Official Title: Telemedicine Optimized Burn Intervention
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Study Protocol and Statistical Design
NCT05019144 Document Date: 7/1/2023

PROTOCOL TITLE:

A Novel Telemedicine Optimized Burn Intervention (TOBI) for Pediatric Burn-injured Patients and Their Caregivers - Phase II

PRINCIPAL INVESTIGATOR:

- Aaron Lesher, MD

1.0 Objectives / Specific Aims

Pediatric burn injury remains a major public health problem, with approximately 120,000 serious pediatric burn injuries annually in the US [15]. Specialized burn center care, similar to medical services delivered at trauma centers, has been associated with improved survival, decreased hospital costs, and shorter lengths of hospital stay [16, 17]. The number of verified burn centers has decreased by 30% since the 1990s, leaving the majority of the US population living more than 2 hours by ground transportation to a verified burn center [18, 19]. 91% of pediatric burn patients are treated in the outpatient setting, often requiring multiple trips to the burn center to ensure that the burn heals without complication [20]. A second key factor in burn care is adherence to prescribed medical treatment. Poor adherence to therapy leads to an increased risk of infection and scarring and decreased range of motion [21-23]. Telemedicine is feasible in burn care [24-26] and facilitates the delivery of care to patients with burn injuries of all sizes [27]. Mobile health (mHealth) technology offers a promising approach to address these geographic barriers [28], but has never been used to provide expert burn care in the home.

A novel smartphone application for burn wound care, called the Telemedicine Optimized Burn Intervention (TOBI), was recently developed to enable burn experts to direct burn wound care while the patient and caregiver are home through text messaging and video-conferencing. The app was designed to bring expert wound care directly to the patient's home to address barriers to healthcare, including high cost burden and time commitment (e.g., geographic limitations, transportation to burn centers, parking, lodging, meals, time away from school and work), particularly for patients/families in rural and medically underserved communities (See Figure 1).

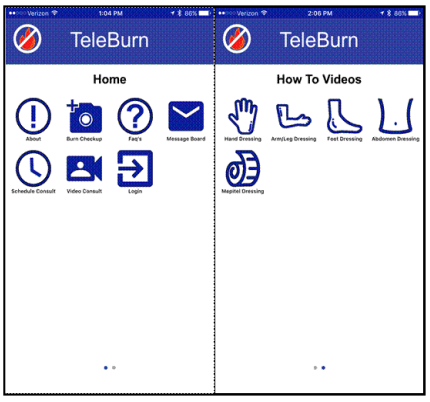

Figure 1. Burn App

The current ongoing Phase I study (**Pro00092341**) aims to refine TOBI, using qualitative research directed at stakeholder feedback, including caregivers and expert burn providers, to make the app/portal more "user-friendly." The ongoing project involves semi-structured interviews, assessment of satisfaction/usability and caregiver well-being and adjustment, and subsequent consumer-driven adjustments to the app to ensure high acceptability and usability. These adjustments will focus on improving patient adherence as well as provider barriers to implementation in preparation for a feasibility RCT.

Following optimization of TOBI app/portal, **the proposed feasibility RCT of burn care utilizing TOBI will be conducted**. The proposed study will recruit 64 patient/caregiver dyads from our pediatric burn center who are under outpatient medical treatment for a partial thickness burn and will randomly assign them to outpatient burn therapy enhanced with TOBI (TOBI) (n=32) vs. standard outpatient face-to-face (FTF) (n=32) therapy.

The **objective** of the proposed study is to assess the feasibility of the TOBI intervention and RCT research protocol in preparation for a subsequent large-scale multi-center RCT comparing outpatient burn care enhanced with TOBI vs. standard care. We will obtain preliminary indicators of effectiveness of the intervention rather than testing hypotheses. Clinical outcomes (burn healing, infection, change in therapy, adherence, and unexpected return to clinic/emergency room) will be assessed during baseline and at clinically determined intervals with (TOBI) or every clinic visit (FTF). We will also assess caregiver self-efficacy, stress, and well-being using psychometrically validated measures to understand whether these factors play a role in service utilization and outcomes. Many factors affect the successful implementation of an intervention that changes clinical practice, like TOBI [69]. The feasibility study is not sufficiently powered to make firm conclusions about TOBI's effectiveness, but will critically assist in identifying barriers to recruitment, retention, and procedures essential toward successfully conducting a large-scale, multicenter RCT. This is consistent with expert recommendations to test the feasibility of conducting an RCT while avoiding hypothesis-testing and yielding data to "debug" the methodology and assess optimal strategies for executing the RCT [69-72].

Aim 1: Assess feasibility of the proposed RCT methodology, including recruitment, participation and attrition, treatment fidelity, safety, and problems associated with equipment.

Aim 2: Obtain estimates of variability for the primary outcome measures: time to treatment of wound complication (e.g., infection, pain, non-healing), patient's sleep, therapy adherence, and FTF clinical visits. These variability estimates are needed to calculate sample size for a subsequent larger, adequately powered RCT to compare the effects of the TOBI intervention with FTF alone.

Aim 3: Examine factors related to caregiver attitudes toward telemedicine and access to health care, as well as caregiver stress, self-efficacy, and well-being in relation to treatment outcomes. Because caregivers randomized to TOBI will be the ones delivering burn treatment under the guidance of a provider through the app, they may experience elevated stress levels and anxiety, and their self-efficacy may influence treatment. Assessing these domains will strengthen our understanding of treatment utilization and outcomes as a function of caregivers' psychological factors. We also would like to assess post-injury caregiver adjustment from a more positive perspective (e.g., personal strengths, relating to others in times of need, spiritual change, appreciation of life), a construct that is conspicuously scarce in the scientific literature on caregivers of burn-injured children. Treatment feasibility and satisfaction will also be assessed.

The proposed mHealth intervention may (1) improve the quality of and access to expert burn care for pediatric surgical patients and their families and (2) relieve the burden on burn providers by allowing them to remotely direct treatment in the patient's home. TOBI has significant clinical utility and strong potential to influence access to care and alter the doctor-patient relationship, enabling healthcare providers to prescribe the right intervention at the right dose at the right time for each patient. Findings from this study will demonstrate the feasibility of testing a scalable, low-cost intervention in a multicenter RCT.

2.0 Background

Access to expert burn care: Pediatric burn injury affects more than 120,000 patients a year, the vast majority affecting children under 6 years of age [15]. Burns are severe injuries requiring highly specialized treatments. Since 1981, the number of accredited or verified burn centers has decreased by 29%, with only 51 centers nationwide verified by the American Burn Association (ABA), and 128 self-reported centers [18, 19, 29, 30]. Unfortunately, this decline in burn centers has led to decreased access to expert burn care for many patients, particularly the rural populations. Nationally, 25%, 46%, and 68% of the US population lives within 1, 2, or 4 hours of a verified burn center; while 41%, 68%, and 91% live within a self-described burn center, with regional variation [18]. Poor access to care is evidenced by inability to pay, lack of insurance, large distances from tertiary care facilities, inadequate knowledge, limited transportation resources and time constraints, especially for working families [31]. In addition, medically-vulnerable populations are more likely to experience inferior outcomes, more likely to have fewer health care choices, and less likely to see a specialist [32]. As burn care has become regionalized, so have the resources and expertise required for high quality care. Errors and delay in treatment occur when burns are treated outside of burn centers [18, 33, 34].

