STU#: STU00217596

PROTOCOL TITLE: Adaptation and Pilot Test of an Electronic Health Record-based Approach to Increase PrEP Knowledge and Uptake: the EMC^2 PrEP Strategy

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STUDY SUMMARY:

Investigational Agent(s) (Drugs or Devices)	
IND / IDE / HDE #	

Indicate Special Population(s)	☐ Children ☐ Children who are wards of the state ☐ Adults Unable to Consent ☐ Cognitively Impaired Adults ☐ Neonates of Uncertain Viability ☐ Pregnant Women ☐ Prisoners (or other detained/paroled individuals) ☐ Students/Employees
Sample Size	225
Funding Source	Merck
Indicate the type of consent to be obtained	☒ Written (online) ☒ Verbal/Waiver of Documentation of Informed Consent ☒ Waiver of HIPAA Authorization ☐ Waiver/Alteration of Consent Process
Site	☐ Lead Site (For A Multiple Site Research Study) ☐ Data Coordinating Center (DCC)
Research Related Radiation Exposure	☐ Yes ☒ No
DSMB / DMC / IDMC	☒ Yes ☐ No

OBJECTIVES:
Aim 1: Refine and implement an electronic health record (EHR)-based strategy as a quality improvement activity that supports informed decision-making and PrEP uptake among women with increased HIV vulnerability in primary care (the EMC^2 PrEP strategy).

Aim 2: Pilot-test the EMC^2 PrEP strategy in primary care to determine its feasibility, acceptability, and preliminary efficacy among women with increased vulnerability to HIV.

Aim 3: Develop a standard operating protocol (SOP) for disseminating the EMC^2 PrEP strategy to a national network of federally qualified health centers.

BACKGROUND:
The overall goal of this study is to implement a EMC^2 PrEP in a partnering clinic to: 1) increase case-finding of women potentially eligible for PrEP; 2) facilitate informed decision-making for HIV prevention; and 3) support PrEP uptake in primary care.

Northwestern University has received funding from Merck to adapt and pilot test, as a quality improvement activity, an electronic health record-based approach to increase knowledge and uptake of pre-exposure prophylaxis (PrEP) for HIV prevention among cisgender women in primary care.

HIV among women in the United States is a significant, yet often overlooked, public health concern. Preventative services are largely geared towards men who have sex with men (MSM). However, in 2018 approximately 1 in 5 individuals who acquired HIV were cisgender women; the vast majority of whom (~85%) acquired the virus through sexual transmission.

A number of biological, structural and sociocultural factors place women at risk of HIV infection, particularly women of color. These include sexually transmitted infections (such as chlamydia, gonorrhea, and syphilis), sexual violence, a lack of consistent condom use, transactional sex,

injection drug use, risky behavior of a male sex partner, and low socioeconomic status. *Many of these factors are difficult to ascertain easily in healthcare settings; however, a positive diagnosis of a bacterial sexually transmitted infection (STI) more than doubles the risk of HIV acquisition.*

PrEP is an antiretroviral medication used to prevent HIV among individuals at increased risk of infection. Unlike condoms, PrEP is a biomedical preventive option women can initiate and use without partner involvement. Clinical trials of PrEP have demonstrated high efficacy among those who adhere to the medication, with results suggesting oral PrEP is 99% effective against HIV acquisition through sexual contact. Currently, the only PrEP available for use among women is a daily pill of emtricitabine and tenofovir disoproxil fumarate. However, numerous trials of other forms, including long-acting pills, injectables, and implants are underway, with some nearing regulatory approval. *As PrEP options expand and evidence accumulates on their effectiveness, strategies will be needed to 'hard wire' PrEP benefit-risk communication and informed decision-making in primary care between women and their providers.*

A recent systematic review revealed women express high interest in PrEP. However, in 2016, the first national data of PrEP users across the United States revealed significant disparities in product use by sex. Although women comprised ~20% of new HIV infections that year, they represented only 7% of PrEP users. Data from Illinois, one of the states with the highest number of PrEP users, has revealed similar disparities. Despite an HIV incidence of 17% among women in 2018, less than 7% of PrEP users in 2019 were women.

Barriers to PrEP uptake among women have been well studied. Known barriers include: low HIV risk perception; lack of PrEP awareness; stigma; concerns about daily pill taking and side effects; costs; medical mistrust; and low provider engagement. Mixed-methods and qualitative studies have emphasized the importance of provider-initiated conversations about sexual health for PrEP uptake among cisgender women. However, a recent systematic review of barriers to PrEP prescribing in the United States noted that the most commonly mentioned barrier was a lack of knowledge among health care providers about PrEP. Among providers who are knowledgeable, researchers have revealed that many are adept at initiating PrEP conversations with MSM, though not with women. This practice not only exacerbates sex disparities in PrEP uptake, but it also results in lower "case finding" or the identification of eligible, female PrEP patients.

Several studies have also noted that primary care providers are well positioned to prescribe PrEP to women who are already engaged in the health system. Women themselves have noted a preference for primary care providers to normalize PrEP conversations and perform regular screening for potential PrEP uptake; this is particularly the case among women who have increased vulnerability to HIV. Yet, while primary care represents the healthcare frontlines for the vast majority of adult women, primary care providers are not always adequately prepared to counsel on, or deliver PrEP.

