Impact VR: An Emotion Recognition and Regulation Training Program for Youth with CD

HM20027823/ NCT06301516

PI: Nicholas Thomson

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INSTRUCTIONS[1]:

- *Use this template to prepare a document with the information from the following sections.*
- *Depending on the nature of your study, some sections may not be applicable to your research. If so mark as "NA". For example, research involving a retrospective chart review may have many sections with "NA." For subsections, like 1.x or 8.x, you can delete it if it's not applicable.*
- *When you write a protocol, keep an electronic copy. You will need to modify this copy when making changes.*
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- *Omit starred (*) items if this is the activation of a protocol at a new site or sites that will be overseen by a principal investigator who will take separate and full responsibility for that site or those sites. Complete by describing information specific to the site(s). Do not repeat information in the approved protocol that applies to all site(s).*

PROTOCOL TITLE:

Impact VR: An Emotion Recognition and Regulation Training Program for Youth with Conduct Disorder

PRINCIPAL INVESTIGATOR:

Name: Nicholas Thomson, PHD
Department: Surgery
Telephone Number: 804-297-5740
Email Address: Nicholas.thomson@vcuhealth.org

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REVISION HISTORY

Revision #	Version Date	Summary of Changes	Consent Change?

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[1] This template satisfies AAHRPP elements 1.7.B, I.8.B, I-9, II.2. A, II.2.I, II.3.A, II.3.B, II.3.C-II.3.C.1, II.3.D-F, II.4.A, III.1.C-F, II.2.D

Contents

1.0 Study Summary

Protocol Information	**Description**
Study Title	Impact VR: An Emotion Recognition and Regulation Training Program for Youth with Conduct Disorder
Study Design	Randomized clinical trial of psychological intervention
Primary Objective	Reduce conduct disorder symptoms
Secondary Objective(s)	Improve emotion recognition
Research Intervention(s)	Impact VR
Study Population	Youth with conduct disorder (aged 10-17 years)
Sample Size	150
Study Duration for individual participants	4 months
Study Specific Abbreviations/ Definitions	CD: CONDUCT DISORDER CU: CALLOUS-UNEMOTIONAL CP: CONDUCT PROBLEMS

2.0 Objectives*

2.1

***SA 1:** To assess youths' acceptability of Impact VR, and make modifications to improve acceptability.*

***SA 2:** Determine the feasibility and usability of the deployment of Impact VR in youth's homes, schools, and mental health settings (e.g., hospitals, clinics).*

***SA 3:** Assess the preliminary efficacy of Impact VR in reducing CD, CU traits, and CP, and improving emotion recognition and regulation using an RCT.*

2.2 We expect youth will find Impact VR acceptable, and the feasibility and usability will be deemed sufficient. We expect participants receiving Impact VR will have improvements in emotion recognition and regulation, and reductions in CD, CU traits, and CP.

3.0 Background*

Conduct disorder (CD) is one of the most prevalent and impairing psychiatric disorders emerging during childhood or adolescence[1–3]. CD is characterized by aggression, antisocial behavior, and the proneness to violate the rights of others. CD is one of the costliest childhood psychiatric disorders, as youth with CD often face lifelong adjustment, mental health, legal, social, occupational, and physical health problems[4,5]. Within the CD diagnosis, a subset of youth (12-46%) display callous-unemotional (CU) traits (termed "limited prosocial emotions"). CU traits denote additional symptoms including a lack of remorse/guilt, a callous lack of empathy, shallow affect, and/or lack of concern about performance[6]. Youth with CD and CU traits are more likely to engage in chronic criminal behaviors and develop psychopathology into adulthood when compared to youth with CD only[7]. Although both CD and CU traits are inextricably linked to poor outcomes for youth, there remains a scarcity of targeted interventions for CD and CU traits. One of the most significant challenges for treatment is that youth with CD are often perceived by providers as treatment-resistant and treatment disrupters[7]. This leads to poor treatment retention and further isolation from treatment opportunities. Further, existing interventions that target antisocial behaviors more generally are costly because they require 24/7 behavioral management therapies[7]. Impact VR is a psychoeducational intervention for improving emotion recognition and regulation, using immersive gameplay and storylines that are relevant to youth. Impact VR uses evidence-based cognitive and dialectical behavioral approaches to improve emotion regulation. At the center of Impact VR is an individualized training program that teaches youth to effectively identify emotional expressions in others. Deficits in emotional expression recognition is thought to play a major role in the development and stability of CD and CU traits, which makes it a key mechanism to target for treatment[7–11]. Thus, Impact VR provides a resource efficient and standardized treatment approach for multiple systems (e.g., schools) to improve mental health for youth by targeting the mechanisms of CD and CU traits.

4.0 Study Endpoints*

Aggression, conduct problems; conduct disorder symptoms; callous-unemotional traits.

