Parent Grant Specific Aims

Integrating Assisted Partner Service and Phylogenetics for HIV-HCV Prevention (1R01DA043409-01)

ABSTRACT: To contain the HIV epidemic in Kenya, innovative strategies are essential to identify and treat key populations such as HIV-infected persons who inject drugs (PWID), and reduce onward transmission to their sexual and/or needle-sharing partners. Our primary objective is to determine how many needle-sharing and sexual partners per HIV-infected PWID accessing HIV testing services can be tested, diagnosed with HIV or HCV, and engaged in care through assisted partner notification services (APS). Aims 2 and 3 leverage APS to identify new HIV and HCV cases and use phylogenetics to characterize modes of transmission and risk factors for ongoing HIV and HCV transmission in this key population.

AIM 1. To determine whether assisted partner notification services (APS) can identify, and link to care, the sexual and needle-sharing partners of HIV-infected and HIV/HCV co-infected PWID. Partner notification and contact tracing will be offered to 1000 PWID who test positive for HIV on initial screening or are known to have HIV (index cases), an estimated 50% of whom will be co-infected with HCV. Through provision of APS, we will identify new cases of HIV and HCV and contact known HIV cases who are not in care.

AIM 2. To define the risk factors for onward HIV transmission among PWID, and to elucidate the role of PWID in the overall Kenyan HIV epidemic, using phylogenetic analysis. We will use HIV *pol* gene sequences, and linked epidemiological data, from 1000 HIV-infected PWID, for advanced phylogenetic analyses.

AIM 3. To characterize the modes and risk factors for onward HCV transmission among PWID using viral phylogenetics. We will use HCV *NS5B* gene sequences, and linked epidemiological data from 1000 HCV-infected PWID, for advanced phylogenetic analyses.

Specific Aims of Proposed Diversity Supplement

This Diversity Supplement will draw upon the Rhodes et al. (2002) risk environment framework and the HIV care continuum to assess health outcomes among HIV-positive PWID in Nairobi, Kenya.[15,28] The risk environment framework suggests HIV drug-related harms (i.e., needle sharing, sexual risk-taking and overdose) are not derived solely from individuals, but rather a product of their surrounding environment. The proposed Supplement employs a sequential mixed methods design, where Aim 1 qualitatively characterizes the Nairobi-specific risk environment within the following four main domains: physical, social, economic, and political environments; with the oversampling of women to provide robust gender-specific environmental influences. Emergent findings (Aim 1) will be incorporated into the parent questionnaire for Aim 2, which will quantitatively assess associations between risk environment and stages of the HIV care continuum (i.e., retention in care, antiretroviral therapy [ART] adherence, and viral load [VL] suppression) among HIV-infected PWID and their sexual and/or needle sharing partners. This will allow us to identify environmental risk factors associated with suboptimal prospective engagement in care (i.e., discontinued care or treatment, no longer virally suppressed) over a 6-month period, which may be unique to PWID in Kenya and ultimately strengthen HIV programs and services targeting this key population, reduce HIV transmission risk and improve health outcomes.

Aim 1: Characterize the risk environment among HIV-positive, PWID index and sexual/needle-sharing partners, by drawing upon the Rhodes et al. (2002) risk environment framework[15,36] and Theory of Gender and Power to a) determine Kenya-specific risk environment factors and b) highlight existing gender differences. Overarching themes will be incorporated into the parent questionnaire in order to gain additional evidence on the effects of the risk environment on HIV care and treatment. *Hypothesis:* We anticipate the following emergent themes related to the four risk environment domains: physical (e.g., injecting in public spaces), social (e.g., sharing drug equipment, policing practices, treatment by medical providers), and political (e.g., supporting needle-syringe programs) environments. We also predict women will reveal factors related to reduced household and community autonomy that impact their ability to engage in HIV care in ways not experienced by men.

Aim 2: Determine risk factors associated with the stages of the HIV care continuum at (a) baseline and (b) over the 6-month follow-up period for HIV-infected PWID participants and their sexual and/or needle sharing partners through a two-step process. At baseline, we will identify environmental factors associated with three stages of the HIV care continuum (e.g., engagement in care, ART adherence and VL suppression), and during the 6-month follow-up, we will assess factors associated with suboptimal HIV care (i.e., discontinued care or treatment, no longer virally suppressed). *Hypothesis:* We predict that individuals further along the HIV care continuum at baseline and compliant with the HIV treatment guidelines will have fewer risk environment barriers, fewer mental health and substance use issues, and more social support compared to individuals in the early stages of the continuum.

A. SIGNIFICANCE

A.1. In Kenya, key affected populations contribute disproportionately to the HIV/AIDS epidemic, and this is likely to increase as HIV prevention and treatment services penetrate the general population but fail to reach marginalized groups.[1,2] Among persons who inject drugs (PWID), HIV prevalence estimates reach 30-50% in men and >50% in women.[2-4] HIV/AIDS represents a large health burden with more than 1.6 million people infected and 36,000 annual deaths.[2] The 2014 Kenyan National Health Survey found that more than half (53%) of people living with HIV were unaware of their status and of those aware of their status, 40% were not on treatment, making them at high risk for disease progression and transmission.[1] Emphasis in Kenya and other parts of sub-Saharan Africa has been on testing the general population, with far less investment in HIV testing and engaging in care within key affected populations, which includes PWID, female sex workers and men who have sex with men.[1] The Kenyan National AIDS Strategic Framework highlights the need to provide evidence-based programs and services to key affected populations, which represents one-third of the newly diagnosed HIV infections.[1,2] The strategic framework was developed around the UNAIDS 90-90-90 Goals, whereby 90% of all people living with HIV will know their status, of those diagnosed 90% will be on antiretroviral therapy (ART), and of those on treatment 90% will be virally suppressed by the year 2020.[5] Progress has been made towards meeting these goals; however, five factors continue to influence new infections within the key affected populations including: 1) Socio-cultural factors (e.g., stigma, discrimination, vulnerability among women); 2) High risk sexual behaviors (e.g., concurrent sexual partners, transactional sex, marginalization of the LGBT community); 3) Biological factors (e.g., low prevalence of male circumcision); 4) Economic factors (e.g., increased labor migration, poverty); 5) Political factors (e.g., weak social and legal protection for key affected populations, high rates of criminalization, poor enforcement of anti-discrimination laws).[1,6,7]

Injection drug use is increasingly contributing to the HIV epidemic with the expansion of drug trafficking networks and an estimated 30,000 PWID in Kenya, 30-50% of whom are likely to be HIV-infected.[8,9,11] Of particular concern are national estimates suggesting 80% of PWID are unaware of their HIV status.[1,12] The vast majority of PWID are concentrated in Nairobi, Mombasa and Kisumu, which have all seen increases in their PWID communities.[11] As regional drug patterns fluctuate, so will the behaviors and patterns of injecting drugs among users, a population known to engage in extremely high-risk HIV behaviors.[3] Needle sharing and unprotected sexual acts with concurrent sex partners, sex workers, and transactional sex partners, increase the risk of HIV transmission between sexual and needle-sharing partners.[10] Women are a minority in the PWID community, but HIV prevalence is estimated to be >50% for this subpopulation in some settings.[13] In order to reach the UNAIDS 90-90-90 goals in Kenya, key populations should be tested frequently, linked to care at the point of diagnosis and be engaged in HIV care in order to achieve viral suppression. This research proposal focuses on the growing group of PWID, who are either HIV-infected or at high risk for HIV infection.

