ASSESSMENT OF A COMPREHENSIVE HIV CLINIC-BASED INTERVENTION TO IMPROVE PATIENTS' HEALTH AND REDUCE TRANSMISSION RISK

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SUPPORTING STATEMENT B

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B. 1. Respondent Universe and Sampling Methods

The respondent universe is all adult HIV-positive patients receiving HIV primary medical care at 6 HIV clinics affiliated with (1) Baylor College of Medicine, Houston, (2) Boston Medical Center, (3) University of Alabama, Birmingham, (4) University of California at San Diego, (5) University of Miami Medical School, and (6) University of Washington.

Respondent eligibility includes all HIV patients 18 years of age and older (19 and older in Alabama) presenting for HIV primary care at the six clinics beginning October 1, 2013.

The method for selecting patients varies depending on the specific outcome or process measure, as described below.

Viral Load and Clinic Attendance Variables

These variables will be obtained from clinics' archived databases and include all patients who attend the clinic beginning in October 1, 2013. We anticipate receiving viral load (VL) and attendance data records for approximately 17,300 patients (Panel A and B combined). This includes existing (i.e., established) patients at the clinics and new patients who enter the clinics during the data collection period.

Behavioral Screener

Three clinics participating in this study are part of the Center for AIDS Research (CFAR) Network of Integrated Clinical Systems (CNICS) and are already conducting screening of patients; these clinics will not do additional screening. At the other three clinics participating in the study, all patients will be asked to complete a brief behavioral screener each time they attend clinic for a primary care exam (approximately every 3 months per patient on average). There will be approximately 9,170 patients at the three non-CNICS clinics. We anticipate a screening rate of 86% (based on the existing screening rate at the three CNICS clinics), yielding screening data from 7,886 patients at the three non-CNICS clinics. No tokens of appreciation will be offered to patients for doing the screener. Medical providers will use this screener information (or the screener information already being collected) as an interventional tool to guide their prevention messages and brief counseling of the patient as needed. The screener information will not be transmitted to CDC or used in the statistical analysis.

Computer-Based Intervention (CBI) Assessment Items

At each of the six clinics, VL detectable patients (e.g., patients whose level of HIV in their blood exceeds 200 copies/mL) are eligible to do the CBI, which includes five assessment items described in supporting statement A. We will approach VL detectable patients when they present for primary care. This includes VL detectable patients who have a history of care at the clinics and new patients who enter the clinics and are VL detectable. We anticipate a total of 7,760 VL detectable patients will be eligible in Panels A and B. Prior intervention studies for HIV-infected persons conducted at clinic settings or other service settings had an average participation rate of 81%.[1-4] We anticipate an 80% CBI participation rate (6,208 of 7,760 VL detectable patients). No tokens of appreciation will be offered to

patients for doing the CBI during a regularly scheduled clinic visit. But if a patient needs to make a special trip to the clinic for purpose of doing the CBI, a token of appreciation will be offered.

Patient "Exit" Survey after Medical Exam

At each of the six clinics, a sample of patients will be surveyed after their primary care exams to document the types of issues (e.g., adherence, attendance, sexual practices) that providers may have discussed during the exams. The first survey will occur prior to the onset of the intervention at the clinic and serve as a baseline; subsequent surveys will be administered quarterly. The same survey items will be used each time. A total of 50 patients (10 per day, Monday through Friday) will be surveyed every 3 months (for 3 years in Panel A clinics and for 2 years in Panel B clinics). Patients will be randomly selected after their primary care exams (not urgent care visits) and asked if they would be willing to answer a few questions. Patients' surveys are not linked across time. Participation is voluntary. No tokens of appreciation will be offer to patients for doing the survey. This type of patient exit survey was used in a recently completed CDC/HRSA funded study conducted at HIV clinics. Of patients approached for the exit survey in that study, 95% participated.

