

Research Protocol

Cooperative Re-Engagement Controlled Trial (CoRECT)

Grantees:

1. Connecticut Department of Public Health
2. Massachusetts Department of Public Health
3. Philadelphia Department of Public Health

Division of HIV/AIDS Prevention
Centers for Disease Control and Prevention

Version: May 22, 2015

TABLE OF CONTENTS

Protocol Executive Summary.....	3
Investigators.....	5
Background.....	7
Objectives.....	9
Study Setting.....	10
Methods and Procedures.....	11
Study Population.....	11
Study Design.....	12
Enrollment.....	12
Randomization.....	20
Blinding.....	21
Health Department Interventions.....	21
Assessment of Standard of Care Clinic Practices.....	22
Data Collection.....	23
Data Management (security, storage, transmission)	25
Data Analysis.....	29
Descriptive Analysis	29
Main Outcomes.....	29
Secondary Outcomes.....	33
Dissemination and Reporting of Results.....	35
Projected Timeline.....	35
Protection of Human Subjects.....	36
References.....	40
APPENDICES.....	41
Appendix A: Study Investigators; Roles and Responsibilities.....	42
Appendix B: Description of participating CoRECT clinics.....	45
Appendix C: Enrollment Databases.....	46
Appendix D: Assessment of Barriers to Care.....	47
Appendix E: Assessment of Clinic Standard of Care Practices.....	51
Appendix F: Data Dictionary	

PROTOCOL EXECUTIVE SUMMARY

The Cooperative Re-engagement Controlled Trial (CoRECT) is funded by CDC through cooperative agreements with the Connecticut State Department of Public Health (in collaboration with Yale University School of Medicine), the Massachusetts State Department of Public Health, and the Philadelphia Department of Public Health to evaluate a combined health department and clinic intervention to improve engagement in HIV care.

Background: HIV antiretroviral therapy (ART) can durably suppress plasma HIV viral load, which restores and preserves immunologic function. Effective ART improves individual survival and quality of life and dramatically reduces further HIV transmission, making it a priority for both individual health and community health. Within the United States, the largest lost opportunity to achieve a suppressed viral load occurs among individuals who have failed linkage to, or retention in, HIV medical care. Health department demonstration projects have suggested that good partnerships and information exchange between health departments and HIV clinics are essential to linkage/ re-engagement programs. The Cooperative Re-Engagement Controlled Trial (CoRECT) will evaluate an intervention to identify HIV-infected persons who are out-of-care and engage them in HIV care.

Summary of objectives: CoRECT will help identify the important components of a data-sharing partnership between health departments and HIV care providers, and determine the extent to which a health department intervention can increase the number of HIV-infected persons out-of-care who: (a) link to an HIV clinic; (b) remain in HIV medical care; (c) achieve HIV viral load suppression within 12 months; and (d) achieve durable HIV viral load suppression over 18 months. We will also measure the cost-effectiveness of this intervention in regards to improved health in the individuals (re)-engaged in HIV care and reductions in further HIV transmission in the community.

Methods summary: Health departments will generate an out-of-care list using HIV laboratory surveillance data; collaborating clinics will concurrently generate out-of-care lists using appointment data. The combined out-of-care list will be reconciled by the health department and clinics, and discussed at monthly case conferences. All individuals determined to be out-of care will be randomized

to receive either: (1) usual linkage and engagement in care services (standard of care [SOC]); or (2) an active health department field services intervention in addition to SOC. The active intervention activities will vary among jurisdictions; however all sites will include field services to locate, contact, and provide assistance, including a same-day appointment, to access HIV medical care.

Study design: Each site will enroll 600 out-of-care HIV-infected individuals (300 per arm) during a two-year enrollment period. An out-of-care individual will be defined as: (1) a person who has received HIV medical care at a CoRECT clinic and then disengages from care; or (2) a person with newly diagnosed HIV infection who has an appointment at a CoRECT clinic, but has not linked to medical care within 90 days.

Intervention: Individuals randomized to the intervention arm will receive field services to locate, contact, and provide assistance to access HIV medical care. Services provided as part of the intervention will vary by jurisdiction, but may include assistance with expedited medical appointments, transportation, access to community resources such as traditional case management, strengths-based case management, or financial incentives (Appendix A).

Primary outcomes: The following outcomes will be compared between out-of-care HIV-infected individuals receiving the study intervention to those receiving usual services:

1. Attend 1 clinic visit within 90 days;
2. Remain engaged in care, defined as 2 clinic visits at least 3 months apart within 12 months;
3. Achieve viral load suppression within 12 months;
4. Achieve durable viral load suppression, defined as 2 consecutive suppressed viral load results at least 3 months apart within 18 months

Timeline: CoRECT is a five-year study (project period: 9/1/2014 – 8/29/19). Enrollment is anticipated to begin in March 2016 after all institutional board review approvals are obtained, and continue through February 2018. All participants will be followed through the end of the study period.

Conclusions: Ultimately, the trial will demonstrate the feasibility of a joint health department – clinic intervention to identify recently out-of-care individuals and the effectiveness of an active health department intervention to (re-)engage these individuals in HIV medical care.

INVESTIGATORS

The Centers for Disease Control and Prevention (CDC) will collaborate with the Connecticut State Department of Public Health (in collaboration with Yale University School of Medicine), the Massachusetts State Department of Public Health, and the Philadelphia Department of Public Health. A complete list of study investigators and description of responsibilities is provided in Appendix B.

Roles and Responsibilities

In accordance with the terms of the collaboration, CDC will work jointly with all 3 health department jurisdictions to develop the research protocol. CDC will not be directly interacting with research participants at the local sites. The study design, procedures, consent forms, data collection instruments, and data archival methods have been developed collaboratively with CDC and investigators from the local sites. The final version of the protocol will be submitted by each health department for local IRB approval. The project will not be implemented until IRB approvals are received from the local health department and all necessary healthcare facilities.

CDC will develop the submission to the Office of Management and Budget (OMB) for review and clearance of data collection conducted in this study. During the OMB approval process, the health departments will not pursue information collection activities.

Data collection will be conducted by the study coordinators. The PIs from the local sites will be responsible for day-to-day oversight of the local project activities. Research sites, in collaboration with CDC, will be responsible for presenting site-specific findings at conferences and preparing manuscripts for publication in peer-reviewed journals. CDC will coordinate all cross-site concepts, carry out all analyses, and write research reports.

Data management and analysis will be the joint responsibility of the health department sites and CDC. Sites will have primary rights to the data and software developed under this trial and will also transfer

data without personal identifiers to CDC monthly. CDC will train sites in data management and in the use of the Secure Access Management System (SAMS) to transmit data files to CDC. CDC will provide all necessary data management guidelines to research sites.

Protocol Development

CDC and the 3 health department jurisdictions will have joint responsibility for the development of the project protocol, which will be reviewed by local IRBs participating in the research project. CDC will organize and conduct site investigators' meetings to discuss the project's progress and plan for the next year's milestones.

Protocol Modifications

All protocol modifications will be approved by local site IRBs. Local IRB approvals will be obtained before protocol changes are implemented. CDC will maintain copies of current local site IRB approval letters and approved consent forms.

BACKGROUND

HIV antiretroviral therapy (ART) can durably suppress the plasma HIV viral load, which improves individual survival and dramatically reduces further HIV transmission. Increasing the number of people living with HIV who access HIV care and achieve viral load suppression is a priority of the National HIV/AIDS Strategy [1]. Within the continuum of HIV care in the United States, improvements in linkage to and retention in effective care provide the greatest opportunity to improve rates of HIV viral suppression. It is estimated that of the 1.2 million persons living with HIV in 2011, only 40% were engaged in HIV medical care and only 30% achieved viral suppression [2]. Moreover, persons not retained in medical care are estimated to account for 60% of HIV transmissions in the United States [3].

Clinical trials with enhanced case management have demonstrated that interventions provided by the health department can improve linkage to care [4] and interventions provided by the clinic can improve retention in HIV care [5, 6]. Although linkage to care has improved in many health department jurisdictions, being linked to care is not enough. There is a need to ensure that: (i) people diagnosed with HIV and linked to care are engaging medical care (i.e., attending their enrollment appointment and returning for follow-up medical appointments); and (ii) people who have disengaged from HIV care (i.e., have missed medical appointments and have not been seen in clinic for more than 6 months) are able to efficiently re-engage in care.

Linkage and re-engagement programs have demonstrated that strong partnerships and information exchange between health departments and HIV treatment clinics can improve HIV care outcomes [7, 8]. People can be identified as disengaged from care based on both laboratory data that is reported to the health department for HIV surveillance (i.e., the absence of reported CD4 or viral load data for more than 6 months) and clinic data (i.e., not attending clinic for more than 6 months). Health department-based re-engagement in care projects have demonstrated that this approach can identify people that case workers can contact and facilitate re-entry into care [8]. Controlled studies are critical to determine the effectiveness of HIV prevention interventions; trials often provide generalizable information that cannot be obtained with observational studies (e.g., HPTN 052 [9]).

CoRECT is a controlled trial to evaluate an intervention to identify HIV-infected persons who are out-of-care and engage them in HIV care. Health department laboratory surveillance data and clinic appointment data will be shared at monthly case conferences to define recent out-of-care HIV-infected individuals. Presumptively out-of-care individuals will be randomized to receive: (1) usual linkage and engagement in care services (Standard of Care [SOC]); or (2) an active health department field services intervention in addition to SOC. The active intervention activities will include field services to locate, contact, and provide assistance (e.g., a same-day appointment, transport) to access HIV medical care. CoRECT will then evaluate if the active intervention resulted in increased (re)-engagement in care, retention in care, and HIV viral load suppression. Ultimately, the trial will demonstrate the feasibility of a joint health department – clinic intervention to identify recently out-of-care individuals and the efficacy of an active health department intervention to (re)-engage these individuals in HIV medical care.

OBJECTIVES

Research objectives:

1. Establish a data-sharing partnership between health departments and HIV care clinical providers designed to identify HIV-infected persons who are out-of-care.
2. Implement an engagement in care intervention to increase the number of HIV-infected out-of-care individuals who: (a) link to an HIV clinic; (b) remain in HIV medical care; (c) achieve HIV viral load suppression within 12 months; and (d) achieve durable HIV viral load suppression over 18 months.

Scientific knowledge to be achieved:

1. Determine the extent to which a health department intervention can successfully engage out-of-care persons in HIV medical care;
2. Describe the key successful components to identify HIV-infected persons out-of-care by a health department – clinic collaboration, and their feasibility;
3. Measure the cost-effectiveness of this intervention in terms of improved health in the individuals (re)-engaged in HIV care and reductions in further HIV transmission in the community.

