CCTG 594

Engagement and Retention in Care for HIV+
(Main Study)

A Multicenter Trial of the California Collaborative Treatment Group (CCTG)

Sponsored by:

The California HIV/AIDS Research Program (CHRP)

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LIST OF ABBREVIATIONS

AE	Adverse Event
ALERT	Active Linkage, Engagement, and Retention to Treatment
ART	Antiretroviral Therapy
ARV	Antiretroviral
CCTG	California Collaborative Treatment Group
CD4	CD4 Lymphocytes
CRF	Case Report Form
CT	Chlamydia
DSMB	Data Safety and Monitoring Board
GC	Gonorrhea
HIV-1	Human Immunodeficiency Virus – 1
ITT	Intention to Treat
LTFU	Lost to Follow Up
MSM	Men who have Sex with Men
NAAT	Nucleic Acid Amplification Test
PID	Patient Identification Number
PLWH	Persons Living With HIV/AIDS
RPR	Rapid Plasmin Reagin
SAE	Serious Adverse Event
SOC	Standard of Care
STI	Sexually Transmitted Infection
TPPA	Treponema Pallidum Particle Agglutination Assay
VDRL	Venereal Disease Research Laboratory

LIST OF TERMS

Lost to follow up: no visit with a prescribing HIV provider in the last 180 days

Out of care: no visit with a prescribing HIV provider in the last 180 days and not on a stable antiretroviral regimen

Retention in care: maintaining at least one visit with a prescribing HIV provider within 180 days

Newly diagnosed patient : someone who has never engaged in HIV care

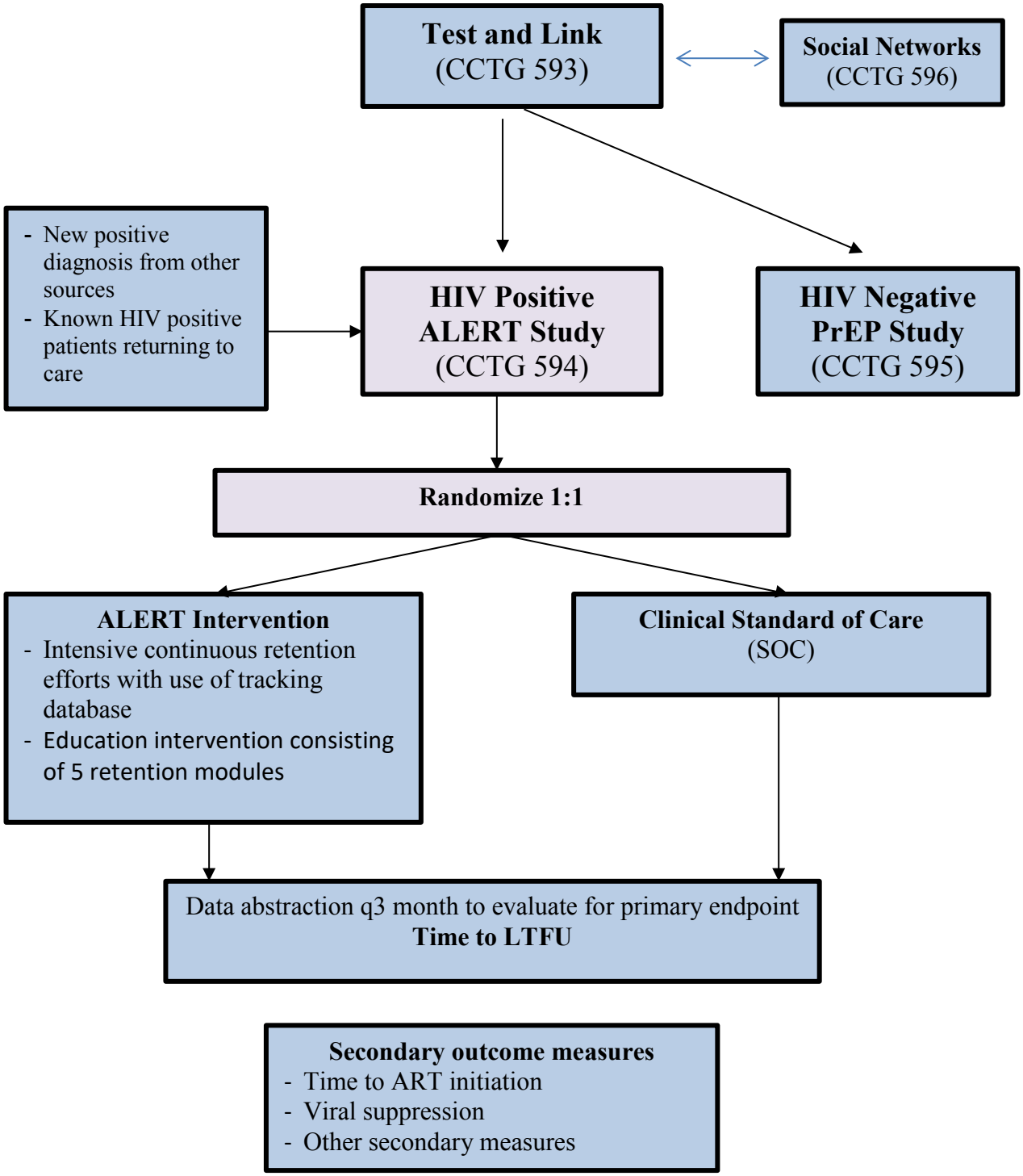
Patient returning to care: a patient previously seen at least once by a prescribing HIV provider who has not seen a prescribing HIV provider in the last 180 days and is not on a stable antiretroviral regimen

Prescribing HIV provider: a licensed HIV care provider who is able to prescribe HIV medications (e.g. an HIV specialty MD, Nurse practitioner, or Physician Assistant)

SCHEMA

Design:	CCTG 594 is a controlled, un-blinded, two-arm, randomized (1:1) clinical trial to evaluate the effectiveness of a clinic-based HIV Active Linkage, Engagement, and Retention to Treatment (ALERT) specialist on improving endpoints of retention in care and maintenance of antiretroviral therapy (ART) as compared to the current standard of care (SOC) in HIV primary care clinics.
Duration:	Each subject will receive follow-up of at least 48 weeks. Follow-up for enrolled patients will continue until the last enrolled patients has been on study for 48 weeks
Sample Size:	A total of 300 subjects will be randomized, 150 per arm.
Study Population:	Eligible subjects will include 1) newly diagnosed HIV-infected individuals entering primary HIV care at one of the CCTG clinics, or 2) previously diagnosed HIV-infected individuals who are "out of care" defined as having no visit with a prescribing HIV provider in the last 180 days and not on a stable ARV regimen.
Stratification:	Subjects will be stratified based on study site and if they are newly diagnosed or returning to care. (See Diagram 1)
Intervention:	Subjects will be randomized (1:1) to either the ALERT Enhanced Retention Intervention Arm or the SOC Arm. Subjects placed into the ALERT Intervention Arm will receive aggressive engagement efforts by the ALERT specialist to ensure visit continuity and retention into care. The ALERT specialist will also administer an education intervention consisting of 5 retention modules designed to improve HIV knowledge and self-efficacy, and will also monitor health care visits and intervene via methods to track, find, and re-engage patients during the study. Patients placed into the SOC arm will receive the HIV care clinic's current standard of care retention services.
Outcomes:	
Primary Outcome:	Time to "lost to follow up" (LTFU) defined as the time from study entry to no visit with a prescribing HIV provider in the last 180 days

DIAGRAM 1: CCTG 594 STUDY SCHEMA



1.0 HYPOTHESIS AND STUDY OBJECTIVES

1.1 Hypotheses

1.1.1 *Primary hypothesis*

Subjects randomized to the ALERT specialist arm will have higher levels of "retention in care," defined as maintaining at least one visit with a prescribing HIV provider within 180 days, compared to subjects in the SOC arm.

