Efficacy Trial of Life Simulation Game to Routinize Adolescent HIV Testing

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Principal Investigators:
Amanda Castel, MD, MPH, George Washington University
Telephone number: 202 994-8325
Daniel Greenberg, Media Rez
Telephone number: 202-483-9411

Co-Investigators and Study Staff:
Dr. Lawrence D'Angelo, MD, MPH Children's National Health System
Connie Trexler, R.N., CPN, MSHS, Children's National Health System

Irene Kuo, PhD, MPH George Washington University
Adam Ciarleglio, PhD, MS George Washington University
Constanza Carney, MPH George Washington University

Gabriel Ralte, Media Rez
Callen Shaw, Media Rez

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I. Background and Rationale

HIV prevalence and diagnosis among youth ages 13-24: HIV testing is a critical first step in the HIV care continuum. Persons unaware of their infection are responsible for an estimated 30% of new infections[1]. Thus, identifying new positives and linking them to care can improve individual and population level outcomes. With guidelines to support routine HIV testing among 13-64 year olds[2], the availability of HIV testing technologies to improve earlier detection of infection, as well as novel effective prevention and treatment interventions, now is a crucial time to ramp up HIV testing initiatives. Goals of the U.S. National HIV AIDS Strategy, Ending the HIV Epidemic Initiative, and the HIV care continuum include reducing the number of people who become infected with HIV by intensifying prevention efforts where HIV is most heavily concentrated[3,4]. For HIV+ adolescents and young adults (AYA), these are particularly critical goals as an estimated 60,300 AYA ages 13-24 are living with HIV infection in the U.S.[5], and AYA account for 21% of new HIV infections[6]. Further, with over 50% of youth in the U.S. unaware they are infected, there are critical gaps in getting at-risk AYA tested for HIV[5]. As AYA, particularly those of color and male youth who have sex with men (MSM), become a leading risk group in the HIV epidemic, creative strategies to support risk assessment, prevent HIV infection, encourage routine HIV testing, and link persons to care are increasingly paramount

High risk behaviors yet poor uptake of HIV testing and pre-exposure prophylaxis (PrEP) among youth in Washington, DC: In Washington, DC, 41% of new HIV diagnoses are among persons ages 13-29; making this the leading age group for new diagnoses[7]. AYA in DC have high rates of gonorrhea and chlamydia with 37% and 52% of diagnoses in 2017, respectively, being among 15-24-year-olds. These diagnoses are indicative of high rates of condomless sex in this age group and AYA may also be exposing themselves to HIV[7]. Data from the 2017 Youth Risk Behavioral Survey (YRBS) conducted in DC among middle (MS) and high school (HS) students found that 14% of students (24% of boys) were sexually active by the age of 11[8]. In addition, almost half (46%) of HS students had ever been sexually active, and 14% had four or more sexual partners, putting them at increased risk for HIV[8]. YRBS data also highlight the gap between sexual activity and receipt of STD and HIV testing with only 18-47% of sexually active students reporting ever being tested for an STD and 19-43% ever being tested for HIV[8]. Finally, these data highlight the need for increased education around HIV prevention with as many as 48% of heterosexual and 39% of lesbian, gay, bisexual MS students not receiving HIV education at school[8].

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Despite engaging in high risk behaviors, and guidelines supportive of routine testing among AYA, numerous studies have shown that AYA do not get tested regularly for HIV, resulting in missed opportunities for early diagnosis and prevention[9-15]. Barriers to testing include providers who often do not assess sexual histories or risk behaviors in adolescent patients[9], yet when offered rapid HIV testing, AYA generally are accepting, willing to get tested, and await receipt of their results[16-21]. Adolescent HIV testing programs, such as that implemented at the Children's National Medical Center (CNMC) Emergency Department and through the DC Department of Health (DOH) School-based Screening Program, found that acceptance of testing was high (73%), significantly associated with the presence of a parent or guardian[16], and influenced by peer responses to testing (internal communication, DC DOH). Other barriers include difficulty identifying and accessing HIV testing sites; low health literacy and beliefs that HIV remains a severe and fatal disease; and lack of self-perceived risk for HIV[15,22-25 26]. Hence there is a need to improve youth understanding of HIV, how to prevent it, behaviors that put one at risk for infection, and to provide them with resources to access HIV testing and prevention options such as PrEP, in a youth-friendly and non-judgmental manner[11,22,27]. A review of HIV testing interventions focused on increasing adolescents' intentions to obtain HIV testing found that facilitators of testing include understanding testing as an essential part of accessing early treatment, helping youth think about future health, and learning how to effectively communicate with their sexual partners[26]. Importantly AYA are more receptive to HIV information when it is provided in an entertaining, exciting, and emotionally engaging format[26,28] and when the material comes from a peer[29 30 31], or is shared over social media.

Aside from HIV testing, use of other HIV prevention interventions such as PrEP has been limited among AYA. However, with the recent FDA expansion of PrEP to adolescents, and the US Preventive Services Task Force Grade A recommendation for PrEP, options for HIV prevention interventions for AYA have expanded[32-34]. Thus, efforts to encourage condom use and safe sex, regular HIV testing, and PrEP will be important in further reducing new infections among AYA.