Outpatient burn wound care: ~91% of serious pediatric burn injuries (those requiring medical treatment) are partial thickness burns (See Figure 2) treated in the outpatient setting, with the majority of care occurring in emergency rooms and outpatient burn or plastic surgery clinics [20]. With increasing emphasis on cost saving, larger burns are increasingly being managed in the outpatient setting [35-37]. The goals of burn wound care are to minimize pain, decrease the risk of infection, promote healthy wound healing, minimize cosmetic deformities, and preserve function [20]. Standard outpatient therapy usually lasts 10-21 days, with the majority of pediatric partial thickness burns healing by 14 days [1]. During this period, the burn wound is assessed for complications including pain, infection, non-healing, and need for operative intervention, with repeat face-to-face clinic visits, one to three times per week, depending on the practice of the burn center [38].

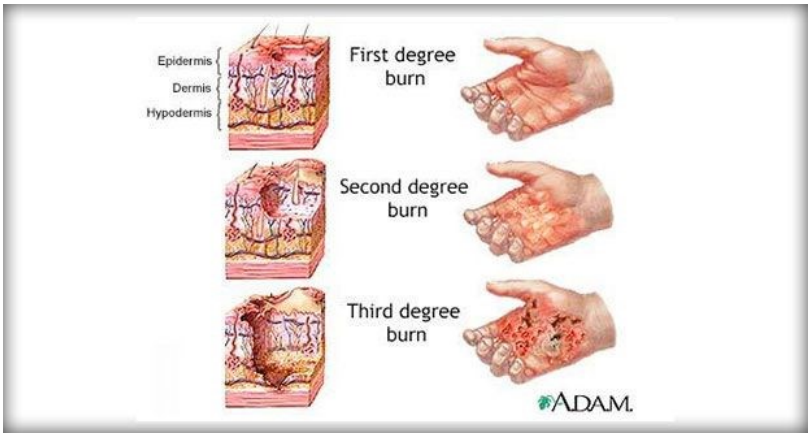

Figure 2. Skin Burn Types.

Adherence to burn wound therapy: To promote recovery after burn injury, appropriate burn care (e.g., wound debridement, dressing changes, range of motion exercises) is critical [22]. Delays in care and poor adherence to prescribed therapies can lead to a higher risk of infection, hypertrophic scarring, contractures, and impaired range of motion [21, 23, 39]. Treatment adherence is defined as "the extent to which a person's behavior coincides with medical or health advice [40]. In outpatient burn care, factors such as discomfort, physical limitations, and lack of information have been associated with non-adherence [39, 41, 42]. Another study demonstrated that having an "expectation of a positive result," "social support," "personal factors" (e.g., use of coping strategies, problem solving, information seeking) were the most common resources used by adults and children to increase adherence to burn care therapy [42]. Adherence of various aspects of burn care has been found to range from poor to good, primarily based on education of patients and communication between the multidisciplinary burn team and the patients and caregivers [23].

Telemedicine use in burn injury: Telemedicine, defined as the remote diagnosis and treatment of patients by means of telecommunication technology, has been used for two decades in burn care [43]. The assessment and treatment of burn injury are ideally suited for the use of telemedicine [24, 44-47]. A systematic review of telemedicine in burns [44] identified 24 studies, the majority with poor methodological detail and no a priori power calculations. Eight studies in the review found that digital imaging was comparable to FTF evaluation. Twelve studies demonstrated proof of concept for decreasing emergency air or ground transfer to burn centers through ER telemedicine carts, but these studies failed to show cost effectiveness and were retrospective. No high quality, prospective RCTs have been performed demonstrating the efficacy of telemedicine on the outcomes of burn patients. Unfortunately, the rapid rise of telemedicine in practice has not been followed by careful validation studies. The last Cochrane review on the effectiveness of telemedicine interventions found a continuing need for larger studies of telemedicine as controlled interventions, with more focus on patients' perspectives with a specific need for collaborative work to generate innovation [48].

Role of mHealth in Burn Care: mHealth, the use of wireless technology in healthcare, is a rapidly growing field in the provision of medical care [49]. Cell phones are utilized by ~95% of adults in the US, with widespread dissemination in all groups irrespective of race/ethnicity, socioeconomic status, or urban-rural classification [50, 51]. Patients and

families are receptive to mHealth programs [52, 53]. To date, pediatric mobile device solutions surrounding the doctor-patient communication have focused on phone calls and SMS messaging related to chronic health conditions, but do not involve direct contact between doctor and patient [54, 55]. Mobile phones have surpassed the minimum requirements needed for burn assessment [56] but rigorous scientific validation to addressing outcomes has not been achieved [57]. A systematic review of smartphone applications in burns found 31 apps in the Google Play Store and 29 in Apple's App store [58]. The apps fell into 4 groups: calculators, information apps, book/journal apps, and games. One app uses store-and-forward images to aid remote doctors in evaluation of acute burns in the office setting [57]. No apps have been developed and evaluated to assist patients and families treating serious burn injury in outpatient settings.

Acceptability of mHealth in healthcare organizations: As patient-generated healthcare data gains traction in medical decision-making, both patients and providers are major stakeholders in the process and content. In Dr. Ruggiero's previous mHealth development work, he found patients desire reminder notifications, instructions and rationale explanations, customizable avatars, incentives and rewards, and clear communication lines, while providers value data management, tracking, and summaries [59, 60]. Increasingly, patients expect healthcare to be "on demand" and "user-friendly," while healthcare systems have lagged behind these expectations. Understanding these stakeholder tensions is imperative to the process of designing effective mHealth systems of care [8]. The rapid evolution of telemedicine has followed the pace of technological advancement, enabling health care entities to provide health care in ever-changing settings, often blurring the lines of traditional care, and thus, the roles of the health care provider [7].

Payer reimbursement of remote patient monitoring (RPM): Billing for physician-based telemedicine services has been a barrier to widespread adoption of telemedicine throughout the United States. Physicians performing telemedicine consultation services to patients remotely in outlying hospitals or clinics are now reimbursed at the same levels as in-person, known as parity, although there is still variation at the state level [61]. While there is no parity payment for physician services provided in the patient's home, Medicare and Medicaid have unbundled the CPT code 99091 to allow for clinician billing of RPM services, specifying the use of digital data transmitted to the physician, billed over a 30-day service period.

3.0 Intervention to be studied

Telemedicine, in various forms, is feasible in burn care [24-26] and facilitates the delivery of care to patients with burn injuries of all sizes [27]. Mobile health (mHealth) technology, offers a promising approach to address barriers [28], but has never been used to provide expert burn care in the home. Smartphone app-based burn injury care exists in practice, although rigorous scientific validation has not been achieved. The MUSC pediatric burn team has partnered with TACHL (Technology Applications Center for Healthy Lifestyles) to provide pediatric patients and their families with state-of-the-art burn care at home using a novel mobile health technology, called the Telemedicine Optimized Burn Intervention (TOBI). TOBI is a smartphone application synced with a portal used by providers, as an adjunct to standard therapy. This burn app provides education through frequently asked questions, instructional burn dressing change videos, and direct communication between patient and burn expert through store-and-forward pictures and videoconferencing.

The ongoing Phase I study (**Pro00092341**) builds upon our proof-of-concept study using a smartphone app to provide expert burn care to children in the home. Feedback from pediatric burn patients, parents, and their health care providers guided initial development and pilot testing of TOBI, which connects clinicians and caregivers through text-messaging, wound image transfer, and video-conferencing. We conducted an open trial (n=32) using TOBI and found high parental and provider acceptability and usability. Comparisons against a historical comparison group suggested quicker time to detect healing, fewer in-person clinical encounters, and greater adherence to treatment among families using TOBI vs. standard care [4]. Rigorous scientific study is needed to validate this novel clinical care pathway as mHealth technology shifts the fundamental structure of the provider-patient relationship. The ongoing Phase I study will culminate with evidence-based optimization of TOBI based on stakeholder feedback prior to the proposed RCT.