STUDY SETTING

Three health departments were selected to participate in CoRECT:

- 1) **Connecticut State Department of Public Health:** In 2012, there were 10,849 prevalent HIV cases in Connecticut. Compared to national data, people living with HIV/AIDS (PLWH) in Connecticut are more likely to have injected drugs, be women, people of color, and be slightly older. Approximately 33% of PLWH are believed to be out-of-care by missing laboratory data. The CT Department of Public Health and Yale University School of Medicine will conduct CoRECT in 24 sites (20 Ryan White A- funded sites, 3 private clinics, 1 Veterans Administration hospital) in the New Haven-Fairfield counties Eligible Metropolitan Area (EMA) and Hartford Transitional Grant Area (TGA). These clinics provide HIV care to >7,500 patients, of which 1,700 are estimated to be out-of-care.
- 2) **Massachusetts State Department of Public Health:** Massachusetts has the highest rate of insured residents (96.6%) in the nation and a well-developed network of hospitals and community health centers for PLWH. However, barriers to engagement and retention in HIV clinical care still remain. Among 18,570 HIV cases in Massachusetts, it is estimated that ~24% of PLWH are currently out of care based on HIV surveillance data. For CoRECT, the MA Department of Public Health will partner with 10 clinical facilities (5 academic centers, 2 community hospitals, 1 public hospital, 2 community health centers) in areas with high HIV prevalence (Boston, Springfield, Cape Cod). These clinics provide care to >6,000 patients, of which 1,300 are estimated to be out-of-care.
- 3) **Philadelphia Department of Public Health:** Philadelphia is the sixth most populous city in the United States with an estimated HIV infection rate of 1.3%, more than three times the national rate. HIV/AIDS in Philadelphia disproportionately affects minority populations; nearly 63% of PLWH are African American, 19.1% are white, and 14.6% are Hispanic. Of the 19,832 cases of HIV, it is estimated that 54% are not receiving regular HIV medical care. In CoRECT, the Philadelphia Department of Public Health will partner with 6 clinical facilities (4 Ryan White clinics, 1 private clinic, 1 Veterans Administration facility). These clinics provide care to ~4,700 patients, of which 1,400 are estimated to be out-of-care.

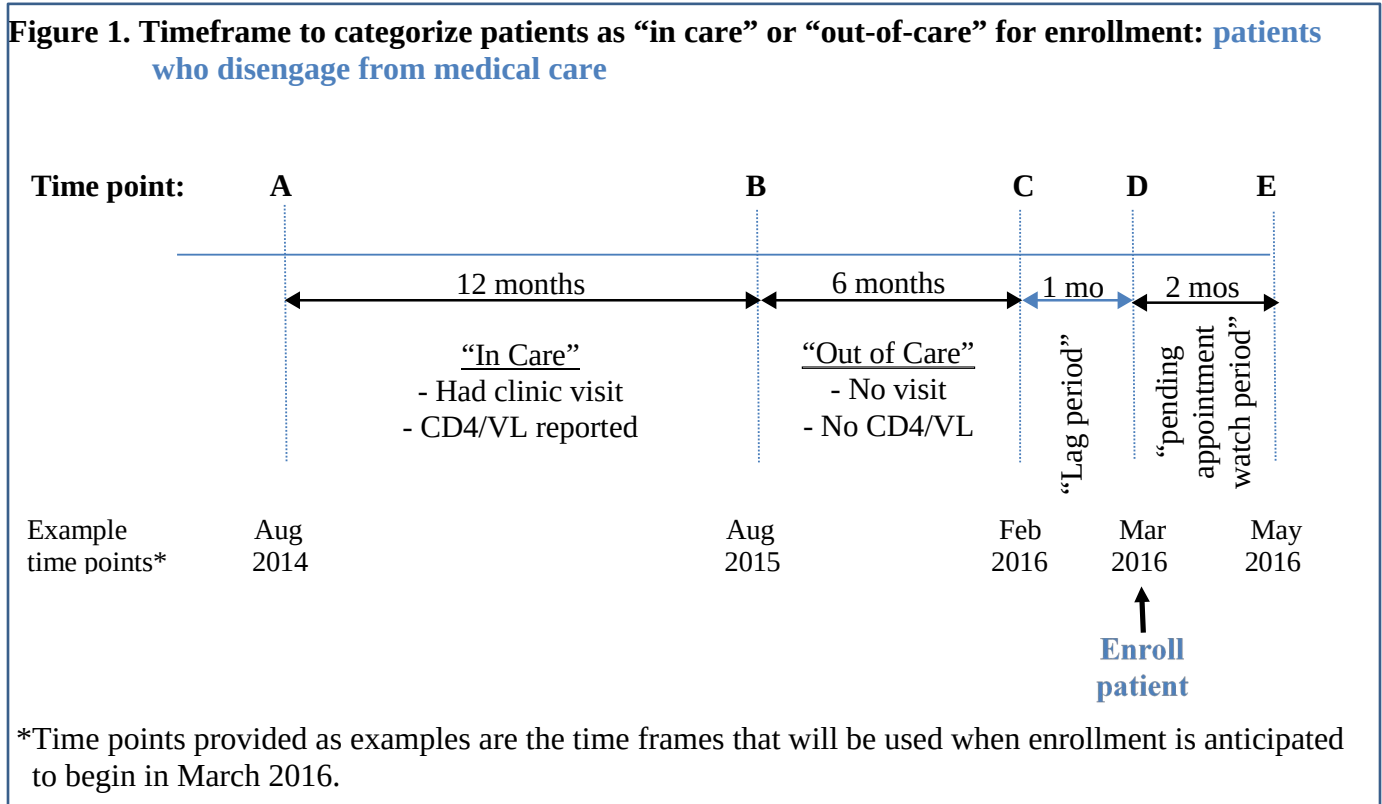
A detailed description of CoRECT clinics in each jurisdiction is provided in Appendix C.

METHODS: STUDY POPULATION

Target Population

1. Residents within the health department jurisdiction who have received HIV medical care at a CoRECT clinic and then disengage by either of the following definitions:
 - i. Clinic definition: did not have a visit with a prescribing provider for 6 months.
 - ii. Health department definition: no CD4 or viral load test result reported to health department surveillance for more than 6 months.
2. Residents within the health department jurisdiction with newly diagnosed HIV infection who have not linked to medical care within 90 days and have either:
 - i. Received, but did not attend, an appointment at a CoRECT clinic; or
 - ii. Attended an enrollment visit but did not receive medical care at a CoRECT clinic.

METHODS: STUDY DESIGN



Enrollment: Patients who disengage from medical care

1. Defining the “in-care” population: Each month, health departments will determine the number of patients who are “in care” at each CoRECT clinic. All patients residing within the health department’s jurisdiction who seek care during a 12-month period (Time A→B; Figure 1) and meet both of the following criteria will be considered “in-care” at a CoRECT clinic:
 - Had at least one visit with a prescribing provider during 12-month period (Time A→B)
 - Had a CD4 or VL associated with the clinic anytime during 12-month period (Time A→B)
2. Defining the “potentially out-of-care” population: All patients who are determined to be “in care” at a CoRECT clinic from Time A→B may be classified as potentially out-of-care if they meet any one of the following criteria (Figure 2):
 - Had no clinic visit with a prescribing provider in 6-month period (Time B→C)
 - Had no CD4 or VL associated with the clinic anytime during 6-month period (Time B→C)

Each month, all CoRECT clinics will generate a list of patients suspected to be potentially out-of-care (i.e., missing a clinic visit or laboratory result) during Time B→C using health records. The health department will *concurrently* generate a list of patients that have neither a CD4 nor VL associated with the clinic during Time B→C. Lists will be reconciled by both the clinics and health department to make a final determination of “potentially out-of-care” status. Any reasons for discrepancies should be documented (Enrollment database; Appendix D).

To allow for potential delays in laboratory reporting and reduce the chance for misclassification, a one month lag period (Time C→D; Figure 1) will be built into the protocol. For example, when looking for out-of-care patients between August 2015 and February 2016, health departments will not start querying laboratory surveillance data until March 2016.

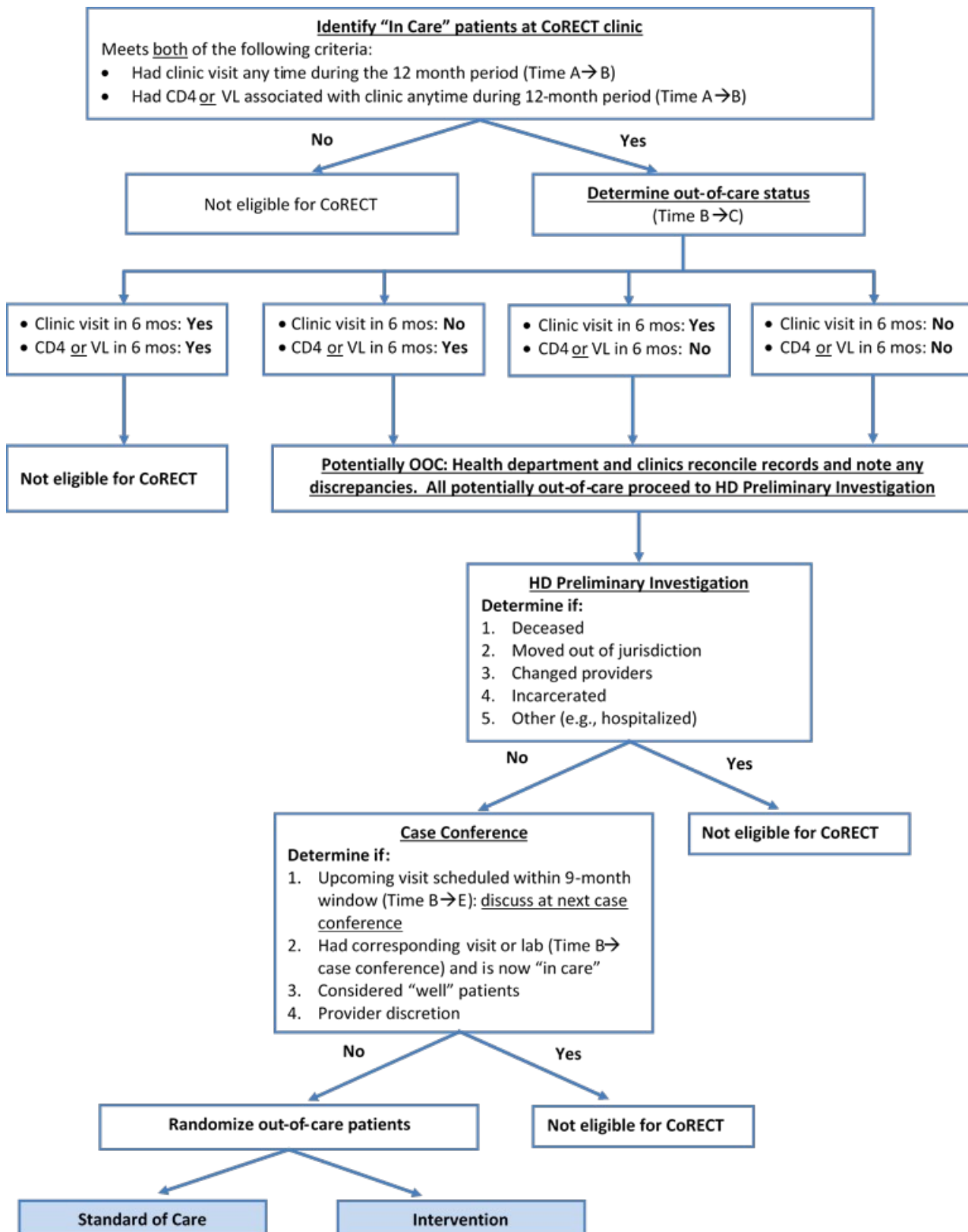
3. Health Department Preliminary Investigation: It is anticipated that several patients will be identified as “potentially out-of-care” by the above definitions; however, further investigation will be necessary to identify whether there are reasons that patients are out-of-care that would not make it appropriate to enroll them into the study. Health departments will cross reference the potentially out-of-care list with multiple other databases (e.g., eHARS, vital statistics, jail/ prison records) to further classify patients into the following categories:
 - **Deceased**: Using vital statistics/ social security databases/ eHARS
 - **Out of jurisdiction**: Either resides out of jurisdiction or has a change of address in eHARS / other software programs
 - **Changed providers**: As evidenced by a CD4/ VL ordered from a different facility/ provider in eHARS
 - **Incarcerated**: As evidenced by jail records or laboratory results from a jail/prison in eHARS
 - **Other**: Other reason why patient may be out-of-care and not able to enroll into CoRECT (e.g., prolonged hospitalization, in hospice care, mental or physical disability that requires assistance with independent activities of daily living that make it impractical to participate.)

