VANDERBILT UNIVERSITY MEDICAL CENTER
HUMAN RESEARCH COMMITTEE
PROTOCOL SUMMARY

PeerNaija: A Mobile Health Platform Incentivizing Medication Adherence Among Youth Living with HIV in Nigeria

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SUMMARY OF STUDY

The scale-up of global antiretroviral therapy (ART) represents an unparalleled global health success story, leading to impressive overall reductions in HIV-related morbidity and mortality. However, adolescents and young adults (AYA), especially those in Sub-Saharan Africa, have largely been left out of this story. While AIDS-related deaths declined by 30% for adults from 2005-2012, they increased by 50% among AYA over the same period, making AIDS the leading cause of death among African youth. AYA living with HIV perform poorly across the entire care continuum. ART adherence is central to effective HIV treatment, but AYA have high rates of virologic failure, virologic rebound after initial suppression, and attrition from HIV care. Unique developmental features of adolescence and young adulthood such as impulsivity, risk-taking, and poor concrete thinking make daily medication adherence even more challenging in this population. In addition, the attitudes and behaviours of young people are often strongly influenced by their peers. This influence can be seen as a powerful incentive for desired behaviours. Much of the literature on incentives for health has focused on financial incentives, which have shown success in promoting health behaviours. There are few data exploring mobile health (mHealth) technologies to exploit social and financial incentives, yet mHealth platforms allow for the delivery of novel behavioural interventions. With the proliferation of mobile phone ownership in Sub-Saharan Africa in general and in Nigeria in particular, such interventions can be delivered where there is greatest need. More than 75% of HIV-infected AYA live in Sub-Saharan Africa, and fully 10% reside in Nigeria.

In this proposal, we will adapt an mHealth application, *PEERNaija,* to leverage both social and financial incentives to improve medication adherence among AYA living with HIV in Nigeria. We will also work with our partners at APIN Public Health Initiatives and NIMR in Nigeria to improve capacity to conduct mHealth research. The *PEERNaija* application will feature daily medication reminders, with individual adherence monitoring, individual adherence scores based on daily monitoring, anonymized peer adherence scores (from peers attending the same clinic; social incentive), and a monthly lottery-based prize for youth with the highest adherence scores (financial incentive). To accomplish these aims, we will build on previous collaborations between Vanderbilt and APIN, a multi-site PEPFAR-supported program serving more than 250,000 persons living with HIV in Nigeria. We will engage key stakeholders in the community through focus groups and key informant interviews to guide iterative adaptation of the app. We will recruit a cohort of 50 HIV-infected AYA to pilot the app and assess feasibility, acceptability, adoption, and preliminary efficacy of important clinical measures (including adherence and virologic suppression). The proposed study will provide important preliminary data for the role of mHealth platforms to harness and deliver social and financial incentives to promote adherence efforts, for vulnerable youth, and for a larger intervention trial evaluating this app among HIV-infected AYA in Nigeria.

1. INTRODUCTION/ BACKGROUND INFORMATION (CITING RELEVANT CRITERIA)

Eighty-five percent of the world's adolescents and young adults (AYA) living with HIV reside in Sub-Saharan Africa. Sub-Saharan Africa (SSA) is home to 12% of the world's population but a staggering 71% of the 36.7 million HIV-infected persons worldwide.[1] Antiretroviral therapy (ART) scale-up has led to unprecedented progress in the global AIDS response, but these gains have not fully benefited the four million AYA (15-24 years) living with HIV.[2] This is especially true in SSA. Over the past decade, while HIV-related deaths decreased by 30% overall, HIV-related deaths among adolescents increased by 50%, making HIV the leading cause of death among this population.[2-4] Nigeria has had the highest annual incidence of perinatally infected children for the past seven years.[5] Coupled with ongoing behavioral transmission, 10% of HIV-infected AYA worldwide now live in Nigeria.[6-8]

