Caregiver Wellness after Traumatic Brain Injury (CG-Well): Protocol for a randomized clinical trial

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ABSTRACT

Introduction: After injury, survivors of moderate to severe traumatic brain injury (msTBI) depend on informal family caregivers. Upwards of 77 % of family caregivers experience poor outcomes, such as adverse life changes, poor health-related quality of life, and increased depressive symptoms. Caregivers frequently report minimal support or training to prepare them for their new role. The majority of previously developed caregiver and caregiver/survivor dyad interventions after msTBI focus on providing information to either survivors only, or to long-term caregivers, rather than to the new caregiver. This manuscript describes the protocol of an ongoing randomized control trial, Caregiver Wellness after TBI (CG-Well), developed to provide education, support, and skill-building to caregivers of adults with msTBI, beginning when the survivor is early in the clinical course.
Methods: Within two weeks of admission to the ICU, participants are randomized to CG-Well online modules (intervention group, n = 50 dyads) or information, support, and referral (ISR) e-bulletins that exist in the public domain (control group, n = 50 dyads) over the first six months after their family member's msTBI. Both groups receive regular phone calls. The primary outcome is intervention satisfaction at six months.
Results: Enrollment began in March 2022 and is projected to complete October 2024. We have enrolled approximately 70 % of participants at this time. Primary analysis completion is anticipated April 2025.
Discussion: This RCT is designed to evaluate caregiver satisfaction by addressing the need for tailored supportive care for caregivers of msTBI beginning during the ICU admission.
Trial registration: Clinicaltrials. gov Registration Number: NCT05307640.

1. Introduction

Traumatic brain injury (TBI) is the leading cause of death and disability in young adults and is projected to remain the highest cause of disability from all neurological diseases worldwide until 2030, at 2–3 times the rate of Alzheimer's disease or cerebrovascular disorders [1,2]. Moderate and severe TBIs (msTBIs) result in a critical illness requiring an intensive care unit (ICU) hospitalization [3]. During and after critical illness, untrained, informal friends and family members of TBI survivors often immediately assume caregiving responsibilities, but few are prepared to do so. Many caregivers report not feeling educated, supported,

or prepared to assume care of the TBI survivor at home [4]. These family and friend caregivers are at risk of developing poor psychological wellbeing [5,6]. Overall, as many as three quarters of TBI caregivers suffer from anxiety and depression [7–15]. In addition to anxiety and depression, caregivers of persons with msTBI have reported a myriad of negative life changes such as loss of a job, financial hardships, social isolation, lack of support from family and friends, and their own health issues [4].

Caregivers of msTBI survivors report the greatest amount of negative life changes shortly after injury, yet no interventions have been developed to support caregivers in this phase of care [4,16]. Prior studies

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have generally enrolled caregivers late after injury. A published review of interventions to support families of critically ill patients found that proactive, early education is pivotal for improved family outcomes, and should include training for caregivers to cope with psychological distress [17]. By waiting until late after injury, only modest effects on caregiver quality of life are noted in other neurological disorders [18–23].

Online interventions to benefit caregivers have advantages compared to phone-only or in-person interventions [24–26]. Online delivery reduces the risk of inconsistently administered interventions [27,28]. The material can be can be accessed privately and conveniently [29–35]. One prior published online intervention exists for adult TBI caregivers and is limited to teaching long-term advocacy [36]. A variety of caregivers, clinicians, and researchers were asked about preferences for modes of delivery, with results mixed across in-person, online, or phone based [37]. For these reasons, we elected to utilize a website for our intervention, Caregiver Wellness after TBI (CG-Well), with regular phone calls to augment the online material.

The purpose of this paper is to describe the protocol for CG-Well, a randomized controlled biobehavioral pilot trial. Examination of satisfaction of the study protocol is the primary outcome. Other focuses of this study are on testing data collection procedures, measurement strategies, optimizing the recruitment plan, monitoring fidelity, and obtaining qualitative data.