Provider Survey

All primary care providers (physicians, physician assistants, nurse practitioners) at each clinic will be asked to complete surveys every three months asking about topics they may have discussed with their patients in the past week. Approximately 120 providers will be asked to participate. The first survey of providers will occur prior to the onset of the intervention at the clinic (baseline) and then the same survey items will be administered quarterly thereafter (total of 4 times per year for 3 years in Panel A clinics and for 2 years in Panel B clinics). A provider's surveys will not be linked across time. Participation is voluntary. No tokens of appreciation will be offered to providers for doing the survey. This type of provider survey was used in a recently completed CDC/HRSA funded study conducted at HIV clinics. Of providers requested to do the pencil and paper survey in that study, 79% completed the survey. We anticipate a higher participation rate in the current study because we will be using electronic surveys with automated reminders.

B. 2. Procedures for the Collection of Information

Setting for Data Collection

The HIV clinic is the setting for the data collection.

Data Transmittal and Security

CDC will establish and host a secure web-based system for receiving and storing all project-related data at CDC. Secure socket layer (SSL) technology will encrypt all incoming data during the transmission process. The encrypted data will be stored in a secure CDC server.

The project computers at the clinics will be connected to the clinics' existing network (wired, WiFi) which will enable access to the Internet for purpose of transmitting data to CDC.

The following safeguards will be in place:

- All encryption device systems will be FIPS 140-2 compliant (federal standard)
- CDC will not receive patient names, medical record numbers, social security numbers, or personally identifiable information.
- No data collected as part of the study will be stored on any project computer or local server at the clinic. All data are encrypted and saved on secure CDC server.
- Only authorized and authenticated CDC-based project staff (project officer, project coordinator, data manager at CDC) will have access to the data sent to CDC.
- Data records received by CDC will only be identified by a unique study ID code number.
- A functional algorithm will be placed on project computers at the sites to convert a patient's medical record number to study ID (the algorithm can also back-convert for study management purposes at the performance sites).
- The algorithm will not be installed on any computers/servers at CDC thus preventing CDC from back-converting a study ID into a medical record number.
- There will be no databases of medical record numbers and study IDs on any project computers or servers at the sites.
- All project computers used at the clinics for purpose of conducting the study will be password protected.
- Only authorized and authenticated project staff at the clinics (clinic-based data manager, project coordinator, and health coach) will have access to the project computers).
- Papers and presentations will report aggregated information and will not contain any identifying information that can be traced back to a respondent.

Methods for Data Collection

Transmittal of clinical variables routinely collected and archived by the clinics: A data manager at each clinic (position funded by the CDC) will electronically transmit clinical variables in batches to CDC on a quarterly basis. These data elements (see list below) are routinely collected and archived by the clinics and used for patient management purposes.

The following clinical data elements available in the clinic's archived database will be electronically transmitted to CDC (for a three-year period beginning on the date of OMB approval).

- All viral load (VL) laboratory results and dates of VL lab tests
- All CD4 cell count and dates of CD4 lab tests
- Attendance for HIV primary care, dates, and dispositions (cancelled, kept, no-show)

The following demographic variables in the clinics' archived databases will also be transmitted to CDC.

- Month and year of birth
- Biological sex
- Ethnicity (Hispanic or Latino; not Hispanic or Latino)

- Race (indicating all categories that apply)
- HIV risk exposure category
- Date first tested HIV positive
- Health insurance status and type of insurance (e.g., Medicaid, Medicare, Ryan White, private)

Behavioral screener: This screener will be available in English, Spanish, and Creole. All patients at the three clinics that are not already conducting behavioral screening of patients will be asked to complete a single-page screener (paper and pencil) each time they come to clinic for primary care (approximately every 3 months). Patients will do the screener in the clinic's waiting room or examining room before seeing the provider that day.

CBI assessment items: The CBI assessment items and audio/visual intervention will be available in English and Spanish. Funds were not available to produce the CBI tool in Creole. Mono-lingual Creole speakers are a very small percentage of patients at only one of the sites (Miami). VL detectable patients will do the CBI while at the clinic, either before or after their primary care exam. Patients at clinic for urgent care visits will not be approached.