5.0 Study Intervention

5.1 Impact VR uses a scaffolding approach to teach youth to identify and understand emotions in others. Impact VR focuses on happy, sad, anger, and fear facial expressions, and a neutral emotional expression. Impact VR has four 20-minute sessions, which include psychoeducational instruction and interactive gameplay to reinforce learning objectives. Session performance is recorded using behavioral and eye-tracking metrics in real time. Using this data in real-time to adjust difficulty ensures youth do not experience floor or ceiling intervention effects, all while maintaining a positive learning environment. Impact VR is a dynamic individualized training program. Impact VR has an integrated pre- and post-assessment for facial expression recognition to track overall treatment progress. Pre-and post-assessments use 360 videos and 3D images of human actors of different ages, gender, and ethnicities, which increases the ecological validity of the assessment to real-life performance. At the start of Impact VR, youth select a companion who provides the psychoeducational content and uses motivational support and positive psychology throughout the sessions. Companions include real and imaginative characters that are all capable of producing clear emotional expressions via emphasized emotional expression diagnostic features. The companions are integrated into storylines to increase the therapeutic alliance.

6.0 Procedures Involved*

Project Overview. We aim to assess the (SA1) acceptability and (SA2) usability of Impact VR, and (SA3) evaluate Impact VR for reducing CD, CU traits, and CP, and improving emotion recognition and regulation. This protocol has been separated based on the specific aims for the study.

SA 1: To assess youths' acceptability of Impact VR and make modifications to improve acceptability.

Specific Aim 1 Protocol: For assessing Impact VR's acceptability, we will recruit 20 youth with CD or conduct problems (10-17 years). Youth will be recruited from the PI's existing dataset from VCU Health's electronic medical records (EMR) via TriNetX (see Recruitment Plan). Our database includes 1310 eligible youth with CD to recruit from. Our current recruitment rate for youth-caregiver dyads (56% male; M_{age}=14.8 years). Eligible youth will be identified using this database. Parents will be contacted by telephone, email, or text to assess their and their child's interest in participating in the focus groups. If the caregiver and youth are interested in the focus groups, they will be invited to attend the groups. Prior to the start of the groups, the caregiver and youth will be provided with an overview of the consent/assent, and then in a private location (i.e., room, space) asked to complete the consent/assent. Once participants have completed the informed consent, participants will engage in the focus group activities. At the end of the focus group (~45 minutes), youth participants will receive $40 for their participation.

Assessing the Acceptability of Impact VR. To measure acceptability for youth, focus groups will be conducted with the participation of 20 youths with CD or conduct problems. A focus group moderator (project coordinator) will be present during these sessions to record qualitative responses and facilitate these sessions. Approximately 3 focus groups with 6-8 youth will be conducted in order to ensure that all primary thematic clusters are detected (Guest et al., 2017). Sessions will be audio-recorded to ensure the accuracy of reporting and these recordings will be transcribed for analyses. The measure of the focus groups will be based on a Sekhon et al.(Sekhon et al., 2017) theoretical framework of acceptability for healthcare interventions(Sekhon et al., 2017) to comprehensively assess acceptability across multiple domains: (1) Affective Attitude (e.g., how do youth feel about Impact VR's specific sessions?), (2) Burden (e.g., any physical symptoms associated with use (i.e., headaches, nausea)?), (3) Perceived Effectiveness (e.g., are the lessons understandable and enjoyable?), (4) Ethicality (e.g., Is the content culturally sensitive and informed?), (5) Intervention Coherence (e.g., is the intervention easy to follow and understand?), (6) Opportunity Costs (e.g., did youth feel like Impact VR was a good use of their time?), (7) and Self-Efficacy (e.g., are youth are able to navigate and learn new skills?). To determine overall acceptability, an 80% acceptability rate will be inferred across groups. If responses fall below 80% acceptability, modifications to improve Impact VR will be made.

Focus groups for acceptability of Impact VR will be held at either VCU or our community partner locations, which include [redacted] and public schools involved in positive youth development and violence prevention initiatives.

Adult participants will be provided information about the study prior to coming to the lab. At arrival at the lab a researcher will explain the consent form to each participant individually in a private room. Once consented, participants will participate in focus group activities. If participants require more time to consider participating they will be provided a copy of the informed consent and contacted at a later date.

SA 2: Determine the feasibility and usability of the deployment of Impact VR in youth's homes, schools, and mental health settings (e.g., hospitals, clinics).

Specific Aim 2 Protocol: For assessing Impact VR's useability, we will recruit 10 youth with CD or conduct problems and their caregivers (n=20), 10 teachers and school counselors, and 10 mental health professionals. Youth and caregivers will be recruited from the PI's existing dataset from VCU Health's electronic medical records (EMR) via TriNetX and via our community partners. Eligible youth will be identified using this database. Eligibility includes being aged 10-17 years old, being diagnosed with CD or having a history of conduct problems, and being English-speaking. Parents will be contacted by telephone, email, or text to assess their and their child's interest in participating in the focus groups. If the caregiver and youth are interested in the focus groups, they will be invited to attend the groups. Prior to the start of the groups, the caregiver and youth will be provided with an overview of the consent/assent, and then in a private location (i.e., room, space) asked to complete the consent/assent. Once participants have completed the informed consent, participants will engage in the focus group activities. At the end of the focus group (~45 minutes), youth participants will receive $40 for their participation. Teachers, school counselors, and mental health professionals will be recruited through the PI's community partners, including [redacted]. Adult participants will be invited to the focus groups where they will be provided an overview of the consent forms and provide consent. This will be conducted in a private location. Once focus groups activities have been completed participants will receive $40 for their participation. Adults must be English-speaking to participate in the focus groups.