Adherence and retention remain major challenges to effective HIV care for AYA. Adolescence and young adulthood is typically considered a period of optimal physical health but is also a vulnerable developmental period for health outcomes.[3] Adolescence is characterized by impulsivity, risk-taking, poor concrete thinking, nascent autonomy, and variable levels of social support; these factors often conflict with behaviour necessary for adherence to chronic medical therapies.[5, 9, 10] While excellent adherence (approximately >90%) is required to effectively control HIV and suppress the virus in the bloodstream, HIV-infected AYA have very poor adherence to life-saving ART.[5, 11, 9, 12-14] Accordingly, AYA show unacceptably high rates of virologic failure (30-50%).[5, 9, 11, 12, 15, 16] Such lapses in treatment have likely driven the increase

in mortality rates for this age group and also pose a great public health risk for HIV transmission.[5, 9, 11, 12]

Peer relationships can be successfully leveraged to promote desirable health behaviors among AYA. Attitudes and behaviors of AYA are strongly influenced by peers.[17, 18] Early research has primarily focused on the link between peer influence and undesirable behaviors, which are sometimes adopted and spread via social networks through a process coined social contagion.[19, 20] Several studies however, highlight the important role of peer relationships on a range of desirable health and social behaviors (e.g.. volunteerism, weight loss).[21, 22] Peer relationships have also been utilized to support outcomes along the entire HIV care continuum, but have not been evaluated extensively among youth in general, and African youth in particular.[23-27] One way in which peer relationships may influence behaviors is through the exertion of descriptive norms (what is most commonly done, or what individuals perceive to be so) and injunctive norms (what ought to be done) for certain behaviors.[28, 29] As such, peer acceptance and alignment with normative behavior may be a powerful social incentive to promote health behaviors in young people. Given limited data on the use of social incentives to support ART adherence for youth, the proposed study will address an important data gap.

Financial incentives have been recognized as a powerful tool for influencing a wide range of health outcomes, including HIV.[30-32] Grounded in principles of behavioural economics and contingency management, financial or other incentives are provided to reward desired behaviors.[33] In the field of HIV, much of the evidence for financial incentives to date has focused on HIV prevention, where incentives have shown great promise.[34-36] Conditional incentives for HIV treatment have been effective in small studies, with absolute increases in adherence ranging from 15% to 25%.[37-39] Similar data are few in resource-limited settings (RLS), but one study from Uganda found small prize incentives resulted in an absolute increase of 23% in adherence to ART for adults.[40] There are no data, however, assessing financial incentives for ART adherence for AYA, especially in RLS. Nonetheless, the provision of rewards for desired behaviours may be a particularly appealing approach for the adolescent brain, which is primed to seek reward.[41]

An mHealth application can integrate motivating incentives with daily medication reminders and peer support to address substantial barriers to adherence. Studies of AYA living with HIV in SSA have identified a range of individual, environmental, structural, and treatment-related factors that impede medication adherence.[42] At the individual level, “simply forgetting to take the dose” is often identified as a barrier to adherence.[42] While this may be due to underlying cognitive dysfunction (from HIV infection itself), competing priorities, or other factors, medication reminders are well suited to address this barrier.[5, 42] Text message reminders can result in significant improvement and up to a doubling of the odds of medication adherence for chronic diseases, including HIV.[43-47] Social support is also an important environmental factor for medication adherence in this vulnerable patient group.[5, 48-50] Young patients who live outside of the home (boarding house, orphanage, etc.) may lack the privacy and support to navigate daily adherence struggles.[45-47] Even those with more traditional living environments may feel secluded, as many studies describe that fear of stigma and disclosure drives patients and families to manage their HIV in isolation.[51, 52] Providing a virtual, peer-based social support group may address an important need for social support, especially in a region where limited clinic-based outreach and largely unavailable adolescent-focused clinical services also threaten adherence.[42]