Table 1. Proposed constructs for drug-risk environment (Rhodes et al.) [14-16]

Categories	Examples of variables
Physical	- Drug-using practices, injecting and commercial sex work locations - Drug injecting in public spaces - Drug availability and purity
Social	- Social and peer group 'risk' norms (e.g., sharing injection equipment) - Local policing practices (e.g., police associated with HIV treatment centers, following formal laws) - Community healthcare (e.g., HIV care), social services and HIV ancillary services - Gender inequities associated with risk - Stigmatization and marginalization of PWID
Economic	- Cost of living and healthcare services (e.g., HIV services, drug treatment, etc.) - Cost of prevention materials (e.g., clean injection equipment, condoms, etc.) - Lack of employment opportunities (both formal and informal)
Policy	- Availability and coverage of clean injection equipment (e.g., needles, cooker, water, etc.) - Policies surrounding harm reduction (e.g., needle exchange programs and possession of syringes) - Policies targeting treatment access for PWID

A.2. Drug risk environments have played a critical role in preventing the forward transmission of HIV within other PWID settings and this proposal aims to understand specific risk factors in Kenya and sub-Saharan Africa that would lead to improving programs and services. Growing evidence highlights the aggregate effects that the surrounding environment has on shaping the HIV risk among PWID.[14-18] Moreover, interventions that target only individual-level factors may be limited in their effectiveness to achieve and sustain change. To address this, Rhodes and colleagues developed a 'risk environment' framework that posits the

consequence of HIV among PWID are not solely derived from individual behavior, but are rather a by-product of the surrounding physical, social, political and economic environment (Table 1).[14,15] The physical environment encompasses fixed features surrounding the PWID community including spaces where drug-use takes place, drug availability and quality, injection practices, and spaces where the buying, selling or trading of sexual acts take place.[15] The social environment includes networks of peers, healthcare providers, figures of authority (e.g., law enforcement), gender inequalities and stigma surrounding the community which have a vital role in HIV risk reduction.[15] In comparison, the economic environment includes financial barriers associated with drug use and HIV risk including the cost of living, expenses tied to injection equipment and employment opportunities, including legal and illegal markets.[15] Finally, the political environment includes laws and policies that determine whether harm reduction strategies are legal, including needle exchange programs and safe haven facilities (i.e., areas where PWID can access healthcare services without harassment)[15]. Considered together, the components of the drug risk environment as a unit of analysis will overcome the limits of individual behaviors, embedded within most HIV prevention interventions, and will convey how drug-related harms intersect with health and vulnerability more generally.[14,15] **This proposed diversity supplement will define facilitators and barriers within the surrounding risk environment for PWID according to their stage in the HIV care continuum (e.g., engagement in care, use of ART and viral suppression) and will provide invaluable information for practical HIV interventions for the PWID community in Kenya.**

A.3. Integrating assisted partner notification services (APS) within existing harm reduction services helps to identify PWID living with HIV, many of whom may not know their status and face unique barriers to accessing and remaining in care and treatment.[19-21] In 2012, Nairobi established its first needle-syringe program (NSP) to curb HIV transmission and provide ancillary medical services (e.g., HIV testing and treatment) within this marginalized group.[22] Traditionally, NSP's have served as harm reduction strategies to prevent new infections and thus reduce forward transmission of HIV, but many are now leveraging their position within the PWID community to provide additional services to address the HIV epidemic.[23-25] For instance, APS is a testing strategy that has been successfully used to test and link thousands of HIV-infected individuals to care in the general population in Kenya, Mozambique, Cameroon and the United States.[19,20] APS involves collecting injection and sexual partner contact information from persons testing positive for HIV, and using health advisors as mediators to offer testing and referrals after notification of exposure.[19,20] The parent grant employs APS, a novel approach in Kenya, through established NSPs. Communication and disclosure of HIV risk behaviors represents a key area of epidemiologic importance in terms of prevention, treatment and the potential for tailored interventions.[26, 27] Previous studies demonstrate that shame and stigma surrounding HIV are associated with non-disclosure (i.e., purposely not discussing drug use and HIV status) and failure to seek care and treatment, which further isolates community members and perpetuates the epidemic.[26] In addition to identifying HIV infections among those unaware of their status, and additional critical part of APS is linking HIV-infected PWID to care services, regardless of their HIV status awareness.[26, 27] While similar studies have been conducted in high and middle-income countries, less is known about the barriers to accessing treatment and retention in care in Kenya. This supplement aims to highlight factors associated with engagement in HIV care, treatment adherence and viral load suppression, in order to improve current programs and services.

A.4. The HIV care continuum provides an underlying framework to track the progress of HIV-positive PWID and their syringe and/or needle-sharing partners through APS.[28,29] The HIV care continuum is a widely-accepted framework that outlines the sequential stages of HIV care that persons living with HIV experience.[28,29] This includes testing persons who are unaware of their HIV status, linking those diagnosed to HIV care, retaining HIV-positive individuals in care, ART adherence, and viral load suppression.[28,29] Loss to follow-up is a significant disruption to this pathway and a common outcome among HIV-positive PWID who face several barriers to accessing HIV care and treatment.[30,31] Challenges to HIV testing and engagement in care include locating 'hidden' or hard-to-reach populations, addressing HIV-related medical expenses, and overcoming mistrust of medical professionals, discrimination and stigma towards PWID.[30,31] Competing needs (i.e., housing, employment, safety) and co-morbidities, mainly mental health issues, sexually transmitted infections, and dual chemical dependencies are all barriers to HIV care in PWID communities.[30,31] In addition, adherence to ART medication can be a challenge for individuals with substance use disorders due to housing insecurity, violence, symptoms of drug withdrawal, and side effects resulting from multiple substances.[32,33] HIV testing is a critical entry point for HIV prevention and treatment (Aim 1, parent grant), but research should also investigate barriers and facilitators to HIV care post-diagnosis and work towards the ultimate goal of HIV viral suppression. Maximizing retention throughout the HIV care continuum will benefit both individuals and the community by improving health outcomes and reducing risk of further HIV transmission.[28,29] Using the HIV care

continuum framework can be a useful tool in evaluating the progress made towards the UNAIDS 90-90-90 Goal, and can be particularly useful in determining the unmet needs of a marginalized community.[33]