Adult participants will be provided information about the study prior to coming to the lab. At arrival at the lab a researcher will explain the consent form to each participant individually in a private room. Once consented participants will participate in focus group activities.

Assessing the Feasibility and Usability of Impact VR. The feasibility and usability of Impact VR will be tested by conducting separate focus groups for (1) 10 youth and their caregivers, (2) 10 teachers and school counselors, and (3) 10 mental health treatment providers. Our sample size is based on prior research suggestions for ideal and effective participant group sizes for usability testing (Macefield, 2009). Self-report surveys and semi-structured interviews will be administered after groups complete parts of Impact VR, with the goal of identifying impactful changes to each session to improve design and usability flaws (e.g., user control, etc.), which will increase deployment success. Youth will be asked to provide perceptions and feedback on the storylines, games, artwork, and aesthetic components of the VR experience. These components will be assessed given the interrelated nature of usability and aesthetics (Lee & Koubek, 2010). Adults will be asked usability questions related to the set-up and use of Impact VR at home, in school, and in mental health settings (e.g., hospital, outpatient clinics). Adults will be asked about Impact VR's progress report data output to evaluate what data is meaningful (e.g., correct vs incorrect number of responses) and how it is best displayed (e.g., percentages vs count, graphs vs text). Improvements to Impact VR will be made prior to the RCT (SA3). For feasibility and usability of Impact VR, we aim to achieve >90% performance and satisfaction rate, and <5% set up error rate, and <0.5% software errors. Adults will provide input from a consumer perspective based on their grouping (e.g., teacher, etc.) to improve our understanding of a commercialization strategy for moving Impact VR to market.

SA 3: Assess the preliminary efficacy of Impact VR in reducing CD, CU traits, and CP, and improving emotion recognition and regulation using an RCT.

Specific Aim 3 Protocol: To test the efficacy of Impact VR, 60 youth with CD and their caregivers will be recruited. Youth-caregiver dyads will be recruited from current research projects conducted by the PI and using VCU Health's electronic medical records (EMR) via TriNetX (see Recruitment Plan). Our database includes 1310 eligible youth with CD to recruit from. Our current recruitment rate for youth-caregiver dyads (56% male; M_{age}=14.8 years) is 57.2% with 91% 6-month retention rate. The RCT testing the efficacy of Impact VR will be conducted at Virginia Commonwealth University. Youth will be eligible to participate if they are in the VCU Health electronic medical records (EMR), they have a current diagnosis of Conduct Disorder (CD), are English speaking, 10 to 17 years of age, have a parent/caregiver that is 18 years old or older. Participants will be excluded if they are non-English speaking (because the intervention and measures are only available in English), are 18 years of age or older, or are incarcerated. We have excluded juvenile offenders in correctional facilities because the interventions cannot be conducted in the prison/correctional environment.

Recruitment plan. Youth with conduct disorder (CD) will participate in all three specific aims: assessing the acceptability (SA1; n = 20), usability (SA2; n = 10), and effectiveness (SA3; n = 60) of Impact VR. Participants involved in SA1 or SA2 will not be recruited to participate in the RCT (SA3). Youth with CD who are aged 10-17 years old and are English speaking will be recruited. Caregivers will only participate in either SA2 (n=10) or SA3 (n=10). Thus, youth-caregiver dyads will be recruited for either SA2 and SA3. Again, participants involved in SA1 or SA2 will not be recruited to participate in the RCT (SA3). We have several sources of recruitment for all participants in this project. Our primary recruitment source is VCU Health's Electronic Medical

Record (EMR) database via TriNetX. A review of the database shows there are currently 1310 eligible participants diagnosed with CD and aged 10-17 years (M_{age}=15 years). This is the same method that Dr. Thomson uses for his NIMH funded research (R01MH123535). Participants will only be invited to participate in the present study if they are not involved in other research or have completed their involvement in the PIs research. Our recruitment rate is 57.2% for this same population (youth with CD aged 10-17 years), with a six-month retention of 91%.

Youth participant inclusion criteria:

Aged 10-17 years old

Identified through the TriNetX database as having a conduct disorder diagnosis

English speaking

Youth participant exclusion criteria:

Youth aged <10 years and >18 years old

Non-English speaking

Youth of caregivers younger than 18 years old.

Adult/caregiver participant inclusion criteria:

Aged 18 years or older

Adult/caregiver participant exclusion criteria:

Aged younger than 18 years

At a recruitment rate of 57.2%, we anticipate the ability to recruit 749 youth with CD (10-17 years). However, we have set our recruitment rate based on our power analyses calculations and taking into account a 9% loss to follow-up rate. Of note, the 91% retention rate is referenced for the PIs current project which includes a 6-month follow-up, whereas the proposed study only has a 3-month follow-up. Therefore, we expect the retention rate to be much higher. We aim to recruit 20 youth for SA1 and 10 youth for SA2, and our power analysis indicated that a sample size of 60 is needed for the RCT (SA3) while accounting for attrition (see Recruitment and Retention Plan). To achieve our total youth sample size of 90 (for all aims), we will need a 6.87% recruitment rate. Thus, we have demonstrated strong feasibility to recruit enough participants for the study from EMRs at VCU Health. However, if our recruitment rate drops below what is required, we have secondary recruitment sources, including the [redacted] Dr. Thomson has support from these community partners. [redacted] Our community partners will display flyers and posters at their facilities, as well as offering flyers and information to eligible participants. The research team will provide a presentation about the research to our community partners staff to encourage recruitment. Eligible and interested participants provide their caregiver's contact details to program staff for the research team to contact them directly. As the Director of Research at VCU Health's IVPP, the PI can also recruit participants with CD from the four youth interventions run by IVPP. Our recruitment rate for this population is high (87%). IVPP provides services to 4000-5000 youth per year who meet the age requirements for the proposed study (10-17 years). Based on a review of the IVPP database, 4% of youth have a current diagnosis of CD and are aged 10-17. Recruiting from IVPP will provide an additional 160-200 eligible participants (37% female). The PI will hold meetings every other week to ensure the recruitment efforts are meeting expectations, and to assess if methods need to be changed to increase recruitment success.