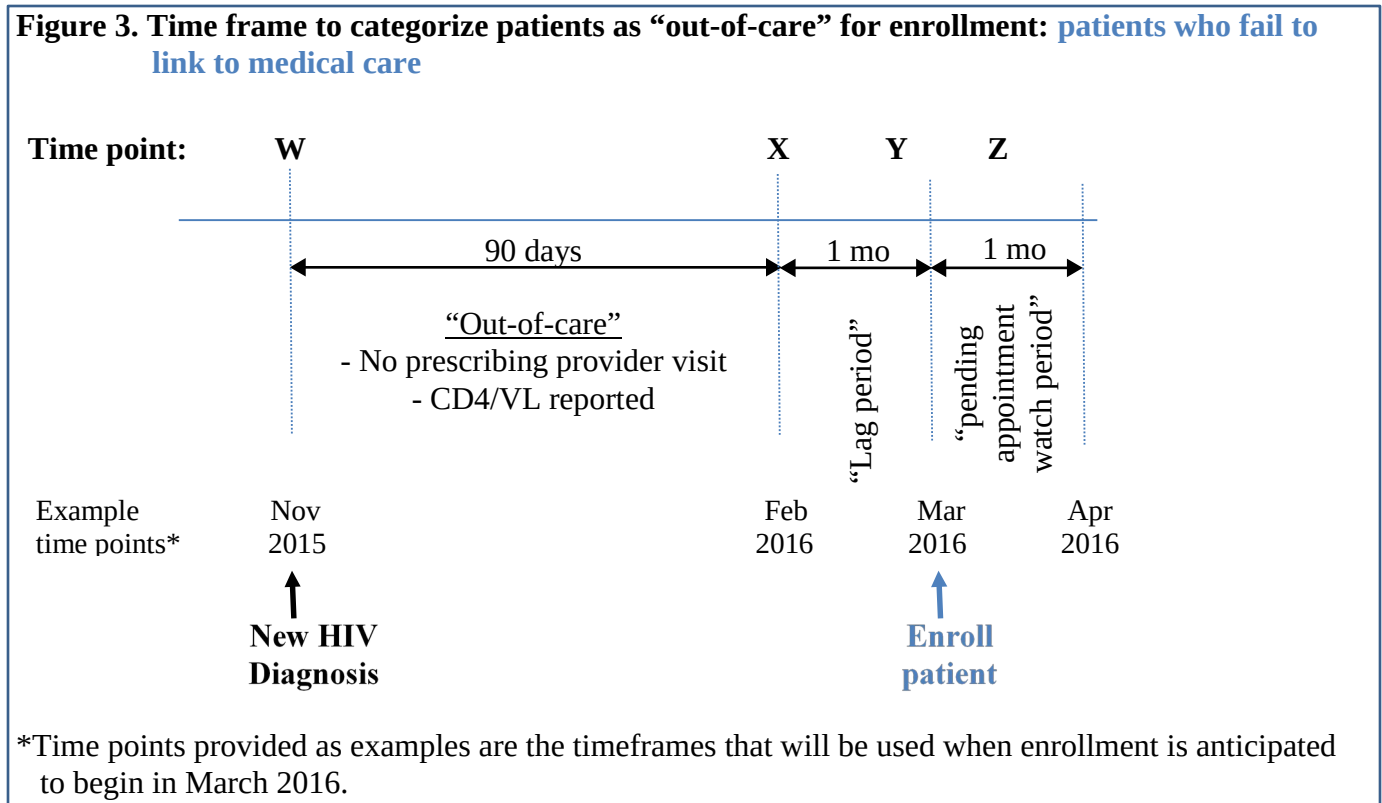
Cases that appear to be out of care by both clinic and health department definitions and are not known to be in one of the above categories will be discussed at a monthly case conference.

4. **Case Conference:** All patients that appear to be out-of care after the health department preliminary investigation will be discussed in monthly case conferences. Health departments will conduct these case conferences with each clinic either in-person or on the phone. During the case conference, all patients who appear to be out-of-care will be discussed individually. The following patients will be removed from the out-of-care list:
- **Upcoming visit:** The patient has an upcoming visit scheduled within 9-months of the “in care” period (Time B→E; Figure 1). During the ‘pending appointment watch period’ (Time D→E), the patient should be kept on the monthly case conference list to determine if the patient keeps the provider appointment and has laboratory results reported. If the patient does not have a provider visit and laboratory result within the 9-month window, and does not meet any of the exclusion criteria described above, this person will be considered out-of-care.
 - **Had recent visit:** If the patient had a provider visit or laboratory result that now classifies the patient as “in care” between Time B and the time when the case conference is held, that patient is excluded from randomization.
 - **“Well” patients:** Based on existing guidelines, HIV care providers may choose to schedule less frequent provider visits and laboratory tests for select patients who are adherent to antiretroviral therapy and have achieved complete viral suppression on repeat evaluation. To be excluded as a “well” patient in CoRECT, the patient must meet both of the following criteria:
 - Evidence of two consecutive “undetectable” viral loads at least six months apart. For this purpose “undetectable” means plasma HIV RNA below the lower limit of detection for the particular test used.
 - No evidence of “detectable” plasma HIV RNA during the “in care” or “out of care” period (e.g., Time A→C; Figure 1).
 - **Other:** Other reason why patient may be out-of-care and not able to enroll into CoRECT (e.g., prolonged hospitalization, in hospice care, mental or physical disability that makes it impractical to participate).
 - **Provider discretion:** There may be rare instances when a patient does not meet the exclusion criteria above, but the provider feels the patient should not be considered “out-of-care.” In these instances, the provider must have a discussion directly with the CoRECT research team

about the rationale for excluding the patient from enrollment. The CoRECT research team will ultimately be responsible for determination of trial eligibility.

Figure 2. Flowchart for enrollment: patients who disengage from medical care





Enrollment: Patients who fail to link to medical care

Any patient with a new HIV diagnosis who is assigned to a CoRECT clinic and fails to link to medical care within 90 days will be considered out-of-care for purposes of CoRECT. The following definitions will be used for enrollment:

1. Assigned to a CoRECT clinic: All patients residing within the health department’s jurisdiction who have a new HIV diagnosis and either:
 - Attended an enrollment visit at a CoRECT clinic; or
 - Received an appointment for a visit at a CoRECT clinic

Several methods may be used to identify patients with new HIV diagnoses who have been assigned to a CoRECT clinic, including surveillance data, clinic appointment information, or a combination of both. National eHARS data will be used to verify that the patient did not have a previous HIV positive test in another jurisdiction.

2. Defining the “potentially out-of-care” population: All patients with new HIV diagnoses who are “assigned” to a CoRECT clinic may be classified as potentially out-of-care if they meet any one of the following criteria (Figure 4):
 - Had no clinic visit with a prescribing provider in the 90-day period (Time $W \rightarrow X$)
 - Had no CD4 or VL during the 90-day period (Time $W \rightarrow X$)

Each month, all CoRECT clinics will generate a list of patients suspected to be potentially out-of-care (i.e., missing a clinic visit or laboratory result) during Time $W \rightarrow X$ using health records. The health department will *concurrently* generate a list of patients that have neither a CD4 nor VL associated with the clinic during Time $W \rightarrow X$. Lists will be reconciled by both the clinics and health department to make a final determination of “potentially out-of-care” status. Any reasons for discrepancies should be documented (Enrollment database; Appendix D).

To allow for potential delays in laboratory reporting and reduce the chance for misclassification, a one month lag period (Time $X \rightarrow Y$; Figure 3) will be built into the protocol. For example, when looking for out-of-care patients between November 2015 and February 2016, health departments will not start querying laboratory surveillance data until March 2016.

