Reducing Challenging Behaviors in Children With Autism Through Digital Health

Study Protocol with Statistical Analysis Plan

NCT05277194

Last Updated: 1/31/2024

Continuing Review

Basic Info

Confirmation Number:	**eaejfifj**
Protocol Number:	**829690**
Created By:	**FLOWERS, TAYLOR**
Principal Investigator:	**NUSKE, HEATHER J**
Protocol Title:	**Development of a Digital Biosensor Stress Alarm for Children with Autism**
Short Title:	**KeepCalm App Development Study**
Protocol Description:	**The primary research goal of the proposed project is to develop a digital emotional stress alarm smartphone application that incorporates wearable biosensor heart rate signaling, for parents and teachers to help them manage challenging behaviors in children with autism spectrum disorder. The secondary aims are to field test the app at preschool, school and home, and establish viable community-based physiological stress recording methods to be used as treatment outcome in intervention studies.**
Submission Type:	**Social and Biological Sciences**
Application Type:	**FULL**

PennERA Protocol Status

Approved (No CR)

Level of IRB Review Required

Expedited Review

The following documents are currently attached to this item:

There are no documents attached for this item.

Summary of protocol modifications approved since last continuing review
Please provide a description of changes which have been reviewed and approved by the IRB since the last continuing review.

Subject Enrollment

Target subject enrollment at Penn

0

Target enrollment at other centers (multi-center study)

0

Number of subjects enrolled at Penn since the study was initiated

0

Actual enrollment at participating centers

0

Number of subjects enrolled at Penn since the last continuing review

Total number of subjects who provided consent

0

Number of subjects determined to be ineligible

0

Number of subjects currently active/on study

0

Number of subjects lost to follow-up

0

Number of subjects no longer participating for other reasons

0

Number of subjects who have completed the study

0

Number of subjects who have withdrawn from the study

0

Race:

American Indian or Alaskan Native

0

Asian

0

Black or African American

0

Native Hawaiian or Pacific Islander

0

White

0

Other

0

Unknown or Not Reported

0

Ethnicity:

Hispanic or Latino

0

Not Hispanic or Latino

0

Gender

Male

0

Female

0

Other

0

Unknown / Not Reported

0

Total

0

Vulnerable Populations

Has your study enrolled pregnant woman?*

No

Has your study enrolled prisoners?*

No

Has your study enrolled children?*

No

Subject Withdrawal

How many subject voluntarily withdrew from the study?

0

How many subjects were withdrawn from the study at the request of the PI/Co-PI?

0

Number of subjects withdrawn due to adverse events/unanticipated problems

0

Subject withdraw reason*
If subjects voluntarily withdrew or were withdrawn, please indicate the reasons.

Issues with recruitment/retention, informed consent, or other issues
If applicable, please provide a brief summary of any difficulty you experienced obtaining/retaining subjects or obtaining informed consent during the entire approval period. Additionally, please indicate if there have been any complaints about the research.

Informed Consent Process*
Recognizing that informed consent encompasses much more than a form or document there are a number of methods employed to educate a potential subject as to what is involved in a particular research project. The forms used are one method for documenting the informed consent process.Is written informed consent required for this project?
No

Is written HIPAA authorization required?*

No

New Findings

Significant preliminary observations/interim findings
Have there been any significant preliminary observations/interim findings during the past approval period. If yes, please describe below.

DMC or DSMB exists*
Does a data monitoring committee (DMC) or data and safety monitoring board (DSMB) exist?
No

DMC or DMB Report Status

The following documents are currently attached to this item:

There are no documents attached for this item.

Multi-site trial summary
If this study is a multi-site trial, provide a narrative summary of any relevant reports that have been received in the past year, regardless of whether the report has been previously submitted to the IRB.

Disclosure of Significant Financial Interests*
Investigators (persons responsible for the design, conduct or reporting of this research protocol) must disclose any of the following financial interests / relationships with any entity that sponsors, provides support, or otherwise has a financial interest in the conduct or outcome of this research protocol (Outside Organization): Payments received for the past 12 months from a publicly traded Outside Organization for personal services (e.g., consulting, lecturing / speaking, service on the Scientific Advisory Board) plus the value of any current equity that when aggregated exceeds $5,000Payments received for the past 12 months from a non-publicly traded Outside Organization for personal services that in total exceed $5,000, or having any equity interestMembership on the governing board of any Outside Organization, including service on its board of directors, or having a position of authority or responsibility to act in its best interests, including being an officer, manager, partner, or limited liability company member with management responsibilityInvestigators must also disclose any financial interest in a drug, device or other product or a competing product (IP rights), regardless of whether the IP has been patented, licensed, or assigned to the Penn, if such IP is being tested, evaluated, or developed in, or if its commercial value could be affected by, this protocol.Investigators are not required to disclose equity in mutual funds and retirement accounts, as long as the Investigator does not directly control the investment decisions made in these vehicles.Does any Investigator (or his or her spouse or dependent children) have a SIGNIFICANT FINANCIAL INTEREST, as defined above?
No

If "YES", was this Financial Interest previously reported to the Conflicts of Interest Standing Committee?
Not Applicable

If "YES", has there been a change regarding this Financial Interest from what was previously reported to the Conflicts of Interest Standing Committee?
Not Applicable

The following documents are currently attached to this item:

There are no documents attached for this item.

Penn Intellectual Property*
To the best of the Principal Investigator's knowledge, does this protocol involve the testing, development or evaluation of a drug, device, product, or other type of intellectual property (IP) that is owned by or assigned to the University of Pennsylvania? Please refer to the Patent and Tangible Research Property Policies and Procedures.
Yes

If yes, please provide any readily available information on such IP. For example, a brief description of the IP, any relevant docket number (if disclosed to the Penn Center for Innovation (PCI), patent application or patent numbers, inventor's names, and/or other relevant details.
Disclosure ID: Web_501954 Inventor: Heather Nuske I have designed a mobile platform application combined with remote sensor physiological recording to identify and alert teachers of heightened stress in students with autism spectrum disorder (ASD) and remind of them of evidence-based practices for assistance in deescalating stress and preventing challenging behaviors. Beyond this initial phase of app development, I plan to adapt this for other children who may experience challenges in the classroom, such as those with anxiety or attention deficit hyperactivity disorder, as well as adapting the technology for self-monitoring of physiological stress by children or adults at school or in other community settings, such as home or work places.

Certification
I have reviewed the Financial Disclosure and Presumptively Prohibited Conflicts for Faculty Participating in Clinical Trials and the Financial Disclosure Policy for Research and Sponsored Projects with all persons who are responsible for the design, conduct, or reporting of this research; and all required Disclosures have been attached to this application.
Yes

Study Completion / Expiration

Study Complete*
Is this study complete?
No

Study Complete - Explanation
If study is completePlease indicate why (eg., research related activities and data analysis are complete, required number of subjects reached, issues with protocol safety,etc.)

The following documents are currently attached to this item:

There are no documents attached for this item.

IRB Approval Expired*
Has IRB approval for this protocol expired or will it expire before the scheduled IRB review?
No

Research During IRB Approval Lapse
If the IRB approval for the protocol has expired or will expire before the scheduled IRB review, confirm that no research related activities occurred/will occur without approval from the IRB unless the PI contacted the Office of Regulatory Affairs and the IRB Executive Chair (or authorized designee) determined that it is in the best interest of subjects to continue during the lapse in IRB approval. For example, in a clinical trial there are (1) subjects who are enrolled but not on intervention, (2) subjects who are on intervention, and (3) subjects who have completed the intervention phase and are in follow up. The IRB Executive Chair must evaluate each of these groups separately regarding continuation of participation in the research after IRB approval has expired.Have any research activities occurred, or will any research activities need to occur, during the lapse in IRB approval?
No

Unanticipated Problems*
Since the last IRB Review, have there been any unanticipated study related events that have not been previously reported to the IRB? If No, do not include these events with this submission. Refer to www.upenn.edu/regulatoryaffairs/index.php?option=com_content&task=view&id=16&Itemid=8
No

The following documents are currently attached to this item:

There are no documents attached for this item.

Adverse Events*
Since the last IRB review, has the profile of adverse events (in terms of frequency, severity, or specificity) changed from previous experience or as documented in the research protocol, informed consent document, or investigator's brochure?
No

The following documents are currently attached to this item:

There are no documents attached for this item.

Documents attached from the IRB protocol application.

The following documents are currently attached to this item:

Informed consent form (consentform_designworkshopsphase1.18.7.18.docx)

Informed consent form (consentform_contextualinquiryphase1.28.17.20_clean.docx)

Informed consent form (consentform_usabilitytestingphase28.17.20_clean.docx)

Informed consent form (parentinformedconsenthipaaauthorizationform1.31.24_clean.docx)

Informed consent form (teacherinformedconsenthipaaauthorizationform1.31.24_clean.docx)

Investigator's brochure/product labeling (mbientlab_metamotionrl.pdf)

Investigator's brochure/product labeling (miofuse.pdf)

Investigator's brochure/product labeling (polarh7.pdf)

Investigator's brochure/product labeling (pulseon.pdf)

Full sponsor's protocol (studyprotocol01-31-24.pdf)

List of Documents Details
Please detail the rationale for why any of the above documents are not attached to the submission (i.e. No Investigator's Brochure, Protocol, or Consent Forms are utilized for this protocol).

Protocol Details

Resubmission*
Yes

Hospital Sites
Will any research activities and/or services be conducted at a Penn Medicine affiliated hospital site?
No

Study Personnel

Principal Investigator

Name:	**NUSKE, HEATHER J**
Dept / School / Div:	**4423 - PS-Mental Health Services**
Campus Address Mail Code	**3309**
Address:	**OFFICE BLDG STE 100** **3535 MARKET ST**
City State Zip:	**PHILADELPHIA PA 19104-3309**
Phone:	**215-746-6041**
Fax:	
Pager:	
Email:	**hjnuske@upenn.edu**
HS Training Completed:	**Yes**
Training Expiration Date:	
Name of course completed :	**CITI Protection of Human Subjects Research Training - ORA**
GCP Training Completed:	**No**
Training Expiration Date:	
Name of course completed :	

Study Contacts

Name:	**DESWERT, SKY**
Dept / School / Div:	**4423 - PS-Mental Health Services**
Campus Address Mail Code	
Address:	
City State Zip:	
Phone:	
Fax:	
Pager:	
Email:	**Sky.Deswert@Pennmedicine.upenn.edu**
HS Training Completed:	**Yes**
Training Expiration Date:	
Name of course completed :	**CITI Protection of Human Subjects Research Training - ORA**
GCP Training Completed:	**Yes**
Training Expiration Date:	**11/09/2024**
Name of course completed :	**Good Clinical Practice: An Introduction to ICH (GCP) Guidelines**

Name:	**KAMEL, RIMA A**
Dept / School / Div:	**4423 - PS-Mental Health Services**
Campus Address Mail Code	
Address:	
City State Zip:	
Phone:	
Fax:	
Pager:	
Email:	**rimak@sas.upenn.edu**
HS Training Completed:	**Yes**
Training Expiration Date:	
Name of course completed :	**CITI Protection of Human Subjects Research Training - ORA**
GCP Training Completed:	**No**
Training Expiration Date:	
Name of course completed :	

Name:	**DUNPHY, MORGAN K**
Dept / School / Div:	**4423 - PS-Mental Health Services**
Campus Address Mail Code	
Address:	
City State Zip:	
Phone:	
Fax:	
Pager:	
Email:	**Morgan.Dunphy@Pennmedicine.upenn.edu**
HS Training Completed:	**Yes**
Training Expiration Date:	
Name of course completed :	**CITI Protection of Human Subjects Research Training - ORA**
GCP Training Completed:	**No**
Training Expiration Date:	
Name of course completed :	