Patient "exit" survey: This patient exit survey will be available in English, Spanish, and Creole. Patients sampled for the quarterly survey will complete it after a primary care exam. A project coordinator will verbally ask the questions and patients will respond privately using an electronic tablet. The survey will not include any personally invasive questions, and will not include patient names, study ID numbers, medical record numbers, or any means of identifying a patient. Patient surveys will not be linked across time. The surveys will include a code to identify the clinic site.

Provider survey: This provider survey will be available in English only. All providers speak and understand that language. Each quarterly period, providers will access the survey using their workplace computers. Automated reminders will be sent to the providers. The provider surveys will not include any personally identifiable information, and surveys will not be linked across time. The surveys will include a code to identify the clinic site.

Statistical Power

The power analyses focus on the population of patients with detectable VL (>200 copies/mL) at baseline because this is the group to whom the intervention is targeted. A separate power analysis was conducted for each of the two primary outcomes: (1) proportion that has an undetectable VL (≤ 200 copies) and (2) proportion who exhibit regular clinic attendance for primary care. Power analyses were also conducted for two secondary outcomes: (1) proportion of patients who self-report on the CBI that they had excellent ability to take all of their ART as prescribed in the past four weeks and (2) proportion who self-report on the CBI that they engaged in HIV sexual transmission risk behavior in the past two months. All power analyses use an alpha of .05 and a two-tailed test. The method for conducting the analysis varies depending on the outcome measure as described below.

Statistical Power for Primary Outcomes (VL Status and Clinic Attendance)

VL status: The power analysis for this outcome was calculated using the group randomized design (Panel A vs. Panel B clinics) taking clinic clustering effects into account (lack of independence among patients within a clinic). The power analysis focuses on patients who have a detectable VL at baseline, and examines the percent of these patients who have an undetectable VL after 12 months of intervention in Panel A clinics. Patients in Panel B serve as a concurrent control group during the first 12 months. The denominator for the analysis will be the total number of VL detectable patients (approximately 7,760 patients; approximately 3,880 per panel). Based on a published longitudinal study,[5] we anticipate that 10% of the VL detectable patients in Panel B (controls) will become VL undetectable by 12 months reflecting general improvement in clinical care practices apart from our project intervention. We have 80% power to detect a study intervention effect that improves the outcome to 20% among Panel A patients relative to the 10% improvement in Panel B patients.

Undetectable viral load	3 Panel B clinics (control)	3 Panel A clinics (intervention)	Power
Improvement compared to control group	10% of 3,880 VL detectable patients become undetectable by 12 months	20% of 3,880 VL detectable patients become undetectable by 12 months	80%

Clinic attendance for primary care: The attendance outcome is the proportion of patients who keep all of their scheduled primary care appointments in a 12-month period following their entry into intervention. The power analysis was calculated using the group randomized design (Panel A vs. Panel B clinics [concurrent control]) taking clustering effects into account. The denominator for the analysis is the approximately 7,760 VL detectable patients (about 3,880 per panel). The percentage of these patients who achieve the outcome after 12 months of intervention in Panel A clinics is compared to the percentage of patients who achieve the outcome in Panel B clinics. We anticipate that the analytic sample size for this attendance variable (obtained from clinics' archived databases) will be the same as the analytic sample size for the VL outcome above. A recently completed retention in care trial found that 25% of non-intervened upon HIV patients kept all of their primary care appointments in a 12-month period.[6] We used this baseline value in our power analysis. We have 80% power to detect an intervention effect that improves the outcome to 40% of patients keeping all primary care appointments in a 12-month period.