Technological interventions, such as serious games, to promote routine HIV testing and PrEP among AYA: Despite data showing that youth prefer to learn about HIV in entertaining formats, social media interventions to promote HIV testing among AYA have been limited. As new technologies are developed, digital gaming has begun to enter the health-promotion lexicon. Use of digital games is highly prevalent among AYA with 60%-97% of teens and young adults reporting playing videogames[35,36]. Digital-game-based interventions, or serious games, have been aimed at promoting health literacy[37], physical health and exercise[38,39], as well as sexual health and HIV prevention among adolescents[40-45]. Though these programs have yielded early success for

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increasing target behaviors among their sample populations, there is limited research on their use in increasing HIV testing among AYA[46-49]. A systematic review identified 55 smart phone, internet and web-based interventions addressing the HIV care continuum, of which only five used gaming approaches[50]. Digital-game-based interventions are a promising strategy for AYA as they overcome traditional barriers to prevention interventions, are broad-reaching, relatively low cost, adaptable, scalable and portable[43]. Evidence also suggests that people who practice new behaviors in virtual environments acquire new skills and are more likely to apply those skills in real-life situations[41,51-55]. Additionally, these games can be used to assess varying levels of exposure to an intervention and have the potential for sustained exposure[41,51].

Use of paradata to enhance interventions: Paradata, i.e., information related to the process of data collection, can be used to assess levels of intervention exposure and can assist in further tailoring interventions to individual AYA. Paradata have been used to assess responses to health surveillance, obesity trials, and to monitor consent rates, data quality, and responses to online interventions and surveys, including technology-based behavioral HIV interventions.[56,57] Paradata can potentially inform which elements of HIV interventions are most useful, should be modified, or removed to increase an intervention's efficacy.[58] By assessing elements of real-time game use such as frequency and time spent playing, and use of gaming incentives, paradata can assist in tailoring game-based interventions in a timely and cost-effective manner.[58]

Given the high rates of HIV among AYA, the need to increase HIV testing and access to prevention interventions, the pervasive use of technology, more specifically gaming, we propose to capitalize on these factors to provide an interactive and entertaining dating-and-life simulation game that will increase HIV knowledge and risk assessment and facilitate access to HIV testing and PrEP. Our proposed intervention offers AYA personally-tailored risk messages and supports their accessibility to HIV testing and prevention services through an innovative gaming approach that is sharable over social media with in-game rewards for sharing the game with peers.

Digital gaming to increase AYA HIV risk assessment, testing, and linkage to care: Our intervention builds on prior formative work and is designed to offer AYA personally-tailored risk messages and supports their accessibility to HIV testing and prevention services through an innovative gaming approach that is sharable over social media with in-game rewards for sharing the game with peers.

I. Study Goals, Objectives and Design

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This study will aim to assess the acceptability, usability and efficacy of using state-of-the-art video game technology to increase HIV testing among adolescents and young adults (AYA) ages 13-24. AYA often lack awareness of their personal risk of contracting HIV and where to go for testing and care. This lack of awareness has contributed to poor uptake of HIV testing among AYA despite engagement in high risk behaviors. The goal of this project is to harness this strong motivation to play games to increase HIV testing. Previous games for behavior change have yielded early success for increasing target behaviors among their sample populations, yet research on increasing HIV testing among AYA through gaming has been limited. This intervention builds on prior formative work and is designed to offer AYA personally-tailored risk messages and supports their accessibility to HIV testing and prevention services through an innovative gaming approach that is sharable over social media with in-game rewards for sharing the game with peers.

The specific aims of the study are as follows:
Aim 1: Determine acceptability of an enhanced life-simulation prototype of a playable interactive game to increase HIV testing.
Aim 2: Conduct pilot field testing of gaming intervention to determine usability.
Aim 3: Determine the efficacy of a life-simulation game in changing HIV testing, knowledge, and risk behaviors among AYA at risk for HIV.

This study will be conducted in various phases. After completion of Aim 1, the details of the additional phases will be submitted for IRB review and approval prior to initiation of the activities.

II. Study Procedures

IRB approval will be obtained prior to initiation of the study. GW will serve as the IRB of record for Media Rez. We will request that GW also serve as the IRB of record for the CNMC site as well as DC Health and Montgomery County DOH. Prior to the Aim 1 focus groups, a subject matter expert will serve as a consultant on v1.0 of the game prototype. This person will be a member of the AYA population whose role will be limited to providing feedback on the initial version of the game so that revisions can be made prior to the focus groups.

A. *Aim 1: Determine acceptability of an enhanced life-simulation prototype of a playable interactive game to increase HIV testing.*

Participant Recruitment

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HIV- AYA ages 13-24 will be enrolled in Aim 1 to participate in a series of focus groups and qualitative discussions.

AYA Participant Selection and Recruitment (N=64)

Participants will be recruited from the CNMC Adolescent clinic, the DC Health Youth Advisory Board (YAB), through peer referral, online using social media (e.g., Facebook, Instagram, SnapChat, etc.) and in the community and by reaching out to local community organizations. If needed, CNMC patients between the ages of 13–24 who have ever been sexually active will be approached during a routine non-HIV clinic visit to the CNMC Goldberg Adolescent Health Clinic to participate in a FG. Potential participants will be informed of the purpose of the study. For all interested youth, the RA will make it clear that focus groups will consist of individuals of similar age and that the first focus group will consist of discussing experiences around HIV testing and opinions about a game prototype. If the patient is interested in participating, consent to share contact information will be obtained (**Appendix 1**). The RA will then screen the participant for eligibility (**Appendix 2**) and if eligible, the RA will add the patient name and contact information to a study specific tracking log so that they can be contacted with details regarding the focus groups (**Appendix 3**). Eligibility of these participants will also be confirmed prior to the start of the focus group. Participants will also be provided a flyer with contact information for study staff (**Appendix 4**) and will be sent reminders about the focus group via the contact information provided in the screener. In order to expand recruitment to AYA who may not be receiving regular outpatient care and therefore may not have been tested for HIV, clinic recruited participants will be allowed to recruit up to 2 peers for the FGs. Peer referrals will use a coupon system in order to ensure confidentiality of the referral process (**Appendix 5**). Peers recruited through the coupon referral system will scan the QR code on the coupon to complete the eligibility screener. If they are eligible for the study, they will be contacted by study staff with information about the date and time of the focus groups. We will primarily work with the DC Health YAB to recruit participants for the FGs, place recruitment flyers with QR codes in the school-based health clinics in DC and Montgomery County, and place ads on social media sites (e.g. Facebook, Instagram, Snapchat, etc.) (**Appendix 4**). Peers who do not complete the eligibility screener prior to the focus group will be screened for eligibility at the time of the focus group.

