INVESTIGATOR STUDY PLAN - TASCS

1. TITLE
Technology-Assisted Systems Change for Suicide Prevention (TASCS)
[NCT04720911]
March 31 2021

2. EXTERNAL IRB REVIEW HISTORY*
N/A

3. PRIOR APPROVALS:
Conflict of Interest (COI): The project has been discussed with representatives from this committee, who deemed a formal review unnecessary at this time: the app is as yet undeveloped and so is not likely to be ready for commercialization for a number of years, at which time UMass is likely to assert its rights to IP.

Electronic Health Record Integration: The focus of this study is to develop and user-test the TASCS app, and to test its potential eventual compatibility with a real EHR by testing its performance in the Epic Sandbox, an open-source test space provided by Epic (not by UMMHC). The current grant does not propose integration of TASCS into the test or production versions of the UMMHC EHR.

4. OBJECTIVES*
See grant: "SPECIFIC AIMS" (p.1) for details.

5. BACKGROUND*
See grant: "RESEARCH PLAN" (p.2-4) for details.

6. INCLUSION AND EXCLUSION CRITERIA*
Inclusion and Exclusion Criteria: See grant: "HUMAN PARTICIPANTS PROTECTION" (p.15) for details. No prisoners will be enrolled (including individuals with ankle monitors) without first obtaining IRB review and approval for this population and without first setting the required prisoner certification in place

For Aim 1, individuals will be eligible to provide input into the development of TASCS if they are aged ≥18 years, and have direct, family or clinical experience of suicidality. They will be excluded if they are medically/cognitively unable to participate or are a prisoner.

For Aims 2 and 3, participants will be invited to participate if they own a smartphone and if they meet the following eligibility criteria:

Eligibility criteria	
Inclusion Criteria	**Exclusion Criteria**
➢ Age ≥18 years ➢ Presenting to the UMMHC EDs ➢ Screened positive for suicidal ideation in the past 2 weeks or attempt in the past 6 months	➢ Medically/cognitively unable to participate in screening or assessment (e.g., sustained altered consciousness, psychosis, hostile behavior, intubation, severe pain) ➢ Currently in state custody ➢ Already enrolled during previous visit ➢ No access to reliable telephone for follow-up

7. STUDY-WIDE NUMBER OF SUBJECTS*
N/A

8. STUDY-WIDE RECRUITMENT METHODS*
N/A

9. STUDY TIMELINES*
The study is anticipated to start July 1, 2020. Aims 1 and 2 (development and user testing) of the project will be completed in the 1st year of the study period. Participation of those involved in Aim 1 and Cycle 1 of Aim 2 will be limited to a once-off encounter. Participants in Cycle 2 of Aim 2 will be asked to complete a one-week follow-up usability survey.

Aim 3 (pilot randomized controlled trial) will be completed in the second year of the project. Participation of those involved in Aim 3 will include a three-month follow-up period after the initial enrollment encounter. The estimated completion date for primary analyses is September 2022. See grant: "TIMELINE" (p.15) for details.

10. STUDY ENDPOINTS*
See grant: "RESEARCH PLAN" (p. 13) for details.

11. PROCEDURES INVOLVED*
For **Aim 1**, the design thinking workshops are described in the grant application under "RESEARCH PLAN" (p.9-10).

For **Aim 2**, participants will be recruited from UMMHC EDs. This will include patients (n~12) and their treating physicians or behavioral health clinicians (n~4). See grant: "RESEARCH PLAN" (p.10) for details on the procedure. We will collect the following:

- Patient case report form, for demographics, psychiatric and suicide history, familiarity with mobile phone/computing technology, self-efficacy/capability
- System Usability Scale (SUS)
- User Engagement Scale (UES)

The second half of these participants (Cycle 2) will also be invited to download the app to their smartphone and followed up to obtain these usability measures again one week after ED discharge ("Cycle 2", RESEARCH PLAN, p.10). Participation will not affect their care, see grant: "HUMAN PARTICIPANTS PROTECTIONS" (p.19-20).