2. Methods

A randomized, controlled, repeated-measures design will be used to investigate the feasibility and satisfaction of the CG-Well intervention relative to an Information, Support, and Referral (ISR) control group. Following baseline data collection, caregivers will be randomized to the CG-Well or ISR group. Both groups will receive weekly calls until the one-month assessment, then monthly calls until the six-month assessment (Fig. 1). All study procedures have been approved by the local Institutional Review Board. Study design was informed in part by previous stroke and pediatric TBI biobehavioral intervention studies, systematic review, Delphi consensus processes, and preliminary qualitative data [4,25,29,38–42].

2.1. Participants

Participants will be 100 msTBI caregiver and survivor dyads from a single center. Research coordinators query the electronic medical record ICU track boards to find eligible caregiver and survivor dyads to approach for enrollment. We define caregivers as a spouse, partner, family member, friend, or neighbor assisting the survivor with activities of daily living and/or medical tasks. Participants will be included if the survivor and caregiver are 18 years old or more, the survivor has a Glasgow Coma Scale (GCS) of 3–12, the survivor is less than two weeks from injury, the dyad is English speaking. Participants will be excluded if the patient is not expected to survive, the caregiver changes, if either member of the dyad is a prisoner, has a pre-existing condition that would interfere with follow-up, or a major prior debilitating neurologic or mental health disorder. If a participant's caregiver changes to a different family member or friend, we will report the information already collected with the enrolled caregiver. In addition, we will report the number of participants who had a caregiver that changed.

2.2. Enrollment and randomization procedures

Coordinators will approach potential participants to explain the study and determine their interest. We will utilize a recruitment plan to include strategies for improving racial diversity since poor caregiving outcomes may be disproportionate based on race or gender [43–45]. Specifically, we will offer flexibility in follow up calls, including weekends and evenings to facilitate the caregiver's busy schedules. We will provide education at the time of consent that their medical information will not be used for other purposes, and will not be exploited, as well as provide information that their participation may benefit future caregivers. Informed consent will be obtained from the caregiver, or legally authorized representative (LAR) following eligibility screening and prior to data collection. Caregiver participants are randomized 1:1 to CG-Well or the ISR control group using a permuted block randomization
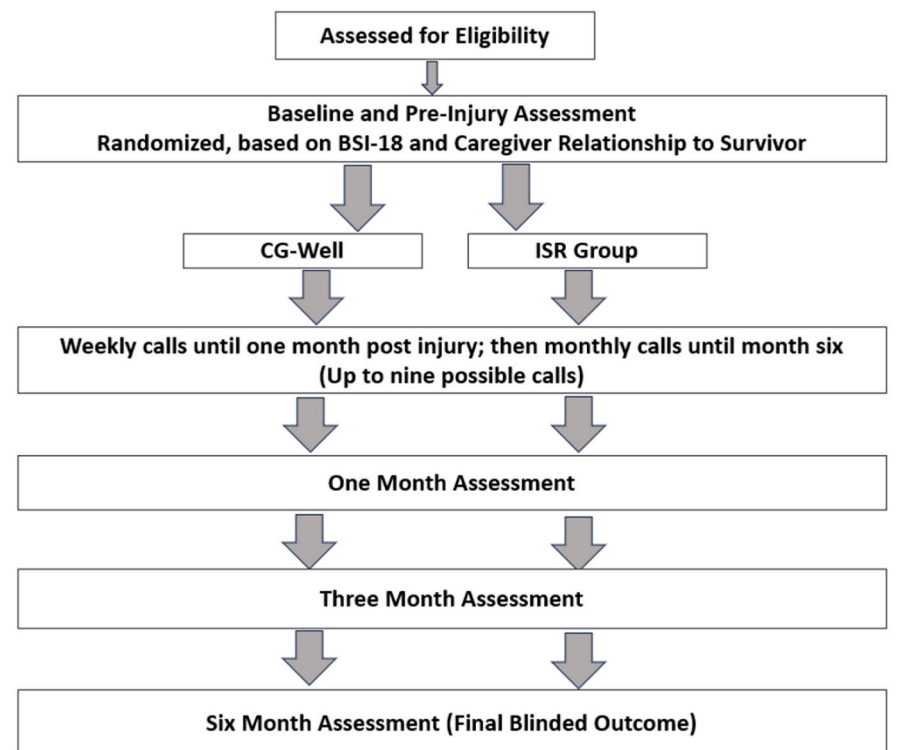