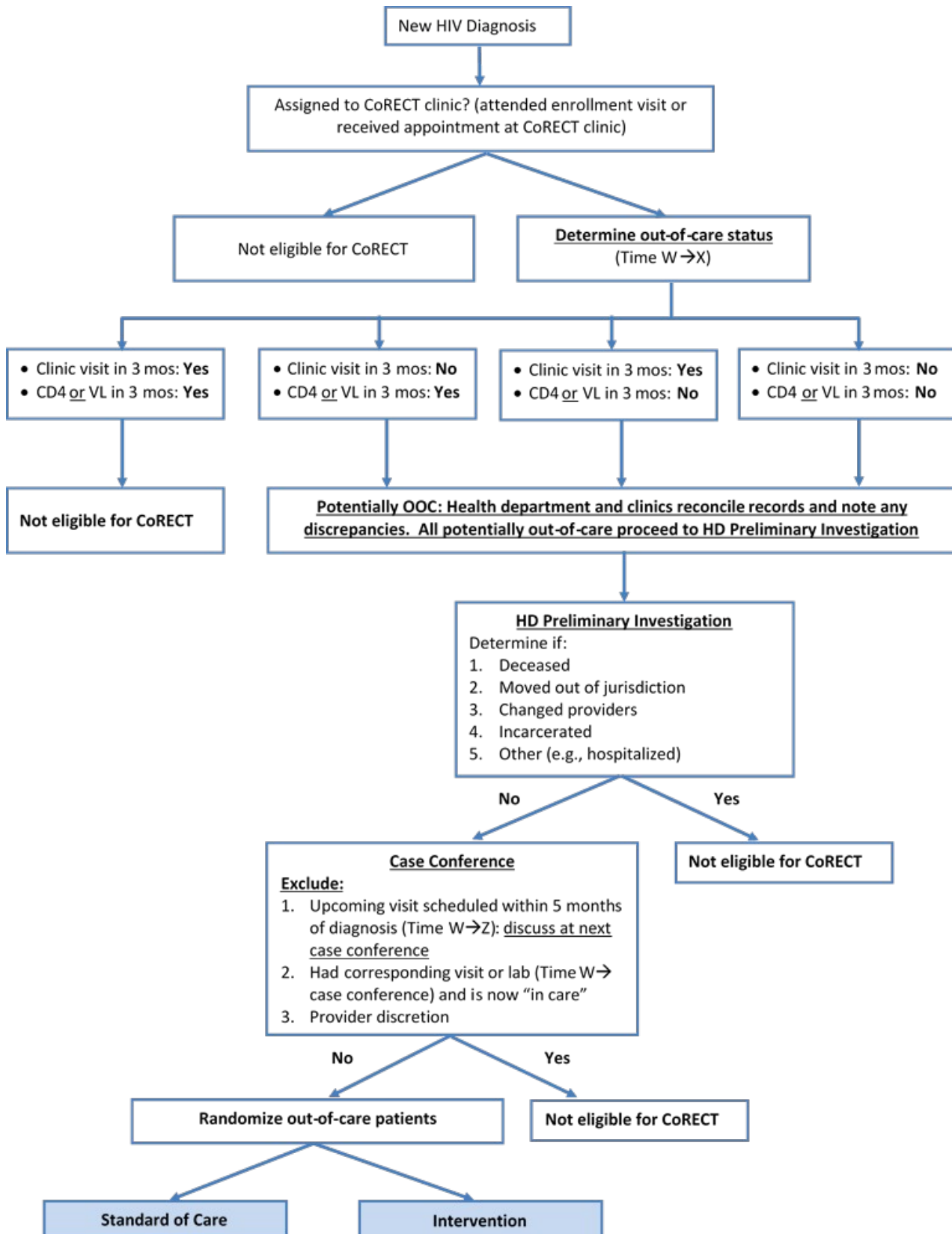
3. Health Department Preliminary Investigation: Health departments will cross reference the potentially out-of-care list with multiple other databases (e.g., eHARS, vital statistics, jail/ prison records) to further classify patients into the following categories:
 - **Deceased:** Using vital statistics/ social security databases/ eHARS
 - **Out of jurisdiction:** Either resides out of jurisdiction or has a change of address in eHARS / other software programs
 - **Changed providers:** As evidenced by a CD4/ VL ordered from a different facility/ provider in eHARS
 - **Incarcerated:** As evidenced by jail records or laboratory results from a jail/prison in eHARS
 - **Other:** Other reason why patient may be out-of-care and not able to enroll into CoRECT (e.g., prolonged hospitalization, in hospice care, mental or physical disability that

requires assistance with independent activities of daily living that make it impractical to participate.)

Cases that appear to be out of care by both clinic and HD definitions, and are not known to be in one of the above categories, will be discussed at a monthly case conference.

4. **Case Conference:** All patients who appear to be out-of care after the health department preliminary investigation will be discussed in monthly case conferences. Health departments will conduct these case conferences either in-person or on the phone. During the case conference, all patients who appear to be out-of-care will be discussed individually. The following patients will be removed from the out-of-care list:
 - **Upcoming visit:** The patient has an upcoming visit scheduled within 5 months since HIV diagnosis (Time W→Z; Figure 3). This patient should be kept on the monthly case conference list to determine if the patient keeps the provider appointment or has laboratory results completed. If the patient does not have a provider visit and laboratory result within this time period, and does not meet any of the above exclusion criteria, this person will be considered out-of-care.
 - **Had recent visit:** If the patient had a recent provider visit that now classifies the patient as “in care” between Time W and the time when the case conference is held, that patient should be excluded from randomization.
 - **Other:** Other reason why patient may be out-of-care and not able to enroll into CoRECT (e.g., prolonged hospitalization, in hospice care, mental or physical disability that makes it impractical to participate).
 - **Provider discretion:** There may be rare instances when a patient does not meet the exclusion criteria above, but the provider feels the patient should not be considered “out-of-care.” In these instances, the provider must have a discussion directly with the CoRECT research team about the rationale for excluding the patient from enrollment. The CoRECT research team will ultimately be responsible for determination of trial eligibility.

Figure 4. Flowchart for enrollment: patients who fail to link to medical care



Randomization

All patients who are determined to be “out-of-care” after the monthly case conference will be randomized to either the standard of care (SOC) arm or intervention arm, generally within 10 days of the case conference.

A block randomization approach will be conducted separately in each jurisdiction:

- *Linkage vs. Re-engagement*: In all 3 jurisdictions, all patients who have not successfully linked to care (i.e., patients with newly diagnosed HIV infection who have not linked to medical care within 90 days) will be randomized separately from patients who have disengaged from care as per the above definitions. This will ensure an equal number of intervention and SOC participants in each group.
- *Randomization by clinic*: Because baseline (re)-engagement practices may vary between clinics, a substantial imbalance between assignment of intervention and SOC participants among clinics could compromise the findings of the study. Given this, the Massachusetts Department of Public Health and Philadelphia Department of Public Health will plan to randomize patients by clinic to ensure there are an equal number of participants in each arm from each clinic.
- *Randomization by county*: Because baseline (re)-engagement practices may vary between counties in Connecticut, the Connecticut Department of Public Health will plan to randomize patients by county.

Randomization is anticipated to begin in March 2016; however, because a large number of out-of-care patients are expected at the beginning of the enrollment period, health departments may choose to phase-in clinic randomization start dates. Patients who are randomized into the study cannot be randomized again (e.g., if patients are successfully re-linked, and then lost to care again).

Misclassification

If a patient is randomized to a study arm and it is later found out that they were actually ineligible for randomization (e.g., the patient was deceased or incarcerated before randomization, but study investigators did not find out until later), the reason for misclassification will be documented. However, following the intent-to-treat approach, patients *will not* be replaced if they are found to be misclassified. A per protocol analysis may be considered beyond the intent-to-treat analysis to determine whether the intervention appears to be more efficacious when such participants are censored.

Blinding

The study coordinator at each site will be responsible for randomizing study participants to either the SOC arm or intervention arm. DIS staff will only receive the list of names of those participants randomized to the intervention arm. The clinics will also be blinded to the randomization results. Although it is likely that some clinic staff may eventually become “un-blinded” to the randomization based on the study design (e.g., if a DIS staff reaches out to the clinic to ask for an expedited appointment for a patient), this level of engagement is necessary and unavoidable by study design.

Health Department Interventions

Individuals randomized to the intervention arm will receive field services to locate, contact, and provide assistance to access HIV medical care. Services provided as part of the intervention will vary by jurisdiction and are described in detail in Appendix A.

The core components of the intervention include the following:

1. *Locating patients*: Health department field specialists or disease intervention specialists (DIS) will begin “actively” locating patients randomized to the intervention during the first 30 days after randomization. Active approaches to locate patients may include phone calls, letters, home visits, and use of patient locator programs (e.g., Lexis Nexis). If a patient is not identified during this 30-day period, DIS will be passively available to assist patients for a minimum of 90 days after randomization (e.g., if patient returns a phone call or responds to a letter).
2. *Contacting patients*: All patients randomized to the intervention arm will be contacted by a DIS, who will confirm the patient’s identify, describe the nature of the intervention (Appendix A), obtain medical release of information (if needed based on the jurisdiction), and obtain informed consent to participate in a survey and DIS-based intervention.
3. *Barriers to Care Assessment*: If the jurisdiction is administering the barriers to care assessment, a standardized tool will be used (Appendix E) to assess barriers to accessing healthcare care (e.g., transportation, financial assistance, housing, substance abuse services, etc.). Informed

consent will be obtained prior to conducting the assessment. In some jurisdictions, patients may be offered an incentive (e.g., gift card) to complete the assessment.

4. *Intervention to Address Barriers to Care:* Specific interventions to address barriers to care will vary by jurisdiction (Appendix A) and may include services such as transportation, assistance with obtaining health insurance, linking patients to community resources, and facilitating expedited appointments with CoRECT clinics. Additional strategies such as strengths-based case management or lottery-based incentives may also be implemented, depending on the jurisdiction.
5. *(Re)-engagement and handoff to the clinic:* All patients must, at a minimum, have a CD4/ viral load test drawn and have a visit with a prescribing provider before DIS will consider the patient (re)-engaged in care. If specific information (such as barriers to care assessment) must be relayed from the DIS to the provider to facilitate retention in care, a protocol will be in place for transfer of sensitive information. Any continued involvement by DIS in the patient's care after (re)-engagement is described in the site-specific protocol (Appendix A).

Assessment of “Standard of Care” Practices

As there is likely to be a change in “standard of care” over the five-year study period, it will be important to understand how the delivery of health services evolves over time at participating CoRECT clinics. Investigators will administer a simple survey at baseline and every six months during the study period (Appendix F). The survey is meant to provide a general sense of current linkage/ re-engagement processes and should be completed by one person (e.g., a clinic administrator) at the CoRECT clinic.

DATA COLLECTION

Study ID Code Numbers

When creating the data transmittals to CDC, the sites will remove all information that can potentially identify a patient (e.g., name, social security number, medical record number used by the clinic to identify a patient). Each site will assign a unique 6-digit identification number to each patient's data using the format below. The study ID code will be linked to the patient's medical record number and these identifiers will be stored in a password-protected network server at each site. The study ID code number will be the only identifying variable in the data transmittals to CDC.

The first digit represents the health department site; the second and third digits represent the CoRECT clinic (Appendix C); and the last three digits identify a unique patient within the clinic:

Connecticut Department of Public Health	100001 through 199999
Massachusetts Department of Public Health	200001 through 299999
Philadelphia Department of Public Health	300001 through 399999

Data Used in the Analysis of CoRECT

The data elements to be used in the research trial are listed in the table below; these data elements are routinely collected in health department surveillance data. Additional data collected from clinical records (e.g., receipt of antiretroviral medications, comorbidities, and appointment information) and relevant data security, storage, and transmission considerations will be discussed in site-specific protocols (Appendix A).

Data Archived by Clinics and Used in the Analysis of CoRECT

The data elements to be used in the research trial are listed in the table below. These data elements are routinely collected in health department surveillance data or clinic medical records for their own patient management purposes. During this project, data managers at each of the health departments will prepare de-identified data files containing these variables on patients enrolled in the trial.

