Integration of Oral HIV Pre-Exposure Prophylaxis into Ambulatory Reproductive Care for Cisgender Women: A Scoping Review and Development of an Evidence-Based Implementation Strategy

by

Sharlay K. Butler

BS, Midland University, 2015

MD, University of Washington School of Medicine, 2019

Submitted to the Graduate Faculty of the

Department of Infectious Diseases and Microbiology

Graduate School of Public Health in partial fulfillment

of the requirements for the degree of

Master of Public Health

University of Pittsburgh

2021

UNIVERSITY OF PITTSBURGH

GRADUATE SCHOOL OF PUBLIC HEALTH

This essay is submitted

by

Sharlay K. Butler

on

April 30, 2021

and approved by

Essay Advisor: Linda Rose Frank, PhD, MSN, ACRN, FAAN, Professor, Graduate School of Public Health, School of Medicine and School of Nursing, Principal Investigator, MidAtlantic AIDS Education & Training Center, Chair, City of Pittsburgh, HIV Commission

Katherine E. Bunge, MD, MPH, Assistant Professor, Department of Obstetrics, Gynecology & Reproductive Sciences, Magee Womens Hospital of the University of Pittsburgh Medical Center, University of Pittsburgh

Integration of Oral HIV Pre-Exposure Prophylaxis into Ambulatory Reproductive Care for Cisgender Women: A Scoping Review and Development of an Evidence-Based Implementation Strategy

Sharlay K. Butler, MPH

University of Pittsburgh, 2021

Abstract

Public Health Significance: Pre-Exposure Prophylaxis (PrEP) is a daily antiretroviral medication to prevent HIV. 20% of new US HIV diagnoses are among women. Although PrEP has been available since 2012, less than 5% of PrEP users are women. Barriers to PrEP use include poor risk assessment by women's health providers, lack of PrEP knowledge among women, and lack of PrEP familiarity among women's health providers. Obstetrician-gynecologists (OB/GYNs) are uniquely positioned to assess women's HIV acquisition risk and increase PrEP utilization.

Objectives: To describe the development of a clinical protocol and provider education series for PrEP delivery in an ambulatory OB/GYN setting.

Methods: An implementation strategy for PrEP delivery was designed based on an informal institutional asset assessment. An evidence-based PrEP protocol was developed with stakeholder engagement. Provider knowledge/familiarity with PrEP was identified as a key barrier to PrEP access and a multi-modal, interactive lecture series was developed in partnership with local community and national HIV/AIDS organizations.

Results: A clinical protocol was distributed. Women's health provider education sessions were held. Studies monitoring the proportion of PrEP prescriptions filled before and after

implementation are ongoing. Demographic data, including reason for initiating and/or discontinuing PrEP will be described.

Discussion: There is little data on implementation of PrEP delivery among OB/GYNs. OB/GYNs are uniquely positioned to increase access and utilization of PrEP among women at risk for HIV acquisition. This evidence-based implementation strategy may provide a model that can be adapted to other women's health ambulatory settings and reduce disparities in PrEP use among women.

Table of Contents

List of Tables

List of Figures

Preface

I would like to thank the faculty, staff, and my classmates at the Graduate School of Public Health who without their unwavering support, I would not have been able to complete this degree. To the medical students, community members, and patients who shared their time and trusted me with their experiences, I am deeply grateful. This essay is dedicated to my family, especially my husband and daughter.

1.0 Section I: Review of PrEP Among Women

In the United States, at the end of 2018, there were approximately 1.2 million people living with HIV in the US, 20% of which were women. It is estimated that 1 in 9 US women living with HIV do not know their HIV status which poses significant treatment and prevention barriers[1]. Among women, HIV disproportionately affects black women. In 2018, 16% of new HIV diagnoses occurred in women with 58% of these incident cases (4,097 of 7110) diagnosed among Black women, who make up only 13% of the population[1]. Indeed, the HIV incidence rate among Black and Latina women is 15 times and 5 times higher than White women, respectively[1]. While sexual contact is the main HIV transmission category among US women, needle-sharing intravenous drug use (nsIVDU) represents a significant means of transmission, particularly among women[1].

The reproductive health of women is also uniquely impacted by HIV infection[2]. Women experience inequity in sequelae of HIV complications of which men do not. These range from higher frequency and severity of sexually transmitted diseases (STDs), abnormal cervical cytology, menstrual irregularities, and the burden of potential vertical transmission during pregnancy[2–14].

In considering gender disparity, HIV risk, and morbidity it is important to acknowledge the burden among transgender individuals. Historically, HIV/AIDS surveillance data has focused on cisgender women because of challenges in identifying and reporting gender identity in HIV surveillance. Transgender-specific data are limited but existing literature reveals that the majority of new HIV infections in transgender people occur in transgender women and almost half of those are among Black transgender women[15]. Hindering our understanding of the epidemic in this population, nearly two thirds of transgender women and men have never been tested for HIV[16].

While the authors acknowledge the limitations of gender identity inclusion in the literature, this report will use the term ‘woman’ to mean cisgender women.

1.1 Mode of Viral Transmission

Empiric data on per contact risk of HIV exposure is limited. Women are at risk for sexual acquisition of HIV through both unprotected vaginal and anal intercourse and the percentage of diagnoses of HIV infection attributed to heterosexual contact is the most common transmission category in the US[1]. Unprotected receptive anal intercourse (URAI) poses the highest transmission risk per sex-act given the significant concentration of immune cells lining the gastrointestinal epithelium that are exposed to HIV-infected genital fluid. URAI is not an uncommon practice among women but is often underreported. Existing data, albeit limited, has found that over 40% of women have engaged in URAI[17,18]. However, HIV transmission risk per-act of URAI does not appear to be different between men and women (approximately one transmission per 72 sex acts) [17,19]. High viral load, the presence of STDs, lack of penile circumcision, as well as other host and genetic factors may also influence the efficiency of HIV transmission[20]. The estimated per-act transmission risk for receptive penile-vaginal intercourse is twice as high as that for insertive penile-vaginal intercourse (1 per 1250 sex acts vs 1 per 2500 sex acts), thus women are more likely to acquire HIV from men than men from women[19,20].

Parenteral transmission through nsIVDU is the second most common transmission category for women in the US[1]. Estimated per-act risk from nsIVDU is approximately 1 in 150 per-act[19]. The percentage of new HIV diagnoses attributed to nsIVDU is increasing with the largest

percentages among American Indian/Alaska Native (43%) and White women (36%). Diagnoses of HIV attributed to perinatal transmission account for ≤1% of cases among all women.[1]

1.2 Review of Biomedical HIV Prevention Strategies for Women

There are many current HIV prevention strategies that target different modes of HIV transmission. Behavioral interventions targeting individual choices and decision-making have been the mainstay of prevention methods for women. These include programs that address barrier protection methods, risk perception, comprehensive sex education (such as STD screening and types of intercourse), and issues of HIV stigma and discrimination[21–23].

One of the most important advances impacting these types of HIV prevention strategies has been the recognition of HIV treatment as HIV prevention. Evidence supporting this concept is derived from several large randomized and observational studies among serodiscordant sexual partners. These studies demonstrated that the risk of sexual transmission of HIV is negligible when a person living with HIV (PLWH) is virally suppressed for at least six months [24–27]. The concept of treatment as prevention is also referred to as U=U, or undetectable equals untransmittable, was included in the 2019 update of the US official HIV treatment guidelines[28].

1.2.1 Oral Pre-Exposure Prophylaxis

Concomitant STDs, inflammation, tissue concentration of immune cells, genital mucosal trauma, and hormonal changes may also mediate infection permissiveness in the cervicovaginal

tissue[29,30]. Female-controlled, discrete, non-coitally dependent interventions are important as they enable women to protect themselves when they may not have the position to negotiate other forms of safe-sex such as male condom use. Thus, female-controlled methods for preventing HIV are critical areas of research and implementation.[31]

In 2012, daily oral tenofovir disoproxil fumarate 300mg/emtricitabine 200mg (TDF/3TC), in combination with safe sex practices, was approved by the Food and Drug Administration (FDA) for use as HIV pre-exposure prophylaxis for all-genders at substantial risk of HIV infection[32] This 2 drug formulation is the only FDA approved oral biomedical PrEP option for women. Oral PrEP prevents HIV transmission through sexual activity when these drug concentrations accumulate in sufficient levels in mucosal tissue to suppress viral replication[30]. TDF and 3TC are nucleoside reverse transcriptase inhibitors and interfere with HIV viral RNA dependent DNA polymerase resulting in inhibition of viral replication.

While oral TDV/3TC is effective and approved for use as PrEP, there is continued research into alternative biomedical interventions. A second formulation of tenofovir, tenofovir alafenamide (TAF) coformulated with 3TC is available as oral PrEP but has not yet been approved for those whose primary risk factor for HIV acquisition is receptive vaginal intercourse[33].

1.2.2 Microbiocides

Microbiocides are products that are designed to prevent the sexual transmission of HIV when applied topically to the vagina or rectum. Some of the earliest female-focused microbiocides trialed were tenofovir-based gels, foams, and films, and most recently, an anti-retroviral impregnated ring[29,34]. Despite early pharmacokinetic data that demonstrated high levels of tenofovir (TDF) concentrations in vaginal mucosa, randomized clinical trials have produced

conflicting results regarding the efficacy of topical TDF-based microbiocides in preventing HIV infection[35]. In a trial that assessed efficacy and safety of a TDF 1% vaginal gel, (CAPRISA 004), the sexual acquisition of HIV was reduced by 39% overall and by 54% in women with high product adherence (adherence >80%) efficacy[36–38]. Two large clinical trials of a dapivirine (DPV)-impregnated vaginal ring, the Ring and MTN-020-ASPIRE, demonstrated reductions in HIV incidence among women by around 30%. This increased to over 70% in subsequent analyses in women who were highly adherent to the product[39,4041,42]. In July of 2020, the European Medicines Agency offered a favorable opinion on the DPV-ring and it is now recommended as a HIV prevention choice for women by the WHO[43–46]. Other promising biomedical interventions, such as cabotegravir (CAB) and islatravir, are currently being evaluated in long-acting injectable and subcutaneous implant formulations of PrEP. Early phase, gender-inclusive studies are ongoing for both antiretrovirals[47,48].

1.3 PrEP Evidence Summary Among Women

The path to proving HIV prevention efficacy of oral PrEP in women has been challenging. Trial results have been conflicting, but the key efficacy study for women has been the Partners PrEP trial (Table 1, 2) [49] This was a randomized control trial (RCT) of oral PrEP use among 4758 heterosexual serodiscordant couples. Sexually active, HIV-1 seronegative women randomized to oral TDF/3TC had a 66% reduction in HIV-1 incidence when compared to women assigned to the placebo arm. This point estimate was lower than the > 90% reduction reported in previous data from studies conducted among men who have sex with men[50]. However, in post-hoc analysis, when serum levels of were used as a proxy for adherence, a 90% reduction in HIV incidence was

observed among women with detectable study drug serum levels. Similar trends have been found in other large RCTs. The TDF2 trial, another key trial reporting oral PrEP efficacy in women, reported transmission risk was decreased by as much as 71% among women who received oral TDF-based PrEP[49,51]. Conversely, 2 major women-only PrEP trials, VOICE and FEM-PrEP, analysis did not demonstrate protective benefit. Post-hoc analysis demonstrated low levels of plasma TDF in study participants, consistent with low drug adherence and thus low prevention[37,38]. In an adherence-based meta-analysis of all randomized clinical trials of PrEP efficacy that included women, oral PrEP was effective in reducing the sexual transmission of HIV (relative risk 0.39, 95% CI 0.25-0.60) when levels of drug adherence were 75% or greater [52].

Table 1 Evidence Summary of Randomized Clinical Trials – HIV Incidence Findings

<table>
<tr><th rowspan="2">Study</th><th colspan="2">Outcome Analyses – HIV incidence (mITT)</th><th colspan="3" rowspan="2">Effect – HR [Efficacy Estimate] (95% CI)</th></tr>
<tr><th>Agent</th><th>Control</th></tr>
<tr><td rowspan="4">Partners PrEP (heterosexual men and women)</td><td rowspan="4">TDF
17infections among 1572 persons

TDF/FTC
13 infections among 1568 persons</td><td rowspan="4">52 infections among 1568 persons</td><td></td><td>TDF</td><td>TDF/FTC</td></tr>
<tr><td>All</td><td>0.33 [67%] (0.19–0.56)</td><td>0.25 [75%] (0.13–0.45)</td></tr>
<tr><td>Women</td><td>0.29 [71%] (0.13–0.63)</td><td>0.34 [66%] (0.16–0.72)</td></tr>
<tr><td>Men</td><td>0.37 [63%] (0.17–0.80)</td><td>0.16 [84%] (0.06–0.46)</td></tr>
<tr><td>TDF2 (heterosexual men and women)</td><td>9 infections among 601 persons

1.2 infections/100 person-years</td><td>24 infections among 599 persons
3.1 infections per 100 person-years</td><td colspan="3">0.38 [62%] (0.17–0.79)</td></tr>
<tr><td>FEM-PrEP (heterosexual women)</td><td>33 infections among 1024 persons

4.7 infections per 100 person-years</td><td>35 infections among 1032 persons
5.0 infections per 100 person-years</td><td colspan="3">0.94 [6%] [a] (0.59–1.52)</td></tr>
<tr><td rowspan="2">VOICE (heterosexual women)</td><td rowspan="2">TDF
52 infections among 993 persons
6.3 infections per 100 person-years

TDF/FTC
61 infections among 985 persons 4.7 infections per 100 person-years</td><td rowspan="2">35 infections among 999 persons
4.2 infections per 100 person-years</td><td colspan="2">TDF</td><td>TDF/FTC</td></tr>
<tr><td colspan="2">1.49 [-50 %][a] (0.97–2.3)</td><td>1.04 [-4%][a] (0.73, 1.5)</td></tr>
</table>

mITT: modified intent to treat analysis; HR: hazard ratio

Adapted from the US Centers for Disease Control and Prevention, US Public Health Service, Preexposure prophylaxis for the prevention of HIV infection in the United States – 2017 update: a clinical guideline. Available at: https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf

[a] Not statistically significant

Table 2 Measures of Efficacy, by Medication Adherence, Percent Reduction in HIV Incidence in Randomized Clinical Trials (95% Confidence Interval)

Study	Modified Intent-to-Treat Efficacy			Efficacy by Self-report Adherence Measures	Efficacy by Pill count Adherence Measures	Efficacy by Blood Detection of Drug Measures[a]
Partners PrEP	All TDF: 67% TDF/FTC: 75%	Men TDF: 63% TDF/FTC: 84%	Women TDF: 71% TDF/FTC: 66%	NR	100% (87–100%)	TDF: 86% (67–94%) TDF/FTC: 90% (58– 98%)
TDF2 (TDF/FTC)	All 63%	Men 80%	Women 49%[b]	NR	NR	TDF detected: 85%[b]
FEM-PrEP (TDV/FTC)	NR			NR	NR	NR
VOICE (TDF, TDF/FTC)	NR			NR	NR	NR

NR, not reported

In fact, the majority of trials showed an "intended use" vs "actual use" phenomenon that parallels familiar issues in contraceptive use and efficacy[31]. Like contraception, PrEP is effective if taken as prescribed. The pharmacokinetics of antiretrovirals in genital mucosal tissues are governed by a number of complex factors. Indeed, PrEP is less forgiving in terms of missed doses when it comes to women[29]. It takes more doses of oral PrEP to achieve protective levels in the vaginal mucosa than the rectal mucosa. Women must ingest a minimum of 6 doses per week to benefit from a protective effect[29,53]. Understanding and identifying barriers to and predictors of adherence is critical in maximizing the impact of PrEP for women[36,37,54–57].