2. RATIONALE/ JUSTIFICATION OF STUDY (CITING RELEVANT CRITERIA)

Preliminary work in Nigeria from Dr. Ahonkhai’s (co-PI) Care4Life program demonstrated, in one retrospective analysis, that 40% of AYA who remained in care one year after starting ART had virologic failure (HIV RNA >1000 copies/mL).[12] In a multisite study of adherence as measured by medication possession ratio (MPR; proportion of prescribed doses of ART picked up from the pharmacy), AYA with MPR >94% had a marked reduction in the risk of virologic failure in the first year on ART compared to those with MPR <80% (aRR 0.43, p<0.001).[53] Nonetheless, 26% of AYA with optimal adherence by MPR (>94%) still had virologic failure, highlighting discordance between ART pick-up from the pharmacy and ART taking behaviour among some youth.[54] **These data underscore need for adherence support measures that help AYA to *take* their medicines, not just *get* them from the pharmacy.** To gain a better understanding of smart phone ownership and use in the proposed study setting, 20 AYA attending an adolescent HIV clinic in Lagos, Nigeria were surveyed; **95% owned a mobile phone (84% with smart phones**) and most were frequent users of SMS/text messaging, instant messaging services, and social media platforms. Thus, our proposed mHealth intervention, which leverages an existing mHealth application focused on improving medication taking for youth with HIV, is well suited to support the adherence needs of AYA in this setting.

3. STUDY OBJECTIVE AND HYPOTHESIS

SPECIFIC AIM: To establish the feasibility, acceptability, and preliminary efficacy of *PEERNaija,* an mHealth intervention designed to harness peer influence as an incentive to promote medication adherence among a pilot cohort of 50 AYA living with HIV in Nigeria.

Hypothesis: PEERNaija will be feasible, acceptable, and show preliminary efficacy in improving ART adherence.

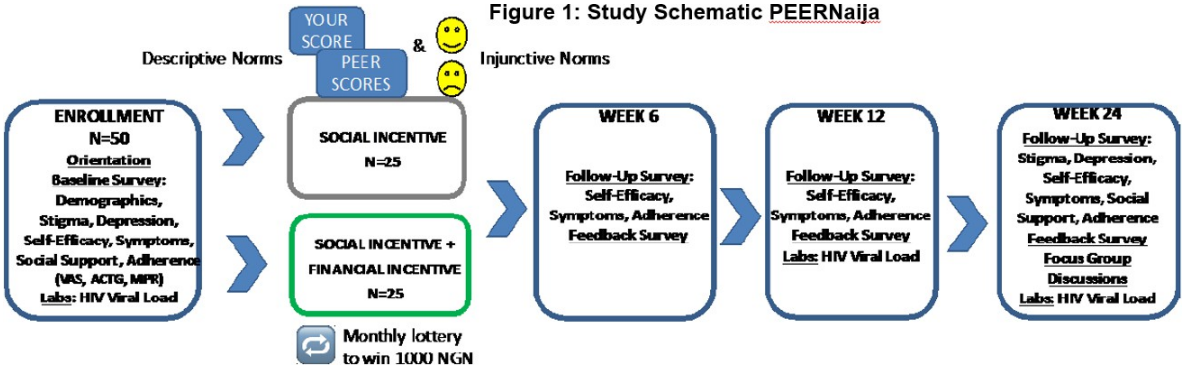
4. METHODS (TO INCLUDE STUDY DESIGN, DETERMINATION OF SAMPLE SIZE, EXCLUSION/ INCLUSION CRITERIA, ANALYSES OF DATA, ETC.)

Eligibility and Enrollment: We will conduct a prospective pilot study of the *PEERNaija* application for 50 AYA living with HIV in Nigeria. Patients will be recruited from the APIN HIV clinic and will be eligible for this study if they 1) own a smartphone (on which they are willing to download *PEERNaija*), 2) are 14-29 years of age, 3) are on ART, and 4) demonstrate the ability read simple text language in English. Patients will provide written informed consent for study participation.

Intervention Description: All participants will receive daily medication reminders, access to the virtual support group, and other key features identified in Aim 1. In addition, participants will be randomized to receive the social incentive (n=25) or the social plus financial incentive (n=25), *PEER*+ and be followed for 24 weeks.

