HRP-503B – BIOMEDICAL RESEARCH PROTOCOL
(2017-1)

Protocol Title: A Digital Intervention for HIV Prevention in Black Adolescent Girls

Principal Investigator: Kimberly Hieftje, PhD

Version Date: 12/10/2021

(*If applicable*) Clinicaltrials.gov Registration #: NCT04108988

INSTRUCTIONS
This template is intended to help investigators prepare a protocol that includes all of the necessary information needed by the IRB to determine whether a study meets approval criteria. **Read the following instructions before proceeding:** 1. Use this protocol template for a PI initiated study that includes direct interactions with research subjects. Additional templates for other types of research protocols are available in the system Library. 2. If a section or question does not apply to your research study, type "Not Applicable" underneath. 3. Once completed, upload your protocol in the "Basic Information" screen in IRES IRB system.

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SECTION I: RESEARCH PLAN

1. **Statement of Purpose:** State the scientific aim(s) of the study, or the hypotheses to be tested.

The purpose of this study is to develop and evaluate an innovative behavioral HIV prevention videogame intervention to bolster motivation and provide skill-building opportunities to improve Black adolescent girls' ability to negotiate around risk including advocating for partner HIV/STI testing, increasing their knowledge and awareness of HIV/STIs, and for reducing sexual risk-taking behaviors (1.e. non-condom use). As a multiplayer videogame, the intervention will be developed and delivered as a social, multiplayer videogame, a compelling context for Black adolescent girls who constantly interact and seek counsel from their peers.

To this end, our Specific Aims, focusing on Black adolescent girls aged 14-18 years, are to:

1. Translate our culturally and socially-tailored card game ***One Night Stan*** to a multiplayer videogame using game design and content experts and focus group input from 30 Black adolescent girls.
2. Conduct a pilot randomized controlled trial comparing the multiplayer videogame ***InvestiDate*** intervention vs. an attention/control non-health-related multiplayer videogame with 80 participants collecting assessment data at baseline, one, and four months to:
    a. Determine the intervention's acceptability and feasibility by collecting quantitative and qualitative data on Black adolescent girls' satisfaction and gameplay experience of the intervention.
    b. Determine the preliminary impact of the intervention on knowledge (information), intentions/attitudes (motivation), social norms, and behavioral skills as related to: i) HIV/STI testing and partner testing and ii) condom use, and iii) sexual risk behavior reduction, such as alcohol and drug use.

2. **Probable Duration of Project:** State the expected duration of the project, including all follow-up and data analysis activities.

    2 years

3. **Background:** Describe the background information that led to the plan for this project. Provide references to support the expectation of obtaining useful scientific data.

    Black women are disproportionately affected by HIV. At current rates, 1 in 32 Black women will be diagnosed with HIV in her life span[1]. Given that Black women are often diagnosed late in the disease process, it is believed that many Black women were, in fact, infected in adolescence[2]. Black adolescent girls between the ages of 14 and 19 are more than twice as likely than White girls (44% vs. 19%, $p = 0.001$) to be diagnosed with an STI ($p = 0.001$)[3]. Alarmingly, STIs are associated with an increase in the risk for HIV acquisition up to two- to fivefold[4-6]. Research suggests that inadequate knowledge about HIV and the role of high-risk behaviors may contribute to the high HIV rates among Black women[7]. For this reason, an early intervention that focuses specifically on Black adolescent girls in high school and that is gender and culturally tailored may decrease their risk for HIV/STIs infection.

    Studies of social and behavioral determinants of disease have increasingly focused on the role of peer group structures on individual outcomes[8,9]. Interactions in peer groups offer opportunities for individuals to exchange and evaluate information, to learn social norms, to develop behavioral skills,

and to influence each other's attitudes and behaviors[10]. These interactions have important effects on knowledge and attitudes about risk, social support for risk and behavioral skills for prevention, and risk or preventive behaviors per se[11]. For instance, a community-based pilot study demonstrated a 72% increase in the number of individuals getting tested for HIV/STI when peers recruited others through their social network [12]. Similarly, a recent study of at-risk Black and Hispanic young women and adolescent girls, aged 13 to 24, found that a female friendship network method of engaging them was successful with increasing HIV testing rates of 90%[13].

Ninety-seven percent of teens ages 12-17 play computer, web, portable, or console games[14], and 94% of girls play video games. Social videogames, or games played with others, are the most popular and most frequently played game genre[15]. Both non-digital and digital games have a well-established role in education[16] because simulated role-playing is a highly effective approach for situated learning[17]. Active participation through simulated role-playing enables individuals to practice behavioral change in a safe and entertaining way[18,19]. Role-playing is a powerful mechanism for influencing people's attitudes[20,21]. Game interventions have demonstrated efficacy in increasing knowledge and affecting behaviors and psychological variables related to health promotion and disease management[22] in areas ranging from depression to medication adherence[23-29]. There is also compelling evidence that individuals who acquire new information, motivation, behavioral skills in a gaming environment are more likely to act in accordance with the new skills in real life[30,31]. Multiplayer social games are often more slowly and deliberately paced than single player games. This may help to create a shared experience with at least one other player, thus allowing for conversations between players and the opportunity to influence attitudes, beliefs, and perceptions around serious topics[32].

