

## Increasing Adoption of HIV PrEP in South Eastern Ontario

### 1. OVERALL GOAL AND SIGNIFICANCE

Canada has endorsed the Joint United National Programme on HIV and AIDS global targets to end the acquired immunodeficiency syndrome (AIDS) epidemic, including reducing new human immunodeficiency virus (HIV) infections to zero, by 2030. Along with the UNAIDS 90-90-90 targets on HIV diagnosis, treatment, and retention in care, HIV pre-exposure prophylaxis (PrEP) will play a key role in reducing HIV incidence in people at risk of HIV acquisition (PRHA). While the optimal target for PrEP coverage in gay, bisexual and other men who have sex with men (GBMSM) is unknown, it has been estimated that 30-50% of behaviourally eligible GBMSM would need to be on PrEP to achieve a 10-year reduction in HIV incidence of 25%. (1) Ontario has had a relatively stable HIV incidence since 2010 despite advances in HIV treatment delivery and retention in care, with 738 incident cases in 2018 and 687 in 2019, of whom 75% were males and 53.6% GBMSM. (2) Thus, eliminating new HIV infections in Ontario will require PrEP being used to its full potential, perhaps with a coverage target higher than 50% and along with other preventative measures.

Ontario is actively working on increasing PrEP uptake through various ways: 1) It has endorsed the Canadian PrEP guidelines and is promoting its adoption via the [ontarioprep.ca](http://ontarioprep.ca) website where PRHA can find essential information about PrEP and locate PrEP prescribers. Similarly, clinicians can find both comprehensive PrEP clinical guidance and tools to set up and run PrEP services at their practices. 2) Ontario offers several options for PrEP coverage through private and public plans including the novel PrEPstart program which covers free PrEP medications for three months thereby supporting users to secure continued PrEP coverage. 3) An online PrEP advertisement campaign is being rolled out directed to GBMSM, trans, and non-binary people on popular social media and redirects them to the [ontarioprep.ca](http://ontarioprep.ca) website resource. And 4) a PrEP utilization monitoring mechanism is in place from IQVIA that longitudinally estimates PrEP dispensing trends.

The Canadian PrEP clinical guidelines were published in late 2017 (3) and Ontario covered PrEP soon after (4). This was followed by an increase of over 700% in PrEP use between 2015 and 2018 (5). By the first quarter of 2020, 8,096 individuals were being dispensed PrEP out of at least 30,000 potential users of whom 77% were in the Greater Toronto Area (GTA) and Ottawa (~6.4 and 1 million people, respectively) and 23% elsewhere in Ontario (7 million people) (6). While there was also increased PrEP use outside of large urban centres, this remains lower in suburban/rural areas of the province. Again, whether or not this level of PrEP use is optimal to achieve PrEP elimination, remains unknown. In the US, a PrEP access gap between urban and rural areas has been documented which persists to date, eight years after PrEP was first approved there (7).

HIV elimination would require that PrEP is offered when needed, and maintained for the duration of a substantial risk of HIV acquisition. Timely use of PrEP can only happen when it can be accessed readily. For PrEP to exert the strongest impact, it needs to be easily accessible at the sites where PRHA seek care, when possible. This can only be done with the full involvement of **primary care providers (PCP)** who would effectively identify PRHA and either offer PrEP or refer to rapidly responsive PrEP services (e.g. sexual health clinics, dedicated PrEP clinics, or PCP with consistent PrEP practice). Failure to perform these activities can result in missed opportunities to prevent HIV acquisition (8, 9).

In Ontario, PrEP was first offered by specialists with high familiarity with HIV medicine. By 2019, 60% of the 1,420 PrEP prescribers in Ontario practiced in the GTA and Ottawa (~ 7.4 million people combined), the cities with the highest PrEP-to-need ratio, 25% and 16%, respectively (6). Of the 41 PrEP clinics listed on the [ontarioprep.ca](http://ontarioprep.ca) website, 17 are in the GTA, and the remaining are distributed across Ontario. The number of PrEP prescribers outside of these clinics is unknown. For instance, a survey in PCP in the Greater Hamilton and Niagara area (n=40), found that only 27% of the family physicians prescribed PrEP (10). Notably, this study did not report the participation rate, but it was probably very low given that over 1,000 PCP practice in this region (11). Besides, a study conducted in Toronto revealed that PRHA preferred to seek PrEP in sexual health clinics rather than from family physicians (12).

**There is a need to increase PrEP adoption/capacity in Southeastern Ontario (SEO).** In Kingston, the Infection and Immunology Clinic (IIC), a subspecialist-led clinic has provided care to people living with HIV (PLH) since the '90s and PrEP since 2014. Between 2018 and 2020, the IIC followed 20-30 PrEP users and currently follows 18 all referred from family physicians or sexual health clinics. Dr. Guan, acting medical officer of health, Kingston Frontenac Lennox and Addington (KFLA), and who as a resident rotated in the IIC, set up nurse-led, medical-directive driven PrEP services in the KFLA sexual health clinic, active since 2020 and currently following 30-40 patients. In response to the COVID-19 pandemic, both clinics provide the bulk of PrEP care by telemedicine. Most PrEP patients seen in the IIC and KFLA

are referred by PCP with low familiarity with PrEP. The trend in referrals has not changed over the last 3 years (15-20/year). The County Drugstore PrEP clinic offers PrEP in Picton. Notably, other than KFLA, no other sexual health clinic under the Hastings and Prince Edward (HPE) districts and the Leeds, Grenville, and Lanark (LGL) districts public health units (PHU) offer PrEP services. The IIC still receives PrEP referrals from the Queen's University student health services (serving over 25,000 students). KFLA offers sexual health services to Saint Lawrence College (approx. 2,400). We ignore if the Loyalist College (approx. 3,500 students) has PrEP services. We do not know the number of PrEP users followed elsewhere in SEO. This may be due to few requests for PrEP services, or other health providers offering this service elsewhere (e.g., via telemedicine). However, we suspect that there are many more people in need of PrEP in SEO than those currently taking it: The SEO catchment population is ~560,000 which renders an estimated GBMSM population of 2,800-8,400 (1-3% of all men) (13, 14). Thus, for a PrEP coverage target of 30% (arguably a modest target) of behaviourally eligible GBMSM (~50%), the range of PrEP-eligible individuals falls between 420 to 1,260 in SEO (15, 16). The 2020 OHTN report on PrEP (unpublished) estimated that there were 144 PrEP users and 62 PrEP prescribers in the Eastern Ontario region (which also includes the population covered by the Eastern Ontario PHU and the Renfrew Health Units) by the first quarter of 2020, a figure three times lower than the lowest estimate of PrEP-eligible individuals only in SEO, which is a portion of the Eastern region. While the PrEP-prescriber-to-need ratio in Eastern Ontario is higher than elsewhere in Ontario, it is unlikely that the current prescribers in SEO can absorb additional PrEP users over time.

