NCT05215262 - TAKE Steps: Motivational Interviewing to Prevent STIs

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Protocol Title: Health Coaching to Improve Comprehensive HIV and Sexually Transmitted Infection Prevention in Adolescent Primary Care

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ABBREVIATIONS AND DEFINITIONS OF TERMS

ACES		Adverse Childhood Experiences Survey
AIM		Acceptability of the Intervention Measure
ATN		Adolescent Trials Network
AYA		Adolescents and young adults
ACT		Acceptance and Commitment Therapy
AE		Adverse event
ASC		Adolescent Specially Care Clinic
CFIR		Consolidated Framework for Implementation Research
CHOP		Children's Hospital of Philadelphia
CRAFFT		Car, Relax, Alone, Forget, Friends. Trouble-Screening Tool
CSR		Chart-simulated recall
EHR		Electronic health record
FIM		Feasibility of Intervention Measure
GSES		Generalized Self-Efficacy Scale
HIV		Human Immunodeficiency Virus
HC		Health Coaching
IAM		Intervention Appropriateness Measure
IRB		Institutional Review Board
MI		Motivational interviewing
NAAT		Nucleic acid amplification test
NIH		National Institute of Health
NIMH		National Institute of Mental Health
PAM		Patient Activation Measure
PCP		Primary care providers
PHI		Private Health Information
PHQ		Patient Health Questionnaire
PrEP		Pre-exposure prophylaxis
RCT		Randomized Control Trial
REDCap		Research Electronic Data Capture
RPR		Rapid Plasmin Reagin
SOC		Standard of Care
STD		Sexually transmitted disease
STI		Sexually transmitted infection

ABSTRACT

Context: (Background)

Pediatric primary care systems are uniquely positioned to reduce HIV and STI incidence in adolescents, despite substantial challenges to sexual health service delivery. Health coaching is a developmentally appropriate and effective method of targeting motivation and behavior change in adolescents.

Objectives: (primary and important secondary objectives)

Primary Aim 1: To adapt a health coaching intervention to provide comprehensive, PrEP-inclusive, HIV and STI prevention for adolescents at elevated risk of HIV in pediatric primary care

Primary Aim 2: To identify contextual barriers and facilitators to implementation of the adapted health coaching intervention in pediatric primary care

Primary Aim 3: To conduct a randomized controlled trial (RCT) to test for the intervention's effect on HIV prevention self-efficacy, as well as feasibility and acceptability among adolescents at high risk of STI and HIV acquisition

Study Design:

Aim 1: Observational cross-sectional study

Aim 2: Observational cross-sectional study

Aim 3: Randomized control trial

Setting/Participants:

All aims: Participants will be recruited in-person or via telephone or email from CHOP Primary Care Clinics. Research activities will also be conducted at the Roberts Center for Pediatric Research, as well as primary care clinics, and on a virtual platform capable of video conferencing using a HIPAA compliant CHOP approved vendor.

In addition, for Aim 1, participants will also be recruited from the Adolescent Specialty Clinic (ASC) at 3550 Market. In addition, participants can be referred by word-of-mouth from other study participants.

Key eligibility criteria

Aim 1: n= 50 male and female participants ages 13-19, with a history of one or more STIs, and can speak and understand written English, and has access to internet, a mobile device or computer, and video conferencing using a HIPAA compliant CHOP approved vendor.

Aim 2: n= 25 clinicians, clinic staff, and administrators who have provided clinical care to patients with STI diagnosis in the past 6 months and can speak and understand written English.

Aim 3: n=150 participants, 75 for each arm (with the chance of more participants in the RCT's intervention arm than control arm if there are changes to the randomization scheme). HIV-negative youth ages 13-19 within 30 days of treatment for an STI diagnosis of incident gonorrhea, chlamydia, trichomonas, or syphilis at the aforementioned clinics, and can speak and understand written English.

