention will be acceptable based on participant satisfaction ratings of ≥70% and qualitative analysis of exit survey responses.

Aim 3 (exploratory): Assess engagement of the mechanistic target (PTSD symptoms) by the mobile application-based exposure therapy intervention (*Messy Memories*). **Hypothesis:** Participants will report improvement in PTSD symptoms, based on pre-/post-intervention decrease in scores on the PTSD Checklist for the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (PCL-5).

2. Study Design

Overall approach: The proposed pilot study will conduct preliminary testing of a novel mobile application (*Messy Memories*) that uses remotely delivered exposure therapy to reduce psychological distress and improve health behaviors in survivors of critical illness. Specifically, we aim to assess the feasibility and acceptability of recruiting and engaging critical illness survivors in the intervention. We also aim to explore the efficacy of the intervention in engaging the mechanistic target (PTSD symptoms) to reduce psychological distress. The results of this initial pilot study will be used to make refinements to the research protocol in preparation for a future adequately powered randomized controlled trial testing whether the intervention can significantly reduce psychological distress and, in turn, improve behavioral outcomes (e.g., medication adherence, physical activity, dietary habits, sleep patterns, substance use) among survivors of critical illness.

Eligibility:

Patients will be included if they meet the following inclusion/exclusion criteria:

Inclusion Criteria:

(1) Age 18 years old or older

(2) Able to speak and write in English

(3) Previously admitted to an ICU

(4) Have internet access (e.g., Wi-Fi)

(5) Have access to an internet-equipped smartphone device (e.g., iPhone, Android)

(6) Meet a minimum threshold of psychological distress related to their prior critical illness as demonstrated by scoring ≥10 points on the PTSD Checklist for the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (PCL-5, see *Measures* section for a complete description).

Exclusion Criteria:

(1) ICU discharge occurred <30 days prior to the time of study enrollment
(2) Score <10 points on the PCL-5 during the initial eligibility screening
(3) Unable to comply with the protocol (either self-selected or indicating that s/he/they cannot complete all requested tasks) for reasons that include, but are not limited to, cognitive impairment (e.g., dementia), alcohol and/or substance abuse, or severe mental illness (e.g., schizophrenia).
(4) Unavailable for follow-up for reasons such as terminal illness and imminent plans to leave the United States (as we have migrant or mobile patients due to their citizenship and work issues).

Intervention: *Messy Memories* is a mobile application that allows users to self-administer exposure therapy techniques outside of the traditional psychotherapy context. The intervention was initially released in a written format for individual self-help, but with the widespread use of smartphones, a mobile version was developed with the potential to further reduce barriers and increase access to mental health care. **Appendix A** shows screenshots of the user view of the various application modules. Please note that these images are only examples of the user interface and do not include every screen the user might see while interacting with the app.

Participants will be asked to engage with the *Messy Memories* application at least 3 days a week for at least 10 minutes each day using their own mobile smartphone device. Participants may proceed through the modules of the application at their own pace and may return to any module as many times as they desire throughout the 6-week intervention period. Mechanistic target and clinical symptom assessments will occur at Week 0 (baseline), Week 3 (mid-intervention), Week 6 (end of intervention), and Week 12 (follow-up). All study procedures, including eligibility screening, consent process, outcome assessments, and exit surveys, will be conducted remotely via telephone or Zoom video conference.

Modules:

- Introduction: Provides a general overview of the application, offers suggestions for its use, describes how stress may impact mental health, and explains how processing difficult memories related to stress may help to improve well-being.
- Memory Processing: Participants recall a difficult ("messy") memory, which they will be asked to audio record, including what they did, felt, thought, smelled, saw, etc. They are then asked questions about what it was like to re-experience the memory, such as what emotions were elicited (e.g., sadness, anger, fear). Next, participants are asked to process what the memory means to them. They are then instructed to listen to their recording of the memory or re-record it as often as they like, until the memory becomes easier to re-

experience. They respond to processing questions each time they listen to or re-record their prior difficult memory.
- Feedback: Shows data from the participant's engagement with the application, including feedback related to memory processing.

Data collected:

- Data directly provided by the participant: While using the *Messy Memories* application, participants will use affect rating sliders to directly input information related to their mood over the past several days, their level of distress before and after processing a difficult memory, and answers to questions about revisiting their difficult memory. Direct recordings of the participant's "messy memory" (audio recorded) will only be available on the participant's smartphone while using the app. These recordings (audio) will not be collected as data.
- Data indirectly provided by the participant: The *Messy Memories* application will also collect data on how long and how frequently participants use the application. Specifically, each response to a prompt within the application will be recorded with a timestamp (date and time) to indicate when the participant provided a particular response.
- Protected Health Information (PHI): The *Messy Memories* application does not collect or store PHI. Participants will be instructed not to record any identifiable information while using the app.

Measures:

Feasibility: To assess feasibility of the intervention, we will determine: 1) the number of participants that are needed to screen and consent; 2) the proportion of eligible participants who accept the offer to participate; 3) the proportion of consenting participants who download the application and initiate the intervention (i.e., log into the app at least once after the baseline visit); 4) the proportion of consenting participants who access the Memory Processing module at least once; 5) the total number of times that the Memory Processing module is accessed; 6) the total number of times that each additional modules (i.e., Introduction, Feedback) is accessed. We will also describe how participants generally engage with the app (e.g., frequency and duration of engagement with each feature). In addition, we will assess the relative efficacy of each of our recruitment strategies.

Acceptability: To assess acceptability of the intervention, participants will be asked to complete an exit survey via telephone interview or self-administered online. The survey will include questions regarding perceptions and feelings about the intervention. Participants will also be asked to provide qualitative feedback on the intervention (e.g., likes, dislikes, suggestions for improvement).