1.1.2 *Secondary hypotheses*

1.1.2.1 Subjects randomized to the ALERT specialist arm will have higher ART uptake compared to subjects in the SOC arm.

1.1.2.2 Use of detailed assessments at study entry will allow for the identification of covariates associated with poor retention and initiation of ART.

1.1.2.3 Use of an ALERT specialist and a structured retention module intervention will modify the impact of covariates on retention and initiation of ART.

1.2 Primary objective

1.2.1 To evaluate the effect of an ALERT specialist on retention in care, based on time to LTFU.

1.3 Secondary objectives

1.3.1 To evaluate the effect of an ALERT worker on the time to initiation of ART per DHHS guidelines.

1.3.2 To assess factors predictive of loss to care, such as demographic, socioeconomic, and psychosocial factors, risk behavior, substance use and psychiatric illness.

1.3.3 To assess if the ALERT intervention mitigates the impact of psychosocial barriers on retention in care and initiation of ART.

1.3.4 To compare in the intervention vs. SOC arm (assessed at 12 month intervals):

1.3.4.1 Baseline and annual scores on standardized assessments of HIV literacy, disclosure and social support, perception of stigma, barriers to care, ART adherence and Intention to Adhere, Beck Depression Index, substance use evaluations, HIV high-risk

transmission behaviors, and measures of self-efficacy

1.3.4.2 Number of visits per year with HIV prescribing provider per year

1.3.4.3 HIV RNA < 50 and 200 copies/mL at 12 months and every 12 months thereafter

1.3.4.4 CD4 cell counts and changes from baseline in CD4 at 12 months and every 12 months thereafter

1.3.4.5 Time to AIDS diagnosis or death

1.3.5 To describe the reasons identified in the refusal survey why patients who are eligible for the study decline study participation

2.0 INTRODUCTION

2.1 Background

Over the last 30 years, HIV infection has evolved from a progressive disease with high mortality to a manageable chronic infection in those patients who adhere to ART with regular appointments for care. Yet, as the Gardner cascade has revealed, progressive gaps in care delivery remain, from the identification of the HIV positive community to adherence to ART resulting in an undetectable viral load (1). Studies suggest that only two thirds of HIV- infected people aware of their serostatus receive HIV care (2), 56% of patients eligible for ART actually receive it (3), and an estimated 20% of HIV-infected persons in the US achieve an undetectable viral load (1).

At community, state, and national levels, a formalized focus on retention assures that HIV-infected populations have improved engagement in their care to assure virologic response to ART and improved health outcomes. Active participation in healthcare, assessed as routine attendance with medical provider visits, improves the likelihood that HIV- infected patients will initiate ART, have improved virologic response and lower mortality (4-8).

In order to improve the success of programs designed to identify HIV- infected individuals earlier in the course of disease, through “test, link to care, plus treat” (TLC+), the focus of research must shift to the primary care HIV clinic to promote interventions which identify barriers and improve retention (9, 10).

2.1.1 Theoretical Framework

Using the guiding framework of the modified ‘Behavioral Model for

Vulnerable Populations', we will construct a responsive behavioral model aimed to improve patient engagement in care (11). This model posits that both patient level [education (literacy), perception of HIV risk/diagnosis/stigma, social support] and clinic level [available services on site (e.g., psychiatric), reminder phone calls] factors are critical barriers to patient engagement with healthcare (6, 10). Addressing a single level or factor of this model is inadequate to sustain meaningful improvement in patient care. Thus, by addressing multiple factors and the complex interplay between them through a structured behavioral intervention, we aim to improve overall patient care linkage and retention.

2.1.2 Factors associated with retention in care

A complex interplay of patient, structural, and process factors result in synergistic barriers to engagement in care (6, 10, 11). For example, social marginalization, active substance use (6) (12) and racial disparities (8) have been identified as predictors of retention in care. HIV related stigma and difficultly navigating the health system can also contribute to poor retention (13), and patients have reported the importance of clinic outreach as a vehicle to improve their HIV knowledge and provide a supportive network (14).

For people with HIV, low health literacy has been associated with lower CD4 counts, higher HIV viral loads, increased hospitalizations, and poorer self-reported health (15), yet rates of health literacy among HIV-infected patients are low, ranging from 15- 49% (16-23). Remarkably, in one study, two thirds of HIV-infected patients with a low health literacy level did not know how to take their medications correctly and 75% did not understand the meaning of CD4 cell count and HIV viral load levels (21). In several studies African American and Hispanic patients had significantly lower health literacy rates compared with other groups (OR of 2.78 and 4, respectively) (22). In another study, African American HIV infected patients were found to be statistically more likely to be non-adherent to ART, yet this difference became non-significant when health literacy levels were included in the model (20). These populations represent a growing proportion of patients with HIV in the US and are highly represented in the CCTG sites proposed in this application (24).

Interventions targeting health literacy have been shown to improve clinical outcomes by our group (25, 26), resulting in a significant sustained increase in knowledge of ART and gain in CD4 cell counts.

Thus, improving health and HIV literacy are potential pathways to successful engagement in, and optimization of HIV care.

Facilitating patient navigation of the complex health system (System Literacy) (27) allows better use of available resources, improves communication and can sustain HIV care over time (engagement). One study in 333 HIV-infected found that 71% of the patients needed at least one support service that was ostensibly available to them through their clinic. Services were not accessed due to lack of information (47%) or other logistical barriers (33%; such as confusing instructions or long waiting lists for services) (28). Similarly, in the UC San Diego Health Systems HIV retention project (29), system navigation was frequently cited as the reason for lack of retention.

Finally, people with HIV report fear of disclosure of their diagnosis and potential stigma as significant barriers to care (13, 30), and to accessing social support networks (31). Behavioral models identify stigma and lack of social support as important factors in an individual's risk for poor engagement, particularly within vulnerable populations (11, 32). Qualitative studies also identify stigma and family support as key factors in patients' ability to engage in HIV care (33), and studies have demonstrated associations between lack of HIV disclosure to support networks and poorer psychosocial, adherence, immunologic, and virologic outcomes (31, 32, 34) (34-38). Furthermore, minority patients are more likely to have concerns about stigma and are more likely to change clinics (30, 39) which may contribute to disparities seen in HIV outcomes in minority patients (40, 41).

We hypothesize that an ALERT specialist, who has access to a tracking database, outreach activity, and a structured behavioral intervention to address the above retention barriers, will improve successful continuity of care and ART initiation.

2.2 Rationale

2.2.1 Study population

The goal of this study is to enhance retention in care amongst those diagnosed with HIV who are at high risk of being LTFU. Based upon the Gardner cascade there is a major drop off from those diagnosed who encounter care and are retained in care over time (1). Thus, we will target those that are encountering care for the first time since HIV diagnosis or who have already met the criteria of having been LTFU, having not been

seen for at least 180 days since first entering care.

2.2.2 Rationale for the use of an ALERT specialist

Retention in care should be defined by both measures of adherence to medical appointments and maintaining visits at regular defined intervals (42, 43). A demonstration project to promote retention in HIV primary care used outreach, advocacy, and support services in a sample of 773 HIV-infected subjects. Participants with nine or more contacts during the first 3 months of their program were half as likely to have gaps in care (defined as 4 months or more) during their first 12 months of follow up (44). In another large non-randomized engagement program including the use of mobile technologies, health educators to facilitate navigation of the health care system, case management to coordinate services, support groups, and peer support, 83% of subjects were still engaged at 12 months. Findings also included improvement of health outcomes as measured by decrease in hospital and ER use ($p<0.0001$) and increases in ART use ($p<0.001$) (45).

