A. SPECIFIC AIMS

HIV pre-exposure prophylaxis (PrEP) is a highly effective HIV prevention strategy and a hallmark of the U.S. Ending the HIV Epidemic initiative. However, there is a large gap between the number of people with an indication for PrEP in the U.S. and actual PrEP use due to complex individual, social, and structural barriers. Patient navigation aims to improve engagement in care through education, support connecting with providers, linkage to related resources, and navigation of multidisciplinary care. It is recommended by CDC as an effective strategy for addressing barriers to PrEP. To date, PrEP navigation programs have focused primarily on PrEP counseling, education, and healthcare navigation with limited opportunities to address the broader social determinants that influence engagement in HIV prevention and contribute to racial/ethnic inequities in HIV.

Since 2017, the Washington State Department of Health (DOH) has contracted diverse local agencies to provide PrEP navigation services to populations with high HIV incidence. In an ongoing DOH-UW implementation science evaluation, agency staff have universally reported a need to better address the social and behavioral health needs of their clients to improve client engagement in PrEP and general well-being. However, PrEP navigation is complex and under-resourced, and it is not known how to effectively and feasibly integrate social and behavioral health services in diverse contexts. Here, we propose a mixed methods implementation science study to identify tailored strategies for integrating social and behavioral health services into PrEP navigation at DOH-funded agencies for future effectiveness and implementation studies. Specifically, at each agency, we aim:

**Aim 1:** To quantify the frequency with which PrEP navigation clients receive social and behavioral health assessments and referrals under the current standard of care.

**Aim 2:** To prioritize strategies for integrating social and behavioral health services into PrEP navigation.

**Aim 3:** To identify facilitators, barriers, and resource needs for prioritized integration strategies.

B. SIGNIFICANCE

B.1. HIV Epidemic in Washington State. As in the U.S. as a whole\(^1,2\), the HIV epidemic in Washington State is concentrated among key populations, particularly men who have sex with men (MSM), and disproportionately affects Black and Latinx people\(^3\). Overall HIV incidence remained stable at >5 per 100,000 adults from 2015-2019, despite achieving WHO’s 90-90-90 goals and being at the forefront of PrEP scale-up\(^3\). To promote PrEP, DOH has established guidance defining priority populations\(^4\), a drug assistance program\(^5\), and supported PrEP navigation programs. Yet, a 2017 statewide survey found that only 28% of MSM with a PrEP indication were using PrEP, with lower use outside King County\(^6\). MSM cited low perceived risk, side effects, cost, and insurance as common barriers. Limited data from other populations, including people who inject drugs (PWID) and people of color (POC), suggest minimal PrEP uptake\(^3\), suggesting need to enhance PrEP activities statewide.

B.2. PrEP Navigation. Patient navigation is a CDC “Effective Behavioral Intervention” for HIV prevention and care\(^7,9\). Through peer or lay health worker-delivered education, counseling, appointment assistance, payer identification, insurance enrollment, adherence support, and behavioral and social services support\(^7\), navigation has potential to address the many individual, social, and structural barriers to PrEP engagement\(^10,11\) and be cost-effective and culturally appropriate\(^8,10\). PrEP navigation services, including most WA DOH-funded programs, have primarily or exclusively focused on PrEP counseling, education, and navigating healthcare and insurance\(^12-18\). Programs that do address broader social determinants have shown promise at increasing PrEP use\(^19-21\). However, given program model, context, and client diversity, identifying which determinants to address and how to effectively and feasibly address them within PrEP navigation is likely to vary substantially across programs.

B.3. Social Determinants of HIV. Social determinants of health are “the conditions in which people are born, grow, live, work and age as well as the complex, interrelated social structures and economic systems that shape these conditions”, such as income, education, housing, health insurance, and structural racism\(^22\). These factors contribute to HIV disparities, including in PrEP use, experienced by POC, MSM, trans, PWID, and immigrant communities\(^2,11,23-29\). The need to address social determinants as part of routine health care\(^30\) and to end the U.S. HIV epidemic\(^23,24,26,31\) is increasingly recognized. As community members, PrEP navigators have unique potential to provide/link clients with relevant services to decrease HIV incidence and improve general well-being.