Innovation

TOBI is an innovative solution to improve access to expert burn care and adherence to burn therapy: The proposed research will capitalize on innovations in technology to improve the efficiency and effectiveness of outpatient burn care. There is a persistent gap between the care that is prescribed and that which is delivered in the outpatient setting [22, 23, 39]. The proposed work takes an innovative approach to meeting this need by increasing access to burn experts through mHealth technology and addressing adherence to prescribed treatment by increasing communication between provider and patients.

TOBI will be applicable and translatable to a broad range of pediatric surgical illness and traumatic illness: This line of work will refine a highly novel, quality of care solution that has strong applicability to a range of pediatric surgical treatments and populations. The use of outpatient burn care as a model intervention for this work is innovative because burn assessment and treatment is well-suited for telemedicine [24, 44-47]. Understanding the needs of patients and parents using the TOBI platform will ensure strong translatability to a wide range of chronic pediatric diseases may be amenable to mHealth remote patient monitoring (RPM), including pectus excavatum, intestinal failure, and adolescent morbid obesity.

TOBI will be a platform for tailoring and personalizing treatment to optimize outcomes: TOBI allows the physician and patient to make faster decisions regarding treatment rather than having the patients and families wait for scheduled clinic appointments, often hours away from home. mHealth offers a distinct advantage to answer the NIH Strategic Objective call for “precision medicine,” to enable healthcare providers to prescribe the right intervention at the right dose at the right time for each patient (Strategic Objective 1) [14].

TOBI is scalable, sustainable technology that overcomes traditional telemedicine barriers: While telemedicine has the potential to bring expert wound care directly to the patient in rural and medically-underserved communities [24, 62, 63], the traditional paradigm of a telemedicine hub-and-spoke model can be a financial burden to health care systems and inefficient for health care providers, leading to inconsistent adoption by hospitals and burn providers [64-66]. Building upon our study aimed at optimization of TOBI, the proposed Phase II study will allow us to explore implementation, scalability, and sustainability barriers with a population and a clinical problem that has not been explored in this way. Phase II study will be submitted as a separate IRB protocol.

4.0 Study Endpoints

Primary endpoints

- Feasibility outcomes:
  - Recruitment (ratio of how many recruited vs. consented; reasons why patients chose not to do the study);
  - Participation/attrition (percentage of those consented and retained over time vs. dropouts; or benchmark for attrition is consistent with similar studies and is 20%; reasons why patients dropped out and from which condition);
  - TOBI treatment fidelity (providers' adherence to the treatment protocol; will use a fidelity checklist each visit which will be self-rated by providers themselves and patients);
  - Safety (AE or SAE, UPs occurrence in both conditions),
  - Problems with technology (number of times problems happened, notes if TOBI did not function correctly [e.g., video breaks down]).

Secondary endpoints

- Clinical outcomes:
  - Time to treatment of wound complication (e.g., infection, pain, non-healing), patient's sleep, therapy adherence, and FTF clinical visits.
- Caregiver factors:
  - Attitudes toward telemedicine, perception of healthcare access, affect, distress/stress, depression, anxiety, self-efficacy, posttraumatic growth.
  - Satisfaction with care

5.0 Inclusion and Exclusion Criteria/ Study Population

Study Population

Participants in the proposed study will be child/caregiver dyads seeking outpatient burn care at MUSC. Caregivers will be parents or legal guardians of the child participant. We expect that females and minorities will be very well represented in this study based on demographic data collected during our retrospective review of pilot data. We anticipate that 40% of youth recruited into the study will be girls. Caregivers' age may vary but the majority will be 25-45 years. Additionally, women are expected to comprise the majority (85%) of participating caregivers. Because mothers are more often the caregivers of injured patients, it is anticipated that more women will be recruited as caregiver providers than men. Participants of all racial/ethnic backgrounds will be eligible for this study. We estimate that Black or African American children and providers will comprise approximately than 50% of our sample. Given the low prevalence of individuals of Hispanic ethnicity in SC (5%) and data from our pilot study, we estimate that our sample will be comprised of approximately 5% of Hispanic youth in this study.

Inclusion Criteria for child/caregiver dyads

Participants will be eligible for enrollment if:

(1) the patient (child) is < 18 years of age;

(2) the patient is diagnosed with a partial thickness burn between <1% TBSA – 20% TBSA by a pediatric burn surgeon;

(3) the burn is being treated with advanced burn dressing therapy (e.g., Silvadene™, Polysporin™, Acticoat™, Mepilex™, or Mepitel™) or skin substitutes;

(4) the burn is evaluated by the MUSC burn team within 72 hours of injury;

(5) the patient's caregiver (parent or legal guardian) is able to speak, hear, and understand English, as determined during study recruitment procedures;

(6) the patient/caregiver owns and is capable of using a smart device (an Android or iOS smartphone) with permission to download TOBI app from the Google Store or AppStore;

(7) able to comply with outpatient clinic visits.

There are no exclusion criteria. All participants who meet inclusion criteria would be eligible to participate in the study.

6.0 Number of Subjects

We will recruit 64 child/caregiver dyads (for a total of 128 people) seeking outpatient treatment at MUSC for acute burn injury.

Consistent with the intent of a feasibility RCT, sample size for this study was determined for pragmatic reasons rather than through formal power calculation. Following the recommendations by Kraemer et al. [73] as well as the CONSORT 2010 statement extension to randomized pilot and feasibility trials [74] the purpose of feasibility/pilot studies is to test recruitment processes, feasibility of the intervention and measurement as well as training protocols, data collection, and data quality control, storage and retrieval processes. Further, Kraemer et al. advise that effect size estimates obtained from pilot studies have insufficient accuracy as useful input for sample size determination for future study design.

We anticipate high feasibility of recruitment of 64 pediatric patient/caregiver dyads with partial thickness burns over 24 months. Our TOBI pilot included recruitment of 32 patient/caregiver dyads, and this recruitment was completed over 9 months with minimal infrastructure. With ~200 outpatient pediatric partial thickness burns cases per year at MUSC and our track record of enrolling participants into clinical studies (including TOBI pilot), an enrollment of ~25% of this sample of ~275 is highly feasible. We had a 74% participation rate in the TOBI pilot, 3-4 times higher than what is needed to meet proposed targets.

7.0 Setting

The proposed study will be conducted at the MUSC campus and remotely via telephone/videoconference and TOBI. Participants will be recruited into the study during their initial visit to the MUSC outpatient burn clinic, hospital floor, or pediatric emergency room for the treatment of pediatric burns. Patients that visit and get discharged from the pediatric emergency room in the after-hours or patients that were missed due to staff unavailability will be contacted by phone by a clinical care team member within 72 hours. Informed consent with caregivers and assent with children, when applicable, will be conducted in a private room at Shawn Jenkins Children's Hospital or virtually at the patient's private location using secure videoconferencing.

8.0 Recruitment Methods

The MUSC Pediatric Burn program provides the only tertiary burn care in the state to >200 pediatric patients annually. We will use a convenience sampling strategy to recruit 64 patient/caregiver dyads who have undergone a face-to-face (FTF) clinical encounter with an MUSC burn professional at the outpatient burn clinic, the hospital floor, or the pediatric emergency room. Patients will be seen in person and prescribed therapy by our burn experts in our standard practice. Patient/caregiver dyads who meet the inclusion criteria will be considered eligible for enrollment.