For the **social incentive**, the application will track the participant's individual adherence score (% of doses taken), track the top scorers (leaderboard), and provide a figure highlighting the proportion of their peers with poor (<80%), medium (80-94%), or high (>94%) adherence scores. The display of the individual's adherence score relative to peer scores is considered a descriptive norm and is meant to portray "what most people are doing," as young people often inaccurately estimate behaviors for their peer groups. Participants will also receive an injunctive norm, or an indication of what they ought to be doing. This will come in the form of an emoji or congratulatory vs. motivating text for those with high or low adherence scores, respectively. When coupled with descriptive norms, injunctive norms have counteracted regression to the mean for individuals who demonstrate desirable behaviors relative to their peers.[28] For the **financial incentive,** the top 5 scorers in the *PEER*+ arm will be eligible win a lottery prize each month of the 24 week pilot of 1000 NGN of "data" that can be directly loaded onto the winner's phone [**Figure 1**]. Behavioral economics theory tells us that individuals are more averse to losses than rewarded by gains, so that even incentives/prizes should be framed in terms of losses.[40] Accordingly, participants in the financial incentive arm will receive weekly motivating messages such as "take your dose today or you lose the chance of winning the lottery." Potential language for these messages will be informed by user-centered feedback in Aim 1.

Figure 1: Study Schematic PEERNaija



Patients will be seen in clinic at enrollment, 6 weeks, 12 weeks, and 24 weeks. At enrollment, patients will complete a comprehensive survey assessing demographics and mobile phone usage patterns. We will also collect data on a range of factors known to impact medication adherence including, depression (WHO SQ-20 scale), self-efficacy (medication taking self-efficacy scale), stigma (Berger's HIV stigma scale), symptoms (HIV symptom severity scale), and social support (SPS-10 scale).[55-58] Adherence will be assessed using from the application itself (percentage of doses completed) and from 3 validated measures: 1) self-reported visual analog scale (VAS), 2) medication possession ration (MPR), and 3) AIDS Clinical Trials Group (ACTG)

adherence questionnaire.[59-61] Baseline CD4 count and HIV RNA will be obtained from the clinic record (within 3 months of enrollment).

Study Outcomes: The outcomes of interest for this study are feasibility, acceptability, adoption, and preliminary efficacy, and will be measured at 24 weeks. Preliminary efficacy will be assessed by comparing change in HIV viral load, and adherence from baseline to 12 weeks, and baseline to 24 weeks. We hypothesize that the *PEERNaija* mHealth application will be feasible and acceptable, and show preliminary efficacy in improving HIV virologic control. The study outcomes will be assessed through a combination of a) questionnaires administered to study participants b) clinical measures or correlates of adherence measured at baseline and at each study visit, and (c) analysis of usage data collected during routine use of the application. Chat feature use will be measured by monitoring the monthly frequency of posts per participant in addition to the thematic content.

Data analysis: Study feasibility and acceptability will be measured by analyzing the content of the feedback surveys at each study visit, and the FGDs at study end. Adoption will be assessed by analyzing usage data. Preliminary efficacy will be assessed by conducting a pre–post comparison of adherence measures, HIV viral load, and adoption measures at baseline, 12, and at 24 weeks in the two study groups (*PEER and PEER+).* De-identified chatroom the chat posts will be downloaded from the coordinator application, and reviewed from weeks 0-12 and 12-24.

5. ETHICAL CONSIDERATION. CONSENT DOCUMENTATION (TRANSLATION TO LOCAL LANGUAGES WHERE APPLICABLE) AND PATIENT INFORMATION LEAFLET (WHERE APPLICABLE)

A. Risks to the Subjects

A.1. Human Subjects Involvement and Characteristics. This study will involve several participants, namely:

- Patients (Aims 1 & 2) Adolescents and young adults (AYA) aged 14-29 years will be recruited from the APIN-managed HIV clinic at the Nigerian Institute for Medical Research. Patients are legally emancipated for HIV care at the age of 15 in Nigeria and can provide consent for clinical care and research participation. For the pilot proposed in Aims 2, Patients will be eligible for this study if they 1) own a smart phone (on which they are willing to download *PEERNaija* 2) are 14-29 years of age, 3) on ART, 4) demonstrate the ability read simple text language in English *"My phone will remind me to take my drugs"*, and 5) have a documented history of poor adherence defined as history of virologic failure in the preceding 3 months, medication possession ratio (MPR) <80%, or referral to clinic counselor for adherence counseling).
- Providers (Aim 1) Providers eligible to participate in this study include physicians, nurses, and counselors whose primary responsibility is for the care of patients living with HIV, and who have focused responsibility for AYA. They will be recruited from the NIMR HIV clinic.
- Other key stakeholders (Aim 1) Important stakeholders who will also participate in this study include parents (of AYA living with HIV), HIV program leaders from NIMR and representatives from the primary public health organization focused on HIV outcomes in the country, Nigeria's National Agency for the Control of AIDS (NACA).