Fig. 1. Study flow.

stratified by type of relationship (spouse vs. adult child/parent) and baseline caregiver depressive symptoms defined as < or > equal to Brief Symptom Inventory-18 (BSI-18)score of 63 [46,47]. The randomization scheme will be accessed by the enrolling study coordinator after the consent process by logging into the REDCap database. Caregivers will not be blinded given the nature of the intervention, but they will not be told if their randomization arm is intervention or ISR.

2.3. Intervention and control delivery

The intervention and control will be delivered in a combination of methods: face to face, if possible, during the initial visit in the ICU; web-based online content; and telephone sessions. If caregivers are unable to access the web-based modules, they will be provided paper copies of the content. Caregivers in both groups will receive up to nine protocolized phone calls. These will occur weekly for the first month after injury, then monthly until month six (Fig. 1). In both groups, calls are scripted, and include items such as: a reminder to review the prior call before the current call, study introductions, receiving an update on the survivor and the caregiver, broadly listening to any recent issues the caregiver is having, time spent in modules, time spent in the call, and time needed for prep and wrap up. In both groups, a call tracking form will be completed for each call. This form is a checklist that includes the time, date, and if the phone call was answered, or if a message was left for the caregiver. In addition, calls in both groups will be recorded and reviewed by the PI to ensure fidelity using a structured checklist [49].

2.4. CG-Well

The development and description of CG-Well has been previously published [37]. CG-Well is a 9-session phone and web-based intervention delivered over six months to improve education, skill building, and support. Caregivers are given resources beginning while the survivor is in the ICU about what they may expect as a caregiver to a person with an msTBI. An overview of the website content is included in Table 1.

Caregivers will receive login information to the CG-Well website to access online modules if enrolled into the CG-Well group. The website contains 43 potential modules for caregivers to review that are tailored to the needs of caregivers of msTBI survivors, in several formats: video, PDF, and links for outside resources. Some examples of modules include: understanding the ICU schedule, early financial and legal issues, feeling angry after the TBI, caregiving basics, caregiver burden, managing medications, and taking care of your own health as a caregiver. The modules will be presented in a recommended order, based on our previously published timeline of caregiver unmet needs [4]; however, caregivers will be able to review the modules in any order. The modules will include three to four questions to assess the caregiver's learning and to help the coordinator better understand any challenges faced within the material, so that content can be reviewed in calls if needed. The modules normalize the caregiver's experience, so that caregivers are able to focus on utilizing resources appropriately. The technology will be initiated in the ICU, and continues as the survivor moves from rehabilitation to home over the first six months. The website is built on Transport Layer Security that ensures encryption, authentication and data integrity for internet connections. Over the modules, caregivers will learn evidence-based problem-solving skills, strategies to meet their goals, cognitive restructuring skills, and coping mechanisms. Participants randomized to the CG-Well group will also receive the ISR materials, which are all publicly available.

Initial calls in the CG-Well group will provide support for technology, introductions to the Brain Injury Association of America (BIAA) and CG-Well websites, and an overview of the study and call schedule. Calls will be protocolized, and tailored to the caregiver's individual needs at the time of the call. The purposes of the CG-Well phone calls will be to assist caregivers with any issues related to accessing the website, guide caregivers to pertinent modules, and reinforce the online modules. In

Table 1
Overview of website content.