Recruitment will be initiated in-person in MUSC's outpatient burn clinic setting, the hospital floor, or pediatric emergency room. Patients/caregivers that visit and get discharged from the pediatric emergency room in the after-hours or patients that were missed due to staff unavailability will be contacted by phone by a member of the clinical care team within 72 hours. Once a possible study candidate dyad is identified, patients will be asked about participating in the feasibility RCT and the study will be explained by study staff, either in-person or by phone/virtually. Study staff will include members of the clinical care team (e.g., burn nurse, physician) and research staff (e.g., clinical trial coordinator). Initial mention of the study will occur with a member of the clinical care team who is also a research team member. If the caregiver expresses interest, study staff will screen potential participants for eligibility and proceed with reviewing informed consent (and assent if applicable) and will address the risks and benefits of the study. For potential participants contacted by phone, the review of informed consent will occur virtually. If potential participants indicate further interest in the study, study staff will obtain written or electronic informed consent from caregivers and assent from children, if applicable. After enrollment, patient/caregiver dyads will be randomized. The randomization scheme will yield at least 32 patients per treatment group.

Pace of patient referral and recruitment will be tracked on a weekly basis by the project team to anticipate, identify, and address potential challenges with recruitment. Our TOBI pilot included recruitment of 32 patient/caregiver dyads, and this recruitment was completed over 9 months with minimal infrastructure. Based on our TOBI pilot recruitment rate, we anticipate high feasibility of recruitment of 64 pediatric patient/caregiver dyads with partial thickness burns over 24 months.

9.0 Consent Process

Informed consent will be obtained from caregivers with legal custody and assent will be obtained from child patients who are 12 years old or older.

Prospective participants will be informed about the study during their FTF clinical encounter with an MUSC burn professional at the outpatient burn clinic, on the hospital floor, or in pediatric emergency room. Patients/caregivers that visit and get discharged from the pediatric emergency room in the after-hours or patients that were missed due to staff unavailability will be contacted by phone and informed about the study by a clinical care team member within 72 hours. Participants will be informed about the project's rationale geared towards evaluating two treatment delivery modalities for burns (TOBI and FTF). If they express interest in the study, study personnel will invite them to complete an informed consent/assent in a private room or virtually at a patient's private location using secure videoconferencing. The study team member will summarize the content of the

informed consent/assent form and ask for any questions. Alternatives to participating in the proposed research will be mentioned; they include continued treatment outside of the study by the health provider who referred them to the study and with whom patients have established care. We will be amendable to patients' preferences. Patients will be informed that declining to serve as a participant in this study will not influence or compromise the quality of their care. If participants express continued interest, study personnel will provide an opportunity for participants (caregivers and children over the age of 12) to review the consent and will obtain written or electronic signature from caregivers and assent from patients who are at least 12 years old. For electronic consent, participants will be invited to join a secure Doxy conference call and will complete an electronic informed consent via Doxy. Participants may also complete electronic informed consent via a REDCap e-consent link (e.g., if Doxy is not working). They will have an opportunity to read it and ask questions. The person obtaining the consent will then sign it in writing or electronically and provide a hard copy or email an electronic copy to the participant via secure MUSC email. Any participant who does not meet study inclusion criteria (as reviewed during the informed consent process) or does not agree to participate, will be excused from the study.

10.0 Study Design / Methods

The RCT will include 64 patient/caregiver dyads recruited from the MUSC outpatient burn clinic, hospital floor, or pediatric emergency room, randomized to burn care enhanced with TOBI (n=32) or FTF standard care (n=32). After obtaining informed consent, the research staff will create a new patient record in the REDCap database and assist (if needed) the caregiver in completing the initial questionnaire battery using the REDCap survey. The baseline questionnaires, completed by the caregiver, will include the demographics form, measures about attitudes toward telemedicine, perception of healthcare access, affect, depression, anxiety, self-efficacy, and peritraumatic distress (see measures attached). All PHI will be protected by a study ID to promote confidentiality The family will receive a ClinCard at the beginning of the study which works like a bank debit card and can be used to purchase goods or services everywhere Debit MasterCard is accepted. Each time they receive payment for participation in this study, the money will be added to the card. Families will receive $20 for completion of baseline assessment.

At the completion of questionnaires, caregivers will be randomly assigned to treatment conditions. Stratified permuted block randomization will be used to assign patients to either the burn care enhanced with TOBI or FTF care only (32 dyads per arm). Assignment will be stratified by provider to ensure balanced enrollment across the treatment arms regardless of numbers enrolled per provider. To minimize the likelihood that the blind will be broken, i.e. the next treatment assignment can be guessed, the block size will be varied.

Chart review will be conducted within approximately 72 hours of enrollment and data will be recorded in a chart review checklist and subsequently transferred into the database (e.g., burn mechanism, % TBSA, burn location, burn depth, date of burn injury, time to medical treatment, type of first clinical encounter [burn outpatient vs. emergency department vs. hospital discharge], and type of dressing).

Patients randomized to FTF will undergo standard burn care including a return follow-up in the burn clinic on a routine basis as prescribed by the clinical burn team (e.g., at least once per week) until the burn has healed. Healing is defined as greater than 95% epithelialization of the burn wound. This will be determined by a clinician.

Patients randomized to burn care enhanced with TOBI will be given instructions and will be aided in downloading TOBI onto their smartphones. Patients with TOBI will be able to use standard FTF care as well. They will demonstrate an ability to use the various components of TOBI during initial visit and enrollment and will be explained how to contact the burn team through the hospital paging operator if TOBI is unavailable. Similar to the FTF group, they will be given oral and written instructions about standard burn care with routine clinical care delivered via TOBI, including a plan to interface with the burn clinicians (text messaging, videoconferencing, or image transfer) on a routine basis. TOBI patients will be scheduled for weekly videoconferencing encounters through the app until the burn has healed. Patients will be asked to come in-person if would complications are noted by a clinician (e.g., non-healing, infection). If technological problems with TOBI are encountered (e.g., video stops working), providers may switch to another secure telehealth platform to provide the necessary care and will document technology issues appropriately, as part of feasibility assessment.

Clinical data will be collected on case report forms by the clinical care team (e.g., burn nurse, physician) and entered into the REDCap database in a coded manner by a research assistant (who is blind to the treatment condition to reduce bias during data entry) at clinically determined intervals per routine care based on clinical judgment with TOBI or FTF (see table below). The duration and number of clinical encounters for both conditions will be guided by best clinical practice and each patient's needs. On average, most burns that meet the study eligibility criteria require 2-5 visits and heal within 2-4 weeks. Case report forms will be generated with study ID only, with no identifiable PHI in order to protect patient's privacy. Data collected at intervals will include adherence to prescribed wound care, change in therapy, wound complications, day of healing, pain scores, sleep problems, unexpected return to clinic or emergency room (see Clinical Case Report Form attached). App metrics, such as number of videoconferences, number of text-messages, number of photos, and scripted messages by burn professional will be recorded by the app software and exported at the end of the study. Images of wounds will not be stored for the purposes of this study. They may be uploaded by clinical care team members into the patient's medical record as part of standard care procedures (outside of the study). Adherence to therapy will be defined as parent/patient performance of prescribed wound care through the end of treatment. Overall compliance with therapy is defined as documentation of healed burn through TOBI or FTF. Clinical data collection will continue until 1 month after the burn is diagnosed as healed by a burn physician in either condition (FTF or TOBI).

At 1-month, caregivers will be asked to complete the post-treatment questionnaires by phone or virtually using the REDCap survey, using a public link and study ID to identify their survey. This assessment will include measures about attitudes toward telemedicine, perception of healthcare access, affect, depression, anxiety, perceived stress, posttraumatic growth, treatment satisfaction, and app feasibility (TOBI only group) (see measures attached). Collected data will be entered into REDCap by the study staff. Overall, participation rate will be recorded. Families will receive $30 following completion of post-treatment assessment.