Data surrounding efficacy of oral PrEP in preventing HIV transmission from IVDU is limited. A randomized, double-blinded, placebo-controlled trial of 2,413 HIV seronegative persons with a history of IVDU in the previous year reported a 51.8% (95% CI 15.3-73.7; p=0.01) reduction in HIV incidence when comparing TDF-based PrEP with the placebo group in an

intention-to-treat analysis. However, in the nested case-control analysis of seronegative participants and those with incident HIV infections in the trial, those with detectable TDF plasma levels had a 70% (95% CI 2.3-90.6; p=0.04) reduction in HIV incidence[58]. In this study, all participants received one or more comprehensive HIV prevention methods (i.e. risk reduction counseling, adherence counseling, condom distribution, and opioid use disorder treatment) and thus it is difficult to parse the isolated efficacy of daily oral PrEP among persons who use IV drugs[59].

1.4 Pregnancy Considerations for PrEP

Pregnancy and lactation represent periods of increased HIV acquisition risk[60]. In a recent analysis of women in serodiscordant relationships, risk of HIV acquisition probability per condom-less sex act steadily increased during each stage of pregnancy and risk was highest in late pregnancy and postpartum[60]. In this study, the risk of HIV acquisition per condom-less sex act was 3 and 4-fold higher in the pregnant and postpartum periods as compared to the nonpregnant period. Some of this risk is thought to be mediated by the hormone related changes in HIV receptor expression, vaginal microbiota, and pregnancy related changes in innate immunity. Additionally, the frequency of sex acts increases in the postpartum period[60].

These data suggest that biological and behavioral changes during pregnancy and the postpartum period increase HIV susceptibility among women. This also carries implications for perinatal transmission which is highest in the setting of maternal viremia. TDF/3TC is routinely part of anti-retroviral therapy during pregnancy for women living with HIV and the majority of safety data come from open-label studies in this population[61,62]. Unfortunately, pregnant women

have been excluded from phase III PrEP clinical trials, but data surrounding peri-conception use demonstrated no difference in fertility rates, congenital anomalies or adverse pregnancy outcomes. Similar findings are supported by the Antiretroviral Pregnancy Registry, which has followed over 20,000 pregnancies with ARV exposure[61–63]. A large meta-analysis and systematic review of data from 19 cohorts representing 22,803 total woman years, reviewed all available data on safety of TDF in pregnancy and lactating persons and their infants. No statistically significant differences were observed in pregnancy incidence, stillbirth/pregnancy loss, preterm delivery less than 37 weeks, low birth weight <2500/<1500g, small for gestational age, birth defects, or infant (>14 days) or maternal mortality [64].

1.5 Breastfeeding Considerations for PrEP

Data on continuing PrEP while breastfeeding has shown that TDF and 3TC are minimally transferred via breastmilk. Breastfed infants are exposed to only 0.5%-16% of the tenofovir dosage that fetuses experienced via placental transfer, and 0.01-0.04% of the recommended weight-adjusted therapeutic dose[65]. In a study of daily oral PrEP in HIV-negative breastfeeding women, tenofovir was not detected in 94% of infant plasma samples obtained on day 7 of PrEP use when maternal drug concentrations were at steady state. Estimated infant doses of TDF and 3TC translated into a <0.01% and 0.5% relative dose when compared to therapeutic doses of these medications for infants[66]. The WHO recommends continuing PrEP if a woman is at continued risk of HIV infection while pregnant and/or breastfeeding[67]. In summary, PrEP use in pregnancy and breast feeding does not appear to be associated with higher risks of adverse

pregnancy and/or infant outcomes. Pregnancy and the postpartum period are periods of heightened HIV risk .

1.6 Unmet PrEP Need Among US Women

Risk of HIV acquisition varies among US demographic groups because HIV risk reflects the likelihood of exposure to HIV. The likelihood that one is exposed to HIV is a function of HIV prevalence in one's community and sexual networks. In addition to women's lack of knowledge about PrEP, challenges to identifying women who might from PrEP, and cost concerns, a lack of infrastructure to provide PrEP for women in venues where they commonly access healthcare poses additional PrEP access barriers. Due to historically gender exclusive marketing of PrEP in the US, there is general misconception that PrEP is only for gay men and is accessed through infectious disease specialists or clinics that primarily serve gay men or MSM[69–81]. This has further exacerbated the disparity in women's access to PrEP.

Unmet PrEP need among women has been defined. Using national HIV surveillance data and statistical modeling, the CDC estimated the proportion of adults with indications for PrEP by transmission risk factor and race/ethnicity[82]. Of the 1.1 million adults with indications for PrEP use, an estimated 176,670 (15%) were women yet when this data was cross-referenced with national pharmacy data during the same time frame, only 2.1% of PrEP eligible women were prescribed PrEP[83,84]. Inequitable prescription of PrEP may further promote racial and ethnic disparities[85]. For example, among the 1,146 women prescribed PrEP in 2016, 554 (48.3%) were white, 297 (25.9%) were black, and 201 (17.5%) were Latina. When compared to the estimated 1.1 million adults with PrEP indications during that same time, 26.3% were white, 43.7% were

black, and 24.7% where Latinx [82,83]. These discrepancies can be described quantitatively by an indicator called the PrEP-to-Need Ration (PNR). PNR represents the ratio of PrEP users to the number of persons newly diagnosed with HIV. It is used to describe whether PrEP use appropriately reflects the epidemic need. A lower PNR indicates more unmet need. In the Western US, this ratio is 25.9 for women but 7.4 among women in the Southern US, where particularly black and women of color are at disproportionate risk of HIV acquisition[86–89]. The inequity gap between those with PrEP indications and those who are actually prescribed PrEP is significant for women and particularly women of color[83].

1.7 PrEP Interest and Utilization Among Women

Clinics focusing on women's health are logical places for women to learn about PrEP and consider their own risk for HIV. Family planning offices, STD clinics, midwifery practices, and OBGYN clinics are all settings with existing structures to support initiation of contraceptive medications, which are also sex-dependent medications that require counseling regarding side effects and monitoring over time. These structures can be easily adapted to provide PrEP to women with risk factors for HIV acquisition. Many studies have sought to assess women's interest in PrEP but few report PrEP utilization in these settings. PrEP interest appears to be as high as 60% among women in family planning clinics, and as high as 82% among women in STD clinics[90,91]. Indeed, qualitative focus groups among women sampled from STD clinics show themes that women are angry they had not previously known of PrEP and expressed interest in initiation including describing PrEP as "life-saving"[92]. However, one survey among PrEP eligible women within Louisiana OBGYN clinics showed that only 54 of 144 (37.5%) women were interested in PrEP.

After counseling on PrEP side effects and monitoring requirements, only 4 (2.8%) remained interested [93]. Notably, of the 54 women who did report interest, 88% felt comfortable discussing PrEP with their OBGYN[93].

Of the limited data reporting PrEP utilization in women, one prospective study among people presenting for HIV testing at a STD clinic in Texas reported actual PrEP utilization among women[94]. Of 109 women who were eligible for PrEP, 27 were interested and 22 initiated PrEP (20%). Comparatively, when PrEP was integrated in a safe syringe program for at-risk women, of 136 women with IV drug use who were approached, 63 women (46.3%) accepted PrEP prescriptions at 1 week. Of these women, 42 (44.2%) reported continuation of PrEP at week 24.

Thus, while women appear to express interest in preventing HIV acquisition, PrEP utilization remains low and may vary by setting[95]. Qualitative studies have described several barriers that impact low PrEP utilization despite high interest among women in options to prevent HIV acquisition. These include challenges in understanding personal HIV risk, prior experiences with HIV (eg family members dying from HIV-related complications), stigma around HIV diagnosis (eg considering it a death sentence), stigma from providers regarding sexual practices, and ongoing structural inequities that perpetuate high HIV vulnerability (eg racism, poverty, intimate partner violence, etc.) [92,96]. The data showing low interest in PrEP among women in OBGYN clinics is concerning when compared to other studies assessing women in family planning and STD clinic settings. More research is needed to identify the pathway from interest in PrEP to actual use of PrEP among women, and to understand what additional barriers there may be within OBGYN offices. However, what is clear is that women deserve non-judgmental care and access to discussions of HIV risk and PrEP counseling from their women's health providers.

2.0 Section II: Leveraging the Unique Position of Women's Health Providers to Increase Access to PrEP

Demand for implementation research that promotes the integration of evidence-based practices, interventions and policies into routine health care and public health settings is increasing. Addressing the intersection of health equity and HIV incidence disparity among women, especially women of color, is challenging. International organizations such as the World Health Organization (WHO) and the US Agency of International Development's (USAID's) Office of HIV/AIDS (OHA) have prioritized implementation science that translates HIV prevention research in to context-informed health practice[97,98]. Implementation science, the study of methods to promote the adoption and integration of evidence-based practices, interventions and policies into routine health care and public health settings, has been central in transitioning health research in to context-informed health practice[97,98]. Implementation science related to PreP and women encourages the integration of multi-level, evidence-based strategies for HIV prevention in women. To help mitigate disparities in PrEP access and utilization among, women's health providers are well positioned to leverage their proficiency in adapting historically gender-exclusive medical care to meet the needs of women, capitalize on their expertise in attention to women's sexual health preferences, and draw from their experience navigating the unique social determinants that mediate their HIV risk.[99]

2.1 Determinant Framework to Assess Facilitators & Barriers to PrEP Implementation

Implementation of PrEP delivery necessitates careful attention to both women's sexual health preferences and the unique social determinants that mediate their HIV risk. The consequences of implementation of PrEP delivery strategies without contextual fit can result in wasted resources, undue burden on clinic structures, and exacerbation of disparate PrEP allocations[99]. Determinant frameworks identify determinants that contextualize the setting in which a strategy or intervention is developed. They do not address how change takes place or describe casual mechanisms. Using determinant frameworks imply a systems approach to implementation strategies and promote structural thinking from the beginning of strategy design[100]. Thus, frameworks and models, such as the socioecological model, that consider the complex relationships between the individual, interpersonal, organizational, community, and policy level factors can facilitate exploration of the population-specific factors that influence PrEP uptake and identify systemic challenges to PrEP implementation strategies[100].

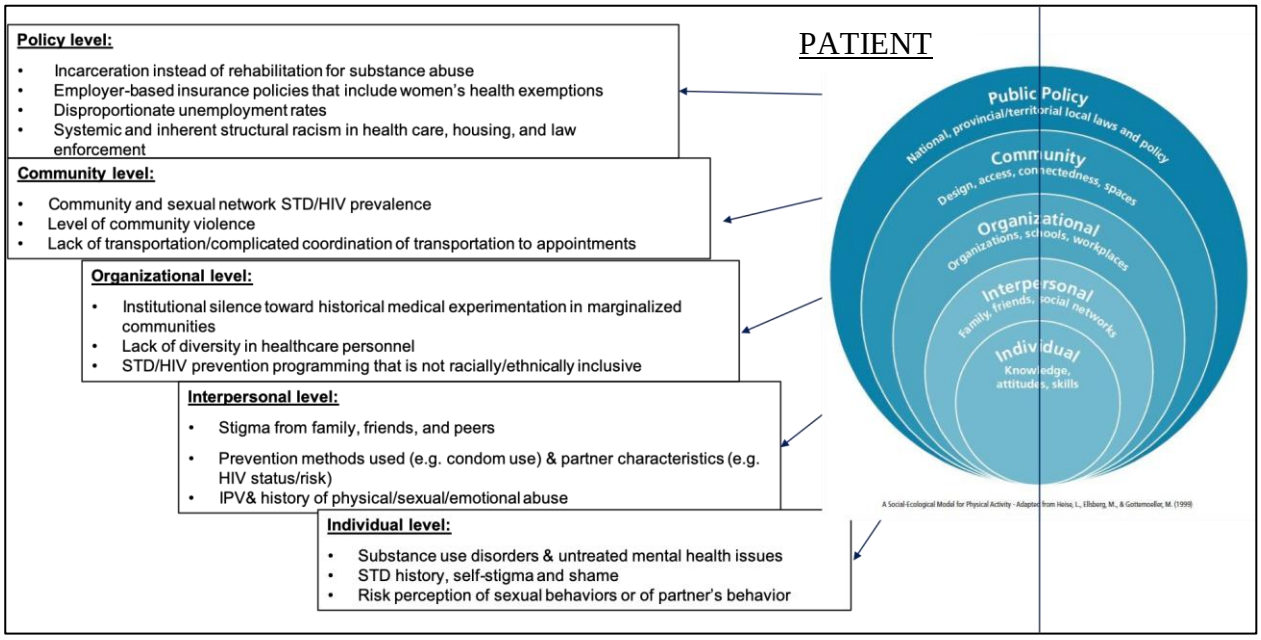
2.1.1 Contextualizing Through the Socioecological Model

At this large urban academic women's hospital, the ambulatory OBGYN clinics were identified as a primary point of access for women with vulnerabilities to HIV acquisition. The clinic receives Title X Family Planning Program grant funding through the Department of Health and Human Services to provide comprehensive family planning and preventative health services for low-income or uninsured persons. This population includes low-income women, women of color, women with opioid and polysubstance use disorders, women experiencing intimate partner violence, unstably housed women, and women with limited English proficiency. To contextualize

the powerful individual, social, community, and structural forces that mediate HIV vulnerability in this population, the socioecological model was applied and social foundations of structural bias, social inequities, and racism were characterized.

Key end users, community, and project stakeholders were engaged to identify relevant factors on each of the levels of the SEM framework. These ranged from patient and provider experiences, local community organizations serving cisgender women who would benefit from PrEP use, and hospital administrators (Figure 1).

Figure 1 The Socioecological Model of the Ambulatory Clinic Setting



Relationships of socio-structural factors unique to the ambulatory care setting were characterized through an extensive literature review key stakeholder input, and informal ambulatory clinic asset and capacity assessment (Table 3).

