College Student Stress: Transitions Over Time

NCT06583096

May 19, 2025

College Student Stress: Transitions Over Time

Protocol Number: 1.0

National Clinical Trial (NCT) Identified Number: NCT06583096

Principal Investigator: Dr. Adam G. Horwitz

Sponsor: University of Michigan, Michigan Medicine

Grant Title: Low Burden Adaptive Mobile Interventions for Mood and Suicide Risk

Grant Number: K23 MH131761

Funded by: NIMH

Version Number: v.1.1

1 May 2025

CONFIDENTIALITY STATEMENT

This document is confidential communication. Acceptance of this document constitutes agreement by the recipient that no unpublished information contained herein will be published or disclosed without prior approval of the Principal Investigator or other participating study leadership and as consistent with the NIH terms of award.

Table of Contents

STATEMENT OF COMPLIANCE

The trial will be carried out in accordance with International Council on Harmonisation Good Clinical Practice (ICH GCP) and the following:

- United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, 21 CFR Part 312, and/or 21 CFR Part 812).

National Institutes of Health (NIH)-funded investigators and clinical trial site staff who are responsible for the conduct, management, or oversight of NIH-funded clinical trials have completed Human Subjects Protection and ICH GCP Training.

The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the IRB for review and approval. Approval of both the protocol and the consent form(s) must be obtained before any participant is consented. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. All changes to the consent form(s) will be IRB approved; a determination will be made regarding whether a new consent needs to be obtained from participants who provided consent, using a previously approved consent form.

INVESTIGATOR'S SIGNATURE

The signature below constitutes the approval of this protocol and provides the necessary assurances that this study will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to local legal and regulatory requirements and applicable US federal regulations and ICH guidelines, as described in the *Statement of Compliance* above.

Principal Investigator or Clinical Site Investigator:

Signed: _____ Date: _____

Name: Adam G. Horwitz

Title: Assistant Professor of Psychiatry, Medical School

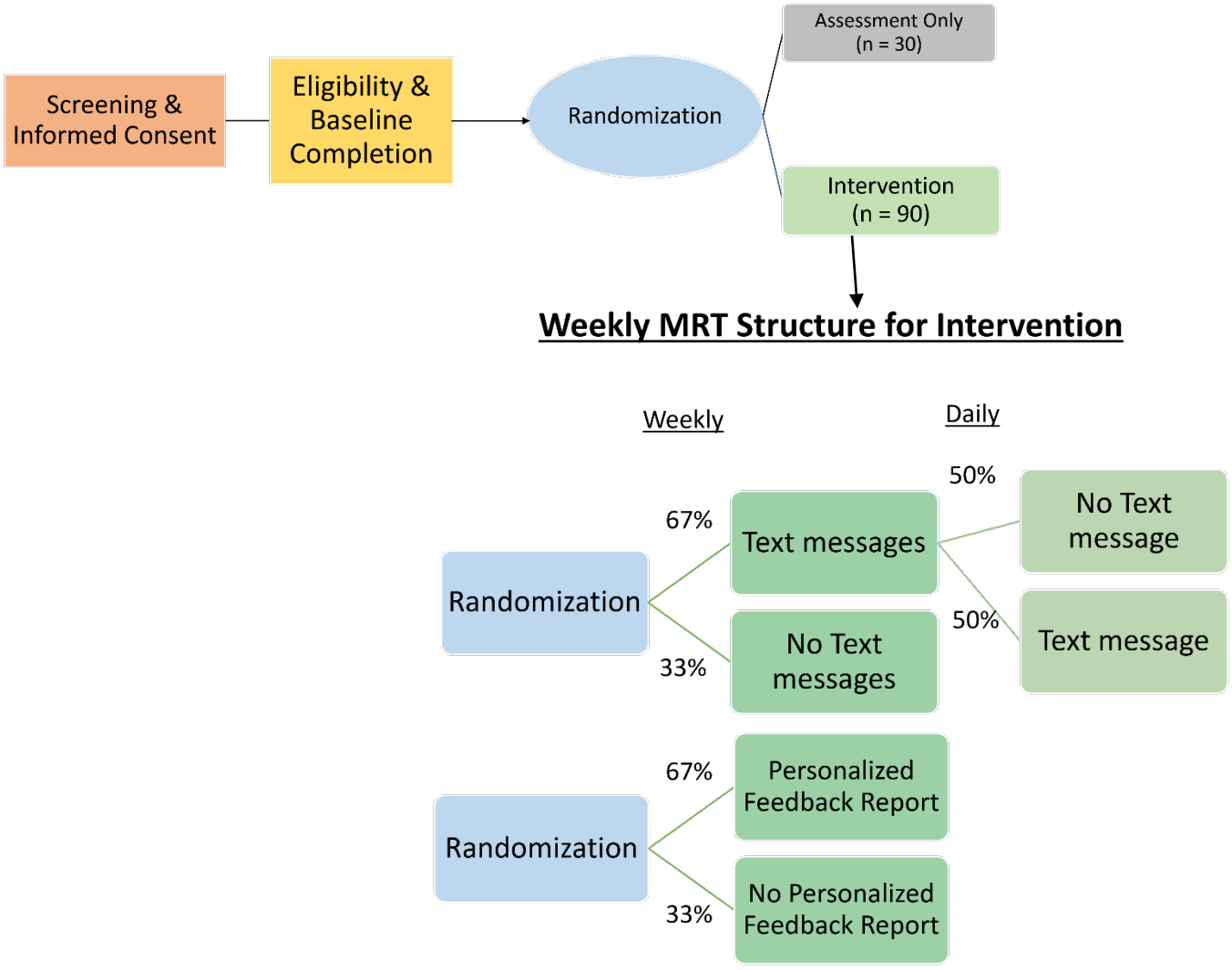
Affiliation: University of Michigan, Michigan Medicine Psychiatry Department
Address: 4250 Plymouth Rd, Ann Arbor, MI 48109
Telephone: 734-764-0231
Email: ahor@med.umich.edu

1 PROTOCOL SUMMARY.

1.1 SYNOPSIS

Title:	College Student Stress: Transitions Over Time
Grant Number:	K23 MH131761
Study Description:	This project will develop a mobile health personalized feedback (PF) intervention for college students at-risk for depressive episodes. Participants will complete daily and weekly assessments, be randomized to receive weekly PF reports regarding mood and stress and be randomized to receive text-messages containing tips/strategies related to self-care, time management, and interpersonal connection/support. We will utilize follow-up surveys and objective indicators of engagement/participation to assess feasibility and acceptability of the intervention. Proposed mechanisms of change (e.g., coping efficacy, perceived stress, readiness for help-seeking) will be assessed by exploring associations of intervention components (i.e., text messages, PF reports) with relevant outcomes.
Objectives:	Demonstrate feasibility, acceptability, and initial impact of mobile health PF intervention on proposed mechanisms of change via a feasibility micro-randomized trial (MRT).
Endpoints:	Participation is complete following the completion of the 6-week follow-up survey.
Study Population:	Participants will be first-year college students, ages 17 or older, recruited from the University of Michigan, Ann Arbor and Flint campuses presenting with mild-to-moderate depressive symptoms who are not receiving professional mental health services.
Phase:	Phase I-II
Description of Sites/Facilities Enrolling Participants:	Participants will be recruited from the University of Michigan, Ann Arbor and Flint campuses via email sent by the university's Registrar.
Description of Study Intervention/Experimental Manipulation:	Participants will be randomized (3:1 intervention-to-control) to receive either 1) weekly surveys only (Assessment-only Condition), or 2) daily and weekly surveys, Personalized feedback reports of symptoms and stress (2:1 randomization to receive/not-receive PF report in a given week), and supportive text messages (2:1 randomization to receive/not-receive messages in a given week; 1:1 daily-level randomization to receive a message during weeks in which randomized to receive messages).
Study Duration:	6 months
Participant Duration:	6 weeks

1.2 SCHEMA



1.3 SCHEDULE OF ACTIVITIES

	Screening	Baseline Survey	Weekly (Every Sunday for 5 weeks)	Daily (42 days; Intervention-only)	6-week follow-up (6th Sunday)
Informed Consent	X				
Demographics	X				
Primary Randomization (Survey Only)		X			
Secondary Randomization (MRT)		X			
Outcome Evaluations					
Flourishing Scale	X		X	*	X
Depression (PHQ-9) and Anxiety (GAD-7)	X		X		X
Coping Self-Efficacy	X		*		X
UCLA-Loneliness Scale	X		X		X
Mental Health Service Utilization	X				X
Pittsburgh Sleep Quality Index-Adapted		X	*		X
Physical Activity (YRBS Adaptation)		X	*		X
Interpersonal Needs Questionnaire (INQ)		X			X
DERS-Emotional Awareness		X	X	*	X
Brief COPE		X			X
National Comorbidity Survey (Suicidal Ideation and Behavior)		X	*		*
Perceived Stress Scale		X	*	*	X
Life Events Checklist (LEC-5)		X			
Readiness for Help-Seeking		X	*		X
Daily Mood				*	
Feasibility/Acceptability Survey					X
Adverse Events Reporting		X			X
Note: X = Full-scale; * = Abbreviated version					

2 INTRODUCTION

2.1 STUDY RATIONALE

Depression is the #1 cause of disease-related disability worldwide and prevalence rates for depression and suicide have increased significantly in the United States over the past 25 years. Young adults, including college students, have especially high rates of depression, yet most individuals with clinically significant symptoms do not seek formal treatment. College students at elevated risk for suicide may decline formal treatment due to barriers such as lack of time, low perceived need for treatment, or limited access to services. Mobile health technologies offer promising new opportunities to overcome these barriers and improve outcomes. Further, the use of mobile technologies allows for the gathering of real-time subjective data, and an ability to respond to mood changes directly with an intervention at the time it is needed. Yet, engagement with mobile health interventions tends to wane quickly, and it is unclear how these interventions can best be implemented in ways that promote sustained health benefits. The present study seeks to develop a low-burden mobile intervention that can help first-year college students more readily identify negative trajectories in their mental health and take steps to facilitate effective coping and/or seek formal help. This two-arm pilot study, with an embedded micro-randomized trial (MRT), will allow us to 1) evaluate the feasibility and acceptability of the study intervention components, 2) examine the initial impact of the study intervention components on the proposed mechanisms of change, and 3) through a series of micro-randomizations, inform an adaptive intervention design that provides personalized feedback or text messages only when it is expected to have a positive impact.