**This project will contribute to HIV elimination in Ontario. We are proposing a mixed methods research and implementation project that will build on the existing health care infrastructure to increase PrEP capacity and adoption among PCP and to integrate PrEP services. Consequently, we expect enhanced HIV prevention that contributes to reaching the OHTN HIV elimination goal by 2026. We propose four aims:**

**AIM 1. Conduct formative work with PCPs to identify 1) the PCP's level of willingness and intention to become consistent PrEP prescribers, and 2) PrEP adoption determinants among PCP, managers, and other key stakeholders, and 3) gather recommendations to address adoption barriers.**

We do not know what the level of PCP's intention and willingness is to offer PrEP in SEO. This is essential to estimate the extent to which PrEP can be scaled up by PCP in the current scenario. Through an online survey and qualitative semi-structured interviews, we will obtain input from PCPs about the factors, barriers, and facilitators for PrEP adoption and what solutions PCPs propose that could increase it. Adoption determinants may be individual, organizational, and contextual. (17)For instance, there is evidence of high levels of support of Ontario nurses for nurse-led PrEP implementation (18). However, Ontario nurses in sexual health clinics perceived that lack of support from physicians was a barrier to PrEP rollout (18). This latter study recommended that the attitudes of physicians supervising these clinics needed to be further understood to effectively engage the potential that sexual health clinics have to offer PrEP services, a task that we will pursue in the proposed project. Given the urgency to increase PrEP adoption, we will also use this opportunity to identify PCPs with high potential to become PrEP-adopters: highly motivated PCP eager to implement PrEP in their practices; and key stakeholders and program managers with high intention to buy-in and support the provision of PrEP services.

**AIM 2. To use the collective experience in PrEP implementation to formulate 1) a training plan for PCPs, and 2) rapid PrEP implementation strategies/protocols that adjust to different clinic settings.** PrEP adoption by PCP is low in SEO despite the availability of online PrEP education resources. This is evident from the fact that only one of seven sexual health clinics in the SEO area offer PrEP. Our team members who are physicians in primary care, public health, global health, and HIV medicine were not aware of the [ontarioprep.ca](http://ontarioprep.ca) website which raised the concern that the PrEP campaign may not be effectively reaching key target populations (e.g. PCP). Besides, there are doubts that the online resources available through [ontarioprep.ca](http://ontarioprep.ca) can effectively translate into increased adoption of PrEP by PCP and sexual health clinics in the absence of other specific efforts. PrEP adoption by PCP has remained low in the US despite having been approved since 2012 (19). There is a risk that a similar situation takes place in SEO (or Ontario in general) with negative repercussions for HIV elimination efforts. Thus, this study will inquire about PCP awareness of the HIV End Game campaign and available PrEP resources in Ontario. By doing this, the study itself will act as an advertising mechanism to increase awareness in contacted PCP. We will then use their collective input to build specific implementation PrEP strategies, **namely rapid implementation strategies**, that could fit different settings in SEO. The input obtained from PCP will be articulated with our team experience on STI and PrEP service implementation, PrEP situational analysis, qualitative research, medical education, and program evaluation. These data will be used to define our study's performance objectives, which are the aspects that need to be subject to change to result in PrEP adoption by

PCP. In this regard, we anticipate that the PrEP service model of the KFLA sexual health clinic can be replicated in other settings: at the HPE sexual health clinic, at the seven LGL sexual health clinics, and potentially also at the student health clinics of Queen's University, St Lawrence and Loyalist College. In Toronto, a sexual health clinic effectively implemented PrEP services using nurses who follow PrEP medical directives. (12) Expecting that knowledge and learning of PrEP-related skills will need to be addressed, we will work jointly with the Queen's University Professional Development and Educational Scholarship (PDES) to define educational performance objectives and develop a PrEP module that effectively addresses knowledge gaps and fit to various learning preferences. Since several learning tools are already in place at [Ontarioprep.ca/clinician/](http://Ontarioprep.ca/clinician/), we will develop tools that complement these without duplicating them. It is expected as well that case discussions, standardized patient-based activities, and the development of medical directives would make part of the educational/implementation strategies to develop.

**AIM 3. To roll out and evaluate a PrEP training program for PCPs.** Once the educational strategies are in place, we will roll them out with the group of PCP who are willing to participate. We will evaluate their impact by measuring several implementation parameters or outcomes: Here, we will need to include the evaluation of the educational program (educational outcomes), plus the impact of the intervention on PrEP outcomes. We will evaluate their impact in terms of reach, effectiveness, adoption, implementation, and maintenance which include answering questions such as the following: 1) Was the educational program appropriate for, acceptable to PCPs? 2) Was it effective to change behaviour? 3) Who was reached? 4) What was the profile of the adopters and non-adopters? 5) What was the fidelity of the PrEP practices performed by new adopters? 4) 4) What was its effectiveness in terms of PrEP prescriptions, number of people offered PrEP, knowledge, and skills to provide PrEP. We expect to find that after the rollout of the training phase, more PCPs would be able to offer PrEP care and that PrEP would be adopted in all or most sexual clinics in SEO.

**AIM 4. To roll out and evaluate rapid PrEP implementation strategies.** Implementation strategies amenable to rapid implementation will be rolled out immediately after PCPs have completed their training. This may or may not, (depending on their nature) be part of the training intervention. Similar to AIM 3, we will evaluate their impact in terms of reach, effectiveness, adoption, implementation, and maintenance. Based on previous experience, these strategies may include the development of medical directives such as the KFLA PrEP program, organizational adjustments, PrEP checklists, expert personalized peer support, enhanced PHU PrEP program advertisement.

