COMIRB Protocol

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Protocol #: 20-0163
Project Title: Information Visualizations to Enhance HIV-Related Communication in Diverse Clinical Settings
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I. Hypotheses and Specific Aims:

Brief background

In preliminary studies, the PI developed and evaluated a set of HIV-related infographics to improve clinician-patient communication and patient outcomes among Latino persons living with HIV (PWH). This work was conducted in the Dominican Republic (DR) and in New York City. Simultaneously, the PI developed a Substitutable Medical Applications and Reusable Technology (SMART)® application (app) compatible with the Fast Healthcare Interoperability Resources (FHIR)®, which is the standard for connecting mobile apps and electronic health records. She has incorporated her evidence-based infographics into this app so her intervention can be scaled up to reach clinicians and their Latino patients living with HIV globally. The next steps in this work are to increase generalizability of the intervention by adapting it to an additional Latino group (persons of predominantly Mexican descent) and to test the efficacy of the intervention to improve clinician-patient communication and health outcomes.

The aims of this study are therefore to:

Aim 1 Adapt previously designed and evaluated infographics for relevance to persons with HIV (PWH) of predominantly Mexican descent through individual interviews and incorporate final infographics into the mobile app prior to the proposed RCT.

Aim 2 Conduct a multi-site randomized controlled trial to assess the efficacy of the intervention (infographics administered through a mobile app) as compared to standard care in improving treatment outcomes (CD4 count, viral load, self-efficacy to manage HIV, among others) of Latino PWH and determine how resultant effects vary over time (baseline to 9-months) and between sites (DR and CO).

Aim 3 Assess implementation factors of integrating the SMART on FHIR app into EHRs through in-depth interviews and leverage findings to ensure the app effectively interfaces with EHRs in the CO and the DR.

Complementary to this work, a better understanding of how distinct Latino groups perceive HIV infection and prefer to communicate regarding HIV is needed so interventions can be modified accordingly. Thus, the last aim of this study is exploratory.

Aim 4 (Exploratory) Conduct in-depth interviews with PWH of predominantly Mexican descent to explore their perceptions of HIV infection and preferences for health communication. Qualitative findings will be integrated with those from the NY and DR cohorts to detail variations and similarities, and identify areas for intervention refinement.

II. Background and Significance:

Latinos are the largest and fastest growing minority group in the United States (US)[1] and they are disproportionately affected by HIV.[2-5] Latinos experience higher HIV prevalence, faster disease progression, more HIV-related deaths, and a marked delay in the diagnosis of new infections.[2,4,6] Many factors contribute to HIV-related health disparities, of which low health literacy (LHL) is a major contributor.[7,8] LHL is an established concern globally[9,10] and Spanish-speaking, less educated, and/or foreign-born Latinos are more likely to have LHL than those born in the US.[9,11] LHL can lead to lesser ability to self-manage which leads to worse health outcomes.[10,12] The proposed intervention is designed to meet the self-management information needs of Latino PWH with LHL, which can lead to better health outcomes.[13-15]

Infographics are technologies that can help clinicians effectively provide health information to individuals with varying language capabilities and LHL.[16,17] Communication regarding complex chronic conditions, such as HIV, is challenging, as providers must provide large amounts of data to patients in a meaningful way.[18] This is especially difficult when a patient's preferred language and culture differs from that of their provider.[2,19] When clinician-patient communication is enhanced, it can lead to better self-management by improving behaviors such as adherence to antiretroviral therapy (ART).[20-22] Infographics can improve clinical communication because, when rigorously designed, they contain a depth and breadth of content displayed in a visually logical way.[23,24] This is useful amidst culture and language differences as infographics provide images familiar to patients, which can help explain complicated processes, augment attention span, and improve information recall.[25-28] Infographics such as the ones in this intervention can, therefore, improve self-management by helping clinicians provide information in an understandable way.[24,28]

Therapeutic communication methods, such as motivational interviewing (MI), targeted at HIV self-management behaviors can help clinicians influence behavior change.[29,30] During MI, specific techniques such as reflective listening and asking open-ended questions are used to emphasize collaboration and acceptance.[29] Incorporating targeted training in this method, even if it is brief,[29,31,32] into interventions enables providers to deliver health education messages that promote healthier behaviors.[29,33] The proposed intervention includes a brief training in MI, so clinicians can more effectively provide information to PWH.