Study Interventions and Measures:

Aim 1: Observational study identifying barriers and facilitators to HIV/STI prevention strategies through surveys, virtual or in-person in-depth interviews and focus groups.

Aim 2: Observational study identifying acceptability, feasibility, and appropriateness of the coaching intervention through survey individual semi-structured interviews and chart-simulated recall.

Aim 3: Randomized controlled trial of the health coaching intervention designed to increase perceived self-efficacy in STI and HIV prevention, using survey measures, interviews, and chart abstraction for outcome measurement.

TABLE 1: SCHEDULE OF STUDY PROCEDURES FOR AIM 3 RCT

Study procedures, by treatment group for the Aim 3 randomized controlled trial.											
	Screening and Enrollment	Baseline		1 Week + 7/- 5 days		1 Month + 30/- 14 days		3 Months + 30/- 14 days		6 Months +/- 30 days	
Study procedure		HC[1]	SOC[2]	HC	SOC	HC	SOC	HC	SOC	HC	SOC
Review of Inclusion / Exclusion Criteria	X	--	--	--	--	--	--	--	--	--	--
Informed Consent	X	--	--	--	--	--	--	--	--	--	--
Randomization	--	X	X	--	--	--	--	--	--	--	--
CASIs[3]	--	X	X	X	--	--	--	X	X	X	X
Health Coaching	--	X	--	X	--	X	--	X	--	--	--
Feedback Interview	--	--	--	--	--	--	--	X	--	--	--
Chart Abstraction	--	X	X	--	--	--	--	X	X	X	X

[1]HC: Health coaching arm

[2]SOC: Standard of care arm

[3]Computer assisted survey instruments

1 BACKGROUND INFORMATION AND RATIONALE

1.1 Introduction

The proposed research seeks to: 1) adapt an existing Health Coaching intervention to focus on comprehensive adolescent biobehavioral HIV/STI prevention; 2) identify barriers and facilitators to intervention implementation in pediatric primary care; and 3) test the intervention in two high STI-incidence pediatric primary care clinics. If successful in accomplishing my aims, I will generate an intervention and dissemination strategy that are feasible to implement in primary care and poised to test whether it improves HIV prevention outcomes while simultaneously launching an independent career in HIV/STI prevention research.

1.2 Name and Description of Intervention

The third aim of this cluster of studies will consist of a randomized controlled trial of a health coaching intervention for adolescents with diagnosed sexually transmitted infections (STIs). The coaching sessions will provide HIV/STI prevention education and teach motivational interviewing (MI) and Acceptance and Commitment Therapy (ACT)-informed behavior change strategies using didactics, role plays, and patient encounter observations.

1.3 Relevant Literature and Data

Pre-exposure prophylaxis (PrEP) is the newest evidence-based practice for HIV prevention in adolescents. PrEP has arrived in the context of disproportionate rates of HIV infection and rising sexually transmitted infections (STIs) in adolescents. While 13-24 years olds comprise ~13% of the U.S. population, they represent 21% of incident HIV cases. STIs in the U.S. are rising dramatically,[1] with ~50% of incident STIs occurring in youth aged 15-24.[2] These statistics highlight the need for new strategies to reduce adolescent HIV and STI incidence. In adult clinical trials, oral tenofovir-emtricitabine (TDF-FTC)-based PrEP has been >90% effective in preventing HIV in highly adherent users.[3,4] The Adolescent Trials Network (ATN) 110/113 trials recently demonstrated PrEP safety in adolescents, leading to expanded Food and Drug Administration (FDA) approval in 2018.[5,6] The Centers for Disease Control and Prevention (CDC) now recommends PrEP for HIV negative individuals who are sexually active and not in a relationship with a recently tested HIV negative partner and have a recent STI, infrequent condom use with partners of unknown or high-risk HIV status, or are men who have sex with men (MSM) with recent condomless anal sex.[7] As prevention options expand, there is a critical need for behavioral HIV prevention interventions to keep pace to ensure that PrEP reaches youth at highest risk of HIV infection.