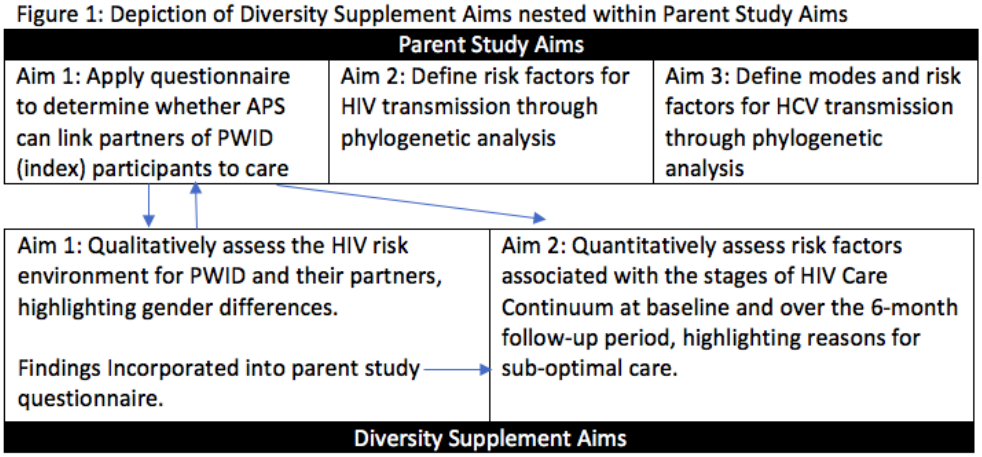
B. APPROACH

Overview of Parent Study & Diversity Supplement

The purpose of the parent study is to determine whether assisted partner notification services (APS) is an effective method for finding and linking newly diagnosed partners to care and to define HIV and HCV risk factors associated with transmission through phylogenetic analysis. HIV-infected PWID are recruited and enrolled from NSP sites and provide contact information for their sexual and/or needle sharing partners. Health advisors attempt to contact partners and offer them HIV testing and counseling. Eligibility criteria for index participants include: current injection drug user, HIV-seropositive, 18 years or older and willing to provide contact information on sexual and/or needle sharing partners. APS is conducted through health advisors who have extensive experience tracing and providing care to this marginalized population. The parent study will undergo pilot testing in January 2018 to ensure that all study staff are trained and all protocols are implemented as intended. Data collection is expected to start in February 2018, with 1000 PWID (index) participants and at least 1000 referred partners (2000 total study participants) enrolled in the study.

The goal of the proposed Diversity Supplement uses a sequential mixed methods study design, where Aim 1 will qualitatively characterize the Nairobi-specific drug risk environment factors among HIV-positive, PWID and their sexual and/or needle-sharing partners, with a particular focus towards gender differences. Emergent findings will be incorporated in the parent study questionnaire. Following the incorporation of emergent risk environment factors into the parent study questionnaire, we will conduct (a) a cross-sectional analysis to assess risk environment factors associated with failures along the HIV care continuum at baseline and (b) and a longitudinal analysis to determine whether risk environment factors are associated with suboptimal outcomes over the 6-month follow-up period (falling out of HIV care, non-ART adherence, unsuppressed viral loads) (Aim 2). The Diversity Supplement will draw upon the existing framework of the parent grant and contribute key findings associated with the Kenya-specific risk environment to the parent study questionnaire, which will provide a tailored approach to addressing the needs of this vulnerable population (**Fig. 1**).

Figure 1: Depiction of Diversity Supplement Aims nested within Parent Study Aims



Study Team

The proposed Diversity Supplement will be attached to the R01 parent grant, "Integrated Partner Services and Phylogenetics for HIV and HCV Prevention." The study team is composed of individuals from the University of Washington (UW), the Kenya Ministry of Health (MOH), Kenya National AIDS and STD Control Program (NASCOP), Kenyatta National Hospital (KNH), Support for Addiction Prevention and Treatment in Africa (SAPTA), and the University of KwaZulu-Natal, Durban, South Africa.

The requested support will be for Ms. X [student], a doctoral student in the Department of Epidemiology at the University of Washington. Ms. X has substantial experience in substance use research along the U.S.-Mexico border, where she worked with scientists from UC San Diego. Her research interests include in the intersecting epidemics of HIV and substance, in both national and global settings. Post-graduation plans include a post-doctorate program that focuses on issues surrounding HIV and substance use, with long-term career plans of building a career in academic research. Ms. X's two primary mentors play integral roles on the parent grant, Drs. Y, (MPI) and Z (Co-I). Dr. Y is a Professor at the University of Washington in the Departments of Global Health, Medicine, and Epidemiology and the Director of the UW Kenya Research and Training Center. She has chaired dissertation committees for 14 doctoral students, most of whom have been in Epidemiology and transitioned into academic careers, and will serve as a primary mentor for Ms. X during the course of the award. Dr. Z is an Infectious Disease Epidemiologist and serves as an Assistant Professor in the Departments of Epidemiology and Global Health. He serves as Ms. X's academic advisor and will be a co-primary mentor, overseeing her academic progress and contributions to the project. Both primary mentors have extensive

experience in working with HIV-positive and key affected populations in Kenya. Three secondary mentors will include a qualitative researcher, Dr. A; a substance use researcher with expertise in environmental risks, Dr. B; and a Kenyan-based clinical researcher, Dr. C. Ms. X will be supported by both primary and secondary mentors until the completion of her study aims and research deliverables.

Study Design Aim 1

Aim 1: Characterize the risk environment among HIV-positive PWID and their partners.

Rationale: The goal of Aim 1, will be to capture subtle differences within the risk environment between (a) men and women and (b) Kenya-specific barriers and facilitators to the HIV care continuum through qualitative inquiry. The risk environment framework by Rhodes et al suggests drug-related harms are not solely derived from individuals, but are the culmination of the surrounding social, physical and political environments.[14-16] While the drug risk environment has been described in other settings in Africa (e.g., South Africa) and elsewhere, there is limited evidence about the risk environment and how it relates to HIV in Nairobi, Kenya.[35] We hypothesize that the risk environment is different in Nairobi based on different governmental policies and distinct community settings, and we will draw on previously described methods and models to define the Kenya-specific risk environment. [13,14,16] In addition, a particular focus will be on power inequities in the drug risk environment that affect women's ability to engage in safe injection practices. Interview questions and qualitative analysis will incorporate the Theory of Gender and Power and the HIV care continuum as underlying frameworks.[28,29,35,36] Program and service providers working with HIV-positive PWID in Nairobi, will be able to use these findings to develop targeted programs in the future that use scientific evidence as a foundation. This information is also useful for research on HIV-positive PWID in the United States, where HIV incidence has increased and harm reduction programs are new or non-existent due to opposing political views (e.g., Southern states).