2.2 BACKGROUND

Depression and suicidal ideation among college students have increased significantly over the past decade (Lipson et al., 2019). Evidence-based treatments, including psychotherapy and medication, have demonstrated effectiveness (Allen et al., 2007; Lee et al., 2019), yet college counseling centers have struggled with long waitlists and insufficient staffing, resulting in many students not receiving needed care (e.g., Auerbach et al., 2016; Xiao et al., 2017). In addition to access barriers, many at-risk students report a lack of time and a perception that their symptoms are not serious enough to require treatment (e.g., Epstein et al., 2010). Early intervention can mitigate the risk for future depressive episodes, yet in many cases, individuals are unaware or unable to name their experiences as symptoms of depression until symptoms are severe and causing significant impairment (e.g., Czyz et al., 2013). There is a significant need for effective, accessible interventions that can promote early recognition of symptoms and overcome common barriers to treatment for college students.

With the ubiquity of smartphones in the US across socioeconomic statuses (Pew Research Center, 2021) and mental health patients (Campbell et al., 2015), mobile interventions offer an accessible modality to deliver care. Advances in mobile technologies have significant potential for reducing barriers to treatment for college students. To date, mobile interventions have not taken full advantage of the unique technological opportunities provided by smartphones to enhance engagement. Namely, mobile technology allows for the collection of ‘real time’ data, which can be used to provide feedback and confront an individual’s lack of awareness or perceived need for intervention (Lattie et al., 2019). Utilizing these data can dramatically transform the delivery of mobile interventions through preventive, adaptive approaches, whereby content is optimized and delivered in response to specific emotional or behavioral changes.

Given the stressors associated with beginning college (Byrd & McKinney, 2012), high prevalence and first onsets of depression, and multiple barriers to mental health care, first-year college students are an ideal, at-risk population to target with a low-burden mobile intervention optimized to prevent the negative progression of depressive symptoms. This study will evaluate feasibility, acceptability, and initial effectiveness of the intervention and explore impact on mechanisms of action.

2.3 RISK/BENEFIT ASSESSMENT

2.3.1 KNOWN POTENTIAL RISKS

The proposed study poses minimal risks. There is a small risk for violation of confidentiality and this risk exists because human participants are providing personal information. Furthermore, as a longitudinal study, we must maintain a link between each student's contact information and their study IDs while the study is active, which is necessary for connecting data at the various follow-up timepoints and providing proper compensation for completed surveys. It also enables us to take appropriate action if a student provides information to suggest imminent risk of suicidal or other dangerous behavior. This risk is related to the damage that could be caused by an inadvertent release of sensitive information (e.g., psychiatric symptoms). Participants will be informed of these risks, the procedures taken to protect their confidentiality, and mandatory reporting requirements in the consent documents. The Risk Management Protocol will be utilized if confidentiality needs to be breached due to a safety concern. Participants could potentially experience emotional discomfort as a result of being asked personal questions about their mental and behavioral health and attitudes related to treatment-seeking. Because the screening portion of the study takes place via Qualtrics surveys, participants will receive crisis and referral information, including local and national resources (e.g., suicide hotlines, crisis text-lines, mental health and substance use treatment, etc.). All participants will also be notified that they are free to terminate the study at any time and may skip any questions that make them uncomfortable.

2.3.2 KNOWN POTENTIAL BENEFITS

Participation in the proposed study may benefit participants in a few ways. Participants completing the screen will receive a list of available resources for crisis management and mental/behavioral health and may choose to seek services with this information. Participants enrolled in the trial will be assessed weekly, and this process may provide an opportunity for reflection on their functioning. Furthermore, those randomized to the intervention condition may also benefit from receiving personalized feedback reports about their symptoms over time and receiving supportive text messages that contain helpful tips and strategies for managing stress. Regarding benefits to others, this research will inform the design of an eventual randomized control trial (RCT) for an adaptive mobile intervention seeking to prevent the negative progression of depressive symptoms, which, if deemed efficacious, has significant public health significance. In sum, the potential benefits for the research outweigh the risks for the participants.

2.3.3 ASSESSMENT OF POTENTIAL RISKS AND BENEFITS

Confidentiality

The study team has considerable experience in maintaining the confidentiality of participant data and has established procedures to ensure data confidentiality. Several steps will be taken to minimize the risk of breaches of confidentiality. Only the designated research staff will have access to research data. Training of staff will include information about the importance of confidentiality and techniques to

maintain confidentiality of all information reported by research participants. Staff will maintain human subjects and confidentiality certifications through the UM Program for Education and Evaluation in Responsible Research and Scholarship (PEERRS) system and will complete CITI Good Clinical Practice (GCP) Training. Consent documents will fully explain the study procedures, potential risks, and potential benefits. In addition, every effort will be made to ensure that study data are always confidential in terms of data storage, so that data cannot be linked to a particular person. Unique identification numbers will be assigned to all participants. Participants' names and study IDs will be kept in a separate file from study data. All linking files will be maintained in a secure password-protected file on a secure server. Electronic data files (e.g. surveys) will be saved with passwords on a secure network and will not contain any identifying information. The "Subject Directory" sheets linking participant IDs to their names will be kept in a password-protected folder on a secure password-protected network. Prior to data entry, all identifying information will be removed, and only the subject IDs will be entered with the study data.

Steps will also be taken to minimize breaches of confidentiality associated with the data collection tools. All study surveys will be developed in Qualtrics (University of Michigan Health System [UMHS]-approved Qualtrics version), with the initial screen/baseline link sent via e-mail and subsequent surveys delivered via text message. Personalized links will be developed for individual participants and processed through a secure study platform that complies with the Health Insurance Portability and Accountability Act (HIPAA) privacy regulations. Similarly, the secure study platform will also be used to deliver the text message intervention component; the platform will be hosted on a server whose data is always encrypted and which is secured in accordance with industry-standard data security practices. Moreover, participants will be informed of the risk that anyone who accesses their phone could see the supportive text messages.

As noted below (managing safety concerns), participants' confidentiality will be breached by the research study only to protect the safety and welfare of research participants and only in accordance with state and federal law. These confidentiality exceptions will be explained in detail as part of the study consent process.

Managing Distress and Safety Concerns

Our team has extensive experience conducting longitudinal research studies with individuals at risk for depression and suicide. Dr. Horwitz will closely supervise research staff to ensure potential safety issues are appropriately addressed in accordance with the protocol. All participants are free to terminate the study at any time or refuse to respond to any questionnaire item. Any suicidal ideation endorsement on the baseline, weekly, or follow-up survey will result in an automated notification informing participants about crisis resources (phone numbers and text line) and recommending use of these resources if they feel unable to resist acting on their suicidal thoughts. Participants will be informed that their survey responses are not monitored by research staff.

Finally, in the event that a participant sends a text message to the phone number used to send daily surveys or supportive text messages, the participants will receive an automated response with information that the phone number does not receive text messages or phone calls and with information about how to contact the study with questions during business hours as well as information for accessing emergency services/immediate support (e.g., crisis line, local emergency department).

3 OBJECTIVES AND ENDPOINTS

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS	PUTATIVE MECHANISMS OF ACTION
Primary			
Feasibility and acceptability of mobile health PF intervention	Completion of the 6-week follow-up survey	This assessment will take place at the completion of the texting program and allow for immediate feedback about their experiences.	N/A
Secondary			
Initial impact of mobile health PF intervention on proposed mechanisms of change	Completion of the 6-week follow-up survey	We will assess whether individuals receiving text-messages or PF reports in a given week demonstrated greater improvements in depressive and anxiety symptoms, perceived stress, flourishing, coping self-efficacy, and readiness to seek help relative to weeks in which they did not receive these interventions.	N/A

4 STUDY DESIGN

4.1 OVERALL DESIGN

This project is a two-armed randomized control trial (RCT) with an embedded MRT aimed to help develop a mobile health intervention for college students at-risk for depressive episodes. Participants will complete daily and weekly assessments, be randomized to receive weekly PF reports regarding mood and stress and be randomized to receive text-messages containing tips/strategies related to self-care, time management, and interpersonal connection/support. We will utilize follow-up surveys and objective indicators of engagement/participation to assess feasibility and acceptability of the intervention. Proposed mechanisms of change (e.g., coping efficacy, perceived stress, readiness for help-seeking) will be assessed by exploring associations of intervention components (i.e., text messages, PF reports) with relevant outcomes. This study has the following aims: 1) demonstrate feasibility and acceptability in intervention components, and 2) examine the initial impact of the mobile health intervention on proposed mechanisms of change. The total time for study completion for an individual participant is 6 weeks, with completion marked as completing the 6-week follow-up survey. The entirety of the study will run for 6 months.