With the near universal adoption of EHRs across the United States, opportunities now exist to increase patient-provider discussion and monitoring of PrEP in primary care with minimal disruption to clinical workflow or timing. EHR alerts have already been used effectively to increase HIV testing in primary care, and efforts are underway to use artificial intelligence within the EHR to predict potentially eligible PrEP users – a technique that relies on existing, yet limited, laboratory data and structured EHR fields. However, no comprehensive EHR-based interventions have been developed to use EHR data for "case-finding" potentially eligible patients, while also facilitating informed decision-making for HIV prevention and supporting PrEP uptake within primary care.

Our team recently developed and evaluated the Electronic health record Medication Complete Communication (**EMC²**) strategy to 'hardwire' provider/patient communication & surveillance of select prescription (R_x) medications. EMC² uses widely available technologies to promote:

- **provider counseling** at the point of care, prompted via EHR 'best practice' alerts (BPAs) linked to the signing of a medication order or a specified diagnosis
- **dissemination of understandable, actionable R_x instructions and risk information** automatically via the EHR or patient portal
- **routine community-based surveillance of R_x use** either by interactive voice response (IVR), text messaging, or EHR patient-portal platforms, to assess patient R_x experiences and notify clinicians of any problems via EHR secured message

To date, the EMC² strategy has been adapted and implemented in a variety of contexts, from higher-risk medications in primary care to knowledge and safe use of opioids in the Emergency Department (See **Table 1**). However, key components of this strategy address many of the well-documented barriers to PrEP uptake in primary care. Importantly, EMC² also promotes patient-provider discussion and decision-making, which will become increasingly important as potential new options for PrEP (e.g. long-acting pills, injectables, implants) may soon become available.

Table 1. EMC2 Strategies Developed by Our Team

R01DK103684	Addressing Higher Risk Medications in Primary Care. Our team developed and is currently evaluating an EMC2 strategy to promote safe use of higher-risk medications for chronic conditions in primary care. This strategy utilized EMC2 core components (BPA, print materials, IVR reports) in Centricity EHR.
R18HS023459	Promoting Safe Opioid Use in the Emergency Department. Members of our team evaluated the use of an adapted EMC2 approach in an ED to support safe opioid use. This strategy used low literacy print materials generated via Epic EHR as well as educational, unidirectional text messaging.
PO4500987425	Educating and Monitoring Patient Understanding and Use of Newly-Prescribed Diabetes Medications. Members of our team have used a patient portal-based EMC2 approach to inform patients about risks surrounding higher-risk diabetes medications in academic, endocrinology and primary care settings.

For this study, we propose to adapt the current EMC² to provide quality improvement to the participating clinics'. The improved activities will:

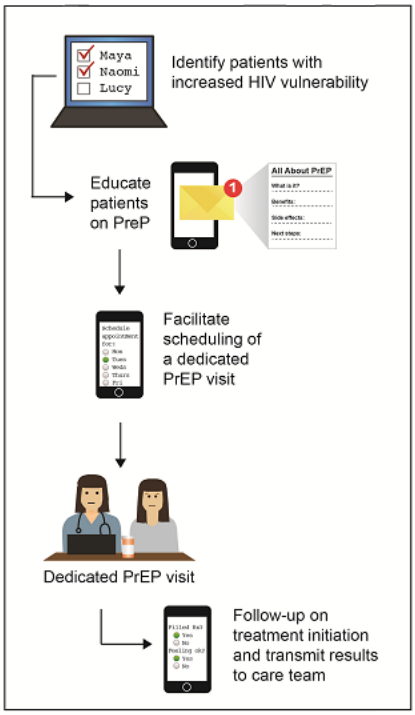
- identify, via the EHR, female patients who have increased vulnerability to HIV
- educate pre-identified patients about PrEP using an interactive, health literacy-appropriate educational tool delivered via the patient portal
- facilitate scheduling of a dedicated PrEP clinic visit with an advanced practice nurse and/or physician for potentially eligible and interested patients

STUDY ENDPOINTS:

Primary outcomes include process outcomes. The primary outcome of interest is PrEP uptake. Rates of PrEP uptake will be compared in the first 6 months between those in the intervention and control arms; a sensitivity analysis will be conducted to examine de-identified rates of PrEP uptake among others during the same timeframe. Other process outcomes of interest will investigate the reliability of the strategy to 1) deliver an educational PrEP decision

guide to women with increased vulnerability to HIV, 2) engage those individuals in the PrEP decision guide, and 3) schedule patients for a dedicated PrEP visit