The integration of evidence-based infographics into EHRs will enable infographics to be easily accessible and efficiently scaled up for use at clinical sites locally and globally. The applicant's previously designed and tested infographics are now automated in a Substitutable Medical Applications and Reusable Technology (SMART)® Application (app) compatible with the Fast Healthcare Interoperability Resources (FHIR)®.[34] This is the standard for communicating between apps and electronic health records (EHR) via an application programming interface (API).[34] The resultant app will enable providers to access evidence-based infographics to facilitate HIV-related communication at a large scale. Unfortunately, electronic health tools, and their advantages, are more widely available in developed settings.[35-37] But, a recent push to develop open-source electronic health records in low and middle income countries will enable FHIR compatible devices to be accessible to those living in limited-resource settings.[38-40] The proposed study will leverage this advancement and provide a valuable platform and guide through which other researchers and developers can expand technologies to meet the needs of organizations and populations in limited-resource settings globally.

Understanding if infographics are acceptable to non-Latino populations is an important step towards generalizability and future scalability of this intervention. As the infographics in this study were designed and tested with Latino persons with HIV, we do not yet know if the infographics are relevant for other populations with HIV. Other US-based races/ethnicities that experience high HIV prevalences and negative HIV-related health outcomes are non-Latino Black and White persons (65% of HIV infections), especially those in high-risk groups such as Men who have Sex with Men and Transgender Women.[3,41,42] Therefore, it is critical to explore if the intervention infographics are meaningful in these populations. As such, we propose an extension of the study to ascertain the perspectives of PWH who identify as Black or White.**III**. **Preliminary Studies/Progress Report**

The PI has rigorously and iteratively developed an intervention to assist clinicians provide HIV-related health information to PWH in several preliminary NINR-funded studies. Her dissertation (T32 NR013454), conducted in the Dominican Republic (DR), identified a need for this type of intervention, among other findings.[43-45] In response, her postdoctoral work (T32 NR007969) was to develop evidence-based infographics to assist clinician-patient communication in the DR,[46,47] as well-designed infographics can improve patients' understanding of concepts and health behaviors.[23,25,26,28] During her K99 (K99 NR017829), the PI first assessed the feasibility of using infographics to improve clinical communication with, and outcomes of, PWH (CD4 count among others) in the DR (first K99 feasibility study). She then adapted infographics to Latino PWH in New York (NY), who are mainly of Dominican origin/descent, and completed a second feasibility trial in New York.

Summary of K99 feasibility study results
Results from the first K99 feasibility study, conducted with a validated methodology in the DR, demonstrate that using infographics to improve clinician-patient communication and health outcomes is feasible and acceptable. Qualitative responses from clinicians who administered the intervention were overwhelmingly supportive of not only continuing to use the intervention, but indicated infographics should be further developed to encompass more topics and be made available outside of the study, to other providers at the clinic. Statistically significant changes were observed in the primary outcome measure (CD4 count) of patient participants between baseline and 9-month visits. As several other outcome measures (viral load, engagement with clinician, HIV-related knowledge) showed statistically significant improvements over this time period as well, it is likely the intervention had a positive effect on these individuals. As with all studies, there were limitations. First, all participants were recruited from one health clinic in the Dominican Republic so results may not be generalizable. The second feasibility trial, recently completed in NY, will provide further evidence of feasibility and usability among a similar population in a different clinical context. Another main limitation of both feasibility studies is that there was not a control group, so from current data we are unable to establish how much of the improvement seen in the Dominican cohort was due to infographics and what was attributable to confounders. When larger cohorts are randomized to the treatment and control groups in the planned multi-site trial during the R00 phase, it will be possible to compare results of participants who received the intervention to those who did not, which will provide further evidence of the actual treatment effect.

