The Substance Abuse Treatment to HIV Care II (SAT2HIV-II) Project

Protocol Version 1.1

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1 BACKGROUND & STUDY SYNOPSIS

1.1 Background

Addressing Substance Misuse in HIV Service Settings

The significance of ending the HIV epidemic. In 2019, the Department of Health and Human Services launched the Ending the HIV Epidemic initiative with the goal of reducing new HIV infection rates by 90% through four key strategies: early diagnosis, rapid treatment to reach viral suppression, prevention, and outbreak response. Achieving this goal is possible with advances in antiretroviral therapies to treat and prevent HIV. Such therapies have significantly improved the quality of life and life expectancy of people with HIV (PWH) and have recently been shown to essentially eliminate the risk of transmitting HIV to sexual partners among PWH who maintain an undetectable viral load. Despite these advances, HIV incidence has remained steady since 2013, with approximately 39,000 new infections annually in the United States.[1] Consequently, HIV remains one of the most significant epidemics in the country, with 1.1 million PWH[2] and $20 billion in annual direct health expenditures for prevention and care.[3] With each new HIV infection having an estimated $400,000 in public health costs, new HIV infections cost the nation approximately $1.6 billion each year. *Innovative strategies that reach the hardest-to-reach populations with the highest rates of transmission will help the Ending the HIV Epidemic initiative achieve its goals.*

The significance of addressing substance misuse among PWH. One of the most significant barriers to ending the HIV epidemic is substance misuse among PWH (misuse of prescription medications, alcohol, or other drugs). Substance misuse among PWH has several adverse consequences that increase the risk of HIV transmission, including decreased adherence to HIV medications,[4-7] poorer viral suppression,[8-10] and increased incidence of risky sexual behaviors such as condom-less sex with partners who are HIV negative or who have an unknown status.[11,12] Substance misuse rates are significantly higher among PWH than in the general population.[13] Recently, Garner and colleagues (2019)[14] found that use disorders for alcohol, opioid, and methamphetamine have the most significant population-level negative impacts for PWH. Few PWH access specialty substance misuse treatment services, even when available,[15,16] highlighting the importance of improving care integration in HIV service settings. *If the Ending the HIV Epidemic initiative is to achieve its target of 95% of persons with diagnosed HIV infection achieving viral suppression, substance misuse among PWH must be addressed to help increase engagement in care and subsequently viral suppression.*

Despite the adverse impacts of substance misuse among PWH, research addressing substance misuse in HIV service settings has been limited,[17-19] with most research to date addressing alcohol misuse in HIV primary care settings.[17,19,20] Dr. Garner's Substance Abuse Treatment to HIV Care (SAT2HIV-I) Project (a dual-randomized, type 2 effectiveness-implementation hybrid trial) focused on HIV service organizations (HSOs) because they are well-positioned to address substance misuse among PWH given that (1) HSOs conduct assessments with clients twice per year, which provides opportunities to screen for and address substance misuse, and (2) relative to time-constrained HIV primary care settings, HSO case management staff

may be better able to make time for identifying and addressing substance misuse.[21,22] We believe that to end the HIV epidemic in the United States, we must target missed opportunities to address substance misuse within HSOs. *Research that focuses on improving treatment for substance misuse within HSOs will have significant contributions to ending the HIV epidemic.*

The significance of integrating motivational interviewing-based brief interventions (MIBIs). Motivational interviewing[23] (MI) is effective for reducing substance misuse; it has more than 25 years of empirical support.[24-27] However, MIBIs have only recently been examined in HIV service settings. Aharonovich and colleagues (2017)[28] found that compared with an educational control, MIBIs delivered in HIV primary care settings significantly decreased the frequency and quantity of non-injection drug use. Similarly, Satre and colleagues (2019)[29] found that MIBIs delivered in primary care settings decreased use of illegal drugs and misuse of prescription drugs. Most recently, Garner and colleagues (2019)[30] found that MIBIs delivered in HSOs significantly reduced substance misuse. *Thus, research supports the effectiveness of MIBIs for addressing substance misuse in HIV service settings.*