Secondary outcomes include psychosocial outcomes. In post-pilot interviews, we will obtain the following measures. Differences between intervention and control groups will be explored. The main secondary outcome is PrEP knowledge measured about 2-6 weeks after randomization to the intervention (receiving the materials) or the control (delayed receipt).
Perceived Risk of HIV. We will use the 8-item Perceived Risk of HIV scale to assess how vulnerable an individual feels to HIV. The scale was developed in the United States and attention was paid to health literacy. Response options vary for each item, though they are measured on a 4-point Likert scale.
PrEP Knowledge. We will use a scale created by our team, drawing from the scale previously created by Welsh for use with men.
PrEP Attitudes. PrEP attitudes will be assessed using a recently developed scale developed that includes 5 items, each measured on a 5-point Likert scale (1=strongly disagree to 5=strongly agree).
Health Literacy. We will assess health literacy skills via the Newest Vital Sign (NVS). Participants will be asked to view a nutrition label and to answer 6 questions about how they would interpret the information. Scores are classified as high likelihood of limited literacy (0-1), possibility of limited literacy (2-3), and adequate literacy (4-6). The NVS has a high correlation with the Test of Functional Health Literacy in Adults and includes both reading and numeracy items.
Health Activation. Patients' engagement in their child's healthcare will be measured using a modified version of our team's 10-item Consumer Health Activation Index (CHAI). Response options are a Likert scale; linear transformation is used to put total scores onto a 0-100 scale, with higher numbers indicating greater activation.
Acceptability of the Strategy. Using 5-point Likert scale response options (1=very unsatisfied to 5=very satisfied), intervention participants will be asked to rate their satisfaction with various strategy components, including the materials, the dedicated PrEP visit, and the clinic follow-up activities.
Demographic Characteristics. We will collect a range of sociodemographic characteristics on the patient. This includes, but is not limited to: age, race/ethnicity, marital status, household income, and insurance status.



STUDY INTERVENTION(S) / INVESTIGATIONAL AGENT(S):
The Figure below provides an overview of key intervention activities.

Briefly, EMC^2 PrEP will help: 1) identify female patients in primary care who are at increased vulnerability to HIV due to prior suspected or confirmed bacterial STIs; 2) identified patients will receive an interactive, and educational PrEP decision guide via the patient EHR portal (they may also receive up to 3 reminders via the EHR portal to view the decision guide); 3) those who are interested in learning more about PrEP will be directed to schedule a dedicated visit with a dedicated PrEP provider; 4) during which PrEP options will be discussed and prescribed as appropriate.

Our pilot study will be conducted at select Northwestern Medicine (NM) primary care, after receiving committee approval to inform potentially eligible women about PrEP by providing them with an educational material that will educate them on PrEP and provide decision support for those who might be interested in speaking with a dedicated PrEP provider about PrEP use. We will not be altering the standard of care; rather, we will be providing additional materials and support to those who may benefit. A recent EHR data pull indicates there are ~1400 female patients who are potentially eligible for PrEP in primary care. For evaluation purposes, these women will be 1:1 randomized to either: 1) immediate receipt of the EMC^2 PrEP strategy as part of the intervention group or 2) a delayed receipt of the EMC^2 PrEP educational materials as part of the control group. Immediate receipt may take place over a rolling period over the course of several months. This not only ensures everyone receives the strategy, but it also allows for a practical rollout that respects the clinic bandwidth. Randomization will occur using a random number generator. EHR data will be evaluated in aggregate to determine, for example, how many women received the PrEP decision guide, opened it, interacted with it, scheduled a dedicated PrEP visit and/or received a PrEP prescription. Data will also be evaluated during the acute period to compare those who immediately received the EMC2 PrEP strategy, and those who were delayed in their receipt of the strategy.

PROCEDURES INVOLVED:

Study Design Overview

To achieve our objectives, mixed-methods research will be conducted to adapt, pilot, and disseminate the EMC^2 strategy for use in PrEP decision making among women in primary care.

Aim 1: Adaptation Phase

During the Adaptation Phase (Aim 1), we will: 1) obtain clinician and EHR analyst input from various committee approval meetings; 2) develop and refine the content of the PrEP decision guide via cognitive interviews with the target audience (N=15), and 3) construct the technological build for both the decision guide and the post-visit treatment initiation questionnaire. A Scientific Advisory Board (N=3) will provide guidance on the strategy and intervention content throughout this process.

Procedures for developing the PrEP decision guide. An interactive and educational electronic PrEP decision guide will be developed for deployment in existing EHR infrastructures (e.g., the patient portal). Iterative development will ensure the decision guide incorporates results from the key informant interviews, a thorough review of the literature, and health literacy best practices. The decision guide will also undergo review by our Scientific Advisory Board before being cognitively tested among women with increased vulnerability to HIV.

The final version of the decision guide will aim to emphasize choice and facilitate informed decision-making for PrEP. The PrEP decision guide will also contain interactive features (such as a video) designed to assess PrEP knowledge and interest. At the end of the guide, users will have an option to schedule a dedicated PrEP visit with an APN.

Procedures for cognitive interviews with patients (N=15). One-time, individual, cognitive interviews lasting ~45 minutes will take place after the key informant interviews. Cognitive interviews provide an opportunity for patients to impart detailed feedback on the MyChart message patients will receive informing them about the PrEP decision guide, the decision guide itself, and the short video that will be embedded within the guide. We will ask questions about the content, readability, understandability and actionability of the material. Attention will be paid

to ensuring the materials are culturally appropriate and non-stigmatizing for a diverse audience. Cognitive interviews will **not** be audio recorded and personal data is not requested; only general feedback solicited on material content, layout, visuals, color, etc. These brief, unstructured interviews (akin to feedback sessions) will be conducted via Zoom or Microsoft Teams. Participants will be told they do not need to have their video cameras on, though they will need to see the materials shown by the Northwestern research coordinator (RC). The RC will also take detailed, de-identified notes for analysis purposes.