Each EMR-identified CD youth and caregiver dyads will be contacted by text, phone, and email. Text messages will be sent three times with the ability for the participant to text back with a response. Phone calls will be made 5 times with each call made at a different time of the day and on different days of the week. A voicemail will be left with a callback number. Emails will be sent to the email address on file. Weekly team meetings will provide the opportunity to make modifications to recruitment procedures based on any feedback. We have found this method to be efficient for recruiting youth and caregivers into research, as evidenced by our current recruitment rate.

Based on our current research projects, we expect that each assessment will last between 90-120 minutes. Thus, the first session will include questionnaires, semi-structured interviews, and an emotion recognition assessment. This assessment is much shorter in length than our current NIMH-funded study (~4 hours).

Prior to coming into the lab eligible participants will be informed about the study and its procedures (including treatment group randomization). Once the interested participants come into the lab to participate, the youth and caregiver will be provided an overview of the consent and assent forms and study design (including treatment group allocation). Caregiver and youth will be consented and assented in separate rooms for privacy. After consent/assent is completed, participants will complete the assessments. Once all assessments are completed, the treatment group allocation will be disclosed to the administrating researcher, youth, and caregiver. This blinded approach to block randomization prevents any bias from occurring during the assessment phase by the researcher. Once participants are randomized the youth will start the intervention tasks. Participants enrolled into Impact VR will be complete the first of four sessions. The four 20-minute sessions will be completed over 4 weeks (one session per week) either in the lab, at the participant's home, school or a mutual private meeting place. This is to help ease participant burden. Participants enrolled into the control group will complete a one-time PowerPoint presentation that provides an overview of emotion expressions and instructions on how to recognize emotions in others.

All participants will complete a 4 week follow-up assessment and a 3 month follow-up assessment. These will be the same measures completed at baseline. Participants will have the option to complete the follow-up assessments online or in-person. Youth and caregiver participants will each receive $75 for each assessment. Follow-up interviews will be scheduled at the end of the prior assessment. To minimize loss to follow-up, participants will be asked to provide their cell phone numbers and up to three contact addresses/phone numbers of close family members or friends who can help the research team contact the participants in case of loss to follow-up. Participants and caregivers will receive two appointment reminders via SMS text message or by a phone call at seven days before their scheduled follow-up assessment, and one day before their scheduled follow-up assessment. If a participant is not available at the scheduled assessment time, then the research team will call the participant and reschedule the meeting. If a participant cannot be reached, the research team will make up to four attempts to contact the participant on different days and times in an effort to conduct the assessment. If the participant does not respond, the research team will contact the family members/friends on the list and ask if they can convey a message with a call back number.

7.0 Data and Specimen Banking*

7.1 Survey data will be stored on RedCap. Participants will not be able to access their data for personal use. Participants will not be able to withdraw their data because the data is de-identified.

8.0 Sharing of Results with Subjects*

8.1 Results will not be shared with participants.

9.0 Study Timelines*

9.1 Describe:

- *4 months.*
- *18 months.*

10.0 Subject Population*

Youth participant inclusion criteria:

Aged 10-17 years old

Identified through the TriNetX database as having a conduct disorder diagnosis

English speaking

Youth participant exclusion criteria:

Youth aged <10 years and >18 years old

Non-English speaking

Youth of caregivers younger than 18 years old.

Adult/caregiver participant inclusion criteria:

Aged 18 years or older

Adult/caregiver participant exclusion criteria:

Aged younger than 18 years

EXCLUDE: Adults unable to consent and Prisoners. This study does not target pregnant women.

11.0 Vulnerable Populations*

11.1 If the research involves individuals who are vulnerable to coercion or undue influence, describe additional safeguards included to protect their rights and welfare.

- *If the research involves persons who have not attained the legal age for consent to treatments or procedures involved in the research* *("children"), review HRP-416 - CHECKLIST - Children to ensure that you have provided sufficient information.*

- *Check if the research involves any of the following groups:*

  n/a ☐ *Wards of the State*
  n/a ☐ *VCU/VCUHS students or trainees*
  n/a ☐ *VCU/VCU Health System employees*
  n/a ☐ *Active military personnel*
  n/a ☐ *Student populations in K-12 educational settings or other learning environments*
  n/a ☐ *Members of a federally recognized American Indian or Alaska Native tribe*

12.0 Local Number of Subjects

12.1 150

13.0 Recruitment Methods

The specific aim assessing the usability of Impact VR will include adult participants. Our goal is to recruit 10 school teachers and counselors (middle and high school), and 10 mental health professionals. These participants will be recruited from our community partners and public schools (see letters of support).