Time Period		Name of Module
Early ICU	The ICU	Understanding Initial Steps
		ICU Schedule and how the ICU works
		Understand the Team Caring for my Loved One
		How to Communicate with the ICU Teams
	Medical Information	Devices, Tubes, Machines
		Prognosis and Likelihood of Improvement
		Early Financial/Legal Issues
	Your Emotions	Managing Your Emotions in the Fast-Paced ICU
		Balancing Life and Time in the ICU
		Feeling Angry After the TBI
Later ICU	The ICU	How to Help my Loved One in the ICU
		Transitioning out of the ICU
	Medical Information	Sharing the Injury with Others
		Finding the Right Skilled Nursing Facility
	Your Life and Emotions	What is Caregiver Burden?
		Building a Support Network Early
		Early Conversations with Children
		Staying Organized
		Problem Solving and Decision Making
After the ICU	Medical Information	Additional Survivor Emotions
		Communication with the Survivor
		Handling the Survivor's Anger and Emotions
	Your Life and Emotions	Caregiver Coping Strategies
		Managing your Anxiety and Stress
		Managing Sadness in the TBI Survivor
		Balancing Caregiving with your Job
		Balancing Caring for Children
		Becoming an Advocate
		Managing Finances
Later Time Points	Medical Information	Arranging Follow-Up Appointments
		Managing Medications at Home
		Assisting with Survivor Mobility
		Cognitive Problems after TBI
		Medical Issues and Complications at Home
	Your Life and Emotions	Taking Care of your Health
		Caregiver Sadness and Depression
		Dealing with Isolation
	Logistical Issues	Caregiving Basics if you are Coming Home
		Preparing your Home
		Activities of Daily Living
		Transportation Needs

addition to the call tracking form, a CG-Well intervention monitoring form will be completed for each call. This form indicates whether the coordinator reviewed notes from the prior call; if the call was completed as scheduled, recorded, and uploaded; which specific modules that are discussed in the call; number of minutes the caregiver spent on each website since the prior call; and information the caregiver found to be useful from the websites. The coordinator will obtain feedback from the caregiver on the prior call, and will document their own feedback about the call. The number of minutes to prepare for the call, complete the call, and wrap up the call will be documented. Any issues with the call will be discussed with the PI and/or additional members of the study team as necessary.

2.5. ISR

Since there are no best practices to support critical care transitions after msTBI, an ISR control group will be utilized. For the purposes of this study, ISR has been adapted for TBI caregivers from the TASKII and TASK III studies of stroke family caregivers [39,48]. The ISR control is

designed to match the time and platform of CG-Well using non-tailored, publicly available information from the BIAA website, delivered as e-bulletins to the caregiver's email. Caregivers in ISR will not receive tailored content.

Similar to CG-Well, ISR includes up to nine protocolized phone sessions. The coordinator will provide non-tailored elements of active listening, empathy, referral to resources, and permission for catharsis in ISR calls. During the first call, the coordinator will review the BIAA website, call schedule, and overview of the study. The coordinator will be trained to not offer tailored advice in ISR calls. This will be assessed by recording calls and monitoring for fidelity [49–51]. Similar to the CG-Well group, an ISR monitoring checklist will be completed by the coordinator for each completed call in the ISR group, in addition to the call tracking form. This checklist will include if the caregiver was reminded of the upcoming call beforehand; if the caregiver was notified he or she was being recorded; and if the call was recorded and uploaded, and if not, why. The coordinator will document in the checklist if the caregiver has reviewed the BIAA website, feedback about the website, and minutes spent reviewing the website. The coordinator will document if active listening techniques were utilized during the call, and that no CG-Well content was shared during the ISR call. The coordinator will have an area in the tracking form to describe their self-reflection about the call, including what could be improved, or areas where the coordinator may feel like she needs more training. Recordings, call tracking forms, and intervention monitoring forms in both groups will be reviewed on an ongoing basis throughout the study to ensure fidelity. In both groups, we obtain information about the patient's level of care at each call, such as whether he or she is at home, inpatient rehabilitation, skilled nursing facility or other location. This will allow us to better understand if or how this impacts the caregiver's wellbeing, as well as describe the complex journey many patients with msTBI have after an injury.