Aim 3 is a pilot randomized controlled trial of 45 ED patients who screened positive during triage for recent active suicidal ideation or suicide attempt. They will be recruited from UMMHC EDs. They will be randomized to one of three TASCS App modalities in the ED (in-person clinician, telehealth clinician, self-directed). All three groups will receive three

counseling calls, access to the TASCS app, and one assessment call in the three months after discharge. See grant: "RESEARCH PLAN" (p.11-13) for details on the procedure. Participation will not affect their care see grant: "HUMAN PARTICIPANTS PROTECTIONS" (p.19-20). Measures to be included are:

Measures at baseline and follow-up **in feasibility trial (Aim 3)**

Construct	Measure
Initial implementation measures	
Usability	System Usability Scale
Acceptability	Qualitative feedback
	Technology Acceptance Model Scale
	User Engagement Scale
Patient-level outcomes	
Suicidal ideation and behavior	Columbia Suicide Severity Rating Scale ;suicide-related ED visits
Intervention targets	
Behavioral activation/effort	Drive subscale of the Behavioral Activation Scale; BH engagement
Perceived social support	Interpersonal Needs Questionnaire; lethal means restriction
Suicide-related impulse control	Mccullumsmith et al. (2014)
Implementation outcomes	
Engagement	Session length, number of features used, screens with most user interaction, completeness of templates
Costs	Clinician time spent and associated costs; billability of services
Reach and retention	Refusals within each arm, number of calls answered, number of app sessions, session frequency patterns, family member registration

Suicide-related visits will be ascertained through medical record review. A HIPAA waiver of authorization will be obtained from the IRB in order to access medical records for to determine eligibility of potential subjects for the subject interviews. Additionally, patients will sign a HIPAA authorization during the consent process.

The measures for Aim 2 are being uploaded with this submission. The remainder of the measures, data collection forms and surveys are still being developed and will be uploaded to the IRB for review and approval prior to implementation.

12. Data and Specimen Banking*

N/A

13. Data Analysis and Management*

See grant: "RESEARCH PLAN" (p.13) and "STATISTICAL DESIGN AND POWER" (p. 26-27) for details.

14. Provisions to Monitor the Data to Ensure the Safety of Subjects*

We will adhere to Investigator Guidance: Prompt Reporting Requirements (HRP-801). See grant: "HUMAN PARTICIPANTS PROTECTIONS" (p.14-23) and DATA SAFETY AND MONITORING PLAN (p.28-29) for details. The emergency number on the app will be for the National Suicide Prevention Lifeline (currently 1-800-273-8255, soon to be 988), a 24/7, toll-free hotline available to anyone in suicidal crisis or emotional distress. Calls to the national number are routed to local centers, which are supported with high-quality training and supervision.

15. Withdrawal of Subjects Without Their Consent*

Due to the sensitive nature of the topics being addressed (mental health, suicide), the investigator's discretion will be used in deciding continued participation in the study. See grant: "HUMAN PARTICIPANTS PROTECTION" (p.22) for further "Withdrawal" details.

16. RISKS TO SUBJECTS*
See grant: "HUMAN PARTICIPANTS PROTECTION" (p.16-21) for details.

17. POTENTIAL DIRECT BENEFITS TO SUBJECTS*
See grant: "HUMAN PARTICIPANTS PROTECTION" (p.23) for details.

18. VULNERABLE POPULATIONS*
Pregnant women: Because pregnant women can have suicide risk, it is scientifically justifiable to include them. For this reason, these patients will be included. No inducements, monetary or otherwise, will be offered to terminate a pregnancy. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy. Individuals engaged in the research will have no part in determining the viability of a neonate

Employees: We will be asking UMMHC clinicians for input on the TASCS apps during their development. Because the study team is comprised of research faculty and the participating clinicians will ED physicians, none of the study team teaches or supervises them or has the ability to influence their grades, academic success, or professional advancement.

Adults unable to consent: A consent mini-quiz will be administered to ensure that all potential subjects possess an understanding of the risks and benefits of study participation. The patient will take a quiz testing their understanding. If a patient obtains a score of less than 80% on the quiz, the research staff will repeat the explanation a second time in even more detail and the patient will re-take the quiz. If the patient obtains a score of less than 80% on the quiz upon re-administration, they will not be invited to participate.