Youth with conduct disorder (CD) will participate in all three specific aims: assessing the acceptability (SA1; n = 20), usability (SA2; n = 10), and effectiveness (SA3; n = 60) of Impact VR. <u>Participants involved in SA1 or SA2 will not be recruited to participate in the RCT (SA3).</u> Youth with CD who are aged 10-17 years old and are English speaking will be recruited. Caregivers will only participant in either SA2 (n=10) or SA3 (n=10). Thus, youth-caregiver dyads will be recruited for either SA2 and SA3. Again, participants involved in SA1 or SA2 will not be recruited to participate in the RCT (SA3). We have several sources of recruitment for all participants in this project. Our primary recruitment source is VCU Health's Electronic Medical Record (EMR) database via TriNetX. A review of the database shows there are currently 1310 eligible participants diagnosed with CD and aged 10-17 years (M_{age}=15 years). This is the same method that Dr. Thomson uses for his NIMH-funded research (R01MH123535). Participants will only be invited to participate in the present study if they are not involved in other research or have completed their involvement in the PIs research.

At a recruitment rate of 57.2%, we anticipate the ability to recruit 749 youth with CD (10-17 years). However, we have set our recruitment rate based on our power analyses calculations and taking into account a 9% loss to follow-up rate. Of note, the 91% retention rate is referenced for the PIs current project which includes a 6-month follow-up, whereas the proposed study only has a 3-month follow-up. Therefore, we expect the retention rate to be much higher. We aim to recruit 20 youth for SA1 and 10 youth for SA2, and our power analysis indicated that a sample size of 60 is needed for the RCT (SA3) while accounting for attrition (see Recruitment and Retention Plan). To achieve our total youth sample size of 90 (for all aims), we will need a 6.87% recruitment rate. Thus, we have demonstrated strong feasibility to recruit enough participants for the study from EMRs at VCU Health. However, if our recruitment rate drops below what is required, we have secondary recruitment sources, including the [redacted] Dr. Thomson has support from these community partners. Dr. Thomson is a member of the Inspire Workgroup, which includes over 30 community partners, public and nonprofit, providing direct services to Richmond youth to reduce the risk of violence, including Richmond Public Schools. Our community partners will display flyers and posters at their facilities, as well as offering flyers and information to eligible participants. The research team will provide a presentation about the research to our community partners staff to encourage recruitment. Eligible and interested participants provide their caregiver's contact details to program staff for the research team to contact them directly. As the Director of Research at VCU Health's IVPP, the PI can also recruit participants with CD from the four youth interventions run by IVPP. Our recruitment rate for this population is high (87%). IVPP provides services to 4000-5000 youth per year who meet the age requirements for the proposed study (10-17 years). Based on a review of the IVPP database, 4% of youth have a current diagnosis of CD and are aged 10-17. Recruiting from IVPP will provide an additional 160-200 eligible participants (37% female). The PI will hold meetings every other week to ensure the recruitment efforts are meeting expectations, and to assess if methods need to be changed to increase recruitment success.

To ensure successful recruitment, the research team will be trained in motivational interviewing techniques and a phone script will be followed when contacting caregivers. Each EMR-identified CD youth and caregiver dyads will be contacted by text, phone, and email. Text messages will be sent three times with the ability for the participant to text back with a response. Phone calls will be made 5 times with each call made at a different time of the day and on different days of the week. A voicemail will be left with a callback number. Emails will be sent to the email address on file. All scripts will be approved by the VCU IRB. Weekly team meetings will provide the opportunity to make modifications to recruitment procedures based on any feedback. We have found this method to be efficient for recruiting youth and caregivers into research, as evidenced by our current recruitment rate.

Based on our current research projects, we expect that each assessment will last between 90-120 minutes. Thus, the first session will include questionnaires, semi-structured interviews, and an emotion recognition assessment. This assessment is much shorter in length to our current NIMH funded study (~4 hours).

As stated above, our current 6-month retention rate for this population is 91%. We will use the same practices to achieve a high retention rate for our 3-month follow-up in the proposed study. To minimize loss to follow-up we will use strategies that we have found to be effective for maintaining participants involved in research at VCU by the PI. At each assessment (baseline and 4 weeks), the research team will update the contact information and schedule the next assessment. The caregiver will provide contact information for three family members or close friends that the research team may contact if the contact details are changed within the follow-up period. The research team will contact the caregiver 1 month and 2 weeks before the scheduled appointment to confirm the times/dates. A text reminder will be sent 24 hours before the scheduled appointment. If a participant cannot be reached, the research team will make up to four attempts to contact the participant on different days and times to conduct the assessment. If the participant does not respond, the research team will contact the family members/friends on the list and ask if they can convey a message with a call back number. Caregivers and youth will each receive $75 for the initial assessment. The youth and caregiver will each receive $75 for each of the follow-up assessments totaling $225 each. We have extensive experience conducting follow-up assessments for high-risk youth in the Richmond City area and have a variety of strategies for tracking and maintaining contact with participants. Our existing retention rate for youth with CD and their caregivers is 91% for 6-month follow-ups.