Specifically, this process includes:
1. Participants will be screened and provide online informed consent prior to participation, including consent to have the interview audio-recorded for note-taking purposes
2. Interviews will be conducted by trained Northwestern research coordinators (RCs) who will use a semi-structured guide to inform the discussion;
3. Participants will also be asked to view, review, and provide feedback on the draft PrEP decision guide material, including the message informing patients they've received the PrEP decision guide in MyChart and an embedded video.
4. Interviews will focus on the material and are not intended to collect personal information.

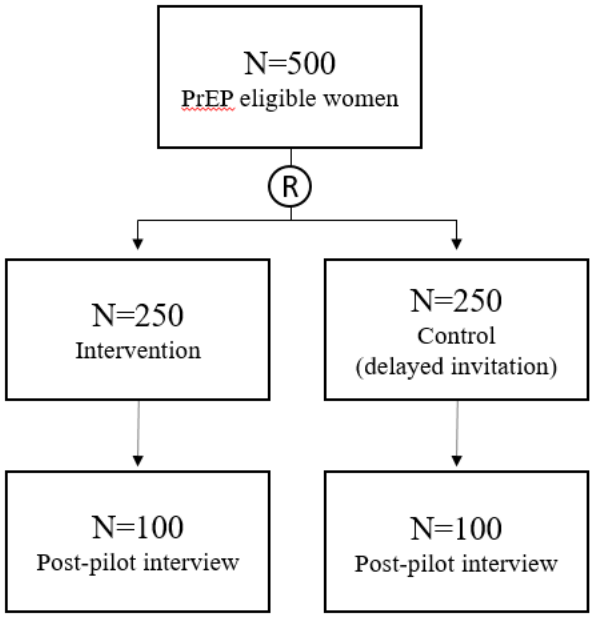
Procedures for the EHR build. Drs. Pack and Bailey (Co-I) will work with NM analysts to build the materials within Epic. Under their direction, clinical informatics staff will build and pilot the strategy in the electronic test environment and implement the strategy after any needed troubleshooting.

Procedures for engaging with the Scientific Advisory Board. During the adaptation phase, we will iteratively work with a Scientific Advisory Board via email and/or videoconferencing platforms for the purpose of obtaining additional scientific guidance on our strategy and content. The board will be comprised of three individuals whose combined expertise will include infectious disease, PrEP, and informatics. The study team will identify individuals with demonstrated expertise through our professional networks at multiple academic institutions and Centers for Aids Research. *This board will also function as a 'mini DSMB'.*

Trial registration. The study protocol will be registered with ClinicalTrials.gov.

Aim 2: Pilot Implementation Phase (Months 10-19)

Procedures for implementing the pilot study. For this 'development of concept' pilot study, the EMC^2 PrEP strategy will be sent to eligible women over a 6-month period at Northwestern primary care practices.



Approximately 1400 women have been identified as potentially PrEP eligible based on a previous EHR data pull. Women will be randomized 1:1 to either *immediately* receive the EMC^2 PrEP strategy (intervention; n=700) or a *delayed* invitation (control arm; n=700). In this manner, all patients will have eventually have the opportunity to receive EMC^2 PrEP materials. Process outcomes may be collected on all these ~1400 women.100 women per arm will be identified and a

post-pilot interview conducted to further evaluate intervention effects.

Procedures for post-pilot interviews (N=200). To further explore intervention effects, the study RC will interview 200 participants approximately 2-6 weeks after they have received the materials or after they have been randomized to the control arm. This includes interviewing 100 participants randomized to the EMC^2 PrEP strategy intervention arm and 100 randomized to the control arm (delayed invitation).

These patients will participate in an interview lasting ~1 hour. This interview will take place either in person, over the phone, or via a secure videoconferencing platform, depending on patient preferences and the status of the COVID-19 pandemic. However, the last 50 intervention arm participants will have their interviews conducted over a secure videoconferencing platform so that the RA can show them the EMC^2 PrEP education materials (the PDF and the video) before initiating the interview questions. Cameras will be turned off and there will be no recording. The purpose is just to ensure these participants have had a chance to view the materials before they answer study interview questions. All questions will be verbally asked by the RA as if the participant were on the phone and data will be captured in REDCap per usual. Interviews with both intervention arm (N=100) and control arm (N=100) patients will include quantitative measures assessing perceived risk of HIV, as well as PrEP knowledge, attitudes, stigma, and information sources. Additionally, we will measure health literacy, health activation, and basic demographic information.

Patients enrolled in the intervention arm (N=100) will also complete measures of satisfaction, specific to each strategy component.

Aim 3: Dissemination activities (Months 20-22)
These activities will be the last to occur. First, to obtain feedback from clinicians at a participating NM primary care practice(s), we will speak with clinic staff during an available business meeting after the completion of the pilot study to gauge their reactions to the approach. We will specifically aim to identify clinic-level barriers to implementation of the EMC^2 PrEP strategy.

The Northwestern research team will then solicit opinions about how best to implement this type of study at AllianceChicago affiliated clinics. To achieve this the research team will speak with current clinic administrators, prescribing providers, or EHR analysts within FQHCs affiliated with AllianceChicago or AllianceChicago itself (N~15).

Together, these activities will directly inform the development of a standard operating protocol that could be used in a future study. Personal data will not be requested. These brief, unstructured interviews (akin to feedback sessions or a business meeting) will be conducted either in person or via a secure webconferencing platform (Zoom or Microsoft Teams).