Other Investigator

Name:	**MANDELL, DAVID S**
Dept / School / Div:	**4423 - PS-Mental Health Services**
Campus Address Mail Code	**3309**
Address:	**3535 Market Street, Rm 3019**
City State Zip:	**Philadelphia PA 19104-3309**
Phone:	**215-573-7494**
Fax:	**215-349-8715**
Pager:	
Email:	**david.mandell@pennmedicine.upenn.edu**
HS Training Completed:	**Yes**
Training Expiration Date:	
Name of course completed :	**CITI Protection of Human Subjects Research Training - ORA**
GCP Training Completed:	**Yes**
Training Expiration Date:	**07/25/2025**
Name of course completed :	**Good Clinical Practice: An Introduction to ICH (GCP) Guidelines**

Responsible Org (Department/School/Division):

4423 - PS-Mental Health Services

Key Study Personnel

Name:	**BROWN, ALYSSA K**
Department/School/Division:	**PS-Mental Health Services**
HS Training Completed:	**Yes**
Training Expiration Date:	
Name of course completed:	**CITI Protection of Human Subjects Research Training - ORA**
GCP Training Completed:	**No**
Training Expiration Date:	
Name of course completed:	

Name:	**DESWERT, SKY**
Department/School/Division:	**PS-Mental Health Services**
HS Training Completed:	**Yes**
Training Expiration Date:	
Name of course completed:	**CITI Protection of Human Subjects Research Training - ORA**
GCP Training Completed:	**No**
Training Expiration Date:	
Name of course completed:	

Name:	**TAN, JESSICA Y**
Department/School/Division:	**SDM Deans Office**
HS Training Completed:	**Yes**
Training Expiration Date:	
Name of course completed:	**CITI Protection of Human Subjects Research Training - ORA**
GCP Training Completed:	**No**
Training Expiration Date:	
Name of course completed:	

Name:	**CROSS, HEAVEN S**
Department/School/Division:	**The College**
HS Training Completed:	**Yes**
Training Expiration Date:	
Name of course completed:	**CITI Protection of Human Subjects Research Training - ORA**
GCP Training Completed:	**Yes**
Training Expiration Date:	**06/12/2026**
Name of course completed:	**CITI Good Clinical Practice (GCP) - OCR**

Name:	**BUI, CAMELLIA N**
Department/School/Division:	**PS-Mental Health Services**
HS Training Completed:	**Yes**
Training Expiration Date:	
Name of course completed:	**CITI Protection of Human Subjects Research Training - ORA**
GCP Training Completed:	**No**
Training Expiration Date:	
Name of course completed:	

Name:	**EMEZIE, AMARACHI E**
Department/School/Division:	**Wharton School**
HS Training Completed:	**Yes**
Training Expiration Date:	
Name of course completed:	**CITI Protection of Human Subjects Research Training - ORA**
GCP Training Completed:	**No**
Training Expiration Date:	
Name of course completed:	

Name:	**KHAN, FARZANA Y**
Department/School/Division:	**SM-DN-Biomedical Graduate Studies**
HS Training Completed:	**Yes**
Training Expiration Date:	
Name of course completed:	**CITI Protection of Human Subjects Research Training - ORA**
GCP Training Completed:	**No**
Training Expiration Date:	
Name of course completed:	

Name:	**ELWASILA, AHMED N**
Department/School/Division:	**The College**
HS Training Completed:	**No**
Training Expiration Date:	
Name of course completed:	
GCP Training Completed:	**No**
Training Expiration Date:	
Name of course completed:	

Name:	**PALERMO, EMMA H**
Department/School/Division:	**Research Services**
HS Training Completed:	**Yes**
Training Expiration Date:	
Name of course completed:	**CITI Protection of Human Subjects Research Training - ORA**
GCP Training Completed:	**No**
Training Expiration Date:	
Name of course completed:	

Name:	**KAHN, ADAM J**
Department/School/Division:	**PS-Mental Health Services**
HS Training Completed:	**Yes**
Training Expiration Date:	
Name of course completed:	**CITI Protection of Human Subjects Research Training - ORA**
GCP Training Completed:	**No**
Training Expiration Date:	
Name of course completed:	

Name:	**YOUNG, AMANDA**
Department/School/Division:	**Health System**
HS Training Completed:	**Yes**
Training Expiration Date:	
Name of course completed:	**CITI Protection of Human Subjects Research Training - ORA**
GCP Training Completed:	**Yes**
Training Expiration Date:	**05/11/2024**
Name of course completed:	**CITI Good Clinical Practice (GCP) - OCR**

Name:	**DE PAIVA, STEICY P**
Department/School/Division:	**The College**
HS Training Completed:	**Yes**
Training Expiration Date:	
Name of course completed:	**CITI Protection of Human Subjects Research Training - ORA**
GCP Training Completed:	**No**
Training Expiration Date:	
Name of course completed:	

Name:	**GRANT, SYDNEY N**
Department/School/Division:	**The College**
HS Training Completed:	**Yes**
Training Expiration Date:	
Name of course completed:	**CITI Protection of Human Subjects Research Training - ORA**
GCP Training Completed:	**No**
Training Expiration Date:	
Name of course completed:	

Name:	**KAUR, ISHA**
Department/School/Division:	**The College**
HS Training Completed:	**Yes**
Training Expiration Date:	
Name of course completed:	**CITI Protection of Human Subjects Research Training - ORA**
GCP Training Completed:	**Yes**
Training Expiration Date:	**01/06/2025**
Name of course completed:	**CITI Good Clinical Practice (GCP) - OCR**

Name:	**KOROBKO, MILANA**
Department/School/Division:	**Health System**
HS Training Completed:	**Yes**
Training Expiration Date:	
Name of course completed:	**CITI Protection of Human Subjects Research Training - ORA**
GCP Training Completed:	**No**
Training Expiration Date:	
Name of course completed:	

Name:	**CHANG, CHERYL**
Department/School/Division:	**Law**
HS Training Completed:	**Yes**
Training Expiration Date:	
Name of course completed:	**CITI Protection of Human Subjects Research Training - ORA**
GCP Training Completed:	**Yes**
Training Expiration Date:	**09/13/2024**
Name of course completed:	**CITI Good Clinical Practice (GCP) - OCR**

Name:	**YOON, JOYCE**
Department/School/Division:	**Health System**
HS Training Completed:	**No**
Training Expiration Date:	
Name of course completed:	
GCP Training Completed:	**No**
Training Expiration Date:	
Name of course completed:	

Disclosure of Significant Financial Interests*
Does any person who is responsible for the design, conduct, or reporting of this research protocol have a **FINANCIAL INTEREST**?
No

Penn Intellectual Property*
To the best of the Principal Investigator's knowledge, does this protocol involve the testing, development or evaluation of a drug, device, product, or other type of intellectual property (IP) that is owned by or assigned to the University of Pennsylvania? Please refer to the Patent and Tangible Research Property Policies and Procedures.
Yes

If yes, please provide any readily available information on such IP. For example, a brief description of the IP, any relevant docket number (if disclosed to the Penn Center for Innovation (PCI), patent application or patent numbers, inventor's names, and/or other relevant details.
Disclosure ID: Web_501954 Inventor: Heather Nuske I have designed a mobile platform application combined with remote sensor physiological recording to identify and alert teachers of heightened stress in students with autism spectrum disorder (ASD) and remind of them of evidence-based practices for assistance in deescalating stress and preventing challenging behaviors. Beyond this initial phase of app development, I plan to adapt this for other children who may experience challenges in the classroom, such as those with anxiety or attention deficit hyperactivity disorder, as well as adapting the technology for self-monitoring of physiological stress by children or adults at school or in other community settings, such as home or work places.

Certification
I have reviewed the *Financial Disclosure and Presumptively Prohibited Conflicts for Faculty Participating in Clinical Trials* and the *Financial Disclosure Policy for Research and Sponsored Projects* with all persons who are responsible for the design, conduct, or reporting of this research; and all required Disclosures have been attached to this application.
Yes

The following documents are currently attached to this item:

There are no documents attached for this item.

Study Instruments

Discuss the particulars of the research instruments, questionnaires and other evaluation instruments in detail. Provide validation documentation and or procedures to be used to validate instruments. For well know and generally accepted test instruments the detail here can be brief. More detail may be required for a novel or new instrument. For ethnographic studies identify any study instruments to be used (i.e. for deception studies) and describe in detail where, when and how the study will be conducted and who or what are the subjects of study. Note: For more information on how to conduct ethical and valid ethnographic research, follow the link For oral histories or interviews provide the general framework for questioning and means of data collection. If interviews or groups settings are to be audio taped or video taped describe in detail the conditions under which it will take place. Include a copy of any novel or new test instruments with the IRB submission.

We propose to develop a digital emotional stress alarm smartphone application (KeepCalm) with community partners, that incorporates wearable biosensor heart rate signaling, for parents and teachers to help them manage challenging behaviors in children with autism spectrum disorder. We propose to conduct the KeepCalm study in three phases, Phase 1 representing contextual inquiry (Design Workshops, Qualitative Interviews, Teacher Needs Assessments and Technical Exploration), Phase 2 representing initial preschool/school/home-based Usability Testing of the technology and Phase 3 representing the Pilot Trial of the app in preschools, schools and/or homes. Phase 1. In Phase 1.1, we will invite approximately 10 participants (adults/verbal youth with autism, parent of students with autism, and teachers and classroom aides/behavior support workers who work with students with autism) to each workshop to co-design the KeepCalm app, with our community partners. Design Workshops will be audio-taped and transcribed in order to comprehensively capture and share the feedback and discussion with community partners with our software development team. In Phase 1.2, we will recruit 20 teachers, 20 parents and 10 school administrators to semi-structured interviews on the acceptability, appropriateness and feasibility of the app (Qualitative Interviews). Classroom aides/ behavior support workers or recruited teams will also be asked to participate, if available. Parents will also be asked for their consent to conduct in-class or in-home observations of their children using the app behavioral logging feature and wearable heart rate tracker so to map physiological stress to challenging behavior episodes (Technical Exploration). Teachers and parents will also be invited to participate in a Needs Assessment so to determine their needs to be incorporated in the programming of the app. KeepCalm App. In partnership with the Department of Biomedical Health Informatics at CHOP, we propose to develop the KeepCalm iPhone application, based on our previously developed Mac desktop application for tracking emotional stress over time using commercially available heart rate monitors (see below). Final app design will be in collaboration with community partners, however initial ideas are that the app could display heart rate relative to resting-state per child, in colored bands (e.g. orange = mild stress, red = high stress), based on our previous work on quantifying cardiac stress in children with autism (see Penn IRB proposal #825953). Teachers and parents will also be able to log behavioral data about the children with autism, including the behavior/context that occurred before any challenging behavior and the supports/strategies they used to manage their childs stress. Sharing of data about the childs management of stress will be sent across home and school in weekly email digests (e.g. top 5 strategies for managing XXXXs stress this week). If adult participants have an iPhone, we will ask them to download the app on their iPhone as we want the app to be embedded in everyday behavior. The initial version will be iPhone only, an Android app version will be made at a later stage. The application may also be designed for iPads/tablets. If any of the adult participants do not have an iPhone, we will loan them one for the week. The app will be password protected and the account will be deleted after the usability testing week. Commercially- Available Heart Rate Monitors Based on our previous benchmarking project (Penn IRB proposal #825953), where we compared commercially-available wearable heart rate monitors against traditional wired ECG, we identified the PulseOn and Mio Fuse wristbands, and the Polar H7 chest-strap as the models we would like to continue this line of work with (see device manuals, attached). Phase 2. In Phase 2, we will conduct app usability testing with 10 student teams (1-2 preschool or elementary school students with autism, and their teacher and classroom aide/behavioral support worker, therefore consisting of up to 40 total participants) for one week each. Each month we will have up to 10 student teams participating in the study for a total of five months. The research team will perform both in-class and in-home behavior tracking of the teachers, classroom aides, parents and child participants using the app and the heart rate and accelerometer devices, to obtain a first-hand look at the practical experience of the prototype, and to examine the emotion regulation strategies that teachers and parents use with children with autism at preschool,