19. MULTI-SITE RESEARCH*
N/A

20. COMMUNITY-BASED PARTICIPATORY RESEARCH*
N/A

21. SHARING OF RESEARCH RESULTS WITH SUBJECTS*
It will be several years before the results of the research are available. If the subjects would like us to try to reach them at that time, we will request that they let us know during the consent process.

22. SETTING
We will recruit participants from all UMMHC EDs (University, Memorial, Marlborough, Clinton and Health Alliance campuses).

23. RESOURCES AVAILABLE

Investigators and key personnel will have undergone mandatory education in human research participants' protection. Educational systems are in place to ensure that all research staff have been through such training and are approved by the IRB Human Subjects department. The responsibilities of investigators and research personnel are as follows:

Contact Principal Investigator. The Contact Principal Investigator will be responsible for overall project governance at UMass, leadership of the Project Team at UMass, protocol development, informing the data analytic plan, and dissemination efforts through professional presentations and peer reviewed journal publications. They will be responsible for overseeing and monitoring patient safety and reporting adverse events, as per IRB protocols.

Multi Principal Investigator and Co-investigators. The Multi Principal Investigator and Co-investigators will provide guidance and expertise on the iterative development of the TASCS, as well as advising on trial methodology as needed.

Project Manager. The Project Manager will be responsible for managing daily operations of recruitment and enrollment including training and supervising the research assistants. They will manage all IRB-related submissions, amendments, and reporting.

Research Clinician(s). Will serve as the study clinician and will perform the TASCS intervention, including the in-ED components and post-ED counseling calls. They will field referrals from the research assistant conducting follow-up assessment calls, if a participant is found to have emerging suicide risk during that assessment call (see HUMAN PARTICIPANTS PROTECTION" (p.17-19).

Research Assistant(s). The research assistant(s) will be responsible for approaching and enrolling participants including carrying out the informed consent process, collecting baseline data, collecting healthcare utilization data, and conducting follow-up assessment calls.

PhD student: The PhD student will be present for usability-focused data collection in Aims 1 and 2 and will assist with transcription and qualitative analyses of anonymized data. She will not be involved in the informed consent process, will not be enrolling patients, and will not conduct trial-related patient data collection like chart reviews or follow-up phone-calls.

Software Engineer. The software engineer(s) will be responsible for programming the TASCS mobile application and ensuring all data is flowing correctly between the mobile application and the secure server. They will have access to data that is entered into the app (such as safety plans and life plans) within the UMass secure environment. Although they may be contractors from WPI or Programination, they will operate within the UMass secure environment and will therefore adhere to the standard protocols and restrictions applied to all individuals working within the that environment. We will assess whether a reliance agreement is necessary for non-UMMS personnel and that any necessary IRB approvals will be in place for them before they interact with subjects or access private identifiable

information about them. PHI will be directly entered by real users into the mobile application during the pilot trial in Aim 3, but not in the user testing phases (Aims 1 and 2). The TASCS mobile application will not store PII/PHI locally on the device.

UMMHC Patient and Family Advisory Council (PFAC). The UMMHC Patient and Family Advisory Council is comprised of several advisory boards that provide input to clinicians and researchers to ensure that programs and interventions are designed to best fit the needs and preferences of patient stakeholders. The facilitators will support us in engaging those with lived experience to advise on the development of TASCS in the Aim 1 design thinking workshops and verification interviews.

24. LOCAL RECRUITMENT METHODS

For **Aim 1**, participants will be invited to participate through the PFAC. We will visit the PFAC to outline the purpose of the study, describe what participation in the design thinking workshop or verification interview would entail, and provide an email address for members to reach out if they have a direct or family lived experience of suicidality and are interested in participating. They will receive a $30 gift-card upon participating.

For **Aims 2 and 3**, Research Assistants (RAs) will review the electronic health record dashboard for patients with positive suicide risk (answered "yes" to suicidal ideation in the past two weeks or a suicide attempt in the past 6 months on the Patient Safety Screener, which is routinely asked by nurses of all patients presenting to acute care). They will document all such patients who present during their shift on a Screening Log, recording demographic details but not patient names. They will use medical records and consultation with clinical staff to determine if an individual is appropriate to approach. All consecutive patients who screen positive for suicide risk will be considered for enrollment. The RA will approach each potentially patient after the patient has been medically assessed and stabilized by medical staff. The RA will explain the nature, purpose, risks, and benefits of the study. If eligible and the patient is interested in participating, the consent mini-quiz will be conducted and written informed consent will be obtained (See CONSENT PROCESS, section #30 below). All patient participants will receive an initial $30 remuneration upon enrollment during their ED visit. Upon participating in the follow-up assessment call, the patient will receive an additional $30 gift-card. There is no compensation for participating in the counseling calls with the study clinician.