We will send out a brief mental health screening survey to 2,500 first-year college students, and anticipate that 425 will consent to participate and complete the screen, and 142 will meet study inclusion criteria for mild-to-moderate depressive symptoms and no current mental health treatment. From this group, we anticipate 120 will provide their cellphone number, complete the baseline survey (~15 additional minutes to 8-minute screening survey), and be randomized into the six-week intervention trial (90 into the 'Pilot MRT' intervention condition, and 30 into the 'Assessment Only'

condition). Participants in the Pilot MRT will complete daily 1-minute (5-item) assessments of their mood, social relationships, emotional awareness, interest in activities, and efficacy to cope with stress. All participants will receive a brief, weekly 10-minute 'Sunday survey' assessing various aspects of their health and well-being. Pilot MRT participants will be randomized each week at a 2:1 ratio to receive (or not receive) a Monday personalized feedback report that provides a graphical depiction summary of their scores up until that point in time on depression, anxiety, perceived stress, and flourishing scales, with a written description of the corresponding severity levels and links to available mental health resources. Pilot MRT participants will also be randomized each week, at a 2:1 ratio, to receive or not receive supportive text messages offering strategies and tips for health promotion and stress management during the week, which includes a daily-level 50:50 randomization (during weeks when randomized to receive texts). At the end of six weeks, all participants will complete a 25-minute follow-up assessment, with additional items for those in the Pilot MRT condition assessing feasibility/acceptability of the PF reports and text-message intervention components.

With respect to randomization procedures, we will pre-randomize specific ID numbers and assign numbers sequentially based on completion of the baseline survey, blocking every 20 participants (15 Pilot MRT, 5 Assessment Only) to ensure balance. Those in the Pilot MRT condition will have further randomizations at the weekly level for six weeks, with each week randomized 2:1 to receive a Monday PF report, and each week randomized 2:1 to receive supportive text messages. As an MRT, we will not block for number of weeks receiving each intervention component, and participants may receive different 'doses' of the intervention components over the course of six weeks. Those randomized to receive supportive messages in a given week, as part of the Pilot MRT condition, will have a daily-level 50:50 randomization to receive or not receive a message. If randomized to receive a message on a given day, the message will be randomly pulled from a pool of 25 messages, with each message assigned a numerical value, and this message will be removed from the available pool once it has been received by a given participant. Participants will receive an average of 14 messages over the course of 6 weeks (i.e., ~4 weeks with messages x ~3.5 messages per week). This randomization will allow for the examination of within-person differences for weeks in which a participant is receiving PF reports versus not receiving PF reports, weeks receiving supportive messages versus not receiving supportive messages, between-person differences for volume of messages received at the weekly level, between-person differences for volume of messages or PF reports over the course of six weeks, and short-term (i.e., next-day) within-person changes associated with messages versus not receiving messages.

Since this is a pilot study, our primary goals are to determine the feasibility and acceptability of the intervention components. We will utilize formal measures of feasibility and acceptability of the intervention components, including degree of agreement with specific statements regarding intervention features (e.g., frequency and timing of assessments, PF reports, and supportive messages; perceptions of confidentiality, helpfulness, usability, etc.), as well as objective data gathered from rates of attrition and adherence to study procedures (e.g., responding to surveys, clicking links to PF reports). While we are not designed to detect an intervention effect, we will explore whether patterns of change are in the desired directions for intervention components at the weekly level, and for overall between group differences in the Pilot MRT and Assessment only conditions. We will also utilize advanced statistical methods outlined in the training plan to identify predictors of change over the course of the study period, which will be used to inform the design of an adaptive version of this mobile intervention that will only send PF reports or messages under specific conditions.

4.2 SCIENTIFIC RATIONALE FOR STUDY DESIGN

An MRT allows individuals to serve as their own control and examine within-subject differences with respect to weeks receiving an intervention versus weeks not receiving an intervention. For this pilot study, we also opted to include a small assessment-only group as a control to examine trends in overall impact of having received the MRT intervention compared to not receiving any of the intervention components.

4.3 JUSTIFICATION FOR INTERVENTION

With rising rates of depression among college students, and college entailing numerous life stressors, our intervention offers an opportunity for students to have greater awareness of changes in their levels of distress and access coping skills during this transitional period. As a pilot trial, we will be seeking feedback about how to best optimize the length of the study and the volume of text messages and PF reports, as well as their content, to balance intervention and habituation. The text-messaging program has the potential to help remind patients to seek out support and engage in coping strategies when experiencing distress and PF reports will raise awareness to students' well-being and present functioning and serve as a possible motivator for formal help-seeking.

4.4 END-OF-STUDY DEFINITION

A participant is considered to have completed the study when they have completed the 6-week follow-up survey.

5 STUDY POPULATION

5.1 INCLUSION CRITERIA

First-year college students (ages of 17 or above) who are full-time or part-time students enrolled at the University of Michigan, Ann Arbor or Flint campuses with mild-to-moderate depressive symptoms, and who are not receiving professional mental health services will be eligible to participate. Students who may be eligible will first be identified through the university's administrative database. Depressive symptoms and current treatment-seeking status will be verified via email administered questionnaires, after obtaining informed consent from interested students.

5.2 EXCLUSION CRITERIA

Exclusion criteria will include: (1) being under the age of 17, (2) currently be receiving mental health therapy/counseling from a healthcare professional, (3) experiencing minimal depressive symptoms (PHQ-9 < 5), (4) experiencing moderately severe to severe depressive symptoms (PHQ-9 >14).

5.3 LIFESTYLE CONSIDERATIONS

N/A

5.4 SCREEN FAILURES

Screen failures are defined as participants who consent to participate in this study but are not subsequently assigned to the study intervention or entered in the study. Individuals who do not meet the criteria for participation in this trial (screen failure) because of meeting one or more exclusion

criteria will not be re-screened, as the initial screening period for this intervention will occur over the course of only two weeks.

5.5 STRATEGIES FOR RECRUITMENT AND RETENTION

We will send out an e-mail to a randomized batch of approximately 2,500 students (2,000 UM-Ann Arbor, 500 UM-Flint), provided by the respective student registries, inviting them to complete an initial 8-minute survey. We anticipate approximately 425 (17%) will consent to participate and complete the ***screening*** survey, and that 142 (33%) will screen as eligible (mild-to-moderate depression symptoms as defined by PHQ-9 score of 5-14; no current MH treatment) for the intervention portion of the study. The screening survey will be administered to all invited participants and takes approximately 8-10 minutes to complete. After initially sending out the screening survey, we will also send two follow-up reminders via email a couple days apart to remind potential participants of the opportunity to participate in the study. Our full sample will be recruited in this ~10-day period.

We anticipate 120 students (85%) will continue to this next phase of the study, provide a cell-phone number, and complete the ***baseline*** survey (all within this same Qualtrics flow as the screening survey). Once the baseline survey has been completed, participants will be randomized 3:1 to a "Assessment Only" (n = 30) or "Intervention" (n=90) condition. Based on student enrollment and screening rates from a prior study, we anticipate our sample to be 67% female, 63% White, 20% Asian, 9% Black, 8% Multi-racial, and 12% Hispanic.

Our research group has developed several successful strategies to improve participant retention. For completion of the baseline survey, daily and weekly assessment surveys, and final follow-up survey we will provide participants with financial compensation in the form of a re-loadable digital Visa card. For the initial completion of the screening survey, participants will be entered into a drawing for one of ten $50 digital Visa cards. For completion of the baseline survey, participants will receive $20. For daily surveys, participants will receive $1 for each completed survey. For weekly assessments, participants will receive $10 for each completed survey. Finally, participants will receive $25 for completing the final, 6-week follow-up survey. Participants will have payments issued each week based on the number of completed surveys.

6 STUDY INTERVENTION(S) OR EXPERIMENTAL MANIPULATION(S)

6.1 STUDY INTERVENTION(S) OR EXPERIMENTAL MANIPULATION(S) ADMINISTRATION

6.1.1 STUDY INTERVENTION OR EXPERIMENTAL MANIPULATION DESCRIPTION

Participants in both the assessment-only and pilot MRT conditions will complete a baseline survey, a weekly Sunday survey, and a 6-week follow-up survey. The following components will be administered only to the Pilot MRT condition:

<u>Daily Surveys</u>

Some research has indicated that completing daily mood reports on their own can serve as an intervention, so brief 5-item/1-minute daily surveys will be completed by the intervention group.