B.4. Integrating Behavioral Health and HIV Services. Populations with high HIV incidence are disproportionately impacted by mental health and substance use disorders, and these disorders – and substance use more broadly – impact HIV risk and adherence to PrEP and antiretroviral therapy\(^22-35\). Co-located HIV and PWID services is common, UNAIDS and the Grand Challenges in Global Mental Health Initiative call for integrated HIV and mental health services\(^36-38\), and lay health workers (e.g. navigators) can effectively deliver evidence-based mental health interventions\(^39\). Integrating assessment, referrals, or delivery of evidence-based behavioral health services in navigation may contribute to addressing the HIV-mental health-substance use syndemic.
C. INNOVATION. Building on a unique academic-health department-community partnership, we propose using novel implementation science methods to develop tailored strategies for integrating social and behavioral health services within community-based PrEP navigation services. We will use real-time web-based polling and “go-zone” analyses to inform group discussion and decision-making within FGDs and nominal group technique (NGT). This has potential to generate results more quickly and increase stakeholder engagement in and ownership of the data and process. Our explicit focus on integrating social and behavioral health services into PrEP navigation and its potential impact on PrEP, general health, and implementation outcomes is innovative. In addition, participating agencies vary in their organizational structure, program models, populations served, and settings, and this programmatic diversity presents an opportunity to identify integration strategies appropriate for implementation across a variety of navigation programs. Quantifying the social and behavioral health service needs of diverse PrEP navigation clients will also be a unique contribution that could motivate service integration.

D. APPROACH

D.1. Multidisciplinary Partnership. At UW, [redacted] is an HIV epidemiologist with experience in behavioral research and program evaluation; Drs. Wagner and Dr. Weiner bring expertise in implementation science, and [redacted] behavioral health clinical services and integration of behavioral health and medical care in low-resource settings. At DOH, [redacted], Community Engagement Coordinator, brings experience in State and local program development and delivery, including as the State PrEP navigation services supervisor.

D.2. Preliminary Studies and Team Expertise. The proposed study builds on work conducted by [redacted], [redacted], and Kyle [redacted] in PrEP services, social determinants of HIV, and implementation science.

2.1. PrEP Navigation Services Implementation. [redacted] and [redacted] collaborate on an evaluation of DOH-funded PrEP navigation services that led to the proposed project (CFAS/CFAR PI [redacted]). Through in-depth interviews with navigators, program leadership, and clients; analysis of program data; time studies; and budget analysis, we are comparing implementation of PrEP navigation at 10 agencies across WA State. Key findings from program interviews include: high variability in approaches to supporting PrEP initiation and retention, and challenges reaching marginalized populations and addressing social and behavioral health needs.

2.2. Socioeconomic Impacts of COVID-19 among MSM. In an annual national cross-sectional survey of MSM, [redacted] found that, early in the COVID-19 pandemic, MSM of color had experienced disproportionate economic impacts, including decreased employment and increased housing instability and need to support family/partners.

2.3. PrEP Promotion via STI Partner Services. [redacted] evaluated integration of PrEP assessment and referral into STI partner services in King County. We found that routinely offering referrals to PrEP providers was feasible and effective at linking MSM to PrEP and that Black and Latinx MSM reported lower PrEP use than other MSM.

2.4. MSM Preferences for App-Based Sexual Health Services. [redacted] partnered with Building Healthy Online Communities (BHOC) on a mixed methods study to prioritize strategies for integrating HIV/STI sexual health services into geosocial networking apps. Our results directly informed BHOC’s work with app companies.