A.2. Sources of material. Data will be obtained through several modalities. A set of data will be obtained through focus group discussions and study questionnaires. We will also collect and use several forms of electronic data, including: (a) data collected as part of routine patient care that is contained within NIMR's electronic health record system, (b) data entered by patients as part of their use of the mHealth application, and (c) logging, activity and location utilized by the mHealth application.

A.3. Potential risks. Overall, potential risks associated with participation in the study are unlikely and of low risk.

- *Physical*. There is a very low likelihood of any physical risk to participants in this project. Patients will be recruited during their routine clinic visits, while non-patient participants will be recruited from within their work location. No participant will be asked to perform any physical activity during the interviews or focus group discussions. Use of the mHealth application will only entail standard activity involving smartphone use, such as typing and swiping fingers on the screen. These have no risk of physical injury.
- *Psychological.* There is a small risk of participants being upset or embarrassed by questions or discussion

items during focus groups or interviews. There might also be a concern that participation or lack of participation in the study would impact the patient-provider relationship, or affect the quality of care received by the participant or offered by the provider.

- *Confidentiality*. mHealth applications to support HIV adherence may force unintended disclosure if provisions are not taken to ensure confidentiality. Examples include the use of non-discreet language identifying the patient as HIV+, displaying medication names, or using symbols or logos associated with HIV if the mobile phone is shared, or the messages received from the application are viewed by others. Unintended disclosure may also occur when researchers "check in" on research participants when applications detect non-adherence. Confidentiality concerns are heightened in the context of HIV because of high rates of stigma in Nigeria and other communities in Sub-Saharan Africa.
- *Privacy.* mHealth applications that exert "continuous surveillance" of participants may be perceived as intrusive or embarrassing and threatening to a participant's privacy. The collection and use of electronic data can raise the concern for loss of privacy and inadvertent access of data by others. Some individuals might also be concerned about privacy of information shared during focus group discussions and interviews.
- *Autonomy*. Adherence monitoring may limit a patient's liberty to be non-adherent. In this way, adherence monitoring or reminders through an mHealth application may limit a patient's autonomy.

B. Adequacy of Protection Against Risks

B.1. Recruitment and informed consent.

- *Informed Consent*: Patient recruitment will be done by trained study staff in a private setting (conference room) in the clinic. The informed consent process begins at pre-study enrollment when study staff explains to the potential participant all the pertinent study information, including: the nature of the study, its purpose, the procedures involved, the expected duration, the potential risks and benefits involved, and any discomfort it may entail. Patients will be asked to explicitly consent to installing the application on their smart phones. Written informed consent, available in both English and three major dialects in the country (Igbo, Yoruba, Hausa), will be obtained from all participants in this study. Based on prior experience enrolling a 700-patient cohort in this setting where fully 100% spoke English and no translation was needed, we anticipate that most participants will be able to write and read in English. As part of the consent process, participants will have the opportunity to request information and pose questions related to the study. As per Nigerian guidelines, "persons aged 13 and above and emancipated minors can consent for themselves without parental consent" in the case on non-therapeutic research (as defined as research that does not involve physical contact through examination, treatment or collection of bodily samples). As such, parent consent will not be required for either focus group or usability testing participation. However, in the case on therapeutic research, defined as physical contact with and taking of bodily fluid from youth, "persons aged 16 and above and emancipated minors can consent for themselves without parental consent". Therefore, in Aim 2, both parental consent and assent from the minor will be required for persons aged 10-15. For children 14-15 years of age, the parent will be required to provide consent.
  Note: For patients consented prior to the amendment on May 20, 2021, the Nigeria-based study coordinator will reach out the currently enrolled study participants and inform them that we will additionally begin monitoring the chatroom for frequency of posts and will download content without participant identification. The participant will be allowed to withdraw from the study if preferred or will be provided with a new consent document that contains a description of the changes.
- *Study Information document:* A detailed informational document will be provided during enrollment. This document will explain the purpose of the study, including: its goals, the procedures associated with enrollment, the risks and benefits of participation, the voluntary nature of this study, and how the findings from this study will be disseminated/published (including details on patient confidentiality), as well as contact information for study participants if they have concerns or questions about their rights as a research participant and/or if they have questions for the study Principal Investigator.
- *Withdrawal of Consent*: Each potential participant will be informed that participation in the study is completely voluntary, that s/he may withdraw from the study at any time, and that refusal to consent or withdrawal of consent at any time will not affect their subsequent care or treatment.
- *Minimizing physical, psychological, and social risks.* Participants will have the freedom not to respond to questions should they be uncomfortable with them. Confidentiality will be discussed and reinforced again at the beginning of each focus group discussion, and all participants will be asked to sign a pledge to not reveal information (including participants' names) from the focus group discussions. Focus group and interview information will be analyzed without including any identifying information, and research data will