Personalized Feedback (PF) Reports

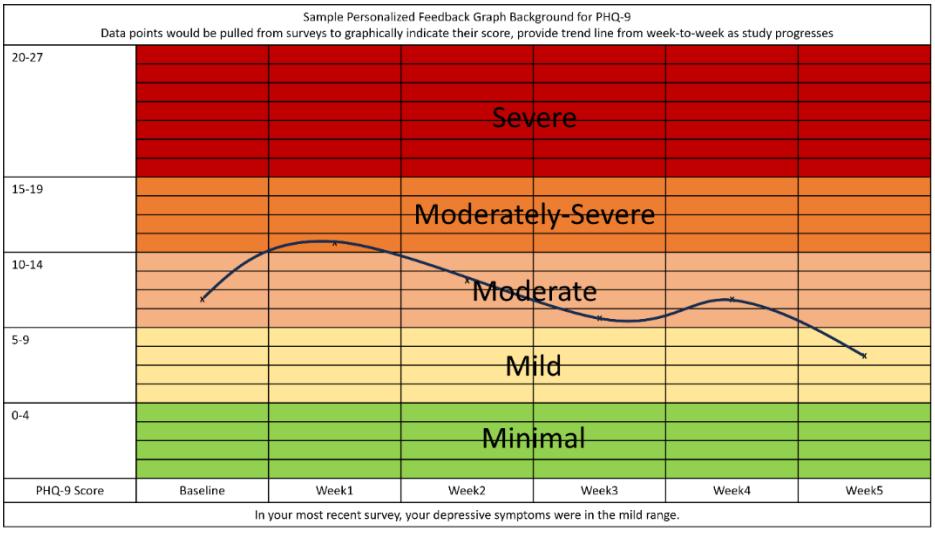
For individuals who are randomized to receive a Personalized Feedback Report, we will send them a text on a Monday with the feedback from their prior survey (Baseline survey in the first week, weekly survey in the next five weeks). There will be graphs for depression, anxiety, stress, and flourishing. The four scales have the following ranges and categories:

Depressive Symptoms (PHQ-9: 0-27): Minimal depressive symptoms (0-4), mild depressive symptoms (5-9), moderate depressive symptoms (10-14), moderately-severe depressive symptoms (15-19), and severe depressive symptoms (20-27).

Anxiety Symptoms (GAD-7: 0-21): Minimal anxiety symptoms (0-4), mild anxiety symptoms (5-9), moderate anxiety symptoms (10-14), severe anxiety symptoms (15-21).

Stress (Perceived Stress Scale-4: 0-16): Low stress (0-5), moderate stress (6-10), high stress (11-16).

Flourishing (Flourishing Scale: 8-56; higher scores are better): Struggling (8-40), Managing (41-47), Thriving (48-56)



At the bottom of the page, there will be a summary statement: “In your last survey, you indicated [Minimal/Mild/Etc.] depressive symptoms, [Minimal/Mild/Etc.] anxiety symptoms, [Low/Moderate/High] stress levels, and results on the Flourishing scale indicated you were [Thriving/Managing/Struggling]. If you feel you might benefit from some support, there are a range of resources available to assist you. Please see {Link: tailored to UM-AA/UM-Flint} for more information.

The graph will highlight where a person is on the week of the PF report and include a trend line for responses leading up to the current week to show changes over time.

Text messages

Text messages will be sent Mondays-Sunday if someone is randomized to receive them in a given week, with a daily 50:50 send/no-send randomization. A bank of 25 text messages will be used for the study, providing tips/strategies across a range of topics, including managing time and academic stressors, recommendations for self-care and mood management, and messages geared towards fostering social connections and support. Participants will be asked to provide a rating for each message they receive to evaluate message helpfulness. Some messages will contain links to videos, websites, or articles for more information on a topic. Please see below for five sample messages:

1. We often default to 'fine' or 'ok' when asked how we're doing. What happens when you open up a bit more next time?
2. Not getting enough sleep? Consider steps you can take to improve your 'sleep hygiene' (link sleep hygiene to: *https://sdlab.fas.harvard.edu/files/sdlab/files/sleephygienechecklistriveweekly.pdf*)
3. When we're our own worst critic, apply the 'reverse' golden rule-- treat yourself how you'd treat your friends.
4. We're not designed to work for hours on end. Consider the Pomodoro method to break things down. (link Pomodoro method to: *https://www.youtube.com/watch?v=mNBmG24djoY*)
5. Being resourceful is a sign of intelligence--asking for help from others when you're struggling is a strength.

6.1.2 ADMINISTRATION AND/OR DOSING

Each participant ID will be pre-randomized to a specific sequence PF reports and text messaging, using a 2:1 ratio for weekly assignment to a PF report, and a 2:1 ratio for receiving text messages during a given week (with daily 50:50 randomization to message/no-message). Participants will, on average, receive 4 personalized feedback reports over the course of six weeks and will receive an average of 14 messages (average of 4 weeks receiving messages and 3.5 messages per week). As an MRT, there will be variation in dosage (e.g., some participants may receive 5 or 6 PF reports and some may receive 2 or 3) for the intervention components. This variability, whereby some weeks will include no texts/PF, PF and no texts, texts and no PF, or both PF and texts, will allow for comparisons that inform an eventual adaptive design.

6.2 FIDELITY

6.2.1 INTERVENTIONIST TRAINING AND TRACKING

The mobile health PF intervention and assessments will be self-guided. Text-messaging, survey assessments, and PF report processes are automated and will not require formal human fidelity training.

6.3 MEASURES TO MINIMIZE BIAS: RANDOMIZATION AND BLINDING

Participants will be assigned sequentially to Study ID numbers that have been pre-randomized with respect to study arm (3:1 ratio, blocking every 20 participants at 15:5). Each study ID will also have a randomized sequence for receiving or not receiving PF reports and/or text messages for weeks 1-6 of the study. Specific text messages will also be randomly pulled from a pool of messages, with previously

used message from a specific participant being pulled for subsequent randomizations (to not send the same message twice to same participant). Assessments are administered electronically and are all self-report. Thus, no blinding procedures are necessary.

6.4 STUDY INTERVENTION/EXPERIMENTAL MANIPULATION ADHERENCE

As a pilot study, we will monitor number of and reasons for withdrawals, and percentage of participants who remain active (i.e. do not request to stop messages), as well as adherence to surveys as indicators of adherence.

6.5 CONCOMITANT THERAPY

N/A

6.5.1 RESCUE THERAPY

N/A

7 STUDY INTERVENTION/EXPERIMENTAL MANIPULATION DISCONTINUATION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1 DISCONTINUATION OF STUDY INTERVENTION/EXPERIMENTAL MANIPULATION

Participants have the option to withdraw from study participation at any time. Those in the intervention conditions will also have the option to withdraw from receiving texts or feedback reports while continuing participation in surveys and follow-up assessments.

7.2 PARTICIPANT DISCONTINUATION/WITHDRAWAL FROM THE STUDY

Participants have the option to withdraw from study participation at any time.

An investigator may discontinue a participant from the study for the following reasons:

- Any event or medical condition or situation occurs such that continued collection of follow-up study data would not be in the best interest of the participant.
- The participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation.

The reason for participant discontinuation or withdrawal from the study will be recorded for acceptability/feasibility tracking purposes.

7.3 LOST TO FOLLOW-UP

A participant will be considered lost to follow-up if they do not complete the six-week follow-up assessment.

Before a participant is deemed lost to follow-up, study staff will make up to two telephone contacts and up to two e-mail contacts following the initial survey invitation.

8 STUDY ASSESSMENTS AND PROCEDURES

8.1 ENDPOINT AND OTHER NON-SAFETY ASSESSMENTS

To recruit participants, we will obtain e-mail addresses of 2,500 first-year undergraduate students from the registrar (2,000 randomly selected from UM-Ann Arbor, and 500 from UM-Flint, which reflects the full annual enrollment of first-year undergraduate students at the UM-Flint campus) and invite them to participate in an 8-minute survey screen of their mental health, with an online consent form. We anticipate approximately 425 students will consent to participate and complete the ***screening survey***, and that 142 students will meet criteria for a positive screen of mild-moderate depressive symptoms (PHQ-9 score of 5-14) and no current psychotherapy for the intervention portion of the study. We anticipate that 85% of the 142 participants who screened eligible for the study will continue to this next phase of the study, provide a cell-phone numbers, and complete the ***baseline survey*** (all within the same Qualtrics flow of the screening survey). The screening survey will be administered to all invited participants who consent to participate and takes approximately 8 minutes to complete. It will be sent out on a Tuesday, with reminders on Friday, and following Monday. Participants are deemed eligible if they score 5-14 on the PHQ-9, denoting mild-to-moderate depressive symptoms ***and*** report they are not currently enrolled in a form of mental health care (e.g., therapy). The baseline survey will be administered to participants screening positive on the screen, when they provide their cell phone number, and takes 10-15 additional minutes to complete. Randomization (3:1 to intervention versus assessment-only) occurs after baseline survey has been completed. Daily surveys will be administered to participants in the intervention group only, and take approximately 1 minute to complete, with links to the survey texted at 8pm each day. Weekly surveys are administered to all participants on Sunday evenings and take approximately ten minutes to complete. The final follow-up survey takes approximately 25 minutes to complete and will be administered to all randomized participants (n=120) on their sixth Sunday of the project. Administration of all surveys will be conducted via an online, automated system (Qualtrics).