school and home. Teachers and parents will be asked to identify periods within the testing week (e.g. 3 x 2-hour periods during in-person or distance learning remote academic instruction) to track their students/childs behaviors and their strategy implementation. No audio or visual recordings will be taken during these sessions, instead the app will be used to log child and teacher/parent behaviors, including child challenging behaviors and teacher/parent intervention strategy implementation, so that a number of quality metrics can be computed and analyzed offline: 1) Clinical Decision Support Success: proportion of emotion regulation strategy app push notifications that result in strategy implementation success, as measured during the behavior tracking sessions during the testing week; 2) False Positives/ Negatives: Proportion of alarms that appear not to be associated with an oncoming challenging behavior (e.g. due to child movement)/challenging behaviors that occurred without an alarm, measured during the behavior tracking session); 3) Artifact Removal: number of heart rate artifacts detected during the testing period; and 4) Offline Mode (proportion of time offline mode is activated over the testing week based on accelerometry [movement] data threshold). The research team will also monitor remotely each teams usage of the app during their respective testing period. Depending on preschool/school/home safety protocols and preferences at the time of this phase of the study, in-person observations by researchers may be also conducted. Throughout the testing week, teachers and parents will also take time-stamped qualitative notes in order to correspond significant behavior or events to the respective physiological reactivity. At the end of the testing week, a 30-minute interview will be conducted with every adult of each team to collect feedback and suggestions for the next app update and will be recorded (with permission). Phase 3. In Phase 3, we will conduct a randomized waitlist-controlled pilot trial of the app with 20 child teams each including a teacher, 1-2 students, and the students caregiver, and a one-to-one aide if they have one and are interested in participating. We anticipate around 50% of teachers will have only one student/caregiver and around 50% of students wont have a one-to-one aide sign up to the study. Therefore, we expect to have a total of 60 participants in the trial. Each team will test the app for a 3-month period and the waitlist group will do so after a 3-month waiting period. Participants will be asked to: 1) Attend an intake meeting once your team has signed up (one parent, one child and one teacher at a minimum) held virtually and/or at the childs preschool, school, home, or another preferred location. During this session participants will be individually briefed on the KeepCalm app and baseline assessments will be completed. This may include a standardized child cognitive assessment if not previously conducted/if scores are unavailable. 2) Before app testing, school personnel will participate in an app training session held virtually and/or at the childs preschool or school and will be given access to the app and the heart rate and movement trackers. 3) School personnel participants will then record at least one baseline heart rate of the child to calibrate the apps stress zone notification to that child. This will be done over a 5-minute period using a wristband or chest-strap heart rate monitor (whichever the child prefers) in which the child is engaged in an activity that is relaxing to them that does not involve much movement (e.g., story reading). 4) Students with autism will wear the heart rate tracker (wristband or chest-strap, whichever they prefer) and movement tracker (belt-clip) to the extent they are able to throughout the school day, each school day throughout the three-month testing period. If a device is uncomfortable for a participant, it can be simply taken off. 5) School personnel will use the app with the child each school day during the three-month app testing period. This may include tracking the students heart rate and movement, entering child data (triggers/ antecedents, challenging behaviors/skills, and intervention strategies), referencing the daily report, using, and exporting the child data figures, accessing and using the intervention strategies resources embedded in the app and/or using the team messaging feature including sending the students parent afternoon notes. Depending on safety protocols and preferences at the time of this phase of the study, in-person observations by researchers may be also conducted. The research team will also monitor remotely each teams usage of the app during their respective testing period. The initial app version is for iPhones, if you do not have an iPhone, one will be loaned to you for the trial. 6) Parents will also use the app during the three-month app testing period. This may include receiving the auto-generated daily report based on the data their childs team enters each school day, using and exporting the child data figures, accessing and using the intervention strategies resources embedded in the app and/or using the team messaging feature including sending their childs teacher morning notes. The initial app version is for iPhones, if you do not have an iPhone, one will be loaned to you for the trial. 7) After app testing has been completed, school personnel and parents will be asked to provide feedback to the research team regarding your experience with the app through a 30-minute interview with a member of the research team. 8) Completing a series of surveys about yourself and/or your child/the student with autism, and your experience using the KeepCalm app. 9) Allow the research team to have access to students Individualized Education Program (IEP) and behavioral plans, if required, for individualizing the app for the student with autism or obtaining past child standardized cognitive assessment scores. As described above, depending on preschool/school/home safety protocols and preferences at the time of

this phase of the study, in-person observations by researchers may be also conducted. No audio or visual recordings will be taken during these sessions, instead the app will be used to log child and teacher/parent behaviors, including child challenging behaviors and teacher/parent intervention strategy implementation, so that a number of quality metrics can be computed and analyzed offline: 1) Clinical Decision Support Success: proportion of emotion regulation strategy app push notifications that result in strategy implementation success, as measured during the behavior tracking sessions during the testing week; 2) False Positives/Negatives: Proportion of alarms that appear not to be associated with an oncoming challenging behavior (e.g. due to child movement)/challenging behaviors that occurred without an alarm, measured during the behavior tracking session); 3) Artifact Removal: number of heart rate artifacts detected during the testing period; and 4) Offline Mode (proportion of time offline mode is activated over the testing week based on accelerometry [movement] data threshold). Questionnaires/ Standardized Instruments. Phase 1. We will also ask participants to fill out the following paper copies of surveys about their perspective on the app, and themselves and the student(s) with autism they are representing: - Acceptability of Intervention Measure (AIM) (Teacher/Aide/Parent) - Intervention Appropriateness Measure (IAM) (Teacher/Aide/Parent) - Feasibility of Intervention Measure (FIM) (Teacher/Aide/ Parent). - Demographic Questionnaire (Teacher/Aide/Parent/Adult), - the Social Communication Questionnaire (SCQ) (Parent). Phase 2. The parents and teachers/aides will fill out a Participant Contact Information Sheet (see attached). Each participant will also complete a Qualtrics based survey (online survey system used by UPenn) regarding about themselves and/or the student with autism, and their experience using the app- based intervention. The following surveys may be included (all attached): - Post-Study System Usability Questionnaire (Teacher/Aide/Parent) - Demographic Questionnaire (Teacher/Aide/Parent) - Comfort Rating Scales (Child, if possible) - Engagement vs. Disaffection with Learning (Teacher/Aide/Parent) - The Institute for Basic Research Modified Overt Aggression Scale (Teacher/Aide/Parent) - Childs Challenging Behaviour Scale (Parent) - Children's Alexithymia Measure (Parent) - Emotion Dysregulation Inventory (Parent) - Emotion Regulation Checklist (Parent) - Home Situations Questionnaire (Parent) - School Situations Questionnaire (SSQ) (Teacher/Aide) Home Situations Questionnaire (HSQ) (Parent) - Motivation Assessment Scale (Teacher/Aide/Parent) - Social Communication Questionnaire (SCQ) (Parent) - System Usability Scale (SUS) (Teacher/Aide/Parent) - Acceptability of Intervention Measure (AIM) (Teacher/Aide/Parent) - Intervention Appropriateness Measure (IAM) (Teacher/Aide/Parent)- Feasibility of Intervention Measure (FIM) (Teacher/Aide/ Parent) - User Burden Scale (UBS) (Teacher/Aide/Parent) Vineland Adaptive Behavior Scales (Parent). All questionnaires are attached. A standardized IQ assessment (Stanford Binet Intelligence Scales 5th edition) will also be conducted with the child at a time convenient for the family (remotely via video conferencing telehealth session, if preferred). The Behavioral Interference Coding Scheme (BICS) clinician report scale will also be used after the IQ assessment, to determine if any interfering behaviors could account for IQ scores. Phase 3. Each participant will complete a Redcap- or Qualtrics-based survey (online survey systems used by UPenn) regarding themselves and/or the student with autism, and their experience using the KeepCalm app. Primary outcome measures include: 1) System Usability Scale (SUS) (Teacher/Aide/Parent); 2) Acceptability of Intervention Measure (AIM) (Teacher/Aide/Parent); 3) Intervention Appropriateness Measure (IAM) (Teacher/Aide/Parent); 4) Feasibility of Intervention Measure (FIM) (Teacher/Aide/ Parent); and a qualitative interview which will assess the intervention's usability, appropriateness, feasibility, and acceptability in a qualitative interview format (Teacher/Aide/Parent). Secondary outcome measures include: 1) School Situations Questionnaire (SSQ) which assesses challenging behaviors within the context of school. The scale assesses both the presence and the severity of challenging behaviors by asking the teacher whether or not a given behavior occurs for that child and to rate the severity. The scale yields two summary scores. The first is the number of problems score which is a sum of the number of problems endorsed, ranging from 0-8 with higher scores indicating greater problems endorsed. The second is the mean severity, calculated as the mean severity for the items endorsed, ranging from 1 to 9 with higher numbers indicating more severe problems (Teacher/Aide); 2) Institute for Basic Research Modified Overt Aggression Scale (IBR-MOAS) which measures the frequency and severity of aggressive behavior episodes. The scale is divided into four components: verbal aggression, aggression against property, autoaggression, and physical aggression. There are 4 items in each category, scored from 0-4 (with higher numbers indicating greater severity) and raters can select as many items as are relevant in the category. The items are then summed within each category to create a summed category score, and then each category is multiplied by its specified weight to give a total weighted aggression score, ranging from 0 to 100, with higher scores indicating greater problems with aggression (Teacher/Aide/Parent); and 3) the Emotion Dysregulation Inventory (EDI) The Emotion Dysregulation Inventory (EDI) measures emotion dysregulation by asking raters to identify how much of a problem certain emotions and behaviors are for the person being rated. The scale

consists of 66 items that are rated for how much of a problem the behavior has been in the last 7 days ("not at all", "mild", "moderate", "severe", "very severe"). These ratings are converted into a numerical rating from 0 ("not at all") to 4 ("very severe"), and then summed to create a total score ranging from 0-264, which higher scores indicating greater emotion dysregulation (Teacher/Aide/Parent). All questionnaires are attached. Other pre-specified measures include: 1) Clinical Decision Support Success: proportion of emotion regulation strategy app push notifications that result in strategy implementation success, as measured during the behavior tracking sessions during the testing week; 2) False Positives/Negatives: Proportion of alarms that appear not to be associated with an oncoming challenging behavior (e.g. due to child movement)/challenging behaviors that occurred without an alarm, measured during the observation session; 3) Artifact Removal: number of heart rate artifacts detected during the testing period; and 4) Offline Mode (proportion of time offline mode is activated over the testing week based on accelerometry [movement] data threshold). Participants will also complete Demographics Questionnaire (Teacher/Aide/Parent) on Qualtrics or Redcap and parents will complete the Social Communication Questionnaire (SCQ) to verify their childs autism diagnosis. If children have recently completed an IQ assessment at school, we will ask for those scores as documented on their IEP. If access to the scores is not possible or no recent assessment has been conducted, Dr. Nuske (PI) will complete a Stanford Binet cognitive assessment as a measure of IQ at a location most convenient to the team (preschool, school or home).

Group Modifications

Describe necessary changes that will or have been made to the study instruments for different groups.
Two items have been added to the Comfort Rating Scales, to measure autism-specific factors relating to sensory sensitivities, Physical Sensation and Attention to Sensation. We used this modification in our previous study (Penn IRB #825953). The Institute for Basic Research Modified Overt Aggression Scale (IBR-MOAS) will be adapted for school-aged children to include the other challenging behaviors of interest (aggression, self-injury, property destruction, escape, climbing furniture, meltdowns).

Method for Assigning Subjects to Groups

Describe how subjects will be randomized to groups.
Treatment groups will be block randomized.