Proctor's Implementation Measures: Three validated measures (Acceptability of Intervention Measure [AIM], Feasibility of Intervention Measure [FIM], and Intervention Appropriateness Measure [IAM]) will be used to assess the acceptability, feasibility, and appropriateness of the *Messy Memories* intervention, respectively.[56] Each measure consists of four items answered on a 5-point scale (1 = *strongly disagree*, 5 = *strongly agree*). Average responses of ≥4 on the AIM, FIM, and IAM are indicative of adequate acceptability, feasibility, and appropriateness, respectively.[56,57]

System Usability Scale (SUS): The SUS is a reliable tool for evaluating the usability of various products and services, including hardware, software, mobile devices, websites, and applications.[58,59] It consists of ten items answered on a 5-point scale (1 = *strongly disagree*, 5 = *strongly agree*). We will use a score ≥68 to indicate adequate usability, in accordance with prior studies.[60]

PTSD symptoms: PTSD symptoms triggered by the prior critical illness and ICU hospitalization will be assessed using the PTSD Checklist for the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (PCL-5).[61] The PCL-5 is an extensively validated self-report measure developed by the National Center for PTSD that corresponds to DSM-5 criteria for PTSD. Patients are provided a list of 20 PTSD symptoms and asked to rate how much they have been bothered by each symptom due to their prior critical illness and ICU hospitalization on a scale of 0 = *not at all* to 4 = *extremely*. We will classify participants with PCL-5 scores ≥34 as having elevated PTSD symptoms, which has been validated as a screening cutoff and used in prior studies of civilian populations.[62-64]

Other psychological symptoms: In addition to PTSD symptoms, we will also assess for symptoms of depression, anxiety, and anxiety sensitivity. Depression will be assessed using the 8-item Patient Health Questionnaire (PHQ-8),[65] with scores ≥10 positive for depression.[66,67] Anxiety will be assessed using the 7-item Generalized Anxiety Disorder (GAD-7) scale,[68] with scores ≥10 positive for anxiety.[69] Anxiety sensitivity will be assessed using the 16-item Anxiety Sensitivity Index (ASI),[70] with scores ≥17 indicating high anxiety sensitivity.[71]

Health behaviors: The International Physical Activity Questionnaire (IPAQ),[72] will be used to measure the type, frequency, and intensity of daily physical activity. The Pittsburgh Sleep Quality Index (PSQI)[73] will be used to measure total sleep duration and sleep quality. Participants will also be asked to report on their patterns of tobacco, alcohol, and substance/drug use.

Post-ICU support: As part of the baseline visit, participants will be asked questions about any medical, psychological, and social support that they may have received after their prior ICU admission. Participants will also be asked about what forms of post-ICU support they think would be helpful for patients and their families.

Sociodemographic and clinical characteristics: Participant sociodemographic information (e.g., age, sex, gender, sexual orientation, race, ethnicity, primary language, educational attainment, occupation, annual household income, marital/partner status, living situation, insurance status) will be self-reported at screening. Participants will also be asked to self-report any comorbid medical or psychiatric conditions, as well as provide information about their prior ICU admission (e.g., location, primary diagnosis, duration of hospitalization, need for intubation/mechanical ventilation, need for renal replacement therapy, need for central line placement).

3. Statistical Procedures

General approach: Given that this pilot study is, by design, not powered to test the effect of our intervention on study outcomes, we do not intend to publish analyses of these effects. Although some have used pilot studies to estimate effect sizes on primary outcomes, we agree with leaders in our field who argue that effect size estimates from small pilot studies are too imprecise to meaningfully inform effect size assumptions or power analyses for larger, later-stage studies. Therefore, we do not provide power calculations for the effects of our intervention on study outcomes. However, we will use estimates from these studies (e.g., standard deviations, attrition rates) to help determine appropriate sample sizes for a future study that is powered to detect meaningful reductions in measures of psychological distress following critical illness.

Descriptive statistics: Categorical data will be presented as percentages and continuous data will be presented as means with standard deviations for normally distributed measures and as medians with interquartile ranges for measures that are not normally distributed. Checks of assumptions (e.g., normality) underlying statistical procedures will be performed and corrective procedures will be applied (e.g., log transformations, nonparametric tests).

Outcomes: The *primary outcomes* are feasibility and acceptability of the *Messy Memories* intervention and research procedures. Feasibility will be based on participant recruitment, retention, and completion rates of ≥70%. Acceptability will be based on participant satisfaction ratings of ≥70% and qualitative analysis of exit survey responses. The *exploratory outcome* is the ability of the *Messy Memories* intervention to engage the proposed mechanistic target, which will be based on pre-/post-intervention change in patient-reported PTSD symptoms specifically triggered by the prior critical illness and ICU hospitalization.

Aim 1: Assess the feasibility of recruiting and engaging critical illness survivors in a mobile application-based exposure therapy intervention (*Messy Memories*). **Hypothesis:** The intervention will be feasible based on recruitment, retention, and completion rates of ≥70%.

Aim 2: Assess the acceptability of recruiting and engaging critical illness survivors in a mobile application-based exposure therapy intervention (*Messy Memories*). **Hypothesis:** The intervention will be acceptable based on participant satisfaction ratings of ≥70% and qualitative analysis of exit survey responses.

Statistical approach for Aims 1 & 2: We will calculate means and standard deviations (or medians and interquartile ranges if variables are non-normal) as well as frequencies and proportions to assess feasibility and acceptability outcomes. T-tests or chi-square tests will be used to compare the demographic and clinical characteristics of 1) eligible patients who did vs. did not enroll in the study and 2) consenting participants who did vs. did not complete the study. Free-text responses from the exit survey will be described qualitatively and used to contextualize our quantitative results and guide future research.

Aim 3 (exploratory): Assess engagement of the mechanistic target (PTSD symptoms) by the mobile application-based exposure therapy intervention (*Messy Memories*). **Hypothesis:** Participants will report improvement in PTSD symptoms based on pre-/post-intervention decrease in scores on the PTSD Checklist for the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (PCL-5).

Statistical approach for Aim 3: We will assess whether the *Messy Memories* intervention engages the mechanistic target (PTSD symptoms) by comparing pre-/post-intervention change in PCL-5 score using one-sample t-tests with comparison values of 0 (i.e., all null hypotheses entail no change in PCL-5 score). Given the exploratory nature of Aim 3, we will focus the interpretation of these analyses on effect sizes (Cohen's D) rather than statistical significance to assess potential signals for intervention effects.