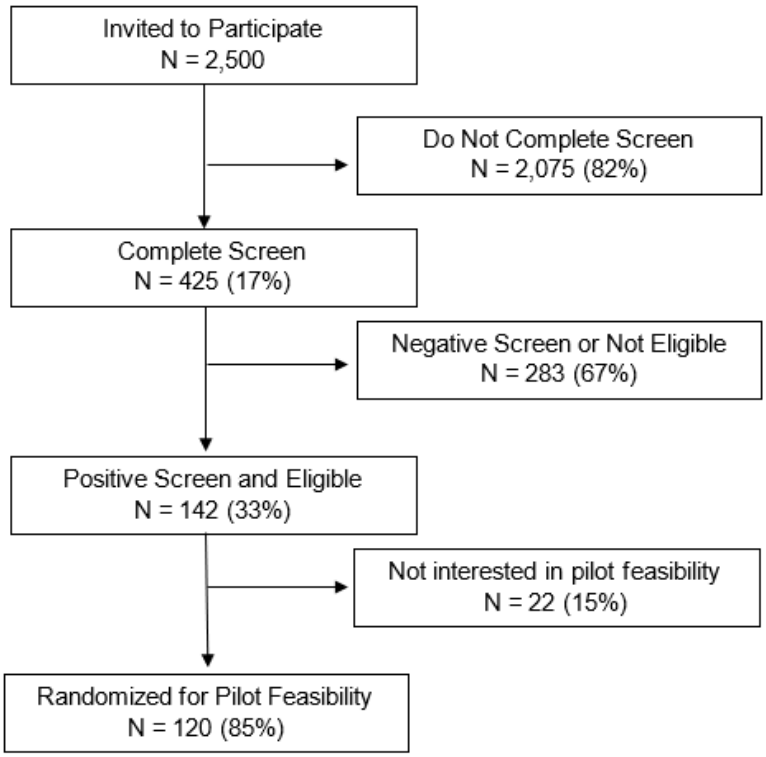


Figure 1. Enrollment Flowchart

Primary Outcomes: The primary outcomes include feasibility and acceptability measured by: (1) percentage of eligible participants who agree to participate, (2) percentage of completed follow-ups, (3) number of and reasons for withdrawals, (4) of those randomized to text-messages, percentage of participants who remain active (i.e. do not request to stop messages), (5) visits/clicks for an individual's

personalized feedback report page, and (6) participant self-reported satisfaction with the intervention components. Participants' feedback will be obtained with Likert scale items and open-ended questions, including overall perspective on personalized feedback reports, and receiving text messages, experience (e.g., ease of accessing intervention components, acceptability of intervention timing, frequency, and duration), and recommended changes.

Additional measures

Daily Survey: The daily survey contains five items that assess: 1) mood (On a scale from 1 (lowest/worst) to 10 (highest/best), how was your mood today? ____), 2) connectedness (My social relationships were supportive and rewarding today (Likert Strongly Disagree (1) to Strongly Agree (7))), 3) coping efficacy (I feel confident that I can cope with the demands and/or stressors in my life (Likert Strongly Disagree (1) to Strongly Agree (7))), 4) Emotional awareness (I was aware of my emotional state and feelings today (Likert Strongly Disagree (1) to Strongly Agree (7))), 5) Interest/energy (I was engaged and interested in my activities today (Likert Strongly Disagree (1) to Strongly Agree (7))).

<u>Screen/Baseline/Weekly/Follow-up Measures</u>

Flourishing (Screen/Weekly/Follow-up). The Flourishing Scale (Diener et al., 2010) is a brief 8-item summary measure of the respondent's self-perceived success in important areas such as relationships, self-esteem, purpose, and optimism. The scale provides a single psychological well-being score (range: 8-56).

Depression (Screen/Weekly/Follow-up). The PHQ-9 (Kroenke et al., 2002) is a 9-item standardized self-report scale for the assessment of depressive symptoms, with a scale range of 0-27.

Anxiety (Screen/Weekly/Follow-up). The GAD-7 (Spitzer et al., 2006) is a 7-item validated self-report scale for the assessment of symptoms consistent with generalized anxiety disorder, with a scale range of 0-21.

Coping self-efficacy (Screen/Weekly-abbv./Follow-up). We use a thirteen-item coping self-efficacy scale (Chesney et al., 2006) to assess confidence in engaging in specific coping strategies when under stress at baseline and follow-up. During weekly assessments, an item from each of the scale's three factors (problem solving, seeking support, stopping unpleasant thoughts/emotions) will be administered.

Loneliness (Screen/Weekly/Follow-up). The UCLA Loneliness scale (Russel et al., 1978) is a self-report measure assessing quality of interpersonal connections and relationships-- we will utilize the 3-item short form for baseline, weekly, and follow-up assessments, which has a scale range of 0-6.

Perceived Stress (Screen/Weekly-abbv./Follow-up). We use the 10-item Perceived Stress Scale (Cohen et al., 1983) at baseline and follow-up assessment; the 4-item PSS short form is used at weekly assessments.

Mental health service utilization (Screen/Follow-up). At baseline, participants will be assessed for lifetime and current use of therapy/counseling from a professional health provider (those currently receiving services are excluded from the trial). At follow-up, participants are asked about any (and number of sessions) counseling or therapy sessions for emotional/mental health in the past six weeks.

Trauma history (Baseline). The Life Event Checklist (LEC-5; Weathers et al., 2013) will ask participants to indicate whether they have every experienced one of twelve types of Criterion A traumatic events, and if so, whether or not these had been experienced in the past 12 months.

Sleep (Baseline/Weekly-abbv./Follow-up). We will use a 9-item adapted version of the Pittsburgh Sleep Quality Index (Buysse et al., 1989) to capture self-report of sleep duration, quality, and sleeping difficulties at baseline and follow-up. Two items focused on sleep duration and quality will be utilized at weekly assessments.

Physical activity (Baseline/Weekly/Follow-up). We use three derived from the Youth Behavior Risk Survey (Grunbaum et al., 2002) to assess frequency and duration of moderate and vigorous exercise at baseline, weekly, and follow-up assessments.

Interpersonal functioning (Baseline/Follow-up). We use 15 items from the Interpersonal Needs Questionnaire (Van Orden et al., 2012), a self-report measure of perceived burdensomeness and thwarted belongingness-- two interpersonal constructs believed to contribute to suicidal desire.

Emotional Awareness (Baseline/Weekly/Follow-up). We use the 6-item subscale 'Emotional Awareness' from the Difficulties in Emotion Regulation Scale (Gratz & Roemer, 2004) at baseline, weekly, and follow-up assessments.

Coping Behaviors (Baseline/Follow-up). We use the 28-item Brief Cope (Carver, 1997) to assess frequency of using 14 specific coping behaviors that encompass various forms of problem-focused coping, emotion-focused coping, and avoidant coping strategies.

Suicidal thoughts and behaviors (Baseline/Weekly—abbv./Follow-up—abbv.). 4 items adapted from the National comorbidity survey will assess history of suicidal thoughts and behaviors at baseline, and two items will assess past-week suicidal thoughts at weekly and follow-up assessments.

Readiness for help-seeking (Baseline/Weekly-abbv./Follow-up). We use four items on a 10-point readiness scale (King et al., 2022) for seeking help from different sources (e.g., family/friends, online resources, professional services, support group) for mental health at baseline and follow-up. Weekly assessments will include two items: readiness for online resources and professional services.

Intervention Acceptability (Follow-up). We use a modified version of the 4-item Acceptability of Intervention Measure (Weiner et al., 2017) to obtain self-report subjective ratings of intervention acceptability and participants will indicate acceptability of numerous intervention features (e.g., frequency/timing of surveys, personalized feedback; confidentiality; satisfaction; helpfulness) using a 7-point agreement scale (strongly disagree to strongly agree).

8.2 SAFETY ASSESSMENTS

There will be no direct contact between participants and study staff, as consent and assessment procedures are completed digitally. Individuals who are deemed ineligible due to elevated depressive symptoms are presented with mental health resources and crisis contacts when exiting the survey platform. Likewise, individuals indicating recent thoughts of suicide are presented with resources and crisis contact information and are informed that study staff do not review their responses.

8.3 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

8.3.1 DEFINITION OF ADVERSE EVENTS

An adverse event is any experience or abnormal finding that has taken place during a research project and was harmful to the subject participating in the research, or increased the risks of harm in the research, or had an unfavorable impact on the risk/benefit ratio.

For this study, expected AE include worsening depressive symptoms and onset of suicidal ideation.

8.3.2 DEFINITION OF SERIOUS ADVERSE EVENTS

Serious adverse event (SAE) is an adverse event that: results in death; is life-threatening (places the participant at immediate risk of death from the event as it occurred); results in inpatient hospitalization or prolongation of existing hospitalization; results in a persistent or significant disability/incapacity; results in a congenital anomaly/birth defect; or based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition.

8.3.3 CLASSIFICATION OF AN ADVERSE EVENT

8.3.3.1 SEVERITY OF EVENT

For adverse events (AEs) not included in the protocol defined grading system, the following guidelines will be used to describe severity.

- **Mild** – Events require minimal or no treatment and do not interfere with the participant's daily activities.
- **Moderate** – Events result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning.
- **Severe** – Events interrupt a participant's usual daily activity and may require systemic drug therapy or other treatment. Severe events are usually potentially life-threatening or incapacitating. Of note, the term "severe" does not necessarily equate to "serious".]