Data analyses will be performed by Dr. Lesher and study coordinator at the completion of the study in aggregate in a blinded fashion to prevent bias as much as possible. Quantitative questionnaire and case report form data will be exported from REDCap and

analyzed using statistical software (e.g., SPSS). Dr. Mueller will oversee Dr. Lesher and the study coordinator in all data analyses.

TOBI	Data Collected	Enrollment	TOBI Video Visit 1	TOBI Video Visit 2	TOBI Video Visit 3	TOBI Video Visit 4	TOBI Video Visit X (possible)	End of therapy (1 month FU)
	Demographics Form	X						
	Chart review data (e.g., burn mechanism, % TBSA, burn location, burn depth, date of burn injury, time to medical treatment, type of first clinical encounter [burn outpatient vs. emergency department vs. hospital discharge], and type of dressing)	X within 72 hrs						
	Caregiver measures: - Attitudes toward telemedicine / technology - Perception of healthcare access - PANAS (affect) - PROMIS-Depression - PROMIS-Anxiety	X						X
	Caregiver measures: - PROMIS-General-Self-Efficacy - PROMIS-Self-Efficacy-Manage-Emotions - Peritraumatic Distress Inventory	X						
	Caregiver measures: - Perceived Stress Scale - Posttraumatic Growth Inventory							X
	Case Report Form: - Clinical endpoints, including pain score, healing, infection, change in therapy, adherence, sleep, unexpected return to ED/clinic	X	X	X	X	X	X	
	Caregiver satisfaction & usability surveys: - Satisfaction questionnaire - MAUQ (app usability) – TOBI only)							X
	Post-treatment data: - Adherence to treatment - Total # of FTF visits - Total # of TOBI visits - Total travel time - Direct cost to patient/caregiver - Return to work/school date							X
	App metrics (# of video-conferences, messages, & photos) – TOBI only							X
FTF	Data Collected	Enrollment	Clinic Visit 1 (date)	Clinic visit 2 (date)	Clinic visit 3 (date)	Clinic Visit 4 (date)	Clinic Visit (possible)	End of therapy (1 month FU)

11.0 Data Management

Regarding data management and storage, all data will be collected using coded questionnaires and case report forms. Only participants' study identification codes will be inputted in computer-based databases. All participants will receive a participant identification number at the time of consent, which will be linked to their data in a master list with participant names and contact information and kept by the PI/study coordinator electronically in password-protected network storage (MUSC Box). Consent forms will be kept either in a locked drawer in the PI's office or electronically in password-protected network storage. Hard copies of the case report forms will also be kept in a locked drawer in the PI's office. Assessments will be administered via in-person or app-based communication, or via REDCap data entry, which will be programmed to check data at the time of entry to ensure that entered values are within the specified range and that items are not inappropriately skipped. The data will be imported directly into a password-protected statistical software data file (e.g., SPSS) stored on MUSC's secure server. The MUSC server has a 1TB hard disk capacity, 4GB of RAM, dual 3000MHz processors, and 100% drive redundancy to safeguard all data and minimize disruptions in the event of hardware failure. The server is protected by the MUSC network, and a secured log-in is required from all users. In addition to these precautions, all personnel will have earned at least a bachelor's degree and have experience in conducting research. All research personnel collecting and handling data will have completed a Human Subjects Research Training course offered through the MUSC Compliance Division and will be supervised by Dr. Lesher to ensure strict compliance with the DSMP. Only IRB-approved study personnel (Dr. Lesher and study team) will have access to data. No data will be released to other agencies unless participants consent to release.

The following data will be collected and analyzed: Feasibility processes include recruitment and drop-out proportions, protocol adherence and patient and provider satisfaction will be assessed at 1 month. We will use 95% CIs for proportions to estimate dichotomous outcomes (proportions of subjects who agree to participate out of the number who are initially approached), the proportion who are adherent to protocol (e.g. opening messages, bi-monthly provider reports), the proportion who report satisfaction with intervention, and the proportion who exit the study prematurely (drop out). In addition, frequency distributions will be developed describing reasons for provider and patient protocol non-adherence, drop out and problems encountered such as technology glitches, etc. For the continuous feasibility measures (e.g., number of technology help requests, provider and patient satisfaction scores from patient surveys and end-of-study interview), frequency distributions and the median and mean responses (with 95% confidence intervals) will be obtained. For relevant categorical feasibility measures, chi-square tests will be used to compare the 2 groups. Pooled *t*-test (or Wilcoxon rank sum tests) will be used to compare the groups for continuous feasibility measures. We will also compare demographic and clinical characteristics for those who were eligible for study versus those who were not eligible and for those who adhered to the study protocol (study completers) versus those who did not adhere (non-adherers and drop-outs).

Quantitative analyses: In preparation for a subsequent adequately powered RCT, the planned primary clinical outcomes will be investigated. Those include variables such as time to healing, time to treatment change, and number of clinical encounters. Determination whether a wound has healed or become infected will be made at routine intervals based on clinical judgement from baseline through the day of burn healing and a final assessment 1 month after it was determined as 'healed'. Analyses for these measures

focus on variability and precision of estimates rather than magnitude of effect sizes. 95% confidence intervals (CIs) of the difference in mean days to healing (or treatment change/infection) between interventions will be obtained. In addition, survival distributions and their 95% CIs will be obtained for each intervention arm using the Kaplan-Meier product limit method. Further, 95% CIs for hazard ratios will be obtained using Cox proportional hazards regression to model time to healing (treatment change) as a function of the intervention. In the future RCT, generalized linear mixed models (GLMM) will be used to obtain estimates of the variances of the clinical outcomes and the covariance structure of longitudinal measures as critical input information for determination of sample size (and hence adequate power) [82, 83]. Frequency distributions of AEs and SAEs will be used to characterize each intervention group. Analyses of caregiver data will include pre- and post-treatment group differences (TOBI vs. FTF) to understand factors related to caregiver well-being and adjustment following mHealth burn treatment and possible predictors of outcomes. These analyses may include mixed design repeated measures analyses of variance (ANOVAs) and regressions.

When the study is concluded, after 6 years all records related to the study will be destroyed. Furthermore, all staff will sign confidentiality agreements, and training sessions will emphasize the critical importance of confidentiality. The likelihood that these methods will effectively protect the confidentiality of participants is considered to be extremely high. Based on our experience with previous research projects, it is believed that these procedures will be effective in protecting confidentiality of subjects and minimizing any potential risk from participation.

12.0 Provisions to Monitor the Data to Ensure the Safety of Subjects

Adverse events (AE), serious adverse events (SAE), and unanticipated problems (UPs) will be monitored throughout the study and any event will be followed to resolution or stabilization. Dr. Lesher is an experienced surgeon specializing in burns, and Dr. Ruggiero, one of Dr. Lesher's mentors, is a licensed clinical psychologist with extensive experience treating victims of traumatic events. In addition to reporting of AEs to MUSC's IRB within 10 days, routine reporting of AEs using NIH's standard AE forms will occur semiannually as determined with NIH staff and the Data and Safety Monitoring Board. All SAEs will be reported immediately to the IRB and the federal funding agency. We will report any unanticipated problems (UPs) to the IRB during Continuous Review and in NIH progress reports unless they are also AEs or SAEs, in which case we will report these events as described above. The Principal Investigator will provide continuous, close monitoring with prompt reporting of adverse events to the IRB and NIH, and will follow MUSC's adverse event reporting policy.