Although effective HIV/STI prevention programs for Black adolescent girls currently exist, including Diffusion of Effective Behavioral Interventions (DEBIs), such as Sisters Informing Healing Living and Empowering (SIHLE), Choosing Life: Empowerment! Action! Results! (CLEAR), and Focus on Youth with Informed Parents and Children Together (FOY+ImPACT)[33], challenges regarding implementation and fidelity have been a concern. Recent studies have cited several barriers to the implementation of HIV/STI prevention interventions, including access to adequately trained providers, staff turnover, resource constraints of agencies, fidelity of the interventions, and challenges of adapting an intervention from one population to another[34-36]. In addition to consistent fidelity and limited demand on program resources, the proposed multiplayer videogame offers some new features that could augment those found in many HIV prevention interventions that target Black adolescent girls as it will: 1) be packaged in a self-contained "vehicle" that is easily accessible and widely available; 2) be interactive with opportunities for players to build and practice skills; 3) allow for Black adolescent girls to engage with others or on their own, increasing their exposure (or "dose") to the intervention; 4) build upon elements that have been identified as being crucial for successful HIV/STI prevention in this population; and 5) not require personnel cost or staff training. Furthermore, given that videogame play is widespread, a game for HIV/STI prevention will allow for greater dissemination of this intervention and potential expansion of this concept to other high-risk populations.

4. **Research Plan:** Summarize the study design and research procedures using non-technical language that can be readily understood by someone outside the discipline. **Be sure to distinguish between standard of care vs. research procedures when applicable, and include any flowcharts of visits specifying their individual times and lengths**. Describe the setting in which the research will take place.

   The purpose of this study is to translate the card game prototype, ***One Night Stan***, into a multiplayer videogame with a focus on empowering Black adolescent girls to assess their risk, improve communication skills, and develop self-efficacy throughout their sexual experiences. By doing so, this digital intervention may provide an opportunity to reduce HIV/STI disparities in Black adolescent girls. To differentiate between the card game and the multiplayer videogame intervention, the videogame intervention has been named ***InvestiDate***.

   The study will take place in two phases. In **Phase 1,** we will conduct four focus groups with five participants each (20 participants) with Black adolescent girls to understand their attitudes, perceptions, and knowledge around communication about HIV/STI testing and condom use with partners. We will conduct focus groups at our partner settings, which include private rooms that we can access. Alternatively, we may conduct focus group sessions through Yale's videoconferencing tool, Zoom. We will then develop an alpha version of the multiplayer videogame ***InvestiDate,*** from the prototype card game, ***One Night Stan***, using formative research and focus group data. Once developed, we will then conduct playtesting with focus groups (two focus groups with five participants each) to develop the beta version of the game. In **Phase 2,** we will pilot test the game intervention with 80 Black adolescent girls (aged 14-18 years) at partner sites in New Haven, Connecticut. Alternatively, we may conduct gameplay sessions through Yale's videoconferencing tool, Zoom, if in person meetings are not possible. If conducted in person, gameplay sessions will take place in private rooms dedicated to the study. If conducted remotely, we will ensure participants have access to a private room and Zoom-capable equipment. Participants will be randomly assigned to ***InvestiDate,*** or a non-health related multiplayer videogame that will serve as an attention/time control condition. All participants will play their assigned videogame for 1-2 hours, on two instances separated by approximately a week for between 2 and 4 hours of gameplay total. They will be evaluated at baseline, one, and four months.

   Setting: For **Phase 1 and Phase 2,** recruitment and enrollment will take place either in person with partner schools and organizations or remotely either in partnership with schools that have agreed to collaborate with us, or through study advertisements placed on social media. Given our ability to play the videogame and collect data remotely, we are seeking additional partnerships with schools nationwide and recruiting participants individually through social media, including Facebook and Instagram. For Phase 1 (focus groups), recruitment may also take place online through social media platforms, including Facebook and Instagram. Focus groups will take place online through Zoom where participants will be able to see and interact with each other.

   Of note, the Principal Investigator, Dr. Kimberly Hieftje will not be involved in any aspects of consenting participants or their parents, the randomization process, data collection or direct performance of data analysis procedures.

   Participants: For **both phases**, participants must be Black heterosexual adolescent girls aged 14 to 18 and currently enrolled in high school. For **Phase 2**, participants must also: 1) be able to participate in web-based videogame (willing to sit for 60-minutes/session to play the game); 2) not have been tested for HIV in the past year; and, 3) be able to provide assent/parental/guardian consent.

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Phase 1: Conduct focus groups and playtesting with Black adolescent girls and develop *InvestiDate* (30 participants): Focus group discussions with Black adolescent girls will inform the new version of the game by providing ideas for content and gameplay around HIV/STI testing, condom use, and sexual risk taking. We have used and refined this iterative process for current videogame projects[15,37-45]. Data collected will be used to inform the development of the multiplayer videogame, ***InvestiDate.*** Example question for the focus groups include, "What are some red flags that teens your age look for when considering dating someone?", "What are some green flags that teens your age look for when considering dating someone?", "What might make it difficult for teens your age to get tested for HIV/STIs?"

The card game prototype ***One Night Stan*** will be adapted as a multiplayer videogame called ***InvestiDate*** and will focus on a slightly younger age group. To do this we use formative research, pilot data, and focus group input to create an updated Game Playbook[37], or intervention manual that will be used to guide the development and design of the game.