Sample size and power estimates: Because the proposed study is a pilot trial, we did not conduct a formal power analysis. We aim to recruit as many participants as possible but selected a minimum n=30 based on pragmatics, the needs of the trial, and previous pilot studies suggesting that this sample size is sufficient to provide an accurate indication of the feasibility and acceptability of the study procedures.

Interim analyses: Given the relatively small sample size of this study and the expected minimal risk of the intervention, no interim analyses are currently planned. However, if concerns arise related to adverse events, then an interim analysis may be conducted and the study may be stopped early depending on the recommendations of the IRB and/or NIA.

Subgroup analyses: Given that this is a stage 1A/1B pilot feasibility study, we do not plan to conduct any pre-specified subgroup analyses.

4. Study Procedures

Provide a detailed description of which procedures are being conducted by Columbia researchers. You may include information about study instruments and study measures.

Recruitment: We aim to enroll ≥30 participants in this pilot study. Potential participants will be identified and recruited using several different approaches, each of which is described below.

1. **Post-ICU support groups**
   We will work with providers at Vanderbilt University Medical Center, University of Pittsburgh Medical Center, UCLA (University of California – Los Angeles), the University of Michigan Medical Center, and other U.S.-based centers who host post-ICU support groups. Led by teams of providers (e.g., physicians, psychologists, social workers), these groups meet regularly via zoom (and/or in person) to provide ongoing practical and psychological support to critical illness survivors. Support group members have all had a prior ICU admission and have experienced varying degrees of psychological distress as a result. Support group leaders have agreed to share the study flyer with their post-ICU support group members. Those who are interested in participating in the study can follow a link or QR code on the flyer, which will direct them to the Qualtrics-based screening information sheet. Those who consent to screen will complete a self-administered study screener on Qualtrics.

   Dr. Liyanage-Don or another member of the study team may also offer a brief live video presentation to post-ICU support groups to describe the study and answer any initial questions the attendees may have about the study. At the presentation, Dr. Liyanage-Don (or a member of the study team) would share the study flyer with the group.

2. **Post-ICU recovery clinics/providers**
   We will work with providers at Vanderbilt University Medical Center, University of Pittsburgh Medical Center, UCLA (University of California – Los Angeles), the University of Michigan Medical Center, and other U.S. based centers who provide multidisciplinary care to patients after an ICU admission. Clinic leaders have agreed to share the study flyer with their post-ICU recovery patients. Those who are interested in participating in the study can follow a link or QR code on flyer, which will direct them to the Qualtrics-based screening information sheet. Those who consent to screen will complete a self-administered study screener on Qualtrics.

3. **Post-ICU patients at Columbia: Direct referrals from outpatient treating clinicians**
   Patients may also be referred directly to the Messy Memories research team by the patient's clinical care team within the ColumbiaDoctors/NYPH healthcare system. We will only accept referrals from providers who confirm that the patient meets the Messy Memories study inclusion and exclusion criteria, deem the patient appropriate for participation, and receive verbal approval from the patient to be contacted by research personnel. The treating clinician will provide patient's first and last name and MRN so that a member of the research team can identify the patient in the electronic health record (EHR) to confirm contact information, English-speaking status and eligibility (as needed). The treating clinician may use an IRB-approved study brochure to introduce the study to their patient should they choose. Please note that this brochure, unlike the study flyer, does not contain any QR codes or links to a Qualtrics information sheet. Once the above steps have been completed, a member of the research team will contact the patient to discuss the study in detail. Patients who express interest in learning more about the study will move forward with the consent to screen, which will be conducted verbally using a screening information sheet. Those who consent to screen will complete a study screener with a member of the study team.

4. **Facebook.com groups (e.g., post-ICU support groups)**
   We may post information about this study on "Facebook" groups. Please note, as most Facebook post-ICU support groups are private groups run by an administrator team, the research team will send the IRB-approved flyer and recruitment language to the administrator or other group member who may post or share this information directly with the group. In cases where the groups are not private, members of the study team may post this language. Interested individuals may click on the link or scan the QR code to navigate to the Qualtrics consent to screen and screener to see if they are eligible or contact the study team and review the consent to screen and screener over the phone if preferred.

5. **CUIMC RecruitMe**
   We may post the study on the "RecruitMe" website (https://recruit.cumc.columbia.edu). Interested individuals may click on the link to the study Qualtrics consent to screen and screener to see if they are eligible or contact the study team and review the consent to screen and screener over the phone if preferred.

6. **ResearchMatch**
   We may post the study on "ResearchMatch" (https://www/researchmatch.org). ResearchMatch will provide the study team with a de-identified list of volunteers that fit the study eligibility criteria. The study team will send a contact message through ResearchMatch to the potential participants. ResearchMatch will provide the study team the contact information for volunteers that reply "yes" to the contact message and consent to their information being shared with the study team. Once contacted by the research team, individuals that express interest in participating in the study will be offered the choice of completing the consent to screen and screener over the phone or via Qualtrics.

7. **ClinicalTrials.gov**
   Individuals who contact study staff to express interest in participating in the study after finding the study on ClinicalTrials.gov may also be recruited. They will be offered the choice of completing the consent to screen and screener over the phone or via Qualtrics.

8. **Sudden Cardiac Arrest Foundation (SCAF)**
   The study flyer may be advertised by SCAF, a community of cardiac arrest survivors, their families, and other advocates. We will provide the study flyer and scripted language to foundation contacts who will share it with the SCAF community (e.g. through their website and/or via their email listserv). Interested individuals may click on the link or scan the QR code to navigate to the study Qualtrics consent to screen and screener to see if they are eligible or contact the study team and review the consent to screen and screener over the phone if preferred.

9. **PACE Study**
   The PACE Study (IRB# AAAT4053) team will share a list of English-speaking former participants of the PACE Study, who agreed to be contacted about future study opportunities, with the Messy Memories research team. The list of former PACE participants will include their MRN, first and last name, language, and contact information. The Messy Memories research team will access the patient's Epic medical record to confirm initial eligibility, contact information, and language. The research team will contact potential participants to discuss the Messy Memories study. Once contacted, individuals that express interest in participating in the study will be offered the choice of completing the consent to screen and screener over the phone or via Qualtrics.