Clinic attendance	3 Panel B clinics (control)	3 Panel A clinics (intervention)	Power
Improvement compared to control group	25% of 3,880 VL detectable patients keep all primary care appointments in 12 months	40% of 3,880 VL detectable patients keep all primary care appointments in 12 months	80%

Statistical Power for Secondary Outcomes (Self-Reported ART Adherence and Sexual Risk Behavior)

Self-reported ART adherence: This variable is collected from VL detectable patients' self-reports on the CBI assessment items. We are not able to analyze the ART adherence outcome using the group randomized design. Rather, this outcome is analyzed as a pre-post change comparing baseline ART adherence (obtained on the first CBI assessment before exposure to the CBI intervention components) and a follow-up CBI assessment (obtained a few months later after exposure to the CBI intervention). The power analysis uses McNemara's test for dependent proportions (percentage of ART patients who report excellent ability to take all of the ART medications as prescribed in the past four weeks; the response scale for this item runs from very poor, poor, fair, good, very good, excellent and has been shown to have a strong correlation with actual VL values of patients[7]). For the power analysis, we focus on VL detectable patients in Panel A during the first year; patients in panel B do not do the CBI in the first year.

Of the total number of 7,760 VL detectable patients, we anticipate that 80% will participate in the CBI (6,208). Approximately half of these will be in Panel A (3,104). Of these, approximately 80% will have been prescribed ART and qualify for this ART adherence outcome (2,483). Of these, we anticipate getting follow-up CBI assessment data on ART adherence from 80% (1,987 VL detectable patients in Panel A). Based on a recent published study,[8] we use a baseline (pre-intervention) value of 55% of non-intervened HIV patients on ART having excellent ability to take all of their ART medications as prescribed. We have >99% power to detect an intervention effect that improves the outcome to 65%.

ART adherence	Panel A: Pre-intervention CBI assessment (baseline)	Panel A: Post-intervention CBI assessment (follow-up)	Power
Improvement from baseline	55% of 1,987 VL detectable patients on ART report excellent ability to take all of their ART medications as prescribed in the past four weeks	65% of 1,987 VL detectable patients on ART are report excellent ability to take all of their ART medications as prescribed in the past four weeks	>99%

Self-report sexual transmission risk behavior: As with the ART adherence outcome, analysis of sexual transmission risk behavior must rely on self-reported data from the CBI. This outcome is examined as a pre-post change based on Panel A patients' baseline CBI assessment (obtained before exposure to the CBI intervention components) and a follow-up CBI assessment (obtained a few months later after exposure to the CBI intervention). The power analysis uses McNemara's test for dependent proportions. For the power analysis, we focus on VL detectable patients in Panel A during the first year; patients in panel B do not do the CBI in the first year.

Of the total number of 7,760 VL detectable patients, we anticipate that 80% will participate in the CBI (6,208). Approximately half of these will be in Panel A (3,104). Of these, we anticipate getting follow-up CBI assessment data on sexual behavior from 80% (2,483 VL detectable patients in Panel A). Our baseline (pre-intervention) value is informed by the findings of a published study of HIV patients assessed at seven HIV clinics.[9] We use a baseline value of 20% of VL detectable patients engaging in

unprotected vaginal or anal intercourse (UVA) with a partner who is HIV-negative or of unknown serostatus (at-risk partner) in a 2-month period. We have >99% power to detect an intervention effect that lowers the percentage to 15%.

Sexual transmission risk behavior	Panel A: Pre-intervention CBI assessment (baseline)	Panel A: Post-intervention CBI assessment (follow-up)	Power
Improvement from baseline	20% of 2,483 VL detectable patients engage in UVA with an at-risk partner in the past 2 months	15% of 2,483 VL detectable patients engage in UVA with an at-risk partner in the past 2 months	>99%

B. 3. <u>Methods to Maximize Response Rates and Deal with Nonresponse</u>

CBI: To maximize participation rate for the CBI, patients will be given an opportunity to do the CBI at the clinic or accessing the tool from their home computer. The CBI items will be computer administered and will maximize response to the items. First, the respondent will hear each question being asked through headphones and will also see the printed question and response categories on the computer screen. Second, each respondent will receive a brief tutorial on using the CBI and how to make a response. Third, the CBI includes programmed skip patterns to smoothly transition the respondent to applicable questions. Fourth, the program includes validity checks to assure the logical consistency of responses, thus maximizing the number of items on which valid data will be collected. Fifth, questions do not include a "don't know" response category unless a "don't know" response is a meaningful answer. We will maximize follow-up administrations of the CBI by using telephone reminders of clinic appointments and scheduling special appointments to come to the clinic to complete the CBI if needed.