Testing Strategies for Implementation and Sustainment

The significance of testing different strategies using type 3 hybrid trial designs. The challenge of implementing evidence-based health interventions (EBHIs) in practice settings is well-documented,[31-35] with estimates suggesting it takes approximately 17 years for 14% of original research to reach patient care.[36] Implementation research aims to improve implementation of EBHIs through "the study of methods to promote the adoption and integration of evidence-based practices, interventions and policies into routine health care and public health settings."[37] Although significant progress has been made, the field of implementation research remains in its infancy. Indeed, implementation research has succeeded in generating many models/frameworks,[38] as well as evidence to better understand key implementation barriers.[39-41] However, implementation research focused on the development and testing of strategies to effectively and cost-effectively address and overcome these barriers has been relatively limited. Additionally, Foy and colleagues (2015)[42] have noted, "If studies evaluating the effects of implementation interventions are to be of relevance to policy and practice, they should have end-points related to evidence-based processes of care." Thus, there is a significant need for implementation research that tests the effectiveness of implementation strategies in improving implementation outcomes and client outcomes, which Curran and colleagues (2012)[43] codified as hybrid trials. Dr. Garner's SAT2HIV-I Project, funded by the National Institute on Drug Abuse (NIDA), addressed this need by using a dual-randomized type 2 hybrid trial design that simultaneously tested the effectiveness of a MIBI to reduce substance misuse and the effectiveness of an innovative implementation strategy called Implementation & Sustainment Facilitation (ISF).[21,22] The SAT2HIV-II Project would address this need by using a type 3 effectiveness-implementation hybrid trial design to compare two strategies in terms of impact on implementation outcomes (primary aim) and client outcomes (secondary aim). This implementation research is especially critical in the context of major public health challenges such as substance misuse among PWH.

Consistent with NIH's encouragement to consider approaches previously used, we propose that the current control condition be the strategy found to be most effective as part of the SAT2HIV-I Project. Thus, the control condition will couple the staff-focused Addiction Technology Transfer Center (ATTC) strategy and the team-focused ISF strategy, which was found to be more effective than the ATTC strategy alone.[30] Consistent with the landmark research of Miller and colleagues (2004),[44] which provided the most rigorous support for the ATTC strategy in preparing staff to implement MIBIs, Dr. Garner and colleagues (2019)[30] found that ISF significantly improved implementation effectiveness (i.e., the *consistency* and *quality* of MIBI implementation). These results advanced implementation research on the effectiveness of facilitation (i.e., a process of interactive problem solving and support that occurs in a context of a recognized need for improvement and a supportive interpersonal relationship).[45-48] Although ISF improved implementation effectiveness beyond the ATTC strategy, our results suggested that room for improvement remained, especially with regard to sustainment.[30] Indeed, even the ATTC+ISF strategy did not appear to be sufficient for MIBI sustainment, with only about one-third of HSOs reporting MIBI sustainment at follow-up. *Thus, we believe building on the promising results of the SAT2HIV-I Project is the next logical step in advancing this area of implementation research.*

The significance of testing Pay For Performance (P4P) as an effective adjunct to the ATTC+ISF strategy. P4P (i.e., providing monetary bonuses for achieving predefined performance targets) has been recommended as a promising strategy to improve the quality of care and address the research-to-practice gap.[49-51] In 2008, the National Institute on Alcohol Abuse and Alcoholism funded Dr. Garner and his research team to conduct a type 3 hybrid trial to test the effectiveness of using P4P to improve implementation outcomes and client outcomes within community-based substance use treatment organizations implementing an EBHI for adolescent substance use.[52] More specifically, the P4P strategy was tested as an adjunct to a multifaceted strategy similar to the ATTC strategy.[53] As described by Garner and colleagues (2012),[54] P4P was found to have a significant impact on implementation outcomes and client outcomes. As such, we hypothesize that the P4P strategy (i.e., ATTC+ISF+P4P strategy) will improve implementation outcomes and client outcomes beyond the ATTC+ISF strategy. Additionally, we hypothesize that the P4P strategy will significantly improve sustainment by offering organizations monetary bonuses for developing a sustainment plan. *Thus, the proposed implementation research is significant because it will test the effectiveness of the P4P strategy as an adjunct to ATTC+ISF strategy, which may affect how the Health Resources and Services Administration (HRSA) funds the AIDS Education and Training Center (AETC) to support future HRSA-funded initiatives focused on improving the integration of MIBIs into HIV service settings.*