DATA AND SPECIMEN BANKING
Participant data will be collected using the Northwestern-based REDCap survey platform. All data will be stored under an ID number. Upon completion of all study activities, a final deidentified dataset will be created. This dataset will be stored indefinitely on the GIM server for secondary analyses. Only authorized personnel will have access to it. Data will be stored on Northwestern encrypted servers and access will be granted through the PI.

SHARING RESULTS WITH PARTICIPANTS
Study results will not be shared directly with participants.

STUDY TIMELINES
In total, this is a 22-month study.

Aim 1: Cognitive Interview Duration
All cognitive interview participants will be involved in the project for the length of their ~45 minute, one-on-one interview on a single day. This is estimated to be approximately 30 minutes for content solicitation, and 15 minutes or less for completion of the demographic questionnaire.

Aim 2: Pilot Study Duration
The EMC^2 PrEP Strategy will be 'turned on' for those randomized to the intervention arm for a total of 6 months. After the 6 months, the EMC^2 PrEP Strategy will be 'turned on' for those randomized to the control arm (delayed intervention). REDCap will be used to facilitate study tracking.

Procedures for analyses will be set up in ample time before the end of the study such that all data can be rapidly analyzed as soon as the intervention timeframe (6 months) has concluded.

INCLUSION AND EXCLUSION CRITERIA

Participants in the cognitive interviews to adapt the EMC^2 strategy (**Aim 1; N=15**), must meet the following eligibility criteria:

1) be an adult (age 18+) woman;
2) self-report interest in HIV prevention (if recruited by Craigslist, social media, etc.)
3) have ever received a positive diagnosis for chlamydia, gonorrhea or syphilis, or have ever received a PrEP prescription (if recruited by the EDW);
4) speak English as their primary language;
5) have access and proficiency using the internet and video conferencing technology;
6) have an active email address;
7) have no severe, uncorrectable visual, hearing or cognitive impairments that would preclude study consent or participation.

For the pilot study (**Aim 2**), we will randomize women who are potentially eligible for PrEP (N~1400; n=700 per arm) to intervention (the EMC^2 PrEP strategy) and control arms (delayed receipt of PrEP education materials). This is similar to a quality improvement activity. To be eligible to receive the EMC^2 PrEP strategy, participants must:

1) be an adult cisgender woman (age 18+) identified in the EHR who:
2) be HIV negative,
3) have received two or more tests in the past 12 months for chlamydia, gonorrhea and/or syphilis,
4) and/or have received a positive diagnosis for at least one of those sexually transmitted diseases (STIs) in the past 6 months;
5) are seen at the participating Northwestern Medicine practice(s);
6) have an active MyChart account;
7) not be currently using PrEP;
8) did not participate in the Aim1 cognitive interviews.

To be enrolled in post-pilot interviews (**Aim 2, N=200; n=100 per arm**), women must additionally (in addition to pilot study eligibility criteria):

1) speak English as their primary language; and
2) have no severe, uncorrectable visual, hearing or cognitive impairments that would preclude study consent or participation.
3) The last 50 intervention arm participants will also need to have access to videoconferencing platform (e.g. Zoom) so that they may view the PrEP education materials (the PDF and the video) before answering the interview questions.

For dissemination activities* (**Aim 3**), we will consult with key informants affiliated with AllianceChicago to explore study expansion. Participants in these consultations will be:

1) current clinicians and/or clinic staff from the participating NM site(s)
2) current clinic administrators, prescribing providers, or EHR analysts within an FQHC partnering with AllianceChicago or AllianceChicago itself

*Aim 3 Dissemination Activities are not considered human subjects research as these individuals are only providing information that will improve the intervention and/or inform the development of a standard operating protocol; no information will be collected about the participants themselves.

VULNERABLE POPULATIONS

We will not include any vulnerable populations in this research.

PARTICIPANT POPULATION(S)

Accrual Number:	Category/Group: (Adults/Children Special/Vulnerable Populations)	Consented: Maximum Number to be Consented or Reviewed/Collected/Screened	Enrolled: Number to Complete the Study or Needed to Address the Research Question
Study-wide	Aim 1: Adults	6000	15
	Aim 2: Adult women	6000	200
Total:		12000	225

RECRUITMENT METHODS

Cognitive interview participants (Aim 1, N=15)

Potentially eligible patients will be identified through various channels. This includes Craigslist, social media (e.g. Facebook), community-based recruitment/snowball sampling, or the Northwestern EDW.

For Craigslist, social media, and community-based recruitment a member of the Northwestern research team will virtually or physically post an ad with select eligibility criteria. Individuals may also be identified through snowball sampling as well as in-person recruitment (e.g. posting/handing out flyers at a community location or event). The research assistant will then call individuals who respond to the ad to introduce them to the study, screen them, and schedule their virtual interview. Criteria will be confirmed over the phone prior to moving forward with consent and scheduling the study interview.

For patients who are recruited through the EDW, we will seek a waiver of HIPPA for recruitment to contact female patients, identified in the EDW, who have ever received a positive diagnosis for chlamydia, gonorrhea or syphilis, or have ever received a PrEP prescription. Trained RCs will review the EDW report and only reach out to those who meet patient eligibility criteria. Criteria will be confirmed over the phone prior to moving forward with the consent process and scheduling the study interview. Due to study timeline restrictions, the study team will not mail out recruitment letters to patients identified through the NM EDW. Instead, a research assistant will call potentially eligible patients who fit our eligibility criteria and/or have provided consent to be contacted for future research opportunities.