2.5. HIV Partner Services Implementation in Kenya. [redacted] and [redacted] are collaborating on a Consolidated Framework for Implementation Research (CFIR)-guided mixed methods study of the effectiveness and implementation of HIV partner services (R01 PI Farquhar).


3.1. Services. DOH contracts diverse local agencies to deliver HIV prevention services to populations with high HIV incidence, including MSM, PWID, and Black and Latinx people. These services are centered on PrEP navigation and include other HIV/STI services that provide opportunities for PrEP recruitment (HIV/STI testing, condom distribution, outreach). Core components of PrEP navigation include: education, support linking to PrEP prescribers, insurance and drug assistance program enrollment, and PrEP retention and adherence support. These services aim to reduce barriers to PrEP, particularly related to knowledge, cost, and healthcare access.

3.2. Settings. Table 1 describes the 9 agencies contracted by DOH to serve priority populations in 9 counties. Although objectives, deliverables, and data systems are mostly consistent across agencies, each agency has developed its own PrEP navigation model, in part defined by agency type, populations served, and local infrastructure. For example, SRHD services are integrated with health department activities including partner services; Gay City has an on-site PrEP clinic; and Entre Hermanos prioritizes outreach, education, and referral
for Latinx MSM. Of the 9 agencies, 8 will participate in this study.

D.4. Study Overview
The proposed study aims to locally tailor strategies for integrating a range of social and behavioral health services into PrEP navigation at 8 diverse agencies across WA State (Figure 1). We will first use client surveys to assess agencies' standard of care, client needs, and perspectives regarding service integration (Aim 1). Second, through a series of group interviews with agency stakeholders, we will elucidate and prioritize service areas (Aim 2, Part 1 FGDs), generate and prioritize integration strategies for selected service areas (Aim 2, Part 2 NGT), and identify facilitators, barriers, and resource needs for implementing prioritized integration strategies (Aim 3 FGDs). Results will be shared with agencies for implementation planning and to identify opportunities to learn and collaborate.

D.5. Aim 1: Evaluate the Standard of Care for PrEP Navigation

5.1. Overview. To evaluate the standard of care, we will conduct web-based quantitative surveys with 40 PrEP navigation clients per agency (total n=320). These surveys will be informed by the Implementation Outcomes Framework (IOF)\(^2\) and assess (a) the frequency with which PrEP navigation clients receive social and behavioral health assessments and referrals and (b) the impact of this standard of care on implementation (acceptability, fidelity), service (effectiveness, patient-centeredness, equity), and client (satisfaction) outcomes.

5.2. Recruitment. Using methods developed for our ongoing evaluation of PrEP navigation implementation, DOH will prepare a list of PrEP navigation clients who received ≥1 service in the past 6 months from participating agencies (~100/agency), and randomly sample clients for study invitation, stratified by agency and time since enrollment in navigation (<6 vs. ≥6 months, DOH-defined initial navigation vs. retention). We will stratify by time since enrollment because practices related to social and behavioral health services may differ during PrEP linkage vs. retention due to greater complexity of navigation during linkage and potentially different effects of these needs on linkage vs. retention on PrEP.

5.3. Data Collection. The survey will be programmed in REDCap\(^3\),\(^4\) and evaluate select IOF constructs (Fig. 2)\(^2\). Questions will address sociodemographics; clients’ social and behavioral health service needs; whether they were asked about/discussed specific service needs as part of navigation (fidelity); if discussed, when this occurred and whether they were offered and accepted referrals or assistance (fidelity); if referred, whether they linked to services (effectiveness); and to prioritize service areas for navigators to address (patient-centered). Service areas include: mental health, substance use, housing, food, employment, transportation, post-incarceration, legal aid, or others. Participants will be asked how offers of these services affected satisfaction with navigation (satisfaction), ability to initiate/maintain PrEP use (effectiveness), likelihood of continuing to engage in and recommending navigation (acceptability) using 5-point Likert scales. Clients with unmet needs will receive a referral list developed with participating agencies and referred to their navigator.