Identifying Implementation Strategies' Mechanisms of Change

Beyond understanding whether or not implementation strategies are effective, it is important that implementation research seeks to better understand *why* and *how* implementation strategies work (i.e., what the mechanisms of change are).[55] Thus, our research will seek to advance implementation research by examining the extent to which implementation climate (i.e., the extent to which the innovation is expected,

supported, and rewarded)[56] mediates the implementation condition to outcome relationship. We focus on implementation climate for several reasons. First, numerous implementation researchers have hypothesized implementation climate as the key construct that may explain the impact of implementation strategies on implementation effectiveness.[57-61] Second, implementation climate is one of the few constructs that has a psychometrically sound and pragmatic measure available.[62] Third and most importantly, the P4P strategy is specifically designed to enhance the dimension of implementation climate that may not be addressed by the ISF strategy (i.e., reward). *Thus, this exploratory aim will help advance knowledge by improving understanding regarding the extent to which implementation climate is a key mechanism of change.*

Public Health Relevance

There is an urgent public health need to end the HIV epidemic and more broadly to identify effective strategies to overcome (not just understand) barriers to implementing and sustaining EBHIs in practice settings. The proposed MIBI for substance misuse has been shown to be effective for reducing substance misuse. Additionally, the ATTC+ISF strategy has been shown to be an effective strategy for implementing this MIBI within HSOs. However, even with the ATTC+ISF strategy, room for improvement remains, especially regarding sustainment. Given P4P has been shown to be highly effective, it may be an effective adjunct to the ATTC+ISF strategy (i.e., ATTC+ISF+P4P strategy > ATTC+ISF strategy). However, due to the strength of the research design (i.e., a 30-site, cluster-randomized, type 3 hybrid trial), we believe implementation research will be advanced significantly even if our hypothesis is not supported (i.e., if the ATTC+ISF+P4P strategy is not able to significantly improve implementation outcomes or client outcomes beyond the ATTC+ISF strategy).

1.2 Study synopsis

The SAT2HIV-II Project is a prospective 30-site cluster-randomized type 3 hybrid trial that is regulated by the Department of Health and Human Services and focused on testing the effectiveness of a Pay For Performance (P4P) strategy as an adjunct to the multifaceted ATTC+ISF strategy, which Garner et al. (2020) found to be the most effective strategy for integrating a MIBI for substance misuse into HSOs. The control condition, which will be provided to all participating HSOs, consists of the following for MIBI staff: 1) a 5-hour online introduction to MI course, 2) three 4-hour virtual training workshops that are focused on the MIBI, 3) standardized feedback reports regarding the fidelity with which each MIBI was implemented, 4) monthly 30-60-minute virtual group consultation calls with an MI expert regarding how to improve fidelity, and 5) monthly 30-60-minute virtual ISF team meetings with an implementation expert. In addition to these strategies, MIBI staff at HSOs randomized to the experimental condition will have the opportunity to earn a $10 bonus for each MIBI implemented, as well as an additional $10 bonus for each MIBI that is rated as meeting or exceeding the quality benchmark (i.e., 80th percentile fidelity score from the SAT2HIV-I Project). For leadership staff at all participating HSOs regardless of condition, participation consists of monthly 30-60-minute virtual ISF team meetings with an implementation expert. Other procedures that are included for research purposes only are online surveys with consenting staff and client participants.

2 OBJECTIVES & OUTCOMES

2.1 Objectives

The objective of the SAT2HIV-II Project is to test the effectiveness of P4P in improving implementation, sustainment, and client outcomes. Specific aims and hypotheses are:

Primary aim: Test the impact of ATTC+ISF+P4P on *implementation outcomes*.

Primary hypothesis: Relative to ATTC+ISF, ATTC+ISF+P4P will achieve significant improvements in staff-level measures of MIBI implementation consistency, MIBI implementation quality, MIBI sustainment consistency, and MIBI sustainment quality.

Secondary aim: Test the impact of ATTC+ISF+P4P on *client outcomes*.