Phase 2: Pilot test *InvestiDate* compared with a control condition: Participants will be randomly assigned to play either ***InvestiDate*** (n=40), or the non-health related attention and time control condition multiplayer videogame (n=40). Participants will be assigned to either the intervention or the control condition using a stratified randomization procedure[46]. Age for the participant and partner testing in the last 30 days will be included in the randomization algorithm. Participants will be randomized by group so that the same group of participants will always play together.

Assessments: We will assess a range of pre-intervention participant characteristics (demographic), process measures, and outcomes (see below in Table 1). All assessments are standardized validated instruments that will be collected in person, using a web-based clinical trial management system we have used with our other studies. Assessments will be collected online using Yale-secured Qualtrics survey collection software. Baseline assessments are designed to ensure that all participants meet eligibility criteria and that important predictor variables are assessed. We will conduct post-intervention assessments immediately after gameplay sessions are completed (one month) with follow-up assessments at four months following enrollment to allow an adequate time for accumulation of outcome events[47].

Table 1: Assessments

Assessment	Base-line	Month 1	Month 4
Participant Demographics (i.e. gender, age, education)	X		
HIV/STI Testing Rates and Partner HIV/STI Testing Rates	X	X	X
Sexual Risk Behaviors—Self-reported measures of sexual intercourse with/without condoms[48]	X	X	X
Vulnerability to Risky Sexual Behaviors[49,50]	X	X	X
Risk Behaviors Associated with HIV/STIs - Youth Risk Behavior Survey[51]	X	X	X
HIV Knowledge (HIV-KQ)[52] (45 item true/false questionnaire)	X	X	X
STI Knowledge (STD-KQ)[53] (27-item true/false questionnaire)	X	X	X
Subjective Norms[54,55]	X	X	X
Intentions[56,57]	X	X	X
Attitudes—Multi-dimensional Condom Attitudes Scale (MCAS)[58]	X	X	X
Self-efficacy in sexual risk behaviors—Sexual Risk Behavior Beliefs and Self-efficacy (SRBBS) Scales[59]	X	X	X
Condom Self-Efficacy (CUSES)[60] (28-item Likert scale)	X	X	X
Sexual Communication[61]	X	X	X
*Satisfaction with game play/acceptability and feasibility (12-item Likert scale)[44]		X	

5. Genetic Testing N/A ☒

6. **Subject Population:** Provide a detailed description of the types of human subjects who will be recruited into this study.

   Adolescents ages 14-18 will be recruited into this study.

7. **Subject classification:** Check off all classifications of subjects that will be specifically recruited for enrollment in the research project. Will subjects who may require additional safeguards or other considerations be enrolled in the study? If so, identify the population of subjects requiring special safeguards and provide a justification for their involvement.

☒Children	☒ Healthy	☐Fetal material, placenta, or dead fetus
☐Non-English Speaking	☐ Prisoners	☐Economically disadvantaged persons
☐Decisionally Impaired	☐ Employees	☐Pregnant women and/or fetuses
☐Yale Students	☐ Females of childbearing potential	

NOTE: Is this research proposal designed to enroll children who are wards of the state as potential subjects?
Yes ☐ No ☒

8. **Inclusion/Exclusion Criteria:** What are the criteria used to determine subject inclusion or exclusion?

   Inclusion/exclusion criteria: For **both phases**, participants must be Black heterosexual adolescent girls aged 14 to 18 and currently enrolled in high school. For **Phase 2**, participants must also: 1) be able to participate in web-based videogame (willing to sit for 60-minutes/session to play the game); 2) not have been tested for HIV in the past year; and, 3) be able to provide assent/parental/guardian consent.

9. How will **eligibility** be determined, and by whom?

   Eligibility will be determined by the research team. If a prospective participant meets the inclusion criteria, they will be eligible to participate in the project.

10. **Risks:** Describe the reasonably foreseeable risks, including risks to subject privacy, discomforts, or inconveniences associated with subjects participating in the research.

The potential risks associated with this study have to do with maintenance of the confidentiality of the identities of the participants enrolled in the study and information relating to them. For focus groups, we will address the risk to confidentiality to participants that are participating in the study and that this cannot be guaranteed given that others will also be participating. However, participants will be told that they should not disclose information about other participants and all participants should respect the privacy of each other. Only participants' ID numbers will be recorded on the electronic assessments themselves to protect confidentiality. Sensitive data is encrypted in transit and in storage. The web data-entry interface allows data entry to be performed from anywhere on the Internet and uses 128-bit secure sockets layer (SSL) security to protect the confidentiality of the data. Playing ***InvestiDate*** may pose a potential psychological risk in that we address sensitive issues around sexual activity and how HIV/STI is transmitted, and the specifics of how certain

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risk behaviors (such as alcohol use) can result in HIV/STI. Additionally, participants may also recognize that they have risked acquiring HIV/STI and may have already acquired these diseases without knowing by confirmatory testing. It also involves interactions with the participants' peers. The assessments and instruments may also present a potential risk given that some of the questions are sensitive in nature and address issues around sexual activity and other risky behaviors.

11. **Minimizing Risks:** Describe the manner in which the above-mentioned risks will be minimized.