Administration of Surveys and/or Process

Describe the approximate time and frequency for administering surveys and/or evaluations. For surveys, questionnaires and evaluations presented to groups and in settings such as high schools, focus group sessions or community treatment centers explain how the process will be administered and who will oversee the process. For instance, discuss the potential issues of having teachers and other school personnel administer instruments to minors who are students especially if the content is sensitive in nature. Describe the procedure for audio and videotaping individual interviews and/or focus groups and the storage of the tapes. For instance, if audio tape recording is to be used in a classroom setting, describe how this will be managed if individuals in the class are not participating in the study. Explain if the research involves the review of records (including public databases or registries) with identifiable private information. If so, describe the type of information gathered from the records and if identifiers will be collected and retained with the data after it is retrieved. Describe the kinds of identifiers to be obtained, (i.e. names, social security numbers) and how long the identifiers will be retained and justification for use.
Phase 1. The two Design Workshops (each approximately 1.5 hours) took place in August 2018, at the Center for Mental Health, or 3535 Market Street, Floor 3, Philadelphia, PA 19104, or at the Center for Autism Research, Roberts Center for Pediatric Research, Childrens Hospital of Philadelphia, 2716 South St, Floor 5, Philadelphia, PA 19146. The PI, Dr. Heather Nuske coordinated the workshops, with the help of the investigators and/or key personnel listed on the project. Surveys will be collected during the workshops. Audio tapes will be taken of the workshops to ensure the discussion and feedback from community partners are comprehensively captured. The contextual inquiry work (Qualitative Interviews, Technical Exploration and Needs Assessment) will be conducted by the research team, under the supervision of Dr. Heather Nuske. Qualitative Interviews will be conducted however is most comfortable for each participant (e.g. in person or via phone). Interviews will be recorded (with permission) for offline qualitative analysis. Technical Exploration child behavior tracking sessions and Needs Assessments will be conducted with teachers and parents at the childs preschool/school/home, according to their preferences and COVID-19 safety protocols, at a time that fits with their schedule. Needs Assessments will also be offered remotely (via phone or video call). As preparatory to the contextual inquiry work described above and throughout the project, the studys expert advisory board

will convene to discuss the COVID-19 pandemic adaptations, map out the assumptions of the app to be further investigated in this phase, and generally discuss study methods and implementation throughout the project. Phase 2. The usability testing with each childs team will be conducted in the childs preschool, school or home. The enrollment meetings (virtual or in-person) with each of the childs team members will involve taking informed written consent, participant characterization (cognitive and language assessment), and video training and review on how to use the app and devices. Questionnaires will be completed via the Qualtrics online survey system. The behavior tracking for the study will involve teachers and parents logging childrens challenging behaviors and any emotion regulation/ behavior management strategies they implement during identified periods within the testing week (e.g. 3 x 2-hour periods during in-person or distance learning remote academic instruction). No AV recordings will be taken during these sessions as logged behaviors will be time stamped within the app. Data will be used to identify 1) Clinical Decision Support Success: proportion of emotion regulation strategy app push notifications that result in strategy implementation success, as measured during the behavior tracking sessions during the testing week; 2) False Positives/Negatives: Proportion of alarms that appear not to be associated with an oncoming challenging behavior (e.g. due to child movement)/ challenging behaviors that occurred without an alarm, measured during the behavior tracking session); 3) Artifact Removal: number of heart rate artifacts detected during the testing period; and 4) Offline Mode (proportion of time offline mode is activated over the testing week based on accelerometry [movement] data threshold). Depending on preschool/school/home safety protocols and preferences at the time of this phase of the study, in-person observations by researchers may be also conducted. Throughout the testing week, teachers and parents will also take time-stamped qualitative notes in order to correspond significant behavior or events to the respective physiological reactivity. At the end of the testing week, a 30-minute interview will be conducted with every adult of each team to collect feedback and suggestions for the next app update and will be recorded (with permission). At the end of the usability testing week, a meeting will be held with each adult participant to review the childs data and conduct an interview on app prototype usability. As the KeepCalm app will continually monitoring heart rate in children during app testing, it is possible the data collected could help to screen for heart rate or cardiac abnormalities in the children that may need to be followed up with their healthcare provider. Parents will be requested to give their permission for Dr. Nuske to communicate any heart rate abnormalities detected as part of the administered Qualtrics survey. The 'KeepCalm App Detection and Communication Plan for Cardiac Abnormalities' plan is attached. Phase 3. The pilot trial testing of the app with each pod/child team will be conducted in the childs preschool, school, and/or home. All meetings will be 30-60 mins and will be delivered either in person or virtually, depending on the participants preference. Meetings will be video/audio recorded for team training and/or transcription purposes. Video and audio files will be stored on a password-protected and HIPAA compliant server and will only be accessible by the research team who have each completed HIPAA training. Questionnaires will be completed via the Qualtrics or Redcap online survey system (see Study Instruments). Child participants will not complete any measures themselves. All information collected through surveys or through the KeepCalm app (childrens nickname, age, triggers, behaviors and intervention strategies and heart rate, and teachers/aides/parents name and email phone number) will be stored in HIPAA compliant servers and will only be accessible by the research team. As described above, depending on preschool/school/home safety protocols and preferences at the time of this phase of the study, in-person observations by researchers may be also conducted. No audio or visual recordings will be taken during these sessions, instead the app will be used to log child and teacher/ parent behaviors, including child challenging behaviors and teacher/parent intervention strategy implementation, so that a number of quality metrics can be computed and analyzed offline: 1) Clinical Decision Support Success: proportion of emotion regulation strategy app push notifications that result in strategy implementation success, as measured during the behavior tracking sessions during the testing week; 2) False Positives/Negatives: Proportion of alarms that appear not to be associated with an oncoming challenging behavior (e.g. due to child movement)/challenging behaviors that occurred without an alarm, measured during the behavior tracking session); 3) Artifact Removal: number of heart rate artifacts detected during the testing period; and 4) Offline Mode (proportion of time offline mode is activated over the testing week based on accelerometry [movement] data threshold).

Data Management

Describe how and who manages confidential data, including how and where it will be stored and analyzed. For instance, describe if paper or electronic report forms will be used, how corrections to the report form will be made, how data will be entered into any database, and the person(s) responsible for creating and maintaining the research database. Describe the use of pseudonyms, code numbers and how listing of such identifiers will be kept separate from the research data.

To ensure the privacy and confidentiality of data for this project we will only store and use the identifiable data at the following locations: 1) Password-protected PCs in locked offices at the University of Pennsylvania. The desktop computer(s) that will access the data will be part of the Center for Mental Health (CMH) domain, with Windows Active Directory group policies in place to distribute and enforce best-practice desktop security policies. Security and software updates are pushed to the system in a timely manner using desktop management tools (Tivoli/BigFix and Windows Automated Update Service). The data on the desktop computer(s) can be encrypted with Bitlocker, PGP Whole Disk Encryption with PGP Virtual Disk which will provide an added layer of data security, or FileVault; 2) On Penn Box, a HIPAA-compliant server used for project file sharing in the context of the teams remote work on the project; and 3) A server at the University of Pennsylvania within the facilities managed room in the data center. A Senior LAN Consultant will upload the data onto the secure production servers (environment and security practices described above). Physical media that are received from the distributer or any physical copies of the data will be encrypted while at rest and will be held in a locked cabinet within the CMH office. Additionally, all PHI data hosted on the server will be accessed over an encrypted VPN connection. Individually identifiable or deducible data will not be transmitted by unsecured telecommunications, which include the Internet, email, and electronic File Transfer Protocol (FTP). Further, the data will not be physically moved or transmitted in any way from the CMH servers or secured desktop(s) without written approval. Physical Security Servers are hosted in dedicated virtual machines running on Dell SAN hardware in the In-formation Systems and Computing facilities managed computer room. The hosting environment SAN and Host Bus Adapters are in a locked Dell rack housed in the Computer Room with restricted door card access to authorized personnel only. There is 24-hours camera surveillance. Business Continuity Server environments get redundant power from independent power feeds. In addition, each of the power sources is UPS protected. There is a Halon fire suppression system, with alarm points below the raised floor and in the ceiling. The virtual machines are hosted in VMWare ESX environments connected to a Dell SAN for shared storage. All virtual machines are stored on the SAN. To minimize downtime caused by hardware failure, the environment is configured for redundancy with multiple ESX hosts, multiple Host Bus Adapters, multiple SAN Switch ports, multiple storage processors, and RAID 5 storage. The server environments are replicated to a secondary site at 3650 Chestnut Street, which has equivalent physical security and also employs all of the security best practices outlined below. The servers are administered by a team of four full-time professional IT staff. The team has over 50 years of combined experience configuring and supporting Windows servers, and all of the staff attend technical training regularly to stay current in best practices for configuring and securing Windows and VMWare environments. Server Security Best Practices In keeping with SANS and Microsoft best practices, all software services and corresponding ports on the servers that are known to be substantial security risks and which are not used by CMH resources are disabled including telnet, and ftp. Security patches are applied promptly and there are standard processes in place for preventive maintenance and monitoring of the servers. Hardware Firewalls - All servers reside behind a cluster of Juniper SSG520 firewalls. A Juniper SSG520 appliance configured in high availability mode acts as a secure gateway between PennNet/Internet (Untrusted Zone) and server resources behind the firewall. A custom firewall policy is developed for each resource hosted on each of the virtual machines. All policies are developed based on service port and PennNet-only IP addresses. VLAN - A Foundry Switch in the TSS managed rack is configured for 4 VLANs to support traffic segmentation behind the SSG520. LTS has access to each VLAN, giving us the ability to place each virtual machine in the appropriate VLAN for another layer of security. SSL Encryption for Web Services - When hosting web servers we only support the use of HTTPS with an SSL certificate to minimize vulnerabilities and exploits common on the standard HTTP port. All port 80 traffic is re- directed to port 443. SSL VPN An SSL VPN supports encryption of traffic between servers and client desktops and laptops. Password Policy - A complex password policy, meeting Microsoft complex password requirements, is in effective in the CMH domain. The password policy requires all CMH domain users to change their domain password every 180 days. Data entered into the KeepCalm app will be stored in a custom-built Amazon server. With regards to security, the KeepCalm app uses Amazon Cognito, which requires multi factor authentication for all users. All data are encrypted in transit via HTTPS/SSL/TLS. The server is necessary to allow for sharing of data amongst educational team members of childrens teams and to allow the research team remote access to the data. Point members of the research team (henceforth Research Specialists) will be responsible for data entry and database management. The Principal Investigator and Research Specialists will ensure that all study personnel are familiar with standardized data entry practices. The Research Specialists will also complete random audits of study files to ensure forms are completed in their entirety and stored in IRB-approved methods. Access to any PHI data will be limited to CMH staff and authorized Research Assistants as well as to the small team of full-time professional IT staff that support the CMH servers

and desktops. In order to be added to the protocol and receive PHI access, CMH staff will demonstrate completion of HIPAA training and will abide by the security procedures enforced within the Windows Active Director domain. At the conclusion of this study, a CMS Certification of Destruction certifying the proper destruction of all data obtained will be completed if destruction is warranted. Lastly, all output containing individual identifiable information is treated as confidential data. This information is never transferred electronically via email or other protocols. Shredders are used on any printed material containing individual identifiers. Clinical personnel assessing children will hold a Bachelors, Masters or doctorate degree. The PI, Heather Nuske who holds a PhD in Psychology will oversee all phases of the project and supervision of any Research Assistants on the testing team.