Post-pilot interview participants (Aim 2, N=200)
We will first seek a waiver of HIPPA for recruitment and to be able to send eligible women the PrEP guide via their MyChart. Then, these potential post-pilot interview participants will be identified via the EDW for post-pilot interviews. This list of patient names, medical record numbers, phone numbers, address, and date of birth will be compiled in a report that can be securely accessed and reviewed by study staff. Reports will be run approximately 2 or more times weekly to identify eligible patients.
Similar to the cognitive interviews, recruitment will be done by the RC via telephone rather than by mailing letters. Patients will be called via telephone within approximately 15 days of receiving the materials (randomization to the intervention arm) or randomization to the control arm. Trained RCs will contact identified patients and if they are interested in participating or learning more about the study, the RC will obtain verbal permission to ask the patient a brief series of questions to verify eligibility. If eligible, RC will obtain electronic informed consent. They will then initiate the post-pilot interview or schedule the interview for a time that is convenient to the participant.

COMPENSATION FOR PARTICIPATION IN RESEARCH ACTIVITIES

Study Activity	Payment Amount
Aim 1: Key Informant interviews with clinicians and administrators	$100
Aim 1: Cognitive interviews with patients	$30
Aim 2: Post-pilot interviews	$45

All compensated participants will be paid at the completion of their interview via the PNC Stored Value Visa Card program (physical gift card) or via the Northwestern Visa Prepaid Card program (virtual gift card). At the end of their interview, participants will be asked which payment type they prefer.

WITHDRAWAL OF PARTICIPANTS

There are no anticipated circumstances when a participant would be withdrawn from the study without their consent. Interviews are all conducted at single time-points, therefore participants will not be asked to participate in any subsequent interviews.

RISKS TO PARTICIPANTS

Participation in this study puts subjects at a minimal risk of discomfort or inconvenience, as they are primarily responsible for providing their own opinions on intervention materials and/or the intervention activities. Participation may make some participants feel uncomfortable, particularly when asked about sensitive topics such as HIV and STIs. Participants will be told they do not need to answer any questions that make them feel uncomfortable. Participation could also result in a loss of privacy, since research and oversight staff may review research findings.

POTENTIAL BENEFITS TO PARTICIPANTS
Participants are not likely to have any direct benefit from being in this research study. However, it is possible that subjects enrolled in the study may indirectly benefit in that they may have, as a result of this study, a better understanding of HIV prevention and PrEP. The results of this study may provide important information regarding how best to increase PrEP uptake among those eligible and interested.

DATA MANAGEMENT AND CONFIDENTIALITY
This is a small pilot study designed to test the feasibility, acceptability, and efficacy of a quality improvement project.

Quantitative Methods. All analyses will be performed using SAS v9.4 (Cary, NC). Descriptive statistics will be first calculated for patient sociodemographic variables, receipt of PrEP (yes/no), variables related to patient satisfaction with the intervention, and process outcomes.

The primary outcomes of interest are PrEP knowledge and PrEP uptake. Rates of PrEP uptake will be compared in the first 6 months between those in the intervention and control arms. Chi-squared tests will be performed with de-identified patient factors, as well as multivariable logistic models, to explore characteristics that may be independently associated with PrEP knowledge and/or receipt of a PrEP prescription. The primary covariate of interest will be the study arm.

Other process outcomes of interest will investigate the reliability of the strategy to 1) deliver an educational PrEP decision guide to women with increased vulnerability to HIV, 2) engage those individuals in the PrEP decision guide, 3) schedule patients for a dedicated PrEP visit, 4) engage patients prescribed PrEP in a portal post-visit treatment initiation questionnaire, and 5) notify prescribers of their patients' treatment initiation barriers. To achieve this, we will identify the percentage of participants randomized to the EMC2 PrEP strategy who complete each step.

Exploratory bivariate analyses will examine whether there are any systematic, statistically significant differences in PrEP knowledge by study arm and between patients who interacted with the PrEP decision guide and those who did not. Specifically, we will use Pearson chi-squared tests or Fisher exact tests for categorical variables and Student t tests for continuous variables. Statistical significance will be defined as alpha<.05.

Confidentiality
Data collected includes consent forms and information collected during the study interviews (demographics, comprehension testing scores, and feedback on the materials). A master study tracking database via REDCap will contain information linking participants to their study ID numbers. This database is secure and only accessible by study personnel. Each participant will be randomly assigned an identification number to ensure confidentiality of data. The RedCap tracking database designed for this study will be the only place where the ID will appear with the participant's name and contact information (address, email, dob, phone number) in the present study. This database will only be accessible by the research team. Survey data and

demographics will be stored in a separate REDCap project. Individual study identification numbers will be assigned to each participant and only this number will appear on the survey. Only study investigators and authorized research personnel listed in the IRB will have access to the data. Qualitative interview data will be audio recorded via a web conferencing service such as Zoom or MS Teams. Efforts will be taken to not record identifiable information. Recordings will be saved directly into the project folder on FSM servers and sent for transcription to a Northwestern-approved vendor. Deidentified transcripts will be kept for analyses purposes. Several methods will be employed to reduce the risk of breach of confidentiality. All personnel involved in data collection will be thoroughly trained in all assessment methods thus ensuring consistent applications of procedures and measurement consistency across participants. All interview data will be automatically saved in the secured, password protected RedCap system. The analyst or project coordinator will downloaded de-identified interview data to secure FSM folder only accessible to the research team. All raw demographic and survey data will be de-identified (with the exception of the study ID number). Under no circumstances will individually identifiable data be released to anyone. Results will be reported as group findings only. Data will be stored on the Northwestern server for the length of the study. All identifiable information will be deleted upon completion of the study.