8.3.3.2 RELATIONSHIP TO STUDY INTERVENTION/EXPERIMENTAL MANIPULATION

All adverse events (AEs) will have their relationship to study procedures, including the intervention, assessed by an appropriately trained clinician based on temporal relationship and his/her clinical judgment. Dr. Horwitz will be responsible for reporting adverse events and serious adverse events. The degree of certainty about causality will be graded using the categories below.

- **Definitely Related** – There is clear evidence to suggest a causal relationship, and other possible contributing factors can be ruled out. The clinical event, including an abnormal laboratory test result, occurs in a plausible time relationship to study procedures administration and cannot be explained by concurrent disease or other drugs or chemicals. The response to withdrawal of the study procedures should be clinically plausible. The event must be pharmacologically or phenomenologically definitive.
- **Probably Related** – There is evidence to suggest a causal relationship, and the influence of other factors is unlikely. The clinical event, including an abnormal laboratory test result, occurs within a

reasonable time after administration of the study procedures, is unlikely to be attributed to concurrent disease or other drugs or chemicals, and follows a clinically reasonable response on withdrawal.

- **Potentially Related** – There is some evidence to suggest a causal relationship (e.g., the event occurred within a reasonable time after administration of study procedures). However, other factors may have contributed to the event (e.g., the participant's clinical condition, other concomitant events). Although an AE may rate only as "possibly related" soon after discovery, it can be flagged as requiring more information and later be upgraded to "probably related" or "definitely related", as appropriate.
- **Unlikely to be related** – A clinical event, including an abnormal laboratory test result, whose temporal relationship to study procedures administration makes a causal relationship improbable (e.g., the event did not occur within a reasonable time after administration of the study procedures) and in which other drugs or chemicals or underlying disease provides plausible explanations (e.g., the participant's clinical condition, other concomitant treatments).
- **Not Related** – The AE is completely independent of study procedures administration, and/or evidence exists that the event is definitely related to another etiology. There must be an alternative, definitive etiology documented by the clinician.]

8.3.3.3 EXPECTEDNESS

Dr. Horwitz will be responsible for determining whether an adverse event is expected or unexpected. An AE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described for the study procedures.

8.3.4 TIME PERIOD AND FREQUENCY FOR EVENT ASSESSMENT AND FOLLOW-UP

The occurrence of an adverse event (AE) or serious adverse event (SAE) may come to the attention of study personnel during review of assessments of a study participant or if a participant makes direct contact with study staff through the project e-mail address. All AEs, not otherwise precluded per the protocol, will be captured on the appropriate case report form (CRF). Information to be collected includes event description, time of onset, assessment of severity, relationship to study procedures, and time of resolution/stabilization of the event. All AEs occurring while on study will be documented appropriately regardless of relationship. Within 48 business hours of learning of these events, the coordinator will then bring all possible AEs to the attention of the PI for evaluation and appropriate reporting. AE's will be assessed by the PI for expectedness (expected, unexpected) and relatedness (definitely related, probably related possibly related, unlikely related, not related). A log of all AE's will be maintained by the study coordinator, and the log will be additionally reviewed for completeness at weekly intervals during the active recruitment period.

8.3.5 ADVERSE EVENT REPORTING

In accordance with U-M IRBMED reporting guidelines, moderate and mild AEs that are expected will not be reported to the IRB. Moderate/mild AEs that are unexpected and definitely or possibly related will be reported to the IRB at the time of scheduled continuing review. Moderate AEs that are unexpected and definitely not related will not be reported to the IRB. A summary of AEs will be reported each year to the IRBMED at continuing review. In addition, we will also follow the NIMH Reportable Events Policy and timeline to promptly report these events to the NIMH as required. Safety events requiring expedited reporting will be sent to the) Chair (and forwarded if necessary to the full board) and program office

within 48 hours of notification of the event. A formal report will be submitted to the IRB and NIH within 7 days.

8.3.6 SERIOUS ADVERSE EVENT REPORTING

In accordance with U-M IRBMED reporting guidelines, study-related, life threatening serious adverse event (SAE) reports will be submitted to IRBMED no later than 7 calendar days after learning of the event. If the SAE is expected, it will be reported within 14 days. For SAEs that are not related to the study, reporting will occur at the time of scheduled continuation, or not at all if determined to be expected, per standard reporting timetable of the U-M IRBMED.

8.3.7 REPORTING EVENTS TO PARTICIPANTS

N/A

8.3.8 EVENTS OF SPECIAL INTEREST

N/A

8.3.9 REPORTING OF PREGNANCY

N/A

8.4 UNANTICIPATED PROBLEMS

8.4.1 DEFINITION OF UNANTICIPATED PROBLEMS

This protocol uses the definition of Unanticipated Problems as defined by the Office for Human Research Protections (OHRP). OHRP considers unanticipated problems involving risks to participants or others to include, in general, any incident, experience, or outcome that meets **all** the following criteria:

- Unexpected in terms of nature, severity, or frequency given (a) the research procedures that are described in the protocol-related documents, such as the Institutional Review Board (IRB)-approved research protocol and informed consent document; and (b) the characteristics of the participant population being studied;
- Related or possibly related to participation in the research ("possibly related" means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- Suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

8.4.2 UNANTICIPATED PROBLEMS REPORTING

Dr. Horwitz will report unanticipated problems (UPs) to the reviewing Institutional Review Board (IRB). The UP report will include the following information:

- Protocol identifying information: protocol title and number, PI's name, and the IRB project number
- A detailed description of the event, incident, experience, or outcome
- An explanation of the basis for determining that the event, incident, experience, or outcome represents an UP

- A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the UP

To satisfy the requirement for prompt reporting, UPs will be reported using the following timeline:

- UPs that are serious adverse events (SAEs) will be reported in accordance with description in section 7.6.4.
- Any other UP will be reported to the IRBMED within 14 business days of the investigator becoming aware of the problem.
- All UPs should be reported to appropriate institutional officials (as required by an institution's written reporting procedures), the supporting agency head (or designee), and the Office for Human Research Protections (OHRP) within 7 days of the IRB's receipt of the report of the problem from the investigator.

8.4.3 REPORTING UNANTICIPATED PROBLEMS TO PARTICIPANTS

If there is a UP that directly impacts a participant, they will be informed within 7 days.

9 STATISTICAL CONSIDERATIONS

9.1 STATISTICAL HYPOTHESES

As a pilot study, our primary goal is to examine feasibility and acceptability with descriptive data, and we therefore do not have formal hypotheses.

9.2 SAMPLE SIZE DETERMINATION

We will be enrolling 120 participants in the study, including 90 for the pilot feasibility micro-randomized trial. The proposed sample size is not based on detecting an intervention effect but on the goals to determine the acceptability of the intervention components, perceived helpfulness of intervention components (e.g., personalized feedback reports, supportive text messages), and feasibility metrics such as rates of attrition and adherence to study procedures. This number of participants will be sufficient to examine feasibility and acceptability and to explore the range and distribution of outcomes.

9.3 POPULATIONS FOR ANALYSES

Analyses will be conducted using an intent-to-treat approach.

9.4 STATISTICAL ANALYSES

9.4.1 GENERAL APPROACH

For descriptive statistics, categorical and continuous data will be presented via percentages, with ranges, means, and standard deviations when applicable. In keeping with an experimental therapeutics model, we will conduct exploratory analyses comparing the intervention and assessment-only group on the proposed mechanisms (e.g., coping self-efficacy, emotional awareness, readiness to seek-help). We will also be able to utilize multi-level models accounting for repeated assessments to examine associations of intervention components with mechanisms of interest at daily and weekly levels. With 50:50

randomizations for supportive text messages during ~4 week of the 6 weeks, there will be approximately 14 messages (3.5 per week x 4 weeks) for 90 participants, yielding approximately 1,260 next-day outcome datapoints. The six assessment points (five weekly assessments and final follow-up) will also allow for up to 540 outcomes (90 participants x 6 assessments) to compare associations of those randomized to receive PF reports and those who did not receive PF reports on a given week (360 with PF reports vs. 180 without PF). Model diagnostics will be utilized to determine whether corrections for autocorrelation or other model violations are necessary. We will utilize multiple imputation strategies to provide estimates and account for missing data, which is expected in the context of studies with daily assessments. Because pilot studies are not specifically powered for efficacy, we will examine if the pattern of change associated with receiving PF reports and/or supportive text messages are in the desired direction.

9.4.2 ANALYSIS OF THE PRIMARY ENDPOINT(S)

The primary outcomes include feasibility and acceptability measured by: (1) percentage of eligible participants who agree to participate, (2) percentage of completed follow-ups, (3) number of and reasons for withdrawals, (4) of those randomized to text-messages, percentage of participants who remain active (i.e. do not request to stop messages), (5) visits/clicks for an individual's personalized feedback report page, and (6) participant self-reported satisfaction with the intervention components.

9.4.3 ANALYSIS OF THE SECONDARY ENDPOINT(S)

N/A

9.4.4 SAFETY ANALYSES

N/A

9.4.5 BASELINE DESCRIPTIVE STATISTICS

Baseline descriptive statistics will be used to verify randomization procedures, including sex, campus, race/ethnicity, and suicide attempt history.

9.4.6 PLANNED INTERIM ANALYSES

N/A

9.4.7 SUB-GROUP ANALYSES

As part of the evaluation of feasibility/acceptability, we will examine whether features of the intervention were moderated by group-level factors such as age, sex, race/ethnicity, or history of formal mental health care.