Radiation Exposure*
Are research subjects receiving any radiation exposure solely because they are enrolled in this protocol? (e.g. X-rays, CT, Fluoroscopy, DEXA, pQCT, FDG, Tc-99m, etc.)?IF YES, the protocol must be approved by the RRSC (Radiation Research Safety Committee). Consult EHRS web site: www.ehrs.upenn.edu/protocols/radiohuman.html for more information.If you have questions, email jjesik@ehrs.upenn.edu or kavyap@upenn.eduIf your protocol includes Nuclear Medicine Procedures, the protocol must be reviewed by the Nuclear Med Operations Committee: https://redcap.link/NMOPS
No

Human Source Material*
Does this research include collection or use of human source material (i.e., human blood, blood products, tissues or body fluids)? IF YES, consult the EHRS web site: www.ehrs.upenn.edu/programs/bio/bbpathogens.html for information on OSHA Bloodborne Pathogens requirements (training, vaccination, work practices and Exposure Control Plan). If you have questions, call 215-898-4453.
No

Image Guided Biopsies*
Does the research involve imaging guided biopsy? IF YES, please contact the Clinical Imaging Core. See https://www.med.upenn.edu/cbi for more details. Any questions should be directed to the Director of Research Operations, Dept of Radiology, Kathleen Thomas.
No

Computerized Tomography (CT) Studies*
Does the protocol involve CT scans that are not considered standard of care and are being performed for research purposes?IF YES, complete the CACTIS Committee Application: https://is.gd/CACTIS and consult CACTIS website: http://www.uphs.upenn.edu/radiology/research/labs/cactis/ for application requirements.
No

CAMRIS and MRI Studies*
Is an MRI scan being performed for research only and NOT considered standard of care (example: specific scanner, parameters or solely for the purposes of research)?NOTE: Research/non-standard use of MRI may include but is not limited to any of the following: Situations in which MRI results may impact subjects current clinical care plan or treatment decisions, such as:The study requires a customized report with specifics regarding the study protocol (i.e., specific measurements or details); Introduction of a device of any kind during the MRI that is not used during a 'standard of care' type scan.Your MRI is not consistent with standard care time points for MRI imaging.Your MRI is not paid for by insurance.IF YES, consult CAMRIS website: https://www.med.upenn.edu/camris/application-and-faq.html for application requirements and required institutional consent form language.
No

Cancer Related research not being conducted by an NCI cooperative group*
Does this protocol involve cancer-related studies in any of the following categories? Therapeutic, Prevention, Supportive Care, Screening, Early Detection, or Diagnostic, Epidemiologic, Observational, Outcome, Ancillary or Correlative. For a description of these categories, see http://www.ctsrmc.org/submitting_a_protocol.php NCI Cooperative Groups are as follows:Alliance for Clinical Trials in OncologyNCI Clinical Trials Group (Canadian Cancer Society) (NCCTG)Children's Oncology Group (COG)NRG Oncology GroupECOG-ACRIN Cancer Research GroupSouthwest Oncology Group (SWOG) IF YES, the protocol must be submitted to the Cancer Center's Clinical Trials Scientific Review Committee for scientific review and approval prior to obtaining IRB approval. Consult the

CTSRMC website: www.ctsrmc.org for application requirements
No

HIPAA / Protected Health Information
Does the research proposal involve accessing (viewing / using), collecting, or disclosing of protected health information (PHI) directly from participants or their medical or dental record for research purposes?
No

CHPS Resources*
Does the research involve CHPS resources?
No

HUP Inpatient Nursing Resources
Does this research include an inpatient admission at HUP?
No

If the answer is YES, indicate which items is is provided with this submission:

Use of UPHS services*
Does your study require the use of University of Pennsylvania Health System (UPHS) services, tests or procedures , whether considered routine care or strictly for research purposes? (UPHS includes all Penn hospitals and clinical practices, including the Clinical Care Associates network of community practices). Examples of UPHS services/tests/procedures includes the Clinical Translational Research Center (CTRC), laboratory tests, use of the pathology lab, cardiovascular imaging tests or radiology imaging tests (whether being billed via the Service Center or through UPHS), other diagnostic tests & procedures and associated professional services, etc.
No

Veteran's Affairs (VA) Patients or Subjects
Does your study involve data from Veteran's Affairs (VA) patients or subjects?
No

If yes, was this approved by the Philadelphia VA?

No

Out of State Research
Will any Penn personnel conduct any research activities outside of the State of Pennsylvania?
No

Research involving Virtua Health
Will any Penn personnel conduct any research activities at a Virtua Health site location, OR in collaboration with Virtua Health System personnel, OR using any Virtua Health System resources (e.g., medical records)?
No

Primary Focus*
Sociobehavioral (i.e. observational or interventional)

Protocol Interventions

x	**Sociobehavioral (i.e. cognitive or behavioral therapy)**
	Drug
x	**Device - therapeutic**
	Device - diagnostic (assessing a device for sensitivity or specificity in disease diagnosis)
	Surgical
x	**Diagnostic test/procedure (research-related diagnostic test or procedure)**
	Obtaining human tissue for basic research or biospecimen bank
x	**Survey instrument**
	None of the above

The following documents are currently attached to this item:

There are no documents attached for this item.

Sponsors

Business Administrator

Name:	**ENGLISH, LATONA**
Dept / School / Div:	**4423 - PS-Mental Health Services**
Phone:	**215-573-7063**
Fax:	**215-349-8715**
Pager:	
Email:	**latona.english@pennmedicine.upenn.edu**

Department budget code

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Funding Sponsors

Name:	**NATIONAL INSTITUTES OF HEALTH**
Type:	**UPENN Federal**

Funding sponsors billing address
If you have selected a commercial or industry sponsor, please provide the appropriate address and contact information for the Sponsor for the purposes of billing for IRB review fees (initial review, continuing review and convened modification fees apply here). If the Sponsor is not industry/ commercial, this information is not necessary to provide with your application.
N/A

Funding sponsors gift
Is this research being funded by a philanthropic gift?
Yes

Regulatory Sponsor

IND/IDE Sponsor

none

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Industry Sponsor

None

Project Funding*
Is this project funded by or associated with a grant or contract?
Yes

Selected Proposals

Proposal No	**Title**
10073891	**Reducing Challenging Behaviors In Children With Autism Through Digital Health**

Sponsor Funding
Is this study funded by an industry sponsor?
No

Status of contract

The following documents are currently attached to this item:

There are no documents attached for this item.

Multi-Center Research

Penn as lead
1. Is this a multi-center study where Penn is serving as the Lead Site or the Penn PI is serving as the Lead Investigator?
Yes

Management of Information for Multi-Center Research
This study represents a research partnership between UPenn and CHOP but at CHOP no human subjects research will take place (this takes place via Penn, at homes, preschools and schools).

Penn irb of record
2. Is this a multi-center study where the Penn IRB will be asked to serve as the IRB of Record for other external study sites?
Yes

Other Sites

Site:	**Children's Hospital of Philadelphia**
Contact:	**Jeffrey Pennington**
Pi:	**Heather Nuske**
Mail:	
Phone:	
Email:	

CHOP operates as a technical site only for the study. Jeffrey Pennington contracted an outside mobile developer who is developing the technology tested in the study. They have no direct contact with any research participants.

Protocol

Abstract
The primary research goal of the proposed project is to develop a digital emotional stress alarm smartphone application that incorporates wearable biosensor heart rate signaling, for parents and teachers to help them manage challenging behaviors in children with autism spectrum disorder. The secondary aims are to field test the app at home and school and establish viable community-based physiological stress recording methods to be used as treatment outcome in intervention studies.

Objectives

Overall objectives
The primary goal of this project is to develop and test an app for managing challenging behaviors in children with autism, incorporating physiological signaling from a commercially-available wearable device, so to measure stress-related triggers to behavior and support the implementation of evidence-based strategies for minimizing challenging behaviors. With this goal, there are two specific aims that will be worked towards. Phase 1 of the project is to design the content, features, and layout of each module of the app-based intervention program using design workshops, in partnership with key stakeholder groups (parents, teachers, teacher aides, and individuals with autism) and with the Translational Informatics Unit at the Children's Hospital of Philadelphia, and conduct contextual inquiry work through stakeholder interviews, behavior tracking sessions and needs assessments. Phase 2 of the project is to prototype, test, and review the app through usability testing with 10 school teams (including 1-2 children with ASD, their teacher, classroom aide/behavioral support worker, and their parents). Phase 3 of the project will be to test the developed app in a pilot randomized waitlist control trial.

Primary outcome variable(s)
The primary outcome variables are app usability, feasibility, acceptability, appropriateness, and burden. This will be tested using the Post-Study System Usability Questionnaire, the System Usability Scale (SUS), Acceptability of Intervention Measure (AIM), Intervention Appropriateness Measure (IAM), Feasibility of Intervention Measure (FIM), User Burden Scale (UBS), and a 30-min interview about app usability at the end of each week- long usability testing and pilot trial.

Secondary outcome variable(s)
Although full app effectiveness will not be tested during the usability testing and pilot trial, the proximal outcome measures to be used in the future randomized control trial will be piloted during these project phases. These include artifact removal rates, offline mode activations (due to excessive movement), false negative rates (number of challenging behaviors that occur without a prior app alarm), early true positive rates (number of emotional learning opportunities provided because the app detected stress signals), and clinical decision support success (proportion of emotion regulation strategy app push notifications that result in strategy implementation success). We will also pilot other more distal outcome measures to be used in the future RCT, including the following questionnaires: the Engagement vs. Disaffection with Learning, Childs Challenging Behaviour Scale, Children's Alexithymia Measure, Emotion Dysregulation Inventory, Emotion Regulation Checklist, Home Situations Questionnaire, School Situations Questionnaire, Institute for Basic Research Modified Overt Aggression Scale and Motivation Assessment Scale.

Background
Challenging behaviors in children with autism spectrum disorder (ASD) have a devastating impact on family well-being (Lecavalier, Leone, & Wiltz, 2006), predict teacher burnout (Hastings & Brown, 2002), and are the most frequent reason youth with ASD are hospitalized (Siegel & Gabriels, 2014). Challenging behaviors top parents' and teachers' lists of problems they want to address (Azad & Mandell, 2016). While challenging behaviors are triggered by different factors (including learnt patterns of responding) and serve different functions, stress-related factors are among the most difficult to treat in individuals with ASD (Powers, et al., 2014). Additionally, they are the most difficult to predict as children with ASD often have difficulty communicating their distress before it is too much for them to handle (Hedman, et al., 2012 and Nuske, Vivanti, & Dissanayake, 2013). However, stress can be

detected through physiological signals (Thayer, Ahs, Fredrikson, Sollers, & Wager, 2012 and Lazarus, Speisman, & Mordkoff, 1963). For example, two case studies of individuals with ASD have shown elevated heart rate before challenging behavior episodes (Barrera, Violo, & Graver, 2007 and Freeman, Grzymala-Busse, Riffel, & Schroeder, 2001). Our pilot data from children with ASD similarly show 21% increase in heart rate in the 2 minutes prior to challenging behavior (Nuske, et al., in prep). Therefore, physiological signaling may provide fine-grained information on the occurrence of stress-triggered behavioral issues. Two additional barriers hinder the evidence-based treatment of challenging behaviors in community settings: caregivers do not always have the time to take, organize and analyze data on what happens before and after challenging behavior episodes (the antecedent-behavior-consequent patterns) and on the success of strategies used; and parents and teachers are not often in constant communication to ensure practice consistency across home and school, which is critical to program success (Hunt, Soto, Maier, & Doering, 2003). The app-based intervention we propose will support and increase the efficiency of community programs by including modules to: 1) communicate childrens stress to their caregivers using physiological signaling; 2) ease the data-taking burden on busy teachers and parents with an easy-to-use interface; and 3) share data among team members to facilitate consistent intervention implementation across home and school. Final app content will be based on stakeholder feedback and evidence-based strategies of functional behavioral assessment, positive behavior support and social-emotional learning programs, and will be designed to help caregivers intervene before the onset of challenging behaviors. References Azad, G. & Mandell, D. S. Concerns of parents and teachers of children with autism in elementary school. Autism 20, 435441 (2016). Barrera, F. J., Violo, R. A. & Graver, E. E. On the form and function of severe self-injurious behavior. Behav. Interv. 22, 533 (2007). Freeman, R. L., Grzymala-Busse, J. W., Riffel, L. A. & Schroeder, S. R. Analyzing the relation between heart rate, problem behavior, and environmental events using data mining system lers. in Computer-Based Medical Systems, 2001. CBMS 2001. Proceedings. 14th IEEE Sym- posium on 1116 (IEEE, 2001). Hastings, R. P. & Brown, T. Coping strategies and the impact of challenging behaviors on special educators burnout. Ment. Retard. 40, 148156 (2002). Hedman, E. et al. Measuring autonomic arousal during therapy. in Proc. of Design and Emotion 1114 (Citeseer, 2012). Hunt, P., Soto, G., Maier, J. & Doering, K. Collaborative teaming to support students at risk and students with severe disabilities in general education classrooms. Except. Child. 69, 315 332 (2003). Lazarus, R. S., Speisman, J. C. & Mordkoff, A. M. The relationship between autonomic indica- tors of psychological stress: Heart rate and skin conductance. Psychosom. Med. 25, 1930 (1963). Lecavalier, L., Leone, S. & Wiltz, J. The impact of behaviour problems on caregiver stress in young people with autism spectrum disorders. J. Intellect. Disabil. Res. 50, 172183 (2006). Nuske, H. J. et al. Physiological precursors to challenging behaviors in children with ASD. (in prep). Nuske, H. J., Vivanti, G. & Dissanayake, C. Are emotion impairments unique to, universal, or specific in autism spectrum disorder? A comprehensive review. Cogn. Emot. 27, 10421061 (2013). Powers, M. D. et al. Behavioral Assessment of Individuals With Autism: Current Practice and Future Directions. Handb. Autism Pervasive Dev. Disord. Fourth Ed. Siegel, M. & Gabriels, R. L. Psychiatric Hospital Treatment of Children with Autism and Serious Behavioral Disturbance. Child Adolesc. Psychiatr. Clin. N. Am. 23, 125142 (2014). Thayer, J. F., \AAhs, F., Fredrikson, M., Sollers, J. J. & Wager, T. D. A meta-analysis of heart rate variability and neuroimaging studies: implications for heart rate variability as a marker of stress and health. Neurosci. Biobehav. Rev. 36, 747756 (2012).