Secondary hypothesis: Relative to ATTC+ISF, ATTC+ISF+P4P will achieve significant reductions in client-level measures of substance use, anxiety symptoms, and depression symptoms.

Exploratory aim: Test the extent to which implementation climate mediates the implementation condition to outcome relationship.

Exploratory hypothesis: Implementation climate will partially mediate the relationship between implementation condition and each of the outcomes in the primary and secondary aims.

2.2 Implementation outcomes

The SAT2HIV-II Project's four implementation outcomes are:

MIBI implementation consistency: The cumulative number of MIBIs that each MIBI staff member implemented during the implementation phase.

MIBI implementation quality: The cumulative sum quality score that each MIBI staff member demonstrated during the implementation phase. Each MIBI session will be rated using the Lyssn Platform and the Independent Tape Rater Scale.[63]

MIBI sustainment consistency: The cumulative number of MIBIs that each MIBI staff member implemented during the sustainment phase.

MIBI sustainment quality: The cumulative sum quality score that each MIBI staff member demonstrated during the sustainment phase. Only the Lyssn Platform will be used to rate each MIBI session during the sustainment phase.

2.3 Client outcomes

The SAT2HIV-II Project's three client outcomes are:

Days using primary substance: The number of days clients used their primary substance (i.e., the substance the client identified a willingness to talk about during the MIBI) during the past 28 days, collected via the Addiction Severity Index—Lite.[64]

Anxiety: The sum of the 7 items included in the Generalized Anxiety Disorder (GAD-7) instrument.[65] Bahorik and colleagues (2016)[66] found reductions in substance use to be associated with reductions in anxiety as measured by the GAD-7.

Depression: The sum of the 8 items included in the Patient Health Questionnaire (PHQ-8) instrument.[67] Bahorik and colleagues (2016)[66] found reductions in substance use to be associated with reductions in depression.

3 SUBJECT SELECTION

Consistent with the goal of the funding opportunity, subjects for the SAT2HIV-II Project are limited to those from HSOs supported by HRSA Ryan White funding. Below are descriptions regarding the selection of HSO staff and client participants, the latter of which are considered a vulnerable population due to having HIV.

3.1 HSO staff

Each collaborating HSO will select their staff to be invited to participate as part of the project. Staff may participate as leadership staff or as MIBI staff.

3.2 HSO clients

All HSO clients who have been diagnosed with HIV and are 18 years of age or older will be invited to participate in the project.

4 INFORMED CONSENT

4.1 HSO staff

A participation agreement, memorandum of understanding, and/or subgrant will be executed between RTI International and each of the project's collaborating HSOs. Each collaborating HSO will select staff to be invited to participate in the project, and all staff must give their informed consent to participate. The project's RTI-based research staff will send each identified staff member an email with a link to the online informed consent. Both the email and the informed consent will emphasize that participation in the project is voluntary and to contact Dr. Garner by phone (919-597-5159) or email (bgarner@rti.org) if they have any questions or concerns.

4.2 HSO clients

During the project's implementation phase, we will seek to inform all HSO clients who have been diagnosed with HIV and are 18 years of age or older about the research project. A copy of the project's participant recruitment flyer will be included as part of the collaborating HSOs' pre-appointment paperwork and posted on the HSOs' bulletin boards and websites. Interested individuals may access the online informed consent via their own internet-capable device or, as described on the recruitment flyer, they may request to use one of the project's electronic tablets. As noted on the recruitment flyer and in the informed consent, individuals may call the project's toll-free number (to be determined) or email the project's email address (sat2hiv@rti.org) with any questions or concerns they have about the project, both of which are monitored by the project's RTI-based research staff.

5 STUDY PROCEDURES

5.1 HSO staff

The expected duration of participation for each HSO staff participant is 19 months. Organized chronologically, below are the study procedures. All online staff surveys will be programmed using Voxco.

Complete baseline staff survey. During month 1, all consenting staff participants will be emailed a unique link to the project's online baseline staff survey, which will take about 25 minutes to complete. Each staff participant who completes the baseline staff survey will receive $25 as compensation.

Complete online introduction to motivational interviewing course. During month 1, all MIBI staff participants will be emailed a link to the project's 5-hour online introduction to motivational interviewing course.