In summary, current literature highlights potential improvements in retention in care, ART use and clinical outcomes in response to various patient engagement interventions. The efficacy of these approaches needs to be determined with randomized clinical trials to evaluate their sustained impact.

3.0 STUDY DESIGN

The CCTG 594 Study is a randomized, two-arm, unblinded, controlled clinical trial to evaluate the effect of an enhanced engagement strategy using an ALERT specialist, as compared to local clinics' SOC, on sustainable engagement in care and uptake of ARVs in a variety of southern California clinical settings. Eligible patients will include those with a new HIV diagnosis and those with prior diagnoses who are out of care. Patients randomized to the intervention arm will have multiple contacts with the ALERT specialist in the form of 5 standardized educational sessions as well as continuous aggressive retention efforts. Engagement and retention efforts in the ALERT arm will follow the algorithm we developed in the pilot project (29). Once a patient has a scheduled appointment, attendance will be tracked. Failed appointments will trigger follow up by an ALERT specialist. Standardized assessments at study initiation and annually will be used to evaluate the psychosocial factors associated with successful retention in care and evaluate the effect of an ALERT specialist on those factors. The primary endpoint will be time to LTFU. The secondary endpoint will include other relevant markers of success in care, including time to initiation of ART.

4.0 SELECTION AND ENROLLMENT OF SUBJECTS

4.1 Inclusion Criteria

4.1.1 HIV-1 infection, as documented by any licensed screening antibody test, such as ELISA, and confirmed by a second antibody test, such as Western blot, or detectable plasma HIV-1 RNA at any time prior to study entry. If an ELISA or Western blot is not available, HIV infection may be documented by two HIV RNA values ≥2000 copies/mL, drawn at least 24 hours apart. The RNA assays must have been run at a CLIA-approved laboratory or equivalent.

4.1.2 18 years of age or older.

4.1.3 Able to give written informed consent.

4.1.4 New patient to the clinic (defined as someone who has never engaged in HIV care) or a patient returning to care (defined as a patient previously seen at least once by a prescribing HIV provider who has not seen a prescribing HIV provider in the last 180 days and is not on a stable ARV regimen).

4.1.5 English or Spanish Speaking.

4.1.6 Registered to receive HIV primary care services at one of the identified CCTG-affiliated clinic, i.e. the Owen Clinic at UC San Diego Health System, Harbor-UCLA Medical Center clinic or Rand Schrader clinic at USC.

4.2 Exclusion Criteria

4.2.1 Unstable neurologic, psychiatric, or physical condition which, in the opinion of the investigator, would limit participation with study procedures for the duration of the study.

4.2.2 A level of drug or alcohol use that, in the opinion of the investigator, would preclude safe participation in the study.

4.2.3 Resident of nursing home or skilled facility.

4.2.4 Pregnant or breastfeeding

4.2.5 Patient's first primary care visit (for new patients) or return to care visit

(for patients returning to care) occurred >60 days ago

4.3 Enrollment Procedures

4.3.1 Prior to implementation of this protocol, sites must have the protocol and consent form approved by their local Institution Review Board (IRB). Sites must be registered with and approved by the CCTG Data Center. Site registration must occur before any subjects can be enrolled in this study.

4.3.2 Once a candidate for study entry has been identified, details of the study will be discussed with the subject. The subject will be asked to read and sign the consent form that was approved by both the local IRB and the CCTG Data Center.

4.3.3 A patient identification number (PID) will be assigned to each patient screened for the study. PIDs should not be reassigned even if the patient fails to enter the study. The PID must be included on every CRF and patient blood sample. Each site must maintain a master list of PID's in a central location. The patient registration and inclusion/exclusion CRF must be completed on the online system.

4.3.4 Once enrolled, participants will respond to the baseline assessment survey, administered with assistance of the study coordinator or ALERT specialist.

4.3.5 Once the survey is completed, participants will be randomized (1:1) to either the ALERT Intervention Arm or the SOC Arm. Subjects randomized to the ALERT Intervention Arm will receive the contact information for the ALERT specialist and will be notified that the ALERT specialist will be contacting them to ensure visit continuity and retention into care. Participants placed into the SOC arm will be notified that they will receive the clinic's current SOC services.

4.3.6 **Refusal Survey Administration**
Patients who meet the inclusion and exclusion criteria of the Engagement and Retention in Care for HIV+ study who decline to participate in the study will be offered a refusal survey. The refusal survey will be administered to patients who verbally consent to participate in the refusal survey administration. The survey will be administered either in written or verbally. No personal health identifying information will be collected as part of this survey. The refusal survey includes questions about age and categorical questions about gender, new to HIV care or

out of care for more than 6 months, race, ethnicity, and the reasons for not participating.

4.37 End of Study Assessment
Study participants in the standard of care and ALERT arms will be contacted at end of study and asked to complete either in person or over the phone a questionnaire about their experiences in the study.

4.4 Co-enrollment

Co-enrollment will be allowed in CCTG 593 and CCTG 596 (Networks Sampling study). For all other studies, co-enrollment will require permission from the CCTG 594 study team.

5.0 INTERVENTION

5.1 ALERT Intervention

5.1.1 Overview

Building from methods previously developed in our pilot retention project (29) we will expand the role of our ALERT specialist to provide on-going engagement in care monitoring and outreach as well as a structured behavioral intervention.

Core training for ALERT specialists will be provided at all consortium care sites. The ALERT specialist should have experience with phone solicitation, customer service, database management and language and cultural competence. During the initial training, skills for navigation of the health systems at each of the three sites will be emphasized. The ALERT specialist will cross train with many clinic personnel to better understand barriers to care; training will include work with the front desk, medical assistants, phone operators, triage nurses and administrative support. The ALERT specialist will also be trained to inform patients about aspects of care including: appropriate estimated visit duration, optimal methods to initiate contact with their provider and education about symptoms which should necessitate immediate health evaluation. A site-appropriate toolbox will be developed (from our pilot retention experience) that includes an algorithmic approach to locate lost patients, a standardized telephone script, creation of a secure visit tracking database, establishment of a secure line for messages from patients to the ALERT specialist and brochures that emphasize engagement awareness.

A summary of the roles, responsibilities, procedures, algorithms, and protocols for the ALERT worker can be found in the *Manual of Operating Procedures* [MOP CCTG 594].

5.1.2 Initial visit

The study coordinator or ALERT specialist will interview patients following their completion of consent and baseline assessment. The ALERT specialist will collect additional pertinent information relative to outreach [MOP CCTG 594: 3.0 Baseline ALERT Specialist Patient Contact Information]. This patient survey will be completed on all patients regardless of randomization to the intervention or the SOC arm. Following survey completion, patients who receive the SOC will receive on-going clinic standards regarding outreach and retention activity. For patients who are randomized to the intervention arm, they will be given a brief overview of the intervention: including anticipated reminder calls about upcoming or needed appointments, follow up outreach for missed visits, and delivery 5 monthly one hour modules related to our HIV coaching intervention.

Patients will also select their preference for communication and outreach activities including: text, voice message, phone call, email, other. Patients will provide optimal secondary recommended approaches for outreach including the ability of the ALERT specialist to contact friends, family, partners, or other persons, and location. Patients will be pro-actively requested to identify and share perceived barriers to engagement in care.