Study Design

Phase*
Phase I

Design
As detailed above, this project will consist of three phases: 1) the design and contextual inquiry phase, when the Design Workshops, Qualitative Interviews, Technical Exploration and Needs Assessments will be conducted, 2) the test and review phase, when the Usability Testing will be conducted, and 3) the trial phase, when the randomized waitlist Pilot Trial of the KeepCalm app will be conducted.

Study duration
The project will last in total for approximately six years, from 2018 2024.Phase 1.1 (Design Workshops) was completed in 2018 and Phase 1.2 (Qualitative Interviews, Technical Exploration and Needs Assessments) will be conducted in the 2020-2021 school year. Phase 2 (Usability Testing) has already commenced and will be completed in the 2021-2022 school year. Phase 3 (Pilot Trial) will be conducted over one-two school years between 2023 and 2025.

Resources necessary for human research protection
Describe research staff and justify that the staff are adequate in number and qualifications to conduct the research. Describe how you will ensure that all staff assisting with the research are adequately informed about the protocol and their research related duties. Please allow adequate time for the researchers to conduct and complete the research. Please confirm that there are adequate facilities for the research.
All research staff will have human subjects training, will be approved on the IRB and will undergo training on the study protocol with the PI of the study before contact with any human subject data. Between the Center for Mental Health , UPenn and the Center for Autism Research, CHOP, there are adequate facilities for the research.

Characteristics of the Study Population

Target population
Phase 1 of the project will include children with autism, parents of individuals with autism, teachers with experience teaching students with autism, and teacher aides that have or are working with individuals with autism. Exclusion criteria in Phase 1.1 includes individuals with autism that are non-verbal as we will as students to verbally report on their experience. Phases 2 and 3 will include preschool children and elementary school children with autism within the School District of Philadelphia and private schools, as well as their parents, teachers, and classroom aides. Children with autism must qualify as having challenging behaviors including but not limited to aggression, escape behaviour, loud noises, non-compliance, property destruction, rigid/inflexible behaviour, self-injury and transition difficulties. The research team will assure all teachers that their employment status will not be affected by their participation or non-participation in this study.

Subjects enrolled by Penn Researchers
310

Subjects enrolled by Collaborating Researchers
0

Accrual
The proposed study will capitalize on the longstanding partnerships between the Center for Mental Health (CMH) at the University of Pennsylvania (Penn) and the School District of Philadelphia. This proposal involves the recruitment of 140 participants: children with autism: 20 (exploratory work), 15 (rapid-cycle prototyping), 30 (pilot trial); parents: 20 (interviews & exploratory work); teachers: 20 (interviews, exploratory work & needs assessment), 10 (rapid-cycle prototyping), 20 (pilot trial); classroom aides: 5 (rapid-cycle prototyping), 10 (pilot trial); school administrators: 10 (interviews.Having successfully completed several much larger studies within the Philadelphia School System over the past 15+ years, we do not anticipate any difficulty meeting the recruitment and retention goals for this project.

Key inclusion criteria
Phase 1.1 of the project will include individuals at least 6 years of age with autism, parents of individuals with autism, teachers with experience teaching students with autism, and classroom aides that have experience working with individuals with autism. Phases 1.2, 2 and 3 will include preschool children and elementary school children with autism (3-13 years old), as well as their parents, teachers, and classroom aides. Children with autism must qualify as having challenging behaviors including but not limited to aggression, escape behavior, loud noises, non-compliance, property destruction, rigid/inflexible behavior, self-injury and transition difficulties. Adult participants will be required to have access to an iPhone in order to test the app. If they do not have one, one will be provided to them for their usability testing week or participation in the pilot trial.

Key exclusion criteria
Exclusion criteria in Phase 1.1 includes individuals with autism that are non-verbal as we will ask individuals to verbally report on their experience.

Vulnerable Populations

x **Children Form**

Pregnant women (if the study procedures may affect the condition of the pregnant woman or fetus) Form

Fetuses and/or Neonates Form

Prisoners Form

Other

None of the above populations are included in the research study

The following documents are currently attached to this item:

There are no documents attached for this item.

Populations vulnerable to undue influence or coercion
We will try to recruit 1-2 adults with autism to partake in the design workshops. We will emphasize to potential participants that participation in the study is completely voluntary and will not affect their relationship with University of Pennsylvania, their school or any other center or service. We will emphasize to teacher and teacher aide participants that employment status will not be affected by their decision to participate or not participate in this study.

Participant recruitment
Please describe the plan to fairly identify and recruit a group of participants that is reflective of the population under study. If this is a multicenter protocol, the recruitment plan should describe the local (Penn) site's plan. Describe: how potential participants may be identified (review of medical records, Slicer Dicer, DAC reports including referrals from physician offices and clinics);who may approach potential participants;methods to achieve a sample representative of the population being studied;what information may be presented to or discussed with them; andthe context and setting in which recruitment will happen.
The research team anticipates using several recruitment methods. Recruitment for each phase will be through the School District of Philadelphia, the Penn Center for Mental Health participant registry, the study expert advisory board, through the teachers who participated in the design workshops lead by Dr. Nuske (who consented to be contacted for app testing) and through ongoing projects led by Dr. Mandell. We will also use study flyers sent through various relevant organizations and listservs, newsletters, internet postings, social media (Facebook and Twitter), and other recruitment tools as needed, and attend parent workshops and autism-related events to recruit. We will also email the teacher listserv from the School District of Philadelphia. We may also use the Recruitment Enhancement Core at CHOP to find participants. The Recruitment Enhancement Core provides assistance with recruitment plan development and may assist in identifying and contacting potential participants using the CRU, the CHOP Recruitment Registry, social media and internal communication resources. The REC also engages community partners and facilitates outreach on behalf of the research Institute and CHOP research studies. We will also upload recruitment text online at CHOP (at the Center for Autism Research's website, CHOP Clinical Trial Finder Page, and This Week @ CHOP). The same text will be used for all three recruitment avenues (see attached online recruitment text). We will also send Parent Permission to Contact forms home with students along with the study flyer. If parents sign the form and send back to school, we will reach out to them to invite them into the study. We also include Spanish versions of the flyer and Parent Permission to Contact form here. We will use a dual recruitment strategy, whereby teachers or parents may be the first contact. If study participation is initiated by teachers, after obtaining Letters of Support from school principals (if required by the School District of Philadelphia or private schools) and consenting teachers, we will send home the referral contact forms via teachers to recruit the parents of their students. Parents will be given the option of contacting the study team directly or returning a referral form giving consent to be contacted. If study participation is initiated by parents, after consenting parents we will send schools the referral contact forms via parents to recruit the childs teachers or reach out to the schools directly to invite teachers to participate, after obtaining Letters of Support from school principals, if required. Then, parents and teachers who agree to be contacted will be called by the research team to explain the study and invite them to participate. Additionally, once teacher consent is completed, classroom aides will also be invited to participate. We

will also ask consented participants for contact information for the other member of their dyad (e.g., parents of consented teachers), so that we may invite them to participate in the study.

Recruitment Materials
Is the research team using any recruitment materials? These may include but are not limited to: phone call scripts, radio/video scripts, flyers/brochures, internet postings, email, letters to potential participants, letters to patient physicians, My Penn Medicine (MPM), other direct messaging, etc. For guidance regarding recruitment materials, please review the IRB's guidance on Participant Recruitment Materials online:https://irb.upenn.edu/recruitment
Yes

Use of Penn Media & Social Media Services
Will the recruitment plan propose to use any Penn media services (communications, marketing, etc.) for outreach via social media avenues (examples include: Facebook, Twitter, blogging, texting, etc.) or does the study team plan to directly use social media to recruit for the research?
Yes

Please identify which method(s) of social media you will utilize, the content of the text to be used, and the method(s) for posting this information (i.e., using Penn supported communication services). When proposing the text to utilize, please be aware of any social media limitations (i.e., number of characters allowed in a tweet) and any appropriate confidentiality practices necessary to be compliant with posting research recruitment text.NOTE: Penn Medicine must utilize one of the centralized PM Facebook Pages:ClinicalResearch@Penn Facebook pagePenn Medicine Facebook page@PennCancer Facebook pageAll clinical research paid Facebook ads must be listed on Clinical Research @ Penn Facebook page,www.facebook.com/ClinicalTrialsAtPenn. Exceptions to the above must get approval from the Penn Medicine Social Media Committee: pennmedicinesocialmediacommittee@uphs.upenn.edu.
Facebook and Twitter will be utilized for recruitment (see attached social media text).

The following documents are currently attached to this item:

There are no documents attached for this item.

Subject compensation*
Will subjects be financially compensated for their participation?
Yes

The following documents are currently attached to this item:

There are no documents attached for this item.

If there is subject compensation, provide the schedule for compensation per study visit or session and total amount for entire participation, either as text or separate document

Participants in the Phase 1.1 Design Workshops will receive compensation of $20 each for each workshop. Phase 1.2 participants will receive $25 each for participation in the interviews, needs assessments and technical exploration (child in-class or in-home behavior tracking/heart rate data collection sessions). Participants in the Phase 2 Usability Testing will receive $25 each at each time point (entry and exit), for a total of $50. Phase 3 pilot trial participants will receive $50 each at each time point (entry, mid-trial and exit), for a total of $150.