Inclusion Criteria

An individual will be eligible for the study if he or she meets all of the following criteria:

- 13-24 years of age

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- Sexually active (self-report)
- HIV negative status (self-report)
- live in the DC, Maryland, or Virginia area and able to attend a FG at CNMC
- Is able to provide informed consent or assent
- Is able to participate in the focus groups
- Is able to complete the surveys and participate in the focus groups in English

AYA Focus Group Conduct (8 focus groups of 4-8 participants, N=64)

Participants will be informed of the date, time and location of the focus group based on their sexual orientation and age. Possible locations for conducting the focus groups include the GW School of Public Health and Department of Epidemiology (private conference room), Children's National Medical Center, any other confidential and safe yet mutually convenient location, or virtually (e.g. through Zoom, Webex, Skype, etc.). We will aim to have 64 total participants for the focus groups but will recruit 100 participants assuming that several will not be available to participate due to unanticipated conflicts. Screeners will be completed and reviewed prior to the start of the focus groups.

We will conduct eight 60-90 minute focus groups (FG) of 4-8 participants each. The 64 AYA participants participating in Aim 1 FGs will be stratified by sexual orientation and age. Four FGs of AYA participants will be conducted with youth who self-identify as heterosexual vs. lesbian gay, bisexual, transgender [LGBT] and youth ages 13-17 vs. 18-24 (n=32). The Media Rez team will make modifications based on the initial FG feedback, after which a second group of new participants (heterosexual vs. LGBT, 13-17 vs. 18-24, n=32) will be recruited and shown the revised game. The objectives of the FG are as follows: 1) to assess participants' understanding of HIV infection and their knowledge and experiences with HIV testing, risk assessment and reduction, and 2) to elicit their perceptions regarding gaming and its potential role in increasing HIV testing. The FGs will cover the following topics (**Appendix 6**):

1) HIV and PrEP knowledge
2) Perceptions and experiences regarding HIV testing
3) Current use of and access to gaming technology (e.g., use of smartphones, game consoles)
4) Perceptions regarding the game enhancements and its potential role in increasing HIV testing and access to PrEP,
5) Perceptions about the role of social media and its influence on HIV testing behaviors,

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6) Opinions regarding effective recruitment approaches through social media

Screen shots from the potential game are included in **Appendix 7**. The game prototype will be demonstrated with emphasis on the enhancements including new locations, interactions where players are learning about HIV, experiencing HIV testing, or learning about PrEP. We will elicit participants' feedback regarding their interest in HIV-related gameplay, and their preferences for particular gaming features, art styles, and animation types.

AYA Surveys:

In addition to qualitative feedback, brief surveys will be administered to AYA electronically (e.g. REDCap, SurveyGizmo) prior to the focus groups to collect information on levels of sexual activity and behaviors related to HIV risk, perceived HIV risk, HIV testing recency and frequency, and use of games and social media (**Appendix 8**). To obtain a preliminary indication of whether the game may increase knowledge around HIV and prevention, brief pre- and post-surveys will be administered to include HIV and PrEP knowledge questions as well as measure perceptions regarding if the game would change participants' intentions to seek HIV testing, PrEP, and to share the game with friends.

AYA Consent Process

At the time of the AYA focus groups, the Research Assistant will have all participants provide verbal informed consent or minor assent. The RA will review the risks and benefits of participating in the study with all focus group members collectively. Group consent will be obtained from adults enrolled in the study via the Aim 1 Adult Focus Group Consent (**Appendix 9**). Group assent will be obtained from adolescents enrolled in the study via the Aim 1 Minor Focus Group Assent (**Appendix 10**). As with our previous studies, we will seek a waiver of parental consent for adolescents ages 13-17 as well as a waiver of documentation of consent. Should a participant decline to participate in the focus group or survey, no information will be collected. In order to minimize the risk of inadvertent disclosure, adolescents will have the option of leaving their copy of the consent form at a secure location at the clinic site.

Data Collection, Management, and Analysis

Data Collection and Management

All focus groups will be audio recorded and a verbatim transcription will be produced via an external service. The transcriptionist will be issued a unique username and password to access the

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secure FTP site where the audiotapes will be stored. The audio files will be downloaded by the transcriptionist and the resulting transcripts will be uploaded back to the FTP site. The resulting text file will be reviewed for quality assurance and entered into a qualitative data analysis software (e.g. NVivo, Atlas.ti).

For the surveys, all data will be manually entered into the REDCap program.

Incentives

Participants will be remunerated with a $10 gift card and $5 metro card. AYA will receive an additional $10 incentive for each peer recruited who participates in the FG, up to $20. Peer referrals will use a coupon system in order to ensure confidentiality of the peer–referral process.

Analysis

Survey data will be cleaned, downloaded and exported into Excel or SAS files and descriptive statistics will be analyzed. Pre- and post-game knowledge levels will be calculated; however, due to the small sample size, no statistical testing will be performed. Qualitative data analysis will include using an a priori and open coding process aimed at identifying relevant themes and categories to inform the development of the game modifications for round 2 FG testing as well as the final game prototype in Aim 2. Key decisions will include potential differences by age and sexual orientation, the types of games, art styles, social features, type/frequency of in-game bonuses, and responses of different kinds of in-game virtual rewards for actions like demonstrating knowledge of HIV risks and virally spreading the game to peers. The Media Rez team will make modifications based on the initial FG feedback (n=32), after which a second group of new participants (n=32) will be recruited using the same methods as described above and shown the revised game. All modifications will be incorporated for the Aim 2 pilot study.