5.1.3 Retention Modules related to our HIV coaching intervention (intervention arm subjects only)

Each patient will receive a one hour coaching intervention starting between 2 weeks and four weeks following enrollment in the study. The coaching intervention will occur in person at the clinic at the time of a routine clinic visit when available and by phone when more convenient to the patient. Each module will provide information and skills that are highly pertinent to HIV care delivery. As part of the 5 retention modules which deliver the HIV coaching intervention, key attention will be to build patient self-efficacy through the use of open ended questions and confidence building. The 5 retention modules include HIV literacy, HIV health systems, Disclosure, Medication adherence and Continuation with

Care, and Self-Efficacy [MOP CCTG 594: 5.0 The 5 Retention Modules for the ALERT specialist]. Consented participants receiving one of the five retention modules may be audio recorded as part of the quality improvement process.

5.1.4 Tracking and outreach

The ALERT specialist will be responsible for tracking the on-going engagement of patients who are randomized into the intervention arm. Patients will be expected to complete visits at a minimum of every 6 months. However, the ALERT specialist will also review chart notes to review the interval that the provider recommended a medical visit. The ALERT specialist will track that the patient makes and keeps an appointment with their primary provider at the suggested interval. If the patient misses a visit at the recommended interval, the ALERT specialist will perform outreach to schedule a return visit, and again track to see that the visit is kept. The ALERT specialist will use a tracking database in order to track patient engagement, their outreach efforts and delivery of the retention modules. The ALERT specialist will record contacts (categorically) both successful and unsuccessful. They will also utilize the baseline patient contact information as well as other key notes in this tracking database. Patients who meet the LTFU primary end point, regardless of study arm will have outreach activity initiated by the ALERT specialist. This will include following the retention tracking algorithm including evaluating whether the patient is incarcerated, providing outreach calls to the patient, and reviewing the medical record. Patients who meet the primary endpoint and are found to be incarcerated will be removed from the study and censored effective at the time of their incarceration. Those who are incarcerated but then return to care upon release, prior to reaching a primary endpoint will be allowed to remain in study. Patients who are confirmed to have changed care provider to an external health facility (such as a different clinic system or a nursing facility) will be assessed for their current engagement in care; those who have completed a clinic visit with a HIV prescribing clinician within the 180 days will be considered engaged in care, and will not be considered LTFU. The ALERT specialist will request access to the patient's new HIV prescribing provider in order to assess continued follow-up care during the course of the study. In addition, if possible, these patients will continue to come to study site for the annual study visit.

6.0 CLINICAL AND LABORATORY EVALUATION

6.1 Table 1: CCTG 594 Schedule of Events

Schedule of Evaluations	Screen	On Study Evaluations											
		Wk 0[1]	Mo 1[2]	Mo 2[2]	Mo 3[2]	Every 3 months	Mo 4[2]	Mo 5[2]	Mo 6[2]	Mo 12	Every 12 Months[5]	Primary Endpoint	EOS Assessment
Informed Consent	X												
Medical History	X												
Examination (targeted)										X	X	X	
Randomization		X											
HIV RNA		X[4]				X[4]				X[4]	X[4]	X[4]	
CD4 cell counts		X[4]				X[4]				X[4]	X[4]	X[4]	
ALERT Specialist retention modules[3]			X	X	X		X	X					
Plasma Storage		X								X	X	X	
Subject self-reported Assessments		X								X	X	X	
Data abstraction (via chart review, no visits)		X				X			X	X	X	X	
In person or phone call													X

[1] Entry must be within 30 days of screening
[2] Planned for monthly intervals but can be done at patient's convenience during course of first year
[3] Interventions only for those in ALERT specialist arm
[4] Abstracted from chart review
[5] annual visits and annual labs should occur within a window of +/- 60 days from the due date. Labs and study visit do not need to occur on the same day.
EOS – End of Study

Figure 2: Detailed flow diagram of CCTG 594 with scheduled events

6.2 Definitions for Schedule of Events – Timing of Evaluations

6.2.1 *Screening Assessment*

Screening visit must occur within 60 days, the patient's first primary care visit (for patients new to care) or their first primary care re-entry visit (for patients returning to care).

A PID will be assigned to each patient screened for the study. PID's should not be reassigned even if the patient fails to enter the study. The PID must be included on every CRF and patient blood sample. Each site must maintain a master list of PID's in a central location. The patient registration and inclusion/exclusion CRF must be completed on the online system.

Screening will be conducted by the study coordinator, Alert specialist or a trained member of the study team and will include medical history, confirmation of HIV test results, evaluation of Inclusion/Exclusion criteria, and signing of study consent form.

Patients who meet the study eligibility but decline to participate will be offered participation in a brief refusal survey. Patients who verbally consent to participate in the refusal survey will be administered the questionnaire in written or verbal format. Patients who were not previously offered will be re-approached while attending their Primary Care clinic visit and will be offered participation in the brief refusal survey.

6.2.2 *Entry Evaluations and Randomization*

Entry must occur within 60 days of the patient's first primary care visit (for patients new to care) or their first primary care re-entry visit (for patients returning to care). At study entry, baseline surveys will be collected utilizing the web-based, computer-assisted system on the study specific portal (to view baseline survey, see Attachment 5, *iPad Assessments for CCTG 594*). The portal will allow private completion of questionnaires without concern that clinic or study personnel can view the subject's responses in order to encourage candor.

Subjects will be randomized (1:1) to SOC or ALERT Intervention study arm. Randomization will be stratified by clinic site and whether the subject is newly diagnosed or returning to care. A total of 300 subjects

(150 per arm) will be randomized and followed for a minimum of 48 weeks. SOC will be the clinic standard.

Samples of plasma will be stored for future assays.

6.2.3 *On-Study Evaluations*

Study specific follow-up visits for each subject will be kept to a minimum in order not to bias the outcome of lost to follow up. Our experience suggests that involvement in a research protocol, with the extra effort the coordinators exert to ensure study follow-up, could easily impact on attendance to clinical care. Thus, for SOC patients, study specific visits will occur yearly preferably in conjunction with a regularly scheduled clinic visits (see below, *yearly study visits*).

In the ALERT intervention arm, the ALERT specialist will conduct 5 monthly educational retention modules (in person or by phone). The ALERT specialist will also continuously monitor and track all health care visits to ensure healthcare continuity, and will intervene using described tools/methods when the subject does not have a visit within a pre-determined interval (see Attachment 4, *Manual of Operating Procedures*, for ALERT Specialist job description, methods, and Retention Modules).

6.2.4 *Data Abstraction*

It is expected that subjects new or returning to care will have regular primary care visits at least 3-4 times in the first year. The ALERT specialist will use the clinic medical record system to abstract data on clinic visits, ART medications, serial HIV RNA and CD4 values, routine CBC and chemistry values, HIV-related and AIDS diagnoses and other medical diagnoses. Data will be entered into the study electronic database. Abstraction will be done at least quarterly for each subject. The ALERT specialist will track the status of each subject and record retention and outreach in the study database. Using data abstracted from the primary care clinic medical records system, the ALERT specialist will record all visits with a prescribing HIV provider, which will document retention as related to the primary study endpoint. For patients in the SOC arm, contact information will be collected for use in the event that the person meets the primary endpoint. Subjects in either arm who reach criteria for the LTFU primary endpoint will be identified by the ALERT specialist. The ALERT specialist will then contact the subject to assure that the patient is not incarcerated or receiving care from an HIV provider at

another facility. Once LTFU is confirmed, the ALERT worker will try to bring the patient in for a primary endpoint visit. All patients will continue to be followed after the primary endpoint (ITT) for assessment of secondary endpoints.