Study Procedures

Suicidal Ideation and Behavior
Does this research qualify as a clinical investigation that will utilize a test article (ie- drug or biological) which may carry a potential for central nervous system (CNS) effect(s)? Centeral nervous system(CNS) effect: the ability of a test article to enter into and potentially interact with the central nervoous system (brain and spinal cord). Clinical Investigation: Any experiment that involves a test article and one or

more human subjects that either is subject to requirements for prior submission to the Food and Drug Adminstration (FDA) under section 505(i) or 520(g) of the Federal Food, Drug, and Cosmetic Act, or is not subject to the requirements for prior submission to the FDA under these sections of the act, but, the results of which are intended to be submitted later to, or held for inspection by, the FDA as part of an application for a research or marketing permit.
No

Procedures
There are three phases of the study: 1) Design and Contextual Inquiry, 2) Usability Testing, and 3) Pilot Trial. Phase 1.1: Design Workshops. This phase of the study has been completed. It took place at the Penn Center for Mental Health, located at 3535 Market Street, Philadelphia, PA, Floor 3, 19104. Five stakeholder groups (parents, teachers, teacher aides, and individuals with autism; total n = 10 per workshop) participated in two Design Workshops, to develop three app modules (1: Physiological stress alarm, 2: ABCs and strategy success logger and 3: Team sharing). App module ideas were finalized during Design Workshops with stakeholders. In Design Workshop 1, we presented initial ideas for the three modules and invite stakeholder feedback on the content, features and use cases of the app, and optimal use cases. Participants were encouraged to write notes and drawings to illustrate their ideas. Dr. Nuske used her expertise in behavioral intervention approaches to frame participants ideas and stimulate discussion on the content, features and use-cases of the app. We also asked participants to fill out the following paper copies of surveys about themselves and the student (s) with autism they were representing: - Post-Study System Usability Questionnaire - Demographic Questionnaire (Family, Adult with autism and Teacher/Teacher aide versions). After the first workshop, the research team (lead by Nuske) and the app-development team (Pennington, Kushleyeva) reviewed the feedback notes and drawings and agreed on a format in which to present the content (What), features (How) and use cases (When) of the app to the stakeholders during the Design Workshop 2. In Design Workshop 2 we gained information about the user interface (layout, usability). After presenting the What, How and When information from ideas generated in Design Workshop 1, the group was divided into two and each were asked to sketch a user interface (app screen layout) of each of the app modules. Dr. Nuske invited the groups to present on their ideas and facilitate a group discussion on the layout of each app module and relevant usability factors. Each Design Workshop lasted for approximately 1.5 hours. Both Design Workshops were audio-taped so systematic reporting of stakeholder feedback can be shared between the research and app- development teams. Following the workshops, the research and app-development team met to re- review the content, features and use cases of each of the app modules in combination with the layout and usability notes and sketches generated. The team reached consensus on each design aspect of the app module prototypes. Following this, Dr. Nuske created a PowerPoint mock-up prototype of the user interface screens and a screen order map, and presented this to the team for review. The prototype was designed as smartphone-compatible for IOS platforms and was based on PowerPoint mock-ups. The app was designed to be smartphone-compatible in order to increase the likelihood that participants will use the app daily. Phase 1.2: Contextual Inquiry. The context inquiry will consist of three parts: 1) Qualitative Interviews, 2) Technical Exploration and 3) Needs Assessments. Qualitative Interviews. To inform iterative development of the app, it is critical to examine the acceptability, feasibility, appropriateness of such an app and associated devices in the context of regulatory and ethical educational frameworks. This will be conducted via teacher, parent and school administrator interviews, in order to understand issues such as teachers use of mobiles/ devices in the classroom, technology self-efficacy/anxiety, perceived value, privacy concerns, and the role of classroom aides in using the app to help to prevent challenging behaviors. Interviewees will indicate their place of preference for the interview if in person and will be offered the option of completing this via phone. Interviews will last 30 mins and will be recorded (with permission). Technical Exploration. In order to further explore the specificity of heart rate increase to challenging behavior in the school and home setting, the best timing for app clinical decision support and the app false positives/negatives (including those related to movement or child factors), parents and teachers will engage in in-class and in-home behavior tracking sessions. After enrollment procedures (same measures as Phase 2), teachers/parents will be given/sent their childs choice of heart rate monitor to wear at preschool, school or home, and, during a period of expected challenging behavior (teacher or parent reported), teachers and parents will log childrens challenging behaviors and emotion regulation/ behavior management strategies in the app alongside continuous heart rate measurement and stress alarm logs. I will also pilot the mBient accelerometers to explore childrens preferences on wrist-worn vs. belt-clip models. Needs Assessments. To ensure that we fully meet teachers and parents needs, and in keeping with the principles of workplace ethnographic research, our needs assessment will include structured in-class observations of teachers (if possible due to COVID-19 policies and preferences),

with follow-up questions using workflow analysis and incident-based cognitive task analysis. Workflow analysis is used to understand how multiple tasks, subtasks, or team work are accomplished according to procedural rules, and can be used to diagram a workflow to understand the context in which systems are implemented. Incident-based cognitive task analysis works to understand barriers and facilitators to achieving a goal (e.g. implementing an emotion regulation strategy) by yielding information about the knowledge and decision-making structures that underlie task performance from real events. During a convenient time for teachers, researchers will observe classroom activities to observe their management of challenging behavior in children with autism. Observations as per above will form the basis of the cognitive task analysis follow-up interview, in which the researcher will refer to events observed to probe for barriers and facilitators to management of stress and prevention of challenging behaviors in children with autism. If an in-class observation is not possible, an interview capturing the same overall themes will be conducted using a semi-standardized interview guide. Participants in each part will also fill out a survey about themselves, and if applicable, the students they teach. Phase 2: Usability Testing. Once the updated prototype is ready for testing, the field-based Usability Testing period will begin with student teams. Each student team will be composed of the individual with autism, their parent, teacher, and classroom aide/behavioral support worker. The research will take place at the home or school of the student with autism. Each of the 10 child teams will test the app for one week, and up to 10 child teams will test the app per testing cycle. Teachers will be provided with a commercially available heart rate recoding monitor (either PulseOn/Mio Fuse wristband, or Polar H7 cheststrap, see attached, whichever is most comfortable for the child) and an mBient accelerometer. Each child will be asked to keep the heart rate and accelerometer on throughout each of the testing school days, during the week-long testing period. We have tested all heart rate models in our previous project on device accuracy and comfort level (Penn IRB# 825953). Each device will connect to the app via Bluetooth. The research team will collect first and last names and emails for team members, so that they can identify one another and receive email notifications, logged behavioral data, and heart rate data from the app. No other information will be collected. Only study members will have access to this information. The app will not collect any other information from participants mobile devices. The app will be removed at the conclusion of the study. In the enrollment session, Dr. Nuske and/or her research team will take a 5-minute baseline recording of the heart rate whilst children watch a relaxing video programmed into the app (Inscapes31), to account for individual differences in baseline physiology. One or two baselines will be taken, at home and/or at school. If two, the lower heart rate averaged over both 5-minute periods (home and school) will serve as the baseline, relative to which the stress alarm zones will be created (e.g. baseline= green zone, stressed= red zone). Dr. Nuske and/or her research team will send instruction videos on how to use or show school staff how to use the heart rate monitor and accelerometer. If possible, the research team will perform in-class and observations of the various stakeholder groups to obtain a first-hand look at the practical experience of the prototype, and to examine the emotion regulation strategies that teachers use with children with autism at school. The research team will also remotely monitor each teams usage of the app during their respective testing period. Throughout the week, teachers and parents will log the childs behavior and emotion regulation/ behavior management strategy they used with their students/child in the app in order to correspond behavior to the respective physiological reactivity. At the end of the testing week, a 30-minute interview will be conducted with teachers, teacher aides and parents to collect feedback and suggestions. The parents and teachers/aides will fill out a Participant Contact Information Sheet (see attached). Each participant will also complete a Qualtrics -based survey (online survey system used by UPenn) regarding about themselves and/or the student/their child with autism, and their experience using the app-based intervention. The following surveys may be included (all attached): - Post-Study System Usability Questionnaire (Parents, Teacher/Aide and Child, if possible given their language level) - Demographic Questionnaire (Family, Adult with autism and Teacher/Teacher aide versions) - Comfort Rating Scales (Child, if possible) - Engagement vs. Disaffection with Learning (Parent, Teacher/Aide and Child, if possible) - Childs Challenging Behaviour Scale (Parent) - Children's Alexithymia Measure (Parent) - Emotion Dysregulation Inventory (Parent) - Emotion Regulation Checklist (Parent) - Home Situations Questionnaire (Parent) - School Situations Questionnaire (SSQ) (Teacher/Aide) - The Institute for Basic Research Modified Overt Aggression Scale (Teacher/Aide) Motivation Assessment Scale (Parent and Teacher/Aide) - Social Communication Questionnaire (Parent) - System Usability Scale (SUS) (Teacher/Aide) - Acceptability of Intervention Measure (AIM) (Teacher/Aide) - Intervention Appropriateness Measure (IAM) (Teacher/Aide) - Feasibility of Intervention Measure (FIM) (Teacher/ Aide) - User Burden Scale (UBS) (Teacher/Aide) Vineland Adaptive Behavior Scales (Parent). A standardized IQ assessment (Stanford Binet Intelligence Scales 5th edition) will also be conducted with the child at a time convenient for the family, via a video call telehealth session or in-person as preferred. The Behavioral Interference Coding Scheme (BICS) clinician report scale will also

be used after the IQ assessment, to determine if any interfering behaviors could account for IQ scores. Feedback on the app will then be considered to create an updated version of the app, which will be used by the next two child teams during the following month. Each child team will be requested to use the app daily during their testing week, especially when the stress alarm signals and after the child experiences an episode of challenging behavior. After each testing cycle (week-long testing with 2 child teams at a time), the app will be updated to incorporate stakeholder feedback. There will be approximately 5 testing cycles during this phase. Phase 3: Each student team will be composed of the child with autism, their parent, teacher, and classroom aide/behavioral support worker (the latter if they have one and they are willing to participate). After screening for eligibility (the SCQ will be administered to parents to verify autism diagnoses in their children), the 20 teams will be randomized to the waitlist (n = 10) or treatment group (n = 10). The treatment (and later, the waitlist) group will use the app for 3 months. After a team has signed up for the study, participants will complete a virtual intake meeting, during which participants will be individually briefed on the KeepCalm app and complete baseline assessments. School personnel will then complete an in-app training session either virtually or in the classroom, during which they will receive access to the KeepCalm app and the heart rate tracker and accelerometer. The research team will also show/instruct teachers how to put the heart rate tracker and accelerometer on the child or assist/instruct the child in putting them on themselves. Participants will download the app onto their own phones or, if they do not have an iPhone, an iPhone will be lent to them for their participation in the project. A member of the research team will also help the school personnel customize the app for their student by showing them how to add the childs profile and their triggers, behaviors/skills and strategies. Standard but editable lists will be programmed into the app for each, including evidence-based proactive and reactive strategies for reducing challenging behaviors and supporting emotion regulation. All teachers recruited will have had professional development and in-class coaching in these strategies by coaches in our center. The research team will administer a fidelity assessment tool to teachers to understand their proficiency in implementing these strategies and provide additional coaching/resources for strategies as needed. Teachers/aides will be provided with a commercially available heart rate tracker (either PulseOn/Mio Fuse wristband, or Polar H7 cheststrap, see attached, whichever is most comfortable for the child) and an mBient accelerometer (see attached). We have tested all heart rate models in our previous project on device accuracy and comfort level (Penn IRB# 825953). Each device will connect to the app via Bluetooth. To sign up to the app, school personnel and parents will enter their name, email and phone numbers and their childs nickname or ID, so that they can each identify the child. Teams will record triggers, behavior/skills and strategies in the app and heart rate and accelerometry data will be recorded from child participants. No other information will be collected. Only team members and the research team will have access to this information. The app will not collect any other information from participants mobile devices. Following this training, school personnel participants will begin testing the app within the classroom. We will support teachers to facilitate their students engagement in research by developing, with advisory board members, and pilot testing an I Can Wear Gadgets protocol. This will likely include heart rate tracker and accelerometer personalization (colors, stickers, etc), visual supports (gadget choice guides, social narratives, first/then boards, etc) and desensitization guidelines (building up from wearing 5 mins, to 10 mins, to 20 mins, etc). We continue to emphasize childrens right to choose to teachers however, if a child expresses they do not want to continue wearing the devices, we will simply take them off. Our prior work involved using some of these components with minimally verbal children but we have not systematically developed, tested or documented these ideas so this would be a novel deliverable of the project. This will be manualized and made publicly available to advance digital health work with individuals with profound autism involving wearable biosensors more broadly. Teachers will initially record at least one baseline heart rate of the child, which will be used to calibrate the apps stress zone notifications for the child. Baseline heart rate is recorded over a 5-minute period, during which the child will be engaged in a relaxing activity. Students will then wear the heart rate tracker and accelerometer each day during the three-month testing period. School personnel will be able to track the students heart rate and movement, enter child data on triggers/antecedents, challenging behaviors/skills, and intervention strategies, view the daily report, export the childs data, and message others on the students team. School personnel will receive text support from the study team during the testing period and will be able to ask questions and troubleshoot any issues that come up during this period. Parents will be able to view the auto-generated daily report for the child, export and build figures of the childs data, access the intervention strategy resources, and use the apps messaging features. The research team will remotely monitor each participants usage of the app during their respective testing period. At baseline, the IQ, SSQ, IBR-MOAS and EDI measures will be taken as well as a demographic survey. The demographic survey will include childs current medications as some as known to affect heart rate. We will ask parents for their childs IEP so we can note their IQ score. If the IQ score was recent (e.g.,

within the last year) and assessed through a standardized test battery, this score will be recorded. If not, a standardized IQ assessment (Stanford Binet Intelligence Scales 5th edition) will also be conducted with the child at a time convenient for the teacher or family, either in- person at school or home, as preferred. Additionally, we will ask for teachers and parents to report on their students/childrens verbal ability to determine whether they meet criteria for being minimally verbal (i.e., 20 functional words). Throughout the trial, the artifact removal success, offline mode activations, implementation success and false positives/negatives measures will be taken. We will use a brief Adverse Events Checklist to be administered to teachers and parents in the treatment group weekly throughout the trial, which may include items related to teachers experiencing stress triggered by monitoring their students stress levels. At mid-trial (6 weeks after baseline) and at post-trial, the SUS, AIM, FIM, IAM, SSQ, IBR-MOAS and EDI measures will be taken and school personnel and parents will provide feedback on their experience with the app during a qualitative interview with a member of the research team. If possible given COVID-19 related school policies and teacher preferences, the research team will perform in-class observations to obtain a first-hand look at the use of the KeepCalm app in the classroom and to clinical decision support success and false positives and false negatives (as described in the outcome measures).