## 2. RESEARCH DESIGN AND METHODS:

**2.1. Overall design:** From the field of implementation science, we will use the Implementation Mapping (IM) methodology to guide the collection of data and accomplish the three aims. (24) This methodology is the most relevant since PrEP is a well-established evidence-based intervention and a provincial implementation strategy is active, but the latter may be falling short of reaching the target populations of adopters (PCP) in SEO. **AIM 1- the formative work-** corresponds to tasks 1 and 2 in IM. In task 1, implementers are identified: we will assess the willingness and intention of PrEP service provision in study participants and identify potential PrEP adopters among the participating PCPs and organizations. In task 2, we will identify barriers and facilitators for PrEP implementation (PCP) which will be mapped according to the implementation science frameworks and behavioral change theories described below. **AIM 2- the development work** -corresponds to Task 3 and 4 of IM. We will select theory-informed, evidence-based, and context-specific interventions to address each identified barrier and enhance facilitators, and formulate implementation strategies and an educational plan (this may use different strategies). In Task 4, we will produce the materials and tools of the educational plan. **AIM 3- rollout and evaluation-** corresponds to Task 5 in IM. Here, we will pilot the educational program and evaluate implementation outcomes. Details of each of the tasks and concrete examples are available in Fernandez et al. (20, 21). To obtain the information on each task, this study uses mixed methods that include a cross-sectional observational study, semistructured interviews, and group discussions. Mixed studies that incorporate qualitative and quantitative paradigms are best suited to study the implementation of interventions or programs as they help understand complex interactions and determinants, provide greater wealth and validity in terms of data collection and analysis, and evaluation (22). Quantitative methods can help confirm hypothesized relationships between intentions, determinants, and outcomes while qualitative methods can explore important contextual factors influencing these relationships, obtain deeper information about reasons for successes and failures, and extract key recommendations for implementation. (21). A pre-and post-intervention design without a control group will be used to evaluate outcomes via survey and semistructured interviews.

**2.2. Setting:** The proposed study will take place in the SEO region, which includes Rural Hastings, Quinte, Rural Frontenac, Lennox, and Addington, Kingston, Lanark, Leeds, and Grenville with a total population of 560,000 of whom 75% reside in medium, small urban centres or rural areas. (23) Health care resources are compiled in the Southeast Health

Line which includes three public health units (PHU): The Hastings Prince Edward PHU, the Kingston, Frontenac, Lennox and Addington PHU, and the Leeds, Grenville, and Lanark District PHU. Local resources include seven sexual health clinics, two in Kingston, one in Belleville, one in Gananoque, one in Brockville, one in Perth, and one in Smith Falls. For the LGBTQ+ community, only the HIV AIDS Regional Services (HARS) and one Transgender Health Clinic operate in SEO, while other resources are in Ottawa and Toronto. Only one clinic specialized in HIV care functions in SEO (IIC, Hotel Dieu Hospital site).

## 2.3. FORMATIVE WORK (AIM 1)

**2.3.1 Sample and study population:** We will invite all health care providers working in sexual health clinics including clinic directors and managers, medical officers of health (if applicable), HIV/STIs program coordinators, and nurses, by fax, mail, or email (PCP in Southeast Health Line  $n \sim 1200+$ ). We estimate that minimum 97 survey participants are needed to identify 50% of the 50% intention to use PrEP with an accuracy of 10%, and a confidence of 95% (59). After the survey, we will use purposeful sampling to select PCP for interviews with an emphasis on variation, (24) that is PCP with either high or low intention of adoption or uptake, so we can capture contrasting profiles and explore determinants. We expect that managers or directors of sexual health clinics and coordinators of PCP general practice offices (if applicable) can inform us about their intention to provide services, barriers, and facilitators at the organizational and external levels.

**2.3.2. Design and Conceptual framework:** We will use a mixed design to gather information on intentions, barriers, and facilitators for PrEP adoption, namely a survey and semistructured interviews. The **Consolidated Framework for Implementation Research** and the **Behavioral Change Wheel** will be used to construct the survey, the qualitative interview guides, the analysis of data, and guide the identification of barriers and facilitators for PrEP adoption. Implementing new services such as PrEP in existing organizations requires changes at the individual and collective (organizational) levels, and changes in structural behaviours and practices (25). Thus, we have chosen the Consolidated Framework for Implementation Research (CFIR) to identify barriers and facilitators to practice change and to provide the tools to design the implementation strategies for PrEP adoption and uptake (26, 27). There are five main domains in the CFIR model each of which may affect the implementation of PrEP (**see Figure 1s** of the supplementary file, obtained from Nolan & Warner (28)). The first domain pertains to the *characteristics of the intervention* which refers to PCP's perceptions of PrEP sources, adaptability, complexity among others. The second domain addresses the *outer setting*, which includes the economic, political, and social context in which the organization resides. In our case, it refers to the political and health systems the PCP practice or sexual clinics are part of. It also includes how providers/clinics incorporate the needs, resources, and preferences of PHRA, guidelines, and other external pressures. *The inner setting*, which refers to the characteristics of the organizations, that is, each of the PCP offices/clinics and sexual health clinics in the SEO. Here, we study aspects related to the organizational structure, the connections with community organizations, the culture, and the implementation climate. The fourth domain deals with the *characteristics of the individuals*, which refers to knowledge, self-efficacy beliefs, etc that PCP have on PrEP. The last domain refers to the *process of implementation*, which involves planning, engaging relevant stakeholders, executing the plan, and reflecting on and evaluating the effort. Recent literature on PrEP implementation in family planning clinics and our work in Colombia demonstrated the utility of the CFIR to identify determinants of success and failure to implement PrEP. (29) We have also selected a second framework, the Behavioral Change Wheel (30) to approach the individuals' perspective, in a manner that complements the fourth CFIR domain, *characteristics of individuals*. We believe this is necessary because the CFIR model does not fully cover the individual factors that lead to a change of behaviour. The BCW is a parsimonious model that synthesizes many theories of behavioural change. At its center is the COM-B model (**Figure 2s** of the supplementary file). The **COM-B** model recognizes that behaviour is part of an interactive system that involves the capacity of an individual or group (physical and psychological), opportunity (social and physical), and motivation (reflexive and automatic); all are constructs or dimensions necessary to produce or change in behaviour (C). The COM-B will inform the learning needs of the PCPs, that will include gaining knowledge, skills, motivations for change, etc, which is required to develop the PrEP curriculum.