10. **Post-ICU patients at Columbia: TRAC requests refreshed by CUIMC IT on a monthly basis as needed**

    Patients identified from TRAC request:
    Potential participants for this study will also be identified through a TRAC request. We will submit a request to TRAC to identify patients who meet the following criteria:

    - 18 years of age or older
    - Preferred language: English
    - Discharged from an ICU at least 30 days prior
    - Living status: not deceased
    - No presence of significant cognitive impairment indicated (e.g., dementia)
    - No presence of significant psychiatric comorbidity indicated (e.g., psychosis)
    - Research Contact Status captured during initial registration: agreed to be contacted about research

    The TRAC request will reflect the following information for patients who meet these criteria:

    - MRN
    - First and Last Name
    - Date of Birth
    - Preferred Language
    - Research Contact Status
    - Date of ICU discharge
    - Date of ICU admission
    - ICD-10 diagnosis code(s) at ICU discharge
    - Patient Contact Information (phone numbers, email)
    - Names of providers in patient's Care Team

The study team will contact the patient's provider (e.g., primary care doctor) to confirm study eligibility. If the provider confirms that the patient is eligible, the study team will contact the patient to introduce the study. The study team may access the patient's medical record to confirm contact information, provider, and eligibility criteria prior to contacting the patient. Patients who are contacted by the study team and express interest in learning more about the study will move forward with the consent to screen, which will be conducted verbally using a screening information sheet. Those who consent to screen will complete a study screener with a member of the study team.

Screening: Upon granting consent to be screened, participants will be asked to complete a brief screening questionnaire (either online or over the phone with the study team) to determine their eligibility for study participation. Individuals completing the screener via Qualtrics will be asked to share their name and contact information so that a study team member can contact them if they screen eligible, if their screener is incomplete or needs clarification, or if they agree to be contacted about future research studies. All participants will be informed of their screening status upon completion of the screener. Those who do not meet study criteria will be thanked for their time and informed that they are not eligible for the study. Those who do meet study criteria will be informed that they are eligible for the study. All individuals who complete the study screener will be surveyed for interest in being contacted for future research studies and/or to provide feedback on the design of research studies.

Potential participants will be asked to report their age (those ages 18 years or older will be eligible to participate) and primary language (those able to speak and write in English will be eligible to participate). Additional sociodemographic information (e.g., sex assigned at birth, gender identity, race, ethnicity, living situation, annual household income, occupation, highest level of education, zip code, health insurance status, marital and partner status) will be collected as part of screening. Potential participants will be asked to report the approximate date of their ICU discharge (those discharged at least 30 days prior to the time of screening will be eligible to participate). Potential participants will be asked to confirm that they have access to both the internet (e.g., Wi-Fi) and to an internet-equipped smartphone device (e.g., iPhone, Android). Potential participants will also be asked to complete the PCL-5 as part of the screening questionnaire (scores ≥10 points are required for study eligibility). Potential participants will also be asked whether they have any physical, psychological, or cognitive condition (e.g., severe dementia, severe mental illness, severe alcohol and/or substance abuse) that would preclude them from completing any aspect of the study protocol.

In all cases, the screening consent process and responding to screening questions is expected to take approximately 25 minutes to complete.

Consent: Individuals who are screened and found to be eligible for the study based on inclusion and exclusion criteria will then be invited to schedule a visit (either by phone or Zoom, depending upon the participant's preference) to undergo a consent discussion for participation in the overall study using a verbal information sheet. On or prior to the visit, a study team member may send a copy of the verbal information sheet via mail or email with the patient's permission. As part of the consent process, the study team member will provide a complete description of the study in clear and easy-to-understand language, including risks and benefits, as well as answer any questions that participants may have after receiving this information. If an eligible participant verbally consents to participate in the study, they will accrue.

All accrued participants will receive a copy of the information sheet via email or mail. Participants will be asked to schedule a time to complete the baseline visit and study staff will confirm their mailing address to send study materials, including instructions for downloading the Messy Memories app, tips for using the Messy Memories app, and mental health resources including study phone numbers to contact study staff. Study phone messages will be checked on a regular basis. Study materials may also be emailed to participants if needed or requested.

Study Visits:

Please note that study staff may email participants to schedule/confirm study visits, send study materials as needed or requested, and/or email questionnaires via Qualtrics. Study staff may also communicate with participants via SMS text messaging using CUIMC-encrypted cell phones available exclusively to study staff to schedule/confirm study visits and/or answer questions should they arise.

"Visit 1"/Baseline Visit (Approximately 60 Minutes): Participants will complete a brief baseline visit via Zoom (or over the phone if preferred). This session (guided by study staff) entails:

1. completing a brief baseline assessment, which will include:
    a. details of the prior ICU admission (e.g., date, location)
    b. comorbid medical and/or psychiatric conditions
    c. psychological symptoms (PHQ-8, GAD-7, ASI)
    d. health behaviors (IPAQ, PSQI, tobacco/alcohol use)
    e. post-ICU support (see *Measures* for full description)
2. downloading the Messy Memories app to their smartphone and logging in with their study-provided login

a. Participants will be advised to reach out to the study team if they forget their login.

3. a brief orientation to the app with suggested guidance for usage

Participant App Usage: Participants will be asked to use the Messy Memories app for 6 weeks beginning the day that all components of the Baseline Visit are complete. This date marks the start of the intervention. Participants will be advised of the date which marks the end of the intervention (6 weeks later). They will be asked to focus on their memory of their ICU experience for memory processing. They will be asked to use the app at least 3 days a week for at least 30 minutes each day. They will be instructed to stop using and delete the app from their phones when their study participation ends.

Post-Baseline Check-In: Participants will receive a phone call from study staff within one week of the baseline assessment to confirm that they are not experiencing any technical difficulties with the app. If a participant expresses distress related (or not related) to the app, study staff will follow safety protocol by sharing the IRB-approved list of resources with the participant over the phone and/or via email and will consult with the study PI.