Participate in virtual motivational interviewing training workshop. During month 2, all MIBI staff participants will be emailed a Zoom training link and passcode for each of the project's three 4-hour motivational interviewing training workshops.

Complete follow-up staff survey. During month 2, after the training workshops, all MIBI staff participants will be emailed a unique link to the project's online follow-up staff survey, which will take about 25 minutes to complete. Each staff participant who completes the follow-up staff survey will receive $25 as compensation.

Submit recording of MIBI roleplay session. Beginning in month 2, after the completion of the project's second motivational interviewing workshop training, all MIBI staff participants will be asked to submit a recording of their MIBI roleplay session that will be conducted with one of their organization's other MIBI staff participants.

Submit recordings of MIBI sessions with client participants. After demonstrating proficiency via a MIBI roleplay session, all MIBI staff participants will be asked to submit a recording for each MIBI session they implement with a client participant.

Review standardized motivational interviewing fidelity feedback reports. Each MIBI session recording will be rated for fidelity, and MIBI staff participants will be asked to review each fidelity feedback report.

Participate in MIBI consultation meetings. Beginning in month 3, all MIBI staff participants will be asked to participate in monthly 30-60-minute virtual group consultation meetings with an MI expert.

Participate in ISF meetings. Beginning in month 1, all staff participants will be asked to participate in monthly 30-60-minute virtual ISF team meetings with an implementation expert.

Complete follow-up staff surveys. At months 7, 13, and 19, all staff participants will be emailed a unique link to the project's online follow-up staff survey, which will take about 25 minutes to complete. Each staff participant will receive $25 as compensation for each follow-up staff survey completed.

5.2 HSO clients

The expected duration of participation for each HSO client participant is about 1 day if the MIBI is not recommended based on their answers on the initial assessment or about 5 weeks if the MIBI is recommended. All online client assessments will be programmed using Voxco. For all online client assessments, client participants will access them either via a unique link that is emailed to them or by entering a unique participant ID that is emailed to them.

Complete initial assessment. All consenting client participants will be asked to complete an online initial client assessment, which will take about 10 minutes to complete. Each client participant who completes the initial client assessment will receive $10 as compensation.

Participate in a MIBI session. Client participants for whom the MIBI is recommended will be asked to participate in a 15-30-minute MIBI session with one of the project's trained MIBI staff, which will be recorded for quality assurance purposes.

Complete pre-MIBI assessment. Client participants who participate in a MIBI session will be asked to complete an online pre-MIBI client assessment, which will take about 20 minutes to complete, immediately prior to receiving the MIBI session. Each client participant who completes the pre-MIBI client assessment will receive $20 as compensation.

Complete post-MIBI assessment. Immediately after receiving the MIBI session, client participants will be asked to complete an online post-MIBI client assessment, which will take about 10 minutes to complete. Each client participant who completes the post-MIBI client assessment will receive $10 as compensation.

Complete 4-week follow-up assessment. Four weeks after receiving the MIBI session, client participants will be asked to complete an online follow-up client assessment, which will take about 10 minutes to complete. Each client participant who completes the follow-up client assessment will receive $10 as compensation. Client participants who complete the follow-up client assessment within 24 hours of being emailed their unique link will receive $10 in bonus compensation. Client participants who complete the follow-up client assessment within 48 hours of being emailed their unique link will receive $5 in bonus compensation.

6 RISKS TO PARTICIPANTS

6.1 HSO staff

The risks of participating in the research itself are considered minimal. Additionally, participating does not include any physical risks. One potential risk is breach of confidentiality, such that unauthorized persons could get access to personal or study-related information. Another potential risk is that staff could feel uncomfortable or anxious about answering some survey questions or having MIBI session recordings rated for fidelity.

6.2 HSO clients

The risks of participating in the research itself are considered minimal. Additionally, participating does not include any physical risks. One potential risk is breach of confidentiality, such that unauthorized persons could get access to personal or study-related information. Another potential risk is that clients could feel uncomfortable or anxious about answering some survey questions or having their MIBI session recorded.