**2.3.3. PCPs survey:** This survey will include PCPs' awareness, intention, and experience with PrEP, as well as individual and contextual barriers and facilitators for PrEP adoption. The online questionnaire was developed using the CFIR framework, COM-B, our previously validated PrEP questionnaire, and other published sources (31, 32). The questionnaire explores several dimensions that are related to providers' intention to manage people on PrEP: knowledge, skills, professional role, beliefs about PrEP characteristics, organizational climate and support, experience in HIV care and/or PrEP, comfort with the assessment of sexual practices, and some basic demographics (33). The concept of *intention to manage people in PrEP* will be defined according to the transtheoretical model of change (34). Thus, PCPs will be found at different stages of PrEP intention, such as unwilling, willing but without clear intention, with a high likelihood of

intention, and those in the action stage (have already started a conversation or have prescribed/counseled people about PrEP). We will also inquire about awareness and visits to the [ontarioprep.ca](http://ontarioprep.ca) website and their impressions on and use of the resources found. This data can be used to identify barriers for utilization of [ontarioprep.ca](http://ontarioprep.ca) resources, inform about the need to train PCP, and identify potential PrEP adopters. The survey will be anonymized, Qualtrics-based, and will be sent to potential participants via fax, email, and/or mail letters. Participants will receive a modest compensation/gift using PayPal or gifts from local stores. Those interested in receiving the compensation/gift will be asked to provide an email address. We will ensure that the email information is not linked to the rest of the survey. A preliminary draft of the survey is available in the supplementary file.

**2.3.4. Semi-structured interviews:** These will be conducted as follows: **1) 10 (MAX 20) PCP** about specific aspects of the practice of PrEP-related care in their offices/clinics. PCPs who have completed the survey will be invited to participate in the interviews. We will invite PCPs who are providing PrEP and those with high intention (very likely to be willing to provide PrEP in the next 12 months) and low intention (unlikely to be willing to provide PrEP in the next 12 months) to inquire about the individual, organizational and political/system barriers, facilitators, and recommendations for PrEP delivery and aspects that they feel are needed for PrEP planning and implementation in their practices. The assumption here is that there may be unidentified factors that could emerge as determinants of success or failure for PrEP adoption/implementation. The interview guide is based on the CFIR and has previously been used in our research in Colombia. (See interview guide in the Appendix) **2) Ten to twenty clinic and/or program managers/directors** will be asked about aspects of the organization and external influences for PrEP implementation. A semi-structured interview guide has been developed and tested in our PrEP project in Colombia which can be adapted for this study. (See interview guide in the Appendix). This in-depth interview will allow us to examine in detail the organizational aspects that may contribute to facilitating the provision of PrEP services. Published evidence and our work in PrEP in Colombia have revealed the importance of the compatibility of organizations with PrEP delivery, the existence of resources, the organizational learning climate, and the presence of PrEP champions as factors for PrEP adoption. (29) All interviews will be conducted via Zoom and audio recorded. A research assistant with experience in qualitative research and/or a master's student in nursing supervised by Dr. Camargo will conduct the interviews. A private company will be hired to transcribe the interviews. All the qualitative data will be imported into patented software to facilitate the analysis of the data (NVivo version 12).

**2.3.5. Analysis:** Quantitative analysis: 1) They comprise the description of data using measures of central tendency, frequencies, and proportions. Comparisons between PCP and 2) factorial and coherence analyzes to reduce the number of items and assess unidimensionality of each of the possible dimensions, e.g. knowledge, skills, professional role, beliefs about PrEP characteristics, organizational climate and support. We will use the exploratory factor analysis, testing first the unidimensionality of each of the proposed dimensions. If power is good, a confirmatory factor analysis will be conducted using SEM. The Cronbach alpha test will be used to examine the internal coherence of each scale as we described elsewhere (35); 3) multivariate models such as the CIBER analysis (36) and multivariate the Latent profile model analysis (29) will be used to identify typologies of PCPs according to intention to adopt PrEP and that share similar CFIR/COM-B factors. For the multivariate analysis, poisson regression will be done to identify the associations between each of the CFIR/COM-B scales and the different outcomes: willing vs. unwilling to provide PrEP care; intention vs non intention; having providing PrEP care vs no previous PrEP experience. The information of the latent profile and CIBER analysis will inform the main determinants to be addressed. Qualitative analysis: All qualitative data will be imported into patented software to facilitate the analysis of the data (Nvivo). The transcription and analysis of the qualitative data will be carried out simultaneously with the generation of data to guarantee research rigor. We will make a hybrid approach using thematic analysis. The analysis will include six steps: 1) development of a coding manual using CFIR and COM-B before the start of the study, 2) application of code templates and coding by two team members, 3) coding comparison and discussion of differences, 4) development of a memo organized by the dimension of CFIR/COM-B using previously published instruments, 5) review of memos by a committee of researchers. An implementation score resembling those used in other publications of CFIR will also be assigned using the memos of each clinic to identify patterns of barriers and facilitators across settings with differential intention stages. Similar studies (37) and previous work in Colombia will serve as a guide for these analyzes.

**From this work we expect two outcomes: 1) The identification of PCPs who are likely to adopt PrEP, and 2) the identification of individual and contextual barriers for PrEP implementation mapped with the CFIR and COM-B model.**

## 2.4. DEVELOPMENT OF THE EDUCATIONAL (TRAINING) PLAN AND RAPID IMPLEMENTATION STRATEGIES (AIM 2)

**2.4.1 Sample and study population:** For this phase of the study, we will invite health care providers working in sexual health clinics including clinic directors and managers, medical officers of health (if applicable), HIV/STIs program coordinators, and nurses, who have already participated in the survey phase. No specific sample size is required for this phase. With the representatives of the stakeholders participating in the study, we will aim to define the strategies needed to address barriers to the adoption of PrEP at the contextual and individual levels.