B. *Aim 2: Conduct pilot field testing of gaming intervention to determine usability.*

Game Design

The research (GW, CNMC) and game production teams (Media Rez) will discuss the Aim 1 results from the adolescents and determine the most optimal set of game features for the Phase II prototype of a life-simulation game in which players can enact real-life behaviors and choices and receive a profile of their HIV-risk. While the Phase I FGs were essential in guiding revisions to

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dialogue, locations, character designs, and interactions, if it is determined that AYA in the Aim 1 FGs do not like the proposed enhancements, we will modify the game accordingly. The risk assessment approach will be informed by existing risk assessment tools and local HIV epidemiology[59-62].

Prototype Production

Once the look and feel has been finalized, the game production team will implement v2.0 of the prototype, creating base code, audio, and 3D art/animation using the Unity "middleware" engine. The prototype will be presented to the research team at regular intervals for assessment and modified according to their feedback.

Prototype Measurement and Analysis

The prototype must pass usability tests by being free of game breaking bugs, onscreen avatars must move precisely under player control, and the risk profiles must accurately track player actions. This production work will be conducted primarily by Media Rez, augmented by subcontractors.

Pilot User Field Testing

Pilot Testing Eligibility and Recruitment (n=10)

We will identify 10 AYA ages 13-24, living in the DC metro area, self-reported HIV negative and ever sexually active, and recruited through social media from either the DC or Montgomery County school-based screening programs or through social media sites such as Instagram, Facebook, or SnapChat (**Appendix 11**). If this proves challenging, we will consider expanding recruitment to local community-based organizations that are not HIV focused and consider recruiting from after school programs or events geared toward AYA. Participants must have their own mobile phone and be willing to use it for study purposes. We will aim to recruit a diverse sample of AYA including those identifying as heterosexual females or males and MSM, as well as a range of ages.

Potential participants will contact the Research Associate (RA) via the Study Management and Retention Toolkit (SMART) to be screened for eligibility (**Appendix 12**) and fraud, and provide electronic informed consent. SMART is a HIPAA-compliant Software as a Service (SaaS) based mobile application that assists with participant recruitment, study implementation, and retention, and manages participant information, including contact information and incentives. SMART includes a participant facing mobile app, which allows for two-way secure messaging, survey

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delivery, secure photo uploads, (which will be used by participants to verify HIV testing and PrEP starts in Aim 3) and longitudinal tracking of participants from screening to study completion. It is compatible on both iOS and Android platforms with messaging through text via a messaging center within the app. Upon enrollment, participants will download the SMART app and complete a brief baseline survey (**Appendix 13**), after which the gaming app will be sent electronically for them to download on their phone. Participants will have unlimited access to all of the game features during the 1-month pilot period.

AYA Consent Process

After participants are screened for eligibility, they will provide electronic consent (**Appendix 14**) or assent (**Appendix 15**). As with our previous studies, we will seek a waiver of parental consent for adolescents ages 13-17 as well as a waiver of written consent for all participants.

Data Collection, Management, and Analysis

Data Collection and Management

User pilot testing will allow us to identify any unanticipated issues with game logins, navigation, functionality, paradata collection, or other unforeseen technical issues. During user-testing, we will monitor game use, HIV testing and PrEP locator use, and access paradata for a 1-month period. We will pilot elements of the survey data collection process to be implemented in Aim 3 including measures of usability, game satisfaction and a modified version of the motivation, attitude, knowledge, and engagement (MAKE) instrument to determine how well the game addresses HIV knowledge and testing. We will collect baseline data on HIV testing and knowledge to preliminarily describe the anticipated characteristics of our online sample (**Appendix 13**).

We will also pilot use of the SMART system for participant screening, survey collection and data management, and trouble-shoot for any issues with phone connectivity, data caching, paradata collection or other potential issues. At the end of the 1-month period, we will conduct brief surveys (**Appendix 16**) and in-depth interviews (IDIs) **(Appendix 17**) with the 10 pilot participants to elicit features of the games and apps that worked well and also identify those that might prohibit full use of the intervention. If participants are unable to secure transportation to GWU, or if we encounter difficulty conducting the IDIs in person, we will conduct them by telephone.

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All IDIs will be audio recorded and a verbatim transcription will be produced via an external service. The transcriptionist will be issued a unique username and password to access the secure FTP site where the audiotapes will be stored. The audio files will be downloaded by the transcriptionist and the resulting transcripts will be uploaded back to the FTP site. The resulting text file will be reviewed for quality assurance and entered into a qualitative data analysis software (e.g. NVivo, Atlas.ti).

Incentives

Based on the results of this testing, we will make any final game modifications. Pilot study participants will be compensated $50 for participating in the pilot ($10 each for the baseline and 1-month surveys, $25 for IDI, $5 for transportation to IDI).

Analysis

Survey data will be cleaned, downloaded and exported into Excel or SAS files. Given the small sample size and objectives of this aim, quantitative analysis will be primarily descriptive to measure usability, acceptability, and satisfaction as well as to confirm baseline characteristics and behaviors of our intended study population. Qualitative analysis will include using an a priori and open coding process aimed at identifying any potential barriers and facilitators to use. Critical and essential modifications will be made to the game, paradata, and SMART data management platforms prior to the randomized trial.

C. *Aim 3: Determine the efficacy of a life-simulation game in changing HIV testing, knowledge, and risk behaviors among AYA at risk for HIV.*

Participant Recruitment

We will enroll 300 sexually active HIV-negative AYA ages 13-24 to participate in a randomized controlled trial with 1:1 randomization to the life-simulation game intervention compared to provision of app-based HIV educational materials on HIV and PrEP.