Quality Assurance:

Training will begin after surveys and interview protocols have been refined and standardized. The PI will lead sessions to orient the research staff to the surveys and study protocols (e.g., interview process, data security). The training will include tailored discussion of 1) roles and responsibilities; 2) HIPAA and IRB mandates (completion of Human Subjects Training Program - CITI; 3) effective recruitment communication and interviewing with attention paid to health literacy and culture; and 4) gathering and recording data including administering the structured survey electronically. Role playing will be used to fine tune training for obtaining informed consent and interviewing patients. Institutional Review Board (IRB) approval will be attained prior to any active recruitment efforts. All interviewers will be required to demonstrate competence in survey administration and to pass a certification test.

Study-wide data management:

- Data Access: Only authorized personnel listed on each institution's IRB will have access to the data.

- Data Storage: The research staff will collect data through the Northwestern RedCap survey platform. Data will be stored in REDCap, a secure, web-based application, and on the Northwestern secure servers for the length of the study. The PI or Data Analyst will download the data from REDCap monthly and save to the "Analytic" folder within the project folder on the FSM department servers which are located in a HIPAA compliant data center. These downloaded data files do not contain any identifiable information, and are identified by project staff by an assigned study ID. Upon completion of all study activities, a final de-identified dataset will be created. This dataset will be stored indefinitely on the GIM server for secondary analyses. Only authorized personnel will have access to the dataset. All identifiable information will be deleted upon completion of the study.

PROVISIONS TO MONITOR THE DATA TO ENSURE THE SAFETY OF PARTICIPANTS

Data Safety and Monitoring Board (DSMB). The Scientific Advisory Board will serve as a mini DSMB. This group will be formed early in the project and be given responsibility to review and approve the methods and analysis plan. It will be organized by Dr. Pack and include an epidemiologist, and two clinical or health services researchers with related expertise. Meetings

will be held via video-conference at least annually to review protocols, procedures, and concerns related to research integrity.

PROVISIONS TO PROTECT THE PRIVACY INTERESTS OF PARTICIPANTS

Information about study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). All study generated datasets will be stored on the FSM server. In order to preserve participants' confidentiality rights, research subjects will be assigned code numbers that will be used to identify all the information collected. Using these codes, none of the collection forms will contain the names of the participants. All electronic data will be stored in on a password-protected computer. A master study tracking database will be created using REDCap and will be kept separate from all study responses that are also collected in REDCap. This database will be kept on a secure server and only accessible by study personnel. Survey data will also be stored in a REDCap. Audio recordings from qualitative interviews will be saved directly into a file on the FSM server from the web conferencing software; these will be sent for transcription. Deidentified transcripts will be kept used for analyses; audio recordings will be deleted at the end of the study. EHR extraction data will be stored on the FSM server. The data will not contain any identifiable information. Individual study identification numbers will be assigned to each participant. The master study tracking REDCap project will include consent data, which includes the participants' name and date of births, and an email to be able to send the electronic consent. REDCap has protections needed for storage of PHI and will restrict data downloads to exclude PHI. These links will be removed after completion of data collection. The REDCap project will only be accessible to authorized study personnel. All personnel involved in data collection will be thoroughly trained. Only information that has been generalized and/or de-identified will be shared.

Subjects will be informed that participation in any part of this research study may result in a loss of privacy, since persons other than the investigators may view their study records if deemed necessary for oversight purposes. However; they will be identified by a unique identification number ("study id"), not by name, and any other identifying information (e.g. personal and/or contact information) will be kept separate from the other data; all information will be kept in secure, password-protected files. Personal information will be encrypted and linked to the study number. Further, subjects will be told that unless required by law, only the study investigators, members of the project staff, and representatives of the Northwestern University and local Institutional Review Boards will have the authority to review any study records. In such case, they too will be required to maintain confidentiality.

Participation in the study poses minimal risk of psychological, social, and economic harm. Informing subjects in advance that they may decline to answer any questions asked during the interview and discussion group will mitigate any risks associated with expressing their opinions (e.g., feeling uncomfortable).

All enrolled participants in Aim 1 will provide online consent. All enrolled participants in Aim 2 will provide electronic consent through REDCap.

COMPENSATION FOR RESEARCH-RELATED INJURY

NA

ECONOMIC BURDEN TO PARTICIPANTS

NA

CONSENT PROCESS

Aim 1 Participants. The Northwestern study team will screen all patients to ensure they meet the study's eligibility criteria. Participants who are recruited for Aim 1 (cognitive interviews) will undergo informed online consent.