7 CONFIDENTIALITY OF STUDY-RELATED RECORDS

The study will be made available for monitoring, auditing, IRB review, and regulatory inspection by providing direct access to study-related source data. Study-related records identifying research participants will be kept confidential (i.e., will only be accessible to the project's authorized research staff) and, to the extent permitted by applicable laws and/or regulations, will not be made publicly available. All study-related records identifying research participants will be destroyed at the end of the study. Recordings of the MIBI sessions will be stored on a HIPAA-compliant cloud managed by Lyssn, with a back-up copy saved on RTI International's enhanced security network server. Recordings of the MIBI sessions will be stored for the duration of the project and destroyed at the end of the project.

8 STUDY OVERSIGHT

Oversight of the study will be the responsibility of the Principal Investigator, including the identification of any conditions that may require premature termination. The study will be made available for monitoring, auditing, IRB review, and regulatory inspection by providing direct access to study-related source data.

9 MONITORING/REPORTING OF DATA AND SAFETY

Responsibility. The research is believed to pose minimal risk to study participants. The Principal Investigator of the research will be responsible for executing the project's data and safety monitoring plan, which will (1) ensure the integrity and security of study data, (2) safeguard the confidentiality of participant data, (3) monitor participant experiences in the study for evidence of potential danger or abuse of the participants or threat of harm by the participants to themselves or to others, and (4) monitor data for possible adverse effects (AEs) of the study and take steps to remedy any that are found.

Data to be collected and monitored. Staff participant data to be collected are staff surveys and digital audio recordings of MIBI staff participants delivering the MIBI. Client participant data to be collected are client assessments and digital audio recordings of MIBI sessions. The staff survey data, client assessment data, and MIBI session fidelity data will be monitored monthly by the data analysis team.

Safety monitoring. An AE is any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's

participation in the research, whether or not considered related to the subject's participation in the research. A serious adverse event (SAE) is one that meets one or more of the following criteria: (1) results in death, (2) is life-threatening (places the subject at immediate risk of death from the event as it occurred), (3) results in inpatient hospitalization or prolongation of existing hospitalization, or (4) results in a persistent or significant disability or incapacity. All research staff will be trained to identify and report AEs and SAEs. Any AE or SAE will be reported to the PI within 24 hours. The PI will record all reported events with start dates occurring from when informed consent is obtained through 7 days (for non-serious AEs) or 30 days (for SAEs) after the last day of study participation. Events will be followed for outcome information until resolution or stabilization. When reporting an AE or SAE, the following will be reported: (1) research protocol information (e.g., title, investigator's name, and IRB number); (2) a detailed description of the adverse event, incident, experience, or outcome; and (3) a description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the AE or SAE. Additionally, to satisfy the requirement for prompt reporting, we will report unanticipated problems using the following timeline:

- Unanticipated problems that are SAEs will be reported to the IRB within 1 week of the PI becoming aware of the event.
- Any other unanticipated problem will be reported to the IRB within 2 weeks of the PI becoming aware of the problem.
- IRB actions (e.g., approval, violations) will be reported to NIDA as part of the annual progress reports.

10 DATA ANALYSIS PLAN

All analyses will follow the intent-to-treat principle and will be conducted using R, SAS, or Mplus. The distribution of each outcome will be examined before analysis. If a distribution exhibits sufficient nonnormality, we will consider other distributions as an alternative to the normal distribution. Doing so will yield more accurate standard errors and p-values. To assess whether distributional choices were appropriate, we will conduct residual diagnostics. Before fitting mixed effects regression models, we will examine variance partitioning between the levels. Intraclass correlations (ICCs) will be estimated and included in publications. Organized by aim, below are descriptions of the sample size, missing data, power, and analysis plan.

Primary Aim. Analyses on the impact of the P4P strategy (i.e., ATTC+ISF+P4P compared to ATTC+ISF) on staff-level outcomes will be analyzed using a three-level mixed-effects regression model (repeated-measures *t* nested in staff *s* nested in organization *o*) with an appropriate distributional assumption. The primary predictor will be the P4P indicator (an organization-level predictor), and its estimated effect is $\boldsymbol{\beta_2}$. Random intercepts $\boldsymbol{\beta_{0so}}$ will adjust for organization differences. Random slopes $\boldsymbol{\beta_{1so}}$ allow for change over time. The basic reduced form of the model is $\boldsymbol{y_{tso} = \beta_{0so} + \beta_{1so}Time + \beta_2 P4P + \varepsilon_{tso}}$. This model will be generalized with a link function if the outcome $\boldsymbol{y_{tso}}$ is nonnormal. Model comparisons will be used to select an appropriate trajectory shape (e.g., linear, quadratic) for the *Time* variable. A sensitivity analysis will

be conducted for each outcome by adding potential staff-level confounders (e.g., sex, race) to the model.