Table 1. Electronic data collected during the study

Data element #	Data element
	Variables collected from surveillance data or assigned by health department
	Collected at enrollment:
1	Unique patient study ID (not clinic ID)
2	Staten0 (eHARS)
3	Month and year of birth
4	Biological sex of patient
5	Ethnicity of patient (OMB categories)
6	Race (OMB categories)
7	HIV exposure risk category
8	Date first tested HIV-positive
9	Lowest known CD4
10	Earliest known CD4 date
11	Trial classification (intervention vs. SOC)
	Collected at each visit:
12	Unique patient study ID
13	eHARS ID
14	Date of laboratory test (CD4 count or viral load)
15	CD4 count
16	Type of HIV-1 viral load assay
17	HIV-1 viral load result
18	Out of range indicator for viral load
	Variables Collected from CoRECT Clinic
	Collected at enrollment:
19	Unique patient study ID
20	CoRECT clinic assigned
21	Date of first visit to this HIV clinic
22	Ever received ARVs at this clinic prior to enrollment
23	Ever achieved viral suppression at this clinic prior to enrollment
	Collected at each visit:
24	Date of scheduled HIV primary care visit
25	Date the HIV primary care appointment was created
26	Type of visit (e.g., laboratory, prescribing provider, case management, social work, etc.)
27	Disposition of the scheduled HIV primary care visit (kept, cancelled, no-show)
28	Primary insurance
29	Prescribed antiretroviral medications (yes/no)

DATA MANAGEMENT

Data Security, Storage, and Transmission

Data Security and Storage

CoRECT data will be subject to the same security and confidentiality requirements as those implemented for HIV surveillance data at state and local project areas, as well as at CDC. These requirements include adherence to CDC guidelines for the security and confidentiality of HIV surveillance data

(<http://www.cdc.gov/nchhstp/programintegration/docs/PCSIDataSecurityGuidelines.pdf>). Specifically, all CoRECT staff will undergo the same security and confidentiality training as that required for health department staff members who conduct HIV case surveillance. While conducting CoRECT, protocols will be strictly followed at the project area and national level to ensure the integrity, confidentiality, and security of all CoRECT data.

HIV case surveillance data are currently collected according to the Assurance of Confidentiality under Sections 306 and 308(d) of the Public Health Service Act (42 U.S.C. Sections 242k and 242m(d)). Information collected in the surveillance system that would permit identification of any individual or establishment is collected with a guarantee that it will be held in strict confidence, will be used only for purposes stated in the assurance, and will not otherwise be disclosed or released without the consent of the individual or the establishment in accordance with Section 306 and 308(d) of the Public Health Service Act. Because data collected for CoRECT constitute data collected for an enhanced surveillance activity, these data will be reported to and maintained by CDC in the same manner as are current HIV surveillance data, and accordingly are covered by the existing Assurance of Confidentiality.

CoRECT interview and abstraction data records will not contain specific personally identifiable information (e.g., name, date of birth, address, social security number). They are linkable to eHARS only through STATENO, the eHARS surveillance numbers. When paper forms are used for interview or abstraction they will be stored under lock and key; information collected on paper will be entered into the appropriate data system at the project area and the paper forms will be destroyed no later than 12 months after the data collection cycle has ended. Any electronic or paper copies of medical records

obtained by the project area will be stored under lock and key and will be destroyed based on the site-specific retention period. Paper or electronic lists that contain personally identifiable information (e.g., patient name, address), such as those that are used for locating patients, will be kept under lock and key and destroyed once they are no longer needed (e.g., when all the eligible persons on the list have been dispositioned, contacted, or determined to be unlocatable) or no later than 24 months after data collection; access to them will be strictly limited. If the contact attempts tracking database is used by the project area, database records will be destroyed no later than 24 months after data collection. Signed informed consent forms for CoRECT will be securely stored separately from the data collection instruments, preferably at the central HIV Surveillance office of the project area, under the same security procedures as those for HIV case surveillance forms. Consent forms will be retained for the duration specified by the state/local surveillance policies.

Portable electronic data collection devices such as laptops or tablet computers used to store interview and other data related to sampled persons must be protected through use of individual passwords, which are known only to the user and to data managers at the project area. The security of the system will meet all Federal Information Systems Management Act (FISMA), OMB, HHS, and CDC IT Security requirements which ensure the confidentiality, integrity, and availability of data on federal information systems. The hard drives of all electronic data collection devices must be encrypted. Data should be uploaded frequently to office computers kept in an area behind a locked door. Portable electronic data collection devices should always be stored in a secure locked location. They should never be stored for extended periods of time, e.g. overnight, in a car.

When traveling into the field to contact patients, CoRECT staff may need to carry identifying and contact information for patients randomized to the intervention. In doing so, staff should take care to limit the amount of information carried to the minimum necessary and to keep the data secure, e.g. in a locked briefcase or other method described in CDC's Data Security and Confidentiality Guidelines for HIV, Viral Hepatitis, Sexually Transmitted Disease, and Tuberculosis Programs (<http://www.cdc.gov/nchhstp/programintegration/docs/PCSIDataSecurityGuidelines.pdf>). Electronic information should be maintained on a password-protected, encrypted device. Additional protections such as biometric authentication are encouraged whenever they are deemed to increase the security of the data.

The interview data warehouse and contact attempts tracking database for each project area will be stored on a secure server with limited access.

Transmission of data from CoRECT clinics to the health department:

Demographic, HIV clinical, attendance data for all patients who are determined to be out-of-care by the above definitions will be maintained on a password-protected file in each CoRECT clinic. The point of contact at each clinic will transmit data to the health department utilizing a FIPS (Federal Information Processing System) Publication 140-2 certified encryption mechanism. Only the data manager and other authorized study staff at the health department will have access to a linked database (i.e., database that includes medical record number and study ID number).

Transmission of data from the health department to CDC:

Health departments will be responsible for aggregating all data from CoRECT clinics and transferring to CDC on a monthly basis. All personally identifying information (e.g., name, date of birth, medical record number) will be removed before being forwarded to CDC. The de-identified file will be encrypted and will only be accessed by local staff who are directly involved with the CoRECT study. Authorized study staff at the health department will transmit the encrypted data files through the Secure Access Management Services (SAMS) to CDC on a monthly basis. SAMS encrypts and prohibits any modification of data in transit between the local health department and CDC. SAMS assures that project sites can only deliver and retrieve authorized information from CDC servers.

The local CoRECT principal investigator and project coordinator will be ultimately responsible for data management, data security, and data transfer. All documents that are locally maintained and have personal identifiers will be secured in locked areas with limited and controlled access according to local procedures. Within these locked areas, study-related records and data will be maintained in secured storage devices (e.g., locked desks, locked filing cabinets, or locked closets). Access to CoRECT study databases will require individual passwords and will be limited to local staff working on the study.

CDC Electronic Data Management

Central data management will be performed by the Epidemiology Branch of the Division of HIV/AIDS Prevention (DHAP). The data from each health department will be downloaded from SAMS to a secure CDC drive that is backed-up daily. Original data received from the sites will be stored separately from SAS data sets. The data on the drive will be stored in folders devoted exclusively to this study and will only be accessible by authorized persons. Individuals will not be identified by name or any other potentially identifying characteristic such as social security number or date of birth on any study forms. Any identification of personal identifying information will be immediately reported to the Information System Security Officer at CDC. The central data set will be maintained at CDC until all study analyses have been completed and all study results have been disseminated after which point these data will be destroyed.

Quality Control

Given the various sources of information for a single person, the possibility exists that information may be entered into the system more than once or that discrepant data may be reported. Data received from the participating sites will be subject to quality control by CDC's CoRECT study data manager, who will write SAS programs to automate the consistency, coherency, and completeness of the data received from the participating sites. The data manager will run series of data validation processes, frequency distributions to look for unexpected patterns in data (outliers), missing data, data that are out of range, and data that are in the wrong format (e.g., character data in field requiring numeric responses). Any errors found will be reported to the participating sites for resolution through the Principal Investigator. Only the sites can correct the data file; no changes to the data will be made by CDC.

DATA ANALYSIS

Descriptive analysis

Baseline characteristics will be compared between the intervention arm and SOC arm to look at the success of randomization. An exploratory analysis of all variables collected (including demographics and relevant clinical characteristics obtained from surveillance data and medical records) will be conducted using the appropriate statistical test based on the structure of the data. Associations between variables of interest will also be tested to inform any potential issues with co-linearity during multivariate analysis.

Descriptive characteristics may be stratified by variables of interest. This might include, but is not limited to, stratification by:

- Newly diagnosed patients vs. re-engagement patients
- Those who received ARVs prior to enrollment vs. those who did not
- Those who were virally suppressed before randomization vs. those who were not
- Reported barriers to care (e.g., transportation, substance abuse)

Health departments and CDC will share responsibility for analysis of data; statistical approaches for the main outcomes will be agreed upon by the jurisdictions and CDC. The same statistical approach will be utilized at all three site for the analysis of main outcomes and for secondary analyses if appropriate

Main Outcomes: There are four main outcomes of the trial:

1. *(Re)-engagement in care:*

Calculate the number and proportion of out-of-care HIV-infected individuals who attend one clinic visit within 90 days of receiving the study intervention compared with SOC.

- a. All patients randomized to either the intervention arm or the SOC arm will be included in the denominator.
- b. Outcomes will be dichotomized as either:
 - i. Attended one clinic visit: patient had a CD4 cell count or viral load result within 90 days of the date of randomization.

- ii. Did not attend one clinic visit: patient did not have a CD4 cell count or viral load result within 90 days of the date of randomization.
- c. Health department surveillance CD4 cell count and viral load reporting data will be used to measure this outcome. Either a CD4 or viral load result must be recorded to be included in the numerator. Patients with evidence of CD4 or viral load results linked to another provider (i.e., not from the initial CoRECT facility), will still be counted in the numerator as patients may have changed providers in the course of engaging in care.

2. Retention in care:

Calculate the number and proportion of out-of-care HIV-infected individuals who remain engaged in care (two clinic visits at least three months apart within 12 months) after receiving the study intervention compared with SOC.

- a. All patients randomized to either to the intervention arm or the SOC arm will be included in the denominator.
- b. Outcomes will be dichotomized as either:
 - i. Remained engaged in care: patient had at least two CD4 cell count or viral load results at least three months apart within 12 months of the date of randomization.
 - ii. Did not remain engaged in care: patient did not have at least two CD4 cell count or viral load results at least three months apart within 12 months of the date of randomization.
- c. Health department surveillance CD4 cell count and viral load reporting data will be used to measure this outcome. Either a CD4 or viral load result must be recorded to be included in the numerator. Patients with evidence of CD4 or viral load results linked to another provider (i.e., not from the initial CoRECT facility), will still be counted in the numerator as patients may have changed providers in the course of engaging in care.

