Title: Efficacy Trial of a Life Simulation Game to Routinize Adolescent HIV Testing

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Aim 3 Statistical Analysis Plan

Analysis Plan: Study Outcome Measures***:*** **The primary outcome measure is *HIV testing*.** We will compare self-reported HIV testing between the two groups at 6 months. We expect that a higher proportion of AYA in the intervention vs. control group will have completed HIV testing at the end of the study. Among a random subsample of participants who report HIV testing, we will elicit a description of the HIV testing process in an attempt to confirm the veracity of their self-reported responses as well as request a secure photo of their test results be sent through SMART. **Secondary outcome measures:** Since self-reported measures tend to overestimate HIV testing[89-92] and given the age range of our participants and potential barriers to receipt of HIV testing among AYA, a secondary outcome will be *intent to test* for HIV[87,93,94]. Intent to test will be assessed using a 6-point Likert scale[87] ranging from "very unlikely" to "extremely likely" to test in response to the question "how likely are you to get tested in the next 6 months?" We will dichotomize this score into "extremely likely" vs. other. We hypothesize that we will see higher intent to test in the intervention vs. control group. Other secondary outcomes will include changes in: 1) HIV knowledge; 2) risky behaviors (e.g., condomless sex); 3) PrEP knowledge, screening, and uptake; 4) risk estimator scores and locator (HIV and PrEP) use, and game usability and acceptability including frequency and duration of use, and reasons for continued/discontinued use.

Statistical Analyses: All statistical analyses will be led by **Drs. Irene Kuo and Adam Ciarleglio** and our DSMB (see letters) will convene quarterly to review the data. Sample Size Considerations: This study aims to assess the efficacy of an interactive technology-based intervention on HIV testing among AYA and is thus powered to determine the efficacy of the intervention. In our pilot study[65], we found that approximately 10% of sexually active AYA reported being tested for HIV in the past 4- 6 months. A sample with approximately 300 subjects (150 per treatment arm) would achieve >80% power to detect a moderate effect corresponding to a difference of at least 13 percentage points (equivalent to a relative risk of 2.3 assuming a 10% prevalence of past 4-6-months HIV testing in the control group) in HIV testing between the intervention and control groups after 6 months using a 2-sided test at a 5% significance level and assuming a 16% attrition rate after 6 months[75]. 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 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 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 timepoint 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 risk for HIV, 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 data from IDIs will be transcribed and involve thematic coding using Atlas.ti version 7.0 to identify themes regarding intervention delivery and acceptability.