not be linked to any other data or record source.

- *Minimizing risks to confidentiality & privacy*. Recognizing that loss of privacy is a serious issue, we have put strong methods in place to protect identifiable data. First, all investigators and research personnel will receive training on protection of human subjects. Second, identifiable information will only be made available to a few specific research personnel who will need access to the data purely for study purposes. All paper records will be stored in secure locked cabinets only accessible to study personnel. Third, the mHealth application will be developed with security as top priority. The security features include storage of data in an encrypted format within a password-protected smartphone, secure https-based data transmission between the mHealth application and the server based at VUMC, robust user-level authentication to access data, and automatic log out after a period of inactivity. Other features that minimize risk to confidentiality and privacy by utilizing neutral signifiers on the application, that would not be readily linked to HIV status (for example using the text "it's time" or another chosen text to pop up on the phone screen when it is time to take an ART dose, not including any symbols or logos readily linked to HIV, and not using the name of the clinic or of antiretroviral medications on the application screen). The choice of text and formatting will be informed by user-centered design. Fourth, patients will provide specific consent for the provision of phone or home-based outreach if the mHealth app signals non-adherence for 5 days or more. This is a practice that patients at NIMR are accustomed to, as phone and/or home-based outreach was standard for patients who defaulted from care before cutbacks in clinic funding. Concerted efforts will be made to minimize the use of any paraphernalia (labeled vehicles, clothing on clinic staff) that might identify participants as HIV patients, and no communication will be initiated in the presence of individuals who are not authorized by the patient to be present. Nonetheless, this risk will be explicitly discussed with participants at the time of enrollment and consent for study participation. Fifth, youth will be counseled on the low risk of data breach with these safeguards, but also on how to further minimize data breach when phones are shared. These safeguards will be present in the demonstration session introducing the participants to the application, and additional steps may be taken to prioritize safety and privacy, as guided by the focus group discussions. Sixth, we will work with the IRBs at Vanderbilt and NIMR to apply for a certificate of confidentiality, to ensure that the information collected through the mHealth application remains secure by preventing the academic institutions conducting the research from disclosing data collected in the course of the study to outside organizations or agencies. This will be an important step to mitigate the potential risk of abuse of data for unforeseen or unanticipated use. Finally, only NIMR staff will have access to data in the electronic health record. Requested clinical data will be shared with the study team and linked to patients in the pilot cohort (Aim 2) using a unique identifier. Identifiable data will be removed and not shared where feasible and also will be removed from servers as soon as is consistent with completing project tasks.
- *Minimizing risks to autonomy.* While the above procedures will address potential risks to autonomy (especially the informed consent procedure and explicitly offering the option to withdrawal consent), it is important to note that studies of SMS reminders for people living with HIV in SSA have suggested that loss of autonomy was not a major concern.[60] On the contrary, patients had a very positive response to electronic adherence reminders which gave patients the sense that their providers really cared for them, and provided the patients with the opportunity to be seen demonstrating their commitment to care [Haberer personal communication].[61]
- *Vulnerable subjects.* While patients may become pregnant during the study, we do not foresee any increased risk for this important population. Rather, we anticipate that women who become pregnant during the course of the study may have greater benefit (than those not in the study) because of the potential adherence benefit, and possible earlier referral and linkage to prevention of mother-to-child transmission services, given their close follow-up in the context of the study. Self-reported pregnancy status will therefore be assessed at each study visit (enrollment, week 6, week 12, and week 24) with prompt referral to prevention of mother to child clinic.