**2.4.2. Design, conceptual framework, and tools:** We will use different qualitative techniques 1) to achieve consensus on 1) barriers and facilitators, 2) implementation strategies and tools, and 3) develop a training model to pilot. Contextual and individual barriers for PrEP adoption will be matched with implementation strategies using the CFIR-ERIC matching tool and the BCW taxonomy, respectively (38, 39). The CFIR-ERIC Matching Tool is a new, freely available tool that helps researchers match barriers that were identified using the CFIR with implementation strategies [4]. This tool was developed by asking 169 implementation experts to select and rank up to seven strategies from the list of ERIC strategies that would best address each CFIR construct. The CFIR-ERIC matching tool is available as an Excel download online at [www.cfirguide.org](http://www.cfirguide.org). We will use it to determine if a determinant was deemed relevant to the implementation strategy under question (yes/no) and generate an output table with the CFIR construct matched to the ERIC strategies with a percentage. The endorsed strategies identified in this process will be mapped with the barriers and facilitators for PrEP adoption using a mapping table (see an example of PrEP study in Colombia Table 1 of the Appendix). The individual barriers identified will be mapped with the COM-B, and the BCW will be used to select functions and behaviour change techniques that will further inform develop the training program (40). Here we will generate a set of strategies that can be promptly put in place and that we refer to as rapid implementation strategies. Barriers that require educational interventions will be handled with a PrEP curriculum as follows: We will develop and deliver the curriculum based on the tenants of constructivism and adult learning theory. Constructivist learning purports that learners construct new knowledge based on the foundations of their existing knowledge through social interactions (e.g., discussions, group work), problem-solving, and support from those who are more knowledgeable in a specific area. (41, 42) While constructivism focuses on learner's interactions, "adult learning theory helps to tailor the experience within a respectful learning environment that acknowledges personal needs". (43) We will follow the guiding principles for effective adult education when developing the curricular interventions: ensure that the learning has utility and facilitates learning; focus on the issues that directly affect the learners; use up-to-date and evidence-based information; create a learning space that is collaborative and safe; anticipate how the learning will be applied in clinical settings, and maximize available resources; expect improvements as a result of the interventions received. (44-47) Curriculum development will include the creation of a planning committee. Guided by Kern's 6-step curriculum design model (Figure 1), the curriculum will be developed based on the findings from the formative work (AIM 1). The six steps include (i) identifying the problem, (ii) identifying the gaps in PCP training (knowledge, skills, and behaviours associated with PrEP processes and prescription), (iii) setting the goals and learning objectives, (iv) identifying the most appropriate educational strategy (e.g., small-group learning, problem-based learning, case-based learning, simulation), (v) implementing the curriculum, (vi) evaluating and providing feedback for improving future interactions. (48, 49) We will incorporate available resources to the curriculum avoiding duplication, e.g. we will not develop audiovisual presentations with the same content already available at [ontarioprep.ca](http://ontarioprep.ca), rather, we will develop or incorporate other resources that fill gaps identified in the formative phase.

**2.4.3. Preliminary work:** Based on work in previous work on PrEP preparedness in Colombia, we have developed a set of performance objectives and determinants mapped with the CFIR and COM-B model (Table 1 and 2 of the Appendix). The main outcomes are mapped with performance objectives which in turn are defined according to the barriers and facilitators that were reported by PCPs in the formative phase. This table will be the starting point for the discussion and will be populated with results from the formative work and discussions with the KFLA sexual health team that implemented PrEP there.

**2.4.4. Discussion sessions with key stakeholders:** We will hold meetings to gather feedback on the matrix developed in 2.4.2. Participants will include possible PCP adopters, clinical managers, implementation experts, and all the research team. We will conduct in-person or online sessions addressing each of the main dimensions of the CFIR as follows 1) one addressing the characteristics of PrEP, 2) one on external influences, such as preferences of participants, and needs in populations, 3) one on organizational performance objectives, and finally, 4) one on individual performance objectives. Each session is expected to last 2-3 hours and will start with the research team presenting a summary of the main results:

barriers and facilitators, followed by a process of reaching a consensus on the findings and on key barriers/facilitators to target, the selection of strategies and tools and a review and final approval of the draft in the last meeting.

**2.4.5. Planning educational committee:** We will work with medical education experts to develop the PrEP curriculum and delivery plan. Since PCPs will have various levels of knowledge, skills, and attitudes, with more positive aspects expected in those already working in sexual health clinics, we will adapt the training modules according to specific educational needs, e.g. low levels of knowledge and experience, high levels of knowledge and experience, etc. To start, we will map all individual performance objectives (obtained in 2.5.4) with information available on [ontarioprep.ca](http://ontarioprep.ca) and other influential training initiatives, such as those of the WHO and PrEP Watch to identify what is available and whatnot. Then, we will meet with our education experts from the Queen's Office of Professional Development and Educational Scholarship (OPDES) in the Faculty of Health Sciences who will guide the design of the PrEP curriculum and its delivery strategies. We will work in sessions of 2 or 3 hours per week until achieving the final version of the curriculum. The OPDES will obtain accreditation the curriculum through the College of Family Physicians of Canada (CFPC) and/or the Royal College of Physicians and Surgeons of Canada (RCPSC).