Education Contacts (weeks 1-24). The ALERT specialist will complete a 5 session educational curriculum called a retention module either in person or by phone to the subjects randomized to the ALERT Intervention arm. The 5 retention modules include instruction about the navigation of HIV health systems, HIV literacy, Disclosure, Medication adherence and Continuation with Care, and Self-Efficacy [MOP CCTG 594: 5.0 The 5 Retention Modules for the ALERT specialist]. The goal will be to present the majority of the material within the first 6 months, however scheduling flexibility will be allowed up to the 12 month time-point in order to maximize opportunities for patients to receive the intervention. Subjects that complete all 5 modules will be asked about their reasons motivating them to 1) participate in the study and 2) completing the 5 modules.

Ongoing Retention Efforts. The ALERT specialist will continuously monitor visit records on all patients in the ALERT specialist Intervention arm and will utilize all tools developed for clinic specific re-engagement to aggressively track, find, and re-engage patients during the study. Monitoring will include missed visits and intervals between scheduled visits. In addition to continuous monitoring for missed appointments, the ALERT specialist will screen the charts of all enrolled subjects every 3 months to evaluate the number of clinic contacts, missed visits, missed attendance of the retention modules, and any other risks for falling out of care.

Yearly Study Visits. For both arms, a study-specific visit will be conducted at yearly intervals from the enrollment date. The annual visits must occur within a 60 day window before or after the due-date. At the annual study visits the baseline study assessments will be repeated along the collection of plasma which will be stored for future assays. Efforts will be made to have these study visits occur around a regularly scheduled clinic visit.

Though every effort will be made to bring all patients in for annual visits within the 60 day window, subjects may remain in the study if the annual visit is missed (i.e., not completed within the 60 day window).

Compensation. Study participants will be compensated for their time at intake, annual, and endpoint visits which are anticipated to require 1-2 hours for questionnaires and collection of lab specimens.

6.2.5 *Primary endpoint visit*

When a participant reaches the primary endpoint of LTFU, every effort will be made to return the participant for an endpoint study visit. If the patient is willing, this visit will include the same assessments and procedures as the annual study visits.

6.3 Special Instructions and Definitions of Evaluations

6.3.1 *Documentation of HIV*

Documentation of HIV-1 infection will be confirmed by reviewing a positive test from any licensed screening antibody test, such as ELISA, and confirmed by a second antibody test, such as Western blot, or detectable plasma HIV-1 RNA at any time prior to study entry. If an ELISA or Western Blot is not available, HIV infection may be documented by two HIV RNA values $\geq$ 2000 copies/mL, drawn at least 24 hours apart. The RNA assays should have been run at CLIA approved laboratory or equivalent.

6.3.2 *Medical and Laboratory History*

At screening, a medical history will be obtained and must be recorded in the source documents. The medical history should include any previous HIV-related diagnoses, malignancies, and AIDS-defining events which will be recorded on the electronic CRF. History will include date of HIV diagnosis, date of last HIV clinic visit (for those returning to care), antiretroviral (ARV) history (if any), concomitant medical conditions, substance use history.

6.3.3 *Medication History*

At screening, a medication history (only of those taken within the last 30 days prior to entry) with actual or estimated start and stop dates should be obtained and recorded in the source documents and the concomitant medication CRF, including:

- All prescription medications, including medications taken for the

treatment or prophylaxis of opportunistic infections.
- Non-prescription medications.
- Alternative therapies and/or dietary supplements.
- Allergies to any medications and their formulations must be documented.

6.3.4 *Concomitant Medications*

At annual study visits concomitant medications of interest taken since the last visit will be recorded in the source documentation and entered into the concomitant medication log CRF.

6.3.5 *ARV Modifications*

All modifications of ART, including initiation of ART, will be recorded on the CRF's at the 3 month data extractions: including initial doses, patient-initiated interruptions, modifications, and permanent discontinuations. ART will also be reviewed and confirmed at the annual study visits.

6.3.6 *Clinical Assessments*

Height and Weight

Height and weight should be documented at study entry and weight documented at annual visits.

Treatment-Limiting Toxicity and Diagnoses

The following should be recorded on the CRFs at the annual study visits, and upon reaching the primary endpoint of LTFU (if possible): AIDS-defining events, ART-limiting toxicity, CV events or non-AIDS-related malignancies, STI diagnoses, new medical conditions and death. The source document must include date of diagnosis and date of resolution.

6.3.7 *Immunologic and Virologic Studies*

Nadir CD4+ T-Cell Count

The subject's prior nadir CD4+ cell count (absolute value and date) should be documented during screening and, when possible, a copy of nadir CD4+ cell count report should be included in the source document. If this documentation is not available, then subject recollection will suffice. For

Subjects who do not know the exact nadir value and for whom there is no source documentation, then recall of the categorical nadir (e.g., < 50, < 100, < 200 cells/mm^3) will suffice.

CD4/CD8 and HIV-1 RNA

At baseline, at all annual study visits, and upon reaching the primary study endpoint (if possible), a CD4/CD8 count and percentage and HIV-1 RNA will be recorded. The results may be obtained via chart extraction, if available from a CLIA-certified laboratory within 60 days of the study visit. If a result is not available within a 60 day window, it will be drawn at the study visit.
To avoid the need for extra blood draws, efforts will be made, via communication with the Primary Care Provider, to have the patient's routine primary care blood draws occur within the 60 day window of the annual study visits.

6.3.8 *Antiretroviral resistance testing*

If patients have had an antiretroviral resistance test during routine care, that data will be collected via chart abstraction.

6.3.9 *Stored Samples*

Stored plasma will be collected at study entry, the annual study visits, and upon reaching the primary study endpoint (if possible). Specimen collection will be encouraged but not mandated. Specimens will be stored at the site's local laboratory and batched shipped to the central laboratory (UCSD) after completion of the study.

Blood volume for stored plasma: 15mL

6.4 End of Study Assessment

6.41 At end of study subjects will be asked (in person or by phone) to complete a short questionnaire assessing the subjects' experiences over the course of the study. Subjects in the intervention will be asked specifically about the different components of the intervention and about other aspects of care that may impact their retention in care. Subjects in the standard of care arm will be asked about aspects of care that may impact retention in care. The survey will be administered to patients who verbally consent to participate. No personal health identifying

information will be collected as part of this survey.

7.0 CLINICAL MANAGEMENT ISSUES

7.1 Toxicity

No toxicities are anticipated as no treatment or invasive procedures are being performed as part of this study.

8.0 CRITERIA FOR EARLY TERMINATION

8.1 Criteria for Study Subject Discontinuation

8.1.1 Pregnancy or initiation of breastfeeding during the study.

8.1.2 Subject request to withdraw participation.

8.1.3 Primary care provider request for subject withdrawal based on the provider's belief that study participation is no longer in subject's best interest.

8.1.4 Medical provider belief that the patient has life threatening clinical condition.

8.1.5 By the discretion of the site IRB, CCTG, or investigator.

8.1.6 The patient is found to be incarcerated at the time of reaching the primary endpoint.

9.0 STATISTICAL CONSIDERATIONS

This section briefly describes the planned statistical analysis. The *Statistical Analysis Plan* (SAP) provides details. If the language in this section differs from the language in the SAP, the SAP takes precedence.

9.1 General Design Issues

This is a 48-week, un-blinded, 2-arm, randomized (1:1) controlled clinical trial.

9.2 Endpoints

Primary Outcome: The CCTG 594 primary outcome is "time to LTFU" defined as the time from baseline visit to meeting the primary endpoint (LTFU defined as: no visit with a prescribing provider for more than 180 days).

9.3 Randomization and Stratification

Once eligibility and consent are confirmed and the baseline survey is completed, randomization will occur using the web-based CFAR BIT data management system. Participants will be randomized (1:1) to either the ALERT Enhanced Retention Intervention Arm or the SOC Arm by the study coordinator or ALERT specialist.

We will stratify randomization by whether the patient is a new HIV diagnosis or a prior diagnosis returning to care and by HIV primary care clinic site.