14.0 Withdrawal of Subjects*

14.1 Participants may be withdrawn from the study if they express harm to themselves or others.

14.2 Participant data will be destroyed/deleted.

15.0 Risks to Subjects*

The most likely risk that we anticipate is that a question on a survey may make a participant feel uncomfortable or fatigued. The risks to participants are clearly outlined in the consent forms. These forms stress that participation is completely *voluntary*. Each participant is informed that they may skip or not answer any question or stop the survey at any time if they are uncomfortable. Participants may withdraw from the study at any point. Participants will be informed that their participation (or not) will have no impact on the healthcare they are receiving at VCU Health. If any participant should become upset, a member of our team will be available to talk with them and to address their concerns. In addition to having immediate access to mental health practitioners as part of our Injury and Violence Prevention Program, we will also offer information about free or low-cost psychological services and provide crisis hotline information as needed. On the consent forms, we indicate that confidentiality will be broken if the participant is in danger of harming himself/herself or others (in which case, we will talk to him or her about our concerns and make appropriate contacts and referrals). Any information of this nature disclosed to study staff will be acted on immediately. The research staff has decades of experience managing populations who are high-risk (to themselves and others) and are trained in de-escalation tactics.

The goal of the VR intervention is to provide youth an immersive, engaging, and therapeutic environment to reduce CD and CU traits. VR environments have been found to cause nausea in some people. It is possible that some youth may experience nausea as a result of the VR environment. However, in research by the PI including over 600 youth and young adults (ages 8-24 years) this has never happened, even when using high intensity stimuli (i.e., roller coaster). Nevertheless, precautions will be taken to prevent the risk of nausea (i.e., having a floor fan for a breeze, youth and caregivers briefed about the intervention before participating, etc.). If a participant reports symptoms of nausea during the VR intervention, then the study will stop and participants will be provided a comfortable resting place, cool drinking water and hand towel, and a receptacle (e.g., waste bin) for emesis. The participant's caregiver will be informed immediately. It is also possible that youth may experience eye fatigue, however, this also has not happened in 45-minute sessions in the PI's previous research involving over 500 youth. In the event this does occur, participants can stop the session at any time. The VR intervention has been developed to be age appropriate and rated.

As with any study being conducted during this pandemic there is the risk of transmission or exposure to COVID-19. SA3 is being conducted at VCU Health. As a Level I Trauma Center, VCU Health has employed a range of COVID-19 procedures to help reduce transmission and exposure to COVID-19 (see section 2b). Further, to prevent spread of COVID-19 all VR headsets will be cleaned with a UV clean box, similar to what is used to clean N95s and medical equipment.

All equipment will be sanitized before and after participants engage in study activities. The procedures have been approved by VCU IRB for existing federally funded research conducted by the PI (HM20022975; HM20021727).

Impact VR has the potential benefit of reducing CD and CU traits, and increasing prosocial behaviors. This service is free to the participant.

16.0 Potential Benefits to Subjects*

Participants involved in the VR intervention may benefit from improvement in emotion recognition and regulation, which may result in improvements in CD, CU traits and conduct problems. For the control group, there may be no direct benefits for the individual. However, rather than providing nothing to control group, we selected a flyer with an overview of how to identify emotional expressions (happy, sad, fear, and anger).

17.0 Data Management* and Confidentiality

Statistical Design and Power

Assessing the acceptability of Impact VR among youth with CD (SA1). To measure acceptability for youth, focus groups will be conducted with the participation of 20 youth with CD. A focus group moderator (project coordinator) will be present during these sessions to record qualitative responses and facilitate these sessions. At least 3 focus groups will be conducted in order to ensure that all primary thematic clusters are detected[59]. Sessions will be audio-recorded to ensure accuracy of reporting and these recordings will be transcribed for analyses. The measure of the focus groups will be based on Sekhon et al.'s[60] theoretical framework of acceptability for healthcare interventions to comprehensively assess acceptability across multiple domains: (1) Affective Attitude (e.g., how do youth feel about Impact VR's specific sessions?), (2) Burden (e.g., any physical symptoms associated with use (i.e., headaches, nausea)?), (3) Perceived Effectiveness (e.g., are the lessons understandable and enjoyable?), (4) Ethicality (e.g., Is the content culturally sensitive and informed?), (5) Intervention Coherence (e.g., is the intervention easy to follow and understand?), (6) Opportunity Costs (e.g., did youth feel like Impact VR was a good use of their time?), (7) and Self-Efficacy (e.g., are youth are able to navigate and learn new skills?). To determine overall acceptability, an 80% acceptability rate will be inferred across groups. If responses fall below 80% acceptability, modifications to improve Impact VR will be made.