IV. Research Methods

A. Outcome Measure(s): Outcomes were selected using a conceptual model depicting distinct pathways through which clinician-patient communication can influence health outcomes.[57] In this model, outcomes that are affected by clinician-patient communication are separated into three distinct categories, proximal, intermediate, and long-term. Table 1 summarizes the corresponding outcome measures and the scale or type of data that will be collected for each.

Please note, the primary outcome of interest is CD4 count, which will be collected with a review of participants' medical records following each study visit. Participants' viral load and current antiretroviral therapy regimen will also be extracted from participants' medical records following each study visit. Other measures will be in the REDCap questionnaires that will be administered using iPads.

B. Description of Populations to be Enrolled:

Individual interviews to adapt infographics to the Latino population of Denver, CO

Patient participants for interviews to identify necessary changes to infographics will be adults (≥ 18 years), Hispanic/Latino, English or Spanish-speaking, and living with HIV. If patient participants are pregnant, they may still be included.

RCT - Interventionists

Inclusion criteria for clinicians who will administer the intervention during the RCT will be those who have offered HIV-related care for greater than one year and are not planning to leave the clinic for the next year.

RCT - Patient participants

Inclusion criteria for patient participants for the RCT will be that patients are adult (≥ 18 years), Hispanic/Latino, English or Spanish-speaking, living with HIV with a detectable viral load (>30 or >40 copies/mL depending on the laboratory test) at any point in the past year or be newly diagnosed with HIV, or have an indication of adherence risk as identified by their provider and be planning to receive care at the study site for the next year. If patient participants are pregnant, they may still be included in the study. Participants from the US site are expected to reflect the demographics of Latino patients at the Center for Positive Health (CPH), who are predominantly male (85%) and Mexican (90%). Participants from the DR will reflect the population at CFLR, which is majority female (57%) and Dominican (81%).

Table 1. Outcome measures

Outcome	Measure
Proximal Outcomes	
Information recall	Questions pertaining to final infographic content
Engagement with clinician	Engagement with Health Care providers Scale*[48]
Satisfaction with care	1. Two questions assessing satisfaction*[49] 2. CHAPS Survey 2.0*[50]
Intermediate Outcomes	
Self-efficacy to manage HIV	Self-efficacy to manage chronic conditions scale*[51]
Adherence	1. SMAQ 6 item scale*[52] 2. Medication possession ratio (MPR)[53,54]
Long-term Outcomes	
Health related quality of life	PROMIS 29*[55]
Health status	1. CD4 count and viral load 2. Health Status Assessment*[56]

Note: * scale validated in Spanish

Key-stakeholders who participate in in-depth interviews

Key-stakeholders for in-depth interviews to assess implementation factors of incorporating the SMART on FHIR app into electronic health records will be clinicians or other employees at both sites who provide HIV-related education to patients, have been working in HIV care for greater than one year, and interact with the electronic health record at their site on no less than a weekly basis.

Usability testing of Creole version of the mobile app

Participants will be employees of the research site in the Dominican Republic who are Spanish/Creole bilingual and provide HIV-related health information to patients in Creole.

Validation of infographics with non-Latino PWH
Inclusion criteria for this phase of the study will be 1) Does not identify as Hispanic/Latino 2) Identifies as White or Black race 3) Has HIV infection, confirmed in electronic health record 4) (≥ 18 years) of age.

C. Study Design and Research Methods

Study Design

This will be a mixed-methods study with several components:

1) Individual interviews (Aim 1)

2) Multi-site randomized controlled trial (RCT) (Aim 2)

3) In-depth individual interviews with Key stakeholders (Aim 3)

4) In-depth interviews with patient participants from the RCT (Aim 4)

5) Interviews with non-Latino PWH (additional component of study added 09/20/23)

Study Settings

The trial will take place at two outpatient clinics specializing in HIV treatment. The US site will be CPH, in Denver, CO and the Dominican site is Clínica de Familia La Romana (CFLR). These are the ideal clinical locations for this trial because they offer services to two large, distinct Latino populations who are the target of this intervention (Mexican and Dominican PWH). Including a site in the US and one in the DR will also further augment intervention generalizability. Additionally, the EHR infrastructures at these sites are ideal for further development of the SMART on FHIR app, which will enable scalability to sites across the US and abroad. CPH in CO uses EPIC as their EHR and CFLR uses the open-source EHR, Odoo. Both systems can interface with SMART apps,[58] and their administrative structures permit app integration with EHRs.