We will apply purposive sampling techniques to oversample marginalized PWID subpopulations that may be most at-risk (e.g., women, participants with sub-optimal HIV care). This recruitment technique, will provide us with robust data from a range of PWID experiences. Data collection will be achieved through in-depth interviews, interviewer field notes, which will be followed by open coding and thematic analysis. Emergent themes from the analysis will be categorized into topologies and then used to develop additional questions of interest for the parent study questionnaire. These additional questions will be incorporated into the baseline and follow-up questionnaire 6-months after the parent study enrollment begins.

Study Design Aim 2

Aim 2: Determine the level of engagement in HIV care and identify key risk factors associated with suboptimal engagement in care among HIV-infected PWID at baseline and over the 6-month follow-up period.

Rationale: The parent study is collecting information on current engagement with the HIV care continuum at baseline and 6-months in order to determine the effects of APS in testing and linking sexual and/or needle-sharing partners into HIV care (Aim 1 of parent study). This Diversity Supplement will assess later stages of the HIV care continuum: engagement/retention, antiretroviral therapy [ART] adherence, and viral load [VL] suppression of both index PWID and their referred partners. This analysis will be useful to HIV care providers and administrators to tailor their services for HIV-positive PWID and those developing prevention strategies for the future.

The parent study questionnaires will be modified to incorporate qualitative findings from Aim 1 of this supplement to determine whether Kenya-specific risk environment factors are associated with the HIV care continuum at baseline (Aim 2a) and sub-optimal care at the 6-month follow-up period (Aim 2b). The final goal of Aim 2, which utilizes baseline and follow-up data collected through the parent study, will prospectively analyze a set of *a priori* risk environment questions that have been identified through previous studies (**Table 1**) and newly developed questions derived from Aim 1 of the proposed supplement. *A prior* and emergent risk environment factors will be assessed according to a patient's level of engagement in the HIV care continuum to highlight factors associated with sub-optimal care (falling out of HIV care, non-ART adherence, unsuppressed viral loads).

The benefit in using a sequential mixed methods approach is that it allows for novel findings and two types of supporting evidence to describe the relationship between drug risk environment and the stages of the HIV care continuum[39]. These findings will support program development efforts targeting the most at-risk PWID sub-populations (e.g., women, non-adherent PLWH) in Nairobi, Kenya. In addition, results will provide scientific evidence for the combination HIV programs that incorporate, both HIV and harm reduction strategies in order to prevent and control the HIV epidemic.

METHODS

This supplement proposes a three-year research and career development plan (**Table 5**) that allows Ms. X to

work alongside her primary and secondary mentors, assist on parent study deliverables and conduct her own project aims that are nested within the existing parent study. Below we highlight the parallel methods of the parent grant and supplement.

1. Recruitment and Enrollment (Parent Study)

1a. Index Recruitment and Enrollment: Peer educators and health advisors will be responsible for disseminating information about the study to PWID presenting at 3 NSP sites. On average, 300 individuals visit the NSP sites each month (100 per site) and are offered HIV and HCV testing when they present for clean needles.[22] For this study, HIV testing occurs as part of standard clinic procedures. If a participant is HIV-positive, either newly diagnosed or known to be infected, individuals are invited to enroll into the study.

Trained health advisors explain the benefits and rationale for providing APS, discuss the importance of HIV care, and describe the process of notifying partners without revealing the identity of the index. They ask participants to provide written informed consent and use a biometric iris scan to assign a unique identifier for each participant, thus enabling the study team to confirm that a person does not enroll into the program more than once. Based on previous pilot studies, recruitment over a 24-month period will yield approximately 1000 index participants.

Partner Recruitment and Enrollment: Health advisors use several different approaches in a stepwise manner to find partners and facilitate HIV testing. First, index patients are asked to provide detailed information on all sexual and/or needle-sharing partners during the last 3 years. Partners who share any drug paraphernalia with the index (*e.g.*, cookers, cotton) will be included. Collection of partner information will include names, telephone numbers and locator information, when available. The health advisors contact the referred partners by phone or home visits using the locator information. Once contacted, study staff extend an invitation to meet at one of the clinics to enroll into the study, where notification of the exposure to HIV is made. In previous studies targeting the general population, on average 1.7 partners were named per index case, of whom about two-thirds were tested.[37] Testing for HIV is offered regardless of enrollment.

For the initial visit, health advisors ask partners about their prior HIV and HCV testing history, determine whether or not they are in care, and counsel them about HIV/HCV prevention. If the partner agrees, HIV testing and counseling is provided according to the Kenya National Guidelines. Health advisors will counsel previously diagnosed PLWH who are out of care about the benefits of care and how they can access care. As with index participants, testing for HIV and HCV is offered regardless of enrollment. Based on previous pilot studies, recruitment over a 12-month period will yield approximately 1000 partners.

1b. Recruitment and Enrollment (Diversity Supplement)

Aim 1: Characterize the risk environment among HIV-positive, PWID and partners.

To collect drug risk environment data, we will invite 30 subjects to participate in in-depth interviews using a combination of purposive and random sampling techniques. The same eligibility criteria used in the parent study will be applied, with the additional exclusion of non-injecting partners (i.e., sexual partners) and newly diagnosed partners, which will be explored in the parent study. To collect a wide range of experiences, our sample will include the following: 10 women (index or partner), 10 participants with sub-optimal HIV care (i.e., not engaged in care, non-adherent to ART, non-virally suppressed) and 10 participants who are adherent to recommendations posited by the HIV care continuum (i.e., engaged in care, adherent to ART, virally suppressed) (n=30).

Participants will be randomly selected from the parent study cohort at the rate of 4 per week during the period of qualitative data collection (2 months). Every Monday, a list of the prior week's enrollments will be generated and categorized according to where they fall in the HIV care continuum using an Excel spreadsheet and their participant ID number. Using the random selection function, we will invite 1 woman, 1 participant with sub-optimal care and 1 compliant participants to complete an in-depth interview with study staff. In scenarios where the parent grant does not recruit participants from each of the three groups (i.e., women, non-compliant, compliant participants), the following week two participants from the absent group will be invited to participate. Oversampling based on specific characteristics will provide insight on risk environment factors within marginalized groups that have traditionally been overlooked in purely quantitative studies. We will preferentially recruit women first, because we anticipate that there will be fewer women in the parent study. After 10 women have been invited to participate in the qualitative interviews, the same random selection procedures will be used to select men. If a participant does not want to participate in a qualitative interview or if the study staff is unable to reach the participant, the same random selection procedures will take place until the full sample is recruited or until conceptual saturation has been reached.[38] In addition, the health advisors and study staff will have the

opportunity to recommend participants for the qualitative interview following the participant's baseline questionnaire responses. For example, a participant who describes a particularly unusual experience surrounding injection drug use or expresses new trends in their community will be considered as a potential candidate for a qualitative interview.

Aim 2: Determine the level of engagement in HIV care and identify key risk factors associated with suboptimal engagement in care among HIV-infected PWID at baseline and over the 6-month follow-up period.