2.6. Safety

Given the assessed low risk of trial participation, serious adverse events and harms are not anticipated. A study-specific data monitoring committee will review data every six months. A suicide protocol will be in place in the event a caregiver reports suicidal ideations during a call. Concerns for abuse or neglect of the survivor will be reported if noted.

2.7. Interventionalist

A trained master's level research coordinator will demonstrate the use of modules (CG-Well) or e-bulletins (ISR) control, and complete the scheduled phone calls in each group. Coordinator training will consist of an 8-hour training session to learn the CG-Well and ISR content. The same coordinator will call participants in both the CG-Well and ISR groups to reduce the possibility that outcomes are related only to a specific group-associated coordinator. All calls will be audio recorded and reviewed by the PI, so treatment fidelity for each group can be regularly monitored. If a deviation from treatment fidelity occurs, this will be discussed between the PI and coordinator, and will be documented.

2.8. Data collection and measurement

Data will be collected at baseline, one month, three months, and six months post-injury (Fig. 1). A research assistant, blinded to the study objectives and randomization, will administer the final outcome questionnaire by phone at six months. Baseline data collection, describing caregivers and survivors' pre-ICU and baseline function may be completed during an in-person meeting in the ICU. All subsequent questionnaires will be completed by phone remotely. All participants will be given $20 at each data collection point for completion of assessments.

2.9. Baseline measures

Baseline measures will include demographic information about the caregiver and survivor. The following will be collected for the caregiver: past medical history, past psychiatric history, pre-injury functional status, family psychiatric history, education level, employment, income bracket, marital status, living situation, phone access, transportation, external responsibilities, social provisions scale, family relationship interaction quality, pre-injury life changes, baseline life changes, pre-injury task difficulty, baseline task difficulty, pre injury threat appraisal, and baseline threat appraisal. Several of these measures will also be obtained again at one month, three months, and six months post injury (Table 2). The following are collected at baseline for the survivors: Injury severity, pre-injury Barthel index, pre-injury Glasgow Outcome Scale Extended, mechanism of injury, age, race and ethnicity, gender, employment, relationship to caregiver, past medical history, past psychiatric history, family psychiatric history, education level, and income bracket.

Most of the scales have strong evidence of reliability and validity, with Cronbach alphas above 0.70 in a variety of samples. Other scales are included either because they are common measures used in clinical practice, or due to conceptual importance. We will assess Cronbach

Table 2
Study measures.

Construct	Measure	Time Obtained
Depression History in survivor, CG, and first-degree relatives	Family History Screen [54]	BL
Survivor Function	Barthel Index [55] and Glasgow Outcome Scale Extended (GOSE) [56,57]	BL, 1m, 3m, 6m
Survivor injury severity	Glasgow Coma Scale (GCS) [56] obtained from medical record	BL
CG and survivor Socioeconomics and Demographics	Sex, age, race, ethnicity, relationship, highest education completed, highest level attempted, employment status, and income bracket of CG and survivor [58]	BL
CG Support and resources	Marital status, living situation (e.g., alone or with others), phone (yes or no), access to transportation (yes or no), external responsibilities (e.g., children in home), Social provisions scale (SPS) [59]	BL, 1m, 3m, 6m
CG - Relationship interaction quality within dyad and the family	McMaster Family Assessment Device, General Functioning Subscale [60] and Life Stressors and Social Resources Inventory pertinent to relationship (spouse, child, family, friend) [61]	BL, 1m, 3m, 6m
CG -Task Difficulty/Burden (Proximal Outcome)	Oberst Caregiving Burden Scale (OCBS) [62]	BL, 1m, 3m, 6m
CG- Appraisal of Caregiving (Proximal Outcome)	ACS Threat Subscale [62]	BL, 1m, 3m, 6m
CG Life Changes (Distal Outcome)	Bakas Caregiver Outcomes Scale (BCOS) [63]	BL, 1m, 3m, 6m
CG and Survivor* Depressive Symptoms (Distal Outcome in CGs)	Brief Symptom Inventory-18 (BSI-18) [47]	BL, 1m, 3m, 6m
Program Evaluation Outcomes		
Feasibility in 100 randomized CG participants	Recruitment, retention, treatment fidelity [50], number of logins, time spent in modules, time spent in phone calls in CG-Well and ISR	BL, 1m, 3m, 6m
CG Intervention Satisfaction (Primary Outcome)	Likert scales of usability, ease of use, acceptability of CG-Well or ISR [38]	6m