A number of precautions will be actively integrated into the research procedures to protect the confidentiality and anonymity of all participants. For participating in Yale's videoconferencing tool, Zoom, participants will be asked to find a secure, private setting, free from others outside the study that may overhear the discussion. All research staff and the staff and volunteers participating in the intervention will be required to complete training in research ethics. Data collection forms will be designated by ID numbers only. A separate master file of names, addresses, contact persons, and telephone numbers, along with the study ID numbers will be maintained in a locked file cabinet in the research team's offices. All data entry and analyses will be completed with ID numbers only. The study will be explained to others, such as the guardian/parent and program staff as a study of child development that will focus on promoting healthy behaviors. In instances in which data are requested from other sources or it is beneficial to the participant to provide information to another individual or agency (e.g. medical personnel) this will only be done with the written permission of the guardian/parent on a "Release of Information" form stipulating who the information is provided to, or received from. The research staff will follow standard confidentiality procedures for research programs.

The research assistant will be available at all times to provide assistance to the participants, answer their questions, and serve as a resource if any distress or concern arises. The research assistant will be available to assist the participants, the community sites staff, and the research staff member administering the assessments if there appears to be any distress around the questions being asked. If participants need additional or more intensive attention, the research assistant will contact Dr. Claudia-Santi Fernandes, our clinical psychologist on the team, who will consult with the team in order to potentially provide consultation resources to the participant.

12. **Data and Safety Monitoring Plan:** Include an appropriate Data and Safety Monitoring Plan (DSMP) based on the investigator's risk assessment stated below. (Note: the HIC will make the final determination of the risk to subjects.)
    a. What is the investigator's assessment of the overall risk level for subjects participating in this study? Minimal risk
    b. If children are involved, what is the investigator's assessment of the overall risk level for the children participating in this study? Minimal risk
    c. Include an appropriate Data and Safety Monitoring Plan. Examples of DSMPs are available here http://your.yale.edu/policies-procedures/forms/420-fr-01-data-and-safety-monitoring-plans-templates for
        i. Minimal risk
        ii. Greater than minimal

The principal investigator is responsible for monitoring the data, assuring protocol compliance, and conducting the safety reviews quarterly. During the review process, the research team will evaluate whether the study should continue unchanged, require modification/amendment, or close to enrollment.

The principal investigator or the Human Investigative Committee (HIC) have the authority to stop or suspend the study or require modifications.

This protocol presents minimal risks to the subjects and Unanticipated Problems Involving Risks to Subjects or Others (UPIRSOs), including adverse events, are not anticipated. In the unlikely event that such events occur, Reportable Adverse Events (which are events that are serious or life-threatening and unanticipated (or anticipated but occurring with a greater frequency than expected) and possibly, probably, or definitely related) or Unanticipated Problems Involving Risks to Subjects or Others that may require a temporary or permanent interruption of study activities will be reported immediately (if possible), followed by a written report within 5 calendar days of the Principal Investigator becoming aware of the event to the IRB via the RNI submission process in IRES IRB and any appropriate funding and regulatory agencies. The investigator will apprise fellow investigators and study personnel of all adverse events that occur during the conduct of this research project through regular study meetings and via email as they are reviewed by the principal investigator. We will use procedures to detect and respond to adverse events that ensure prompt discovery of any adverse events and to minimize their effects. There is adequate surveillance and protections to discover adverse events promptly and keep their effects minimal. Data and safety monitoring procedures in this study include collection and monitoring of paper-based questionnaires and an organizational structure of clearly defined tasks assigned to all research personnel involved in the conduct of this study. We will keep a thorough record of research activities and completion of scheduled assessments.

We have established a Data Safety and Monitoring Board (DSMB) composed of two experts, Dr. Trace Kershaw and Dr. Cindy Crusto, in clinical trials in young teens and in statistical analysis of clinical trials to oversee the safety and data integrity of this study. DSMB will also review the progress of the study.

Dr. Trace Kershaw, Department Chair and Professor of Social and Behavioral Sciences, focuses on the social and structural determinants of health (e.g., sexual health, substance use, mental health, reproductive health) among adolescents and emerging adults. His current focus is using innovative technologic methods to understand how social and geographic context influence their behaviors and health. Further, he is an expert in developing interventions aimed to improve the health and well-being of adolescents and emerging adults.

Cindy A. Crusto, Ph.D., Associate Professor of Psychiatry, Yale University School of Medicine, is the Director of Program and Service System Evaluation at The Consultation Center. Dr. Crusto has more than 20 years of experience in developing, implementing, and evaluating preventive interventions in schools and community agencies. She also has extensive experience providing training and technical assistance to schools and to community-based organizations on the evaluation of prevention programs. She is interested in culturally relevant interventions for children from racial/ethnic minority and low-income backgrounds and in school-based behavioral health services.

d. For multi-site studies for <u>which the Yale PI serves as the lead investigator</u>:
   i. How will adverse events and unanticipated problems involving risks to subjects or others be reported, reviewed and managed? *Write here*
   ii. What provisions are in place for management of interim results? *Write here*
   iii. What will the multi-site process be for protocol modifications? *Write here*

13. Statistical Considerations: Describe the statistical analyses that support the study design.

All of the statistical analyses, including ensuring the completeness and integrity of the data is being carried out by the Yale Center for Analytical Studies (YCAS) in conjunction with the personnel overseeing CTMS. YCAS is a relatively new center for collaborative science. Developed in partnership with the Yale Center for Clinical Investigation and the Yale School of Public Health (YSPH), YCAS brings together existing academic strengths in biostatistics, epidemiology, health economics and health services research at Yale. Their collaborative teams provide expertise in the design, conduct and analysis of health and healthcare studies, methodological development and education and training to Yale and the extended research community. YCAS operates in a vital and expanding YSPH community of scholars engaged in research that enhances the quality of the analytical and computational tools needed to effectively use the data being generated by rapidly advancing technology. Hence, it serves as a nexus for clinical investigators and analytical scientists with common interests to nurture the development and application of new approaches to design and data analysis.