Table 3 Social Inequality Factors that Impact HIV Vulnerability in the Ambulatory Clinic Population

Determinants of HIV Vulnerability	Identified Examples
Structural Barriers	• Provider lack of knowledge & comfort prescribing PrEP • Intimate Partner Violence • Historical trauma & medical mistrust • 'Chief complaint' disclosure in making clinic appointment through central scheduling
-isms	• Racism (ie "clinic patient" code) • Classism (ie HIV risk implied by class) • Linguicism • Ageism (ie not screening postmenopausal women for HIV)
Social Determinants of Health	• Lack of provider diversity • Community stigma around condom use, seeking HIV testing
Structural Biases	• Limited clinic hours/no walk-in clinic • Lack of childcare for kids < 2 yo
Political Determinants of Health	• Lack of contact tracing policy in clinic
Economic Determinants of Health	• Hospital parking fees, public transportation issues • Lab fees outside of clinic fees • Co-pays, co-insurance fees

In applying the SEM from the vantage of the OBGYN provider, a key gap in the capacity of the ambulatory clinic to integrate PrEP into routine preventative care for cisgender women was low provider knowledge and comfort level in prescribing PrEP. Identifying this critical gap in PrEP delivery formed the basis of developing an evidence-based implementation strategy for integrating PrEP into the ambulatory OBGYN clinic in the form of a targeted provider education series and adapted evidence-based PrEP prescribing guidelines

2.2 Creating Awareness & Interest: Assessing HIV Risk in Women

Paramount to optimizing PrEP uptake in US women is performing adequate HIV risk assessment and helping women to recognize their risk. Inadequate HIV risk assessment results in providers being less likely to classify a woman as "eligible" for PrEP[89,99,101]. Clinical guidelines for implementation of PrEP are published by the US Centers for Disease Control and US Public Health Service's Preexposure Prophylaxis for the Prevention of HIV Infection in the United States-2017 Update: A Clinical Practice Guideline. The document summarizes PrEP safety and efficacy data, provides eligibility criteria for PrEP, outlines parameters for providing and discontinuing PrEP, and includes strategies for medication adherence and HIV risk reduction[102].

Table 4 Comparison of the Two Versions of PrEP Eligibility Criteria Within the US Centers for Disease Control and Prevention Guidelines

Version of Criteria	Population		
	Men who have sex with men (MSM)	Heterosexual Women and Men	Persons who inject drugs (PWID)
Summary of Guidance for PrEP Use	- HIV(+) sexual partner - Recent bacterial STD (gonorrhea, chlamydia, and/or syphilis) - High number of sex partners - History of inconsistent/no condom use - Commercial sex work	- HIV(+) sexual partner - Recent bacterial STI (gonorrhea or syphilis) - High number of sex partners - History of inconsistent/no condom use - Commercial sex work - In high HIV+ prevalence area or network	- HIV(+) injecting partner - Sharing injection equipment
Recommended Indications for PrEP Use	- Adult person o without acute or o established HIV o infection - Any sex with opposite partners in past 6 months - Not in a monogamous partnership with a recently tested, HIV(-) partner AND 1+ of the following: o Any anal sex without condoms (receptive or insertive) in past 6 months o A bacterial STD (gonorrhea, chlamydia, and/or syphilis) diagnosed or reported in past 6 months	- Adult person o without acute or o established HIV o infection - Any sex with opposite sex partners in past 6 months - Not in a monogamous partnership with a recently tested, HIV(-) partner AND 1+ of the following: o Is a man who has sex with both women and men (behaviorally bisexual; see also recommended indications for MSM) o Infrequently uses condoms during sex with 1+ partners of unknown HIV status who are known to be at substantial risk of HIV infection (PWID or bisexual male partner) o Is in. an ongoing sexual relationship with an HIV(+) partner o Is an ongoing sexual relationship with an HIV(+) partner o A bacterial STD (gonorrhea, syphilis in women or men) diagnosed or reported in past 6 months	- Adult person without acute or established HIV infection - Any injection of drugs not prescribed by a clinician in past 6 months AND 1+ of the following: o Any sharing of injection or drug preparation equipment in past 6 months o Risk of sexual acquisition (see also recommended indication for MSM and heterosexually active men and women)

The guidelines define PrEP eligibility criteria separately for men who have sex with men, heterosexual men and women, and people who inject drugs. These guidelines are presented in 2 different versions throughout the document - the 'summary of guidance' table (p 13) and the 'recommended indications for PrEP use' (p 36-38). In its current form, the 2 versions of the are inconsistent in critical ways for women who have risk factors for sexual transmission of HIV.[102] For example, using the summary of a guidance criteria, a woman meets indications for PrEP based on her individual risk behavior. Whereas by way of the recommended indications criteria, that

same women would be required to also have knowledge of their partner's HIV risk factors to meet criteria for PrEP. Additionally, this latter set of criteria includes stipulations that a woman be able to recognize that she has a bacterial STD, despite the fact that these infections can potentially be asymptomatic. This is problematic because many providers decide whether to discuss PrEP based on these inadequate risk assessments [89,99,101–103].

The CDC guidelines are the most widely adopted resource for guiding PrEP service delivery in the US, with 84% of states and Washington DC having state-level eligibility criteria that was adapted from or linked to the CDC guidelines[101,103]. However, the guidelines have received growing scrutiny regarding their poor sensitivity in being able to consistency identify persons who are at risk for HIV acquisition[85,104,105]. Identified discrepant eligibility criteria that disproportionately affect heterosexually active women include: indeterminant categorization of individual and structural drivers of HIV risk, vague guidance on PrEP use in the setting of condom use and/or viral suppression status of sex partners in serodiscordant couples, and perfunctory limitations of sex and gender identity language. These eligibility screening gaps in the guidelines risk further deepening disparities in PrEP access for women – particularly those of color[85,101,103].

A recent study examined the ability of the 2 CDC guideline versions to assess PrEP eligibility among women who self-disclosed as having existing HIV risk factors and/or endorsed motivation to use PrEP. Over 11,000 women receiving care at a Planned Parenthood center were surveyed online. The survey assessed PrEP interest, self-perceived HIV risk, and sexual health, relationship, and behavioral risk factors for HIV acquisition. HIV-negative women who completed all survey items to determine PrEP eligibility were included in the analytic sample (n=679). Of the women who reported known HIV risk factors, motivation to take PrEP, or both in the online survey, 82.3% of them were eligible for PrEP by summary of guidance criteria compared to 1.5%

when recommended indications criteria was applied. These data highlight the inconsistency and insensitivity of current guidelines to adequately identify women who could benefit from PrEP[101].

In another study, the CDC eligibility criteria for PrEP were applied to a cohort of women without HIV who were enrolled in the Southern US sites of the Women's Interagency HIV Study (a multicenter, observational cohort study of US women living with HIV or are at risk of acquiring it)[89,106]. In this analysis, only 32% of women with pre-defined HIV risk factors met PrEP eligibility. When the data was modeled to identify correlates of PrEP eligibility, factors such as educational level and history of sexual violence were associated with PrEP eligibility. These factors are not currently included in the CDC guidelines[89]. These data signify the critical need to address how women are screened for HIV risk and PrEP eligibility. There is a growing body of evidence that acknowledges the shortcomings of how women are currently assessed for HIV risk and calls for reform of the guidelines to align the 2 sets of criteria and increase women's PrEP access[85,101,107,108].

3.0 Section III: Evidence Based Implementation Strategy for Integration of PrEP into Routine Reproductive Health Care

There is limited literature describing the development of evidence-based strategies and interventions to integrate oral PrEP into ambulatory reproductive health care for cisgender women[99,109]. Currently, there are no high quality evidence-based or evidence-informed interventions or best practices for increasing PrEP initiation and uptake among cisgender women[110]. A strategy to implement an evidence-based intervention, such as oral PrEP, involves end user engagement, integrated knowledge translation, and structural thinking in its design. In this section, the process of developing an evidence-based implementation strategy for integrating PrEP into a large, urban academic ambulatory OBGYN clinic will be described

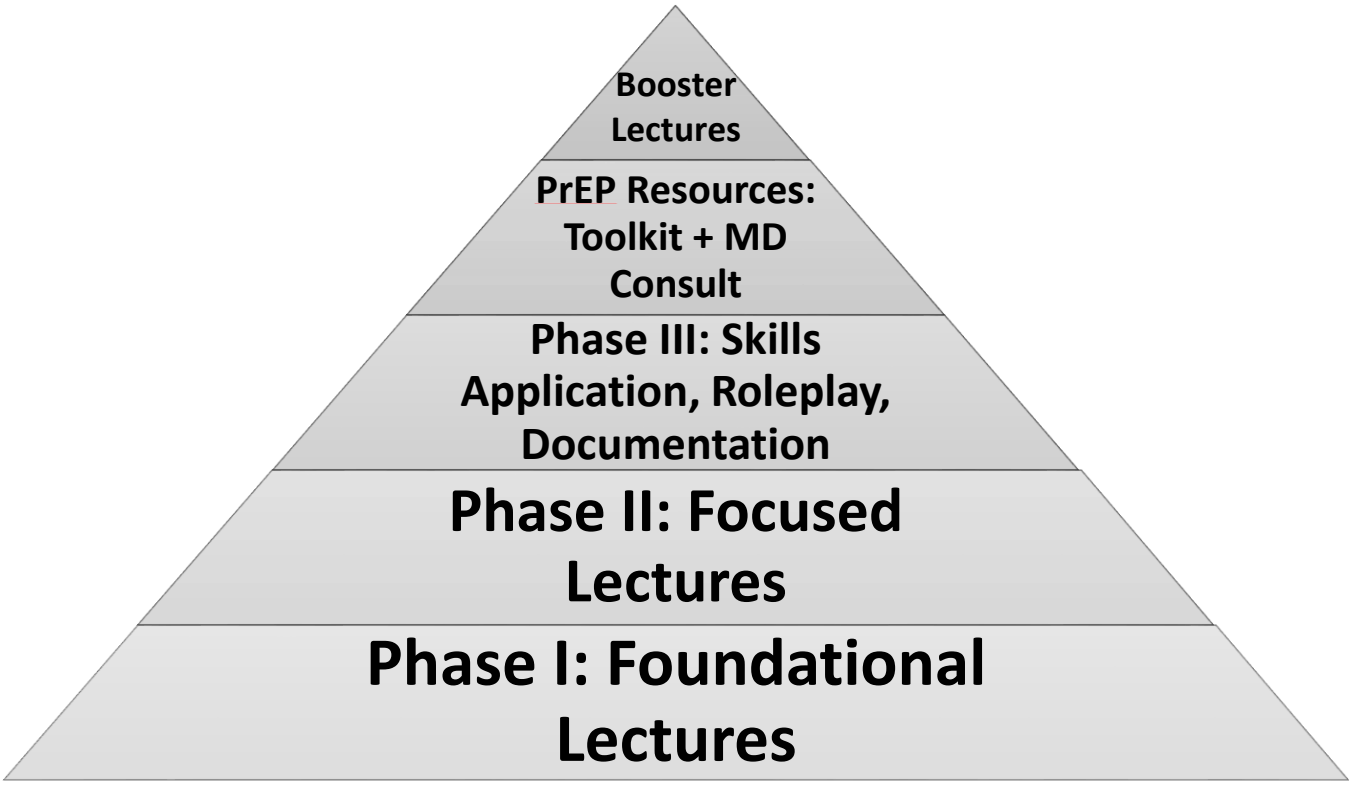
3.1 Building Knowledge & Commitment: Addressing Provider Education Gaps in PrEP Knowledge

HIV vulnerability in women is in part mediated by complex psychosocial and structural factors and may be amplified by reproductive health providers' lack of familiarity with PrEP and comfort with prescribing PrEP[111]. In a survey administered to US OBGYN providers, 685 of providers had heard of PrEP but only 3% had ever prescribed it, even though 78% of providers considered their patient population to be at-risk for HIV infection[112]. Other themes that emerged were lack of comfort with current safety and efficacy data of PreP and uncertainty if PrEP could be continued in a pregnant patient or not. 71% and 35% of providers reported these concerns[112].

At a national level, a survey of family planning providers showed less than 50% of providers were comfortable with PrEP efficacy data and ordering the correct HIV test after an HIV exposure. Targeted curriculum to improve basic PrEP knowledge foundation that is tailored for pregnant, breastfeeding, and non-pregnant women are necessary[111,112].

To build provider educational capacity, a targeted educational series was developed to address gaps in provider PrEP knowledge and familiarity in prescribing PrEP, identifying women who would benefit from PrEP, and improve provider comfort in caring for pregnant, lactating, and non-pregnant women who use PrEP. A multi-modality learning approach was employed through the development of a targeted education series for providers in the ambulatory OBGYN clinic. An educational lecture series was developed to align with adult learning styles including interactive facilitated roleplay, interval "booster" education sessions to promote individual knowledge and skill retention, and succinct high-yield content review didactics. The following sections describe the three phases of the targeted education series for women's health providers (Figure 2).

Figure 2 Components of Provider Education Series



3.1.1 Target Audience

The target audience for the provider education series included all practitioners who delivered direct patient care in the ambulatory OBGYN Clinic. This included medical assistants, nurses, certified nurse midwives, nurse practitioners, physician's assistants, medical students,

OBGYN residents, and OBGYN faculty. The core demographic audience consisted primarily of physician assistants, OBGYN residents and faculty. Lecture content was made accessible to all patient care provider types.

3.1.2 Curriculum Design & Development

Lecture format consisted of traditional in-person didactic mode, remote-virtual didactic mode, and a recorded structured case presentation with facilitated role-play stratified by learner level. In addition to the evidence-based clinical protocol, resources to support PrEP providers prescribing and managing PrEP in women were developed in collaboration with the Mid-Atlantic AIDS Education Training Center (MAAETC). The MAAETC is one of eight regional Ryan White federally funded centers in the US that is administered by the Health Resources and Services Administration under the department of Health and Human Services. Among many roles in helping meet the goals of the US National HIV/AIDS strategy, the center provides training to health care professionals and organizations on the prevention, diagnosis, and treatment of HIV. In this capacity, the MAAETC also provided technical and program evaluation support during the interactive role-play session, as well as HIV expert clinics to facilitate the role-play session. The following subsections will describe each phase of the educational series.

3.1.2.1 Phase I of Provider Education Series: Foundational Lectures

Two foundational lectures were delivered to providers in lieu of a regularly scheduled weekly educational conference. Foundational lecture content was developed to address known PrEP knowledge gaps among OBGYNs[111,112]. Content areas included a review of the properties of oral PrEP, data regarding PrEP safety and efficacy in women who are non-pregnant, pregnant,

and/or lactating, PrEP eligibility criteria for women and important discrepancies in national guidelines that pertain to women as discussed above[101,103], how to prescribe and monitor PrEP in the ambulatory setting, introduction to an evidence-based clinical protocol adapted to the ambulatory OBGYN clinic setting (the development of which is discussed in the following sections), and introduction to PrEP documentation and prescription in the electronic medical record (Appendix 1).