AYA Participant Selection and Recruitment (N=300)

To enroll a sample representative of diverse racial/ethnic and sexual behaviors, as well as a sample of non-clinic attending AYA, recruitment will occur primarily through social media. We will place targeted advertisements toward MSM and Black and Hispanic AYA on social media sites such as Facebook, Instagram, Twitter, SnapChat, YouTube and Spotify . If this proves challenging,

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we will consider expanding recruitment to local community-based organizations that are not HIV focused and consider recruiting from local public school, after school programs, local colleges and universities, or events geared toward AYA. Additionally, we will place study fliers with QR codes at the DC Health and Montgomery County School Based Health programs. Interested AYA will click on an advertisement or QR code and complete an online screener to determine their age, gender, sexual behaviors and orientation, state of residence, and availability of a reliable cell phone. Those recruited through social media advertisements will first be directed to a website with information about the study and a link to complete two preliminary questions asking age and place of residence. If potential participants meet preliminary eligibility criteria, they will be directed the online screener to determine their age, gender, sexual behaviors and orientation, state of residence, and availability of a reliable cell phone. Additionally, we will be utilizing peer referrals. Participants will be allowed to recruit up to 3 peers. Participants will be given unique links to share with peers, this will ensure confidentiality of the referral process. REDCap will be used to generate peer referral links, screen potential participants, and record and manage the eligibility screener surveys for peer recruited participants. Peers recruited through the peer referral system will click on the link to complete the eligibility screener on REDCap. Participants will receive an additional $10 incentive for a peer recruited who participates in the RCT. We anticipate needing to screen 1,750 AYA over a 12-month period to successfully enroll 300 participants. We anticipate high rates of initial ineligibility using this approach due to issues such as incomplete screeners and fraudulent accounts, and a 15% consent refusal.

Inclusion Criteria

An individual will be eligible for the study if he or she meets all of the following criteria:

- age 13-24
- self-reported HIV negative or unknown status
- self-reported ever sexually active
- resident of the DC metropolitan region which includes DC, Maryland and Virginia for at least the next 6 months
- Is able to provide informed consent or assent
- able to complete all study procedures in English
- has own mobile phones and be willing to use them for the study.

Fraud Detection

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While online recruitment is ideal to identify our population of interest, there is the risk for fraud and we have implemented a comprehensive fraud detection protocol. Prior to randomization, a comprehensive procedure to reduce the risk of fraud will be implemented and will include review of baseline enrollment data for suspicious responses or duplicates, not revealing eligibility criteria to ineligible participants, immediate verification of cell phone numbers via SMS text, and email.

AYA Consent Process

After participants are screened for eligibility and fraud, they will provide electronic consent or assent through REDCap. As with our previous studies, we will seek a waiver of parental consent for adolescents ages 13-17 as well as a waiver of documentation of consent.

Study arm randomization

Once verified and consented, participants will be randomized 1:1 to one of two study arms for a 3-month period: 1) **the intervention arm** in which they have unlimited access to the games, risk assessment tool, and HIV and PrEP locators embedded within the game; or 2) the **control arm** in which participants will have access to an HIV educational app curated from existing resources including the CDC website on HIV, the HIV risk assessment tool and the HIV and PrEP locator websites. Participants will be randomized in blocks of six, stratifying by age (13-17, 18-24) and sexual behavior (LGBT vs. heterosexual), using a random number generator for assignment. Randomization will occur through REDCap. Once enrolled, they will complete a baseline survey through REDCap, and will receive a link to download either the gaming or control app to their personal smart phone.

Intervention condition

Intervention participants will have access to the full-study game inclusive of revisions from Aims 1 and 2, the CDC HIV risk estimator, HIV testing locator, and PrEP locator links for 3 months from the time of enrollment. The game is both IOS and Android compatible.

Intervention delivery

After providing informed consent, and completing the baseline survey through REDCap, participants in the intervention arm will receive a link to download the game. Once downloaded, participants will have access to the game for a 3-month period, with up to 30 hours of content available. Participants will be asked to opt in to receive up to 4 notifications. Notifications will occur after the first 7 days of no game activity, and at 30, 60 and 90 days after enrollment. All

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notifications will occur once. We will track use of the app including time spent on specific game aspects, clicks on specific content, risk scores, and use of the locators, similar to the paradata collected in Aim 2.

Control condition

Control arm development

Prior to roll out of the intervention, the Media Rez Team, along with the clinical research team will develop an app that will include basic information on HIV basics (e.g., routes of transmission, data on the epidemiology of HIV among youth), prevention information, and information on HIV testing and PrEP, as well as a link to the HIV risk estimator, and HIV testing and PrEP locators. (See screenshots)

Control arm delivery

After providing informed consent, and completing the baseline survey through REDCap, participants in the control arm will receive a link to download this informational app containing this content and have unlimited access to the app for a 3-month period. Participants will be asked to opt in to receive up to 4 notifications. Notifications will occur after the first 7 days of no app activity, and at 30, 60 and 90 days after enrollment. All notifications will occur once. The control app is both IOS and Android compatible. We will track use of the app including clicks on specific content, risk scores, and use of the locators.

Technical Support

In the event that a participant is in need of technical support, the research coordinator will facilitate the interaction between the Media Rez team members and the participant by scheduling a zoom call. The Media Rez team will interact directly with participants for technical support only. This interaction may include a zoom video chat, where the Media Rez team may see the participants faces.