Focus Groups: Data will be analyzed using the principles of grounded theory, using the constant comparative method for systematic inductive analysis[62]. The transcripts from focus groups will be reviewed by members of the research team jointly who will perform data coding. We will develop the codes in a step-wise fashion[63], beginning with the creation of an initial code structure from the first two transcripts that are independently reviewed by each team member. All focus groups will be analyzed before initiating subsequent focus groups and new concepts will be used as probes in the subsequent interviews. To enhance inter-rater reliability, focus group transcripts will be independently reviewed and coded by each researcher and coding will be compared for agreement. Manual coding will then be electronically applied to the textual data using Dedoose a software program designed to facilitate the analysis of qualitative data. Data collected will be used to inform the development of the multiplayer videogame, ***InvestiDate.***

Data Analyses General Considerations: Statistical procedures and models for analyzing data have been selected according to the research hypotheses being investigated and the types of data available. In general, we will use two-tailed tests and p-values smaller than 0.05 will be considered to indicate statistical significance. When necessary, however, we will use appropriate adjustment of the level of significance (alpha) to account for multiple statistical tests. All statistical analyses will be conducted on an intention-to-treat sample using either SPSS/SAS statistical packages. Baseline characteristics will be analyzed using descriptive statistics. We will use baseline, one-month, and four-month data to estimate effect sizes for the primary outcome[125]. Given the limited sample size (n=80), we anticipate that the power of this study to identify small but significant effect sizes will be low. A strength of this design is that it provides a number of perspectives from which to view treatment effects, including a treatment condition, a control condition, and a follow-up period. The results will inform the sample size calculation for a subsequent full-scale randomized trial.

We will evaluate the preliminary efficacy of ***InvestiDate*** at increasing HIV/STI testing and partner HIV/STI testing. We will test the hypothesis that individuals who play ***InvestiDate*** will report more

HIV/STI testing and partner testing in comparison to the control condition. We will conduct a longitudinal analysis using a hierarchical linear mixed models approach to compare participants in the intervention group to participants in the control group on reported participant and partner HIV/STI testing from baseline across all follow-up assessments (i.e., baseline, one month and four months). Hierarchical modeling will allow us to account for the fact that the data are nested as the participants will play the game in groups. An advantage of mixed models is that participants with missing data need not be excluded as all available data are used in estimating parameters. We will also use logistic regression models to determine if any relevant baseline variables are associated with improvement in reported HIV/STI testing or partner testing (constructed as a binary outcome (Yes/No). We plan to evaluate the prognostic significance of a small set of predictor variables (e.g., intentions, attitudes, self-efficacy, social norms, and knowledge) and use them as covariates in the primary analysis. All of these analyses will be exploratory given the study sample size.

SECTION II: RESEARCH INVOLVING DRUGS, BIOLOGICS, RADIOTRACERS, PLACEBOS AND DEVICES

A. RADIOTRACERS ☒N/A

B. DRUGS/BIOLOGICS ☒N/A

C. DEVICES ☒N/A

SECTION III: RECRUITMENT/CONSENT AND ASSENT PROCEDURES

1. Targeted Enrollment: Give the number of subjects: 250
   a. Targeted for enrollment at Yale for this protocol: 110
   b. If this is a multi-site study, give the total number of subjects targeted across all sites: n/a

2. Indicate recruitment methods below. Attach copies of any recruitment materials that will be used.

☒ Flyers	☐ Internet/web postings	☐ Radio
☒ Posters	☐ Mass email solicitation	☐ Telephone
☐ Letter	☐ Departmental/Center website	☐ Television
☐ Medical record review*	☐ Departmental/Center research boards	☐ Newspaper
☐ Departmental/Center newsletters	☐ Web-based clinical trial registries	☐ Clinicaltrails.gov
☐ YCCI Recruitment database	☒ Social Media (Twitter/Facebook):	
☐ Other:		

3. Recruitment Procedures:

a. Describe how potential subjects will be identified. SEE BELOW

b. Describe how potential subjects are contacted. SEE BELOW

c. Who is recruiting potential subjects? SEE BELOW

The study will be advertised via posters and flyers located and circulated at the partnering schools. The opportunity to participate in the study will also be announced in classrooms at our participating schools. The study will also be advertised through social media, including Facebook and Instagram. Participation in this study will be strictly voluntary, confidential and non-discriminatory. Participants interested in participating in our study will follow a link displayed on the flyers and social medial advertisements to a Yale Qualtrics webpage where they will fill out a form with basic demographic information (age, race, sexual orientation) and their contact information (email and phone number) and the parent/guardian contact information (email) for participants younger than 18. All participants who fill out the Qualtrics form will receive an email

from the project director/research assistant with details about the study and exclusion/inclusion criteria. If the participant is under 18, the research staff member will email the parental information sheet to the parent and contact them by email or phone to obtain written consent. If either the participant or the parent do not wish to be in the study or have their child participate in the study, no further contact will be made. Participants that meet the requirements and after consent or parent permission and assent have been obtained, will be enrolled in the study by the project director/research assistant. For focus groups, participants will also be recruited through the use of social media sites, including Facebook and Instagram. Participants will be asked to click on a link in the ad, which will take them to the Yale Qualtrics webpage where they will fill out a form with basic demographic information (age, race) and their contact information (email and phone number) and parental contact information (email and phone number) if the participant is under 18. If participants meet eligibility criteria, a research staff member will email the potential participant the focus group information sheet for them to review and set up a time to contact them by phone to review the study and obtain verbal consent. If the participant wishes to participate in the study and is under 18, the research staff member will email the parental information sheet to the parent and contact them by phone to obtain verbal consent. If either the participant or the parent do not wish to be in the study or have their child participate in the study, no further contact will be made. Focus groups will take place through Zoom where participants will be able to see and interact with each other.