All index patients and partners enrolled in the study will be included in a cross-sectional analysis to identify factors, including *a priori* and emergent risk environment factors, associated with levels of engagement in the HIV care continuum (Aim 2a). In addition, index and HIV-positive partners will be followed up for 6-months. As part of this supplement, data collection at baseline and 6-months will follow the same protocol as outlined by the parent study, but the questionnaires will have additional survey questions incorporated from Aim 1. After the follow-up period, participants will be assigned to one of four groups (e.g., adherent to the HIV care continuum, fallen out of HIV care, non-ART adherence, unsuppressed viral load), with great emphasis on the sub-optimal care groups. The goal will be to determine which risk factors are related to the stages of HV care continuum, with sub-analyses evaluating gender differences and other vulnerable populations.

2. Data Collection

2a. Index and Partner Data Collection (parent study): At baseline and 6-month follow-up, all participants will complete in-person interviews conducted by health advisors to capture detailed sociodemographic and behavioral data. These data will be collected on mobile tablets using the Open Data Kit (ODK) platform. Participants will answer more sensitive questions (e.g., needle sharing behaviors, injection and sexual partners, and sexual behavior) by self-administered questionnaire via a mobile tablet with an interactive ODK interface.

2b. Index and Partner Data Collection (supplement): (Aim 1) We will develop a semi-structured in-depth interview guide that will be administered by a trained qualitative interviewer with experience working with PWID. At present, the parent grant does support qualitative research, but the study team does consist of several qualitative researchers. Under the scope of the Diversity Supplement, current study staff will complete a brief training on the qualitative study protocol, which includes both in-depth interview training and post-interview reflection notes. The in-depth interview guide will include two parts. Part I will include a brief quantitative section that assesses demographic characteristics including: age, gender, education, general location of residence, drugs/substances of choice and routes of administration, frequency of drug use, languages spoken, and country of origin. This will provide the interviewer with basic demographic information, personal drug use behaviors, and will establish a rapport with the participant. Part II will include a series of open-ended questions designed to elicit descriptions of the participant's experiences related to drug risk environment and HIV care. To elicit female PWID experiences of the risk environment, we will incorporate questions using a Theory of Gender and Power as our underlying framework.[36] Interviews will be 30-60 minutes in duration, depending on participant responses, and all interviews will be audio recorded. Following the interview, the audio recorded file will be uploaded to a secured server for transcription and translation by a study staff member. Audio recordings will be cross-checked by another team member for quality control purposes, whereby a study staff member will listen to the audio recording while reading the transcript to capture any inaccuracies in the transcript. In addition, the qualitative interviewer will take field notes during and after the interview to capture any additional information on the quality of the interview, general thoughts, nonverbal behavior and participant's demeanor using an Interviewer Feedback Form. Weekly team meetings will be scheduled to discuss interview content and update interview questions in response to emergent information. Interviews will conclude after all 30 participants are recruited or when conceptual saturation is reached, whereby study staff repeatedly hear similar experiences and perspectives on topics of interest and no new information will be gained by conducting additional interviews.[38]

Using a sequential mixed methods model, unique findings from Aim 1 will be incorporated into the parent study baseline and follow-up questionnaire at 6-months after initial study enrollment, which will omit participants enrolled in the first six months.[39] However, the participants that are enrolled in the parent study during the first six months of study recruitment, will be eligible to conduct qualitative interviews. This contribution to the parent study questionnaire will allow us to collect Nairobi-specific environmental risk factors which may be contributing to the HIV care for PWID communities.

(Aim 2) Emergent findings drawn from thematic analysis in Aim 1, will be incorporated into the parent study questionnaire. The data collection process will remain the same throughout the study, with the added benefit of incorporating targeted risk environment questions gain from Aim 1.The baseline and 6-month follow-up questionnaire currently have *a priori* risk environment questions, which address the following topics: drug-

use practices (i.e., drug preparation and administration), type of injection locations, drug purity and quality, social norms (e.g., sharing injection equipment), policing practices and harassment, healthcare access (i.e., HIV care and drug treatment options), intimate partner violence, community violence, cost of living, employment, costs associated with drug use, and the use of syringe exchange programs.[15-17]

3. Analysis Plan

3a. Data Analysis and Management (parent study): The parent study will manage study data and conduct analysis using STATA version 14.0 (College Station, Texas, USA).

3b. Analysis Plan (supplement): (Aim 1) Study transcripts and interviewer notes will be saved on a secured server until preliminary analysis begins. Codebook development will involve two study team members, including the Diversity Supplement applicant, independently reading through six randomly chosen transcripts. Members will generate a list of codes based on the interview guide (i.e., deductive approach) and emergent themes (i.e., inductive approach). Codes will be arranged in a hierarchical structure by parent codes (e.g., physical, social, economic, political codes, gendered perspectives) and corresponding sub-codes for each level. Two analysts will code each transcript and meet weekly to discuss and refine the codebook as needed. Qualitative analysis is an ongoing, iterative process, whereby the content of the qualitative interviews will be discussed at weekly team meetings so that members can discuss topics of interest, as well as new topics that emerged during interviews. Based on these initial team discussions, study team members may choose to modify the in-depth interview guide to illicit information on novel findings.[38] MAXQDA 10 (VERBI, Marburg, Germany) will be used to manage and analyze transcript data, including interviewer notes, into one integrated system. Overarching themes found in the qualitative analysis will be incorporated in the quantitative parent questionnaire, in an effort to triangulate the data sources. In triangulation, efforts are made to increase study validity and reduce methodological biases, by drawing upon the strengths of two methods.[38]

(Aim 2) As part of her training, Ms. X will be required to complete a formal data analysis plan prior to conducting her analyses in both Aim 1 and 2. Her approach will be based on the current scientific literature and only when it is approved will she carry out her analysis. This was added to the timeline, indicting a Q2 and Q4 deadline. The first statistical analysis (Aim 2a) will characterize the baseline study sample according to the HIV care continuum and identify factors associated with being 1) engaged in care (one medical visit in the last 6-months, but no longer 3-months since last missed appointment); 2) ART adherent (qualitatively assess whether the participant adhered to their treatment regimen "all of the time") over the last 6-months; and 3) virally suppressed (≤ 1000 copies/ml). Antiretroviral treatment (ART) adherence will be assessed by asking participants a series of questions whether they have ever been prescribed ART medication, currently taking ART medication or stopped taking ART. For those currently prescribed ART medication, we will define participants as adherent if they self-report taking ART "all of the time" versus "most of the time", "rarely (adhered)" and "did not take ART medication at all." Participants self-reporting that they took ART most of the time, rarely and not at all within the last 6-montns will be deemed ART non-adherent. In addition, participants indicating that they have not been prescribed ART or stopped taking ART for more than one week will be coded as ART non-adherent. The cut-off for viral load suppression will be defined as ≤ 1000 copies/ml (i.e., virally suppressed) and more than 1000 copies/ml (i.e., not virally suppressed.) A chi-squared test will be used for binary demographic variables and a t-test will be used for categorical variables in assessing differences within the three HIV care continuum categories using a .05 significance cut-point. In addition, logistic regression will be used to examine demographic correlates of each outcome category.