Individual interviews to adapt infographics to Colorado context

To satisfy Aim 1, *to adapt previously designed and tested infographics for relevance to persons with HIV (PWH) of predominantly Mexican descent through individual interviews and incorporate final infographics into the mobile app prior to the proposed RCT,* up to 15 individual interviews will be conducted (in English and in Spanish) with PWH after they attend a regularly scheduled clinic visit. During interviews, infographics (n=16) will be shown and participants' feedback on their interpretability and acceptability and suggestions for refinement will be solicited. Interviews will be audio recorded and transcribed, then transcripts will be reviewed to extract meaning and identify necessary refinements to infographics. Corresponding refinements will be incorporated into infographics prior to the proposed trial.

SMART on FHIR App Development

A prototype of the app will be ready for the proposed trial, with a planned start date in January 2021. But, because full integration with the EHR at both sites by then is not feasible, the EHR functionality of the app will be continuously developed, separate from the trial, so the final product of this study will be a functional app that can be incorporated into the EHRs at both sites. To maintain intervention fidelity, the prototype will be used throughout the trial.

Infographic Intervention

Intervention infographics are available in English and in Spanish and were created using a rigorous iterative design process.[46] They are intended to assist clinicians deliver patient education through culturally appropriate and visually appealing representations of key HIV-related concepts, systematically identified in a preliminary study.[47] For the trial, up to five clinicians at each site will be selected to use infographics. These "interventionists" will first attend a training, held by the study team, on how to use infographics to guide education using motivational interviewing (MI),[30] the mobile health application that contains the infographics, and on how to maintain intervention fidelity.[59,60] During training, key concepts of infographics and MI will be reviewed then attendees will conduct "mock visits" to review learned components of MI, the mobile application and infographic content, confirm understanding of study procedures, and ensure interventionists uniformly administer the intervention. Additional training sessions will be held during the study to reinforce interventionists' ability to implement learned skills. Also, during the second training session, interventionists will complete a questionaire (the system usability scale (SUS)) to assess usability of the mobile health app containing infographics. During the study, in normal clinic visits, interventionists will use MI and infographics to guide education with participants using the infographics that will appear in the app, easily accessible on iPads. If a provider is conducting a telehealth visit with a study participant in the treatment group, during times of COVID-19 surges or for any other reason, they will have paper copies of the infographics to show participants during video visits.

Table 2. Study activities at each visit in the RCT

Time point	Activity and group (Treatment (Tx), Control (Cl), or Both)
Baseline	• Randomization • Baseline assessment (Both) • Standard Care (Cl) • Exposure to intervention (Tx)
3 months	• Standard Care (Cl) • Exposure to intervention (Tx) • Follow-up assessment (Both)
6 months	• Standard Care (Cl) • Exposure to intervention (Tx) • Follow-up assessment (Both) • In-depth interviews with PWH begin (Both)
9 months	• Follow up assessment (Both)
Study end	• Follow-up interviews for interventionists (5 per site) • In-depth interviews with key stakeholders (15 per site)

RCT study procedures

During recruitment, clinic staff at each site will work closely with the Research Assistants (RA) to identify eligible participants on or before each recruitment day by verifying eligibility criteria in the electronic health records (EHR).

At the DR site, the RA will notify clinic staff of eligible participants at the beginning of each recruitment day. Then, when an eligible participant presents to the clinic for their regularly scheduled appointment, initial contact will be made by clinic staff (face to face) who will introduce the study by providing a brief description of the study using the approved recruitment script and will then introduce interested participants to the RA, who will further explain the study, confirm eligibility, and complete informed consent and randomization.