Participants will be provided with an age-appropriate description of the study and told about what they might expect. In describing the study to the participant, the purpose of the study will be described as "finding out how teen girls can make choices that are healthier for them". In describing the study to the guardian/parent, we will indicate that the study will focus on promoting healthy behaviors in adolescence and on providing strategies to assist adolescents in making decisions about the many challenges they face; particularly as they relate to risky behaviors, including sex. If a participant or their guardian/parent indicates that they do not wish to participate, there will be no further involvement in the study.

4. Assessment of Current Health Provider Relationship for HIPAA Consideration:

Does the Investigator or any member of the research team have a direct existing clinical relationship with any potential subject?

☐Yes, all subjects

☐Yes, some of the subjects

☒No

If yes, describe the nature of this relationship. *Write here*

5. Request for waiver of HIPAA authorization: (When requesting a waiver of HIPAA Authorization for either the entire study, or for recruitment purposes only. Note: if you are collecting PHI as part of a phone or email screen, you must request a HIPAA waiver for recruitment purposes.)

Choose one:

☒ For entire study – for Focus Group participants/parents only – waiver of written authorization

☐ For recruitment/screening purposes only

☐ For inclusion of non-English speaking subject if short form is being used and there is no translated HIPAA research authorization form available on the University's HIPAA website at hipaa.yale.edu.

i. Describe why it would be impracticable to obtain the subject's authorization for use/disclosure of this data: *Write here*

ii. If requesting a waiver of **signed** authorization, describe why it would be impracticable to obtain the subject's signed authorization for use/disclosure of this data: A waiver will be obtained given that we will not obtain any identifying or personal health information from participants as part of the focus group.

The investigator assures that the protected health information for which a Waiver of Authorization has been requested will not be reused or disclosed to any person or entity other than those listed in this application, except as required by law, for authorized oversight of this research study, or as specifically approved for use in another study by an IRB.

Researchers are reminded that unauthorized disclosures of PHI to individuals outside of the Yale HIPAA-Covered entity must be accounted for in the "accounting for disclosures log", by subject name, purpose, date, recipients, and a description of information provided. Logs are to be forwarded to the Deputy HIPAA Privacy Officer.

6. **Process of Consent/Assent:** Describe the setting and conditions under which consent/assent will be obtained, including parental permission or surrogate permission and the steps taken to ensure subjects' independent decision-making.

Participation in this study will be strictly voluntary, confidential and non-discriminatory. The study will be advertised via posters and flyers located at partner schools and through emails sent directly to students and announcements made during class. The study will also be advertised through social media, including Facebook and Instagram. Potential participants will fill out an eligibility survey through the Yale Qualtrics webpage where they will provide basic demographic information (age, race, sexual orientation) and their contact information (email and phone number) and parental contact information (email and phone number) if the participant is under 18. If participants meet eligibility criteria, a research staff member will email the potential participant the study information sheet for them to review and set up a time to contact them by phone or zoom to review the study and obtain verbal consent. If the participant wishes to participate in the study and is under 18, the research staff member will email the parental information sheet to the parent and contact them by email to obtain written consent. We will provide, via email, the adolescents and their parents with an age-appropriate description of the study and told about what they might expect. In describing the study to the participant, the purpose of the study will be described as "finding out how teens can make choices that are healthier for them". In describing the study to the guardian/parent, we will indicate that the study will focus on promoting healthy behaviors in adolescence and on providing strategies to assist adolescents in making decisions about the many challenges they face; particularly as they relate to risky behaviors, including sex. For the focus groups we will employ waived signature of consent. Parents who do not wish for their children to participate will contact the project director. For the evaluation, we will obtain informed written assent from the participant and written informed consent from their guardian/parent. For both phases, if a participant or their guardian/parent indicates that they do not wish to participate, there will be no further involvement in the study. We will also obtain agreement from the appropriate administrator at the participating program.

For both phases, participants will also be recruited through the use of social media sites, including Facebook and Instagram. Participants will be asked to click on a link in the ad, which will take them to the Yale Qualtrics webpage where they will fill out a form with basic demographic information (age, race) and their contact information (email and phone number) and parental contact information (email and phone number) if the participant is under 18. If participants meet eligibility criteria, a research staff member will email the potential participant the focus group information sheet for them to review and set up a time to contact them by phone to review the study and obtain verbal consent. If the participant wishes to participate in the study

and is under 18, the research staff member will email the parental information sheet to the parent and contact them by phone to obtain verbal consent. If either the participant or the parent do not wish to be in the study or have their child participate in the study, no further contact will be made. Focus groups will take place through Zoom where participants will be able to see and interact with each other.