5.4. Analysis. We will describe proportions of clients who report needing, being asked about, offered, and accepted referrals/assistance for each service area. We will compare proportions asked about any behavioral health (mental health/substance use) and social service (remaining services) by time since enrollment,
race/ethnicity, and population, adjusting for agency using log-binomial regression [equity]. We will summarize Likert scale responses using means and standard deviations. Analyses will be conducted overall and by time since enrollment.

5.5. Power calculations. We powered this aim to compare the proportion of participants asked about services by time since enrollment (ratio N_{<6mo}/N_{≥6mo}=1) and race/ethnicity (N_{POC}/N_{NW}=0.5) using \( \chi^2 \) tests for differences in 2 independent proportions assuming 2-sided \( \alpha = 0.05 \) and 80% power. Depending on outcome prevalence (range = 10-50%), minimum detectable differences with an N of 320 range from 11-18% for these comparisons.

D.6. Aim 2: Prioritize strategies for integrating social and behavioral health services into PrEP navigation

6.1. Overview. At each agency, HIV/STI prevention staff (e.g. navigators, HIV/STI testing staff, prevention managers) and other key stakeholders (e.g. leadership, case management staff) will be invited to participate in a two-part group interview process: (1) FGDs to explore PrEP navigation clients’ needs and prioritize service areas for integration into PrEP navigation, followed by (2) NGT to identify, characterize the feasibility and effectiveness of, and prioritize integration strategies for providing/linking clients with these services.

6.2. Part 1: Focus Group Discussions

6.2.1. Elucidating Client Needs. The facilitator will use a semi-structured question guide to explore the social and behavioral health service needs of PrEP navigation clients; how they impact PrEP uptake, retention, and general well-being; and the agency’s current policies and practices in these areas, then present aggregate data from Aim 1 for participants to respond to. Service areas to be discussed are described in Aim 1 above.

6.2.2. Prioritizing Service Areas for Integration. The facilitator will then guide staff in developing criteria for prioritizing services. Criteria may include: prevalence of the need; perceived impact of addressing the need on PrEP use or other health outcomes; availability of resources; contribution of the need to racial/ethnic inequities; or others. Aim 1 data will be available for consideration. Participants will vote on criteria anonymously in real time using a rank-order question programmed by study staff in Poll Everywhere, a web-based audience response system. The group will select criteria based on majority opinion, then use these criteria to vote on service areas to prioritize using a rank-order poll followed by group discussion.

6.2.3. Analysis. FGDs will be conducted by a facilitator with support staff for poll development and note-taking and be audio-recorded and transcribed. Cross-cutting and diverging themes regarding clients’ social and behavioral health needs at each agency will be identified using the Framework Method, a directed content analysis approach that uses deductive coding based on a pre-developed framework or conceptual model\(^{55}\). Two analysts will pull excerpts from transcripts and categorize responses into the coding categories using a matrix format to organize and synthesize content into summarized themes.

6.3. Part 2: Nominal Group Technique

6.3.1. Data Collection and Analysis. Within one month, participants will reconvene for a second meeting using NGT to identify and prioritize strategies for integrating the social and behavioral health services areas selected in Part 1. NGT is a structured process that combines individual and group phases to brainstorm ideas and build consensus\(^{56-59}\). Strengths include separating ideas from participants, giving ideas equal consideration and equal voices to participants, and systematizing evaluation of ideas. Our approach comprises 5 steps adapted to include “go-zone” rating and analysis: (1) silent individual generation of ideas in writing; (2) round-robin listing of ideas; (3) group discussion of ideas, e.g. clarifying, merging, and adding new ideas into a final list; (4) individually rating ideas; and (5) “go-zone” analysis and discussion [Fig 3, adapted from \(^{60,61}\)]. In these final 2 steps, participants will rate each strategy in the final list for perceived effectiveness and feasibility using 5-point Likert scales. Ratings will be entered into a REDCap survey programmed by study staff between steps 3 and 4 to include all named strategies. Following survey completion, data will be exported for visualization using “go-zone” plots for each service area and discussed as a group in step 5. “Go-zone” plots are scatterplots of mean scores for each
strategy, divided into 4 zones using the mean of each dimension. Here, quadrant I contains strategies with high feasibility and effectiveness ratings, and quadrant II strategies with low feasibility and high effectiveness. Participants will select quadrant I/II interventions to discuss in Aim 3.