Curriculum development and operationalization

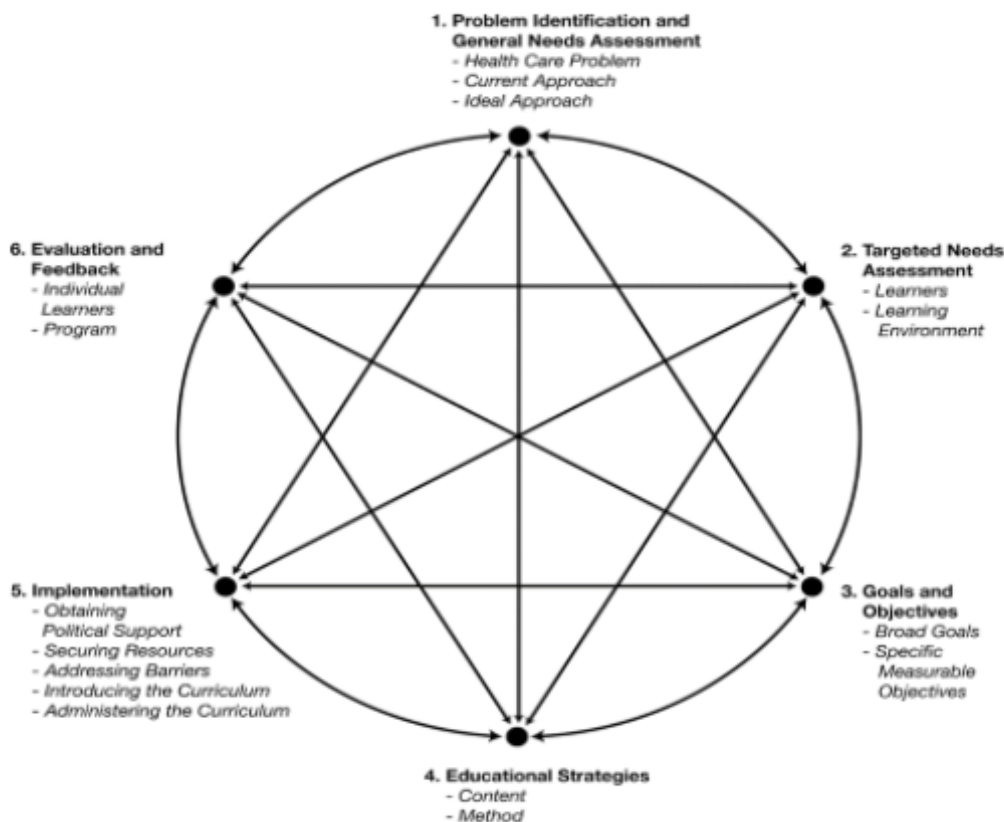


Figure 1. A Six-Step Approach to Curriculum Development Obtained from reference (48)

**2.4.6. Analysis:** most of the work of this phase is based on a deliberative process, and we will not collect data. The discussion will generate a matrix of barriers/facilitators and implementation tools/strategies. An example of these matrices is available in tables 1 and 2 of Fernandez et al. paper and the book of Susan Michie (21, 30).

The expected two outcomes of this phase are 1) a matrix of recommendations and possible strategies for adoption at the organizational level, and 2) the curriculum for a PrEP training program for PCPs.

## 2.5. ROLL OUT AND EVALUATION TRAINING PROGRAM (AIM 3)

**2.5.1. Sample and study population:** All PCPs initially invited to formative work will be invited to the training program; we expect PCP with high intention to offer PrEP to participate; all participants of the training program will be part of the evaluation sample. We do not have a predetermined sample for this study, but we expect to train at least 60 PCPs through this study. Three months after completion of the training conduction, a sample of participants in the program will be invited for personal interviews. Interviews will be conducted until saturation is obtained.

**2.5.2. Design and conceptual model:** An outcome-based mixed method design will evaluate the training program. We will collect quantitative information using and a pre-/post training study with no control arm to assess effectiveness, and group discussion and semistructured interviews with participating PCPs to explore other aspects of the program evaluation (see table 4 in the Appendix). The main evaluation questions are developed using the RE-AIM framework. The framework includes five dimensions, Reach, Efficacy or Effectiveness, Adoption, Implementation, and Maintenance. The evaluation questions are: **at the PCP level** 1) who are we reaching with this training program? What are the characteristics of the PCPs reached with the training program? 2) What are the important outcomes expected with the program? How likely is it that the initiative achieves the outcomes? What are the challenges to achieving them? And 3) what are the aspects of the program that are more acceptable and appropriate? What aspects of the program work? 4) How likely is it that the program will produce lasting effects in the participants? and **at the program level**, 1) what was the fidelity of the training program? 2) What was the feasibility of the program in terms of adherence and level of exposure?

**2.5.3. Delivery of the PrEP curriculum:** during the initial phases of this study, we will ask PCPs about learning preferences. Different options will be discussed: A mixed online/in-person training, full online sessions, in-person face-to-face sessions, standardized patients, case discussions, setting up a PrEP clinic, preparing medical directives. We will work with them to define the best ways to deliver the program and with the guidance of the Queen's University Faculty of Health Sciences office for Professional Development and Educational Scholarship.

**2.5. 4. Program logs:** During each session of the program logs will be created to 1) measure attendance, 2) assess the acceptability, and 3) fidelity of the session.

**2.5.5. Pre and post-training questionnaire:** we will assess program outcomes before, immediately after, and 3 months later (this will be updated once the program is in place): PrEP knowledge, attitudes towards PrEP, initiation of or referral for PrEP (number of patients, and demographics on patients), comfort assessing sexual history and counseling skills. The final questionnaire that will be used to assess the effectiveness of the training program and will be developed according to the educational objectives identified in the curriculum. All sociodemographic characteristics and aspects related to the intention to use PrEP found in the formative work will be included here so we can compare those who received training with those not exposed to the program in various aspects.

**2.5.6. Semi-structured interviews:** This will allow us to assess appropriateness, acceptability, mechanisms through which the educational intervention works, and feedback about the program. A preliminary guide for the interview is included in Table 5 of the Appendix. Qualitative data will be recorded using Zoom, transcribed, and de-identified. Participants will be interviewed by one of the RA or a master's student with experience in qualitative research.

**2.5.7. Analysis:** The quantitative analysis will consist of a descriptive analysis of the RE-AIM outcomes using some indicators as presented in Table 5 of the Appendix. We will assess the change in knowledge, skills, and comfort in providing PrEP pre and post-training using the T-paired and the McNemar tests. If the sample is appropriate we will adjust for the demographic and previous HIV experience of participants. Qualitative analysis will consist again of a mixed approach, using inductive and deductive methods using as main codes aspects related to program acceptability, feasibility, appropriateness, effectiveness, and recommendation. The analysis will be conducted by RA with the support of the research team.

## **2.6. ROLL OUT AND EVALUATION OF RAPID IMPLEMENTATION STRATEGIES (AIM 4)**

**2.6.1. Sample and study population:** We will invite participants whose profile suggested a high intention to start offering PrEP in their practice settings.



**2.6.2. Design:** First, we will present the rapid implementation strategies identified in AIM 2 and potential ways to use them. These strategies may include medical directives, PrEP program, organizational adjustments, PrEP checklists, expert personalized peer support, enhanced PHU PrEP program advertisement among others. Second, we will hold meetings with managerial and clinical leadership of different practice settings to define the mode and timing of each rapid implementation strategy deemed relevant to each setting. Then, we will then allow them time to perform the rollout activities. This may take one to three months.