3. Viral suppression:

Calculate the number and proportion of out-of-care HIV-infected individuals who achieve viral load suppression, defined as viral load < 200 copies/mL, within 12 months of the study intervention compared with SOC.

- a. All patients randomized to either the intervention arm or the SOC arm will be included in the denominator.
- b. Outcomes will be dichotomized as either:
 - i. Achieved viral load suppression: suppressed viral load result *any time* within 12 months of the date of randomization.
 - ii. Did not achieve viral load suppression: either there was no evidence of viral load suppression within 12 months of the date of randomization or the patient had no viral load results.
- c. Health department surveillance viral load reporting data will be used to measure this outcome. Patients with evidence of a viral load result linked to another provider (i.e., not from the initial CoRECT facility), will still be counted in the numerator as patients may have changed providers in the course of engaging in care.

4. Durable viral load suppression:

Calculate the number and proportion of out-of-care HIV-infected individuals who achieve durable viral load suppression of the study intervention compared with SOC. To achieve durable viral load suppression, the following must be documented: (1) the most recent viral load in the 18-month follow-up period after randomization is <200 copies/mL; and (2) the viral load immediately prior to, but at least three months apart from, the most recent viral load is <200 copies/mL; and (3) all viral load results between time (1) and time (2) are <200 copies/mL.

- a. All patients randomized to either the intervention arm or the usual services arm will be included in the denominator.
- b. Outcomes will be dichotomized as either:
 - i. Achieved durable viral load suppression: met all three criteria for durable viral load suppression
 - ii. Did not achieve viral load suppression: did not meet all three criteria for durable viral load suppression
- c. Health department surveillance viral load reporting data will be used to measure this outcome. Patients with evidence of a viral load result linked to another provider (i.e., not from the initial CoRECT facility), will still be counted in the numerator as patients may have changed providers in the course of engaging in care.

Hypotheses

- *Null hypothesis:* The same proportion of patients will achieve the main outcomes (viral load suppression, (re)-engagement in care, retention in care, durable viral load suppression) in both the intervention group and the SOC group.
- *Alternative hypothesis:* The proportion of patients that achieve the main outcomes (viral load suppression, (re)-engagement in care, retention in care, durable viral load suppression) will be different between the intervention group and the SOC group.

Sample Size and Statistical Power

To have adequate power to detect at least an absolute increase of 10 percentage points in the proportion of patients in the intervention arm who achieve a main outcome (e.g., viral load suppression), the trial needs approximately 600 out-of-care HIV-infected individuals (300 per arm; Table 2). A combined collaborating clinic population of 3,000 – 6,000 patients would likely be required to enroll 600 out-of-care persons over a two-year period.

Table 2. Sample Size Calculations for the Main Study Outcomes

		Proportion Achieving Main Outcome in Intervention Arm										
		0.2	0.25	0.3	0.35	0.4	0.45	0.5	0.55	0.6	0.65	0.7
Proportion Achieving Main Outcome in SOC Arm	0.1	174	90	57								
	0.2			250	121	74						
	0.3					300	141	83				
	0.4							325	150	87		
	0.5									325	147	83
	0.6											

Analysis of Main Outcomes

The main outcome measures will be analyzed using an “intent-to-treat” approach; all participants randomized in the study will be included in the analysis regardless of disposition or acceptance of the intervention. If a CD4 or viral load result is missing, it will not be counted in the numerator (i.e., it will be presumed “failure”). A per protocol analysis may be considered, as a secondary analysis, beyond the intent-to-treat analysis to determine whether the intervention appears to be more efficacious when participants who were misclassified at randomization are censored.

Regression analysis, using an appropriate model based on the structure of the data, will be used to evaluate multivariate models. Any baseline characteristics (e.g., Table 1) that are found to be statistically different between intervention and control group *and* that are felt to be potentially confounding the association between the intervention and the outcome will be considered in the multivariate model. The most parsimonious model is desired — only those variables that substantially confound the relationship between the intervention and the outcome and remain statistically significant will remain in the final model.

Secondary Outcomes

1. *Measurement of time-dependent variables* (e.g., association between intervention and time to (re)-engagement or time to viral load suppression) using Cox proportional hazard models
2. *Measurement of viral load as a continuous outcome variable*: Changes in viral load (e.g., geometric mean) over time will be compared between the intervention group and SOC group.
3. *Stratified analysis*: Although the study was powered to detect a 10% absolute increase in the main outcomes among those in the intervention group compared to the SOC group, exploratory data analysis may suggest that the intervention worked differently among certain subgroups of (patient, clinical, and clinic-level variables). Secondary stratified analyses may be considered on a case-by-case basis if driven by the data; however, these analyses cannot be planned *a priori*.

4. Measure viral suppression among persons living with diagnosed HIV in the jurisdiction and HIV Care Continuum (that includes HIV testing and diagnosis, linkage to HIV medical care, continuous engagement in HIV medical care, initiation of antiretroviral therapy, and suppressed viral load) at the beginning and end of the study to estimate what impact this intervention can potentially have at the community level.
5. Describe reasons identified at monthly case conferences that explain care status misclassifications of HIV-infected individual (i.e., out-of-care individuals that are actually in-care and vice versa) by either health department lab-based metrics or clinic appointment-based metrics
6. Evaluate the prevention effectiveness of the study intervention using a costs vs. effectiveness or costs vs. utility-type model. The model may include any projected improvements in individual health (QALYs) and any projected reductions in HIV transmission.

DISSEMINATION AND REPORTING OF RESULTS

CoRECT study results will be disseminated at (i) internal presentations to CDC's Division of HIV/AIDS Prevention and at the study sites; (ii) conferences such as the National HIV Prevention Conference (NHPC), the Conference on Retroviruses and Opportunistic Infections (CROI), Infectious Disease Society of America, or the Council of State and Territorial Epidemiologists; and (iii) as manuscripts published in the peer-reviewed literature.

Topics for dissemination will include aggregated results from data-to-care activities, public health interventions to improve (re)-engagement in care, and cost effectiveness. All publications and external presentations derived either from site-specific or from aggregate data collected under this study must be cleared by CDC's Division of HIV/AIDS Prevention.

PROJECTED TIMELINE

February–August 2015 — Finalize protocols, submit, and obtain IRB approvals

January 2016 — Obtain OMB approval

March 2016 — Begin enrolling patients

August 2019 — Complete data collection

PROTECTION OF HUMAN SUBJECTS

Waiver of Informed Consent for Enrollment in the Research Trial

Based on 45 CFR 46.116(d), the IRB is requested to waive specific informed consent for enrollment into CoRECT study. To summarize, the research components of this study include:

- (a) Establishing a data-sharing partnership between health departments and HIV care clinical providers to identify HIV-infected persons who are out-of-care

- (b) Evaluate a public health intervention to increase the number of HIV-infected individuals out-of-care who (i) link to an HIV clinic; (ii) remain in HIV medical care; (iii) achieve HIV viral load suppression; (iv) achieve durable HIV viral load suppression.

This waiver is requested because individuals in both study arms will be receiving routine public health services. The following four requirements of 45 CFR 46.116(d) are met:

1. *The research involves no more than minimal risk to the participants:*

- Patient confidentiality: the risk of access to protected health information (PHI) is minimal as all data will be maintained on password-protected files and transmitted via a FIPS 140-2 certified encryption algorithm. Data sharing will only occur between designated CoRECT study team participants at the clinics, health departments, and CDC. Any data in paper form will be maintained in a secure location and access will be restricted to CoRECT study investigators. All CoRECT staff will comply with local requirements for training with regards to human subjects research and HIPAA requirements. In addition all data will be de-identified (i.e., removal of name, birth date other than year of birth) prior to analysis and before transfer to CDC.
- Patient privacy: Patients randomized to the intervention arm may become upset when they are contacted by the health department to (re)-engage them in care. However, in all three health jurisdictions, contacting individuals with a reportable infectious disease is a routine public health activity conducted by epidemiologists and DIS. This risk can be minimized by ensuring that staff members comply with all protocols.

The minimal risk criterion, therefore, are met in that the probability and magnitude of harm or discomfort anticipated from enrolling into this study are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine public health activities.

2. *The waiver or alteration will not adversely affect the rights and welfare of the participants.*

- Surveillance data has long been used to inform and initiate public health intervention for infectious disease. With respect to HIV/AIDS, however, use of disease surveillance data to drive public health intervention and to monitor engagement in care is novel. Given the efficacy of antiretroviral therapy in facilitating sustained viral suppression, a public health

intervention to facilitate (re-)engagement in HIV medical care represents an important opportunity to maximize “treatment as prevention” in order to substantially decrease incident infections, to improve health outcomes for people living with HIV/AIDS, and to promote health equity.

- All 3 jurisdictions have the legal and regulatory authority to collect information necessary to investigate, prevent, and control diseases of public health significance. DIS already receive training to find, counsel, and elicit sexual contacts of persons with priority STIs. In some jurisdictions, DIS also perform outreach and engagement in care work for individuals with acute HIV infection identified through laboratory surveillance data. Thus, the proposed project is an expansion of existing roles for health department personnel.
- The welfare of some individuals randomized to the intervention arm may be enhanced if DIS are successful at facilitating (re-)engagement in HIV care. Patients in the SOC arm may also benefit by having their out-of-care status brought to the attention of their clinicians, who may also offer reengagement services through their existing clinic protocols.

3. *The research could not practicably be carried out without the waiver or alteration.*

The goal of the trial is to evaluate an intervention to actively engage out-of-care persons compared to standard of care. Informed consent prior to randomization would not be possible because out-of-care persons are often difficult to locate (an expected outcome in both study arms); requiring informed consent for enrollment creates logistical complications that could impact the health department’s ability to carry out the intervention. Moreover, if patients are contacted to obtain informed consent before randomization, this would function to some degree as an intervention, which could compromise the findings of the study.

4. *Whenever appropriate, the participants will be provided with additional pertinent information after participation.*

As part of the health department’s routine services and activities, all participants randomized to the intervention arm will be provided with information about HIV clinical care and community resources to address barriers to care. Patients in the SOC arm who (re-)engage in clinical care will also have access to this information.

Patients randomized to the intervention arm will be asked to consent to an in-depth interview regarding access to care, reasons for falling out of care, barriers to remaining in care and what they may need to maintain care and health (Appendix E). Because collection of this information goes beyond routine HIV/AIDS surveillance and may be of a sensitive nature, informed consent will be obtained before participation in the interview.

Participants will be fully informed of the purpose of the study, procedures, risks, and benefits of participation as well as protection of privacy. Participants will be made aware of the activities requested of them if they participate in the survey, the duration of the survey, and informed that they may withdraw from the interview or refuse to answer any question in the survey without penalty and without jeopardizing any aspect of their care at the clinic. If the jurisdiction is administering the barriers to care assessment, participants will be informed that information provided in the assessment may be shared with their medical provider as needed to facilitate (re)-engagement in medical care. They will be informed that the study will be applying for a Federal Certificate of Confidentiality which means that, under most circumstances, the investigators cannot be forced to reveal information that may identify participants. They will be informed that only a study code number, not names, will be used to identify all data collected in the study.

