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Title: PlusCare: Mobile Platform to Increase Linkage to Care in Adolescents Living With HIV/AIDS
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Study Objective and Overview: To conduct a mixed-methods, non-randomized pre-post study to test PlusCare, a mobile application, in real-world clinical settings. In a Phase I project, members of the research team demonstrated the acceptability and feasibility of PlusCare, a mobile application system developed by Dimagi, Inc. to support HIV case management for youth living with HIV (YLH) aged 13 to 25 years old. In this Phase II SBIR project, we will enhance the PlusCare system to best serve the team-based care delivery model identified in Phase I and test it in a non-randomized, pre-post intervention study conducted in multiple clinical settings. The objective of this Phase II project is to test and demonstrate the effectiveness of PlusCare on HIV case management process and care continuum outcome measures.

Study Design: Patients and case managers (CMs) will be recruited from three HIV case management programs in two hospitals in the metro Boston area. Patients will use the PlusCare application for 12 months, while CMs will use the system for at least 15 months in order to account for rolling patient recruitment (i.e., 3 months to enroll target number of patients). We will perform a process and outcomes evaluation of the system to determine the effect of the PlusCare intervention on HIV health status and case management outcomes.

Patient Selection and Inclusion/Exclusion Criteria: A research assistant (RA) will recruit CMs (N=20) and patients (N=50).

The patient eligibility criteria are as follows:
Inclusions:
1) between 13-25 years old,
2) patient of the BCH HAPPENS or BCH CHAP program,
3) HIV-positive,
4) own or ability to access a smartphone (e.g., iPhone, Android) for one year, and
5) be in care for at least 1 year prior (for access to historical control data)

Exclusions:
1) Non-English speaker or
2) Visually or hearing impaired

These criteria were selected to ensure the focus and inclusion of YLH to fulfill the purpose and function of this proposed application for case management to serve this population, who most benefit from the support for care and services that the case management model provides. Additionally, our team wanted to ensure that the patients would be able to run the PlusCare app on their device for the needed length for the study.

The CM eligibility criteria are as follows:
Inclusions:

1) are actively employed BCH and
2) perform case management duties with HIV-positive patients 13-25 years old

Description of Study Treatments or Exposures/Predictors: Study participants will be given a username and access to the PlusCare app on their own personal devices. CMs will have access to the mobile app available on a study tablet that will be provided to each program or web app accessible from their own work computers.

Definition of Primary and Secondary Outcomes/Endpoints: Primary outcomes will be CD4 count, viral load, and HIV medical visit frequency. Secondary outcomes include emergency room visits and hospitalizations, adherence, patient reported quality of life, system usage data (such as log-ins) and system usability and satisfaction. This is detailed further in the table below:

Patient Measures	**Pre**	**Post**			**Data Source**
	1-year prior	**Base**	**6-mos**	**12-mos**	
Baseline Demographics					
Current gender[1], sexual orientation identity (BRFSS[2]), age/date of birth, income & employment (STRIVE[3]), years since diagnosis, time spent in case management, housing stability, insurance, retention and quality of care, treatment		x			Survey, EHR
Experience with Technology		x			Survey
Primary Outcomes					
CD4, viral load[4]	x	x		x	EHR (Lab data)
HIV medical visit frequency and gaps[4]	x	x		x	Billing data, EHR
Secondary Outcomes					
ED visits, hospitalizations	x	x		x	Billing data, Survey
Patient-centered: Quality of Life (CDC HRQOL-14), self-efficacy (based on chronic disease scale)		x	x	x	Survey
System: Usage (log in frequency, dwell time)				x	System data
System: Usability and Satisfaction[5]				x	Survey

Data Collection Methods, Assessments, Interventions and Schedule (what assessments performed, how often)
For case managers:

Baseline assessment and in-person training. Enrolled CMs will attend an in-person training session, which will be led by a RA with a Dimagi study team member with technical experience in the development of PlusCare. A baseline survey will be administered to collect basic demographic data (e.g., age, sex, race, ethnicity, education), information on professional role and experience (e.g., job title, years of CM experience, number of patients managed), and experience with technology. In the training session, Ease of training and feasibility of this model of patient registration will be assessed in this study through qualitative feedback collected from CMs at the end of the study.

Intervention. All CMs will have access to PlusCare via mobile app installed on a study tablet or web app accessible from any computer for at least a period of 15 months to accommodate for rolling patient enrollment. During this study period, data on CM usage of PlusCare will be collected passively through the tablet as well as through web app access and outputted as daily usage logs.

End-of-Study Interview with CMs. Towards the end of the study period (i.e., 15 months after Baseline), CMs in each program will be re-contacted by the respective study RA at each site to participate in a one-hour focus group. Focus groups will comprise 2-8 participants and will be led by the study RA in a private setting. For those who are unable to attend a scheduled focus group, a separate structured one-on-one interview will be scheduled.

CM participant compensation. CMs will be compensated $50 for completing the Baseline Assessment and Training Session and $100 for completing the End-of-Study Interview. If a CM drops out of the study before the end of the study due to circumstances unrelated to the study (e.g., change in employment), s/he will still have an opportunity to participate in an end-of-the-study interview and will receive $100 for completion of that study activity. Any CMs who are newly employed during the 15-month period will be recruited to participate in the study and compensated in the same fashion.