"Visit 2"/3-Week/Mid-Intervention Questionnaire (Approximately 25 minutes): Approximately three weeks after the start of the intervention (Baseline Visit) participants will be asked to complete a questionnaire by telephone or video consisting of the PCL-5, PHQ-8, GAD-7, ASI, IPAQ, and PSQI. If a participant expresses that they will not be available to complete the questionnaire by telephone or video, or if the study team is unable to reach the participant, the study team will send the questionnaire to the participant via Qualtrics. Those who do not complete the survey will remain on the study, and this task will be listed as "not completed" and included as part of analysis.

6-Week/End of Intervention Call: A member of the study team will call the participant within one week prior to the end of the intervention to remind the participant of the date when the intervention ends and that they are to stop using the Messy Memories app at that time. This call can also be used to schedule the 6-week/Post-Intervention Questionnaire.

"Visit 3"/6-Week/Post-Intervention Questionnaire (Approximately 40 minutes): Approximately six weeks after the start of the intervention (Baseline Visit) participants will be asked to complete another questionnaire by telephone or video consisting of the PCL-5, PHQ-8, GAD-7, ASI, IPAQ, PSQI, substance use measures, implementation measures (e.g., feasibility, acceptability, appropriateness, satisfaction), and qualitative feedback on the intervention (e.g., likes, dislikes, suggestions for improvement). If a participant expresses that they will not be available to complete the questionnaire by telephone or video, or if the study team is unable to reach the participant, the study team will send the questionnaire to the participant via Qualtrics. Those who do not complete the survey will remain on the study, and this task will be listed as "not completed" and included as part of analysis.

"Visit 4"/12-Week/Follow-Up Questionnaire (Approximately 30 minutes): Approximately six weeks after the end of the intervention, participants will be asked to complete one final questionnaire by phone consisting of the PCL-5, PHQ-8, GAD-7, ASI, IPAQ, PSQI, and substance use measures. If a participant expresses that they will not be available to complete the questionnaire by telephone or video, or if the study team is unable to reach the participant, the study team will send the questionnaire to the participant via Qualtrics. Those who do not complete the survey will remain on the study, and this task will be listed as "not completed" and included as part of analysis.

Compensation:

Participants will be compensated a total of $120 if they complete all components of the study in the form of TruCentive electronic gift cards. This compensation will be allocated in the following amounts:

- $30 for completion of all components of the Baseline Visit (completing questionnaires, downloading the app, and being onboarded to the app with study staff)
- $30 for completion of the 3-Week/Mid-Intervention Questionnaire
- $30 for completion of the 6-Week/Post-Intervention Questionnaire
- $30 for completion of the 12-Week/Follow-up Questionnaire

Participants who complete only part of a questionnaire (50%, for example) will *not* receive partial compensation for that questionnaire. Participants may, however, skip any question(s) that they do not feel comfortable answering, and this will not impact their compensation for the study.

All compensation will be provided via TruCentive e-gift cards sent to subjects by email, SMS text message or both. Each TruCentive electronic gift card will allow participants to choose from a list of pre-approved businesses at which they may use each card (including Target, Amazon, Starbucks, Chipotle, etc.).

Participants will receive instructions for utilizing TruCentive.

5. Risks

Study procedures (i.e., completing questionnaires such as the PCL-5, answering Messy Memories app questions, and, as applicable, recording and processing distressing memories of prior ICU experiences in the *Messy Memories* app) present minimal risk. Exposure treatments pose some risk of psychological discomfort, but participants will not be required to interact with the app any more than they choose to and can discontinue using the app at any time without penalty. The questions asked and the thoughts evoked during the course of this research study pose minimal risk of psychological discomfort, and participants may skip any question or questionnaire that they choose. Participants will be made aware of these risks and will be assured that they can terminate their participation in the study at any time without penalty. Mental health resources will be provided to all participants.

A potential risk of this study is violation of participant privacy, since patient medical information will be used as a source of data. Special protections against this risk will be provided (see below). Although the *Messy Memories* application does not directly collect or store protected health information, it is possible that participants may enter personally identifiable information into the free text fields within the application. To mitigate against this, participants will be instructed not to enter any personally identifiable information into the free text fields at any time while using the application. In addition, direct recordings of participants' prior distressing memory (audio recorded) will **not** be stored on the *Messy Memories* application nor collected as study data. The study-provided login to access the Messy Memories app will **not** contain any identifiable information. Participants will contact the study team if they require any assistance with the study login.

6. Benefits

There is no direct benefit to subjects who participate in this study.

Improved psychological symptoms and adherence to health behaviors: Participants may benefit from the intervention in terms of decreased psychological distress and posttraumatic stress disorder (PTSD) symptoms related to their prior critical illness. This may help participants become more adherent to their medical treatments and develop adaptive health behaviors. Participants may also benefit from the attention they receive from study personnel.

Contributions to scientific/medical knowledge: While participants in this study may not directly benefit from their participation, we anticipate the results from this study will benefit future research seeking to reduce psychological distress and improve health behaviors after prior critical illness experiences.

7. Alternatives

The alternative is not to participate in the study. Participants will be assured that they can decide at any point to discontinue participation with absolutely no consequences. Additionally, the Principal Investigator may withdraw participants from the study after enrollment upon further examination of eligibility criteria and/or at their professional discretion.

8. Data and Safety Monitoring

As this study presents minimal risk to participants, data and safety monitoring will be conducted by the study staff as directed by the principal investigator. Investigators and research staff will meet weekly to discuss any issues or concerns with the study, in particular, whether there were any unexpected complaints about the study procedures or questionnaires, or whether there were any breaches in data confidentiality (which will be reported to the IRB as required by policy). If unexpected complaints about the procedures or questionnaires are generated, then the study may be stopped or altered prior to recruiting the full sample.

The Study Principal Investigator (PI), Nadia Liyanage-Don, MD, and Dr. Ian Kronish, a board-certified general internist, will be responsible for ensuring participants' safety. The investigators will be informed of unanticipated problems or unexpected serious adverse events that may be related to the study protocol as soon as they occur, and they will notify the Institutional Review Board, in compliance with policy.