Data Collection, Management, and Analysis

Data collection and Management

Data will be collected via surveys through REDCap at baseline, 1, 3, and 6 months . The IDIs will be completed through a Zoom call at 6 months . As in Aim 2, we will utilize REDCap to manage all

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participant screening, recruitment, enrollment, retention, survey completion and remuneration. REDCap will be used to screen potential participants who are referred by a peer.

Survey Domains

Surveys will collect information on the following validated domains: self-reported sexual and HIV risk behaviors, self-perceived risk for HIV, perceived norms, barriers to HIV testing, reported HIV testing and PrEP uptake, behavioral intentions including intent to test for HIV, to seek PrEP, and to reduce risky behaviors, self-efficacy, game use, interest, acceptability, and usability. In order to minimize non-response rates and social desirability bias with respect to self-reported data, all surveys will be sent to participants via a a web link using the REDCap system. This approach avoids potential transportation issues and reliance on in-person data collection for most of our study outcomes.

Paradata and Game Use Monitoring

We will monitor the intervention in real-time using game data and paradata. This contextualized use data will allow us to assess game use patterns throughout follow-up and assist in quantifying exposure levels to the gaming elements and locators. Examples of paradata to be collected will include length of time using game, game content accessed, risk assessment scores, and frequency of use of locators.

In-depth interviews

After completion of the 3 month survey, a purposely selected subset of intervention participants (n=25), will be asked to conduct an in-depth “exit” interview (IDI) regarding their experience being in the study, feedback regarding the game, and to more fully describe how they played the game, how it changed their HIV knowledge, self-perceived risk, and describe any risk reduction approaches they may have undertaken during the study period. To obtain a range of perspectives, we will seek feedback from participants stratified by sexual behaviors (heterosexual vs. LGBT), age group (13-17 vs. 18-24), whether they sought and received HIV testing, and levels of game play and locator use based on the paradata (none, low-moderate, high use). The IDIs will be conducted over a Zoom call after the 3-month study follow-up. We will use a semi-structured interview guide and all interviews will be audio recorded. If we encounter difficulty conducting the IDIs in person, we will conduct them by telephone or by Zoom.

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All IDIs will be audio recorded and a verbatim transcription will be produced via an external service. The transcriptionist will be issued a unique username and password to access the secure FTP site where the audiotapes will be stored. The audio files will be downloaded by the transcriptionist and the resulting transcripts will be uploaded back to the FTP site. The resulting text file will be reviewed for quality assurance and entered into a qualitative data analysis software (e.g. NVivo, Atlas.ti).

Incentives

Participants will be remunerated in increasing amounts with electronic gift cards. All participants will receive: $30 for the baseline, $25, $25, and $40 for the 1, 3, and 6-month surveys, respectively. IDI participants will receive an additional $30 gift card.

Retention protocol

Given the importance of retention in being able to accurately assess the intervention effect, we will obtain participant contact information including email addresses, social media information, and the participant's cell phone numbers (verified at the time of enrollment). The RA will be in regular contact with participants to support downloading of the app/game, conduct check-ins, and provide study reminders and updates. The participant will be sent a reminder of an upcoming survey 2 weeks and then 1 week prior to survey date. If participants do not complete the follow-up surveys, the link will be resent and participant contacted at 24, 48, and 72 hours after sending the initial notification to remind them to complete it. If there is no response, the study RA will contact the participant to confirm receipt of the link and to assist them in completing it. Participants will have up to 2 weeks to complete the survey. If a participant is not responsive after 10 attempts, we will consider him/her lost to follow up. Based on these measures and previous studies which use similar procedures, we anticipate an 84% retention rate over a 6-month period.

Sample Email:
Hi (enter participant name),
Thank you for taking the time to talk about the study today.

To recap to our conversation, these are the next steps:
1) You should have received a REDCap link to review the consent form- please check your spam if you haven't received it. After reading the consent form, please let me know if you have any

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questions. Please select if you'd like to move forward and participate by selecting "yes" or "no". The consent form can be downloaded from REDCap if you'd like to keep it for your record.
2) After I receive your completed consent form, I will send you a link to complete the baseline survey and the download information for the app or game.
3) After receiving the completed baseline survey, I will send you your gift card incentive.
Thanks so much for your time, and let me know if you have any questions.

Best,
(enter RA name)
Sample Text:
Hi (enter participant name), this is (enter RA name) from GWU. I noticed that you have not completed the baseline survey. Did you receive the link or are you having trouble completing it? Let me know if you need me to resend the link or how I can help.

Analysis

The primary outcome measure is *HIV testing*. This will be measured as self-reported HIV testing in the past 1, 3, and 6 months. To minimize social desirability bias in reporting HIV testing, for all participants who report testing, we will attempt to validate reported testing by eliciting a description of the HIV testing process. We will compare self-reported HIV testing between the two groups at1, 3, and 6 months.

A secondary outcome will be *intent to test* for HIV. Intent to test will be assessed using a validated 6-point Likert scale. Other secondary outcomes will utilize previously published questions and validated scales and include changes in: 1) HIV knowledge; 2) risk perception and behaviors (e.g., condomless sex); 3) PrEP knowledge, screening, and uptake 4) risk estimator scores and locator (HIV and PrEP) use; and 5) game usability and acceptability including frequency and duration of use, and reasons for continued/discontinued use.

Intervention Effect Analysis

All data will be inspected for inaccurate input (e.g., out-of-range values, implausible means and variation). We will first summarize the outcome measures descriptively overall and within each intervention arm at each time point. We will make every effort to obtain all data. Any patterns of missingness will be investigated and reported. Sensitivity analyses, including rerunning analyses

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with imputed values for missing data, will be conducted to assess any impact of missingness on the study findings. All primary analyses will be conducted using an intent-to-treat approach. The primary analysis will focus on differences between the treatment and control groups at the 6-month follow-up visit using a Chi-squared test for independence (the outcome will be taken as having ever had an affirmative response on the outcome measure during the 1,3, and 6-month study period). We will also investigate differences between rates of HIV testing in the treatment and control groups, stratifying by age (13-17 vs. 18-24) and sexual orientation (LGBT vs. heterosexual identity).