At the US site, the RA will identify eligible participants for recruitment days the day before. Then, the RA will call eligible participants to confirm eligibility and explain the study by providing a brief description using the approved recruitment script. If a potential participant is interested, they will be invited to come to the clinic an hour before their scheduled appointment to complete the study visit. When a participant presents to the clinic, the RA will further explain the study, confirm eligibility, and complete informed consent and randomization. If the baseline/enrollment visit will be completed virtually, the procedures for recruitment/enrollment will be exactly the same, they will just be conducted over the phone or via a HIPAA compliant platform such as Skype or Zoom. During virtual enrollment visits, the RA will complete informed consent electronically through REDCap.

Permuted block randomization stratified by clinical site will be computer generated a priori and placed in ordered opaque envelopes by a study team member who is not recruiting; thus, group assignments will be blind to the study team.[61] Procedures will then take place as described in Table 2.

Time intervals of study visits (baseline, 3-, 6-,and 9-months) were selected as CD4 count and viral load may change at three months after ART initiation.[62] Study participants will have visits with interventionists (treatment group) or other providers (control group). Prior to the study, standard education at each site will be evaluated to ensure the only difference between treatment and control groups is the infographic intervention. The intervention will not be administered at 9-month visits to enable assessment of long-term effects. No extra time will be allowed for intervention study visits and participants will be reminded of visits via phone. Half of intervention visits (randomly selected) will be audio recorded and a checklist of intervention components will be independently completed by two study team members, then compared to verify intervention fidelity.

In-depth interviews with key stakeholders

Semi-structured individual interviews will be conducted with up to 15 clinicians at each site who provide patient education to establish preferences and recommendations for integrating the app into each EHR (Aim 3). Interview guides will be rigorously developed[63] and questions will be guided with a theoretical model.[64]

Usability testing of Creole version of the mobile application

As the study team had the opportunity to translate the mobile application for this project into Haitian Creole, we will recruit five additional clinic employees who provide HIV-related health education to PWH to use and evaluate the Creole version of the app. Following recruitment, they will complete informed consent and then will participate in a 1 hour training session, conducted by the study team, where they will learn about the infographics in the app and also learn about the app itself. These five participants will then use the app with patients who speak Creole for two weeks. Then, they will participate in a focus group where they will provide feedback on the app and suggestions for improvement. During the group, participants will be provided prinotouts of the infographics and of the screens in the mobile app so they can make changes to the Creole versions directly. They will also complete the SUS, the same usability scale that the study interventionists completed.

Assessment of infographics with non-Latino PWH

We will recruit an additional 50 PWH (N=25 Black and N=25 White) from the Center for Positive Health at Denver Health to help us understand if infographics are meaningful to non-Hispanic/Latino Persons with HIV. During Recruitment, Medical Assistants at the Center for Positive Health will introduce eligible participants (as confirmed in their medical records) and if they are interested in participating, will refer them to speak with an on site study team member. The study team member will then further explain the study, answer any questions. When interested and eligible patients agree to participate, the on-site study team member will complete verbal informed consent (see attached document) and complete the study visit.

During the visit, the study team member will show participants all of the infographics in the set and ask them questions about each one. After seeing the full set of infographics, participants will answer a set of questions that is about infographics generally and will then complete a very short (3 question) recorded interview to ascertain their perspectives of infographics and their potential use in the clinic.

After completion of the study visit, the study team member will provide the participant with a $40 gift card for their time.

At study completion, we will provide a $50 gift cards to the Medical Assistants and clinic staff who assist in recruiting.

D. Description, Risks and Justification of Procedures and Data Collection Tools

Description of data collection tools

D.1. Individual interviews to adapt infographics to the Colorado context.

Participants will initially complete a brief demographic questionnaire. Then, they will complete individual interviews with a study team member. Interviews will be audio recorded and later professionally transcribed.

D.2. RCT

D.2.1. Medical record review

Data will be extracted from medical records after each study visit and will include **the primary outcome CD4 count** as well as most recent viral load and currently prescribed ART regimen.