Assess the feasibility and usability of the deployment of Impact VR in youth's homes, schools, and treatment settings (SA2). The feasibility and usability of Impact VR will be tested by conducting separate focus groups for (1) 10 youth and 10 caregivers, (2) 10 teachers and school counselors, and (3) 10 mental health treatment providers. Focus groups will be kept to 6-7 people within their respective group (e.g., 6-7 caregivers, 6-7 teachers and school counselors, etc.). Our sample size is based on prior research suggestions for ideal and effective participant group sizes for usability testing[61]. Self-report surveys and semi-structured interviews will be administered after groups complete Impact VR, with the goal of identifying impactful changes to each session to improve design and usability flaws (e.g., user control, etc.), which will increase deployment success. Youth will be asked to provide perceptions and feedback on the storylines, games, artwork, and aesthetic components of the VR experience. These components will be assessed given the interrelated nature of usability and aesthetics[62]. Adults will be asked usability questions related to the set-up and use of Impact VR at home, in school, and in mental health settings (e.g., hospital, outpatient clinic). Adults will be asked about Impact VR's progress report data output to evaluate what data is meaningful (e.g., correct vs incorrect number of responses) and how it is best displayed (e.g., percentages vs count, graphs vs text). Improvements to Impact VR will be made prior to the RCT (SA3). For feasibility and usability of Impact VR, we aim to achieve >90% performance and satisfaction rate, and <5% set up error rate, and <0.5% software errors. In preparation for the Phase II STTR, adults will provide input from a consumer perspective based on their grouping (e.g., teacher, etc.) to improve our understanding of a commercialization strategy for moving Impact VR to market.

Evaluate Impact VR for reducing CD, CU traits, and CP, and improving emotion recognition (SA3). Descriptive statistics will be computed for baseline characteristics with means and standard deviations reported for continuous variables, and counts and proportions for categorical variables. Data will be examined to ensure statistical assumptions are satisfied, and if necessary, normalizing transformations or non-parametric tests will be used. To assess the preliminary efficacy of the intervention, we will estimate the mean (or median) change of the outcome variables at each follow-up time point. For each outcome, we will examine the mean difference in change between the intervention and control group between baseline and 3-month follow-up with their corresponding 95% confidence intervals. To assess preliminary efficacy, we will test for change in each outcome from baseline to 3-month follow-up using a paired t-test (or Wilcoxon signed-rank test) using an alpha of 0.05. Statistically significant change will be considered evidence of preliminary efficacy. Lastly, we will estimate the variance of each outcome at the two follow-up time points. These values will be used to determine the sample size required for a future randomized control trial. The estimates and data gathered from this RCT will be used to inform the design of the future confirmatory trial and to show a "signal" that the intervention can provide meaningful changes. All analyses will be completed using the R statistical software.

SA3 Sample size justification and handling of missing data. The goal of SA3 is assess preliminary effectiveness of Impact VR and obtain estimates of variability to guide a larger RCT in Phase II. Prior research recommends a sample size of at least 12 per group for a pilot study to estimate the variance of treatment effects[63], as the gain in precision of the estimate of variance diminishes once a sample size reaches 12[63]. Our sample size of $N = 60$ ($n = 30$ per treatment group) for the RCT exceeds this recommendation so we can obtain precise estimates of the variance for the main outcomes. The estimates of variability will be appropriately stable for use in the sample size plan for a future trial which will be adequately powered to detect the minimal meaningful effects. Considering the precision of the estimate of variance, the standard error of the variance is given by $S^2\sqrt{2/(n-1)}$ where S^2 is the variance and n is the sample size. With a sample size of 30 per group, we will have a standard error that is 0.28 times the variance, or 28% of the estimated variance (for a variance of 10, the standard error would be 2.8), accounting for up to 10% attrition. In addition to adequacy for estimating variability for future sample size planning, we will also be able to estimate proportions with 95% confidence intervals within ± 0.19 for proportions of 0.5 to ±011 for proportions of 0.9 for each group. In addition to the sample size being adequate for estimating group variances, it also provides adequate power to test for change from baseline to follow-up within group. Specifically, we will have 80% power to detect a standardized effect size *dz* of 0.56, a medium effect size according to Cohen, assuming 10% attrition. Given our ability to estimate the group-level variances, and power to detect change from baseline to follow-up, we consider the sample size appropriate for completing the aims of this study. Missing data analysis will examine any variables associated with the likelihood of having missing data. These factors, baseline outcomes and demographics will be used in a multiple imputation model to impute missing data. To prevent biased estimates of variances and means observed, we will apply joint multiple imputation (J-MI). J-MI performs well in sample sizes as small as 50 with up to 30% missing data[64].

17.1 *Describe the steps that will be taken to secure the data (e.g., training, authorization of access, password protection, encryption, physical controls, certificates of confidentiality, and separation of identifiers and data) during storage, use, and transmission. If the study will code the research data by replacing subjects' names and/or other identifiers with assigned subject IDs, describe the following:*

- *How subject IDs will be generated/assigned (e.g., random, sequential)*

Random

- *Whether a key will be retained linking subject IDs to identifiers, and if so where the key will be stored, who has access to key, and when key will be destroyed*
- *Linking keys will be stored separately from the data, in a secured/locked office*

Select all that apply to ***paper*** *research material:*

X *Maintaining control of paper documents at all times, including when at off-campus location*

X *Storing paper documents in a secure location accessible only by study team*

X *Promptly transcribing, scanning, or abstracting data from paper into electronic platform and destroying the paper copy*

Select all that apply to ***electronic*** *research material:*

X *Use VCU-approved methods of data storage, transmission, and transfer (see https://dms.vcu.edu)*

X*Using individual logins/separate accounts on shared devices*

X *Using VCU approved data collection tools and apps (e.g., REDCap, Qualtrics)*

X *Consulting with VCU Information Security when using non-VCU approved data collection tools (https://ts.vcu.edu/askit/essential-computing/information-security/)*

17.2 *N/A*

17.3 Describe how data or specimens will be handled study-wide:

- *Survey data will be held for upto 5 years*

17.4 If you plan to retain screening data collected by phone or other methods for people who decline to participate, describe this, including the rationale for retaining the information and for how long (e.g., end of the study).