For patients*:*

In-person baseline interview. Upon receiving written assent or consent, the RA will then proceed to administer a baseline assessment and a semi-structured, open-ended interview. The RA will be responsible for registering the patient into the PlusCare system and setting up the patient's contacts. A parent handout about the study will be prepared for distribution to patients who wish to share information with a parent about the study. All patients will install the PlusCare application on their own smartphone, with assistance from the RA if needed. Once PlusCare has been installed and the patient has successfully demonstrated that s/he can 1) access the app from his/her smartphone and 2) receive incoming SMS messages from the CM, the patient will be actively enrolled for one year.

Intervention. All patients enrolled in the study will have access to all of PlusCare's functionalities for a period of at least 12 months starting from the time they are enrolled. App activity will be monitored throughout the 12-month period.

Monthly Adherence Assessment. A validated one-item medication adherence assessment will be administered once a month; this assessment consists of patients' self-reported rating of their perceived ability to take all of their medications as prescribed in the past month.[6,7] Patients will receive an SMS message alerting them to submit a response to the adherence assessment from within the PlusCare app, thus ensuring individuals' responses remain confidential. While the method of self-report may be subject to recall and social desirability bias

compared to other more objective measures such as digital medicine systems or pharmacokinetic measures, it has the advantage of being feasible and acceptable and less susceptible to misestimation due to device non-use and pocket dosing or overestimation due patients opening the device without removing pills.[8] Based on findings from adherence studies, including our previously funded SBIR project (ARemind), adherence reminders are effective in collecting timely, reliable measures of adherence and we recognize that there is a potential that they may be associated with a decrease in HIV-1 RNA viral load.[9,10]

Retrospective data. The study RA will access key variables of interest from the patient's electronic case management records (via PowerChart) and administrative and hospital billing data dating back 1 year from date of enrollment for initial cost-effectiveness analysis that will contribute to the evaluation and commercialization plan. Key variables will include viral load and CD4 counts from lab results and medical visit frequency and gaps consistent with standards for Ryan White Foundation-funded programs.[4]

6-Month and 12-month Follow-up Assessment. At the 6-month and 12-month time point, the site RA will contact each patient to complete assessment items online. The RA will disseminate an online survey to the patient. Responses will be collected via a CommCare survey form and stored in the CommCare server.[11] Patients will have the option of completing this assessment in person if they prefer, but compensation will remain the same as a remote assessment.

Safety plan. Before completing the surveys potential participants will read and sign an informed consent. This form will document a potential participant's understanding that if they identify any level of emotional distress above baseline on survey questions, the results will be flagged and e-mailed to a member of the study team**.** Participants will subsequently be contacted by the study team member or another mental health provider within two business days to have a safety check-in. No items have explicit safety concerns such as suicidality. We will also document a potential participant's understanding that if we identify during surveys/screening any heavy or dangerous use of substances in the past 30 days, we will report the use to their provider for safety. Participants will be given a mental health resource list at the time of consent in case they experience emotional distress at any point throughout the course of the study.

Statistical Analysis Plan

The study analysis will follow an *intention-to-treat* approach to determine PlusCare's effect on outcomes related to HIV case management. Our primary outcomes will include Ryan White Program core performance measures[4] (HIV viral suppression, HIV medical visit frequency, and gaps in medical visits). Secondary outcomes will include proximal outcomes (medication adherence), patient-centered outcomes (quality of life, self-efficacy), and system usage and usability. Usage data collected passively from the system from both patients and CMs will be analyzed to assess trends in system usage (e.g., what module was accessed by patients most frequently, how many documents were sent by CMs) and system usability will be assessed via the SUS administered at the end of the study.[5] Baseline characteristics of our sample were summarized with descriptive statistics (mean, median, SD, frequency) and a Wilcoxon test for significance will be used to assess PlusCare's impact on our outcomes of interest pre- and post-intervention and a repeated measures analysis will be used to determine changes in outcomes assessed at each respective time point during pre- and post-intervention. Under the

assumption that some individual specific effects are uncorrelated with the independent variables while some other effects are correlated, we will use mixed effects modeling to account for both time-variant and time-invariant factors. Initial cost-effectiveness analysis will be performed following methods used in previous studies.[12–15] Data on HIV medical visit frequency and gaps and ED visits and hospitalizations will be used to perform this analysis. The monetary benefit from the PlusCare intervention arises from the cost savings as a result of reduction in hospital visit frequency between pre- and post-intervention. We will compute preliminary cost-effectiveness of the PlusCare intervention by comparing the cost savings attained with the program cost of the case management program using Net Present Value (NPV = *Present Value of Cost Savings – Present Value of Program Costs*) and the Return on Investment (ROI = *Present Value of Cost Savings / Present Value of Program Costs*). We hypothesize that the use of PlusCare will have a positive effect on the return on investment. All statistical analyses were performed using R statistical software (R Foundation for Statistical Computing, Vienna, Austria) or SAS software, version 9.2 (SAS Institute, Cary, NC) and a two-tailed P-value of the test < 0.05 was considered statistically significant.

Statistical Power and Sample Considerations

The power calculation was based on N=50 patients. With a confidence level of 95%, there is 81% power to detect a 38% change in log10 HIV viral load in patients pre- and post-intervention.[16]

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