Compensation will be carried out through the Bank of America (BoA) reloadable gift card system, which is HIPAA compliant and in line with the University system for dispatching compensation to study participants. The participant's contact details (name, address, phone number, and possibly social security number) must be shared by the research team with BoA in order for BoA to disburse the card. The BoA card will be delivered to the participant within 10 days of enrollment and will be reloaded upon the completion of their follow up calls. Cash can then be withdrawn from these cards, without a fee at BoA ATMs or $1.50 at non-BoA ATMs. For any participants without a stable address, "anonymous" BoA cards will be given during the initial and follow-up encounters (these cards are not reloadable and have a 3-year expiration date). Participants will be made aware of the process when they enroll in the study. The research team will destroy the personal information that is needed for the BoA gift card no later than six years after study closure.

25. LOCAL NUMBER OF SUBJECTS

In Aim 1 (design thinking workshop and verification interviews), an estimated 16 participants will be enrolled. In Aim 2 (usability assessment), an estimated 12 patients (and four clinicians) will be enrolled. In Aim 3, 45 participants will be enrolled, leading to a total of 73 participants.

26. CONFIDENTIALITY

Potential risks due to loss of confidentiality will be minimized by having all information collected and handled by research staff trained to deal appropriately with sensitive clinical issues. All research personnel will receive training in research ethics. All information will be treated as confidential material and will be available only to research and clinical staff. Audio recordings of all interviews will be obtained, unless the participant declines. The sound files will be recorded on digital voice recorders then downloaded to a password-protected folder on a secure drive hosted by UMass. After downloading to the secure drive, the recordings will be erased from the voice recorders. This will be described in the consent form, and patients can opt out of the recordings. All surveys will be digital and entered directly into REDCap. Any paper-based materials, like consent forms, will be kept in locked filing cabinets in a locked office. Data entered into the TASCS application will live within the UMass secure environment and will be de-identified before being exported outside that environment for analysis. All datasets will be handled in a HIPAA compliant manner, will be password-protected, and the analytic dataset will be de-identified. For additional information on processes to mitigate loss of confidentiality, please see grant "HUMAN PARTICIPANTS PROTECTION" (p.16-23).

As of October 1, 2017, all NIH funded research collecting or using identifiable, sensitive information will automatically be issued a certificate of confidentiality (aka applications are no longer needed). The NIH is no longer using physical certificates, but rather the Notice of Award and Grants Policy Statement will suffice as documentation of CoC protection. See link below for the full policy details. https://grants.nih.gov/grants/guide/notice-files/NOT-OD-17-109.html

27. PROVISIONS TO PROTECT THE PRIVACY INTERESTS OF SUBJECTS

The following security protocols will be applied to all data: physical protections - all databases and systems will be hosted behind the firewall by UMass Medical School and employ user authentication and role-based security for access. Standard security access procedures designed by UMass Medical School will be used to ensure that only authorized research staff has access to the study data. All paper-based materials, like consent forms, will be kept in locked files; logical protections. All datasets will be handled in a HIPAA compliant manner, will be password protected, and the analytic dataset will be de-identified.

A HIPAA waiver of authorization will be obtained from the IRB in order to access medical records for to determine eligibility of potential subjects for the subject interviews. Additionally, patients will sign a HIPAA authorization during the consent process. If the patient is excluded or refuses, this information, along with the reason for exclusion, will be documented on the Screening Log to allow comparisons of those enrolled vs. not enrolled, which will allow the team to assess representativeness of the sample. See Screening Log SOP (attached) for further details.