Patient and provider surveys: These self-administered surveys will be completed using an electronic tablet (for the patient surveys) or a laptop/desktop computer (for the providers). Both surveys are very brief which should prevent tedium and reduce the likelihood of non-response due to burden. Both surveys will have programmed skip patterns and validity checks.

Patient behavioral screener: Patients will be asked to complete this brief screener while waiting to see their provider. The clinic receptionist will give the form to the patient when the patient checks in. A nurse will collect the form, check for completeness, and deliver the completed form to the primary care provider as part of the paperwork for that patient.

Transmittal of clinical variables routinely collected and archived by the clinics: This transmittal of information does not involve participant response to any surveys. A data manager at each clinic will electronically transmit clinical variables to CDC. The clinic data manager will work with the data manager at CDC to ensure that all variables requested are transmitted to CDC, that the data are formatted correctly, that there are no out of range values, and no cases of missing data (e.g. a VL value is present but not a date).

B. 4. Tests of Procedures or Methods to be Undertaken

The data collection forms have already been reviewed by the investigators and staff participating in the project. All of the forms and procedures will be pilot tested with six HIV patients and three primary care providers at the participating clinics. The data collection forms for the patients will undergo a translation/back translation process to ensure consistency between English, Spanish, and Creole versions.

B. 5. Individuals Consulted on Statistical Aspects and Individuals Collecting and/or Analyzing Data

Individuals consulted on statistical aspects of the study design
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REFERENCES

1. Chesney MA, et al. Effects of a behavioral intervention to reduce risk of transmission among people living with HIV. JAIDS 2007;44:213-221.

2. Kalichman SC, et al. Integrated behavioral intervention to improve HIV/AIDS treatment adherence and reduce HIV transmission. American Journal of Public Health 2011;101:531-538.

3. Lightfoot M, et al. Efficacy of brief interventions in clinical care settings for persons living with HIV. JAIDS 2010;53:348-356.

4. McKirnan DJ, et al. The treatment advocacy program: a randomized controlled trial of a peer-led safer sex intervention for HIV-infected men who have sex with men. Journal of Consulting and Clinical Psychology 2010;78:952-963.

5. Althoff KN, Buchacz K, Hall I, et al., U.S. trends in antiretroviral therapy use, HIV RNA plasma viral loads, and CD4 T-lymphocyte cell counts among HIV-infected persons, 2000-2008. *Annuals of Internal Medicine*, 2012;157:325-335.

6. Gardner LI, Marks G. Preliminary findings from the CDC/HRSA retention in care project. P resented at the 7th International Conference on HIV Treatment and Prevention Adherence, Miami, Florida, June 3-5, 2012.

7. Feldman BJ, Fredericksen RJ, Crane PK, et al. Evaluation of the single-item self-rating adherence scale for use in routine clinical care of people living with HIV. AIDS and Behavior 2012, e-published ahead of print.

8. Simoni JM, Huh D, Frick PA, Pearson CR, Andrasik MP, Dunbar PJ, Hooton TM. Peer support and pager messaging to promote antiretroviral modifying therapy modifying therapy in Seattle: a randomized controlled trial. *JAIDS*, 2009;52:465-473.

9. Gardner LI, Marks G, O'Daniels CM, Wilson TE, Golin C, Wright J, Quinlivan EB, Bradley-Springer L, Thompson M, Raffanti S, Thrun M. Implementation and evaluation of a clinic-based behavioral intervention: Positive STEPS for HIV patients. *AIDS Patient Care and STDs*, 2008;22:627-635.