**2.6.3. Evaluation:** We will apply questionnaires to the participants at 6 and 12 months to inquire about the impact of each implementation strategy in terms of Reach, Efficacy or Effectiveness, Adoption, Implementation, and Maintenance (see Table 5 for details on measured aspects).

**2.6.4. Analysis:** The quantitative analysis will consist of a descriptive analysis of the RE-AIM outcomes using some indicators as presented in Table 5 of the Appendix. We will describe the characteristics of the clinics that implemented PrEP vs those that did not to identify factors that affected these outcomes. This can be done either quantitatively using the chi-square test or t-test, or qualitatively. Qualitative analyses will consist of a mixed approach, with inductive and deductive methods using as main codes aspects related to program acceptability, feasibility, appropriateness, effectiveness, and recommendations. The analysis will be conducted by a RA with the support of the research team.

**2.7. Key stakeholders and Engagement activities:** Participation of key stakeholders is a fundamental aspect for effective scale-up of PrEP (25). The interaction of PCP (in general practice, emergency departments, sexual health clinics) with PRHA creates opportunities for PrEP and PEP utilization. PHUs run health promotion and disease prevention programs including sexual health. PrEP is an area of interest for HARS, the Faculty of Health Sciences of Queen's University, and the three PHUs of SEO (see letters of support). PCP including family physicians, nurse practitioners, and physicians, and nurses working in sexual health clinics will be invited to participate in the study data collection, design of interventions, generation of implementation strategies and protocols, and dissemination of results. Medical officers of health, program managers, and staff of the three SEO PHUs are essential players for the implementation of sexual health prevention programs. They run the sexual health programs at each PHU and can assess their capacity, readiness and make decisions regarding the type, level, and scope of involvement of each PHU in HIV prevention programs and PrEP services. We will engage stakeholders using various approaches. First, we have developed this project with input from key stakeholders, and we will seek to involve all relevant stakeholders with more diverse backgrounds. This advisory committee will interact regularly during the first six months. Secondly, all stakeholders will be key informants in all phases of the project. They will participate in surveys, in-depth interviews, discussions, and planning meetings. Third, we will hold planning meetings with representatives of all stakeholders. Finally, we will count on the expertise of OPDES to review the instruments of the formative phase, ensure all key components of adult learning are taken into account and oversee the evaluation of the educational intervention.

**2.8. Overview of the current environment, including barriers and facilitators:** The Times Higher Education Impact Rankings, reported Queen's University in the first place in Canada thanks to social impacts locally and abroad. (50) Queen's University is especially interested in contributing to the seventeen United Nations' Sustainable Development Goals. (51) Goal 3 is Good Health and Well-Being and goal 5 is Gender Equality. Thus, the overall climate in our institution is favorable for studies like the one we propose. The COVID-19 pandemic has increased general awareness of the need to tackle infectious diseases that are preventable, treatable, or curable. There is an active collaboration of Queen's University on Lyme disease, COVID-19, HIV treatment, HIV PrEP with the KFLA and HPE Public Health Units, and there is renewed interest and need to escalate PrEP and sexually transmitted infection care and research. In addition, the division of infectious disease has consistently over the years delivered continued medical education to PCP in SEO and supported HIV clinic rotations for Queen's University family medicine and preventive medicine residents. Finally, the current head of the Queen's Department of Public Health Sciences, and co-investigator of this study is an infectious disease physician with expertise in PrEP and sexually transmitted infections. These factors will likely facilitate the conduction of the proposed study. Another aspect that will facilitate the conduction of this project is the fact that the principal applicant and two of the co-researchers (BEA, PC) have led a similar study in Colombia with a national scope. Briefly, we have used the COM-B and CFIR framework to develop surveys (already validated) for PRHA and health care providers and these have been adapted to this project. We have conducted quantitative and qualitative analyses of the data collected in Colombia and measured health care providers and PHRA intention to adopt/uptake PrEP. We are now conducting focus groups with PRHA to share results and identify determinants to be targeted to achieve change. We have presented these results at a national meeting in Colombia and conducted four focus groups with health care providers to identify priorities for intervention, performance objectives, and possible strategies to implement PrEP in

existing HIV clinics (In Colombia PrEP was approved in 2019, but very few providers offer it). Potential barriers include a low rate of participation of PCP in an ongoing pandemic, although we expect less disruption in the months to come as COVID-19 vaccination advances. Importantly, the COVID-19 pandemic has boosted the use of online communication, a tool that is becoming the norm. We are now partnering with OPDES to harness their educational expertise for this project.

**2.9. Challenges, limitations, and proposed solutions:** Recruitment of an adequate sample may be challenging due to the low response rate common in PCP surveys. Family physicians and nurse practitioners are busy and may not readily respond to survey invitations. To tackle this challenge, we will send several reminders (up to three) asking them to participate, provide a modest compensation, and ask influential peers to support our invitations within their interaction with colleagues and through active collaboration with leaders from the Queen's University Department of Family Medicine. We have previously achieved a response rate of 40% in Colombia combining emails, regular mail, and fax. A response rate of 15-20% would suffice for the present study (approx. 150-200 participants from 1,200 invited).

**2.10. Ethical aspects of the project:** Our team has conducted a situational analysis for PrEP in Colombia and is familiar with the process for ethics approval with Queen's University. First, this study will request informed consent from each participant for the research assessment they are asked to participate in. For instance, informed consent will need to be provided before proceeding with the surveys, before proceeding with the interviews, before proceeding with focus groups. Anonymity will be protected for all surveys, privacy and confidentiality will be ensured for interviews and focus groups. Modest compensation will prevent undue coercion.

**2.11. Adaptations to COVID-19 epidemic.** Overall, the feasibility of this study does not seem to be affected by the ongoing COVID-19 epidemic. Interviews with PCP participants and focus groups will be conducted via Zoom. Currently, all healthcare facilities in Ontario have guidance to provide care to patients either in-person or via telemedicine. Therefore, no further adaptation is needed for this activity. Telemedicine will be a crucial part of the conversation when designing intervention strategies, specifically when considering populations residing far from health care facilities. While efforts will be made to build PrEP capacity that covers most areas of the SEO, given the geographical extension of rural Ontario, telemedicine will likely become a practical solution for certain areas.