28. COMPENSATION FOR RESEARCH-RELATED INJURY

This research involves no more than minimal risk or harm to subjects. However, the subjects will be informed during the consent process of the following: "The University of

Massachusetts Medical School does not provide funds for the treatment of research-related injury. If you are injured as a result of your participation in this study, treatment will be provided. You or your insurance carrier will be expected to pay the costs of this treatment. No additional financial compensation for injury or lost wages is available."

29. ECONOMIC BURDEN TO SUBJECTS

There will be no costs for which subjects may be responsible for due of participation in the research.

30. CONSENT PROCESS

For Aim 1, we propose a waiver of written documentation of consent for advisors participating in the design workshops and verification interviews. The research involves no more than minimal risk of harm to subjects and involves no procedures for which written documentation of consent is normally required outside of research context. Study procedures will be described verbally. An information sheet will be provided to the clinicians informing them about the study and that their participation is voluntary. The participants will be asked for permission to record the meetings for the purposes of notetaking. The recordings will be stored on a secure UMMS server and destroyed at the end of the study period, as described in Section 26. Confidentiality. In the event it becomes appropriate to provide participants with additional pertinent information after participation, we will seek the guidance of the IRB.

Patients:

For Aims 2 and 3, the RA will approach each patient after the patient has been medically assessed and stabilized by medical staff. They will explain the nature, purpose, risks, and benefits of the study. A five-item, multiple-choice consent mini-quiz will be administered to ensure that all potential subjects possess an understanding of the risks and benefits of study participation. Content will differ for patients depending on what participation entails, for Cycles 1 and 2 of Aim 2 and for Aim 3. If a patient obtains a score of less than 80% on the quiz, the research staff will repeat the explanation a second time in even more detail and the patient will re-take the quiz. If the patient obtains a score of less than 80% on the quiz upon re-administration, they will not be invited to participate. If the patient agrees to participate, electronic written informed consent will be obtained.

Clinicians: Waiver of written documentation of consent will be obtained for the clinicians in Aim 2. Being limited to user feedback, the research involves no more than minimal risk of harm to subjects and involves no procedures for which written documentation of consent is normally required outside of research context. Study procedures will be described verbally. An information sheet will be provided informing clinicians about the study and that their participation is voluntary. In the event it becomes appropriate to provide participants with additional pertinent information after participation, we will seek the guidance of the IRB.

31. PROCESS TO DOCUMENT CONSENT IN WRITING

Patients: The consent process will be conducted in-person; the research staff will review the consent form with the participant in REDCap. The participant and the research staff will both electronically sign through REDCap's "Wet Signature" feature, as required by UMMS. The participant will then choose whether they would like to receive an emailed PDF copy of the

consent or a paper copy of the consent. . Documentation of consent will be done in accordance with *HRP-803 INVESTIGATOR GUIDANCE: Documentation of Informed Consent*.

Waiver of written documentation of consent will be obtained for Aim 1 advisors and Aim 2 clinicians. The research involves no more than minimal risk of harm to subjects and involves no procedures for which written documentation of consent is normally required outside of research context.

32. DRUGS OR DEVICES

Based on the FDA's Policy for Device Software Functions and Mobile Medical Applications (2019), TASCS is unlikely to be subject to regulatory requirements because (1) it resembles examples given under Appendix B for which the FDA intends to exercise enforcement discretion because they pose lower risk to the public and (2) will neither transform a mobile platform into a regulated medical device nor connect to an existing device type for purposes of controlling its operation, function, or energy source (Appendix C). Towards the end of the study period, we will revisit this issue based on the eventual functionality of the TASCS and initiate the 513(g) process as appropriate.

Statistical Analysis Plan

STATISTICAL DESIGN AND POWER

In this two-year R34, data will be used primarily to iteratively improve the TASCS and assess feasibility and acceptability of pilot implementation in the emergency department. In Aim 1, we will build the TASCS using input and feedback from empaneled stakeholders. In Aim 2, we will obtain introduce the TASCS to emergency department patients with suicide risk to examine usability and acceptability in vivo. Finally, in Aim 3, we will conduct a pilot feasibility trial with three arms:

(1) In-person clinician-administered TASCS ED App in the ED followed by telephone coaching calls, facilitated by the Post-ED Clinician App, and access to the Post-ED Patient and Family App
(2) Telehealth-based TASCS in the ED followed by telephone coaching calls, facilitated by the Post-ED Clinician App, and access to the Post-ED Patient and Family App
(3) Self-administered TASCS in the ED followed by telephone coaching calls, facilitated by the Post-ED Clinician App, and access to the Post-ED Patient and Family App

Data analyses will proceed with an intent-to-treat approach. Statistical significance will be at $p < .05$ and analyses will occur via IBM® SPSS® Statistics V21 and SAS 9.4 statistical software package (SAS Institute Inc, Cary, NC).