The second statistical analysis will longitudinally compare factors associated with sub-optimal care and non-adherence of ART using bivariate and multivariate analysis. This prospective analysis, will draw from data collected at two time-points per participant (i.e., baseline and 6-month follow-up), with enrollment for the current supplement beginning 6-months after the parent study enrollment. If the participant does not present for their 6-month follow-up appointment, they will be given a 3-month grace period to complete their follow-up questionnaire. If the participant does not return after 3-months (a total of 9-months after baseline), the participant will be deemed lost to follow-up and considered not engaged care and non-adherent to ART medication. Univariate statistics and multivariate logistic regression models will assess relationships between predictors and outcomes of interest (i.e., sub-optimal HIV care), using a 0.05 significance cut-off. Models will adjust for age, marital status, years lived in Nairobi, children, clinic location, time since HIV diagnosis, methadone use and housing type. Known risk environment variables will include transactional sex, sex work, violence (perpetrated by police, gang members, sex partners), drug of choice, access to drugs, drug quality, injection practices (e.g., injecting alone, rushed injections), injection spaces (e.g., access to running water, sanitation), access to clean needles, and shared injection equipment. All statistical analysis will be conducted using STATA version 14.0

(College Station, Texas, USA).

Sample size calculations: In total, the parent study will enroll 1000 index participants and at least 1000 sexual and/or needle-sharing partners. Early pilot studies indicated that 300 participants visited the three study locations per month.[37] As such, we expect 28 index participants and 25 partners (total 53 participants) will enroll into the parent study each month. Aim 2 will include a sub-sample of the parent study, starting with participants enrolled 6-months after the initial enrollment date in order to incorporate findings from Aim 1. This leaves our analysis with 1682 participants, including index participants and partners. Based on previous studies, we expect that 60-70% of HIV-positive PWID will be engaged in care, 50-60% will be ART adherent and 40-50% will be virally suppressed.

For Aim 2a, we can expect a minimum detectable association of odds ratio (OR)=1.31 for factors associated with engagement in HIV care at the time of enrollment, assuming a baseline prevalence of engagement in care of 60% and prevalence of exposure (i.e., environmental risk factor) of 50%, with 80% power and α=0.05 using a 2-sided χ^2 test. We can expect a minimum detectable association of OR=1.59 with a baseline prevalence of engagement in care at 70% and prevalence of the exposure of interest at 10% (**Table 2**).

Table 2. Factors associated with baseline engagement in care

Baseline Prevalence of Engagement in Care	Prevalence of "Exposure" Factor	Minimum Detectable OR
70%	10%	1.59
70%	20%	1.44
70%	50%	1.36
60%	10%	1.51
60%	20%	1.38
60%	50%	1.31

For Aim 2b, which assesses engagement in care at the 6-month follow-up period, we highlight two groups of participants. **Table 3** assumes 80% power to get the minimum detectable risk associations for participants who were not engaged in HIV care at baseline but engaged in care at the 6-month follow-up visit. When prevalence of the exposure of interest (i.e., risk environment factor) is 20-50% in the population and the incidence of being engaged in care is 20% among those not in care at baseline, then we can expect a minimum detectable relative risk (RR) between 1.54-1.68, whereas if the incidence of being engaged in care were 80%, we can expect a minimum detectable RR between 1.11-1.14. **Table 4** assumes 80% power to get the minimum detectable risk associations for participants who were engaged in HIV care at baseline, but not at the 6-month follow-up visit. When prevalence of the exposure of interest (i.e., risk environment factor) is 20-50% in the population and the incidence of discontinuing care is 10%, then we can expect a minimum detectable RR between 1.60-1.74, whereas if the incidence of discontinuing care is 30%, we can expect a minimum detectable relative risk between 1.28-1.35.

Table 3. Incidence of 6-month engagement in care among those initially not engaged in care

Prevalence of the Exposure (i.e., environmental risk factor)	Incidence of **engagement in care** in the "Unexposed"	Minimum detectable RR
20%	20%	1.68
20%	50%	1.31
20%	80%	1.14
50%	20%	1.54
50%	50%	1.25
50%	80%	1.11

Table 4. Incidence of sub-optimal care at 6-months (i.e., initially in care at baseline, but discontinued care at 6-months)

Prevalence of the Exposure (i.e., environmental risk factor)	Incidence of **discontinuing care** in the "Unexposed"	Minimum detectable RR
20%	10%	1.74
20%	20%	1.47
20%	30%	1.35
50%	10%	1.60
50%	20%	1.38
50%	30%	1.28

Study timeline: We anticipate Aim 1 will take place over Q1-Q3 and Aim 2 will take place over Q3-Q9 (36 months total). Timeline of study and career development activities are provided in **Table 5**.

C. CAREER DEVELOPMENT PLAN

Overview: We propose a 36-month research and career development plan for Ms. X, a doctoral student at the University of Washington Department of Epidemiology. Ms. X earned an MPH from Emory University, Rollins School of Public Health. She was awarded a Hispanic-Serving Health Profession Schools Fellowship, which transitioned into full-time employment for 3.5 years in academia at the University of California, San Diego, CA. Prior to matriculating at UW, she spent two years as an Epidemiologist for Los Angeles County Department of Public Health, HIV and STD Programs, Research and Innovation Unit. Her post-graduation plans include pursuing a career in academia, where she will apply mixed methods approaches in addressing issues of substance use and HIV/AIDS, making her an excellent candidate for a NIDA Diversity Supplement. She is familiar with the topics being investigated under the current parent grant including experience working with PWID

communities along the U.S.-Mexico Border and evaluating HIV care continuum programs during her time at Los Angeles County.