After initial recruitment and screening by phone, subjects will be informed about the nature of the study by a trained RC and asked to provide online consent. Participants will be provided a consent form. Informed consent will be viewed as a process, i.e. at several times during review of the IRB approved consent document, the subject will be asked to explain in their own words what their understanding of the consent. This will enable the research personnel to enter into a dialogue with the subject and ensure that the subject understands that he/she is free to withdraw at any time without penalty. Information will be provided to the subjects in terms that they can fully understand. They will be informed that they may withdraw from the study at any time and given contact information for the PI and RC. There will be no exertion of any overt or covert coercion. They will be encouraged to ask questions prior to giving consent.

If a patient agrees to participate after the RC reads the consent, the RC will digitally sign their own name on the form using REDCap. This signed consent form will be saved on a secure FSM server, in a project folder only accessible by IRB approved personnel. Subjects will also be mailed or emailed the consent forms to keep for their records.

Aim 2 Participants. Patient participants who are recruited for participation in the post-pilot interviews (Aim 2) will provide electronic consent with HIPPA authorization. Prior to the post-pilot interview, participants will electronically provide consent. Similar to the consent process for Aim 1, the RC will send patients a link to REDCap by email to be able to read through the consent with the RC. Informed consent will be viewed as a process, i.e. at several times during review of the IRB approved consent document, the subject will be asked to explain in his/her own words what his/her understanding of the consent. This will enable the research personnel to enter into a dialogue with the subject and ensure that the subject understands that he/she is free to withdraw at any time without penalty. Information will be provided to the participants in terms that they can fully understand. There will be no exertion of any overt or covert coercion. They will be encouraged to ask questions prior to giving consent. Participants will be informed about the nature of the study by a CITI certified RC and asked to provide consent. Additionally they will be notified that only those contents of their medical record that are necessary to evaluate the effectiveness of the intervention will be released to the research team at Northwestern. They will be informed that they may withdraw from the study and stop the interview at any time; they will be given contact information for the PI and study coordinator. The patient will then complete an electronic consent and HIPAA Authorization through REDCap. Patients will be informed they can print their screen to keep a copy of the consent, or we can mail or email them a blank copy of the consent document for their records. Prior to completing the phone interview, the RC will review the electronic consent with the patient and confirms the consent was properly signed and completed.

Non-consenting patients. Participants in the post-pilot interviews (Aim 2) are consenting to post-pilot interviews; however, because of the nature of implementing the EMC^2 PrEP intervention other eligible patients will receive the EHR components of the intervention without being approached for consent or enrolled in the study (this is similar to a quality improvement activity). Patients will receive educational materials via their EHR portal about PrEP and HIV prevention. For these patients receiving the intervention, but not approached or consented for post-pilot interviews, we request a waiver of informed consent because: 1) this is a low-risk study, in particular, it is research designed to evaluate an educational strategy, 2) it would not be feasible to conduct the study as intended if obtaining individual informed consent were necessary, 3) informed consent from each participant would threaten the scientific validity of the study (in this

case it would be impossible to evaluate real-world dissemination and implementation of the intervention) and 4) for the patients receiving the intervention, but not completing follow-up, no patient data are collected that would not be routinely collected in usual care without consent. This specific strategy of "turning on" an EHR intervention has been previously approved by the IRB at Northwestern University.

NON-ENGLISH SPEAKING PARTICIPANTS

NA

WAIVER OR ALTERATION OF CONSENT PROCESS

Waiver of HIPAA Authorization are requested to identify subjects (patients) prior to enrollment into the study.

A waiver of consent for eligible patients to receive intervention materials (the PrEP decision guide) is requested. Education materials will be offered as an option for all patients to see and respond to on their own accord, regardless if they consent to the study or not as this will be the clinic standard of care. Materials will inform patients about PrEP, a service that is already offered at the clinic. Because PrEP is most useful to individuals who face an increased vulnerability to HIV, it is prudent to target materials to individuals who have a clinical indication of vulnerability due to recent STI testing and/or diagnoses. Furthermore, targeting as opposed to sending the material to all patients, will help to not overwhelm the practice, should the materials create increased interest in PrEP.

PROTECTED HEALTH INFORMATION (PHI AND HIPAA)

This study involves the use of Protected Personal Health Information for Aim 2 participants. All enrolled participants in Aim 2 will provide electronic consent with HIPAA authorization for the collection of all data, including review of the patient's medical record.

Waiver of HIPAA Authorization are requested to identify subjects (patients in Aims 1 and 2) prior to enrollment into the study. The following will be collected for eligible patients

- Names
- Street address, city, county, ZIP code
- Date of Birth
- Telephone numbers (home, cell, work)
- Email
- Medical Record Numbers
- HIV testing results
- Sexually Transmitted Testing and/or Illnesses

QUALIFICATIONS TO CONDUCT RESEARCH AND RESOURCES AVAILABLE

The research team is comprised of 5 PhD and/or MD level researchers, and 1 research coordinator (with experience on similar projects). Pack (PI) will manage the team, which includes experts in health literacy (Bailey, Pack), primary care (Liebovitz; Vasiloff), infectious disease (Masters), HIV prevention and PrEP (Liebovitz, Masters, Vasiloff, Pack) and health information technology (Liebovitz, Bailey).

MULTI-SITE OR COLLABORATIVE RESEARCH:

STU#: STU00217596

NA