In addition, a Data and Safety Monitoring Board (DSMB) will be formed to ensure the ongoing safety of the participants. Should we encounter AEs, SAEs, or UPs, such as worsening of symptoms or distress, patients may be hospitalized for higher level of care and may undergo an operation if the burn converts to a deeper burn or if an infection occurs. A patient may also need to be escalated to inpatient care due to distress during wound care. The PI will appoint members from diverse disciplinary backgrounds that are not involved in the project. The chairperson of this committee will be Dr. Michael Yost, PhD. Dr. Yost is a full professor and Vice Chairman for Research in the Department of Surgery. He has held numerous grants and has expertise in monitoring clinical trials. Dr.

Rupak Mukherjee, PhD has agreed to serve as the biostatistician on the DSMB. Dr. Mukherjee is a staff scientist and statistician in the Cardiovascular Research Laboratory at MUSC. Dr. Ashley Hink has agreed to serve as the expert in the therapeutic area of burn surgery. D. Hink is a burn and trauma surgeon in the Department of Surgery, with an active research interest in firearm injury prevention. The Board will monitor subject participation and safety issues with a focus on study enrollment in process, study safety, and data integrity. They will be sent tables with de-identified data prior to each semiannual meeting for their review. For the duration of the RCT, including the follow-up, the board will meet semiannually to review data and monitor any potential concerns that have developed. Safety monitoring will involve review of cases involving AEs or UPs where continuing the intervention could create safety concerns, ongoing review of potential risks and our measures in place to protect participants against foreseeable risks, review of consent procedures, and review of participant privacy protections and security of data collected by our system. MUSC will have full and instant access to all reports and data reviewed by the DSMB. This will ensure adherence to the monitoring plan and requirements for reporting AEs, SAEs, and UPs. The PI also will have the ability to call an unscheduled in-person meeting in the event of any AEs, UPs, or SAEs that arise with the project. The Board also will be responsible for following up on requested actions based on recommendations from the Board in response to an AE. Outcome of SAEs will be written in the form of a report reported to the MUSC IRB and NIH.

13.0 Withdrawal of Subjects

Participants may refuse to take part in or stop taking part in this study at any time. Should they decide to withdraw after enrollment, they will be encouraged to contact the PI, who is also a burn surgeon, to discuss their decision and continuity of care outside of the study. Their decision not to take part in the study will not affect their current or future medical care or any benefits to which they are entitled. The investigators and/or the sponsor may stop participants' involvement in this study at any time if they decide it is in their best interest. The investigator and/or sponsor may also do this if participants do not follow the investigator's instructions.

14.0 Risks to Subjects

1. The research material obtained from human participants in this protocol will include questionnaire data and case report forms clinical data. Breaches of confidentiality are a concern with web-accessible components of any study. However, we have taken many steps to protect participant information, including only using study ID numbers on all questionnaires and storing data on secure, password-protected servers. Only the study team will be able to see this information.
2. It is possible that the questionnaires may make participants feel upset. These reactions will be normalized and appropriate resources and/or referrals to a mental health provider (outside of the study) may be provided.
3. Risks associated with TOBI vs. standard FTF burn care:
    - We do not anticipate more than minimal risk to participants in this study as study procedures closely follow those used in routine clinical care. Because the intervention includes the use of a smartphone technology in addition to standard therapy FTF therapy if needed, there is minimal risk above the risk normally incurred by undergoing standard medical treatment. A potential risk is the possibility that burn care delivered through TOBI is worse than care delivered in person (FTF). Although numerous studies suggest that the burn care can be

safely delivered through telemedicine, the TOBI intervention may not accurately portray the burn injury. In practice, the TOBI arm of the RCT includes the use of a smartphone technology in addition to standard therapy. Because patients in the TOBI arm are allowed to return in person for FTF care, there is minimal risk above the risk normally incurred by undergoing standard medical treatment. For example, it is possible that a participant might experience a burn complication at home that is not properly detected through use of the TOBI intervention. Burn complications include infection, pain, and non-healing. If there is an issue with technology, or image/video transfer is inadequate, these issues will be noted and the patient will be evaluated in the standard manner, in clinic face-to-face or in the emergency department. Patients in the standard therapy arm will be evaluated in clinic or emergency room, which is the standard of care. Nevertheless, we do have a specific protocol should a participant have an adverse event as a result of participation in this study.

- Patients in both groups will receive an initial FTF visit either in the burn clinic, hospital, or emergency department. In routine outpatient burn care, the primary risks of burn treatment include burn wound infection, non-healing, and pain. Burn wound infection is the highest risk complication, but, fortunately, is very uncommon in pediatric burn wounds. In adults, burn wound infection approaches 5% in some studies. Data of the incidence of outpatient burn wound infection in children is incomplete, although anecdotal evidence from our practice suggests that outpatient burn wound infection is extremely uncommon. In our pilot series of 32 patients treated with TOBI, none had burn wound infection. Burn wound infection would be normally assessed on visual inspection of the wound and a clinical history of fever. In order to mitigate the small, potential risk of burn infection that is misdiagnosed by using TOBI communication, each daily digital interaction (e.g., video-conferencing, or image-transfer) will be prompted with a dialogue box asking the caregiver if the patient has had a fever in the last 24 hours. This will enhance detection of fever in a burn wound infection patient. In terms of other short-term complications measured, including non-healing or pain, if there is a suspicion that these two clinical outcome measures were inadequately treated by TOBI, the patient will be requested to make a FTF visit.
- Dr. Lesher is a licensed surgeon in South Carolina and has over 12 years of experience assessing and treating patients with burn injury. He will closely supervise all study staff, and will hold weekly meetings with the team during the initial recruitment of patients. He and his partners will provide burn care using both modalities, as is their current clinical practice. All burn surgeons and therapists at MUSC will undergo training in the study procedures. All staff will have cell phone numbers where Drs. Lesher and Ruggiero will be available. Dr. Lesher will coordinate his schedule with staff to ensure that he is available during any staff-patient interactions. In the rare instance where he cannot be reached, Dr. Ruggiero will serve as the clinical backup and will follow these protocols and standards.

15.0 Potential Benefits to Subjects or Others

The potential benefit to participants is that the services they receive may be more helpful or convenient than other available services, although this cannot be guaranteed. For example, if the patient/caregiver dyad is in the group that proves to be better than the other group in this study, the dyad may benefit from this study. Youth and their caregivers receiving services using the TOBI app, will have access to a resource that has potential to improve clinical outcomes, including burn healing time, faster treatment of burn wound complications, decrease travel time, and promote greater adherence to burn wound therapy.

It is hoped that the information gained from this study will help in the treatment of future patients with burn injury. Completion of this study may improve the quality of and access to expert burn care for pediatric surgical patients and their families and may relieve the burden on burn providers by allowing them to remotely direct treatment in the patient's home. The proposed study is a feasibility RCT in MUSC's burn center done in preparation for a subsequent large-scale multi-site RCT. This study will provide valuable data toward understanding how mHealth resources can affect the delivery of healthcare and improve healthcare access and clinical outcomes while leveraging a scalable, sustainable technology platform. It also will set the stage to address key questions around the implementation, dissemination, and sustainability of technology-facilitated treatment approaches in clinical practice settings. The proposed approach is highly sustainable due to low costs of disseminating these resources, and therefore has the ability to have wide reach and impact in the general population.

16.0 Sharing of Results with Subjects

Research results obtained from this study will not be disclosed to participants directly.