D.2.2. Baseline assessments

Baseline assessment will be administered either virtually or in-person at baseline visits and will collect demographics (age, length of time living with HIV, sex, gender, income, level of education among others), assess health literacy levels with two validated assessments, the Short Assessment of Health Literacy - Spanish & English (SAHL S&E)[65] and the Newest Vital Sign (NVS),[66] include a measure of acculturation, the Short Acculturation Scale for Hispanics (SASH),[67] and all other outcome measures not extracted from medical records (Table 1).

D.2.3. Follow up assessments

Follow up assessments will be administered either virtually or in-person at 3-, 6-, and 9-month visits and will include outcome measures (Table 1) and open-ended questions exploring infographic usability, satisfaction with infographic design, and recommendations for improvement. Questions regarding interventionists' communication strategies and intervention delivery will be included to further assess intervention fidelity and enable assessment of providers' communication variability.

D.2.4. Semi-structured in-depth interviews

In depth interviews with patient participants at the CO site will be conducted using a rigorously developed iterative interview guide.[63] Interviews at the CO site will include questions and probes to generate an explanatory model of participants' experience living with HIV and communicating about it in a clinical setting,[68] this data was already collected from participants in the DR and NY in preliminary studies. Questions to obtain feedback on how to adapt infographics and clinical communication will be included for all participants. Interviews will be audio recorded and later transcribed.

D.2.5. Follow up interviews with interventionists

Final interviews with interventionists will explore clinicians' perspectives on the use of visual communication aids (infographics) during clinic visits (barriers and facilitators), explore their experiences working with participants in the study, and identify areas where infographics can be further refined. Interviews will be audio recorded and later transcribed.

D.3. In-depth interviews with key stakeholders

In depth interviews will be conducted with up to 15 clinicians at each site who provide patient education to establish preferences and recommendations for integrating the app into each EHR (Aim 3). Interview guides will be rigorously developed[63] and questions will be guided with a theoretical model.[64] Interviews will be audio recorded and later transcribed.

E. Interviews with non-Latino PWH

Interviews with non-Latino PWH will be conducted using an interview guide that includes the questions to ask for each infographic, the set of questions to ask after the participant has seen the entire set of infographics as well as the three interview questions to ask during the recorded portion of the interview.

Potential Risks

In all research there is a risk of a loss of confidentiality. Possible additional risks are detailed below.

In initial individual interviews, participants may feel uncomfortable discussing HIV or answering questions about infographics.

In the RCT, interventionists will be trained in a new communication technique (motivational interviewing) and will be using the intervention during clinic setting so no more than minimal risks beyond their normal daily work are anticipated. Patient participants in the RCT will receive health information using infographics (intervention group), otherwise they will receive standard care. Both treatment and control group participants will complete baseline and follow up questionnaires at all study visits with a study team member. Therefore, participants may feel uncomfortable with questions asked. Also, two study visits will be randomly selected to be recorded, which may make participants feel uncomfortable.

Though it is unlikely because interviews will not include sensitive questions, key-stakeholders may also feel uncomfortable answering questions in an interview setting.

Participants may have difficulty accessing study visits in virtual formats. If this case presents itself, the RA will provide additional assistance as needed to help them gain familiarity with the electronic platforms to be used.

The study team will strictly adhere to the procedures detailed in this protocol, including methods to mitigate risks to participants.

Justification of procedures

Because this study involves no more than minimal risks to participants, the above described procedures and data collection techniques are justified as they are all necessary to satisfy the research aims of this study. Additionally, having the option to complete visits virtually or in-person will ensure maximum safety for patients and providers in times of COVID-19 surges.

E. Potential Scientific Problems

As attrition may be a concern in hard to reach populations,[69] we accounted for 22% attrition in our sample size calculations. To encourage retention, as was successful in the K99 trial in the DR, participants will be reminded of visits via phone calls prior to study visits and incentives appropriate for each site will be provided. Recruitment will be monitored to ensure a sufficient pace of enrollment and timelines will be extended if needed.