In some cases, we may conduct focus groups through Yale's video conferencing service, Zoom. To obtain verbal consent, the Research Assistant will discuss the study with their guardian/parent and obtain verbal assent from the participant and verbal consent from their guardian/parent. At the beginning of the Zoom meeting, participants will be provided with an age-appropriate description of the study and told about what they might expect. In describing the study to the participant, the purpose of the study will be described as "finding out how kids can make choices that are healthier for them". In describing the study to the guardian/parent, we will indicate that the study will focus on promoting healthy behaviors in adolescence and on providing strategies to assist adolescents in making decisions about the many challenges they face; particularly as they relate to health relationships and dating. If a participant or their guardian/parent indicates that they do not wish to participate, there will be no further involvement in the study. We will work with our study partners to identify potential participants; study partners will email our approved flyer to those that may fit within our study inclusion criteria (black teen girls aged 14-18). Participants that are interested in participating in the focus groups may reach us through the phone number or email listed on the approved flyer.

7. Evaluation of Subject(s) Capacity to Provide Informed Consent/Assent: Indicate how the personnel obtaining consent will assess the potential subject's ability and capacity to consent to the research being proposed.

   This research does not involve subjects with limited decision-making capacity. Parents and adolescents will be provided with an age-appropriate description of the study and told about what they might expect. In describing the study to the participant, the purpose of the study will be described as "finding out how kids can make choices that are healthier for them". In describing the study to the guardian/parent, we will indicate that the study will focus on promoting healthy behaviors in adolescence and on providing strategies to assist adolescents in making decisions about the many challenges they face; particularly as they relate to risky behaviors, including sex. For focus groups, we will employ waived signature of consent. Parents who do not wish for their children to participate will contact the project director. For the pilot randomized controlled trial, we will obtain informed written assent from the participant and written informed consent from their guardian/parent.

8. Non-English Speaking Subjects: Explain provisions in place to ensure comprehension for research involving non-English speaking subjects. If enrollment of these subjects is anticipated, translated copies of all consent materials must be submitted for approval prior to use.

   Non-English Speaking Subjects will not be able to participate in this project.

As a limited alternative to the above requirement, will you use the short form* for consenting process if you unexpectedly encounter a non-English speaking individual interested in study participation and the translation of the long form is not possible prior to intended enrollment? YES ☐ NO ☒

Note* If more than 2 study participants are enrolled using a short form translated into the same language, then the full consent form should be translated into that language for use the next time a subject speaking that language is to be enrolled.

Several translated short form templates are available on the HRPP website (yale.edu/hrpp) and translated HIPAA Research Authorization Forms are available on the HIPAA website (hipaa.yale.edu). If the translation of the short form is not available on our website, then the translated short form needs to be submitted to the IRB office for approval via modification prior to enrolling the subject. ***Please review the guidance and presentation on use of the short form available on the HRPP website.***

If using a short form without a translated HIPAA Research Authorization Form, please request a HIPAA waiver in the section above.

9. Consent Waiver: In certain circumstances, the HIC may grant a waiver of signed consent, or a full waiver of consent, depending on the study. If you will request either a waiver of consent, or a waiver of signed consent for this study, complete the appropriate section below.

☐Not Requesting any consent waivers

☒Requesting a waiver of signed consent:

☐ Recruitment/Screening only *(if for recruitment, the questions in the box below will apply to recruitment activities only)*

☒ Entire Study (Note that an information sheet may be required.) – For focus group participation only.

For a waiver of signed consent, address the following:

- Would the signed consent form be the only record linking the subject and the research? YES ☒ NO ☐
- Does a breach of confidentiality constitute the principal risk to subjects? YES ☒ NO ☐

OR

- Does the research pose greater than minimal risk? YES ☐ NO☐
- Does the research include any activities that would require signed consent in a non-research context? YES ☐ NO ☐

☐ Requesting a waiver of consent:

☐ Recruitment/Screening only *(if for recruitment, the questions in the box below will apply to recruitment activities only)*

☐ Entire Study

For a full waiver of consent, please address all of the following:

- Does the research pose greater than minimal risk to subjects?
  ☐ Yes *If you answered yes, stop. A waiver cannot be granted.*
  ☐ No
- Will the waiver adversely affect subjects' rights and welfare? YES ☐ NO☐
- Why would the research be impracticable to conduct without the waiver? *Write here*
- Where appropriate, how will pertinent information be returned to, or shared with subjects at a later date? *Write here*

SECTION IV: PROTECTION OF RESEARCH SUBJECTS

Confidentiality & Security of Data:

1. What protected health information (medical information along with the HIPAA identifiers) about subjects will be collected and used for the research? *Name, Address, Telephone Number, Email Address, reported HIV/STI testing status and test results, sexual activity status*

2. How will the research data be collected, recorded and stored? All data collected from the assessments will be entered directly into the secure web-based system, Yale Qualtrics, which is Yale's enterprise-wide data management system. Research staff will enter the data into the Yale Qualtrics system. To assess acceptability and feasibility, directly following completion of the intervention, we will collect quantitative and qualitative data on the intervention participants' experiences of the game intervention.

3. How will the digital data be stored? ☐CD ☐DVD ☐Flash Drive ☐Portable Hard Drive ☒Secured Server ☐Laptop Computer ☐Desktop Computer ☐Other

4. What methods and procedures will be used to safeguard the confidentiality and security of the identifiable study data and the storage media indicated above during and after the subject's participation in the study?