References

1. Lesher, A.P., et al., *Effectiveness of Biobrane for treatment of partial-thickness burns in children.* J Pediatr Surg, 2011. **46**(9): p. 1759-63.
2. Lesher, A.P., et al., *Outcome of splenectomy in children younger than 4 years with sickle cell disease.* J Pediatr Surg, 2009. **44**(6): p. 1134-8; discussion 1138.
3. Mouw, E., et al., *Use of an ethanol lock to prevent catheter-related infections in children with short bowel syndrome.* J Pediatr Surg, 2008. **43**(6): p. 1025-9.
4. Garcia, D.I., et al., *Expert Outpatient Burn Care in the Home through Mobile Health Technology.* J Burn Care Res, 2018.
5. Lesher, A.P. and S.R. Shah, *Telemedicine in the perioperative experience.* Semin Pediatr Surg, 2018. **27**(2): p. 102-106.
6. Mathhew Harting, M., MS; Austin Wheeler; Todd Ponsky; Benedict Nwomeh; Chuck Snyder; Nick Bruns; Aaron Lesher; Samir Pandya; Belinda Dickie; Sohail Shah (In Press). , *Telemedicine in Pediatric Surgery.* Journal of Pediatric Surgery.
7. Currell, R., et al., *Telemedicine versus face to face patient care: effects on professional practice and health care outcomes.* Nurs Times, 2001. **97**(35): p. 35.
8. Sanger, P.C., et al., *A patient-centered system in a provider-centered world: challenges of incorporating post-discharge wound data into practice.* J Am Med Inform Assoc, 2016. **23**(3): p. 514-25.
9. Arbra, C.A., et al., *Time to reintroduction of feeding in infants with nonsurgical necrotizing enterocolitis.*J Pediatr Surg, 2018.
10. McClain, L., et al., *Laparoscopic needle-assisted inguinal hernia repair in 495 children.* Surg Endosc, 2015. **29**(4): p. 781-6.
11. Hebra, A., V.A. Smith, and A.P. Lesher, *Robotic Swenson pull-through for Hirschsprung's disease in infants.* Am Surg, 2011. **77**(7): p. 937-41.
12. Lesher, A.P., et al., *Recurrence of midgut volvulus after a Ladd procedure.* Am Surg, 2010. **76**(1): p. 120-2.
13. Lesher, A.P., J.M. Kratz, and C.D. Smith, *Removal of embedded central venous catheters.* J Pediatr Surg, 2008. **43**(6): p. 1030-4.

14. Health, T.N.I.o., *National Institute of Health Strategic Plan Fiscal Years 2016-2020.* https://www.nih.gov/sites/default/files/about-nih/strategic-plan-fy2016-2020-508.pdf.
15. D'Souza, A.L., N.G. Nelson, and L.B. McKenzie, *Pediatric burn injuries treated in US emergency departments between 1990 and 2006.* Pediatrics, 2009. **124**(5): p. 1424-30.
16. Sheridan, R.L., *Burn care: results of technical and organizational progress.* JAMA, 2003. **290**(6): p. 719-22.
17. Sheridan, R., et al., *Early burn center transfer shortens the length of hospitalization and reduces complications in children with serious burn injuries.* J Burn Care Rehabil, 1999. **20**(5): p. 347-50.
18. Klein, M.B., et al., *Geographic access to burn center hospitals.* JAMA, 2009. **302**(16): p. 1774-81.
19. Saffle, J.R., *The 2002 Presidential Address: N.P.D.G.B. and other surgical sayings.* J Burn Care Rehabil, 2002. **23**(6): p. 375-84.
20. Warner, P.M., T.L. Coffee, and C.J. Yowler, *Outpatient burn management.* Surg Clin North Am, 2014. **94**(4): p. 879-92.
21. So, K., et al., *Effects of enhanced patient education on compliance with silicone gel sheeting and burn scar outcome: a randomized prospective study.* J Burn Care Rehabil, 2003. **24**(6): p. 411-7; discussion 410.
22. Lloyd, E.C., et al., *Outpatient burns: prevention and care.* Am Fam Physician, 2012. **85**(1): p. 25-32.
23. Szabo, M.M., et al., *Patient adherence to burn care: A systematic review of the literature.* Burns, 2016. **42**(3): p. 484-91.
24. Theurer, L., et al., *American Telemedicine Association Guidelines for Teleburn.* Telemed J E Health, 2017. **23**(5): p. 365-375.
25. den Hollander, D. and M. Mars, *Smart phones make smart referrals: The use of mobile phone technology in burn care - A retrospective case series.* Burns, 2017. **43**(1): p. 190-194.
26. Hoseini, F., H. Ayatollahi, and S.H. Salehi, *systematized review of telemedicine applications in treating burn patients.* Med J Islam Repub Iran, 2016. **30**: p. 459.
27. Atiyeh, B., S.A. Dibo, and H.H. Janom, *Telemedicine and burns: an overview.* Ann Burns Fire Disasters, 2014. **27**(2): p. 87-93.
28. Parvizi, D., et al., *The use of telemedicine in burn care: development of a mobile system for TBSA documentation and remote assessment.* Ann Burns Fire Disasters, 2014. **27**(2): p. 94-100.
29. Association, A.B., *Burn Care Resources in North America.* Chicago: American Burn Association, 2004.
30. Brigham, P.A. and E. McLoughlin, *Burn incidence and medical care use in the United States: estimates, trends, and data sources.* J Burn Care Rehabil, 1996. **17**(2): p. 95-107.
31. Freiburg, C., et al., *Effects of differences in percent total body surface area estimation on fluid resuscitation of transferred burn patients.* J Burn Care Res, 2007. **28**(1): p. 42-8.
32. Berkebile, B.L., I.W. Goldfarb, and H. Slater, *Comparison of burn size estimates between prehospital reports and burn center evaluations.* J Burn Care Rehabil, 1986. **7**(5): p. 411-2.
33. Lasser, K.E., D.U. Himmelstein, and S. Woolhandler, *Access to care, health status, and health disparities in the United States and Canada: results of a cross-national population-based survey.* Am J Public Health, 2006. **96**(7): p. 1300-7.
34. Cook, N.L., et al., *Access to specialty care and medical services in community health centers.* Health Aff (Millwood), 2007. **26**(5): p. 1459-68.