9.4.8 TABULATION OF INDIVIDUAL PARTICIPANT DATA

N/A

9.4.9 EXPLORATORY ANALYSES

All planned exploratory analyses should be specified in the protocol.

Because pilot studies are not specifically powered for efficacy, we will examine if the pattern of change associated with receiving PF reports and/or supportive text messages are in the desired direction. We will also examine whether dose of an intervention (e.g., numbers of texts, number of weeks with texts,

number of personalized feedback reports) had a directional influence on mechanisms of interest. We will also explore whether randomization to the intervention group had an impact on mechanisms of interest relative to those in the assessment-only condition.

10 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1 REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

10.1.1 INFORMED CONSENT PROCESS

10.1.1.1 CONSENT/ASSENT AND OTHER INFORMATIONAL DOCUMENTS PROVIDED TO PARTICIPANTS

Consent forms describing in detail the study intervention, study procedures, and risks will be given to the participant and participants will confirm their review of the document and consent to participate prior to initiating the survey. The study consent form and the e-mail invitation documents are provided as supplements to this protocol.

10.1.1.2 CONSENT PROCEDURES AND DOCUMENTATION

Participants will be invited via e-mail to participate in the study and be provided with an electronic consent form that can be viewed and downloaded. Participants will be informed of the general nature of the study, expectations for their participation, the voluntary nature of their participation, the risk/benefits, limitations to confidentiality, and that they may withdraw from the study at any time. As a digital study, formal written consent will be waived and participants will be required to attest that they have reviewed the consent form and wish to participate prior to proceeding to the screening survey. A waiver for parental consent will be obtained so that 17-year-old first-year college students may participate in the study.

10.1.2 STUDY DISCONTINUATION AND CLOSURE

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. If the study is prematurely terminated or suspended, the Principal Investigator (PI) will promptly inform study participants, the Institutional Review Board (IRB), and sponsor/funding agency and will provide the reason(s) for the termination or suspension. Study participants will be contacted, as applicable, and be informed of changes to study visit schedule.

Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants
- Demonstration of efficacy that would warrant stopping
- Insufficient compliance of study staff to the protocol (i.e., significant protocol violations)
- Data that are not sufficiently complete and/or evaluable
- Determination that the primary endpoint has been met
- Determination of futility

The study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the funding agency, sponsor, IRB, Food and Drug Administration (FDA), or other relevant regulatory or oversight bodies (OHRP, DSMB).]

10.1.3 CONFIDENTIALITY AND PRIVACY

The study team has considerable experience in maintaining the confidentiality of participant data and has established procedures to ensure data confidentiality. Several steps will be taken to minimize the risk of breaches of confidentiality. Only the designated research staff will have access to research data. Training of staff will include information about the importance of confidentiality and techniques to maintain confidentiality of all information reported by research participants. Staff will maintain human subjects and confidentiality certifications through the UM Program for Education and Evaluation in Responsible Research and Scholarship (PEERRS) system and will complete CITI Good Clinical Practice (GCP) Training. Consent documents will fully explain the study procedures, potential risks, and potential benefits. In addition, every effort will be made to ensure that study data are always confidential in terms of data storage, so that data cannot be linked to a particular person. Unique identification numbers will be assigned to all participants. Participants' names and study IDs will be kept in a separate file from study data. All linking files will be maintained in a secure password-protected file on a secure server. All data and assessments will be coded with this ID rather than with a name. Electronic data files (e.g. surveys) will be saved with passwords on a secure network and will not contain any identifying information. The "Subject Directory" sheets linking participant IDs to their names will be kept in a password-protected folder on a secure password-protected network. Prior to data entry, all identifying information will be removed, and only the subject IDs will be entered with the study data.

Steps will also be taken to minimize breaches of confidentiality associated with the data collection tools. Baseline and follow-up surveys will be developed in Qualtrics (University of Michigan Health System [UMHS]-approved Qualtrics version). No identifying information will be collected via Qualtrics. Daily messages sent to participants will be sent via text messages to participants' phones using a secure study platform; the platform complies with the Health Insurance Portability and Accountability Act (HIPAA) privacy regulations. The platform will be hosted on a server whose data is encrypted at all times and which is secured in accordance with industry-standard data security practices. Moreover, participants will be informed of the risk that anyone who accesses their phone could see the supportive text messages. Participants will be encouraged that they can further protect their privacy by password-protecting their phone/device.

Participants' confidentiality will be breached by the research study only to protect the safety and welfare of research participants and only in accordance with state and federal law. Although study assessments will not ask about child abuse, in the unlikely event that a participant self-discloses the abuse of a child, staff will be trained to report this information to local child protective services/family independence agencies. These confidentiality exceptions will be explained in detail to participants as part of the study consent process.

It is NIH policy that the results and accomplishments of the activities that it funds should be made available to the public (see *https://grants.nih.gov/policy/sharing.htm*). The PI will ensure all mechanisms used to share data will include proper plans and safeguards for the protection of privacy, confidentiality, and security for data dissemination and reuse (e.g., all data will be thoroughly de-identified and will not

be traceable to a specific study participant). Plans for archiving and long-term preservation of the data will be implemented, as appropriate.

Certificate of Confidentiality: To further protect the privacy of study participants, the Secretary, Health and Human Services (HHS), has issued a Certificate of Confidentiality (CoC) to all researchers engaged in biomedical, behavioral, clinical or other human subjects research funded wholly or in part by the federal government. Recipients of NIH funding for human subjects research are required to protect identifiable research information from forced disclosure per the terms of the NIH Policy (see *https://humansubjects.nih.gov/coc/index*). As set forth in 45 CFR Part 75.303(a) and NIHGPS Chapter 8.3, recipients conducting NIH-supported research covered by this Policy are required to establish and maintain effective internal controls (e.g., policies and procedures) that provide reasonable assurance that the award is managed in compliance with Federal statutes, regulations, and the terms and conditions of award. It is the NIH policy that investigators and others who have access to research records will not disclose identifying information except when the participant consents or in certain instances when federal, state, or local law or regulation requires disclosure. NIH expects investigators to inform research participants of the protections and the limits to protections provided by a Certificate issued by this Policy.

10.1.4 FUTURE USE OF STORED SPECIMENS AND DATA

Data collected for this study will be analyzed and stored at the University of Michigan for a minimum of three years after the conclusion of the award or public release, whichever comes later. After the study is completed, the de-identified, archived data will be transmitted to a public repository and stored for use by other researchers, including those outside of the study. Permission to transmit data will be included in the informed consent.

10.1.5 KEY ROLES AND STUDY GOVERNANCE

Principal Investigator
Adam Horwitz, PhD, Assistant Professor
University of Michigan Medical School
4250 Plymouth Rd., Ann Arbor, MI, 48109
734-764-0231
ahor@umich.edu

10.1.6 SAFETY OVERSIGHT

While we are specifically targeting students with mild-to-moderate symptoms of depression, there may be students whose symptoms worsen over the course of the study (as we would expect among first-year college students, regardless of study participation). Participants reporting suicidal thoughts in Qualtrics surveys will receive an immediate response including crisis hotline telephone numbers and the local Psychiatric Emergency Department.

As the PI, Dr. Horwitz will ensure that all relevant University of Michigan IRBMED policies, procedures, and stipulations are being followed. He will be responsible for ensuring that research staff adhere to the IRBMED policies, including: 1) all participants will understand and agree to an electronic consent form before participating; 2) all participants will be provided with a copy of the informed consent; 3) strict adherence to participant's right to withdraw or refuse to answer any questions will be maintained; 4) the assessments will be completely confidential and no names will be associated with the assessment data; 5) identifying information will be kept separate from the actual participant data; 6) all identifying information will be locked/saved with passwords on secure servers; 7) participants will be informed in writing in the consent form how to contact the PI and IRB office with any questions or concerns.

10.1.7 CLINICAL MONITORING

Study monitoring will be conducted to ensure that the rights and well-being of participants are protected, that the reported data are accurate, complete, and verifiable, and that the conduct of the study is in compliance with the protocol and with applicable regulatory requirements. Dr. Horwitz will be responsible for monitoring the data safety and quality. All research projects involving human participants require approvals from the University of Michigan Medical School's Institutional Review Board (IRBMED). Annual reviews will be conducted by IRBMED, including the number of subjects screened, enrolled, and withdrawn. The IRB will also review protocol deviations, adverse events, and complaints that arise in connection with the study. As the PI, Dr. Horwitz will ensure that all relevant IRBMED policies, procedures, and stipulations are being followed.

10.1.8 QUALITY ASSURANCE AND QUALITY CONTROL

An emphasis will be placed on maintaining strict patient confidentiality. No participant names will be associated with the data. Forms containing identifying information will be kept separate from participant study data and electronic files will be password protected on secured servers. The study platform is HIPAA compliant and will use a secure SMS service (Twilio) to deliver text messages to participants. When data from Qualtrics is downloaded by investigators, the aggregated dataset will contain no PII. Quality control and reliability of assessments will be monitored by the PI, Dr. Horwitz. He will meet weekly with research assistants on the project to monitor the quality of the data files and identify any inconsistencies that may require adjustment to the programming of the Qualtrics survey or study platform.