Secondary Aim. Analyses on the impact of the P4P strategy (i.e., ATTC+ISF+P4P compared to ATTC+ISF) on client-level outcomes will be analyzed using a three-level mixed-effects regression model (clients *c* nested in staff *s* nested in organization *o*), with an appropriate distributional assumption. The primary predictor will be organizational-level condition assignment (ATTC+ISF+P4P condition = 1; ATTC+ISF condition = 0), and its estimated effect is $\boldsymbol{\beta_2}$. Random intercepts $\boldsymbol{\beta_{0so}}$ will adjust for organization and staff differences. Random intercepts will adjust for organization and staff effects on the relationship between baseline client outcomes and the follow-up outcome $\boldsymbol{\beta_{1so}}$. The basic reduced form of the model is $\boldsymbol{y_{cso(follow-up)} = \beta_{0so} + \beta_{1so} y_{cso(baseline)} + \beta_2 P4P + \varepsilon_{cso}}$. A sensitivity analysis will be conducted for each outcome by adding potential staff-level and client-level confounders (e.g., sex, race) to the model.

Exploratory Aim. For the exploratory aim, we will use the staff-level data and client-level data used above, as well as the average implementation climate score for each MIBI staff member (i.e., the hypothesized mediator). We will apply a Baron-and-Kenny-style mediation approach, which uses centering within context and includes a group mean at level three. Step 1 is that the outcome will be regressed on the condition variable (ATTC+ISF+P4P condition = 1; ATTC+ISF condition = 0) in a multilevel regression. Step 2 is that the outcome will be predicted by both condition and the group mean-centered mediator (i.e., implementation climate) in a multilevel regression. Step 3 is that the mediational effect will be calculated by subtracting the estimated coefficient associated with condition in Step 2 from the estimated coefficient associated with condition in Step 1. This method will allow the between-group mediation effect to be partitioned from the within-group mediation effect, which is important because between-group mediation is the effect of interest. Significance of the mediation effect will be calculated using the Freedman and Schatzkin *t* statistic.

11 INTENDED USE OF THE DATA

The data collected as part of this research is primarily intended to help improve generalizability of knowledge about how best to improve integration of care for HIV and substance misuse within HIV service settings. The data is also intended to help contribute to generalizable knowledge about how to reduce the research-to-practice gap, which is a significant problem across numerous areas of health.

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13 GLOSSARY OF ABBREVIATIONS

AE ..... Adverse effect

AETC ..... AIDS Education and Training Center

AIDS ..... Acquired immunodeficiency syndrome

ATTC ..... Addiction Technology Transfer Center

EBHI ..... Evidence-based health intervention

GAD-7 ..... Generalized Anxiety Disorder-7 instrument

HIPAA ..... Health Insurance Portability and Accountability Act

HIV ..... Human immunodeficiency virus

HRSA ..... Health Resources and Services Administration

HSO ..... HIV service organization

ICC ..... Intraclass correlation

ID ..... Identifier

IRB ..... Institutional review board

ISF ..... Implementation and Sustainment Facilitation

MI ..... Motivational interviewing

MIBI ..... Motivational interviewing-based brief intervention

NIDA ..... National Institute on Drug Abuse

P4P ..... Pay for performance

PHQ-9 ..... Patient Health Questionnaire-9 instrument

PI ..... Principal investigator

PWH ..... People with HIV

RTI ..... Research Triangle Institute

SAE ..... Serious adverse event

SAS ..... Statistical Analysis System

SAT2HIV-I ..... Substance Abuse Treatment to HIV Care I Project

SAT2HIV-II ..... Substance Abuse Treatment to HIV Care II Project