CG = Caregiver; BL = Baseline; At baseline, caregivers were asked to provide information about their status at the time of enrollment, as well as how they believed they felt two weeks prior to the injury. *Survivor BSI-18 is only obtained if the survivor is able to speak on the phone at 6-month post injury.

alpha for internal consistency for all scales in the proposed sample prior to analyses.

The BSI-18, which measures depressive and anxiety symptoms, will be collected at baseline in caregivers and will be utilized for randomization purposes [46]. In addition, caregivers will be randomized based on their relationship to the survivor.

2.10. Primary outcome/satisfaction

The primary outcome is caregiver satisfaction at six months, which is a 16-item questionnaire was adapted from Bakas's prior work [38]. Items query subjects' responses to the various components of the intervention (e.g., content, timing, and length of sessions), and will be used for future intervention modification.

2.11. Secondary outcomes/preliminary efficacy

A battery of caregiver secondary measures will be assessed to explore preliminary efficacy of the trial, including: Oberst Caregiving Burden Scale (proximal outcome), ACS Threat Subscale (proximal outcome), Bakas Caregiver Outcome Scale (distal outcome), and BSI-18 (distal outcome). We will also obtain the following survivor outcomes at one, three, and six Months: Barthel Index, Glasgow Outcome Scale Extended (GOSE), and BSI-18, so that we can explore the role of survivor functional outcomes on caregiver outcomes.

2.12. Feasibility outcomes

To explore feasibility, we will compute the number of participants screened per month, enrolled per month, proportion of eligible caregivers who enroll, retention rates, fidelity, and proportion of outcome measures completed. We will collect attendance in modules, length of time in modules and calls, number of logins, and module completion.

2.13. Exploratory outcomes

We will explore how baseline factors affect responses to CG-Well compared to ISR control as exploratory outcomes. Caregiver satisfaction will be evaluated within the following subgroups: caregiver with a history of depression, dyad and family relationship quality, type of caregiver, caregiver support, caregiver resources, and TBI severity. Cutpoints will generally follow these proposed values, but may be altered based on number of patients enrolled per subgroup. The relationship of baseline characteristics to proximal (OCBS, ACS) and distal (BCOS, BSI-18) outcomes will be evaluated as well.

3. Data management

All study data and tracking will be entered into REDCap (www. REDCap.org) [52]. All analyses will be carried out using SAS software (SAS Institute Inc., Cary NC). Typical of longitudinal studies we anticipate having missing data, but will make every effort to avoid missing data at the start. Our approach will be to first assess the reasons and patterns of missing data and understand the distribution of missing data, allowing us to assess whether an assumption of missing completely at random is reasonable or whether missingness is conditional on another variable in the dataset. Descriptive statistics will compare characteristics of participants with and without missing data. If missing at random, we will incorporate variables that are identified to be related to the missingness in the analysis using multiple imputation if the amount and distribution of missing data seems likely to affect the study results. A data safety monitoring board will be in place to review data quality control, queries, adverse events, and safety every six months.