Intervention fidelity and contamination are concerns as participants may be scheduled to see the incorrect provider, providers may use infographics with control group participants, or simply may not use infographics. Intervention fidelity will be assessed by providers, patients, and a study team member, and contamination addressed with intent-to-treat analysis**.**

F. Data Analysis Plan

Sample size calculations

Individual interviews

Up to 15 participants will participate in individual interviews. This sample size was established as 15 participants are likely to be able to identify 90% of usability concerns in informatics-based studies[70] and as few as 10 are likely to achieve saturation in qualitative studies on specific themes (e.g. the experience of living with HIV) with relatively homogenous samples (e.g. Latino persons of predominantly Mexican origin/descent living in Denver, CO).[71]

RCT – Interventionists

Up to 5 interventionists at each site will be purposefully selected to participate. This sample size is based on preliminary feasibility studies.

RCT – patient participants (n=164, 82 at each site, 41 per group)

To establish sample size for the RCT, we used a longitudinal power analysis approach for testing the “time averaged difference” in two group means for a continuous outcome over time.[72] This effect size is analogous to Cohen’s D: $(\mu_1-\mu_2)/\sigma$, where μ_1, μ_2 are the outcome means (averaged over time) in the treatment and control groups, and σ is the standard deviation of the outcome (assumed constant over time and equal for both groups).[73] Assuming a slightly less than “medium” effect size of D=0.45,**[73]** 80% power, and two-sided significance level $\alpha=0.05$, the required total sample size ranges from 68-126 depending on the assumed constant pairwise correlation between the 4 repeated measures (which we varied from 0.25 to 0.75) (Table 3). We conservatively assume a correlation of 0.75 which requires a total sample size of 126. To account for 22% attrition, higher than our attrition rate that we experienced in the pilot tests in the Dominican Republic (16%) to account for complications with this hard to reach population of Denver, we increased the sample size to 164 (161.5 rounded up to ensure equal numbers in each group).

Interviews with key stakeholders

Up to 15 interviews with key stakeholders will be conducted at each site (CO and DR). This is based on estimates that 12 interviews per site can lead to saturation of identified themes.[74,75]

Summary of total sample size per site:

DR total # of participants to be consented to achieve study aims: 100
(maximum recruitment at this site will be 115 to account for failures and withdrawals).

Denver Health total # of participants to be consented to achieve study aims: 121
(maximum recruitment at this site will be 140 to account for failures and withdrawals).

Analytic plan for each study aim

Aim 1: See individual interviews in section C above.

Aim 2: *Conduct a multi-site randomized controlled trial to assess the efficacy of the intervention (infographics administered through a mobile app) as compared to standard care in improving treatment outcomes (CD4 count, viral load, self-efficacy to manage HIV, among others) of PWH and determine how resultant effects vary over time (baseline to 9-months) and between sites (US and CO).*

Table 3. Necessary sample size for testing the time-averaged difference between two groups of equal size

	ρ (constant correlation of 4 repeated measures over time)		
Effect Size (Average diff. in 2 group means over time, analogous to Cohen's D: $(\mu_1-\mu_2)/\sigma$)	0.25	0.50	0.75
0.20 (Small)	344	491	638
0.35	113	161	209
0.40	86	123	160
0.45	68	97	126
0.50 (Medium)	55	79	103
0.80 (Large)	22	31	40

Note: Calculations with 80% power and $\alpha=0.05$ with 4 repeated measures assuming exchangeable/ constant pairwise correlation "ρ" varied from 0.25 to 0.75.

Primary Analysis: A linear mixed effect model (LMM) will be used to compare the effects of the two groups (treatment vs. standard of care) on the primary longitudinal outcome of CD4 count between baseline and the three follow up visit time points (3-, 6-, and 9-months). Subject-specific random intercepts and slopes will be used to model heterogeneity in the subjects' trajectories. Three primary tests will be considered: 1) testing the time-averaged difference in the outcome between the two treatment groups (main effect for treatment), and 2) test whether change-over-time differs between the two treatment groups (treatment*time interaction), and 3) test whether the treatment effect differs between the two sites (treatment*site interaction and treatment*site*time interaction).