If participants incidentally disclose that they are experiencing severe symptoms related to anxiety, depression, psychological distress, or suicidal ideation at any point in the study the study team will follow a standardized safety protocol. This will include reminding participants of available mental health resources provided at the beginning of the study to all participants, offering a phone call with a study PI/MD within 24 hours, encouraging participants to stop using the Messy Memories app if they feel it is causing excessive distress, and encouraging participants to seek medical and/or psychological care with a doctor or mental health professional. All instances of incidentally reported severe psychological distress will be communicated to a Study PI/MD within 24 hours. The Study PI/MD will determine next steps and follow-up with the participant as deemed appropriate.

The study team will collect required demographic data to report to the NIA as required via CROMS (Clinical Research Operations and Management System).

A description of the study will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify participants. At most, the website will include a summary of the results.

References

1. Jackson JC, Hart RP, Gordon SM, Hopkins RO, Girard TD, Ely EW. Post-traumatic stress disorder and post-traumatic stress symptoms following critical illness in medical intensive care unit patients: assessing the magnitude of the problem. *Crit Care*. 2007;11(1):R27.

2. Bienvenu OJ, Neufeld KJ. Post-traumatic stress disorder in medical settings: focus on the critically ill. *Curr Psychiatry Rep*. 2011 Feb;13(1):3-9.

3. Wade D, Hardy R, Howell D, Mythen M. Identifying clinical and acute psychological risk factors for PTSD after critical care: a systematic review. *Minerva Anestesiol*. 2013 Aug;79(8):944-63.

4. Jones C, Bäckman C, Capuzzo M, Flaatten H, Rylander C, Griffiths RD. Precipitants of post-traumatic stress disorder following intensive care: a hypothesis generating study of diversity in care. *Intensive Care Med*. 2007 Jun;33(6):978-85.

5. Davydow DS, Gifford JM, Desai SV, Needham DM, Bienvenu OJ. Posttraumatic stress disorder in general intensive care unit survivors: a systematic review. Gen Hosp Psychiatry. 2008 Sep-Oct;30(5):421-34.

6. Parker AM, Sricharoenchai T, Raparla S, Schneck KW, Bienvenu OJ, Needham DM. Posttraumatic stress disorder in critical illness survivors: a metaanalysis. Crit Care Med. 2015 May;43(5):1121-9.

7. Diagnostic and Statistical Manual of Mental Disorders: DSM-5. 5th ed., American Psychiatric Association, 2013.

8. Herridge MS, Cheung AM, Tansey CM, Matte-Martyn A, Diaz-Granados N, Al-Saidi F, Cooper AB, Guest CB, Mazer CD, Mehta S, Stewart TE, Barr A, Cook D, Slutsky AS; Canadian Critical Care Trials Group. One-year outcomes in survivors of the acute respiratory distress syndrome. N Engl J Med. 2003 Feb 20;348(8):683-93.

9. Herridge MS, Tansey CM, Matté A, Tomlinson G, Diaz-Granados N, Cooper A, Guest CB, Mazer CD, Mehta S, Stewart TE, Kudlow P, Cook D, Slutsky AS, Cheung AM; Canadian Critical Care Trials Group. Functional disability 5 years after acute respiratory distress syndrome. N Engl J Med. 2011 Apr 7;364(14):1293-304.

10. Dowdy DW, Eid MP, Sedrakyan A, Mendez-Tellez PA, Pronovost PJ, Herridge MS, Needham DM. Quality of life in adult survivors of critical illness: a systematic review of the literature. Intensive Care Med. 2005 May;31(5):611-20.

11. Dowdy DW, Eid MP, Dennison CR, Mendez-Tellez PA, Herridge MS, Guallar E, Pronovost PJ, Needham DM. Quality of life after acute respiratory distress syndrome: a meta-analysis. Intensive Care Med. 2006 Aug;32(8):1115-24.

12. Magruder KM, McLaughlin KA, Elmore Borbon DL. Trauma is a public health issue. Eur J Psychotraumatol. 2017 Oct 9;8(1):1375338.

13. Pericot-Valverde I, Elliott RJ, Miller ME, Tidey JW, Gaalema DE. Posttraumatic stress disorder and tobacco use: A systematic review and meta-analysis. Addict Behav. 2018 Sep;84:238-247.

14. Kearns NT, Carl E, Stein AT, Vujanovic AA, Zvolensky MJ, Smits JAJ, Powers MB. Posttraumatic stress disorder and cigarette smoking: A systematic review. Depress Anxiety. 2018 Nov;35(11):1056-1072.

15. Zen AL, Whooley MA, Zhao S, Cohen BE. Post-traumatic stress disorder is associated with poor health behaviors: findings from the heart and soul study. Health Psychol. 2012 Mar;31(2):194-201.

16. van den Berk-Clark C, Secrest S, Walls J, Hallberg E, Lustman PJ, Schneider FD, Scherrer JF. Association between posttraumatic stress disorder and lack of exercise, poor diet, obesity, and co-occuring smoking: A systematic review and meta-analysis. Health Psychol. 2018 May;37(5):407-416.

17. Shemesh E, Rudnick A, Kaluski E, Milovanov O, Salah A, Alon D, Dinur I, Blatt A, Metzkor M, Golik A, Verd Z, Cotter G. A prospective study of posttraumatic stress symptoms and nonadherence in survivors of a myocardial infarction (MI). Gen Hosp Psychiatry. 2001 Jul-Aug;23(4):215-22.

18. Shemesh E, Yehuda R, Milo O, Dinur I, Rudnick A, Vered Z, Cotter G. Posttraumatic stress, nonadherence, and adverse outcome in survivors of a myocardial infarction. Psychosom Med. 2004;66:521-526.

19. Kronish IM, Edmondson D, Goldfinger JZ, Fei K, Horowitz CR. Posttraumatic stress disorder and adherence to medications in survivors of strokes and transient ischemic attacks. Stroke. 2012;43:2192-2197.

20. Edmondson D, Horowitz CR, Goldfinger JZ, Fei K, Kronish IM. Concerns about medications mediate the association of posttraumatic stress disorder with adherence to medication in stroke survivors. Br J Health Psychol. 2013;18:799-813.