CDC guidelines situate PrEP within comprehensive HIV/STI prevention care.[7] Patients must be monitored every three months for risk reduction counseling, HIV, and STI testing. Given the dramatic recent rise in adolescent STIs and potential STI increases in PrEP users, PrEP must also be paired with STI prevention approaches.[8] Unfortunately, while PrEP is known to be effective and safe for adolescents, <2% of PrEP prescriptions are for adolescents <18 years. To move PrEP to scale, research is needed to determine **who** should be involved in PrEP delivery, **what** the behavioral targets are for risk reduction, **which**

factors may serve as barriers to uptake, **when** the optimal time is for linkage to PrEP, and **how** to best intervene to increase HIV and STI prevention behavior in adolescents.

Pediatric primary care systems are uniquely positioned to reduce HIV and STI incidence in adolescents, despite substantial challenges to sexual health service delivery. While most youth will be in the care of a pediatrician when their STI or HIV infection occurs, currently, there is no evidence-based comprehensive biobehavioral HIV prevention framework for integrating PrEP in pediatric primary care. The U.S. Preventative Services Task Force (USPSTF), CDC, and American Academy of Pediatrics (AAP) all recommend routine HIV/STI screening and counseling at primary care visits, and the USPSTF recently gave PrEP a Grade A recommendation for individuals at high risk of HIV infection.[9-13] However, there are significant discrepancies between guidelines and current practice. A survey of U.S. pediatric primary care providers (PCPs) found that <50% recommended routine STI and HIV testing to their adolescent patients.[14] The most common barriers to sexual health delivery are lack of time and provider self-efficacy.[15] Addressing all currently recommended prevention topics AND delivering PrEP to high-risk youth would require a substantial increase in the time currently allotted for pediatric visits. Since 'buying' providers additional time to provide comprehensive prevention is infeasible, this research will adapt a theory-driven health coaching intervention to increase HIV/STI prevention behavior in adolescents, paired with clinician delivery of PrEP.

Health coaching is a developmentally appropriate and effective method of targeting motivation and behavior change in adolescents. Coaches utilize motivational interviewing (MI) to facilitate behavior change, and strategies grounded in Acceptance and Commitment Therapy (ACT),[16] a mindfulness-informed cognitive behavioral therapy, to educate, create prevention social norms, and nurture self-efficacy to adopt and sustain target behaviors. Coaches are typically allied health professionals who complete manualized and certified training.[17] Coaching interventions are generally intensive programs that involve weekly-monthly 30-60 minute sessions over 1-6 months. Although time-intensive, a USPSTF systematic review found that only high-intensity risk reduction interventions (>2 hours total) significantly reduce STIs in adolescents.[18,19] While PCPs are essential for PrEP delivery, the counseling time needed to create effective behavior change is infeasible in the routine office setting. Instead, this counseling can be delivered by coaches who can meet repeatedly with patients to develop and enact tailored risk reduction plans and then partner with PCPs who can prescribe PrEP. Cost-benefit analyses demonstrate that health coaching can lead to significant savings in expenditures for >20 chronic health conditions, making it a promising option for high-value care delivery.[20]

To create an effective AND scalable intervention, we aim to develop and test an intervention that has the capacity to be implemented in pediatric primary care. Most HIV and STI prevention interventions have focused on key sub-populations of adolescents such as young men and transgender women who have sex with men (YMSM/TW) who comprise the vast majority of incident HIV infections, or young women who carry the disproportionate burden of morbidity associated with STIs but are overlooked in PrEP interventions.[21-23] However, in primary care, there is a need for interventions such as health coaching which can be broadly applied to adolescents, but tailored to the needs of specific

demographic populations. Lastly, while coaches may be essential in moving youth toward PrEP uptake, PCPs will be necessary for prescription and medical management. Unfortunately, even among Adolescent Medicine specialized pediatricians, only 35% have prescribed PrEP and the odds of prescription are double in those who feel confident in their PrEP knowledge.[24] Therefore, for this research, we will involve multi-level stakeholders in implementation research addressing the integration of coaching and, in tandem, PrEP delivery in primary care.