Secondary Analyses: The same analysis plan will be repeated with the remaining longitudinal outcomes Table 2 of the Research Strategy section of this application. Linear mixed effect models (LMM) will be used for continuous outcomes (CD4 count, viral load, knowledge questions, engagement with health care provider scale, satisfaction with care,

self-efficacy, health related quality of life PROMIS-29), logistic generalized linear mixed effect model (GLMM) will be used for the dichotomous adherence score (SMAQ-6), and ordinal GLMM will be used for the health status assessment score while LMM will be used for the additional health status continuous score. Lastly, as a simpler alternative to longitudinal mixed effect models (that use all time points), standard general linear models will be used to model outcomes at 9 months adjusting for baseline, thus testing whether an outcome differs between the two interventions at 9 months.
The System Usability Scale (SUS) that providers complete during the second training session will be scored according to published guidelines.[76]

D.9.4. Aim 3: *Assess implementation factors of integrating the SMART on FHIR app into EHRs through in-depth interviews and leverage findings to ensure the app effectively interfaces with EHRs in the CO and the DR.*

Transcripts from key stakeholders at each site will be analyzed using directed content analysis to identify implementation factors regarding the SMART app's integration with EHRs.[77-80] Key considerations to enhance perceived usefulness and ease of use will be identified and incorporated into the final app.

D.9.5. Exploratory Aim 4: *Conduct in-depth interviews with PWH in CO to explore their perceptions of HIV infection and preferences for health communication. Qualitative findings will be integrated with those from the NY and DR cohorts to detail variations and similarities, and identify areas for intervention refinement.* To deeply and rigorously explore participants' perceptions of HIV infection and how they influence clinical communication, explanatory models of HIV infection among PWH at each site will be generated.[68,81-83] Directed content analysis guided by McGuire's Classic Input-Output Framework for Constructing Persuasive Messages will be used to analyze transcripts from in-depth interviews.[84] Gioia's methodology will be followed to enhance qualitative rigor.[85] Results from each cohort (DR, CO, and NY) will be synthesized and integrated to establish variations and similarities in the HIV experience among distinct Latino cultures as well as establish how their unique perspectives shape intervention design and delivery.

Usability testing of Creole version of the app

Changes to the app will be made directly on the paper copies provided during the group. The scores of the SUS will be calculated according to the instrument guidelines.

Validation of infographics with non-Latino PWH

Quantitative data from the questionnaire that will be administered during interviews will be scored and descriptive statistics calculated. Audio recordings will be transcribed and analyzed for patterns. Representative quotes will be extracted.

E. Summarize Knowledge to be Gained

HIV continues to be a global concern, but the focus on HIV treatment and research have shifted from considering HIV to be a devastating acute condition to a chronic condition that is manageable with optimal self-management and treatment adherence. This shift in attention and disease progression requires persons living with HIV to effectively manage their health for long periods of time. However, individuals with limited health literacy may have difficulty accessing and using the health information that enables this extended health management, especially when they are presented with information that is not culturally relevant or is language inappropriate. This study will contribute evidence to support the provision of health information to diverse Latino populations in numerous ways.

This study aims to develop and evaluate an evidence-based and culturally appropriate technology (infographics embedded in a mobile application) to facilitate HIV-related communication between Latino persons living with HIV and their clinicians. By incorporating these evidence-based infographics into an app that interfaces with EHRs both locally and globally, this work will contribute to the informatics literature regarding the effective development and implementation of SMART on FHIR apps at a global scale. Additionally, it will provide valuable information regarding the effectiveness of infographics at improving clinical communication between patients and providers, which has widespread relevance to the growing information visualization literature. Additionally, there is little in the literature regarding effective ways to tailor interventions to heterogeneous groups, as an intervention designed for one Latino group may not be relevant to others. This work will provide evidence-based guidance regarding methods to effectively tailor health related interventions to diverse Latino groups. Furthermore, this intervention is scalable and will be accessible to clinicians working with Latino patients with low health literacy in the United States and around the world.

Including an additional portion in this study to ascertain if the infographics are meaningful and acceptable to non-Latino persons with HIV will provide preliminary data about the generalizability of these infographics and set the stage for further scalability of the intervention so that more individuals in need are likely to benefit from it.

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