21. Cusack K, Jonas DE, Forneris CA, Wines C, Sonis J, Middleton JC, Feltner C, Brownley KA, Olmsted KR, Greenblatt A, Weil A, Gaynes BN. Psychological treatments for adults with posttraumatic stress disorder: A systematic review and meta-analysis. Clin Psychol Rev. 2016 Feb;43:128-41.

22. Rothbaum BO, Meadows EA, Resick P, Foy DW. Cognitive-behavioral therapy. In: Foa EB, Keane TM, Friedman MJ, editors. Effective treatments for PTSD: Practice guidelines from the International Society for Traumatic Stress Studies. New York (NY): Guilford Press; 2000. p. 320–25.

23. Institute of Medicine. Treatment of PTSD: An assessment of the evidence. Washington (DC): Institute of Medicine;2007. p. 84.

24. National Institute for Clinical Excellence. Post-traumatic stress disorder (PTSD): The management of PTSD in adults and children in primary and secondary care. London (England): National Institute for Clinical Excellence; 2005.

25. Foa EB, Kozak MJ. Emotional processing of fear: Exposure to corrective information. Psychol Bull. 1986;99(1):20–35.

26. Rauch S, Foa E. Emotional Processing Theory (EPT) and exposure therapy for PTSD. J Contemp Psychother. 2006;36(2):61–65.

27. Foa EB, Riggs DS. Posttraumatic stress disorder following assault: Theoretical considerations and empirical findings. Curr Dir Psychol Sci. 1995;4(2):61–65.

28. Foa EB, Rauch SA. Cognitive changes during prolonged exposure versus prolonged exposure plus cognitive restructuring in female assault survivors with posttraumatic stress disorder. J Consult Clin Psychol. 2004;72(5):879–84.

29. Keane TM, Fairbank JA, Caddell JM, Zimering RT. Implosive (flooding) therapy reduces symptoms of PTSD in Vietnam combat veterans. Behav Ther. 1989;20(2):245–60.

30. Boudewyns PA, Hyer L. Physiological response to combat memories and preliminary treatment outcome in Vietnam veteran PTSD patients treated with direct therapeutic exposure. Behav Ther. 1990;21:63–87.

31. Glynn SM, Eth S, Randolph ET, Foy DW, Urbaitis M, Boxer L, Paz GG , Leong GB, Firman G , Salk JD, Katzman JW, Crothers J. A test of behavioral family therapy to augment exposure for combat-related posttraumatic stress disorder. J Consult Clin Psychol. 1999;67(2):243–51.

32. Schnurr PP, Friedman MJ, Engel CC, Foa EB, Shea MT, Chow BK, Resick PA, Thurston V, Orsillo SM, Haug R, Turner C, Bernardy N. Cognitive behavioral therapy for posttraumatic stress disorder in women: A randomized controlled trial. JAMA. 2007;297(8):820–30.

33. Cahill SP, Rauch SA, Hembree EA, Foa EB. Effect of cognitive-behavioral treatments for PTSD on anger. J Cogn Psychother. 2003;17(2):113–31.

34. Foa EB, Hembree EA, Cahill SP, Rauch SA, Riggs DS, Feeny NC, Yadin E. Randomized trial of prolonged exposure for posttraumatic stress disorder with and without cognitive restructuring: Outcome at academic and community clinics. J Consult Clin Psychol. 2005;73(5):953–64.

35. Watts BV, Schnurr PP, Mayo L, Young-Xu Y, Weeks WB, Friedman MJ. Meta-analysis of the efficacy of treatments for posttraumatic stress disorder. J Clin Psychiatry. 2013;74(6):e541-50.

36. Rauch SA, Eftekhari A, Ruzek JI. Review of exposure therapy: a gold standard for PTSD treatment. J Rehabil Res Dev. 2012;49(5):679-87.

37. McLean CP, Levy HC, Miller ML, Tolin DF. Exposure therapy for PTSD: A meta-analysis. Clin Psychol Rev. 2022 Feb;91:102115.

38. DuHamel KN, Mosher CE, Winkel G, et al. Randomized clinical trial of telephone-administered cognitive-behavioral therapy to reduce post-traumatic stress disorder and distress symptoms after hematopoietic stem-cell transplantation. J Clin Oncol. 2010 Aug 10;28(23):3754-61.

39. Pacella ML, Armelie A, Boarts J, et al. The impact of prolonged exposure on PTSD symptoms and associated psychopathology in people living with HIV: a randomized test of concept. AIDS Behav. 2012 Jul;16(5):1327-40.

40. Shemesh E, Annunziato RA, Weatherley BD, et al. A randomized controlled trial of the safety and promise of cognitive-behavioral therapy using imaginal exposure in patients with posttraumatic stress disorder resulting from cardiovascular illness. J Clin Psychiatry. 2011 Feb;72(2):168-74.

41. New Freedom Commission on Mental Health. Achieving the promise: transforming mental health care in America. Final report. Rockville, MD: DHHS; 2003. 113 p. Pub. No. SMA-03-3832.

42. Stecker T, Fortney JC, Hamilton F, Ajzen I. An assessment of beliefs about mental health care among veterans who served in Iraq. Psychiatr Serv. 2007;58(10):1358–61.

43. Workforce issues: integrating substance use services into primary care. Proceedings; 2011 Aug 10–11; Washington DC. Washington DC: Substance Abuse and Mental Health Services.

44. Kuehn BM. Military PTSD Care. JAMA. 2012;308(8):753.

45. Morland LA, Wells SY, Glassman LH, Greene CJ, Hoffman JE, Rosen CS. Advances in PTSD Treatment Delivery: Review of Findings and Clinical Considerations for the Use of Telehealth Interventions for PTSD. Curr Treat Options Psychiatry. 2020 May 30:1-21.

46. Cigrang JA, Rauch SA, Mintz J, Brundige AR, Mitchell JA, Najera E, Litz BT, Young-McCaughan S, Roache JD, Hembree EA, Goodie JL, Sonnek SM, Peterson AL; STRONG STAR Consortium. Moving effective treatment for posttraumatic stress disorder to primary care: A randomized controlled trial with active duty military. Fam Syst Health. 2017 Dec;35(4):450-462.