3.1.2.2 Phase II of Provider Education Series: Focused Lectures

Given the differentiated range of training-level and experience among the primary target residence audience, content lectures were stratified to meet the focused needs of novice learners. In this clinical setting, interns (i.e. physicians in their first year of subspecialty training) faced both lack of content exposure and lack of logistical experience in the ambulatory clinic. To address this unique intersection of differentiated learner needs, interns identified focused content areas to receive additional education in. The clinic administrative chief resident (i.e. senior resident physician in final year of subspecialty training) provided additional collateral information regarding facilitators and barriers to the operationalization of PrEP delivery in the ambulatory OBGYN clinic. These systemic and logistical learning points were incorporated into the focused lecture through structured case presentations followed by discussion questions requiring hypothetical navigation of clinic infrastructure and electronic medical records. Active learner engagement was facilitated through the use of an online, freely available audience response tool. This effortful retrieval practice also allowed for real-time identification of knowledge gaps which facilitated instruction adaptation to address these areas. Focused content areas included the review of PrEP medication properties and side effects, HIV risk assessment in women, patient counseling points regarding PrEP use, discontinuation, efficacy, and safety.

3.1.2.3 Phase III of Provider Education Series: Skills Application, Facilitated Roleplay, Electronic Medical Record Adaptation

To promote integration and application of PrEP knowledge, an interactive facilitated role-play training session was developed. A structured case study simulating a telemedicine visit between a pregnant patient and her provider was developed and filmed. In this clinical scenario, the "patient" discloses behavioral risk factors that increase her risk of STI/HIV acquisition. Specific communication skills and learning objectives were developed to help the "provider" and "patient" model a conversation on how to navigate HIV risk assessment in women, discussing PrEP, reviewing safety and efficacy in pregnancy and lactation, and logistical skills in optimizing use of patient encounter notes and PrEP medication order sets in the electronic medical record. Payment options were also reviewed. video clips were interjected with narrated slides to highlight key learning points and skills that had been demonstrated in the role play, resident, and faculty learners were stratified into novice to advanced experience group. Two structured clinical cases were developed and specific communication skills and learning objectives were developed for the "patient" and "provider" role. These included knowledge application skills in counseling about the safety and efficacy of PrEP use in pregnancy and communication skills through the practice of helping a patient recognize her personal HIV risk. A complete description of training case scenarios, lists of skills, learning goals are detailed in Appendix B. Expert clinicians in HIV medicine and patient-centered communication were present to facilitate discussions and provide real-time feedback to leaners.

At the conclusion of the facilitated role-play case scenario, each learner participant was guided through navigation of the electronic medical record to complete PrEP related note

documentation, medication orders, counseling documentation, and return visits for PrEP monitoring. See Appendix C for complete collection of electronic medical record tools.

A point of care reference for providers was developed and produced by the MAAETC. The point of care reference is a succinct review of HIV risk assessment and prevention counseling unique to women. Counseling points include messaging specifically for HIV testing during specific times in reproductive care (i.e. pregnancy, rapid testing during labor and delivery). See Appendix D.

3.1.2.4 Evaluation of Provider Education Series

Evaluation of the provider education series was limited to the interactive skills-based session. MAAETC evaluation tools were administered via an online, secure digital platform to participants. Twenty-nine participants attended the skills-based educational session, 20 of which were resident physicians. The post-session survey evaluated multiple domains of provider confidence in identifying appropriate candidates for PrEP, prescribing it, and counseling women about PrEP use. Additional domains included provider likelihood to use the knowledge/skills gained in the learning experience and degree to which the training positively or negatively impacted their current clinical practice regarding management of PrEP in women. See Table 5 for complete descriptive statistics.

Table 5 Evaluation Results from MAAETC

	Extent to which residents plan to use the knowledge/skills gained in the learning experience in their HIV prevention care, >moderate amount	Extent to which residents plan to use the knowledge/skills gained in the learning experience in their HIV screening practices, > moderate amount	Extent to which residents intend to seek additional training from HIV experts	Degree to which residents agree that training met expectations and stated learning objectives, >Agree strongly
Resident response	100% (n=5)	80% (n=4/5)	60% (n=3/5)	100% (n= 5/5)

Overall response rate was low (n=5), however, favorable responses were notable in key evaluative domains. 100% of residents indicated that they planned to use the knowledge/skills gained in the learning experiences in their delivery of HIV prevention and screening services. 60% of residents indicated that they intended to seek additional training from HIV experts as a result of the learning experience and 100% expressed strongly that they were satisfied with the training program as a whole.

3.1.2.5 PrEP 'Booster' Education Sessions

Short interval, succinct review lectures were designed to facilitate knowledge and skill retention among providers. Content topics include foundational knowledge review as well as provider generated content topics that are stratified by learner-level. See Appendix A.

3.2 Promoting Action & Adoption: Implications for OBGYN Training

Learning to assess HIV risk in women and being able to provide PrEP is an important opportunity for OBGYN's to improved HIV prevention in women – particularly for those women disproportionately affected by the HIV epidemic in the US. Integrating PrEP education into OBGYN training is integral to maintaining comprehensive, equitable HIV prevention care delivered by physicians that serve as critical access points for women's healthcare. As PrEP delivery modalities continue to evolve, OBGYN's are poised to be central in helping to meet the diverse needs of women's unique HIV prevention needs.

3.3 Pursuing Integration & Sustained Use: Adaptation of Evidence-Based Implementation Guidance for PrEP Delivery to Meet Women's Needs

To develop a clinical protocol that detailed practice standards of operations and clinical guidance for prescribing and monitoring PrEP for women, individuals from key stakeholder groups such as pharmacy, social work, clinic administration, and the various levels of providers were identified. Hospital leadership was involved early in the protocol development to ensure institutional support and oversight. As discussed above, the most widely adopted clinical guidance for prescribing PrEP are those published by the CDC[103]. With key stakeholder input, an institutional protocol to support ambulatory OBGYN providers in prescribing PrEP was adapted to meet the needs of the women cared for in this clinic setting. Existing electronic medical record resources for medication order sets, patient counseling, and note templates were adapted from the

hospital system electronic repository. The following sections describe the adapted components of PrEP delivery guidance for women.

3.3.1 Laboratory Testing[102]

Prior to initiating PrEP, women should be screened for signs and symptoms of acute HIV infection in the prior month (i.e. a flu-like illness with fevers, unintentional weight loss, or malaise. Based on timing of last high-risk exposure event, HIV testing should be performed to confirm seronegativity. Contraindications to oral PrEP containing TDF/3TC include a creatinine clearance (CrCl) of less than 60mL/min and a weight above 35 kg. Therefore, baseline serum CrCl must be drawn. Hepatitis B status should be assessed and if non-immune, vaccination should be offered. TDF has partial-activity against hepatitis B, and thus it is important to determine immunity so as to avoid precipitation of the hepatitis B virus (HBV) if PrEP is discontinued. Hepatitis B infection is not a contraindication to PrEP use and linkage to an experienced HBV provider is recommended for patients found to be HBsAg positive. Women who are non-immune to HBV should be vaccinated. Other STD screening, such as gonorrhea, chlamydia, trichomonas, and syphilis should be offered for all receptive sexual sites if indicated by sexual practices.

3.3.2 Providing PrEP[102]

Oral PrEP is prescribed as a fixed dose combination of 300mg TDF and 200mg 3TC as a single daily dose. A 90-day supply is typically prescribed. The safety or efficacy in preventing HIV acquisition with alternative dosing schedules such as on-demand PrEP (pre/post sex dosing only), intermittent, or other episodic schedules have not been studied in women and are not FDA

approved for PrEP. PrEP among women should be taken daily, and adherence is critical to effective HIV prevention. Side-effects of PrEP are uncommon and usually dissipate within the first month of use. Referred to as "start-up syndrome," short-term initiation side effects include headache, nausea, and flatulence. Serious side effects are rare but may include proximal renal tubulopathy (Fanconi syndrome), lactic acidosis, elevated liver enzymes 2.5 times the upper limit of normal, and decreased bone density. Women should be counseled about signs or symptoms that indicate need for urgent medical care such as severe muscle pain and weakness, jaundice, and fragility fractures[113]. Lastly, effective risk-reduction and prevention methods, such as condoms or substance abuse treatment referral, should accompany PrEP prescription.

3.3.3 Insurance Coverage and Financial Support for PrEP

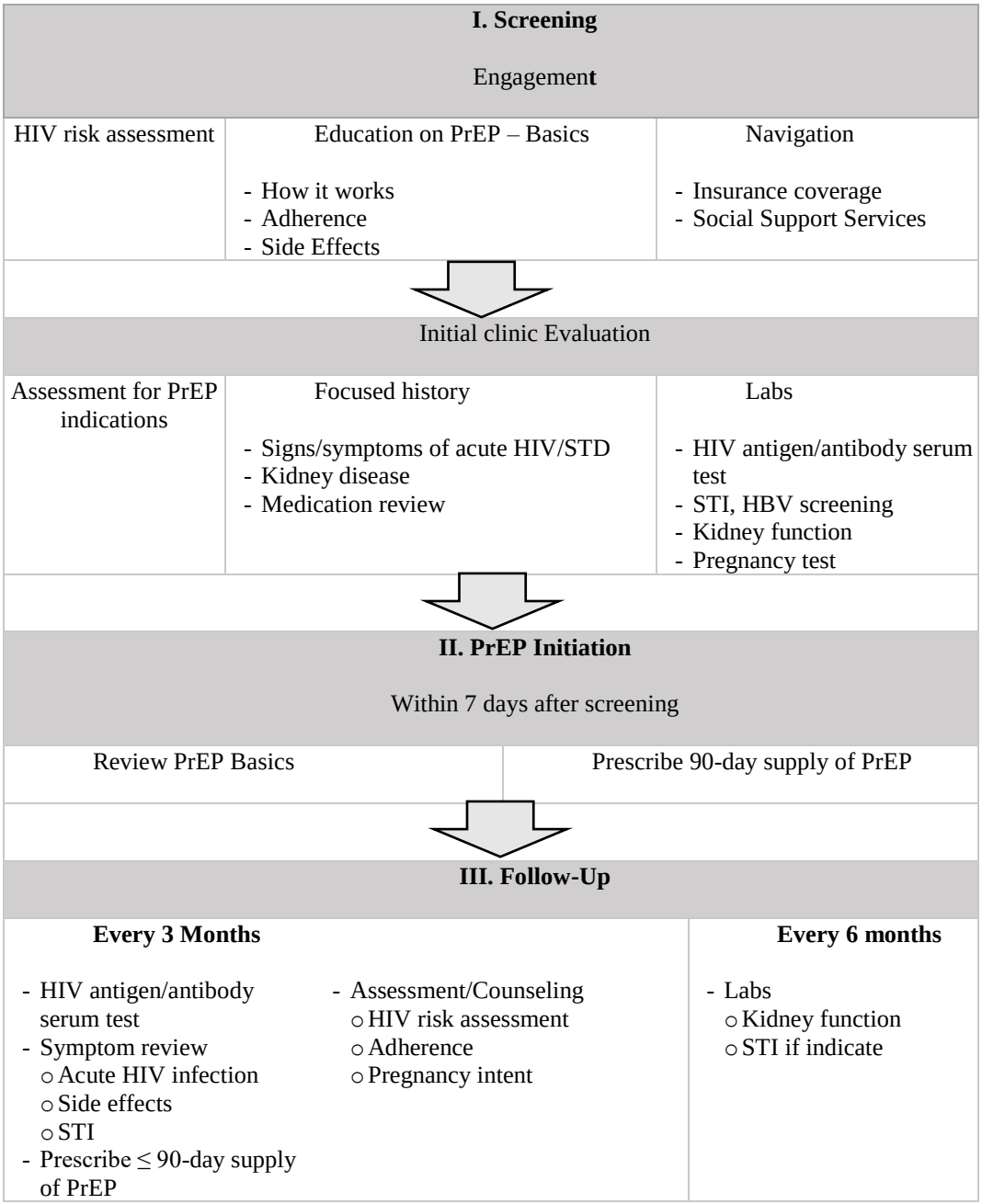
Financial coverage for PrEP includes both insurance coverage, private, and federal subsidies. Many insurance plans will cover the cost of PrEP. However, for uninsured or underinsured patients, financial support programs are available such as the Gilead Advancing Access and Copay Assistance Programs (available at: https://www.gileadadvancingaccess.com/), and "Ready, Set, PrEP" through the Department of Health and Human Services (available at: https://www.gileadadvancingaccess.com/copay-coupon-card)

3.3.4 PrEP Monitoring[102]

The follow up for PrEP should occur at 3 months intervals for the duration of time that a woman is taking PrEP. Three months follow up visits involve re-assessment of HIV risk factors,

side effect profile, and patient desire to continue PrEP use. Repeat HIV testing should always occur in addition to STD and urine pregnancy testing if applicable. Assessment of creatinine level should occur initially at 3 months and then every 6 months thereafter. PrEP should be discontinued in the event of a positive HIV test result, or if the CrCl >60ml/kg. If there is a steadily declining CrCl despite <60ml/kg, PrEP should still be discontinued. If there is concern for adverse renal effects, the patient should be referred to a nephrologist. A summary figure of the adapted CDC guidelines is shown in Figure 3 below:

Figure 3 Summary of the PrEP Care System for Women



Adapted from the US Centers for Disease Control and Prevention, Pre-exposure Prophylaxis (PrEP Care System). Available at: ***Pre-exposure Prophylaxis (PrEP) | Prevent | Effective Interventions | HIV/AIDS | CDC***

4.0 Summary

When taken as indicated, PrEP can reduce the risk of acquiring HIV from unprotected sex by over 90% and more than 70% from injection drug use[106]. Pregnancy and the postpartum period are periods of heightened HIV acquisition. These findings underscore the need for continued counseling on the risk of HIV acquisition and options for biomedical HIV prevention in all stages of reproductive life. The continuum of HIV prevention for women should also include structural interventions that aim to address underlying factors that make women vulnerable to HIV acquisition. While these are some of the most difficult interventions to undertake, they may be the most cost-effective approaches to mitigate the historical trauma, systemic inequity, and social determinants that mediate HIV vulnerability[116]. Examples of structural interventions include programs that promote gender equality, decriminalization of sex work, and programs that increase access to school education for young girls[116–118].

PrEP options are changing for women and new delivery systems will provide long-awaited choice in HIV prevention options for women. OBGYNs and reproductive health providers are uniquely positioned to identify women who would benefit from PrEP and provide it in trusted clinical settings. PrEP implementation strategies that consider the complex interplay of psychosocial factors that mediate HIV risk for women can help guide translation of innovative PrEP research into clinical practice. Targeted curriculum to improve OBGYN competence in prescribing PrEP to women has significant potential to increase PrEP access for them.