The training goals of this Diversity Supplement build upon Ms. X's graduate-level training in qualitative research methods, while improving her understanding and application of advanced statistical methods. As such, Aim 1 uses a qualitative approach to characterizing community-specific HIV risks and Aim 2 uses quantitative research methods to evaluate the HIV care continuum in our study and determine reasons for sub-optimal HIV care. Ms. X will be based within the Department of Epidemiology at the University of Washington, and her research training activities will consist of 9-months of in-country fieldwork, one-year of coursework in advanced qualitative methods, two-years of coursework in advanced epidemiology and biostatistics methods, applied research study planning and implementation, attending HIV and substance use seminars and workshops, and dissemination of her findings through abstract preparation and manuscript development. Her deliverables will include three independent analyses, which will be submitted as three abstracts to scientific conferences and three publications to peer-reviewed journals (**Table 5**). In addition to fulfilling milestones, Ms. X will serve as an integral research team member, attending team meetings, providing input on study-related decisions and assisting in mid-year evaluations so that she experiences the various phases of the grant lifecycle. She is committed to working with PWID, both internationally and domestically, to reduce the burden of HIV and associated co-morbidities, which is the overarching goal our parent study. **The contributions of the proposed Diversity Supplement will support Ms. X's career development and provide important contributions to the scientific literature. By characterizing the Nairobi-specific drug risk environment, highlighting factors associated with each stage of the HIV care continuum, and conducting a longitudinal analysis on factors associated sub-optimal HIV care, this supplement will be able to provide recommendations for future HIV programs and services that serve PWID, both nationally and globally.**

Table 5. Timeline of proposed research and career development objectives and milestones by 3-month quarter

	Activity	2018			2019				2020				2021
		Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12
Training	Coursework												
	Seminars (Table 7)												
	Summer Institute on Addiction[1]												
	General Exam												
R01	Study Enrollment												
	Study Follow-up												
	Systematic Review												
Aim 1	Develop Study Materials												
	Data Collection - Interviews												
	Codebook Development												
	Thematic Analysis												
Aim 2	Integration of additional questions to survey												
	Data Collection												
	Data Cleaning												
	Analysis Plan (Aim 2a & 2b)												
	Data Analysis												
Training	Manuscript Preparation												
	Conference Attendance												
	Dissertation Defense												
	Travel to Kenya[2]												

[1]Q2 recently accepted to the Summer Institute of Addiction, University of Amsterdam, which is supported by NIDA

[2]Q2 travel provided through Ottenberg-Winans Fellowship, University of Washington, Department of African Studies and GO-Health Fellowship offered through the University of Washington, Department of Global Health

C1. Career Development & Training Activities:

The training plan for Ms. X will allow her to complete her doctorate degree and prepare her for a successful career in academic research as an epidemiologist focused on issues of substance use and HIV. She will dedicate 36-months to her training and research by committing 50% of her time to her academic coursework and 50% of time to the Diversity Supplement. For the duration of the Diversity Supplement, Ms. X will have two primary mentors: Dr. Y (MPI) is a Professor at the University of Washington (UW) in the Departments of Global Health, Medicine and Epidemiology and Dr. Z (Co-I) is an Assistant Professor at the University of Washington (UW) in the Departments of Epidemiology and Global Health. Secondary mentors, will provide expertise in qualitative methods, drug risk environment and in-country fieldwork. Outlined below is the didactic training and

research plan (**Table 5**) and mentorship plan (**Table 7**).

In addition to the required course work for the Epidemiology Doctoral Program, training activities will include additional coursework in qualitative research methods, journal clubs, and seminars. These courses and fieldwork experiences, combined with dedicated mentorship from Drs. Y and Z, will provide an ideal environment for Ms. X's career advancement. Objectives include training as an independent mixed methods investigator, focused on issues of substance use in communities with a high prevalence of HIV. This includes completion of doctoral-level coursework in advanced epidemiology and qualitative methods, completing fieldwork, conducting data analysis, first-authoring abstracts and manuscripts, successfully passing qualifying exams and dissertation defense, and developing a job-talk in preparation for her next steps as a post-doctorate candidate.

<u>Career Development Objective 1:</u> To develop advanced epidemiology and qualitative analyses techniques by completing doctorate-level coursework and additional courses that emphasize mixed methods. In addition, she will gain applied research training as a member of the research team for the parent grant.

<u>a) Complete doctorate-level coursework in advanced epidemiology methods and qualitative research:</u> Ms. X will complete her coursework in advanced epidemiology methods by Quarter 4, in addition to advanced qualitative methods offered through the UW Department of Global Health and the Jackson School of International Studies. Her coursework plan details the courses needed to complete deliverables associated with each of the proposed aims (**Table 6**).

Table 6. Aims, Deliverables and Training Supported by Diversity Supplement

	Aim 1: Characterize the risk environment among PWID	**Aim 2:** Evaluate risk environment factors, gender and the stages of the HIV care continuum
Deliverables (Deadline)	**1 abstract (Q7)** **1 manuscript (Q8)**	**2 abstracts (Q3, Q11)** **2 manuscripts (Q6, Q10)**
Applied Coursework	**Q3 Courses** 1. International Bioethics, Social Justice and Health Seminar (GH 590/LAW 506) **Q4 Courses** *2. Research Methods for Social and Contextual Determinants of Health (EPI 548)* **Q5 Courses** 3. Qualitative Methods (GH 590)	**Q1 Courses** 1. Advanced Epidemiology Methods II (EPI 516) *2. Psychiatric Epidemiology (EPI 546)* **Q3 Courses** 3. Current Literature in Epidemiology (EPI 591) **Q4 Courses** 4. Statistical Methods of Spatial Epidemiology (BIOST 555)
Completed Coursework	1. Qualitative Data Analysis (JSIS 512) 2. Built Environment (ENVH 538)	1. Epidemiology Methods I (EPI 512) 2. Epidemiology Methods II (EPI 513) 3. Advanced Epidemiology Methods I (EPI 515) 4. Categorical Analysis Epidemiology (EPI 536) 5. Survival Data Analysis in Epidemiology (EPI 357)
Additional coursework:	**Q1 Courses** 1. Preparing & Writing Research Proposals (EPI 588) 2. Program Seminar: Current literature in Epidemiology (EPI 592) ***Q2 Courses*** *3. Responsible Conduct of Research: Global and Local (EPI 586)* *4. Summer Institute on Addiction (University of Amsterdam)* ***Q3 Courses*** *5. Addiction: Mechanisms, Prevention and Treatment (CONJ 556)* ***Q5 Courses*** *6. Drugs and Behavior (PSYCH 420)* *7. Drugs and Society (LSJ 376)*	

<u>b) Applied research training, fieldwork and data collection:</u> Ms. X will play an integral role on our research team by assisting with survey development, developing Standard Operating Procedures (SOPs), collaborating with data managers, assisting with progress reports, and conducting analyses. In addition, she will continue to attend all research team meetings and presentations. Ms. X will travel to our study site in Nairobi, Kenya, at least three times with a cumulative duration of 9 months. While in Nairobi, she will be accompanied by our study liaison, Dr. C, who is a co-Investigator and has lived in Nairobi for the last 4 years. The cost of travel, room and board will be supported through sources at the University of Washington. Ms. X is currently the recipient of the Ottenberg-Winans Fellowship through the Department of African Studies and she will also be applying to additional funding opportunities through the Departments of Global Health and Epidemiology. Our team has been successful at attaining these travel awards in the past and will not be drawing upon the parent grant to supplement travel. While in Kenya, Ms. X will have the opportunity to experience data collection for both the qualitative and the quantitative portion of her aims (**Table 5**). While Ms. X has contributed to multiple grants, our goal is to provide her experience in working with a new population of PWID living with HIV in Kenya, which will present a different set of risks from the surrounding environment compared to populations she has worked with previously. Skills gained through her work in Nairobi, Kenya, can be applied to settings that mirror Nairobi's high HIV prevalence and newly established harm reduction programs (e.g., Southern states).