10.1.9 DATA HANDLING AND RECORD KEEPING

10.1.9.1 DATA COLLECTION AND MANAGEMENT RESPONSIBILITIES

Data collection will be the responsibility of the research staff under the supervision of the PI. The PI will be responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data. Data will be collected only with informed consent. The primary sources of data will be gathered via questionnaires collected at: (1) screening/baseline survey, which will be collected through an e-mailed Qualtrics survey link; (2) weekly (six time-points) follow-up assessments, which will be collected through a texted Qualtrics survey link; and (3) daily surveys (intervention-only group), which will be collected through a texted Qualtrics survey link. Assessment instruments have been used widely and evaluated for their appropriateness with participants. Participants will provide qualitative data at the end of the trial

concerning acceptability of intervention components as well as input on barriers and facilitators to participation to inform future implementation.

10.1.9.2 STUDY RECORDS RETENTION

Study documents will be retained for a minimum of 3 years.

10.1.10 PROTOCOL DEVIATIONS

This protocol defines a protocol deviation as any noncompliance with the clinical trial protocol, International Council on Harmonisation Good Clinical Practice (ICH GCP), or Manual of Procedures (MOP) requirements. The noncompliance may be either on the part of the participant, the investigator, or the study site staff. As a result of deviations, corrective actions will be developed by the site and implemented promptly. Because study participation is voluntary, participants not completing aspects of the study are not considered protocol violations. Protocol deviations will be sent to the reviewing Institutional Review Board (IRB), NIMH, and DSMB per their reporting requirements.

10.1.11 PUBLICATION AND DATA SHARING POLICY

This study will be conducted in accordance with the following publication and data sharing policies and regulations:

National Institutes of Health (NIH) Public Access Policy, which ensures that the public has access to the published results of NIH funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive PubMed Central upon acceptance for publication.

This study will comply with the NIH Data Sharing Policy and Policy on the Dissemination of NIH-Funded Clinical Trial Information and the Clinical Trials Registration and Results Information Submission rule. As such, this trial will be registered at ClinicalTrials.gov, and results information from this trial will be submitted to ClinicalTrials.gov. In addition, every attempt will be made to publish results in peer-reviewed journals. Data from this study may be requested from other researchers by contacting the PI. Considerations for ensuring confidentiality of these shared data are described in Section 10.1.3.

10.1.12 CONFLICT OF INTEREST POLICY

The independence of this study from any actual or perceived influence is critical. Therefore, any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this trial will be disclosed and managed. Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is appropriate to their participation in the design and conduct of this trial. The study leadership in conjunction with the NIH has established policies and procedures for all study group members to disclose all conflicts of interest and will establish a mechanism for the management of all reported dualities of interest.

10.2 ADDITIONAL CONSIDERATIONS

N/A

10.3 ABBREVIATIONS AND SPECIAL TERMS

Abbv.	Abbreviated
AE	Adverse Event
CFR	Code of Federal Regulations
CMP	Clinical Monitoring Plan
COC	Certificate of Confidentiality
CRF	Case Report Form
DCC	Data Coordinating Center
DHHS	Department of Health and Human Services
DSMB	Data Safety Monitoring Board
EC	Ethics Committee
eCRF	Electronic Case Report Forms
EMA	Ecological Momentary Assessment
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
ICH	International Council on Harmonisation
IRB	Institutional Review Board
IRBMED	Institutional Review Board Medicine
ISM	Independent Safety Monitor
ITT	Intention-To-Treat
MOP	Manual of Procedures
MRT	Micro-randomized Trial
NCT	National Clinical Trial
NIH	National Institutes of Health
OHRP	Office for Human Research Protections
PF	Personalized Feedback
PI	Principal Investigator
QA	Quality Assurance
QC	Quality Control
RCT	Randomized Control Trial
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SMC	Safety Monitoring Committee
SOA	Schedule of Activities
SOP	Standard Operating Procedure
UP	Unanticipated Problem
US	United States

10.4 PROTOCOL AMENDMENT HISTORY

*The table below is intended to capture changes of IRB-approved versions of the protocol, including a description of the change and rationale. A **Summary of Changes** table for the current amendment is located in the **Protocol Title Page**.*

Version	Date	Description of Change	Brief Rationale
v.1.0	07/08/2024	Not applicable; this is the first version of the protocol	Not applicable; this is the first version of the protocol
v.1.1	5.1.2025	Updated enrollment to reflect 120 recruited	IRB amendment

11 REFERENCES

Allen NB, Hetrick SE, Simmons JG, Hickie IB. Early intervention for depressive disorders in young people: the opportunity and the (lack of) evidence. *Med J Aust*. 2007;187(S7)

Auerbach RP, Alonso J, Axinn WG, et al. Mental disorders among college students in the World Health Organization world mental health surveys. *Psychol Med*. 2016;46(14):2955-2970.

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

Byrd DR, McKinney KJ. Individual, interpersonal, and institutional level factors associated with the mental health of college students. *J Am Coll Health*. 2012;60(3):185-193.

Campbell B, Caine K, Connelly K, Doub T, Bragg A. Cell phone ownership and use among mental health outpatients in the USA. *Pers Ubiquitous Comput*. 2015;19(2):367-378.

Carver CS: You want to measure coping but your protocol's too long: consider the brief COPE. *Int J Behav Med.* 1997, 4:92-100.

Chesney MA, Neilands TB, Chambers DB, Taylor JM, Folkman S. A validity and reliability study of the coping self-efficacy scale. *Br J Health Psychol.* 2006; 11(3): 421-37.

Cohen S, Kamarck T, Mermelstein R: A Global Measure of Perceived Stress. *J Health Soc Behav.* 1983, 24:385-396.

Czyz EK, Horwitz AG, Eisenberg D, Kramer A, King CA. Self-reported barriers to professional help seeking among college students at elevated risk for suicide. *J Am Coll Health*. 2013;61(7):398-406.

Diener E, Wirtz D, Tov W, Kim-Prieto C, Choi D-w, Oishi S, Biswas-Diener R: New Well-being Measures: Short Scales to Assess Flourishing and Positive and Negative Feelings. *Soc Indic Res.* 2010, 97:143-156.

Epstein RM, Duberstein PR, Feldman MD, et al. “I didn’t know what was wrong:” how people with undiagnosed depression recognize, name and explain their distress. *J Gen Intern Med*. 2010;25:954-961.

Gratz KL, Roemer L: Multidimensional assessment of emotion regulation and dysregulation: Development, factor structure, and initial validation of the difficulties in emotion regulation scale. *J Psychopathol Behav Assess.* 2004, 26:41-54.

Grunbaum, J. A., L. Kann, S. A. Kinchen, et al. Youth risk behavior surveillance-United States, 2001. *MMWR Surveill. Summ.* 51:1-62, 2002.

King CA, Eisenberg D, Pistorello J, Coryell W, Albucher RC, Favorite T, Horwitz A, Bonar EE, Epstein D, Zheng K: Electronic bridge to mental health for college students: A randomized controlled intervention trial. *J Consult Clin Psychol.* 2022, 90:172-183.

Kessler, R.C., Berglund, P., Chiu, W.T., Demler, O., Heeringa, S., Hiripi, E., Jin, R., Pennell, B.-E., Walters, E.E., Zaslavsky, A. and Zheng, H. (2004), The US National Comorbidity Survey Replication (NCS-R): design and field procedures. Int. J. Methods Psychiatr. Res., 13: 69-92.

Kroenke K, Spitzer RL, Williams JB. The PHQ-9: Validity of a brief depression severity measure. *J Gen Intern Med.* 2002;16(9):606-613.

Lattie EG, Lipson SK, Eisenberg D. Technology and college student mental health: Challenges and opportunities. *Front Psychiatry*. 2019;10:246.

Lee YY, Stockings EA, Harris MG, et al. The risk of developing major depression among individuals with subthreshold depression: a systematic review and meta-analysis of longitudinal cohort studies. *Psychol Med*. 2019;49(1):92-102.

Lipson SK, Lattie EG, Eisenberg D. Increased Rates of Mental Health Service Utilization by U.S. College Students: 10-Year Population-Level Trends (2007–2017). *Psychiatr Serv*. 2019;70(1):60-63.

Pew Research Center. Mobile fact sheet. 2023. Accessed 2023 August 02, 2023. *https://www.pewresearch.org/internet/fact-sheet/mobile/*

Russell D, Peplau LA, Ferguson ML: Developing a measure of loneliness. *J Pers Assess.* 1978, 42:290-294.

Spitzer RL, Kroenke K, Williams JBW, Lowe B. A brief measure for assessing generalized anxiety disorder. *Arch Intern Med.* 2006;166:1092-1097.

Van Orden KA, Cukrowicz KC, Witte TK, Joiner TE: Thwarted belongingness and perceived burdensomeness: construct validity and psychometric properties of the Interpersonal Needs Questionnaire. *Psychol Assess.* 2012, 24:197-215.

Weathers FW, Blake DD, Schnurr PP, Kaloupek DG, Marx BP, Keane TM. (2013). The Life Events Checklist for DSM-5 (LEC-5). Instrument available from the National Center for PTSD at *www.ptsd.va.gov*

Weiner, B.J., Lewis, C.C., Stanick, C. et al. Psychometric assessment of three newly developed implementation outcome measures. Implementation Sci 12, 108 (2017).

Xiao H, Carney DM, Youn SJ, et al. Are we in crisis? National mental health and treatment trends in college counseling centers. *Psychol Serv*. 2017;14(4):407.