Appendix A Provider Education Series Phase I & II: Foundational and Focused Lectures

1) https://docs.google.com/presentation/d/1S12PzYkBfKmjKjEwQoF1VeIraE5qAXT3b4re-oPAoTI/edit#slide=id.g882bb5cc19_0_95
2) https://docs.google.com/presentation/d/1YA3_9YonS8Qx789595IlLoM4M2O2BpeV/edit#slide=id.p1

Appendix B Provider Education Series Phase III: Structured Case Scenarios and Facilitated Roleplay Guide

Appendix B.1.1 Structured Case Scenarios

Breakout Session Format Options:

- Zoom breakout sessions with expert clinicians as facilitators
- **Option 1:** Volunteer provider and patient each read case scenario. List of "objectives" reviewed by each participant. Act out scene, facilitator interjects to emphasize key points or answer questions
- **Option 2:** Volunteer pair picks and objective to role play through. Facilitator gives feedback/answers questions, and emphasizes learning points
- **Option 3:** Free-style role play. Participants can propose their own case scenarios, choose Case 2 or parts of it, or choose an objective(s) from case 1 or 2 to role play through.

Case 1:

Patient: You are a 22 yo G2P1 @ 17wga, presenting for routine obstetric care. You disclose that you are very stressed out by the FOB. You've been in an on and off relationship for several years but he is the FOB of your first child. He was recently incarcerated in South Carolina and returned to Pittsburgh several months ago and moved in with you because he had nowhere else to stay. He is the FOB of this pregnancy but you know he has been unfaithful since he's been back. You received a call from a public health contact tracer last week notifying you that you

may have been exposed to syphilis through a sexual contact. You have not had any other sexual partners in the last 2 years. Fortunately, all of your testing was negative. Your partner admitted to having one other partner but you suspect that he has had multiple since he has been back. You do not have any other information on his outside relationships.

Goals for the Patient:

- Disclose each of the following risk factors through the interview. If the provider does not illicit risk factor, creatively bring them up in the conversation
    - Bacterial STDs
    - Unsure of partner's sexual relationships (number of partners, consistent condom use)
    - Partner's recent incarceration (1 in 5 persons in prison are HIV+. RF include dirty injection equipment & IVDU, consensual/non-consensual/coercive/transactional sex, dirty/bootleg equipment for tattooing)
    - Inconsistent condom use

Provider: You are an OBGYN in the OPC. Your next patient is a 22 yo pregnant patient who is here for routine obstetric care. You do not find anything out of the ordinary on your precharting but your MA lets you know that the patient seems upset prior to seeing her.

Goals for the provider/Skills to practice:

- Identify risk factors for HIV
- Communicate risk assessment to patient

- Ask about PrEP
- Discuss PrEP benefits/efficacy, risks, alternatives
- Review pregnancy and breastfeeding safety data
- Locate and utilize Epic note type, problem-based dot phrase, order set
- Be aware of patient payment options

Case 2:

Patient: You are a 24yo with two children, who was recently called about a positive gonorrhea test. You are coming in for treatment. You have sex with multiple partners, sometimes more than one at a time. She sometimes you use condoms and no other forms of birth control. You have never heard of PrEP. You feel silly that you have been having sex with so many people, but aren't aware of the risk for STDs or HIV. You are interested in learning about PrEP but don't want to use PrEP yourself.

Goals for the Patient:

Disclose each of the following risk factors through the interview. If the provider does not illicit risk factors, creatively bring them up in the conversation

- Bacterial STD
- Multiple sexual partners, Unsure of partner's sexual relationships (number of partners,
- consistent condom use
- Inconsistent condom used
- Discuss your interest in earning about PrEP

- Convey limited understanding of HIV risk factors

Provider: You are an OBGYN in the OPC. Your next patient is coming in for gc+ treatment. You do not find anything out of the ordinary on your precharting.

Goals for the provider/Skills to practice:

- acquire information about her sexual practices
- support her sexuality while also counseling about PrEP

Appendix B.1.2 Filmed Sample Case and Facilitate Roleplay Script

Video Link: https://pitt.app.box.com/s/iym2qr0vyh43n7ik0uj7y2v5kjzp4lv7

Roleplay Script

Setting: Recorded Telemedicine Visit - Zoom

Scene 1: MD is in his office chart reviewing his next patient

Dummy patient in Epic: Zzzpco, Adultfemale - 742174275

Opens Chart, flashes to still screen with narrated description

"22 yo G2P1 @ 37wga presents for routine obstetric care." MA gives you a heads up that the patient seems upset but did not disclose anything to her

The objectives of this visit are to:

- Identify risk factors for HIV
- Communicate risk assessment to patient

- Ask about PrEP
- Discuss PrEP benefits/efficacy, risks, alternatives
- Review pregnancy and breastfeeding safety data
- Locate and utilize Epic note type, problem-based dot phrase, order set
- Be aware of patient payment options

Scene 2: MD "enters" the virtual patient room, pregnant person as patient

MD: Hi Ms. Williams, how are you feeling today?

Patient: I'm ok, just stressed.

MD: Oh yeah? How so? What has been going on?

Patient: Well, my fiancé has been cheating on me and I'm scared that I'm going to catch something from him. I'm scared that it will affect the baby. I got a call from the public health department that I might have been exposed to syphilis and I needed to get tested. I've only been with him but I've suspected that he has been with other women since he's been back. I didn't have any symptoms, but I got tested for everything and all of my testing came back negative.

MD: OMG I'm so sorry to hear this. This sounds so stressful!

Patient: Thank you, yeah it has been. When I confronted him about the call, he eventually came clean about cheating on me last month and getting treated for chlamydia and syphilis. He swore it was only one woman but I think it's been a lot more based on some rumors I've heard.

MD: Thank you for sharing all of this with me, I'm really glad all of your testing has come back and I share your concern that his actions could put you and the baby at risk for STDs. Are you and your partner still having sex?

Patient: Not since I got that call. But he's the father of both of my children and we're working on things. He got out of jail in South Carolina and came straight here because he really doesn't have anywhere else to go.

MD: I hear you, life isn't always straight forward. But I do want to help you stay protected from STDs if you have sex with him again. Do you use condoms when you have sex with him?

Patient: No. He hates them and I don't like them either.

Narrated break

<u>Identify risk factors for HIV:</u>

- Bacterial STDs
- Unsure of partner's sexual relationships (number of partners, consistent condom use)
- Partner's recent incarceration (1 in 5 persons in prison are HIV+. RF include dirty injection equipment & IVDU, consensual/non-consensual/coercive/transactional sex, dirty/bootleg equipment for tattooing)
- Inconsistent condom use

MD: Ok, that's not uncommon to hear. Condoms are a good barrier protection from STDs but there are other things outside of sex that can increase your risk of contracting an STD like HIV too. I know that you have not used drugs before, but do you know if your partner has ever used drugs like heroin or meth?

Patient: He hates needles.

MD: That's fair. Has he used these drugs in any other ways? Like taken pills or smoked them?

Patient: Yeah, that's why he was locked up for 6 months in South Carolina. He was smoking heroin and got caught with some old friends that were selling it.

MD: I see. Do you know much else about his drug use history? Do you know if he's ever traded sex for things like drugs?

Patient: No.

MD: Ok, and one last question to help me understand some of his risk. Do you know if he's ever had sex with someone who has tested positive for HIV?

Patient: I have no idea. But who knows? He got syphilis and chlamydia from someone, so I doubt he's asking them about HIV.

MD: Unfortunately, there aren't any medications that prevent STDs but there is one that can help protect you in case you are exposed to HIV in the future. Have you ever heard of PrEP before?

Narrated break

Highlight how risk assessment was communicated to patient:

- Asked her to reflect on a "high risk" sexual behavior of her partner
- Helped patient recognize risks associated with his lack of monogamy which in turn, puts her at risk for STDs/HIV
- Acknowledged concern about her risk for STD/HIV acquisition
- Asked about PrEP

Patient: Yeah, but I thought it was only for gay men

MD: it is actually approved for women too! PrEP reduces the risk of contracting HIV by 99%.

Patient: wow! Can I use it while I'm pregnant?

MD: Yes! The data we have now is limited but has shown that PrEP is safe during pregnancy and breastfeeding.

Narrated break

Discuss PrEP benefits/efficacy

- Reviewed pregnancy and breastfeeding safety data

Patient: ok, what are the side effects?

MD: A mild headache and nausea are the most common side effects

Patient: Does my insurance cover this medication?

MD: It depends, but we have many ways of helping people get this medication covered. After our visit, social work will come by and help you find coverage.

Patient: How do I take PrEP? Do I have to have any special tests before starting?

MD: We'll need to get a baseline HIV test and some basic labs to check your kidney function. In very rare cases, PrEP can affect how your kidneys filter things and may cause decreases in bone strength over time.

Patient: Ok. So how often do I need to take this medication

MD: PrEP is a daily medication that you take for as long as you need! Especially for women, adherence is very important. There isn't much room for missing doses, women need to take at least 6 doses per week in order to be maximally protected against HIV.

Narrated break

<u>Discuss PrEP risks and side effects</u>

- Be aware of payment options
- List payment options on screen that are in ambulatory OBGYN clinic

Scene 3: Back to MD's electronic medical record screen.

Show MD opening Pre-exposure prophylaxis Smart set

Click note type

Click Meds, labs, level of service, diagnosis

RTC in 6 months

Add patient discharge instructions

Show MD adding to the problem list: Counseling about HIV

Add dot phrase: .OPCprep

End scene

Narrated ending

PrEP Toolkit

- Reminder of clinical protocol
- Use point of care pocket cards/keep on personal cell phone
- Reproductive Infectious Disease team available for point of care consults
- Online location of video for reference
- MAAETEC website and resources

Appendix C Electronic Medical Record Adaptations & Documentation

Appendix C.1 PREP NEW PATIENT NOTE

PrEP History and Physical

Referred to clinic by:

HPI:***

This is a @AGE@ year old {PREP GENDER:31661} here for a new PrEP visit.

HIV Risk factor is {HIV RISK FACTORS:31662}.

Reason for interest in PrEP: ***

Sex partners are {PREP SEX PARTNERS:31663}. Has engaged in condomless

{PREP CONDOMLESS SEX:31664} sex in the past 12 months.

Last condomless penetrative sex (anal/vaginal): ***

Flu like illness in the past 4 weeks {Yes No:31668}.

Date of Last HIV test: ***

PAST MEDICAL HISTORY

@PMH@

History of kidney disease {Yes No:31668}.

Other Past Medical History:

Medications

@MEDC@

SUBSTANCE USE HISTORY

@SOC@

Adherence History: Reports {PREP ADHERENCE:31666} missed doses in the past week.

@LMP@

REVIEW OF SYSTEMS:

Fever: {Yes No:31668}

Lymphadenopathy: {Yes No:31668}

Diarrhea: {Yes No:31668}

Nausea: {Yes No:31668}

Rash: {Yes No:31668}

Urethral Discharge: {Yes No:31668}

Rectal Discharge: {Yes No:31668}

Vaginal Discharge: {YES NO NA:15678}

PHYSICAL EXAMINATION

The patient is a {:11314} @SEX@ in {PACT Status:30685}.

@VS@

Affect: {PACT AFFECT:29079}

Eyes: {PACT EYES:30686}

ENT: {PACT HEENT:29080}

Respiratory: {PACT RESPIRATORY:30687}

Cardiovascular: {HEART ID:11343}

Gastrointestinal: {GIMA ABDOMEN EXAM:11341}

Genitourinary: {PACT GENITOURINARY:30688}

Skin: {IDPE SKIN:60028}

Lymphatic: {IMMUNE/LYMPHATICS ID:11334}

Most recent HIV result: @LASTLAB(HIV1AB,HIVP24AGSCREEN,HIV2AB)@

Most recent Creatinine result: @LASTLAB(SCREAT)@

Most recent Syphilis Screen result: @LASTLAB(SYPHILISIGG)@

Most recent Gonorrhea result:@LASTLAB(GCAMPLIFIED)@

Most recent Chlamydia result:@LASTLAB(CHLAMYDIATRACHOMATISAMPLIFIED)@

Current PrEP regimen:

***

This is a @AGE@ year old {PREP GENDER:31661} here for a new patient visit.

HIV Risk factor is {HIV RISK FACTORS:31662}.

Would like to start use of PrEP. Discussed the importance of adherence. Other HIV prevention modalities such as barrier protection discussed as part of a risk mitigation plan. Discussed risks of PrEP including risk compensation, potential for resistance, and toxicities/side effects. Understands the importance of regular assessments including regular HIV testing and creatinine monitor to ensure safety while on PrEP. Understands the risks and benefits and would like to proceed with taking PrEP. Discussed need to perform STI testing with patient and the role of condom use given that PrEP does not offer protection against STIs.

@ORDERSENC@

@IMMR@

Follow up in {MONTHS:14410}.

Appendix C.2 PREP FOLLOW UP NOTE

This is a @AGE@ year old {PREP GENDER:31661} here for a follow-up PrEP visit.

{PREP GENDER:31661}

- Cis-male
- Cis-female
- Transgender male
- Transgender female
- Gender non-conforming individual
- Other

Last Labs:

Most recent HIV result: @LASTLAB(HIV1AB,HIVP24AGSCREEN,HIV2AB)@

Most recent Creatinine Clearance vs CREATININE W/GFR VS BMP

Most recent Syphilis Screen result: @LASTLAB(SYPHILISIGG)@

Most recent Gonorrhea result:@LASTLAB(GCAMPLIFIED)@

Most recent Chlamydia result:@LASTLAB(CHLAMYDIATRACHOMATISAMPLIFIED)@

Pregnancy/Birth Control Evaluation:

Current birth control method: {ANNUAL CONTRACEPTION:20532}

{ANNUAL CONTRACEPTION:20532}

- None
- Combined Pill

- Condoms
- Depo-Provera
- Diaphragm
- Essure
- Liletta
- Mirena
- Nexplanon
- NFP
- Nuvariing
- Paragard
- Patch
- Progestin-only Pill
- Skyla
- Tubal Ligation
- Vasectomy
- Withdrawal
- ***

If not on effective birth control, understands the risks/benefits of continuing PrEP in pregnancy or while attempting to get pregnant. {YES/NO:63} If no, patient referred to provider. {Yes No:31668}.

PrEP Maintenance Questions:

Have you had any side effects to the PrEP medication? {yes no:26423}, {PrEP Side Effects:28887}

{PrEP Side Effects:28887}

- Headache
- Nausea
- Flatulence
- Abdominal pain
- Diarrhea
- other

Patient counseled on supportive measures (Tylenol, ibuprofen, simethicone, hydration) for side effects. {yes no:26423}

Flu like illness in the past 4 weeks {Yes No:31668}. If yes, patient referred to provider. {Yes No:31668}.