   Data will be stored in Yale's secured online data collection system, Yale Qualtrics. Paper assessments will be kept in a locked filing cabinet in the PI's office.

All portable devices must contain encryption software, per University Policy 5100. If there is a technical reason a device cannot be encrypted please submit an exception request to the Information Security, Policy and Compliance Office by clicking on url http://its.yale.edu/egrc or email it.compliance@yale.edu

5. What will be done with the data when the research is completed? Are there plans to destroy the identifiable data? If yes, describe how, by whom and when identifiers will be destroyed. If no, describe how the data and/or identifiers will be secured.

   Data collected in the study will reside in our computerized database and electronic storage mechanisms. All data analyses will be performed under approved HIC protocols. Digital files of the focus groups will be destroyed at the end of the study.

APPROVED BY THE YALE UNIVERSITY IRB 12/19/2021

6. If appropriate, has a Certificate of Confidentiality been obtained? A CoC automatically covers this study due to its NIH funding.

SECTION V: POTENTIAL BENEFITS

Potential Benefits: Identify any benefits that may be reasonably expected to result from the research, either to the subject(s) or to society at large. (Payment of subjects is not considered a benefit in this context of the risk benefit assessment.)

It is anticipated that the Black adolescent girls enrolled in this study should benefit directly from the study as the purpose of the study is to reduce their risk for HIV/STI by improving their negotiation and communication skills around condom use and partner HIV/STI testing. It is hypothesized that the participants assigned to the multiplayer videogame, ***InvestiDate***, will have higher rates of condom use and reported partner HIV/STI testing at 4 months following study enrollment as compared to the control group. This research has the potential to benefit a large number of Black adolescent girls around the country and worldwide, because if the intervention is shown to be effective, then this program can be replicated elsewhere in the U.S. and in countries where resources are lacking and interventions for HIV/STI risk reduction are limited. The potential benefits to all participants are great while strict precautions are being taken to protect the confidentiality and well-being of participants, as has been described above. Thus, the potential benefits to the participants outweigh the potential risks.

SECTION VI: RESEARCH ALTERNATIVES AND ECONOMIC CONSIDERATIONS

1. **Alternatives:** What other alternatives are available to the study subjects outside of the research?
   Not participating in the study
2. **Payments for Participation (Economic Considerations):** Describe any payments that will be made to subjects, the amount and schedule of payments, and the conditions for receiving this compensation.

   We will compensate focus group participants and participants who participate in pilot testing with gift cards with monetary value of $30. Participants in the pilot randomized controlled trial will be given a gift card incentive of $30 for completion of each assessment for a total of $120 (4 assessments total) for study participation.

3. **Costs for Participation (Economic Considerations):** Clearly describe the subject's costs associated with participation in the research, and the interventions or procedures of the study that will be provided at no cost to subjects.

   No costs to subjects will be incurred.

4. **In Case of Injury:** This section is required for any research involving more than minimal risk, and for minimal risk research that presents the potential for physical harm (e.g., research involving blood draws). N/A

   a. Will medical treatment be available if research-related injury occurs? *Write here*

   b. Where and from whom may treatment be obtained? *Write here*
   c. Are there any limits to the treatment being provided? *Write here*
   d. Who will pay for this treatment? *Write here*
   e. How will the medical treatment be accessed by subjects? *Write here*

IMPORTANT REMINDERS

Will this study have a billable service? Yes ☐ No☒

A billable service is defined as any service rendered to a study subject that, if he/she was not on a study, would normally generate a bill from either Yale-New Haven Hospital or Yale Medical Group to the patient or the patient's insurer. The service may or may not be performed by the research staff on your study, but may be provided by professionals within either Yale-New Haven Hospital or Yale Medical Group (examples include x-rays, MRIs, CT scans, specimens sent to central labs, or specimens sent to pathology). Notes: 1. There is no distinction made whether the service is paid for by the subject or their insurance (Standard of Care) or by the study's funding mechanism (Research Sponsored). 2. This generally includes new services or orders placed in EPIC for research subjects.

If answered, "yes", this study will need to be set up in OnCore, Yale's clinical research management system, for Epic to appropriately route research related charges. Please contact oncore.support@yale.edu

Are there any procedures involved in this protocol that will be performed at YNHH or one of its affiliated entities? Yes ☐ No ☐

If Yes, please answer questions a through c and note instructions below.

a. Does your YNHH privilege delineation currently include the specific procedure that you will perform? Yes ☐ No ☐

b. Will you be using any new equipment or equipment that you have not used in the past for this procedure? Yes ☐ No ☐

c. Will a novel approach using existing equipment be applied? Yes ☐ No ☐

If you answered "no" to question 4a, or "yes" to question 4b or c, please contact the YNHH Department of Physician Services (688-2615) for prior approval before commencing with your research protocol.

IMPORTANT REMINDER ABOUT RESEARCH AT YNHH

Please note that if this protocol includes Yale-New Haven Hospital patients, including patients at the HRU, the Principal Investigator and any co-investigators who are physicians or mid-level practitioners (includes PAs, APRNs, psychologists and speech pathologists) who may have direct patient contact with patients on YNHH premises must have medical staff appointment and appropriate clinical privileges at YNHH. If you are uncertain whether the study personnel meet the criteria, please telephone the Physician Services Department at 203-688-2615. By submitting this protocol as a PI, you attest that you and any co-investigator who may have patient contact has a medical staff appointment and appropriate clinical privileges at YNHH.

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