Secondary Analyses

We will perform a longitudinal analysis on the repeated measures from each subject using logistic mixed effects models with a subject-specific random intercept. In each model, we will include time as a 4-level categorical predictor (with baseline serving as the reference level) as well as a treatment indicator and time-by-treatment interaction. We will jointly test the interaction coefficients to determine if the effect of treatment varies over time. If the effect is found to vary over time, we will test the intervention effect at each time point and characterize the difference between the treatment and control groups using risk differences and their corresponding 95% confidence intervals (CIs). If no evidence of a time-by-treatment interaction is present, we will refit the logistic model without the interaction terms and provide the overall intervention effect and its corresponding 95% CI. Furthermore, we will provide a descriptive analysis for each secondary outcome overall and within each intervention arm at each time point. Self-reported survey data, including self-perceived HIV risk, HIV knowledge indicators, and risk behavior indicators, among others, will be compared between the treatment and control groups using t-tests for continuous measures and Chi-squared tests for categorical measures. The corresponding group differences (in mean scores or proportions) and their 95% CIs will be reported. Within the intervention group, we will investigate whether game-use changes over time and whether there exists a dose-response relationship between various game-use indicators (e.g. amount of time playing the game) and the various survey responses, including HIV testing, intent to test for HIV, PrEP uptake, and intent to seek PrEP as well as the other secondary outcomes.

Qualitative analysis will include using an a priori and open coding process aimed at identifying themes regarding intervention delivery and acceptability.

Human Subjects Considerations

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The protocol team is requesting the IRB grant a waiver of parental permission to obtain contact information and for participation in the focus groups for youth participants between the ages of 13 and 17 years old and in the Aim 3 Efficacy trial. Adolescents who are sexually active may not have disclosed their behaviors to a parent or guardian. Under 45 CFR 46.408 (c), an IRB has the authority to waive parental permission if it determines that "a research protocol is designed for conditions or a participant population for which parental or guardian permission is not a reasonable requirement to protect the participants" and "an appropriate mechanism for protecting the children who will participate as research participants is substituted" and "that the waiver is not inconsistent with Federal, State, or local law." Rationale for requesting a waiver of parental consent among adolescents who have not disclosed their sexual initiation to their parents/guardian is as follows:

- This study is not considered greater than minimal risk. The probability of harm from participating in this study is no greater than that occurring in routine care.
- The CNMC and other clinics that may participate that provides HIV- and sexual health-related care to adolescents and most other community agencies offering these services are confidential and do not require parental/legal guardian notification or permission to treat under state regulations.
- Contacting a parent/legal guardian could potentially put some youth at risk for abuse or ousting from the home if parents/guardians are not aware of their risk behaviors.
- If adolescents have not disclosed their sexual initiation to parents/guardians, a requirement for parental permission in this type of study could not only affect a person's willingness to participate, but could also potentially impact the ability of researchers to engage in this type of HIV-related research with youth.
- Adequate protection has been substituted by the mechanisms in place to protect the privacy and confidentiality of participants and by the treatment referrals offered if needed.

The protocol team is also requesting the IRB grant a waiver of documentation of consent for all participants. Under 45 CFR 46.117 (c), an IRB has the authority to waive the requirement to obtain signed informed consent for some or all subjects if the research presents no more than minimal risk of harm to subjects and involves no procedures of which written consent Is normally required outside of the research context. Rationale for requesting a waiver of documentation of consent is as follows:

- This study is not considered greater than minimal risk. During this study, AYA will engage in minimal risk focus groups to discuss their HIV and PrEP knowledge, perceptions and experiences regarding HIV testing, and current use of and access to gaming technology, perceptions regarding social media and the game enhancements and their potential role in

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increasing HIV testing and access to PrEP. AYA will also participate in a pilot trial and randomized control trial where they will either have access to the life-and-dating simulation game or app-based HIV educational materials on HIV and PrEP.

- Verbal or electronic consent will be obtained from all participants. Prior to conducting the focus groups, the researchers will make sure that all participants understand the information presented in the consent form and are comfortable to proceed. The informed consent will be read in its entirety to all participants while they follow along, participants' comprehension of the study will be assessed, and any questions that participants may have will be answered by research staff before participants are asked to indicate verbal consent. Each participant will be offered a copy of the informed consent or assent document; however, youth will also have the option of not taking a copy of the informed consent so as to protect their confidentiality. For the pilot trial and RCT, the informed consent or assent will be read in its entirety by all participants, any questions that participants may have will be answered by a Research Assistant. The electronic consent of efficacy trial participants will be recorded electronically in REDCap. Each participant will be offered an electronic copy of the informed consent document; however, youth will also have the option of not receiving a copy of the informed consent so as to protect their confidentiality

Risks and Benefits

The sources of data will be participant focus group and interview data, participant survey data, and paradata. All eligible patients will be asked to participate in the focus groups, pilot testing, or the efficacy trial, at which point they can either accept or refuse to participate. Study participation will not affect the routine medical services provided to patients and should not detract from the overall HIV testing efforts. Participants will be informed that they can chose to not answer a question and/or can chose to discontinue the focus groups, interviews, or surveys at any point and that doing so will in no way affect the care and services they receive at the clinic.

There are no risks that are more than minimal for participating in this study. None of the procedures, situations, or materials will be hazardous to personnel or clinic patients. There may be minor discomfort in answering questions regarding HIV knowledge and risk; however, these are commonly used questions when conducting HIV-related research.