In a typical week, how many days do you forget to take your PrEP medication? ***

If missing any doses, counseled on adherence and risk of HIV. {yes no:26423}

Do you wish to continue PrEP? {yes no:26423} If no, document why patient is discontinuing and proceed to discontinuation section. Why discontinuing? ***

Discussed the importance of adherence. Understands the risks and benefits of continuing PrEP. {YES/NO:63}

Discussed need to perform STI testing with patient and the role of condom use given that PrEP does not offer protection against STIs. {YES/NO:63}

Every 3 months:

HIV testing ordered: {Yes No:31668}.

Syphilis testing ordered: {Yes No:31668}.

GC/CT test sent to lab: {Yes No:31668}. Sites Sent: Urine, Genital swab, Pharyngeal, Rectal

Urine pregnancy test result today: {POSITIVE/NEGATIVE:13559::" Negative"}.

Every 6 months:

Creatinine Clearance ordered: {Yes No:31668}.

Creatinine Monitoring:

Creatinine Clearance at initiation of PrEP: ***

Last Creatinine Clearance level? ***

If using Truvada, Creatinine Clearance <60ml/kg, patient referred to provider {yes no:26423}

If using Descovy, Creatinine Clearance <30ml/kg, patient referred to provider {yes no:26423}

If Discontinuing PrEP:

Reason for discontinuing PrEP? ***

HepB carrier? {Yes No:31668}.

If yes, the patient was counseled on risk of Hepatitis flare and to present for care if experiencing yellow-skin, fevers, right upper quadrant pain. {Yes No:31668}.

Patient counseled on risk of HIV transmission after discontinuation of PrEP and ongoing risk reduction through condom use and post-exposure prophylaxis. {Yes No:31668}.

Patient counseled on need for HIV repeat screening if electing to imitate PrEP again? {Yes No:31668}

Appendix C.3 Problem List Dot Phrase

Discussed the patient's eligibility for PrEP, reviewed 99% risk reduction of acquiring HIV when PrEP is used daily (in women, need at least 6 doses weekly of Truvada to achieve GU levels that are protective, 4 doses per week to achieve levels protective in rectal mucosa). Patient has heard of Truvada and is accepting. Discussed that she should have baseline HIV testing prior to starting any PrEP method (in addition to baseline Cr testing).

[ ] document neg HIV test

[ ] assess for any sx of acute HIV infection

[ ] Serum Cr >60

[ ] Meet with SW to discuss payment

[ ] Truvada (TDF/FTC) 90-day supply

[ ] Monitoring:

-Serum cr at 3 mos, then 6 mos thereafter (or however long using PrEP), -STD testing q 3-6 mos or as needed.

-pregnancy test q 3 mos

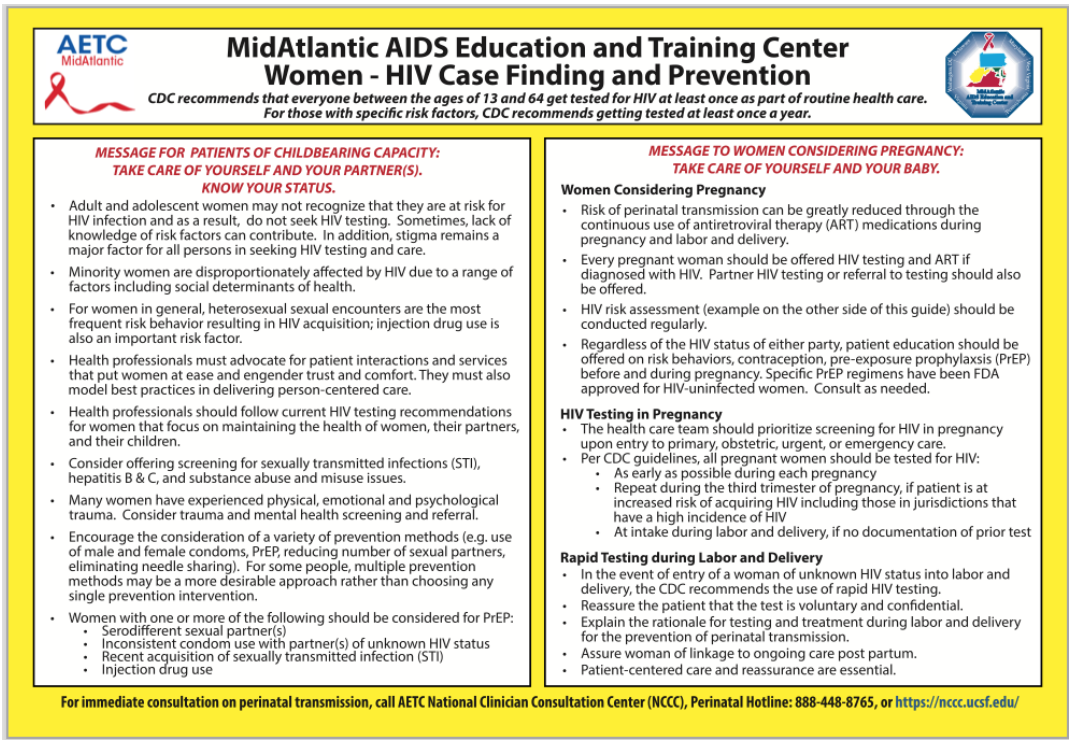
*Descovey was approved for PrEP 10/2019, however, is not approved for receptive vaginal sex.

Is approved for receptive anal intercourse.

Appendix C.4 PrEP Smartest

Go to “smart sets”-->PrEP smartest → open smart set and navigate through each section.

Appendix Figure 1 MAAETC Point-of-Care Reference



AETC MidAtlantic

MidAtlantic AIDS Education and Training Center
Women - HIV Case Finding and Prevention

CDC recommends that everyone between the ages of 13 and 64 get tested for HIV at least once as part of routine health care. For those with specific risk factors, CDC recommends getting tested at least once a year.

MESSAGE FOR PATIENTS OF CHILDBEARING CAPACITY: TAKE CARE OF YOURSELF AND YOUR PARTNER(S). KNOW YOUR STATUS.

- Adult and adolescent women may not recognize that they are at risk for HIV infection and as a result, do not seek HIV testing. Sometimes, lack of knowledge of risk factors can contribute. In addition, stigma remains a major factor for all persons in seeking HIV testing and care.
- Minority women are disproportionately affected by HIV due to a range of factors including social determinants of health.
- For women in general, heterosexual sexual encounters are the most frequent risk behavior resulting in HIV acquisition; injection drug use is also an important risk factor.
- Health professionals must advocate for patient interactions and services that put women at ease and engender trust and comfort. They must also model best practices in delivering person-centered care.
- Health professionals should follow current HIV testing recommendations for women that focus on maintaining the health of women, their partners, and their children.
- Consider offering screening for sexually transmitted infections (STI), hepatitis B & C, and substance abuse and misuse issues.
- Many women have experienced physical, emotional and psychological trauma. Consider trauma and mental health screening and referral.
- Encourage the consideration of a variety of prevention methods (e.g. use of male and female condoms, PrEP, reducing number of sexual partners, eliminating needle sharing). For some people, multiple prevention methods may be a more desirable approach rather than choosing any single prevention intervention.
- Women with one or more of the following should be considered for PrEP:
  - Serodifferent sexual partner(s)
  - Inconsistent condom use with partner(s) of unknown HIV status
  - Recent acquisition of sexually transmitted infection (STI)
  - Injection drug use

MESSAGE TO WOMEN CONSIDERING PREGNANCY: TAKE CARE OF YOURSELF AND YOUR BABY.

Women Considering Pregnancy

- Risk of perinatal transmission can be greatly reduced through the continuous use of antiretroviral therapy (ART) medications during pregnancy and labor and delivery.
- Every pregnant woman should be offered HIV testing and ART if diagnosed with HIV. Partner HIV testing or referral to testing should also be offered.
- HIV risk assessment (example on the other side of this guide) should be conducted regularly.
- Regardless of the HIV status of either party, patient education should be offered on risk behaviors, contraception, pre-exposure prophylaxis (PrEP) before and during pregnancy. Specific PrEP regimens have been FDA approved for HIV-uninfected women. Consult as needed.

HIV Testing in Pregnancy

- The health care team should prioritize screening for HIV in pregnancy upon entry to primary, obstetric, urgent, or emergency care.
- Per CDC guidelines, all pregnant women should be tested for HIV:
  - As early as possible during each pregnancy
  - Repeat during the third trimester of pregnancy, if patient is at increased risk of acquiring HIV including those in jurisdictions that have a high incidence of HIV
  - At intake during labor and delivery, if no documentation of prior test

Rapid Testing during Labor and Delivery

- In the event of entry of a woman of unknown HIV status into labor and delivery, the CDC recommends the use of rapid HIV testing.
- Reassure the patient that the test is voluntary and confidential.
- Explain the rationale for testing and treatment during labor and delivery for the prevention of perinatal transmission.
- Assure woman of linkage to ongoing care post partum.
- Patient-centered care and reassurance are essential.

For immediate consultation on perinatal transmission, call AETC National Clinician Consultation Center (NCCC), Perinatal Hotline: 888-448-8765, or https://nccc.ucsf.edu/

MESSAGE TO ALL WOMEN:

KNOW YOUR STATUS. CARE FOR YOURSELF, PARTNER(S), CHILDREN.

- In all clinical settings, privacy in the clinical encounter is essential.
- Introduce yourself as well as other clinicians and students who may be in the room. If the patient objects, respect their wishes.
- Use active listening skills, listen with intent to learn how the woman is feeling while assessing their knowledge of HIV and pregnancy.
- Reassure the woman that it is her decision to make regarding testing, treatment and care for herself and child.
- Respect and support the person's autonomy and right to make decisions.
- Be comfortable with pauses to allow the woman to ask questions.
- Be aware of the body language and facial expressions of you and the patient.
- Specific consent forms for HIV testing are NOT required, general consent in primary care is sufficient in most states. Please check state-specific laws for more information or contact the MAAETC for assistance.
- Assess the woman's family planning needs, by asking:
  - Are you considering becoming pregnant?
  - Are you currently using birth control? If so, what type?
  - Have you been pregnant before?
  - If you have been pregnant, how many pregnancies to term?
  - Were there any problems with your pregnancies?
  - Are you interested in learning more about family planning?
- Consider cultural beliefs and practices in helping to plan care with the patient.
- Frame questions in a way that supports risk reduction.
- Consider literacy and attempt to ascertain that the woman grasps information.

MIDATLANTIC AIDS EDUCATION AND TRAINING CENTER
University of Pittsburgh, Graduate School of Public Health
Department of Infectious Diseases and Microbiology
www.maaetc.org

GENERAL HIV RISK ASSESSMENT

SAMPLE SEXUAL HEALTH HISTORY TAKING SCRIPT

- "Good morning, my name is_____ and I am a (discipline). You can call me _____. How would you like to be addressed?" "Before we begin, are there issues that are of concern to you?"
- "The questions that I am going to ask will help to assess your sexual health risks. Just so you know, I ask all of my patients these questions. Is it OK to go ahead and ask you questions?"
  - When was the last time you had sex?
  - How many sex partners have you had in the past week? Past month?
  - Can you share the gender of people with whom you're having sex?
  - What kind of sex do you have or have you had?
    - Genital – penis in vagina
    - Anal – penis in anus
    - Oral – mouth on penis, vagina or anus
  - Do you use drugs or alcohol before or during sex?
  - How often do you use a condoms?
  - Have you been tested for STIs?
  - Have you had an STI in the past?
  - Have you ever had sex in exchange for money, housing, food, clothing, drugs or other gifts?
- Can I assist in making referral for other clinical services?
- What kind of support resources can I help you obtain?
- Do you have other needs for your children and family?

HRSA, HIV/AIDS Bureau, Office of Program Support Grant No. U1OHA29295
Please refer to the most recent guidelines.
Last Modified: September 18, 2020

References

ACOG (2013). Addressing Intimate Partner Violence Reproductive and Sexual Coercion: A Guide for Obstetric, Gynecologic, Reproductive Health Care Settings, Third Edition. [online] Available at: https://www.futureswithoutviolence.org/userfiles/file/HealthCare/Reproductive%20Health%20Guidelines.pdf [Accessed 6 Aug. 2019].

CDC. A Guide to Taking a Sexual History. [online] Available at https://www.cdc.gov/std/treatment/sexualhistory.pdf [Accessed 6 Aug. 2019] CDC. (2019). Women | Gender | HIV by Group | HIV/AIDS |

CDC. [online] Available at: https://www.cdc.gov/hiv/group/gender/women/index.html [Accessed 6 Aug. 2019].

The Henry J. Kaiser Family Foundation. (2019). Women and HIV/AIDS in the United States. [online] Available at: https://www.kff.org/hivaids/fact-sheet/women-and-hivaids-in-the-united-states/ [Accessed 6 Aug. 2019].

Lincoln, P. (May 8, 2019). HIV and Women: Barriers to Care. [Webinar] In MidAtlantic AETC Wednesday Webinar series: HIV and Women. Retrieved from: http://aetc.adobeconnect.com/ptv189aqdyvd/

US Preventive Services Task Force. Pre-exposure Prophylaxis for the Prevention of HIV Infection: US Preventive Services Task Force Recommendation Statement. JAMA. 2019;321(22):2203–2213. doi:10.1001/jama.2019.6390

Bibliography

1. HIV Surveillance Report 2018 (updated). 31:119.

2. Currier JS. Management of Long-Term Complications of HIV Disease: Focus on Cardiovascular Disease. *Top Antivir Med*. 2018;25(4):133-137.