9.4 Sample Size and Accrual

9.4.1 *Power and Sample Size Justification*

The primary outcome for this study is to compare the time to LTFU. A secondary outcome is time to initiation of ART. Sample size calculations were based on a two-sided, two-sample log-rank test to compare the differences in time to the primary endpoint proportions between the intervention arm and the standard of care arm.

Since attrition is a component of the composite endpoint, attrition rates are not used as an adjustment in the power calculations. Assuming 150 subjects per group in each of the two groups (for a total of 300 subjects), we have 87% power to detect a difference of 15%, assuming a time without a composite endpoint rate of 70% in SOC arm and that the intervention arm will increase the time without an endpoint (to a rate to 85%). This corresponds to a hazard ratio of 2:19. Table 5 shows other possible standard of care rates between arms (and hazard ratios), and corresponding statistical power. The calculations assume that the hazard rates are proportional.

Table 5: Power based on a two-sided, log-rank test with alpha=0.05 and N=150 per arm (total N = 300)

Composite rate without Endpoint in SOC (%)	Composite rate without Endpoint in Intervention (%)	Corresponding Hazard Ratio (HR)	Statistical Power (%)
65	80	1.93	82
65	85	2.65	97
70	85	2.19	87
75	87.5	2.15	78
75	90	2.73	92
80	92.5	2.86	87
80	95	4.35	97

9.5 Monitoring

Monitoring will be conducted monthly by the core protocol team to assess for accrual and data completeness.

9.6 Analyses

9.6.1 *Statistical Analysis Plan*

In general, analyses will incorporate the intent-to-treat principle, namely, all randomized participants will be included in the analysis. The primary analysis compares the ALERT Intervention to the SOC arm. For all secondary analyses of interest, no adjustments for multiple comparisons will be made, and a p-value of 0.05 will be considered statistically significant. Demographic and baseline measurement variables will be summarized via standard descriptive statistics.

9.6.2 Analysis of Primary Outcome

A survival analysis of "time to LTFU" will be conducted. LTFU is defined as no visit with a prescribing HIV provider in the last 180 days. Time-to-LTFU will be calculated as total days between the first visit and the date when the participant reaches the definition of LTFU.
For example, a subject has his first visit on Jan 1, 2013, and another visit on Mar 1, 2013. If the subject does not have any visits thereafter, or does not have any visits until >180 days later, the subject will be counted as reaching the primary endpoint of LTFU. In this case, the subject would be LTFU if no visit occurred before Aug 27, 2013, (which is 180 days past Mar 1st). The "time-to-LTFU" will be the time period between Jan 1, 2013 and Aug 27, 2013.

At the end of the study, patients who have not reached the primary endpoint will be censored at the time of their last quarterly data extraction.

Patients who meet the primary endpoint and are found to be incarcerated will be removed from the study and censored effective at the time of their incarceration. Those who are incarcerated but return to care upon release, prior to reaching a primary endpoint, will be allowed to remain in study. Patients who change care provider to an external health facility (such as a different clinic system or a nursing facility) will be assessed for their current engagement in care; those who have completed a clinic visit with a prescribing clinician within the 180 days will be considered engaged in

care, and will not be considered LTFU. If possible, these patients will continue to come in for annual study visits.

The null hypothesis is that the median time-to-LTFU estimated using the Kaplan-Meier method will be identical in both groups. The log-rank test will be used to test the null hypothesis against the alternate hypothesis that the median time-to-LTFU is not the same between the groups.

In addition, to assess the factors associated with time-to-LTFU, Cox regression models will be performed on two subgroups, looking at each arm separately. The model will have time to LTFU as the outcome, baseline variables such as demographic, socioeconomic, psychosocial factors, risk behavior, substance use and psychiatric illness as predictors.

Randomization will be stratified by clinic site and whether the subject is newly diagnosed or returning to care. A total of 300 subjects (150 per arm) will be randomized and followed for a minimum of 48 weeks. SOC will be the clinic standard.

9.6.3 Analysis of Secondary Outcomes

Main Secondary Outcome: The CCTG 594 secondary outcome is time to initiation of ART. A survival analysis of time to initiation of ART will be conducted. Time to initiation of ART will be calculated as total days between the first visit to the ART start date. For those participants who do not start ART, the time to initiation of ART will be censored to the participant's last visit date.

The NULL hypothesis is that the median time to initiation of ART estimated using the Kaplan-Meier method will be identical in both groups. The log-rank test will be used to test the null hypothesis against the alternate hypothesis that the median time to initiation of ART is not the same between the groups.

In addition, to assess the factors associated with time to initiation of ART, Cox regression models will be performed on two subgroups, looking at each arm separately. The model will have time to initiation of ART as the outcome, baseline variables such as demographic, socioeconomic, psychosocial factors, risk behavior, substance use and psychiatric illness as predictors.

9.6.4 Other Secondary Analyses

Descriptive analyses will be conducted for all the secondary analyses including comparisons between randomized groups on the following measures:

- Baseline and follow-up scores on HIV and health literacy assessments, disclosure rates, adherence, and measures of self-efficacy
- Number of primary care visits per year
- HIV RNA < 50 and <200 copies/mL at years 1 and 2
- CD4 cell counts and changes from baseline in CD4 at years 1 through 2
- Scores on Beck Depression Index
- Substance use
- HIV high-risk transmission behaviors
- Time to AIDS diagnosis or death
- Reasons eligible patients decline study participation

For patients who meet the primary endpoint (LTFU) but subsequently return to care, secondary analyses will measure the proportion returning in the intervention vs. SOC arm and the time between their last and return visit with a prescribing provider.

Fisher's exact test will be used for categorical variables; T-test (or Wilcoxon Rank Sum test, if parametric assumptions fail) will be used for continuous variables.

10.0 DATA COLLECTION AND MONITORING AND ADVERSE EVENT REPORTING

10.1 Records to be kept

Case report forms (CRF's) will be provided for each subject. Subjects must not be identified by name on any CRF's. Subjects will be identified by the PID provided by the CCTG Data Unit upon registration and the linkage to the PID will be kept in paper copy only in a locked cabinet in a secure office at the study sites available only to the site investigators. Surveys performed electronically will be automatically stored in the electronic database secured by the CFAR BIT group for the CCTG.

The contact information collected by the ALERT specialist will be collected on a paper form. This will be stored in a secured locked file cabinet within a locked office at the AVRC.

10.2 Role of Data Management

10.2.1 Instructions concerning the recording of study data on CRF's will be provided by the CCTG Data Unit.

10.2.2 It is the responsibility of the CCTG Data Unit to assure the quality of computerized data for this study.

10.3 Clinical Site Monitoring and Record Availability

10.3.1 Site monitors provided by the CCTG will visit participating clinical research sites to review the individual subject records, including consent forms, CRF's, supporting data, laboratory specimen records, and medical records (physicians' progress notes, nurses' notes, individuals' hospital charts), to ensure protection of study subjects, compliance with the protocol, and accuracy and completeness of records. The monitors also will inspect sites' regulatory files to ensure that regulatory requirements are being followed.

With their permission, consented participants receiving one of the five retention modules may be audio recorded as part of the quality improvement process related to the ALERT Specialist. The audio recording will not have any participant related identification. This recording will be securely disposed and not used directly for research purposes.

10.3.2 The investigator will make study documents (e.g., consent forms and CRF's) and pertinent hospital or clinic records readily available for inspection by the local IRB or the site monitors.

10.4 Serious Adverse Experience (SAE) Reporting

Serious adverse events are not expected in this study. All serious adverse experiences must be documented on the Serious Adverse Experience (SAE) Reporting Form within 5 working days of site awareness of the event and submitted to the CCTG Data Unit.