There are minimal risks to participants in the survey. A few questions on the survey ask about alcohol and drug use and may make some participants feel uncomfortable. Also, some participants may have concerns about being identified as a participant in the study and that providers may obtain personal information about them. To minimize these risks, patients may refuse to answer any question in the survey. To maintain confidentiality, all identifying information including name and other personal identifiers will be maintained with strict confidentiality protocols. Electronic data will be managed under password protected computer programs on a secured data network. Filing cabinets are maintained in offices with limited and controlled access and all computers and the electronic health records are accessible only by authorized personnel with proper usernames and access codes. In addition, no identifying information will be sent to CDC.

A checkbox on the assessment tool (Appendix E) will be used to indicate that the patient has given informed consent to participate in the interview. Written documentation of informed consent will not be obtained by asking the patient to sign their name.

Anticipated Benefits

This study affords considerable individual medical and public health benefits. Given the efficacy of antiretroviral therapy in facilitating sustained viral suppression, a public health intervention to facilitate (re)-engagement in HIV medical care represents an important opportunity to maximize “treatment as prevention” in order to substantially decrease incident infections, to improve health outcomes for people living with HIV/AIDS, and to promote health equity. The health of patients in the intervention arm may improve if DIS are successful at facilitating (re)-engagement in HIV care and initiation of antiretroviral therapy to suppress HIV viral load. Patients in the SOC arm may also benefit by having their out-of-care status brought to the attention of their clinicians, who may also offer reengagement services through their existing clinic protocols.

Vulnerable Populations

- No participants under the age of 18 will be participating in the study.
- Pregnant women may also be enrolled in the study. The level of risk is minimal and there are potential benefits for enrollment in the study, such as (re)-engagement in HIV care, initiation of antiretroviral therapy, and viral load suppression.

References

1. The White House Office of National AIDS Policy. *National HIV/AIDS Strategy*. Available at: <http://www.whitehouse.gov/administration/eop/onap/nhas>. Accessed: 30 January 2015.
2. Bradley, H., et al., *Vital Signs: HIV diagnosis, care, and treatment among persons living with HIV--United States, 2011*. MMWR Morb Mortal Wkly Rep, 2014. **63**(47): p. 1113-7.
3. Skarbinski, J., et al., *Human Immunodeficiency Virus Transmission at Each Step of the Care Continuum in the United States*. JAMA Intern Med, 2015.
4. Gardner, L.I., et al., *Efficacy of a brief case management intervention to link recently diagnosed HIV-infected persons to care*. AIDS, 2005. **19**(4): p. 423-31.
5. Gardner, L.I., et al., *A low-effort, clinic-wide intervention improves attendance for HIV primary care*. Clin Infect Dis, 2012. **55**(8): p. 1124-34.
6. Gardner, L.I., et al., *Enhanced personal contact with HIV patients improves retention in primary care: a randomized trial in 6 US HIV clinics*. Clin Infect Dis, 2014. **59**(5): p. 725-34.
7. Dombrowski JC. *Testing, Linkage and Retention in Care: Getting Control of the Cascade in Seattle*. National Summit on HIV and Viral Hepatitis Diagnosis, Prevention, and Access to Care, Washington, DC, November 26–8, 2012.
8. Udeagu, C.C., et al., *Lost or just not following up: public health effort to re-engage HIV-infected persons lost to follow-up into HIV medical care*. AIDS, 2013. **27**(14): p. 2271-9.
9. Cohen, M.S., et al., *Prevention of HIV-1 infection with early antiretroviral therapy*. N Engl J Med, 2011. **365**(6): p. 493-505.

Connecticut Department of Public Health (DPH)

- Heidi Jenkins: Principal Investigator; Program Director, Connecticut DPH
- Frederick Altice, MD, MA: Co-Investigator; Research Director; Yale University School of Medicine
- Merceditas Villanueva, MD: Co-Investigator; Clinical Services Director; Yale University School of Medicine

Massachusetts Department of Public Health (DPH)

- Alfred DeMaria, MD: Principal Investigator; Medical Director/ State Epidemiologist, Massachusetts DPH
- Liisa Randall, PhD: Co-Investigator/ Project Manager; Director of Healthcare Planning, Massachusetts DPH

Philadelphia Department of Public Health (DPH)

- Kathleen Brady, MD: Principal Investigator; Medical Director, Philadelphia DPH
- Crystal Lucas, Project Coordinator, Philadelphia DPH
- Greta Anshuetz: DIS/ STD Surveillance Manager, Philadelphia DPH

Centers for Disease Control and Prevention (CDC)

- To be determined: Project Officer; Medical Officer, Division of HIV/AIDS Prevention (DHAP), CDC.
- Paul Weidle, PharmD, MPH: Co-Investigator; Team Leader, Health Services Research for Prevention with Positives, DHAP, CDC
- Kathy Byrd, MD, MPH: Co-Investigator; Medical Officer, DHAP, CDC
- Lytt Gardner, PhD: Co-Investigator; Epidemiologist, DHAP, CDC
- Gary Marks, PhD: Co-Investigator; Senior Research Psychologist, DHAP, CDC
- Simone Gray, PhD: Co-Investigator; Statistician, DHAP, CDC
- Azfar Siddiqi, PhD, MS, MD: Co-Investigator; Senior Service Fellow, DHAP, CDC
- Nasima Camp, MPH: Project Coordinator; ICF/ DHAP, CDC
- Lois Conley, MPH: Collaborator, Epidemiologist; DHAP, CDC
- Phil Peters, MD: Collaborator; Medical Officer; DHAP, CDC
- Kate Buchacz: Collaborator; Epidemiologist, DHAP, CDC
- Ram Shrestha, PhD: Collaborator; Economist, DHAP, CDC
- Ann Do, MD: Collaborator; Associate Chief of Science, Epidemiology Branch, DHAP, CDC
- Irene Hall, PhD, MPH: Collaborator; Chief, HIV Incidence and Case Surveillance Branch, DHAP, CDC
- Taraz Samandari, MD, PhD: Collaborator; Chief, Epidemiology Branch, DHAP, CDC

ROLES AND RESPONSIBILITIES

The principal investigators/ health departments will have primary responsibility for:

- Collaborating with other award recipients and CDC to develop a single, unified protocol for CoRECT and submitting the protocol for IRB approvals as required locally.
- Identifying patients out-of-care and randomizing to either active intervention or usual services.
- Enrolling an adequate number of out-of-care HIV-infected individuals as determined by the study protocol and the program requirements.
- Following out-of-care HIV-infected individuals as determined by the study protocols.
- Establishing procedures to maintain the rights and confidentiality of all out-of-care HIV-infected individuals evaluated in this trial.
- Performing data analyses as determined in the study protocol.
- Collaborating with CDC and other grantees to disseminate study results at national or international meetings and publishing research findings in peer-reviewed scientific literature.
- Participating in routine conference calls with CDC project officer(s) and research team.
- Hosting CDC project officer(s) for site visits.
- Developing data management systems to collect information necessary for the project. Use the eHARS system to collect as much project data as is feasible to avoid duplication of data collection.
- Transferring data for central analysis monthly.
- Attending initial and annual meetings with other CDC- funded grantees to promote research dissemination and networking among investigators.
- Reporting surveillance and program results as required by local law.
- PUBLICATIONS: Publications, journal articles, etc. produced under a CDC grant support project must bear an acknowledgment and disclaimer, as appropriate, for example: “This publication (journal article, etc.) was supported by the Cooperative Agreement Number above from the Centers for Disease Control and Prevention. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the Centers for Disease Control and Prevention”. In addition, the PI/PD must provide to CDC Program the abstracts or manuscripts prior to any publication related to this funding. The grantee will not seek to publish results and findings from this project without prior approval and clearance from CDC.
- Awardees will retain custody of and have primary rights to the data and software developed under these awards, subject to Government rights of access consistent with current DHHS, PHS, and CDC policies.

CDC staff have substantial programmatic involvement that is above and beyond the normal stewardship role in awards, as described below:

- Providing technical assistance as needed in the design and conduct of the research.
- Facilitating and assisting in the development of a research protocol for IRB review by all cooperating institutions participating in the research project. A CDC engagement determination will determine if the CDC IRB will also need to approve the protocol.
- Obtaining Office of Management and Budget approval per the Paperwork Reduction Act
- Assisting, as needed, in designing a data management system.
- Facilitating storing of aggregate data with participating recipients.
- Collaborating with grantees to disseminate study results at national or international meetings and publishing research findings in peer-reviewed scientific literature.

- Conducting site visits to ensure that collaborating clinics are properly selected, collaborations outlined in proposals are appropriate, the community is involved in the research activities, and investigators are complying with the research protocol.
- Conducting meetings of the study investigators to facilitate the exchange of research progress among recipients and to offer additional technical expertise for the conduct of research.

Health departments will update accordingly

Health departments will update accordingly

CoRECT: Barriers-To-Care AssessmentInformed Consent

You are being asked to participate in a research study by [name of institution] and the Centers for Disease Control and Prevention. The purpose of the study is to learn whether additional services offered by the health department will help improve patients' attendance in clinic. In order to do this, we would like to interview you about any difficulties you may have in coming to your regular clinic appointments. Before you decide if you want to be interviewed, I want to tell you more about what it means to be in the study. Please ask me any questions you may have.

If you agree to be interviewed, I will ask you a series of questions about any difficulties you may have in coming to your regular clinic appointments. The interview will take less than 30 minutes. There are minimal risks to you if you take part in the interview. A few questions ask about alcohol and drug use and may make you feel uncomfortable. If you give consent, some of the information from the interview may be given to your medical providers to help connect you with resources to keep you in care. You may refuse to answer any question in the interview. There are no direct medical benefits to you by participating; however, you will receive help in overcoming obstacles to seeking medical care. The results from this study may help us improve services provided to other patients in the future.

All of the information you give us will be kept private to the extent allowed by law. This study has a Federal Certificate of Confidentiality. This means we cannot be forced to give out any information such as medical information, survey information, or other information that can identify you. Any information collected from you as part of this interview will be destroyed within 12 months after you are interviewed. After your information is destroyed, there will be no way to link you personally to your interview

You are free to participate in the interview or not. If you do not participate, you will not lose any services or medical care at the clinic. If you decide to participate, you may refuse to answer any question or simply not talk about a matter that you do not wish to discuss study. In that case too, you will not lose any services or medical care at the clinic. We will not let you be a part of the study if you are not able to give legal consent to be in the study.