3. King EM, Albert AY, Murray MCM. HIV and amenorrhea: a meta-analysis. *AIDS Lond Engl*. 2019;33(3):483-491. doi:10.1097/QAD.0000000000002084

4. Mills JC, Pence BW, Todd JV, et al. Cumulative Burden of Depression and All-Cause Mortality in Women Living With Human Immunodeficiency Virus. *Clin Infect Dis Off Publ Infect Dis Soc Am*. 2018;67(10):1575-1581. doi:10.1093/cid/ciy264

5. Cejtin HE, Kalinowski A, Bacchetti P, et al. Effects of human immunodeficiency virus on protracted amenorrhea and ovarian dysfunction. *Obstet Gynecol*. 2006;108(6):1423-1431. doi:10.1097/01.AOG.0000245442.29969.5c

6. Schoenbaum EE, Hartel D, Lo Y, et al. HIV infection, drug use, and onset of natural menopause. *Clin Infect Dis Off Publ Infect Dis Soc Am*. 2005;41(10):1517-1524. doi:10.1086/497270

7. Ellerbrock TV, Chiasson MA, Bush TJ, et al. Incidence of cervical squamous intraepithelial lesions in HIV-infected women. *JAMA*. 2000;283(8):1031-1037. doi:10.1001/jama.283.8.1031

8. Duerr A, Kieke B, Warren D, et al. Human papillomavirus-associated cervical cytologic abnormalities among women with or at risk of infection with human immunodeficiency virus. *Am J Obstet Gynecol*. 2001;184(4):584-590. doi:10.1067/mob.2001.111791

9. Jamieson DJ, Duerr A, Burk R, et al. Characterization of genital human papillomavirus infection in women who have or who are at risk of having HIV infection. *Am J Obstet Gynecol*. 2002;186(1):21-27. doi:10.1067/mob.2002.119776

10. Barbosa C, Macasaet M, Brockmann S, Sierra MF, Xia Z, Duerr A. Pelvic inflammatory disease and human immunodeficiency virus infection. *Obstet Gynecol*. 1997;89(1):65-70. doi:10.1016/s0029-7844(96)00387-0

11. LaGuardia KD, White MH, Saigo PE, Hoda S, McGuinness K, Ledger WJ. Genital ulcer disease in women infected with human immunodeficiency virus. *Am J Obstet Gynecol*. 1995;172(2 Pt 1):553-562. doi:10.1016/0002-9378(95)90572-3

12. Clark RA, Brandon W, Dumestre J, Pindaro C. Clinical manifestations of infection with the human immunodeficiency virus in women in Louisiana. *Clin Infect Dis Off Publ Infect Dis Soc Am*. 1993;17(2):165-172. doi:10.1093/clinids/17.2.165

13. HIV and Women's Health Issues. https://www.hiv.gov/hiv-basics/staying-in-hiv-care/other-related-health-issues/womens-health-issues

14. Global HIV & AIDS statistics — 2020 fact sheet. https://www.unaids.org/en/resources/fact-sheet

15. Becasen JS, Denard CL, Mullins MM, Higa DH, Sipe TA. Estimating the Prevalence of HIV and Sexual Behaviors Among the US Transgender Population: A Systematic Review and Meta-Analysis, 2006-2017. *Am J Public Health*. 2019;109(1):e1-e8. doi:10.2105/AJPH.2018.304727

16. Transgender People. https://www.cdc.gov/hiv/group/gender/transgender/index.html

17. Baggaley RF, White RG, Boily M-C. HIV transmission risk through anal intercourse: systematic review, meta-analysis and implications for HIV prevention. *Int J Epidemiol*. 2010;39(4):1048-1063. doi:10.1093/ije/dyq057

18. Jenness SM, Neaigus A, Murrill CS, Wendel T, Forgione L, Hagan H. Estimated HIV incidence among high-risk heterosexuals in New York City, 2007. *J Acquir Immune Defic Syndr 1999*. 2011;56(2):193-197. doi:10.1097/QAI.0b013e318202a9c4

19. Patel P, Borkowf CB, Brooks JT, Lasry A, Lansky A, Mermin J. Estimating per-act HIV transmission risk: a systematic review. *AIDS Lond Engl*. 2014;28(10):1509-1519. doi:10.1097/QAD.0000000000000298

20. de Vincenzi I. Comparison of female to male and male to female transmission of HIV in 563 stable couples. European Study Group on Heterosexual Transmission of HIV. *BMJ*. 1992;304(6830):809-813. doi:10.1136/bmj.304.6830.809

21. Barré I. HIV Implementation Science: What It Is and Why It Matters. https://2012-2017.usaid.gov/comment/reply/213646

22. Health Systems Global. "Statement on Advancing Implementation Research and Delivery Science." www.healthsystemsglobal.org/the-irds-statement/

23. Lancaster KE, Hetrick A, Jaquet A, et al. Substance use and universal access to HIV testing and treatment in sub-Saharan Africa: implications and research priorities. *J Virus Erad*. 2018;4(Suppl 2):26-32.

24. Cohen MS, Chen YQ, McCauley M, et al. Antiretroviral Therapy for the Prevention of HIV-1 Transmission. *N Engl J Med*. 2016;375(9):830-839. doi:10.1056/NEJMoa1600693

25. Donnell D, Baeten JM, Kiarie J, et al. Heterosexual HIV-1 transmission after initiation of antiretroviral therapy: a prospective cohort analysis. *Lancet Lond Engl*. 2010;375(9731):2092-2098. doi:10.1016/S0140-6736(10)60705-2

26. Rodger AJ, Cambiano V, Bruun T, et al. Sexual Activity Without Condoms and Risk of HIV Transmission in Serodifferent Couples When the HIV-Positive Partner Is Using Suppressive Antiretroviral Therapy. *JAMA*. 2016;316(2):171-181. doi:10.1001/jama.2016.5148

27. Bavinton BR, Pinto AN, Phanuphak N, et al. Viral suppression and HIV transmission in serodiscordant male couples: an international, prospective, observational, cohort study. *Lancet HIV*. 2018;5(8):e438-e447. doi:10.1016/S2352-3018(18)30132-2

28. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. https://gallery.mailchimp.com/6041fabfe630690490d7da99d/files/061cb070-2470-4b4c-a80c-3a0d6d266590/Treatment_Guidelines_December_2019.pdf

29. Cottrell ML, Srinivas N, Kashuba AD. Pharmacokinetics of antiretrovirals in mucosal tissue. *Expert Opin Drug Metab Toxicol*. 2015;11(6):893-905. doi:10.1517/17425255.2015.1027682

30. Trezza CR, Kashuba ADM. Pharmacokinetics of antiretrovirals in genital secretions and anatomic sites of HIV transmission: implications for HIV prevention. *Clin Pharmacokinet*. 2014;53(7):611-624. doi:10.1007/s40262-014-0148-z

31. Seidman D, Weber S. Integrating Preexposure Prophylaxis for Human Immunodeficiency Virus Prevention Into Women's Health Care in the United States: *Obstet Gynecol*. 2016;128(1):37-43. doi:10.1097/AOG.0000000000001455

32. Hunt A. FDA In Brief: FDA continues to encourage ongoing education about the benefits and risks associated with PrEP, including additional steps to help reduce the risk of getting HIV. U.S. Food & Drug Administration. https://www.fda.gov/news-events/fda-brief/fda-brief-fda-continues-encourage-ongoing-education-about-benefits-and-risks-associated-prep

33. Hare C, Coll J, Ruane P, et al. *THE PHASE 3 DISCOVER STUDY: DAILY F/TAF OR F/TDF FOR HIV PREEXPOSURE PROPHYLAXIS*. Kaiser Permanente San Francisco Medical Center http://www.croiconference.org/sessions/phase-3-discover-study-daily-ftaf-or-ftdf-hiv-preexposure-prophylaxis#

34. Thomson KA, Baeten JM, Mugo NR, Bekker L-G, Celum CL, Heffron R. Tenofovir-based oral preexposure prophylaxis prevents HIV infection among women: *Curr Opin HIV AIDS*. 2016;11(1):18-26. doi:10.1097/COH.0000000000000207

35. Patterson KB, Prince HA, Kraft E, et al. Penetration of tenofovir and emtricitabine in mucosal tissues: implications for prevention of HIV-1 transmission. *Sci Transl Med*. 2011;3(112):112re4. doi:10.1126/scitranslmed.3003174

36. Abdool Karim Q, Abdool Karim SS, Frohlich JA, et al. Effectiveness and safety of tenofovir gel, an antiretroviral microbicide, for the prevention of HIV infection in women. *Science*. 2010;329(5996):1168-1174. doi:10.1126/science.1193748

37. Marrazzo JM, Ramjee G, Richardson BA, et al. Tenofovir-Based Preexposure Prophylaxis for HIV Infection among African Women. *N Engl J Med*. 2015;372(6):509-518. doi:10.1056/NEJMoa1402269

38. Van Damme L, Corneli A, Ahmed K, et al. Preexposure Prophylaxis for HIV Infection among African Women. *N Engl J Med*. 2012;367(5):411-422. doi:10.1056/NEJMoa1202614

39. Nel A, van Niekerk N, Kapiga S, et al. Safety and Efficacy of a Dapivirine Vaginal Ring for HIV Prevention in Women. *N Engl J Med*. 2016;375(22):2133-2143. doi:10.1056/NEJMoa1602046

40. Baeten JM, Palanee-Phillips T, Brown ER, et al. Use of a Vaginal Ring Containing Dapivirine for HIV-1 Prevention in Women. *N Engl J Med*. 2016;375(22):2121-2132. doi:10.1056/NEJMoa1506110

41. Brown E, Palanee-Philips T, Marzinke M, et al. Residual dapivirine ring levels indicate higher adherence to vaginal ring is associated with HIV-1 protection. In: Vol Abstract TUAC0105LB. ; 2016.

42. Montgomery E, van der Straten A, Chitukuta M, et al. Key insights into acceptability and use of the vaginal ring: results of the MTN-020 ASPIRE trial qualitative component. In: Vol Abstract WEPEC265. ; 2016.

43. *Dapivirine Ring*. International Partnership for Microbiocides https://www.ipmglobal.org/our-work/our-products/dapivirine-ring

44. Annalene Nel1, Neliette Van Niekerk1, Ben Van Baelen2, Zeda Rosenberg3. HIV INCIDENCE AND ADHERENCE IN DREAM: AN OPEN-LABEL TRIAL OF DAPIVIRINE VAGINAL RING. In: Vol ABSTRACT NUMBER 144LB. SESSION NUMBER O-13. ; 2018. https://www.croiconference.org/abstract/hiv-incidence-and-adherence-dream-open-label-trial-dapivirine-vaginal-ring/#:~:text=The%20trials%20demonstrated%20that%20the,and%20adherence%20to%20ring%20use.

45. Jared Baeten, Thesla Palanee-Phillips, Nyaradzo Mgodi, Ashley Mayo, Annalene Nel, Zeda Rosenberg, Sharon L. Hillier, Elizabeth Brown. HIGH UPTAKE AND REDUCED HIV-1 INCIDENCE IN AN OPEN-LABEL TRIAL OF THE DAPIVIRINE RING | CROI Conference. In: ; 2018. Accessed November 19, 2019. http://www.croiconference.org/sessions/high-uptake-and-reduced-hiv-1-incidence-open-label-trial-dapivirine-ring

46. WHO recommends the dapivirine vaginal ring as a new choice for HIV prevention for women at substantial risk of HIV infection. World Health Organization. Published January

26, 2021. https://www.who.int/news/item/26-01-2021-who-recommends-the-dapivirine-vaginal-ring-as-a-new-choice-for-hiv-prevention-for-women-at-substantial-risk-of-hiv-infection

47. Schürmann D, Rudd DJ, Zhang S, et al. Safety, pharmacokinetics, and antiretroviral activity of islatravir (ISL, MK-8591), a novel nucleoside reverse transcriptase translocation inhibitor, following single-dose administration to treatment-naive adults infected with HIV-1: an open-label, phase 1b, consecutive-panel trial. *Lancet HIV*. 2020;7(3):e164-e172. doi:10.1016/S2352-3018(19)30372-8

48. GSK Clinical Trials VH. Pharmacokinetic Study of Cabotegravir Long-acting in Healthy Adult Volunteers. https://clinicaltrials.gov/ct2/show/NCT02478463?term=cabotegravir&draw=2&rank=3

49. Baeten JM, Donnell D, Ndase P, et al. Antiretroviral Prophylaxis for HIV Prevention in Heterosexual Men and Women. *N Engl J Med*. 2012;367(5):399-410. doi:10.1056/NEJMoa1108524

50. Grant RM, Lama JR, Anderson PL, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *N Engl J Med*. 2010;363(27):2587-2599. doi:10.1056/NEJMoa1011205

51. Thigpen MC, Kebaabetswe PM, Paxton LA, et al. Antiretroviral Preexposure Prophylaxis for Heterosexual HIV Transmission in Botswana. *N Engl J Med*. 2012;367(5):423-434. doi:10.1056/NEJMoa1110711

52. Hanscom B, Janes HE, Guarino PD, et al. Brief Report: Preventing HIV-1 Infection in Women Using Oral Preexposure Prophylaxis: A Meta-analysis of Current Evidence. *J Acquir Immune Defic Syndr 1999*. 2016;73(5):606-608. doi:10.1097/QAI.0000000000001160

53. Anderson PL, Glidden DV, Liu A, et al. Emtricitabine-Tenofovir Concentrations and Pre-Exposure Prophylaxis Efficacy in Men Who Have Sex with Men. *Sci Transl Med*. 2012;4(151):151ra125-151ra125. doi:10.1126/scitranslmed.3004006

54. Kashuba AD, Patterson KB, Dumond JB, Cohen MS. Pre-exposure prophylaxis for HIV prevention: how to predict success. *The Lancet*. 2012;379(9835):2409-2411. doi:10.1016/S0140-6736(11)61852-7

55. McCormack S, Dunn DT, Desai M, et al. Pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): effectiveness results from the pilot phase of a pragmatic open-label randomised trial. *The Lancet*. 2016;387(10013):53-60. doi:10.1016/S0140-6736(15)00056-2

56. Helen Rees1, Sinead A. Delany-Moretlwe1, Carl Lombard2, Deborah Baron1, Ravindre Panchia4, Landon Myer3, Jill L. Schwartz5, Gustavo F. Doncel5, Glenda Gray2. FACTS 001 Phase III Trial of Pericoital Tenofovir 1% Gel for HIV Prevention in Women. In: *Preventing HIV and HSV-2: What Will It Take?*. Vol ABSTRACT NUMBER 26LB. ;

2015:SESSION NUMBER O-1. https://www.croiconference.org/abstract/facts-001-phase-iii-trial-pericoital-tenofovir-1-gel-hiv-prevention-women/

57. Montgomery ET, van der Straten A, Chitukuta M, et al. Acceptability and use of a dapivirine vaginal ring in a phase III trial. *AIDS Lond Engl*. 2017;31(8):1159-1167. doi:10.1097/QAD.0000000000001452

58. Choopanya K, Martin M, Suntharasamai P, et al. Antiretroviral prophylaxis for HIV infection in injecting drug users in Bangkok, Thailand (the Bangkok Tenofovir Study): a randomised, double-blind, placebo-controlled phase 3 trial. *The Lancet*. 2013;381(9883):2083-2090. doi:10.1016/S0140-6736(13)61127-7

59. Karim SSA. HIV pre-exposure prophylaxis in injecting drug users. *Lancet Lond Engl*. 2013;381(9883):2060-2062. doi:10.1016/S0140-6736(13)61140-X

60. Thomson KA, Hughes J, Baeten JM, et al. Increased Risk of HIV Acquisition Among Women Throughout Pregnancy and During the Postpartum Period: A Prospective Per-Coital-Act Analysis Among Women With HIV-Infected Partners. *J Infect Dis*. 2018;218(1):16-25. doi:10.1093/infdis/jiy113

61. Pyra M, Anderson PL, Hendrix CW, et al. Tenofovir and tenofovir-diphosphate concentrations during pregnancy among HIV-uninfected women using oral preexposure prophylaxis. *AIDS Lond Engl*. 2018;32(13):1891-1898. doi:10.1097/QAD.0000000000001922

62. Vernazza PL, Graf I, Sonnenberg-Schwan U, Geit M, Meurer A. Preexposure prophylaxis and timed intercourse for HIV-discordant couples willing to conceive a child: *AIDS*. 2011;25(16):2005-2008. doi:10.1097/QAD.0b013e32834a36d0

63. *THE ANTIRETROVIRAL PREGNANCY REGISTRY INTERIM REPORT 1 JANUARY 1989 THROUGH 31 JANUARY 2020*. Registry Coordinating Center; 2020. www.APRegistry.com

64. Mofenson LM, Baggaley RC, Mameletzis I. Tenofovir disoproxil fumarate safety for women and their infants during pregnancy and breastfeeding: *AIDS*. 2017;31(2):213-232. doi:10.1097/QAD.0000000000001313

65. Hu X, Wang L, Xu F. Guides concerning tenofovir exposure via breastfeeding: A comparison of drug dosages by developmental stage. *Int J Infect Dis*. 2019;87:8-12. doi:10.1016/j.ijid.2019.07.023

66. Mugwanya KK, Hendrix CW, Mugo NR, et al. Pre-exposure Prophylaxis Use by Breastfeeding HIV-Uninfected Women: A Prospective Short-Term Study of Antiretroviral Excretion in Breast Milk and Infant Absorption. Mofenson LM, ed. *PLOS Med*. 2016;13(9):e1002132. doi:10.1371/journal.pmed.1002132

67. World Health Organization. *WHO Technical Brief: Preventing HIV during Pregnancy and Breastfeeding in the Context of Pre-Exposure Prophylaxis (PrEP).*; 2017.