The benefits of participating in the study are neither direct nor long-lasting. Participants will receive appropriate remuneration for their participation in the various study aims. This will be the first study to our knowledge in the District of Columbia to systematically test the efficacy of a life-and-dating

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simulation game to increase HIV testing among AYA. Additionally, the results will be helpful in informing future programs and interventions developed by the pediatric HIV treatment community, videogame developers and researchers.

Subject Confidentiality

Informed consent will be required for participation in the focus groups pilot testing, and intervention. Each study participant will be assigned a pseudonym to participate in the focus groups and interviews. Study participation will not affect the receipt of HIV-related care and treatment services at the clinic. Lastly, the consent process, focus groups, and in-depth interviews will be completed in private rooms and areas that will allow for privacy and confidentiality. There is the risk of parents/guardians of minors finding out they are involved in the study. If contacted by a parent/guardian we will not disclose a participant's enrollment, the study eligibility criteria, nor share participant-specific information.

During recruitment for the Aim 1 focus groups a tracking log will be maintained of patient names and telephone numbers so that participants can be contacted for the focus groups. The log will only be accessible to authorized clinic and study staff. The log will be securely housed at GW by study staff in either locked file cabinets or a secured password protected computer. Once recruitment is complete, the records will be destroyed. The files will be electronically destroyed through deletion and paper copies will be shredded. Surveys will be labeled with a study ID. For Aims 2 and 3, a tracking log will be maintained of participant contact information including email addresses, social media information, and the participant's cell phone numbers as part of the intervention retention protocol. The log will only be accessible to authorized clinic and study staff. The log will be securely housed at GW by study staff in either locked file cabinets or a secured password protected computer. Once recruitment is complete, the records will be destroyed. The files will be electronically destroyed through deletion and paper copies will be shredded. Surveys will be labeled with a study ID.

The subjects will be informed that all transmission of study data will bear only their unique ID codes, and only investigators directly involved in the study will have access to the identifying information stored in locked cabinets or password protected computers and study drives. Participants will be informed that individual results will not be shared and only aggregate results will be disclosed at study completion. Summary statistical data stratified by age, race or other categories may be released. However, if the total information will allow identification of the exact

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person(s), the information will not be released. We will adapt measures successful in other studies to reduce the risk of potential breaches by using passwords, not sending any sensitive information, and eliciting AYA's preferred method of communication and receipt of study information (e.g., surveys, incentives).

Withdrawal from the Study

A subject may withdraw from this study at any time without impacting the care they receive at the clinic. However, information collected prior to withdrawal may still be used or disclosed after withdrawal.

Confidentiality

All data collection will be confidential. Focus group information will never include a participant's real name as participants will be assigned a pretend name or pseudonym. Surveys will only be identified through the Survey ID. Data will be entered directly into REDCap and all paper files stored in a locked-secured file cabinet. REDCap is a secure, password-protected survey database to which only PIs and sub-PIs will have access. Only non-identifiable data will be used in the analysis of the survey information collected.

REDCap

REDCap will be used to manage survey data in Aim 1, 2, and 3. REDCap is a secure web application designed exclusively to support data capture for research studies. REDCap is HIPAA compliant. George Washington University is a REDCap partnering institution and has provided designated usernames and passwords to study staff for this research project. All data once collected is stored on the GWU servers thus, no project data are ever transmitted at any time by REDCap from that institution to another. All data will be downloaded into SAS and or Excel for analytic purposes. Please see the attached description of REDCap security procedures

Study Files and Record Retention

During the data collection period, qualitative data will be posted temporarily on a secure FTP site. All study staff will be issued a unique username and password to access the FTP site for the purposes of transferring data. Once the data collection period ends, study data will be permanently stored on a drive housed at GW. The investigator shall retain records required to be maintained for

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at least a period of three years after which they will be destroyed. The data from REDCap will be deleted, as will recordings from the interviews.

Analysis Plan

Quantitative Data Analysis

Detailed analysis plans are described above.

Qualitative Analysis

Thematic coding and analysis of the focus group and interview data will be conducted and pertinent themes will be used to summarize the data collected.

Presentations and Publications

The information gathered from this study will be used to inform stakeholders about how best to address HIV testing among at-risk AYA. The de-identified dataset will be analyzed and the findings disseminated via the peer-reviewed literature and at national conferences. Game design will be informed from these findings and the intent is to develop and design additional studies based on these findings.

Collaborators

This study will take place at CNMC, GWU and the Media Rez laboratories. Dr. Lawrence D'Angelo leads the CNMC Burgess Adolescent HIV clinic and will facilitate participant recruitment.

Funding

Dr. Castel and Mr. Greenberg have received funding from the National Institutes of Health National Institute of Child Health and Human Development for this 3-year intervention study.

Costs to Subjects/Subject Compensation

There is no cost to the participants for participating in the study elements. Participants will be remunerated for their participation in each aim of the study.

Anticipated Study Timeline

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Appendices

1. Aim 1 Consent to Share Contact Information
2. Aim 1 Eligibility Screener
3. Aim 1 Focus group recruitment log
4. Aim 1 Recruitment Flyer for AYA Focus Group Participants
5. Aim 1 Peer Referral Coupon
6. Aim 1 FG Protocol Surveys
7. Aim 1 Game Screen Shots
8. Aim 1 Pre-FG Survey
9. Aim 1 Adult Focus Group Consent
10. Aim 1 Minor Focus Groups Assent
11. Aim 2 and 3 Social Media Advertisements
12. Aim 2 Eligibility Screener
13. Aim 2 Baseline Survey
14. Aim 2 Adult Pilot Consent
15. Aim 2 Minor Pilot Assent
16. Aim 2 1-Month Survey
17. Aim 2 In-Depth Interview Guide
18.

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