1.4 Compliance Statement

This study will be conducted in full accordance all applicable Children's Hospital of Philadelphia Research Policies and Procedures and all applicable Federal and state laws and regulations including 45 CFR 46. All episodes of noncompliance will be documented.

The investigators will perform the study in accordance with this protocol, will obtain consent and assent, and will report unanticipated problems involving risks to subjects or others in accordance with The Children's Hospital of Philadelphia IRB Policies and Procedures and all federal requirements. Collection, recording, and reporting of data will be accurate and will ensure the privacy, health, and welfare of research subjects during and after the study.

2 STUDY OBJECTIVES

The overarching purpose of this study is to optimize HIV and STI prevention delivery in primary care by adapting, optimizing, and testing a youth-focused, health coaching intervention to deliver comprehensive HIV/STI prevention, including PrEP, to high-risk adolescents.

2.1 Primary Objective (or Aim)

There are three primary aims to this study:

Primary Aim 1: To adapt a health coaching intervention to provide comprehensive, PrEP-inclusive, HIV and STI prevention for adolescents at elevated risk of HIV in pediatric primary care

Primary Aim 2: To identify contextual barriers and facilitators to implementation of the adapted health coaching intervention in pediatric primary care

Primary Aim 3: To conduct a randomized controlled trial (RCT) to test for the intervention's effect on HIV prevention self-efficacy, as well as feasibility and acceptability among adolescents at high risk of STI and HIV acquisition.

3 INVESTIGATIONAL PLAN

3.1 General Schema of Study Design

The project will be conducted as part of a K23 career development award with three aims. Each aim represents a sub-study of the overarching study to achieve the overall goal. Aims 1 and 2 will occur sequentially and each should take approximately a year to complete. The results of Aim 1 and 2 will go to inform the randomized control trial (RCT) in Aim 3. However, Aim 3 enrollment can occur even if there is no enrollment in Aim 2. Aim 3 will occur over a 12-18-month period.

Aim 1: Observational, qualitative, cross-sectional study (n~50). Youth with complete one of five focus groups (~5-8 youth per group) or an in-depth interview to identify barriers and facilitators to HIV/STI prevention behavior to be addressed in the intervention and determine preferences for intervention format and delivery strategy. Participants will also complete a brief CASI at the time of study enrollment after informed consent. At the end of each focus group and in-depth interview, we will remind participants of where they can access sexual health and preventative care services and we will share the clinics' contact information. It is of note that Aim 1 focus groups might not occur if any conditions prohibit the gathering of focus groups within the primary care setting.

Aim 2: Observational, mixed methods using chart stimulated recall (CSR), in-depth interviews, and quantitative measurement of acceptability, feasibility and appropriateness of the PrEP-inclusive coaching intervention in pediatric primary care. Participants will complete a single study visit with completion of CSR, semi-structured audio-recorded interviews, and a computer assisted survey instrument (CASI) delivered on a secure tablet or laptop with acceptability, feasibility, and appropriateness measures.

Aim 3: We will conduct 1) an iterative pilot phase followed by 2) a small RCT assessing intervention effect on the intermediate target of prevention self-efficacy. Pilot testing will occur over a 3-month period to prime intervention for implementation, with the aim of recruiting n=10 pilot participants. Pilot phase participants will follow the same study procedure timeline as participants randomized to the coaching intervention arm of the RCT, excluding the 6-month follow-up visit. Pilot participants will not be followed in the RCT or contribute outcome data. At the end of every health coaching visit (the baseline, 1-week, 1-month and 3-month visits), pilot phase participants will complete a brief feedback interview to ensure face validity and identify areas needing refinement. Feedback will be incorporated into the study design, with amendments submitted to the IRB as needed. The RCT will randomize youth with recent STI 1:1 to the coaching intervention vs a standard of care (SOC) control. If difficulty retaining coaching participants during the RCT generates a disparity in evaluable participants per arm, the RCT's randomization scheme will be changed to 2:1, intervention vs SOC, to balance numbers of evaluable participants per arm. Both arms (intervention and SOC) will have data collection visits at the baseline, the 3-month, and the 6-month-follow-up time points. In addition, the intervention group will have health coaching sessions at baseline, 1 week, 1 month and 3 months. At the end of the 3-month health coaching visit, a sample of RCT phase participants assigned to the intervention arm will complete a brief feedback interview to ensure face validity and identify areas needing refinement for future studies.