### 3. AREAS OF LEARNING AND IMPROVEMENT

Many effective interventions are available to prevent HIV transmission including condom use, PrEP, post-exposure prophylaxis (PEP), combination antiretroviral treatment of chronic HIV infection, among others. However, the challenge common to them all is at the implementation stage. For instance, the ongoing COVID-19 pandemic has shown at least two important observations: The first is that one size does not fit all - province-wide school closures in response to COVID-19 hotspots negatively affected school children in low-prevalence areas and added negligible benefit to epidemic control. The science table has now recommended that individual PHU, better informed of their districts, guide the COVID-19 response in what pertains to school opening/closures. (52) The second is that even after effective vaccines have become available, barriers to their use persist which need to be understood and addressed following scientific evidence. This study offers an opportunity to learn about what is working and not with the current PrEP rollout effort and how to improve it.

1. Although Ontario is moving towards PrEP implementation, there must be recognition that the approaches designed based on large urban centres might need adjustments or modifications if they are to work for people residing in smaller cities and rural communities. We believe that this project can help us learn about such differences, how stakeholders can collaborate to address the limitations of the current implementation efforts to make them more effective in suburban and rural communities.
2. The execution of the implementation elements of this research project can consolidate existing collaborative efforts between academic HIV specialists, sexually transmitted infections experts, public health leadership, primary care providers, academic family medicine physicians, and community leaders. The expected interaction between HIV/PrEP experts and PCP in this project can contribute to integrating practice silos via discussion sessions, educational interactions and probable subsequent colleague peer support relationships encouraged by the project.
3. Regarding patient-centered care, we expect that PHUs would end up playing a very active role in advertising PrEP services built from the project in a longitudinal manner, which constitutes population-focused prevention and health promotion and may increase the efficiency of PrEP provision (and possibly uptake) by supporting the implementation of PrEP services in their sexual health clinics. Similarly, the practice of PrEP by PCP will likely result

in some cases of early HIV detection, which would result in timely referral to HIV treatment services within the SEO.

4. The rapid implementation strategies generated are expected to be feasible pathways for execution within a timeline of few months. We will pursue the execution and evaluation of such strategies as part of this project to effectively increase capacity within a short period of time.
5. We will expect to have a curriculum for PrEP training that takes into account the knowledge, skills, motivation, and opportunities of PCPs which will synergize with the available resources at ontarioprep.ca.
6. We will incorporate the fundamentals of PrEP and PEP into the undergraduate and graduate teaching curriculum at Queen's university, with special focus on teaching PrEP and PEP to family medicine and Emergency medicine trainees.

#### 4. IMPACTS

We expect that this project will to increase the capacity for PrEP provision in SEO, and maximize its sustainability for the time needed to eliminate HIV/AIDS in Ontario.

**Short-term goals:** This study will help 1) Identify the factors that affect the adoption of PrEP among in SEO, which may help inform other areas in Ontario and Canada, 2) implement and evaluate the effect of a PrEP training curriculum to increase PrEP adoption in PCPs; 3) apply rapid implementation strategies in the currently available health care resource infrastructure; 4) we expect that introducing several elements of the educational curriculum to teaching the fundamentals of PrEP and PEP in the undergraduate and graduate programs at Queen's university (with special focus on teaching PrEP and PEP to family medicine and Emergency medicine trainees) will enable graduating physicians to rapidly adopt these interventions early in their independent practices.

**Medium terms goals:** We will likely conduct a study of execution of implementation strategies generated with this study and measure impact. Hence, we expect to 1) increase the capacity of the healthcare system to prevent HIV and/or detect it early; 2) we will also increase the capacity of the healthcare system to timely detect and treat sexually transmitted infections and 3) we will inform other suburban/rural areas (in Ontario and elsewhere) on feasible strategies to increase PrEP adoption/uptake.

**Long-term goals:** we believe that the strategies to increase the capacity of PCP to offer PrEP in suburban and rural SEO can be also rolled out elsewhere and can help sustain PrEP access over the time needed to eliminate HIV in Canada and elsewhere.

#### 5. EVIDENCE SHARING PLAN

We will use different approaches to disseminate the results of this project, as follow:

1. Presentations to key audiences: At Queen's University: Results of this study will be presented at rounds in the Department of Medicine, Department of Public Health Sciences, and Department of Family Medicine locally in Kingston: We will present the results at HARS and other community organizations as requested. At the regional level: We will present the results of the study at the PHU in SEO in continued medical education activities for family physicians in SEO and others in the province as requested. At the provincial level: we will present the study results at the OHTN annual conference and elsewhere if invited. At the national level: we will submit results for poster/oral presentation at the CAHR conference. Internationally, we will submit the results of this study for publication in high-impact journals and to international conferences, e.g. CROI, IAS conferences.

2. Targeted dissemination workshops: The Queen's University department of medicine participates in continued medical education of family physicians. These are excellent opportunities to disseminate the results of this study and further encourage PrEP adoption in the region. We will also pursue short workshops specifically addressing physicians working in emergency departments of hospitals around the region who often see patients seeking post-exposure prophylaxis or care for sexually transmitted infections.

3. Web page: We will create a study webpage to present the study to the public, and to disseminate study results.

4. Targeted messages: We will prepare messages to PCP around the region that fit one single page to share key learned points from the study and prompt them to seek additional information on ontarioprep.ca and/or our study website and look for PrEP resources or peer support regarding PrEP adoption. This may be expanded provincially if found suitable.

Academic	Practice	Policy
Conference papers	Upload study results via Study Web page, OHTN webpage, CATIE, PHU websites	PHU may introduce PrEP policies within their sexual health clinics and sexual health programs
Peer-reviewed, open-access journal publications	Targeted workshops on PrEP implementation for PHU, sexual health units, and PCP in Ontario.	These local policies will be shared with other PHUs to promote change.
Invited Lectures	Targeted workshops in community organizations HARS, Street Health, universities/colleges student health services	
	Podcasts e.g. new PrEP champions recently adopting PrEP and PrEP user on experience navigating new PrEP capacity	

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