6.3.2. Potential integration strategies. Types of integration strategies may include: assess and provide tailored resource list, make initial connection to external provider, provide ongoing navigation to support external service provision, link to services within agency providing PrEP navigation, or direct service delivery by PrEP navigator. Prior to NGT sessions, study staff will review the literature for evidence-based integration strategies, and the facilitator will introduce these ideas during the round-robin merging of ideas if not raised by participants.

6.3.3. Rationale for “go-zone” rating and analysis. Based on preliminary data from our ongoing navigation evaluation, resource constraints (e.g. staffing, costs) are likely to be key considerations in determining feasibility. However, integration strategies that may be perceived as having the greatest potential effectiveness may also be more resource-intensive (e.g. direct service delivery by navigators) and therefore seen as less feasible. The proposed adaptation will ensure that prioritization is explicitly informed by these characteristics and offer participants opportunities to discuss integration strategies that are feasible in the short-term and those that could be built towards for increased impact. It also captures data on perceptions of each strategy for analysis.

6.4. Synthesizing Results. We will summarize agencies’ prioritized service areas and integration strategies next to agency characteristics: type, populations served, geography, size, and navigation caseload.

D.7. Aim 3: Identify facilitators, barriers, and resource needs for prioritized integration strategies

7.1. Focus Groups Discussions. We will conduct a CFIR-guided FGD with the HIV prevention team and other stakeholders at each agency (8 FGDs) to elucidate determinants of implementation for integration strategies prioritized in Aim 2. With 39 constructs associated with effective implementation across 5 domains, CFIR is adaptable and can guide systematic assessments of barriers and facilitators. Question guides will be based on validated CFIR tools, focusing on select constructs (Table 2). FGDs will examine 1-2 integration strategies per service area/agency (up to 6 strategies/agency) and will be audio-recorded and transcribed.

7.2. Analysis. We will use a framework-guided rapid analysis approach comprising the following: (1) develop a matrix with key CFIR domains and, as needed, other prevailing themes, (2) two coders read transcripts in-depth, (3) coders read all FGD notes, (4) coders re-read transcripts and extract key quotes that align with specific domains into the matrix, and (5) consolidate matrices by organization and service area to identify key themes and patterns at these levels. CFIR constructs will be used to identify potential determinants of implementation.

8. Possible Complications/Alternative Plans. COVID-19 has resulted in uncertainty and change that may affect perspectives on expanding PrEP navigation and the context for implementation planning. Communication will be critical to understand changes in context and adapt data collection and interpretation. In the absence of routine program data, we will use client self-report to assess the standard of care, which will be subject to social desirability and recall bias. Integrating systematic needs assessments would be an intervention in itself and was therefore not feasible for assessing standard of care. If client response rates are low, we can consider weighting estimates for non-response, triangulating client data with a navigator survey, and increasing the sample.

9. Future Research Directions. This research will establish a menu of locally-tailored strategies for integrating social and behavioral health services into PrEP navigation and identify barriers to and resources needed for implementation. We will pursue NIH funding to evaluate the effectiveness and implementation of these strategies for improving PrEP and other client outcomes and understand the effects of social determinants in this context.