3.1. Data analysis

3.1.1. Primary outcome/satisfaction

The primary outcome, satisfaction ratings, obtained from the Caregiver Satisfaction Scale (CSS) [62] (usability, ease of use, acceptability) will be summarized as a total satisfaction score and by subscales (usefulness, ease of use and acceptability) by intervention group using descriptive statistics, including mean and 95 % CI. Items will be rated on a 5-point Likert scale (1 = strongly disagree to 5 = strongly agree). Average scores will be computed for each subscale (usefulness, ease of use, and acceptability) and total score (satisfaction) so that all scores range from 1 to 5. CSS scores, total and subscales, will be compared between groups using two-sample t-tests or nonparametric alternative, if the normality assumption appears violated. If covariate adjustment is needed, differences between groups will be evaluated using a generalized linear model.

3.1.2. Secondary outcome/feasibility

We will monitor feasibility outcomes by obtaining screening and recruitment rates, attrition rates, acceptability, and fidelity ratings of both ISR and CG-Well procedures. The fidelity ratings have been developed from prior published fidelity checklists [49–51]. We will report the number screened per month, number enrolled per month, proportion of screened eligible caregivers who enroll, retention rates, fidelity, and proportion of outcome measures completed. We hope to exceed the following thresholds: enrollment of three dyads per month, enrollment of 50 % of eligible caregivers who are approached, and 80 % retention, defined as the proportion of outcome measures completed. We will report attendance in modules, and length of time in modules and calls. These measures will be summarized using descriptive statistics. We will use descriptive statistics to summarize multiple aspects of study feasibility, including acceptability (percentage of approached and eligible caregivers who consent to the study), tolerability (percentage of consented and enrolled caregivers who complete the study in both arms), and adherence (descriptive statistics summarizing the rate of caregiver completing the scheduled sessions for both arms).

3.1.3. Secondary outcome/preliminary efficacy

Preliminary efficacy outcomes of the intervention will include proximal outcomes in caregivers, which are outcomes we hypothesize may be moderators of the distal outcomes, such as the Oberst Caregiving Burden Scale which measures task difficulty, and the ACS Threat Subscale which measures Appraisal of Caregiving. Distal outcomes in caregivers will include the Bakas Caregiving Outcome Scale, which measures Caregiver Life Changes, and the BSI-18, which measures depressive symptoms. Descriptive statistics and graphics will be used to evaluate these preliminary efficacy outcomes from ICU stay to 1, 3, and 6 months by intervention group, using an intent-to-treat (ITT) approach. We will compute a mean and 95 % CI for the change from baseline to 1, 3, and 6 months for each outcome. If covariate adjustment is needed, differences between groups will be evaluated using a generalized linear mixed model, taking into account the correlation among repeated measures. At each follow-up, we will compute mean differences and 95 % CI between groups to evaluate trends in outcomes.

3.1.4. Exploratory outcomes

Generalized linear regression models for the Caregiver Satisfaction Scale (CSS) including interaction terms between treatment groups and variables defining the above subgroups (caregiver with a history of depression, dyad and family relationship quality, life stressors and social resources, type of caregiver, caregiver support, caregiver resources, and TBI severity) will be applied. The distribution of CSS will be assessed for normality; if appropriate, we may apply a transformation or utilize a suitable link function. The effect of CG-Well on CSS will be estimated in subgroups and expressed as unadjusted means with 95 % confidence intervals and interaction p-values. These analyses will be analyzed

under the ITT principle. We will similarly explore the response to CG-Well on proximal and distal outcomes based on subgroups by evaluating the change from baseline to 1, 3, and 6 months for each outcome using generalized linear mixed models with an interaction term between treatment group and subgroup. Subgroup point estimates with 95 % confident intervals will be computed.

3.1.5. Sample size Calculation

Sample size is based on the primary outcome of caregiver satisfaction total score at 6 months. A sample size of 40 in each group achieves 80 % power to detect a mean difference in satisfaction of 0.4 between groups, with an estimated standard deviation (SD) of 0.60 in both groups using a two-sample *t*-test with a significance level of 0.05. This detectable difference is lower than published differences [38]. This sample size was also determined by balancing realistic recruitment estimates and minimal sample requirements for planned analyses [53]. To account for deaths and drop-outs, we will enroll 50 dyads in each group. We have enrolled approximately 70 % of participants at this time.