11.0 HUMAN SUBJECTS

11.1 IRB Review and Informed Consent

This protocol and the informed consent document and any subsequent modifications will be reviewed and approved by the IRB or ethics committee responsible for the oversight of the

study. A signed consent form will be obtained from the subject. The consent form will describe the purpose of the study, the procedures to be followed, and the risks and benefits of participation. A copy of the consent form will be given to the subject.

Patients who meet the inclusion and exclusion criteria who decline to participate in the Engagement and Retention in Care for HIV+ study will be offered a refusal survey. The refusal survey will be administered to patients who verbally consent to participate in the refusal survey.

11.2 Subject Confidentiality

All laboratory specimens, evaluation forms, reports, and other records that leave the site will be stripped of any patient identifiers (name, birthdate, medical record number) and identified by the coded PID only to maintain subject confidentiality. All records will be kept locked. All computer entry and networking programs will be done with coded numbers only and analyzed centrally without any possibility of linking subject identity with subject data. Clinical information will not be released without written permission of the subject, except as necessary for monitoring by IRB and governmental agencies.

11.3 Study Discontinuation

The study may be discontinued at any time by the IRB or other government agencies as part of their duties to ensure that research subjects are protected.

12.0 PUBLICATION OF RESEARCH FINDINGS

Publication of the results of this trial will be governed by CCTG policies.

13.0 BIOHAZARD CONTAINMENT

As the transmission of HIV and other blood-borne pathogens can occur through contact with contaminated needles, blood, and blood products, appropriate blood and secretion precautions will be employed by all personnel in the drawing of blood and shipping and handling of all specimens for this study, as currently recommended by the Centers for Disease Control and Prevention and the National Institutes of Health.

All infectious specimens will be transported using packaging mandated in the Federal Code of Regulations, CDC 42 CFR Part 72. Please also refer to individual carrier guidelines, e.g., FedEx, Airborne, for specific instructions.

14.0 REFERENCES

1. Gardner EM, McLees MP, Steiner JF, Del Rio C, Burman WJ. The spectrum of engagement in HIV care and its relevance to test-and-treat strategies for prevention of HIV infection. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. [Research Support, N.I.H., Extramural Review]. 2011 Mar 15;52(6):793-800.
2. Fleming PLB, R.H.; Sweeney P.A.; Daniels, D.; Karon, J.M.; Janssen R.S., editor. HIV Prevalence in the United States, 2000. 9th Conference on Retroviruses and Opportunistic Infections; 2002 February 24-28, 2002; Seattle, WA.
3. Teshale EK, L.; Harris, N.; et al., editor. Estimated number of HIV-infected persons eligible for and receiving HIV antiretroviral therapy, 2003 - United States [abstract 167]. 12th Conference on Retroviruses and Opportunisitic Infections; 2005 2005; Boston, Massachusetts; Alexandria, VA.
4. Giordano TP, Hartman C, Gifford AL, Backus LI, Morgan RO. Predictors of retention in HIV care among a national cohort of US veterans. HIV Clin Trials. [Research Support, N.I.H., Extramural Research Support, Non-U.S. Gov't]. 2009 Sep-Oct;10(5):299-305.
5. Mugavero MJ, Lin HY, Allison JJ, Giordano TP, Willig JH, Raper JL, et al. Racial disparities in HIV virologic failure: do missed visits matter? J Acquir Immune Defic Syndr. [Research Support, N.I.H., Extramural Research Support, Non-U.S. Gov't]. 2009 Jan 1;50(1):100-8.
6. Ulett KB, Willig JH, Lin HY, Routman JS, Abroms S, Allison J, et al. The therapeutic implications of timely linkage and early retention in HIV care. AIDS Patient Care STDS. [Research Support, N.I.H., Extramural]. 2009 Jan;23(1):41-9.
7. Giordano TP, Gifford AL, White AC, Jr., Suarez-Almazor ME, Rabeneck L, Hartman C, et al. Retention in care: a challenge to survival with HIV infection. Clin Infect Dis. [Research Support, N.I.H., Extramural Research Support, U.S. Gov't, Non-P.H.S.]. 2007 Jun 1;44(11):1493-9.
8. Mugavero MJ, Lin HY, Willig JH, Westfall AO, Ulett KB, Routman JS, et al. Missed visits and mortality among patients establishing initial outpatient HIV treatment. Clin Infect Dis. [Research Support, N.I.H., Extramural Research Support, Non-U.S. Gov't]. 2009 Jan 15;48(2):248-56.
9. Cheever LW. Engaging HIV-infected patients in care: their lives depend on it. Clin Infect Dis. [Comment Editorial]. 2007 Jun 1;44(11):1500-2.
10. Christopoulos KA, Das M, Colfax GN. Linkage and retention in HIV care among men who have sex with men in the United States. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. [Research Support, N.I.H., Extramural Research Support, Non-U.S. Gov't Review]. 2011 Jan 15;52 Suppl 2:S214-22.
11. Gelberg L, Andersen RM, Leake BD. The Behavioral Model for Vulnerable Populations: application to medical care use and outcomes for homeless people. Health Serv Res. [Research Support, U.S. Gov't, P.H.S.]. 2000 Feb;34(6):1273-302.
12. Tobias C, Cunningham WE, Cunningham CO, Pounds MB. Making the connection: the importance of engagement and retention in HIV medical care. AIDS Patient Care STDS. [Research Support, N.I.H., Extramural Research Support, Non-U.S. Gov't Research

Support, U.S. Gov't, P.H.S.]. 2007;21 Suppl 1:S3-8.
13. Seekins DS, A.; Juday, T.; Stryker, R.; Das, A.;, editor. Barriers to accessing HIV testing, care, and treatment in the United States. XVIII International AIDS Conference; 2010 July 18-23; Vienna, Austria.
14. Rajabiun S, Mallinson RK, McCoy K, Coleman S, Drainoni ML, Rebholz C, et al. "Getting me back on track": the role of outreach interventions in engaging and retaining people living with HIV/AIDS in medical care. AIDS Patient Care STDS. [Research Support, U.S. Gov't, P.H.S.]. 2007;21 Suppl 1:S20-9.
15. Kalichman SC, Rompa D. Functional health literacy is associated with health status and health-related knowledge in people living with HIV-AIDS. Journal of acquired immune deficiency syndromes. [Research Support, U.S. Gov't, P.H.S.]. 2000 Dec 1;25(4):337-44.
16. Kalichman SC, Ramachandran B, Catz S. Adherence to combination antiretroviral therapies in HIV patients of low health literacy. J Gen Intern Med. [Research Support, U.S. Gov't, P.H.S.]. 1999 May;14(5):267-73.
17. Kalichman SC, Benotsch E, Suarez T, Catz S, Miller J, Rompa D. Health literacy and health-related knowledge among persons living with HIV/AIDS. Am J Prev Med. [Comparative Study Research Support, U.S. Gov't, P.H.S.]. 2000 May;18(4):325-31.
18. Kalichman SC, Pope H, White D, Cherry C, Amaral CM, Swetzes C, et al. Association between health literacy and HIV treatment adherence: further evidence from objectively measured medication adherence. J Int Assoc Physicians AIDS Care (Chic). [Research Support, N.I.H., Extramural]. 2008 Nov-Dec;7(6):317-23.
19. Paasche-Orlow MK, Cheng DM, Palepu A, Meli S, Faber V, Samet JH. Health literacy, antiretroviral adherence, and HIV-RNA suppression: a longitudinal perspective. J Gen Intern Med. [Comparative Study Multicenter Study Randomized Controlled Trial Research Support, N.I.H., Extramural]. 2006 Aug;21(8):835-40.
20. Osborn CY, Paasche-Orlow MK, Davis TC, Wolf MS. Health literacy: an overlooked factor in understanding HIV health disparities. Am J Prev Med. [Research Support, U.S. Gov't, P.H.S.]. 2007 Nov;33(5):374-8.
21. Wolf MS, Davis TC, Cross JT, Marin E, Green K, Bennett CL. Health literacy and patient knowledge in a Southern US HIV clinic. Int J STD AIDS. [Research Support, Non-U.S. Gov't]. 2004 Nov;15(11):747-52.
22. Drainoni ML, Rajabiun S, Rumptz M, Welles SL, Relf M, Rebholz C, et al. Health literacy of HIV-positive individuals enrolled in an outreach intervention: results of a cross-site analysis. J Health Commun. [Research Support, U.S. Gov't, P.H.S.]. 2008 Apr-May;13(3):287-302.
23. Waite KR, Paasche-Orlow M, Rintamaki LS, Davis TC, Wolf MS. Literacy, social stigma, and HIV medication adherence. J Gen Intern Med. [Multicenter Study]. 2008 Sep;23(9):1367-72.
24. Hall HI, Song R, Rhodes P, Prejean J, An Q, Lee LM, et al. Estimation of HIV incidence in the United States. Jama. [Research Support, U.S. Gov't, P.H.S.]. 2008 Aug 6;300(5):520-9.
25. Dowse RB, K.; Browne, S.H., editor. Use of patient information leaflets on antiretroviral medication incorporating pictograms for low literate HIV patients significantly