This information will be retained to ensure we do not contact people who have declined again. This data will be deleted once recruitment ends.

18.0 Provisions to Monitor the Data to Ensure the Safety of Subjects*

This section is required when research involves more than Minimal Risk to subjects.

18.1 Describe: n/a

19.0 Provisions to Protect the Privacy Interests of Subjects

19.1 Describe the steps that will be taken to protect subjects' privacy interests. "Privacy interest" refers to a person's desire to place limits on whom they interact or whom they provide personal information.

Select any of the following that apply:

x *Conducting study activities in locations that maximize privacy*

x *Verifying identify before discussing personal information*

x *Asking the subject if they are comfortable answering in the location*

x *Asking the subject if they are comfortable with others present*

x *Offering alternate ways to respond (e.g., pointing, writing)*

x *Using generic signs on research rooms and spaces*

x *Some questions may be skipped*

x *Using Study IDs instead of direct identifiers*

n/a *Using mailing techniques that do not include study name or identifiers*

x *Working only in locations the study team can ensure privacy*

x *Storing study material in locations restricted to study team access*

n/a *Obtaining explicit parental permission before sharing photos/recordings of children*

19.2 Describe what steps you will take to make the subjects feel at ease with the research situation in terms of the questions being asked and the procedures being performed. "At ease" does not refer to physical discomfort, but the *sense of intrusiveness a subject might experience in response to questions, examinations, and procedures.*

Participants will be made aware that there involvement is completely voluntary and they may choose to answer/not answer any of the survey questions.

19.3 Indicate how the research team is permitted to access any sources of information about the subjects.

Dr. Thomson's team is employed at VCU and therefore has access to the required resources

19.4 Select all identifiers that will be collected at any time as part of this study (including for recruitment, data gathering, data analysis, etc.), even if the data will eventually be anonymized:

X *Names*
☐ *Geographic Locators Below State Level*
☐ *Social Security Numbers*
X *Dates (year alone is not an identifier)*
☐ *Ages over 89 (age under 89 is not an identifier)*
X *Phone Numbers*
☐ *Facsimile Numbers*
X *E-mail Addresses*
X *Medical Record Numbers*
☐ *Device Identifiers*
☐ *Biometric Identifiers*
☐ *Web URLs*
☐ *IP Addresses*
☐ *Account Numbers*
☐ *Health Plan Numbers*
☐ *Full Face Photos or Comparable Images*
☐ *License/Certification Numbers*
☐ *Vehicle ID Numbers*
☐ *Other Unique Identifier*
☐ *No Identifiers*
☐ *Employee V#*

20.0 Compensation for Research-Related Injury

20.1 If the research involves more than Minimal Risk to subjects, describe the available compensation in the event of research related injury.

N/A

20.2 Provide a copy of contract language, if any, relevant to compensation for research-related injury.

N/A

21.0 Economic Burden to Subjects

21.1 Describe any costs that subjects may be responsible for because of participation in the research.

There is no cost to participants

22.0 Consent Process

22.1 Indicate whether you will you be obtaining consent, and if so describe (describe for different groups if multiple): yes

- *Who will obtain informed consent*
    - *The study team (PI or research assistants)*
- *Where will the consent process take place.*
    - *At VCU*
- *How the consent process will be conducted (e.g., electronic, face-to-face, phone or video). If electronic, describe platform.*
    - *Face to face*
- *Any process to ensure ongoing consent.*
- *Whether you will be following HRP-090 - SOP - Informed Consent Process for Research. If not, describe:*
    - *We will follow HRP-090. However, we are only requesting consent from one parent. This is because requiring two parents will result in severely limiting recruitment opportunities for youth, who often come from single-parent households. Requiring two parent signatures would discriminate eligible participants based on parent relationship status. This study would not be able to be completed if it required two parent signitures.*
    -

Non-English Speaking Subjects

- *This study only includes English speaking participants.*

Waiver or Alteration of Consent Process (consent will not be obtained, required information will not be disclosed, or the research involves deception)

- *N/A*

Subjects who are not yet adults (infants, children, teenagers)

- *SEE SECTION 6.*

Cognitively Impaired Adults

- *Describe the process to determine whether an individual is capable of consent or assent. The IRB allows the person obtaining assent to document assent on the consent document and does not routinely* *require assent documents and does not routinely require cognitively impaired adults to sign assent documents.*

Participants will be assessed during the consent/assent process by assessing consent/assent content understanding.

Adults Unable to Consent

- *See section 6*

23.0 Process to Document Consent in Writing

23.1 Consent will be completed in person using paper documents.

23.2 If your research presents no more than minimal risk of harm to subjects and involves no procedures for which written documentation of consent is normally required outside of the research context, the IRB will generally waive the requirement to obtain written documentation of consent.

24.0 Setting

24.1 Describe the sites or locations where your research team will conduct the research.

- *VCU West Hospital; IVPP Research Lab*

25.0 Resources Available

25.1 Describe the resources available to conduct the research: For example, as appropriate:

Dr Thomson has all the required resources to complete the study.