35. Morgan, E.D., S.C. Bledsoe, and J. Barker, *Ambulatory management of burns.* Am Fam Physician, 2000. **62**(9): p. 2015-26, 2029-30, 2032.
36. Jansen, L.A., et al., *Reduced length of stay in hospital for burn patients following a change in practice guidelines: financial implications.* J Burn Care Res, 2012. **33**(6): p. e275-9.
37. Brandt, C.P., et al., *Complete integration of inpatient and outpatient burn care: evolution of an outpatient burn clinic.* J Burn Care Rehabil, 1998. **19**(5): p. 406-8.
38. Coffee, T., Brandt, CP, Yowler, CJ. , *Risk factors for burn wound infections in the outaptient burn patient.* Journal of Burn Care Research, 2007. **28**(2): p. S62.
39. Johnson, J., et al., *Compliance with pressure garment use in burn rehabilitation.* J Burn Care Rehabil, 1994. **15**(2): p. 180-8.
40. Horwitz, R.I. and S.M. Horwitz, *Adherence to treatment and health outcomes.* Arch Intern Med, 1993. **153**(16): p. 1863-8.
41. Ripper, S., et al., *Adherence to pressure garment therapy in adult burn patients.* Burns, 2009. **35**(5): p. 657-64.
42. Stewart, R., et al., *Pressure garment adherence in adult patients with burn injuries: an analysis of patient and clinician perceptions.* Am J Occup Ther, 2000. **54**(6): p. 598-606.
43. Holt, B., et al., *Telemedicine use among burn centers in the United States: a survey.* J Burn Care Res, 2012. **33**(1): p. 157-62.
44. Wallace, D.L., et al., *A systematic review of the evidence for telemedicine in burn care: with a UK perspective.* Burns, 2012. **38**(4): p. 465-80.
45. Ajami, S. and A. Arzani-Birgani, *Fast resuscitation and care of the burn patients by telemedicine: A review.* J Res Med Sci, 2014. **19**(6): p. 562-6.
46. Wirthlin, D.J., et al., *Telemedicine in vascular surgery: feasibility of digital imaging for remote management of wounds.* J Vasc Surg, 1998. **27**(6): p. 1089-99; discussion 1099-100.
47. Roa, L., et al., *Digital imaging in remote diagnosis of burns.* Burns, 1999. **25**(7): p. 617-23.
48. Ekeland, A.G., A. Bowes, and S. Flottorp, *Effectiveness of telemedicine: a systematic review of reviews.* Int J Med Inform, 2010. **79**(11): p. 736-71.
49. Kashgary, A., et al., *The role of mobile devices in doctor-patient communication: A systematic review and meta-analysis.* J Telemed Telecare, 2017. **23**(8): p. 693-700.
50. Poushter, J., *Smartphone Ownership and Internet Usage Continues to Climb in Emerging Economies* 2016. http://www.pewinternet.org/fact-sheet/mobile/. *Mobile fact sheet*. 2016.
51. McGillicuddy, J.W., et al., *Patient attitudes toward mobile phone-based health monitoring: questionnaire study among kidney transplant recipients.* J Med Internet Res, 2013. **15**(1): p. e6.
52. Jenkins, C., et al., *Stroke patients and their attitudes toward mHealth monitoring to support blood pressure control and medication adherence.* Mhealth, 2016. **2**.
53. Kashgary, A., et al., *The role of plasma exchange in treating post-transplant focal segmental glomerulosclerosis: A systematic review and meta-analysis of 77 case-reports and case-series.* BMC Nephrol, 2016. **17**(1): p. 104.
54. Badawy, S.M., et al., *Text Messaging and Mobile Phone Apps as Interventions to Improve Adherence in Adolescents With Chronic Health Conditions: A Systematic Review.* JMIR Mhealth Uhealth, 2017. **5**(5): p. e66.
55. Shokrollahi, K., et al., *Mobile phones for the assessment of burns: we have the technology.* Emerg Med J, 2007. **24**(11): p. 753-5.
56. Wallis, L.A., et al., *A Smartphone App and Cloud-Based Consultation System for Burn Injury Emergency Care.* PLoS One, 2016. **11**(2): p. e0147253.
57. Wurzer, P., et al., *Smartphone applications in burns.* Burns, 2015. **41**(5): p. 977-89.
58. BE, B. *Development and design of an mHealth resource to improve behavioral PRACTICE*

during child mental health treatment. in *MUSC Health Center for Telehealth Research Seminar Series*. 2017. Charleston, SC.
59. BE, B., *PRACTICE: A mobile application to increase homework use and engagement during child mental health treatment*, in *Medical University of South Carolina Department of Psychiatry and Behavioral Sciences Annual Update in Psychiatry*. Charleston, SC.
60. Harvey, J.B., et al., *Utilization of Outpatient Telehealth Services in Parity and Nonparity States 2010- 2015.* Telemed J E Health, 2019. **25**(2): p. 132-136.
61. McWilliams, T., et al., *Telehealth for paediatric burn patients in rural areas: a retrospective audit of activity and cost savings.* Burns, 2016. **42**(7): p. 1487-1493.
62. Wallace, D.L., et al., *Telemedicine for acute plastic surgical trauma and burns.* J Plast Reconstr Aesthet Surg, 2008. **61**(1): p. 31-6.
63. Wallace, D.L., R.W. Smith, and M.A. Pickford, *A cohort study of acute plastic surgery trauma and burn referrals using telemedicine.* J Telemed Telecare, 2007. **13**(6): p. 282-7.
64. Nguyen, L.T., et al., *Telemedicine follow-up of burns: lessons learned from the first thousand visits.* J Burn Care Rehabil, 2004. **25**(6): p. 485-90.
65. Saffle, J.R., et al., *Telemedicine evaluation of acute burns is accurate and cost-effective.* J Trauma, 2009. **67**(2): p. 358-65.
66. Shah, A., et al., *Epidemiology and profile of pediatric burns in a large referral center.* Clin Pediatr (Phila), 2011. **50**(5): p. 391-5.
67. Stoyanov, S.R., et al., *Mobile app rating scale: a new tool for assessing the quality of health mobile apps.* JMIR Mhealth Uhealth, 2015. **3**(1): p. e27.
68. Tickle-Degnen, L., *Nuts and bolts of conducting feasibility studies.* Am J Occup Ther, 2013. **67**(2): p. 171-6.
69. Thabane, L., et al., *A tutorial on pilot studies: the what, why and how.* BMC Med Res Methodol, 2010. **10**: p. 1.
70. Abbott, J.H., *The distinction between randomized clinical trials (RCTs) and preliminary feasibility and pilot studies: what they are and are not.* J Orthop Sports Phys Ther, 2014. **44**(8): p. 555-8.
71. Leon, A.C. and L.L. Davis, *Enhancing clinical trial design of interventions for posttraumatic stress disorder.* J Trauma Stress, 2009. **22**(6): p. 603-11.
72. Kraemer, H.C., et al., *Caution regarding the use of pilot studies to guide power calculations for study proposals.* Arch Gen Psychiatry, 2006. **63**(5): p. 484-9.
73. Eldridge, S.M., et al., *CONSORT 2010 statement: extension to randomised pilot and feasibility trials.* Pilot Feasibility Stud, 2016. **2**: p. 64.
74. Julious, S.A., *Designing clinical trials with uncertain estimates of variability.* Pharmaceutical Statistics, 2004. **3**(4): p. 261-268.
75. Keith, R.E., et al., *Using the Consolidated Framework for Implementation Research (CFIR) to produce actionable findings: a rapid-cycle evaluation approach to improving implementation.* Implement Sci, 2017. **12**(1): p. 15.
76. Yamamoto, L.G., et al., *Telemedicine using the internet.* Am J Emerg Med, 1996. **14**(4): p. 416-20.
77. Teddlie, C., Tashakkori A. , *Foundations of mixed methods research*. 2009, Los Angeles: Sage.
78. M, P., *Qualitative research & evaluation methods*. 2002, California: Sage publications.
79. Sandelowski, M., *Whatever happened to qualitative description?* Res Nurs Health, 2000. **23**(4): p. 334- 40.
80. Graneheim, U.H. and B. Lundman, *Qualitative content analysis in nursing research: concepts, procedures and measures to achieve trustworthiness.* Nurse Educ Today, 2004.

24(2): p. 105-12.
81. Hedeker, D. and R. Gibbons, *Longitudinal data analysis* 2006, New Jersey: John Wiley & Sons.
82. McCulloch, C. and A. Searle, *Generalized, Linear and Mixed Models*. 2001, New York: John Wiley & Sons.
83. Julious, S.A. and R.J. Owen, *Sample size calculations for clinical studies allowing for uncertainty about the variance.* Pharmaceutical Statistics, 2006. **5**(1): p. 29-37.
84. Moser, Albine, and Irene Korstjens. "Series: Practical guidance to qualitative research. Part 3: Sampling, data collection and analysis." *European Journal of General Practice* 24.1 (2018): 9-18.