increaseas drug knowledge, self-efficacy and improves CD4 count. International AIDS Society; 2011; Rome, Italy.
26. Dowse RR, T.; Browne, S.H. Developing visuals for communicating antiretroviral side effect information to a low-literate target population. African Journal of AIDS Research. 2010 December 2010;9(3).
27. Hede K. Agencies look to patient navigators to reduce cancer care disparities. J Natl Cancer Inst. [News]. 2006 Feb 1;98(3):157-9.
28. Wohl AR, Carlos JA, Tejero J, Dierst-Davies R, Daar ES, Khanlou H, et al. Barriers and unmet need for supportive services for HIV patients in care in Los Angeles County, California. AIDS patient care and STDs. [Research Support, Non-U.S. Gov't]. 2011 Sep;25(9):525-32.
29. Sitapati AM, Limneos J, Bonet-Vazquez M, Mar-Tang M, Qin H, Mathews WC. Retention: building a patient-centered medical home in HIV primary care through PUFF (Patients Unable to Follow-up Found). J Health Care Poor Underserved. [Research Support, Non-U.S. Gov't Research Support, U.S. Gov't, P.H.S.]. 2012 Aug;23(3 Suppl):81-95.
30. Johnson MO, Chesney MA, Neilands TB, Dilworth SE, Remien RH, Weinhardt LS, et al. Disparities in reported reasons for not initiating or stopping antiretroviral treatment among a diverse sample of persons living with HIV. Journal of general internal medicine. [Comparative Study Randomized Controlled Trial Research Support, N.I.H., Extramural]. 2009 Feb;24(2):247-51.
31. Wolitski RJ, Pals SL, Kidder DP, Courtenay-Quirk C, Holtgrave DR. The effects of HIV stigma on health, disclosure of HIV status, and risk behavior of homeless and unstably housed persons living with HIV. AIDS and behavior. [Randomized Controlled Trial Research Support, U.S. Gov't, P.H.S.]. 2009 Dec;13(6):1222-32.
32. Kalichman SC, Simbayi LC. HIV testing attitudes, AIDS stigma, and voluntary HIV counselling and testing in a black township in Cape Town, South Africa. Sex Transm Infect. [Research Support, U.S. Gov't, P.H.S.]. 2003 Dec;79(6):442-7.
33. Singh B, Sabin S, Rofim O, Shaha A, Har-El G, Lucente FE. Alterations in head and neck cancer occurring in HIV-infected patients--results of a pilot, longitudinal, prospective study. Acta Oncol. 1999;38(8):1047-50.
34. Vyavaharkar M, Moneyham L, Tavakoli A, Phillips KD, Murdaugh C, Jackson K, et al. Social support, coping, and medication adherence among HIV-positive women with depression living in rural areas of the southeastern United States. AIDS patient care and STDs. [Multicenter Study Research Support, N.I.H., Extramural]. 2007 Sep;21(9):667-80.
35. Stirratt MJ, Remien RH, Smith A, Copeland OQ, Dolezal C, Krieger D. The role of HIV serostatus disclosure in antiretroviral medication adherence. AIDS and behavior. [Research Support, N.I.H., Extramural]. 2006 Sep;10(5):483-93.
36. Ammassari A, Trotta MP, Murri R, Castelli F, Narciso P, Noto P, et al. Correlates and predictors of adherence to highly active antiretroviral therapy: overview of published literature. Journal of acquired immune deficiency syndromes. [Research Support, Non-U.S. Gov't Review]. 2002 Dec 15;31 Suppl 3:S123-7.
37. Voigt K. Incentives, health promotion and equality. Health Econ Policy Law. 2010 Sep

21:1-21.

38. Ramadhani HO, Thielman NM, Landman KZ, Ndosi EM, Gao F, Kirchherr JL, et al. Predictors of incomplete adherence, virologic failure, and antiviral drug resistance among HIV-infected adults receiving antiretroviral therapy in Tanzania. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. [Research Support, N.I.H., Extramural Research Support, Non-U.S. Gov't]. 2007 Dec 1;45(11):1492-8.
39. Bird JD, Fingerhut DD, McKirnan DJ. Ethnic differences in HIV-disclosure and sexual risk. AIDS Care. [Comparative Study Research Support, U.S. Gov't, P.H.S.]. 2011 Apr;23(4):444-8.
40. Pence BW, Ostermann J, Kumar V, Whetten K, Thielman N, Mugavero MJ. The influence of psychosocial characteristics and race/ethnicity on the use, duration, and success of antiretroviral therapy. J Acquir Immune Defic Syndr. [Research Support, N.I.H., Extramural Research Support, Non-U.S. Gov't]. 2008 Feb 1;47(2):194-201.
41. Smith KY, Patel P, Fine D, Bellos N, Sloan L, Lackey P, et al. Randomized, double-blind, placebo-matched, multicenter trial of abacavir/lamivudine or tenofovir/emtricitabine with lopinavir/ritonavir for initial HIV treatment. Aids. [Multicenter Study Randomized Controlled Trial Research Support, Non-U.S. Gov't]. 2009 Jul 31;23(12):1547-56.
42. Horstmann E, Brown J, Islam F, Buck J, Agins BD. Retaining HIV-infected patients in care: Where are we? Where do we go from here? Clin Infect Dis. [Review]. 2010 Mar 1;50(5):752-61.
43. Petry NM. Contingency management treatments: controversies and challenges. Addiction. [Editorial Research Support, N.I.H., Extramural]. 2010 Sep;105(9):1507-9.
44. Cabral HJ, Tobias C, Rajabiun S, Sohler N, Cunningham C, Wong M, et al. Outreach program contacts: do they increase the likelihood of engagement and retention in HIV primary care for hard-to-reach patients? AIDS Patient Care STDS. [Research Support, U.S. Gov't, P.H.S.]. 2007;21 Suppl 1:S59-67.
45. Hightow-Weidman LB, Jones K, Wohl AR, Futterman D, Outlaw A, Phillips G, 2nd, et al. Early linkage and retention in care: findings from the outreach, linkage, and retention in care initiative among young men of color who have sex with men. AIDS Patient Care STDS. [Research Support, U.S. Gov't, P.H.S.]. 2011 Aug;25 Suppl 1:S31-8.