6. STATISTICAL ANALYSIS PLAN (SAP)

Primary Outcomes

Primary outcomes are feasibility, acceptability, and appropriateness of the PEERNaija app. These will be assessed through Weiner's validated feasibility of intervention measure (FIM), acceptability of intervention measure (AIM), and appropriateness of intervention measure (IAM) at six months. The FIM, AIM, and IAM surveys each contain four statements and participants are asked to rate their level of agreement to each statement on a Likert scale of 1-5, with 1 being "completely disagree" and 5 being "completely agree."

Participants will answer study team-generated questions assessing the acceptability and appropriateness of individual app features and the app overall via feedback questionnaires administered at 12 and 24 weeks.

Secondary Outcomes
Secondary outcome is preliminary efficacy on vial load. This will be assessed by comparing change in HIV viral load (from baseline to 24 weeks), and self-reported adherence from baseline to 12 weeks, and baseline to 24 weeks. ART adherence will also be assessed at baseline and six months using a visual analogue scale where participants indicated the percentage of prescribed ART doses taken over the past 30 days.

Additional covariates are assessed at baseline, and include depression, digital health care literacy, self-reported ART self-efficacy and adherence, HIV stigma, social support, and alcohol and substance use. Depression was assessed through the Patient Health Questionnaire, version 9 (PHQ-9). The PHQ-9 contains 9 items on the frequency of depressive symptoms in the past two weeks; total scores range from 0-27 and higher scores indicate a higher severity of depressive symptoms. Digital health care literacy will be assessed through the Digital Health Care literacy scale. The Digital Health Care Literacy Scale contains 3 items on comfort and ability with using technology; total scores range from 0-12 and higher scores indicate higher literacy. ART self-efficacy will be assessed through the HIV Medication Taking Self-efficacy Scale (MT SES). The MT SES contains 16 items on confidence in managing HIV treatment; total scores range from 1-10 and higher scores indicate higher self-efficacy. HIV stigma was assessed through Berger's HIV Stigma Scale. Berger's stigma scale contains 40 items on perceived stigma, fears related to disclosure, negative self-image due to HIV status, and perceived community stigma; total scores range from 40-160 and higher scores indicate higher HIV stigma. Social support will be assessed through the Social Provisions Scale. The Social Provisions Scale contains 24 items on support individuals receive from their social networks; total scores range from 24-96 and higher scores indicate higher social provisions. Alcohol and substance use was assessed through the CRAFFT screening tool. CRAFFT contains 3 items on substance use in the past twelve months; total scores range from 0-3 and higher scores indicate a need for further assessment.

Analysis Plan
Descriptive analyses will be performed to describe the distributional statistics of interested variables, including demographic variables, clinical, and psychosocial characteristics, at baseline and during follow-up assessments. For continuous variables, the mean and standard error will be reported; for categorical variables, frequencies and percentages will be presented.

Comparisons of primary outcomes (feasibility, acceptability and appropriateness) will be performed by comparing mean FIM, AIM, and IAM scores respectively between PEERNaija and PEERNaija+ at 24 weeks using two-sample t-tests. These constructs will additionally be addressed by comparing questions from feedback questionnaires, specifically assessing percentage of reminders received and whether or not reminders or chat messaged were intrusive, whether it was helpful to see their peers' adherence scores, whether they would use the app after the study, and whether they would recommend the app to a peer.

Comparisons between secondary outcomes (viral load and self-reported adherence) will be assessed by conducting a pre–post comparison of adherence measures at baseline, 12, and at 24 weeks, and pre-post comparison of viral load measures at baseline and 24 weeks in the two study groups (*PEERNaija and PEERNaija+),* using paired tests (e.g., paired t-tests, signed rank tests, or McNemar's tests, as appropriate), with a significance level set at $p \leq .05$ (2-tailed test). Further, self-reported preliminary efficacy will be assessed via response to feedback questionnaire question asking whether the app helped them to miss fewer medication doses and responses across study groups using Chi-square tests.

To further explore associations between outcomes and variables of interest, univariate regression analyses will be performed. Linear regression will be applied to continuous outcomes, including the primary outcomes (FIM, AIM, and IAM score) and self-reported adherence; while logistic regression will be used for binary outcomes such as viral suppression status at the study end.