Career Development Objective 2: To develop a strong publication portfolio with three first-authored manuscripts, in addition to three abstracts that will be presented at scientific research conferences.
In her role on the parent grant, Ms. X will have the opportunity to develop databases, conduct data cleaning, generate regular reports, and perform advanced analyses for both the parent study and the proposed Diversity Supplement. Her work on the proposed research project will give Ms. X opportunities to critically read and summarize the literature, including HIV care, injection drug use, and drug risk environments. Following the completion of her analyses, Ms. X will be mentored in how to succinctly communicate results on national and global platforms, which will include presenting at scientific conferences and publishing manuscripts (**Table 6**).

Career Development Objective 3: To develop a competitive application for post-doctorate positions, including developing a job-talk presentation. During Quarters 10-12 of the Diversity Supplement, we will be training and positioning Ms. X for the next phase in her career. She aims to apply to post-doctorate positions with mentors that work both nationally and internationally on the co-occurring risks of substance use and HIV/AIDS. In addition, her analysis will provide her with robust pilot data for submitting a NIDA training grant (e.g., NIDA K-award).

Table 7. Frequency of Ms. X's proposed research and career development meetings

Planned Meetings	Weekly	Bi-weekly	Monthly
Meeting with MPI (Dr. Y)		x	
Meetings with Co-I and Academic Advisor (Dr. Z)	x		
Research Study Team Meetings	x		
Consultant Meetings (Drs. A & B)			x
Training Seminars *(Research Area)*			
UW CFAR Seminars *(HIV/AIDS)*			x
UW Alcohol and Drug Abuse Institute Seminars *(Substance use)*			x
Journal Club Meetings *(Epidemiology Methods)*		x	
Workgroup on Social Determinants of Health *(Epidemiology Methods)*		x	
Kenya Research and Training Center Seminar *(HIV/AIDS)*	x		

Primary Mentors
Dr. Y (Multiple Principal Investigator) is a Professor at the University of Washington (UW) in the Departments of Global Health, Medicine and Epidemiology. She is the Multiple Principal Investigator for the "Integrated Partner Services and Phylogenetics for HIV and HCV Prevention," the parent grant under which we are applying for this diversity supplement. In addition, she is currently the Principal Investigator of two Fogarty International Center (FIC) HIV research training grants focused on trainees from Kenyatta National Hospital, the Ministry of Health and the Kenya Medical Research Institute (KEMRI). Dr. Y will provide career development guidance and mentorship in research to the Diversity Candidate for the duration of the award. Mentorship will be provided during one-on-one calls/meetings or joint mentor meetings and will serve to guide Ms. X as she conducts her proposed research analysis. We are not requesting salary support for Dr. Y on this Diversity Supplement.

Dr. Z (Co-Investigator) is an Assistant Professor at the University of Washington (UW) in the Departments of Epidemiology and Global Health. He is Ms. X's Academic Advisor and will be her direct point of contact throughout the Diversity Supplement to ensure that she completes the proposed aims and the requirements of doctorate program. He is currently the Co-Investigator on the parent study and provides technical expertise on HIV and Hepatitis C on the project. We are not requesting salary support for Dr. Z on this Diversity Supplement

Secondary Mentors
Dr. A (Consultant), is a Professor in Psychology and Adjunct Professor in Global Health at the University of Washington. She is the Co-Director of the Program on Global Mental Health and is active in the UW Center for AIDS Research (CFAR), Socio-behavioral and Prevention Research Core and Assistant Director of its Substance Use Working Group. She is currently a consultant on the parent study, contributing her expertise in qualitative research. We are not requesting salary support for Dr. A on this Diversity Supplement.

Dr. B (Consultant), is the Director of the Alcohol and Drug Abuse Institute, Professor in Psychiatry and Behavioral Sciences, and Adjunct Professor in the Departments of Global Health, Health Services and Psychology at the University of Washington. He serves on NIDA's National Drug Abuse Treatment Clinical Trials Network (CTN), where he chairs the Research and Development Committee and is a member of the Publications Committee. We are not requesting salary support for Dr. B on this Diversity Supplement.

Dr. C (Co-Investigator) is an Acting Instructor/Infectious Disease Fellow at the University of Washington. She is currently living in Nairobi, working on two studies that are investigating the risks of HIV and Hepatitis C in PWID. She is a very familiar with the needle exchange programs, recruitment sites and Nairobi-based study staff. In

addition to working with Ms. X on an analysis plan, she will provide mentorship while in Nairobi, Kenya during the data collection phase. We are not requesting salary support for Dr. C on this Diversity Supplement.

C2. Mentorship Timeline

The proposed Diversity Supplement will build a foundation for Ms. X to achieve her professional goals of becoming an independent HIV and substance use researcher. All of Ms. X's mentors have a successful track record of mentoring candidates pursuing careers in academic research and will provide a strong support network to ensure that she achieves her goals. To ensure successful completion of her doctorate degree and training, Drs. Y and Z and will conduct weekly meetings with Ms. X on her academic progress (**Table 7**). Over the last 20 years, Dr. Y has mentored 80 graduate students, post-doctoral fellows, and junior faculty at the University of Washington who are now successful researchers and public health practitioners. Dr. Z is an alumnus from the University of Washington, Department of Epidemiology, and he has worked with Dr. Y for the last 10 years in Nairobi, Kenya. Dr. Z is Ms. X's academic advisor and has mentored multiple epidemiology students. He will partner with Dr. Y to provide mentorship in the form of one-on-one teaching, ensuring academic advancement, troubleshooting data analysis issues and verifying that milestones are met. In addition, regular biweekly and monthly meetings will occur with study collaborators Dr. A, who will provide topic-specific and qualitative methods guidance, and Dr. B, who will provide input on the Rhodes et al. risk environment framework. Ms. X will continue to build on her training by attending seminars and workshops offered through the University of Washington's Center for AIDS Research (CFAR) and the Alcohol Drug Abuse Institute (ADAI), which focus on innovative HIV and substance use research projects. These activities will help Ms. X build a foundation in academic research and prepare her for a post-doctorate level position.

C3. Impact of research and career development experiences on the Diversity Supplement Candidate

At the completion of the proposed Diversity Supplement, Ms. X will successfully defend her dissertation, prepare and submit abstracts to scientific meetings and conferences, and first-author a minimum of three manuscripts, in preparation of her next steps in academia. Drawing from her proposed data analysis, Ms. X will be able to incorporate her findings into a K-award for the next phase of her career as a post-doctorate researcher. Dr. Y has experience in mentoring 5 K-award recipients, which will be an invaluable resource that Ms. X can draw upon. The proposed Diversity Supplement will serve as a foundation for a long-term academic research career for Ms. X, which will enhance diversity within the field of academic substance use research.

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