The following documents are currently attached to this item:

There are no documents attached for this item.

Deception
Does your project use deception? Deception could be considered any direct misinformation presented to the subject or omission of key information pertaining to the design or nature of the project.
No

International Research
Are you conducting research outside of the United States?
No

Analysis Plan
Given the nature of the project of designing and testing usability of the KeepCalm app rather than conducting definitive effectiveness testing, analysis will be mostly limited to descriptive statistics on app usability, at all phases of the project. Based on Schnall et al. (2016), we expect to achieve app usability scores on the PSSUQ of under 2 (1= perfectly usable 7=unusable), by the end of usability testing. The pilot randomized field trial of the KeepCalm app in Phase 3 is designed to test usability and implementation aspects, rather than effectiveness. Data from the pilot trial will be written into a paper on the usability, acceptability, feasibility, appropriateness and technical reliability of the m-health EMORE app incorporating HR tracking for children with ASD and challenging behaviors. Preliminary effectiveness data will also be presented in an exploratory (underpowered) 2 groups (treatment, waitlist) x 2 time periods (entry, exit) repeated-measures ANOVA. We predict participants will assign high app usability, acceptability, feasibility and appropriateness scores following treatment. We also predict satisfactory proximal effectiveness (80% clinical decision support success rates, 20% false positive and negative rates) and lower post-treatment severity and frequency of challenging behaviors in the children with ASD. To inform future work in the area we will run a conditional logistic regression to examine if heart rate increase/heart rate variability decrease is predictive of challenging behavior vs. non-challenging behavior. Given the sample size this analysis will be under-powered, therefore interpretation will be based on odds ratios rather than p-values. I will also use qualitative methods (interviews with teachers and classroom aides) to examine acceptability, feasibility, and appropriateness of the m-health app, as per Phase 1.2.

The following documents are currently attached to this item:

There are no documents attached for this item.

Data confidentiality

- x **Paper-based records will be kept in a secure location and only be accessible to personnel involved in the study.**
- x **Computer-based files will only be made available to personnel involved in the study through the use of access privileges and passwords.**
- x **Prior to access to any study-related information, personnel will be required to sign statements agreeing to protect the security and confidentiality of identifiable information.**
- x **Wherever feasible, identifiers will be removed from study-related information.**

A Certificate of Confidentiality will be obtained, because the research could place the subject at risk of criminal or civil liability or cause damage to the subject's financial standing, employability, or liability.

A waiver of documentation of consent is being requested, because the only link between the subject and the study would be the consent document and the primary risk is a breach of confidentiality. (This is not an option for FDA-regulated research.)

- x **Precautions are in place to ensure the data is secure by using passwords and encryption, because the research involves web-based surveys.**
- x **Audio and/or video recordings will be transcribed and then destroyed to eliminate audible identification of subjects.**

Subject Confidentiality

Paper-based records will be kept in a secure location and only be accessible to personnel involved in the study. Electronic files will only be made available to personnel involved in the study through the use of access privileges and passwords. Prior to access to any study-related information, personnel will be required to sign statements agreeing to protect the security and confidentiality of identifiable information. Whenever feasible, identifiers will be removed from study-related information. Precautions are in place to ensure the data is secure by using passwords and encryption, because the research involves web-based surveys. Audio recordings will be transcribed and/or coded and then destroyed within 2 years to eliminate identification of subjects except where participant consent for future studies has been given. In the KeepCalm app we will collect first names and emails so that team members can identify one another and receive email notifications from app data, which will be based on logged behavioral data and heart rate data only. App accounts will be deleted after the study.

Sensitive Research Information*

Does this research involve collection of sensitive information about the subjects that should be excluded from the electronic medical record? [NOTE: This does not apply to: 1) research information that would not normally be included in the electronic medical record or 2) information that is in the electronic medical record as part of clinical care.]

No

Subject Privacy

Privacy refers to the person's desire to control access of others to themselves. Privacy concerns people, whereas confidentiality concerns data. Describe the strategies to protect privacy giving consideration to the following: The degree to which privacy can be expected in the proposed research and the safeguards that will be put into place to respect those boundaries. The methods used to identify and contact potential participants. The settings in which an individual will be interacting with an investigator. The privacy guidelines developed by relevant professions, professional associations and scholarly disciplines (e.g., psychiatry, genetic counseling, oral history, anthropology, psychology).

Data from the study will only be shared with personnel that is on the study. Data in the KeepCalm app will be shared amongst school team members as explained on the informed consent form. Participants who have given written indication of wanting to be contacted for future research will be contacted my email or phone and invited to participate. The researchers will interact with participants during the design workshops at UPenn or CHOP, at homes and at the school. Professional conduct will be expected by each member of the research team, and will be overseen by the PI, Dr. Nuske, in accordance with the privacy guidelines developed by the discipline of psychology.

Disclosures
Will any data or specimens from Penn participants OR other research generated work product (e.g., intellectual property) be disclosed to any individuals, entities, or vendors, etc. outside of Penn?
No

*Data Protection**

- x **Name**
- x **Street address, city, county, precinct, zip code, and equivalent geocodes**
- x **All elements of dates (except year) for dates directly related to an individual and all ages over 89**
- x **Telephone and fax number**
- x **Electronic mail addresses**
- x **Social security numbers**
- **Medical record numbers**
- **Health plan ID numbers**
- **Account numbers**
- **Certificate/license numbers**
- **Vehicle identifiers and serial numbers, including license plate numbers**
- **Device identifiers/serial numbers**
- **Web addresses (URLs)**
- **Internet IP addresses**
- x **Biometric identifiers, incl. finger and voice prints**
- x **Full face photographic images and any comparable images**
- **Any other unique identifying number, characteristic, or code**
- **None**

Does your research request both a waiver of HIPAA authorization for collection of patient information and involve providing Protected Health Information ("PHI") that is classified as a "limited data set" (city/town/state/zip code, dates except year, ages less than 90 or aggregate report for over 90) to a recipient outside of the University of Pennsylvania covered entity?
No

Tissue Specimens Obtained as Part of Research*
Are Tissue Specimens being obtained for research?
No

Tissue Specimens - Collected during regular care*
Will tissue specimens be collected during regulator clinical care (for treatment or diagnosis)?
No

Tissue Specimens - otherwise discarded*
Would specimens otherwise be discarded?
No

Tissue Specimens - publicly available*
Will tissue specimens be publicly available?
No

Tissue Specimens - Collected as part of research protocol*
Will tissue specimens be collected as part of the research protocol?
No

Tissue Specimens - Banking of blood, tissue etc. for future use*
Does research involve banking of blood, tissue, etc. for future use?
No

Genetic testing
If genetic testing is involved, describe the nature of the tests, including if the testing is predicative or exploratory in nature. If predictive, please describe plan for disclosing results to subjects and provision of genetic counseling. Describe how subject confidentiality will be protected Note: If no genetic testing is to be obtained, write: "Not applicable."
Not applicable

Consent

1. Consent Process

Overview
After participants are recruited and once communication is established between the research team and each interested participant, the screening process will begin in order to determine eligibility. Once the invitees are determined eligible, the research team will schedule a meeting with them, or will send the Informed Consent and/or Informed Consent Form and HIPAA Authorization Form via a Qualtrics or Redcap link for the respective phase of the project they wish to participate in. These consent forms include a description of the study and expected roles and responsibilities of the participant, risks and benefits to participants, and confidentiality procedures (see attached). For Phase 1.1, the research team will take written informed consent from participants individually before beginning the design workshop. For Phases 1.2, 2 and 3, the research team will take written informed consent from participants individually during the initial scheduled meeting or via Qualtrics or Redcap. Parents and teachers will consent separately, before the testing/trial period begins. The consent forms also clearly state that participation in the study is completely voluntary, and participants can drop out of the study without penalty at any time. All consent forms follow the guidelines outlined by the University of Pennsylvania, the School District of Philadelphia, and ethical guidelines set forth by the state and federal governments. Documentation of subject consent will be stored in a locked file in the PI or designees office at each study site or in one of the HIPAA-compliant servers described above.

Children and Adolescents
Parents will indicate on the consent form they fill out electronically (sent via email or text) that their child is either 1) capable of providing assent and has freely assented to take part in this study; 2) capable of providing assent and has decided NOT to take part in this study; or 3) not capable of providing assent (parent has consented so they will take part in the study).

Adult Subjects Not Competent to Give Consent
We are planning on enrolling 1-2 adults with autism in phase 1 of the project, but we do not anticipate enrolling adults that are not able to give consent, as we are screening out individuals with autism with a verbal delay, due to the nature of Phase 1 of the project, to gather, verbally, impressions and feedback on the app development.

2. Waiver of Consent

Waiver or Alteration of Informed Consent*
No Waiver Requested

Minimal Risk*

Impact on Subject Rights and Welfare*

Waiver Essential to Research*

Additional Information to Subjects

Written Statement of Research*
No

If no written statement will be provided, please provide justificiation

The following documents are currently attached to this item:

There are no documents attached for this item.

Risk / Benefit

Potential Study Risks
It is possible that some participants may experience discomfort in talking about their experiences and emotions as part of the discussions in the design workshop or throughout the usability testing week. In the design workshops there is a potential risk of breach of confidentiality. We have taken steps to protect your privacy. However, we cannot guarantee that other group members will not share any information outside of the group. Children may experience some discomfort from wearing the heart rate monitor and/or accelerometer. Children will be able to choose the device they feel most comfortable in; wristband and chest-strap versions will be available. Children will be asked to wear the device throughout the day. If the device is uncomfortable to the child, they can simply take it off. The research team will document device usage via the end of week interview and with the Comfort Rating Scales. After explaining the study protocol to participants during the consenting/assenting process, we will emphasize that participation is voluntary and that they may terminate their participation in the testing any time.

Potential Study Benefits
There are no direct benefits to participants for participating in this study. However, this study is expected to improve our understanding of how to measure emotional stress and minimize challenging behavior in children with autism.

Alternatives to Participation (optional)

Data and Safety Monitoring
The PI (Dr. Heather Nuske) will closely monitor safety, privacy, and data integrity throughout the project.

The following documents are currently attached to this item:

There are no documents attached for this item.

Risk / Benefit Assessment
There is minimal to no risk associated with this study.

General Attachments

The following documents are currently attached to this item:

There are no documents attached for this item.