10. Timeline. Milestones include project implementation planning with agencies and DOH, developing SOPs and data collection tools, and obtaining ethical approvals (mos 1-6); implementing and analyzing Aim 1 survey (mos 7-12); implementing Aim 2 FGDs and NGT (mos 10-15) and Aim 3 FGDs (13-18); qualitative analysis (mos 13-21); manuscript preparation, results dissemination, and feedback/planning with agencies/DOH (mos 18-24).
REFERENCES


PROTECTION OF HUMAN SUBJECTS
Justification of Human Subjects Research Exemption

The proposed human subjects research falls under Exemption 2.iii. The only involvement of human subjects will be survey procedures in Aim 1 with clients at 8 agencies contracted by the Washington State Department of Health (DOH) to provide HIV prevention services. Because we will record information in a manner that the identity of participants can readily be ascertained and any disclosure outside the research poses risks to the subjects, our study protocols (including recruit, informed consent, and data security procedures as described below) will be reviewed by the University of Washington Human Subjects Division and Washington State IRB. All procedures will be conducted in accordance with 45 CFR Part 46.

In Aims 2 and 3, we will conduct group interviews with up to 80 HIV prevention staff and other stakeholders at DOH-contracted agencies to participate. Because these interviews will address only their perspectives on their clients’ needs, their work, and strategies for enhancing PrEP navigation services, the data will not be identifiable private information about these participants, and they are not considered human subjects per 45 CFR Part 46. Study staff will review a study information sheet with all potential participants prior to group interviews, provide opportunities for questions, and emphasize that participation is voluntary and will not affect employment.

Aim 1 Procedures & Human Subjects Protections
A. Recruitment. DOH staff responsible for program monitoring and evaluation of PrEP navigation services at participating agencies will develop a list of all active PrEP navigation clients (defined as receiving ≥1 service in the past 6 months) from Provide, the statewide database used by agencies for documenting PrEP navigation services. They will then use a random sequence generator to sample clients, stratified by agency and time since enrollment in navigation (<6 vs. ≥6 months). Study staff will provide DOH a list of client-specific URLs for the survey in REDCap. (REDCap is a secure web-based survey and data management platform with HIPAA-compliance capability and IRB-approved electronic consent procedures.) DOH will then send a letter to clients informing them of the study, including the unique link, and provide study staff at UW with a list of sampled clients, contact information, demographics, last service date, and agency matched with the client-specific survey URL. Study staff will follow up with clients who have not completed the survey within one week and make up to 5 contact attempts over 2 weeks until clients are either defined as lost to follow-up or refuse participation.
B. Informed Consent. The REDCap survey will begin with a web-based informed consent process approved by the UW Human Subjects Division, including a detailed description of the study and potential risks, benefits, and alternatives to participation. A contact number and email for study staff will be provided in case of questions. The information page will emphasize that participation is voluntary; that participants can refuse to participate, answer any question, or end their participation at any time without penalty; and that such refusals will not affect service provision at participating agencies or from DOH. Participants will electronically sign the informed consent form.
C. Risks to Participants. The potential risks of participating in the quantitative survey include loss of privacy related to any personal experiences or information participants choose to disclose in the survey and psychological discomfort related to being asked about sensitive information, including service needs related to mental health, substance use, housing, legal aid, and others.
D. Participant Compensation. Participants will be offered $25 online gift card for participation in the 20-30 minute survey. Upon completion of the main survey, participants who wish to receive compensation will be linked to a separate, unlinked survey to submit an email address to send the gift card to.
E. Data Security/Protections against Risks. All study procedures will occur at a location of participants’ choosing, and study staff will encourage participants to complete the survey in a private location in all communication. Survey data will be linked to participant data from Provide using a code only; the survey will include no identifiable information. The smartphone used for communication with participants will be password protected, encrypted, and kept in a locked office when not in use. Identifiable data from Provide will be sent from DOH to UW staff in a password-encrypted file via secure file transfer protocol. Data will be stored on networks maintained in a secure area, and data with identifiers will be stored separate from survey data in their own password-encrypted network folders. All portable media will be encrypted per department policy. When identifiable data are no longer needed, they will be destroyed.