There is no cost to you for being in this study. We will give you \$20 gift card after you complete the computer survey as a thank you for your time. There will be no other reimbursements.

Checked box indicates that the statement has been read to the participant, all of the participant's questions have been answered, and the participant verbally agrees to be interviewed.

People can have many different types of problems getting their HIV care. Think of the reasons why you may not have gotten the HIV care you needed or that was recommended for you. Please indicate “Yes” or “No” for all of the following reasons for why you may not have gotten necessary HIV care in the past 6 months (or 3 months for linkage to care patients).

1. I felt good	Yes	No	Decline
2. My CD4 count and viral load are good	Yes	No	Decline
3. Did not think I am HIV positive	Yes	No	Decline
4. I didn't want to think about being HIV positive	Yes	No	Decline
5. I did not know when to follow-up with my healthcare provider	Yes	No	Decline
6. I felt sick	Yes	No	Decline
7. Medication side effects	Yes	No	Decline
8. I felt depressed	Yes	No	Decline
9. I didn't like the way that I was treated at the clinic in the past	Yes	No	Decline
10. The clinic facility (hours, location, or wait-time) is inconvenient	Yes	No	Decline
11. I did not want to be seen at the HIV clinic	Yes	No	Decline
12. I do not trust doctors	Yes	No	Decline
13. I did not know where to go for medical care	Yes	No	Decline
14. I had problems getting through to someone in the office to make an appointment	Yes	No	Decline
15. I couldn't get an appointment with the provider I like	Yes	No	Decline
16. It took too long to get an appointment	Yes	No	Decline
17. I had problems finding a provider who speaks my language	Yes	No	Decline
18. I forgot about my appointment	Yes	No	Decline
19. I had problems getting child care	Yes	No	Decline
20. I didn't have health insurance	Yes	No	Decline
21. I did not have enough money to pay my co-pay	Yes	No	Decline
22. I was afraid it might cost too much	Yes	No	Decline
23. I couldn't get the time off work or school	Yes	No	Decline
24. I had other responsibilities	Yes	No	Decline
25. I had problems getting transportation to my appointment	Yes	No	Decline
26. I was too drunk or high	Yes	No	Decline

- 27. There is no cure for HIV so I don't need to go to the doctor Yes No Decline
- 28. I didn't want to go to the doctor until I told my friends/family Yes No Decline
- 29. I don't need to go to the doctor because God will cure me Yes No Decline

30. Of the reasons mentioned, what was the *main* reasons (up to three) that you didn't go to a doctor, nurse, or other health care worker for HIV medical care during the last 6 months (or within 3 months for linkage-to-care patients)? _____

In this next section, I will list some services that you may have needed to help you get medical care. For each service, please indicate "Yes", "No", or decline to answer whether you tried to access this service in the past 6 months (or within 3 months for linkage-to-care patients). If you needed the service, please indicate whether you were able to get the service when you wanted it.

	A. Did you need [Interviewer: insert service] during the past 6 months?	B. Were you able to get [Interviewer: insert service] during the past 6 months?
27. Counseling services. <i>These are services for when you need someone to talk to when you feel anxious, sad, down in the dumps, depressed or have emotional problem.</i>	<input type="checkbox"/> Yes (Go to the box to the right) <input type="checkbox"/> No (Skip to the box below) <input type="checkbox"/> Decline	<input type="checkbox"/> Yes <input type="checkbox"/> Sometimes <input type="checkbox"/> No
28. Substance abuse treatment. <i>This includes treatment or counseling for drugs or alcohol.</i>	<input type="checkbox"/> Yes (Go to the box to the right) <input type="checkbox"/> No (Skip to the box below) <input type="checkbox"/> Decline	<input type="checkbox"/> Yes <input type="checkbox"/> Sometimes <input type="checkbox"/> No
27. Housing services. <i>These are services to help you find a suitable place to live. These do not include financial assistance for paying your rent or mortgage.</i>	<input type="checkbox"/> Yes (Go to the box to the right) <input type="checkbox"/> No (Skip to the box below) <input type="checkbox"/> Decline	<input type="checkbox"/> Yes <input type="checkbox"/> Sometimes <input type="checkbox"/> No
28. Emergency financial	<input type="checkbox"/> Yes (Go to the box to the right)	<input type="checkbox"/> Yes

<p>assistance. <i>These are emergency services to help you pay for things like utilities (electricity, heating oil, natural gas), housing (rent or mortgage payment), and medications, when other resources are not available.</i></p>	<p><input type="checkbox"/> No (Skip to the box below) <input type="checkbox"/> Decline</p>	<p><input type="checkbox"/> Sometimes <input type="checkbox"/> No</p>
<p>29. Employment assistance. <i>These are services to help you find a job or get work.</i></p>	<p><input type="checkbox"/> Yes (Go to the box to the right) <input type="checkbox"/> No (Skip to the box below) <input type="checkbox"/> Decline</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> Sometimes <input type="checkbox"/> No</p>
<p>30. Transportation. <i>These are transportation services provided directly to you or through a voucher to help you get to HIV medical appointments or go to HIV-related health services such as case management.</i></p>	<p><input type="checkbox"/> Yes (Go to the box to the right) <input type="checkbox"/> No (Skip to the box below) <input type="checkbox"/> Decline</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> Sometimes <input type="checkbox"/> No</p>
<p>31. Help with getting groceries, meals. <i>This includes things like food vouchers or food stamps, food pantry packages, or pantry bags, meals delivered to your home.</i></p>	<p><input type="checkbox"/> Yes (Go to the box to the right) <input type="checkbox"/> No (Skip to the box below) <input type="checkbox"/> Decline</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> Sometimes <input type="checkbox"/> No</p>
<p>32. Help with getting benefits. <i>This includes help qualifying for things like health insurance (Medicaid, Medicare, or private insurance), Ryan White services, social security, welfare or unemployment.</i></p>	<p><input type="checkbox"/> Yes (Go to the box to the right) <input type="checkbox"/> No <input type="checkbox"/> Decline</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> Sometimes <input type="checkbox"/> No</p>
<p>33. Other: _____</p>	<p><input type="checkbox"/> Decline</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> Sometimes <input type="checkbox"/> No</p>

The next 3 questions are about where you have stayed or lived in the past 6 months.

34. In the past 6 months, at how many different places have you lived?

- 1 2 3 or more Decline

35. Where are you currently staying or living?

- In my own home or apartment
 In someone else's (friend, relative, etc.) home or apartment
 Some other type of living arrangement (e.g., multiple people's homes/moving from house to house, hotel/motel, shelter, residential treatment program, boarding house, group home, halfway house, on the streets/in a car/park/abandoned building)

36. During the past 6 months, have you been incarcerated (in jail or prison) for at least 48 hours?

- Yes No Decline

The following questions are about recent drug or alcohol use. I would like to remind you that your responses will be kept confidential. You may decline to answer any item.

37. In the past 30 days, have you injected drugs (e.g. injected heroin or cocaine)?

- Yes No Decline

38. In the past 30 days, have you used the following drugs?

- | | | | |
|--|------------------------------|-----------------------------|----------------------------------|
| Crack (rock, gravel) | <input type="checkbox"/> Yes | <input type="checkbox"/> No | <input type="checkbox"/> Decline |
| Powder cocaine (snort, blow) | <input type="checkbox"/> Yes | <input type="checkbox"/> No | <input type="checkbox"/> Decline |
| Heroin, not injected (horse, smack, tar) | <input type="checkbox"/> Yes | <input type="checkbox"/> No | <input type="checkbox"/> Decline |
| Methamphetamines (meth, crystal meth, speed, crank, ice) | <input type="checkbox"/> Yes | <input type="checkbox"/> No | <input type="checkbox"/> Decline |
| Marijuana or hashish (pot, weed) | <input type="checkbox"/> Yes | <input type="checkbox"/> No | <input type="checkbox"/> Decline |
| Party drugs (Ecstasy, Special K, GBH) | <input type="checkbox"/> Yes | <input type="checkbox"/> No | <input type="checkbox"/> Decline |
| Prescription painkillers without a prescription (Codeine, Morphine, Demerol, Darvon, Oxycontin, Vicodin, Dilaudid) | <input type="checkbox"/> Yes | <input type="checkbox"/> No | <input type="checkbox"/> Decline |

39. In the past 30 days, have you had 5 or more alcoholic drinks (beer, wine, or hard liquor) in 1 day?

- Yes No Decline

CoRECT: Assessment of Clinic Standard of Care Practices

Point person at your clinic for CoRECT

Name: _____

Phone: _____

Email: _____

“Out of care” patients

1. Do you currently have a protocol in your clinic to contact patients who are out of care?

- Yes No

2. If so, how do you define “out of care” in your clinic? How do you identify those that are “out of care” (e.g., electronic records, paper)?

3. Who is responsible for conducting outreach for patients that are out of care?

- | | |
|---|--|
| <input type="checkbox"/> Receptionist | <input type="checkbox"/> Practice manager |
| <input type="checkbox"/> Medical assistant | <input type="checkbox"/> Medical director |
| <input type="checkbox"/> Nurse | <input type="checkbox"/> Dedicated team other case manager |
| <input type="checkbox"/> Mid-level practitioners (APRN or PA) | <input type="checkbox"/> Peer |
| <input type="checkbox"/> Nurse case manager | <input type="checkbox"/> Physician/ provider |
| <input type="checkbox"/> Other _____ | |

4. If you have a protocol, what type of outreach do you conduct for out of care patients? How often?

Process	Frequency (e.g., every missed appointment, if no appointment in six months, etc.). If you do not conduct this type of outreach, write “N/A”
Telephone calls	
Letters	
Referral to case manager	
Other: _____	

Other: _____	
--------------	--

5. Has your protocol been revised or updated in the last six months? *Explain:*

Missed appointments

6. Do you currently have a protocol in your clinic to contact patients who have missed appointments? Yes No

7. Who is responsible for conducting outreach for patients that have missed appointments?

- | | |
|---|---|
| <input type="checkbox"/> Receptionist
<input type="checkbox"/> Medical assistant
<input type="checkbox"/> Nurse
<input type="checkbox"/> Mid-level practitioners (APRN or PA)
<input type="checkbox"/> Nurse case manager
<input type="checkbox"/> Other _____ | <input type="checkbox"/> Practice manager
<input type="checkbox"/> Medical director
<input type="checkbox"/> Dedicated team other case manager
<input type="checkbox"/> Peer
<input type="checkbox"/> Physician/ provider |
|---|---|

8. If you have a protocol, what type of outreach do you conduct for patients that have missed appointments? How often?

Process	Frequency (e.g., every missed appointment, if no appointment in six months, etc.). If you do not conduct this type of outreach, write “N/A”
Telephone calls	
Letters	
Referral to case manager	
Other: _____	
Other: _____	

9. Has your protocol been revised or updated in the last six months? *Explain:*

Health departments will update accordingly