A. Aim 2: Usability Testing. Analyses will center around assessing usability, acceptability, and needs for program updates based on users' experiences. We will apply descriptive statistics to assess participants' comments and questions related to specific program/equipment features and global assessments. Usability outcomes will be: 1) ability to use the program and equipment without staff assistance after training (yes/no), 2) time (in minutes) to complete the TASCS process once trained, and 3) total number of deviations from the direct path of completing TASCS procedures after training. The stopping point for testing will be having three patients rate the platform as having a SUS score of ≥ 80. We will track and store usage statistics, including time on each page and time in app. Google Analytics will constitute a secondary source of statistics.

B. Aim 3: Feasibility Trial. It is important to note that, being an initial feasibility trial, the study is not powered to find a difference between arms and we are not seeking to compare TASCS to treatment-as-usual to examine effectiveness. Rather we are seeking to describe the usability and acceptability of different modes of delivering TASCS in the ED, of the Post-ED Clinician App, and the Post-ED Patient and Family App, to examine potential intervention targets, and to examine the utility of our chosen measures at baseline and follow-up.

Initial analyses will compare the three treatment groups on baseline demographic and clinical variables using a chi-square test (for categorical variables) and analysis of variance (for continuous variables). Variables that significantly differ between groups or are theoretically important will be used as covariates in multivariate analysis, when appropriate. We will proceed with intent-to-treat analyses. Baseline and three-month usability and acceptability analyses will compare the three treatment groups using analysis of variance. The behavioral outcome in the feasibility trial will be occurrence of any suicidal behavior (attempt, preparatory, aborted or interrupted attempt, death by suicide) and categorical level of ideation during three-month follow-up. Analyses will compare the three arms via chi-square for suicidal behavior and Kruskal-Wallis test for ordinal level of suicidal ideation. Changes in suicidal behavior and suicidal ideation over time will be examined using McNemar (overall) and Friedman tests (by

arm) respectively. To elucidate the impact of intervention components on intervention targets, we will use t tests to compare our three main intervention targets at follow-up (social support, behavioral activation, and impulse control) between those who did and did not receive the intervention component specific to that target, and will use t tests to examine the association between intervention targets and patient outcome (occurrence of any suicidal behavior and presence of active suicidal ideation at follow-up). For all analyses, effect sizes will be estimated, with parametric and non-parametric statistics as appropriate.

Sample size justification. For our development and usability testing, we will engage 12 individuals with lived experience for persona testing in Aim 1 and 12 ED patients for in vivo usability testing in Aim 2. This number was chosen because a sample of 10 users can identify 95% of usability problems[1] including in persons with serious mental illness.[2] The sample size for the feasibility trial (n=45) is based on the same principle, allocating 15 patients in each of the three arms and allowing for moderate attrition over the three-month follow-up period. Because of the funding mechanism and our focus on platform development, the feasibility trial is **not** powered to test hypotheses but rather to inform the feasibility of the intervention and data collection measure for a future large-scale implementation trial. With significance set at 0.05 and assuming a power of 0.80, a sample size of 45 participants across three arms will allow us to detect a large effect size of f=0.48 in usability and acceptability scores and w= 0.46 in dichotomous suicidal behavior outcome.

REFERENCES

1. Faulkner L. Beyond the five-user assumption: Benefits of increased sample sizes in usability testing. *Behav Res Methods, Instruments, Comput*. 2003;35(3):379-383. doi:10.3758/BF03195514.
2. Ben-Zeev D, Kaiser SM, Brenner CJ, Begale M, Duffecy J, Mohr DC. Development and usability testing of FOCUS: a smartphone system for self-management of schizophrenia. *Psychiatr Rehabil J Rehabil*. 2013;36(4):289-296. doi:10.1037/prj0000019.