4. Discussion

Whereas attention in the ICU is traditionally paid to the patient, our intervention will target the caregiver. This trial, comparing CG-Well to an ISR control group, will evaluate the satisfaction of a tailored intervention targeted toward meeting the needs of caregivers of patients who have sustained an msTBI. In addition, numerous secondary outcomes will be obtained that will both inform future CG-Well iterations, and impact the msTBI caregiver literature as a whole. This intervention fills a gap for an intervention that can be accessible, private, and acceptable to caregivers. We will start the program while the survivor is early in his or her course of injury. By doing so, we hope to proactively intervene, thus reducing stigma for caregivers to obtain help later if needed.

4.1. Future work

Findings from this study will be reported in line with CONSORT standards, and will inform the possibility of a future larger-scale trial. If our approach is supported, it will inform interventions that help manage the negative adverse impacts of msTBI to caregivers, that may be used in other neurocritical care patient populations, and interventions that may sustain over the long term. Given the burden of msTBI, and the increasing numbers of msTBI within the population, there may be larger societal impacts of CG-Well.

5. Limitations

To reduce the possibility of the trial simply measuring the effects of two different coordinators, the same study coordinator will administer the phone calls in both arms of the intervention. Thus, it is possible that elements of CG-Well may be revealed to participants enrolled in the ISR cohort, which would potentially impact fidelity and reduce the effects of the CG-Well intervention. To decrease the chance of this occurring, we will transcribe and review all calls in both groups, and we will monitor treatment fidelity of the protocol with a standardized checklist [50]. Our fidelity plan includes assessing each session for any such contamination. It is likely that some caregivers will experience significant benefits by being randomized to the ISR group. However, the use of an ISR control group in previous studies suggests that this possibility is limited [48]. We do not have the ability to control for the education, support, or skills that caregivers may obtain in other ways outside this study, such as from inpatient rehabilitation, physician specialists, or online support groups. We do not formally collect information about the other types of information caregivers receive outside of this study, but this information will be collected in future studies. Finally, we acknowledge that msTBI caregivers that meet our inclusion and exclusion criteria are a smaller population, however, we anticipate that many of our findings may be

translatable to caregivers of other neurocritical care patient populations.

6. Conclusions

Our rigorously designed pilot trial has the potential to have a positive impact on caregivers. It may also inform future larger studies of CG-Well. Since we plan to determine ways that CG-Well needs to be tailored based on psychosocial and contextual factors of dyads, we may better understand the types of caregivers who may be most responsive to CG-Well. Given the increasing numbers of msTBI, this intervention has the potential the improve the care of a wide range of survivors and their caregivers, and may ultimately be able to be modified for other neurocritical illnesses and injuries.

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CRediT authorship contribution statement

Natalie Kreitzer: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Stephanie Fink:** Writing – review & editing, Project administration, Methodology, Investigation, Data curation. **Opeolu Adeoye:** Writing – review & editing, Methodology, Investigation, Funding acquisition, Data curation, Conceptualization. **Brad Kurowski G:** Writing – review & editing, Supervision, Methodology, Investigation, Funding acquisition, Data curation, Conceptualization. **Shari Wade:** Writing – review & editing, Supervision, Methodology, Investigation, Funding acquisition, Conceptualization. **Heidi Sucharew:** Writing – review & editing, Supervision, Software, Resources, Project administration, Funding acquisition, Formal analysis, Data curation. **Tamilyn Bakas:** Writing – review & editing, Writing – original draft, Visualization, Supervision, Resources, Methodology, Investigation, Funding acquisition, Data curation, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Dr. Kreitzer is on the speaker bureau of Astra-Zeneca (Andexxanet Alfa), is an independent neurotrauma consultant for National Football League, and speaks for EMCREG-International. None are topics that are related to the submitted manuscript.

Data availability

Data will be made available on request.

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