47. Mealer M, Conrad D, Evans J, Jooste K, Solyntjes J, Rothbaum B, Moss M. Feasibility and acceptability of a resilience training program for intensive care unit nurses. Am J Crit Care. 2014 Nov;23(6):e97-105.

48. Pfizer-funded effort; Rauch and Foa, unpublished.

49. Miner A, Kuhn E, Hoffman JE, Owen JE, Ruzek JI, Taylor CB. Feasibility, acceptability, and potential efficacy of the PTSD Coach app: A pilot randomized controlled trial with community trauma survivors. Psychol Trauma. 2016 May;8(3):384-392.

50. Kuhn E, Kanuri N, Hoffman JE, Garvert DW, Ruzek JI, Taylor CB. A randomized controlled trial of a smartphone app for posttraumatic stress disorder symptoms. J Consult Clin Psychol. 2017 Mar;85(3):267-273.

51. Cox CE, Hough CL, Jones DM, Ungar A, Reagan W, Key MD, Gremore T, Olsen MK, Sanders L, Greeson JM, Porter LS. Effects of mindfulness training programmes delivered by a self-directed mobile app and by telephone compared with an education programme for survivors of critical illness: a pilot randomised clinical trial. Thorax. 2019 Jan;74(1):33-42.

52. Stolz T, Schulz A, Krieger T, Vincent A, Urech A, Moser C, Westermann S, Berger T. A mobile app for social anxiety disorder: A three-arm randomized controlled trial comparing mobile and PC-based guided self-help interventions. J Consult Clin Psychol. 2018 Jun;86(6):493-504.

53. Franklin JC, Fox KR, Franklin CR, Kleiman EM, Ribeiro JD, Jaroszewski AC, Hooley JM, Nock MK. A brief mobile app reduces nonsuicidal and suicidal self-injury: Evidence from three randomized controlled trials. J Consult Clin Psychol. 2016 Jun;84(6):544-57.

54. Kazemi DM, Borsari B, Levine MJ, Shehab M, Nelson M, Dooley B, Stinson B, Fang F, Li S. Real-time demonstration of a mHealth app designed to reduce college students hazardous drinking. Psychol Serv. 2019 May;16(2):255-259.

55. Gál É, Ștefan S, Cristea IA. The efficacy of mindfulness meditation apps in enhancing users' well-being and mental health related outcomes: a meta-analysis of randomized controlled trials. J Affect Disord. 2021 Jan 15;279:131-142.

56. Proctor E, Silmere H, Raghavan R, et al. Outcomes for implementation research: conceptual distinctions, measurement challenges, and research agenda. Adm Policy Ment Health. 2011 Mar;38(2):65-76.

57. Weiner BJ, Lewis CC, Stanick C, et al. Psychometric assessment of three newly developed implementation outcome measures. Implement Sci. 2017 Aug 29;12(1):108.

58. Brooke J. SUS: A quick and dirty usability scale. Usability Eval Ind. 1995;189.

59. Bangor A, Kortum P, Miller J. Determining What Individual SUS Scores Mean: Adding an Adjective Rating Scale. J Usability Stud. 2009;4:114-123.

60. System Usability Scale (SUS). https://www.usability.gov/how-to-and-tools/methods/system-usability-scale.html.

61. Weathers FW, Litz BT, Keane TM, Palmieri PA, Marx BP, Schnurr PP. The PTSD Checklist for DSM-5 (PCL-5). 2013. Scale available from the National Center for PTSD at www.ptsd.va.gov.

62. Bovin MJ, Marx BP, Weathers FW, Gallagher MW, Rodriguez P, Schnurr PP, Keane TM. Psychometric properties of the PTSD Checklist for Diagnostic and Statistical Manual of Mental Disorders-Fifth Edition (PCL-5) in veterans. Psychol Assess. 2016 Nov;28(11):1379-1391.

63. Bliese PD, Wright KM, Adler AB, Cabrera O, Castro CA, Hoge CW. Validating the primary care posttraumatic stress disorder screen and the posttraumatic stress disorder checklist with soldiers returning from combat. J Consult Clin Psychol. 2008 Apr;76(2):272-81.

64. Creamer M, Bell R, Failla S. Psychometric properties of the Impact of Event Scale - Revised. Behav Res Ther. 2003 Dec;41(12):1489-96.

65. Kroenke K, Spitzer RL, Williams JB. The PHQ-9. Journal of general internal medicine. 2001;16(9):606-613.

66. Kroenke K, Strine TW, Spitzer RL, Williams JB, Berry JT, Mokdad AH. The PHQ-8 as a measure of current depression in the general population. Journal of affective disorders. 2009;114(1):163-173.

67. Shin C, Lee SH, Han KM, Yoon HK, Han C. Comparison of the Usefulness of the PHQ-8 and PHQ-9 for Screening for Major Depressive Disorder: Analysis of Psychiatric Outpatient Data. Psychiatry Investig. 2019 Apr;16(4):300-305.

68. Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med. 2006 May 22;166(10):1092-7.

69. Plummer F, Manea L, Trepel D, McMillan D. Screening for anxiety disorders with the GAD-7 and GAD-2: a systematic review and diagnostic metaanalysis. Gen Hosp Psychiatry. 2016 Mar-Apr;39:24-31.

70. Reiss S, Peterson RA, Gursky DM, McNally RJ. Anxiety sensitivity, anxiety frequency and the prediction of fearfulness. Behav Res Ther. 1986;24(1):1-8.

71. Allan NP, Raines AM, Capron DW, Norr AM, Zvolensky MJ, Schmidt NB. Identification of anxiety sensitivity classes and clinical cut-scores in a sample of adult smokers: results from a factor mixture model. J Anxiety Disord. 2014 Oct;28(7):696-703.

72. Craig CL, Marshall AL, Sjöström M, Bauman AE, Booth ML, Ainsworth BE, Pratt M, Ekelund U, Yngve A, Sallis JF, Oja P. International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc. 2003 Aug;35(8):1381-95.

73. Buysse DJ, Reynolds CF 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res. 1989 May;28(2):193-213.