7. POTENTIAL VALUE OF RESULTS (OUTCOME OF STUDY)

This proposal will provide important data for the potential role for smartphones in delivering incentive-based medication adherence interventions along with essential peer support for vulnerable youth living with HIV. The project will serve as the basis for a larger R01-supported intervention trial evaluating this mHealth application in a critically important region of the world for AYA with HIV, while building capacity for a large programmatic

network to conduct future mHealth research in this setting. The proposed intervention has the potential to improve medication adherence, and therefore virological control and survival in a very high-risk patient population.

8. LIST OF INVESTIGATORS. INVESTIGATOR SPECIALTY AND COLLABORATORS (ATTACH CVS OF INVESTIGATORS NOT MORE THAN 3 PAGES, LETTER OF COLLABORATION/SUPERVISION, ETC.)

Our **multidisciplinary team** will be led by PI **Dr. Aima Ahonkhai** (Assistant Professor, Medicine, Vanderbilt University Medical Center, VUMC), an HIV specialist, epidemiologist, outcomes researcher, and founder of the *Care4Life* Research Program in Nigeria. She will oversee all aspects of this project and coordinate between the study teams in the U.S. and Nigeria. **Dr. Martin Were** (Associate Professor, Biomedical Informatics and Medicine, VUMC; Director, Institute for Bioinformatics, Moi University, Kenya) will lead the informatics team in adapting and customizing the proposed application. Drs. Ahonkhai and Were will lead the mHealth research course. **Dr. Carolyn Audet** (Assistant Professor, Health Policy and Preventive Medicine, VUMC), a medical anthropologist with expertise in adapting, implementing, and evaluating behavioral interventions, will guide qualitative analysis informing application adaptation and development. **Dr. Bryan Shepard** (Associate Professor, Biostatistics, VUMC) is a senior biostatistician who will ensure sound study design and guide the quantitative analysis. **Dr. Prosper Okonkwo,** CEO of APIN, has extensive experience in service delivery and program management and will serve as the in-country lead investigator. **Dr. Nadia Dowshen** (Assistant Professor, Pediatrics, Adolescent HIV Program Director, Children's Hospital of Philadelphia) is the developer of the prototype application, *TreatYourSelf.* She will share code an expertise particularly in the adaptation phase. **Dr. Sandra Amaral** (Assistant Professor, Pediatrics, Children's Hospital of Philadelphia) will provide guidance on the design and delivery of social and financial incentives for AYA. **Drs Oliver Ezechi**, Director of Research, and **Dr. Agatha David**, Head of Clinical Sciences Department, both of the Nigerian Institute for Medical Research, will serve as advisors, meeting biannually with the PIs and key investigators. **Dr. Zaidat Musa** (Biostatistician, Monitoring and Evaluation Unit Head, NIMR) and **Ifeoma Idigbe** (Medical Sociologist/Clinical Counselor, Head of HIV Testing Services and Counseling, NIMR) will provide oversight onsite and serve as liaisons between NIMR and VUMC, meeting biweekly with the PIs and key investigators.

9. TIMEFRAME:

TIMELINE & DELIVERABLES								
				10-	13-	16-		22-
Month	**1-3**	**4-6**	**7-9**	**12**	**15**	**18**	**19-21**	**24**
Recruit and consent cohort								
Pilot mHealth app								
Data analysis								
Manuscripts (M) and R01 preparation					M		M R01	M

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11. ATTACHMENTS/ENCLOSURES

APPENDIX A. QUESTIONNAIRE AND FGD GUIDE
- A.1 PeerNaija Pilot AYA Questionnaire
- A.2 PeerNaija Pilot Close Out Focus Group Guide

APPENDIX B. CONSENT DOCUMENTS
- B.1 Pilot Testing Self Consent Form
- B.2 Pilot Testing Parent Consent Form

APPENDIX C. LETTERS OF SUPPORT
- C.1 APIN Public Health Initiatives
- C.2 Children’s Hospital of Philadelphia

APPENDIX E. RECRUITMENT FLYERS
- E.1 Participant Recruitment Flyer

APPENDIX F. GRANT
- F.1 Notice of Award