68. National Library of Medicine. *Emtricitabine in Drugs and Lactation Database*.; 2018.

69. Whitfield THF, John SA, Rendina HJ, Grov C, Parsons JT. Why I Quit Pre-Exposure Prophylaxis (PrEP)? A Mixed-Method Study Exploring Reasons for PrEP Discontinuation and Potential Re-initiation Among Gay and Bisexual Men. *AIDS Behav*. 2018;22(11):3566-3575. doi:10.1007/s10461-018-2045-1

70. Morgan E, Moran K, Ryan DT, Mustanski B, Newcomb ME. Threefold Increase in PrEP Uptake Over Time with High Adherence Among Young Men Who Have Sex With Men in Chicago. *AIDS Behav*. 2018;22(11):3637-3644. doi:10.1007/s10461-018-2122-5

71. Chan PA, Mena L, Patel R, et al. Retention in care outcomes for HIV pre-exposure prophylaxis implementation programmes among men who have sex with men in three US cities. *J Int AIDS Soc*. 2016;19(1):20903. doi:10.7448/IAS.19.1.20903

72. Holloway IW, Dougherty R, Gildner J, et al. Brief Report: PrEP Uptake, Adherence, and Discontinuation Among California YMSM Using Geosocial Networking Applications. *JAIDS J Acquir Immune Defic Syndr*. 2017;74(1):15-20. doi:10.1097/QAI.0000000000001164

73. Zucker J, Carnevale C, Richards P, et al. Predictors of Disengagement in Care for Individuals Receiving Pre-exposure Prophylaxis (PrEP). *J Acquir Immune Defic Syndr 1999*. 2019;81(4):e104-e108. doi:10.1097/QAI.0000000000002054

74. Brooks RA, Cabral A, Nieto O, Fehrenbacher A, Landrian A. Experiences of Pre-Exposure Prophylaxis Stigma, Social Support, and Information Dissemination Among Black and Latina Transgender Women Who Are Using Pre-Exposure Prophylaxis. *Transgender Health*. 2019;4(1):188-196. doi:10.1089/trgh.2019.0014

75. Dubov A, Galbo P, Altice FL, Fraenkel L. Stigma and Shame Experiences by MSM Who Take PrEP for HIV Prevention: A Qualitative Study. *Am J Mens Health*. 2018;12(6):1843-1854. doi:10.1177/1557988318797437

76. Pinto RM, Berringer KR, Melendez R, Mmeje O. Improving PrEP Implementation Through Multilevel Interventions: A Synthesis of the Literature. *AIDS Behav*. 2018;22(11):3681-3691. doi:10.1007/s10461-018-2184-4

77. Lankowski AJ, Bien-Gund CH, Patel VV, Felsen UR, Silvera R, Blackstock OJ. PrEP in the Real World: Predictors of 6-Month Retention in a Diverse Urban Cohort. *AIDS Behav*. 2019;23(7):1797-1802. doi:10.1007/s10461-018-2296-x

78. Hevey MA, Walsh JL, Petroll AE. PrEP Continuation, HIV and STI Testing Rates, and Delivery of Preventive Care in a Clinic-Based Cohort. *AIDS Educ Prev*. 2018;30(5):393-405. doi:10.1521/aeap.2018.30.5.393

79. Arnold T, Brinkley-Rubinstein L, Chan PA, et al. Social, structural, behavioral and clinical factors influencing retention in Pre-Exposure Prophylaxis (PrEP) care in Mississippi. *PloS One*. 2017;12(2):e0172354. doi:10.1371/journal.pone.0172354

80. Krakower D, Maloney KM, Powell VE, et al. Patterns and clinical consequences of discontinuing HIV preexposure prophylaxis during primary care. *J Int AIDS Soc*. 2019;22(2):e25250. doi:10.1002/jia2.25250

81. Laborde ND, Kinley PM, Spinelli M, et al. Understanding PrEP Persistence: Provider and Patient Perspectives. *AIDS Behav*. 2020;24(9):2509-2519. doi:10.1007/s10461-020-02807-3

82. Smith DK, Van Handel M, Grey J. Estimates of adults with indications for HIV pre-exposure prophylaxis by jurisdiction, transmission risk group, and race/ethnicity, United States, 2015. *Ann Epidemiol*. 2018;28(12):850-857.e9. doi:10.1016/j.annepidem.2018.05.003

83. Huang YA, Zhu W, Smith DK, Harris N, Hoover KW. HIV Preexposure Prophylaxis, by Race and Ethnicity — United States, 2014–2016. *MMWR Morb Mortal Wkly Rep*. 2018;67(41):1147-1150. doi:10.15585/mmwr.mm6741a3

84. All State PrEP Data Sets. AIDSVu. https://aidsvu.org/resources/ downloadable-maps-and-resources/

85. Calabrese SK, Krakower DS, Mayer KH. Integrating HIV Preexposure Prophylaxis (PrEP) Into Routine Preventive Health Care to Avoid Exacerbating Disparities. *Am J Public Health*. 2017;107(12):1883-1889. doi:10.2105/AJPH.2017.304061

86. 2018 Annual HIV Surveillance Report.pdf. Accessed December 3, 2019. https://www.health.pa.gov/topics/Documents/Programs/HIV/2018%20Annual%20HIV%20Surveillance%20Report.pdf

87. Cairns G. PrEP programmes & uptake. nam aidsmap. Published July 4, 2020. https://www.aidsmap.com/news/jul-2020/least-28000-women-united-states-have-started-prep

88. Guest J, et al. PrEP update in women in the US from 2012-2017. In: Vol Abstract 9302. ; 2020.

89. Patel, MD, MS AS, Goparaju, PhD L, Sales, PhD JM, et al. PrEP Eligibility Among At-Risk Women in the Southern United States: Associated Factors, Awareness, and Acceptability. *J Acquir Immune Defic Syndr*. 2019;80(5):527-532. doi:10.1097/QAI.0000000000001950

90. Garfinkel DB, Alexander KA, McDonald-Mosley R, Willie TC, Decker MR. Predictors of HIV-related risk perception and PrEP acceptability among young adult female family planning patients. *AIDS Care*. 2017;29(6):751-758. doi:10.1080/09540121.2016.1234679

91. Khawcharoenporn T, Kendrick S, Smith K. HIV risk perception and preexposure prophylaxis interest among a heterosexual population visiting a sexually transmitted infection clinic. *AIDS Patient Care STDs*. 2012;26(4):222-233. doi:10.1089/apc.2011.0202

92. Goparaju L, Experton LS, Praschan NC. Women want Pre-Exposure Prophylaxis but are Advised Against it by Their HIV-positive Counterparts. *J AIDS Clin Res*. 2015;6(11). doi:10.4172/2155-6113.1000522

93. Carley T, Siewert E, Naresh A. Interest in Pre-exposure Prophylaxis (PrEP) for HIV is Limited Among Women in a General Obstetrics & Gynecology Setting. *AIDS Behav*. 2019;23(10):2741-2748. doi:10.1007/s10461-019-02529-1

94. Flash CA, Adegboyega OO, Yu X, et al. Correlates of Linkage to HIV Preexposure Prophylaxis Among HIV-Testing Clients: *JAIDS J Acquir Immune Defic Syndr*. 2018;77(4):365-372. doi:10.1097/QAI.0000000000001605

95. Roth AM, Tran NK, Felsher MA, et al. Integrating HIV pre-exposure prophylaxis with community-based syringe services for women who inject drugs: Results from the Project SHE demonstration study. *JAIDS J Acquir Immune Defic Syndr*. 2020;Publish Ahead of Print. doi:10.1097/QAI.0000000000002558

96. Mayer KH, Agwu A, Malebranche D. Barriers to the Wider Use of Pre-exposure Prophylaxis in the United States: A Narrative Review. *Adv Ther*. 2020;37(5):1778-1811. doi:10.1007/s12325-020-01295-0

97. Harding T, Oetzel J. Implementation effectiveness of health interventions for indigenous communities: a systematic review. *Implement Sci*. 2019;14(1):76. doi:10.1186/s13012-019-0920-4

98. Cáceres CF, Mayer KH, Baggaley R, O'Reilly KR. PrEP Implementation Science: State-of-the-Art and Research Agenda. *J Int AIDS Soc*. 2015;18(4 Suppl 3):20527. doi:10.7448/IAS.18.4.20527

99. Seidman D, Weber S. Integrating Preexposure Prophylaxis for Human Immunodeficiency Virus Prevention Into Women's Health Care in the United States: *Obstet Gynecol*. 2016;128(1):37-43. doi:10.1097/AOG.0000000000001455

100. Nilsen P. Making sense of implementation theories, models and frameworks. *Implement Sci*. 2015;10(1):53. doi:10.1186/s13012-015-0242-0

101. Calabrese SK, Willie TC, Galvao RW, et al. Current US Guidelines for Prescribing HIV Pre-exposure Prophylaxis (PrEP) Disqualify Many Women Who Are at Risk and Motivated to Use PrEP: *JAIDS J Acquir Immune Defic Syndr*. 2019;81(4):395-405. doi:10.1097/QAI.0000000000002042

102. Centers for Disease Control and Prevention: US Public Health Service: Preexposure prophylaxis for the prevention of HIV infection in the United States—2017 Update: a clinical practice guideline. Published March 2018. Accessed December 8, 2019. https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf

103. Calabrese SK, Krakower DS, Willie TC, Kershaw TS, Mayer KH. US Guideline Criteria for Human Immunodeficiency Virus Preexposure Prophylaxis: Clinical Considerations

and Caveats. *Clin Infect Dis Off Publ Infect Dis Soc Am*. 2019;69(5):884-889. doi:10.1093/cid/ciz046

104. Sullivan PS, Rosenberg ES, Sanchez TH, et al. Explaining racial disparities in HIV incidence in black and white men who have sex with men in Atlanta, GA: a prospective observational cohort study. *Ann Epidemiol*. 2015;25(6):445-454. doi:10.1016/j.annepidem.2015.03.006

105. Lancki N, Almirol E, Alon L, McNulty M, Schneider JA. Preexposure prophylaxis guidelines have low sensitivity for identifying seroconverters in a sample of young Black MSM in Chicago. *AIDS Lond Engl*. 2018;32(3):383-392. doi:10.1097/QAD.0000000000001710

106. Women's Interagency HIV Study (WIHS). National Institute of Allergy and Infectious Diseases. https://www.niaid.nih.gov/research/womens-interagency-hiv-study

107. Ojikutu BO, Mayer KH. Hidden in Plain Sight: Identifying Women Living in the United States Who Could Benefit From HIV Preexposure Prophylaxis. *J Infect Dis*. 2020;222(9):1428-1431. doi:10.1093/infdis/jiz416

108. Preexposure prophylaxis for the prevention of human immunodeficiency virus. *Obstet Gynecol*. 2014;(6):123:1133.

109. Seidman DL, Weber S, Timoney MT, et al. Use of HIV pre-exposure prophylaxis during the preconception, antepartum and postpartum periods at two United States medical centers. *Am J Obstet Gynecol*. 2016;215(5):632.e1-632.e7. doi:10.1016/j.ajog.2016.06.020

110. HIV/AIDS Prevention Research Synthesis Project. Compendium of Evidence-Based Interventions and Best Practices for HIV Prevention. Centers for Disease Control and Prevention. Published online March 29, 2021. Accessed April 2, 2021. https://www.cdc.gov/hiv/research/interventionresearch/compendium/index.html.

111. Seidman D, Carlson K, Weber S, Witt J, Kelly PJ. United States family planning providers' knowledge of and attitudes towards preexposure prophylaxis for HIV prevention: a national survey. *Contraception*. 2016;93(5):463-469. doi:10.1016/j.contraception.2015.12.018

112. Kole M, Scott M, Brar I, Sangha R. Do You PrEP? Knowledge and Practice Among Obstetrician and Gynecologists in an Inner City Hospital [16Q]. *Obstet Gynecol*. 2019;133(1):185S-185S. doi:10.1097/01.AOG.0000558937.64362.d3

113. Truvada (emtricitabine and tenofovir disoproxil fumarate) tablets, for oral use [Package insert].

114. Centers for Disease Control and Prevention. Pre-exposure prophylaxis (PrEP). https://www.cdc.gov/hiv/risk/prep/index.html

115. World Health Organization. WHO EXPANDS RECOMMENDATION ON ORAL PREEXPOSURE PROPHYLAXIS OF HIV INFECTION (PrEP). https://apps.who.int/iris/bitstream/handle/10665/197906/WHO_HIV_2015.48_eng.pdf;jsessionid=750D54CDE134ADD6D33FFF9C18735616?sequence=1

116. Adimora AA, Auerbach JD. Structural interventions for HIV prevention in the United States. *J Acquir Immune Defic Syndr 1999*. 2010;55 Suppl 2:S132-135. doi:10.1097/QAI.0b013e3181fbcb38

117. Edmonds K. Beyond Good Intentions: The Structural Limitations of NGOs in Haiti. *Crit Sociol*. 2013;39(3):439-452. doi:10.1177/0896920512437053

118. Footer KH, Silberzahn BE, Tormohlen KN, Sherman SG. Policing practices as a structural determinant for HIV among sex workers: a systematic review of empirical findings. *J Int AIDS Soc*. 2016;19:20883. doi:10.7448/IAS.19.4.20883