3.1.1 Screening Phase

Aim 1: Participants for the virtual or in-person in-depth interviews and focus groups will be identified through the CHOP STI testing database, a data platform with >20,000 HIV/STI testing encounters (2014-present) which updates in near-real time using a business intelligence application (Qlik, Radnor, PA). The password-protected dataset application is only accessible to the principal investigator (PI) and the study team. Potential subjects will be identified using the protocol inclusion and exclusion criteria. Study staff be provided a list of potential participants via the Pediatrics Research Consortium (PeRC) and will confirm participant eligibility criteria in the electronic health record (EHR), based on age and prior STI status. Participants can also be recruited in-person by the research team from the CHOP Adolescent Specialty Clinic and referred into the study by word-of-mouth from existing study participants. For all participants, consent for the study will occur via a Research Electronic Data Capture (REDCap) form and can occur in-person or via a secure online form emailed from the REDCap platform. Participants will not be told on the consent form that they are being recruited because they are diagnosed with an STI. This is because knowing this information would inform the participants of the health information of the others in the focus group. Given the sensitive nature of the data and enrollment of minor adolescents, per the guidance of the CHOP REDCap team, participant's personal email addresses will be collected via the consent form to mitigate the use of any potential auto-default parent/guardian email addresses via MyCHOP, and to ensure participants receive a copy of their signed/e-signed consent form.

Aim 2: Clinical provider participants will be identified through assistance by PeRC. We will solicit a list of names and emails of those who are in the clinical practices meeting the inclusion criteria at CHOP Karabots and Cobbs Creek clinics. All potential participants will be sent an email through the secure CHOP system asking if they are interested in participating in a research study and detailing brief study information. From an email survey link, potential participants can access the secure REDCap screening survey to determine eligibility.

Aim 3: Potential clinical trial participants will be identified and referred for recruitment by any of three strategies: 1) when nurses or clinical providers call with positive STI results, they will provide adolescent patients with information about the study; 2) the STI database will be checked daily by the study team to identify new STI diagnoses and obtain the confidential contact information for potential participants to contact them directly by phone; and 3) potential participants will be approached in-person at the time of STI testing or treatment. Screening for the study will occur via a REDCap form and can occur in person or by phone.

3.1.2 Study Treatment Phase

Aim 1: No intervention

Aim 2: No intervention

Aim 3: The study treatment phase for the RCT will consist of data collection and health coaching visits over a 6-month period (see Table 1: Schedule of Study Procedures for Aim 3

RCT). The health coaching sessions will consist of HIV and STI prevention education, motivational interviewing, and acceptance and commitment therapy.

3.1.3 Follow-up Phase

Aim 1: No intervention

Aim 2: No intervention

Aim 3: All RCT participants will have a 6-month follow-up visit. Participants in the intervention arm will be able to attend the follow-up visit if they attend at least one of the health coaching visits. For both arms, the follow up visit will consist of the same data collection (CASIs and chart abstraction) as the 3-month visit.

3.2 Allocation to Treatment Groups and Blinding

Aim 1: N/A

Aim 2: N/A

Aim 3: Non-stratified 1:1 randomization will occur at baseline using the REDCap randomization tool based on randomization tables. The study team will not be able to change study groups for participants once randomization has taken place. The randomization will not be blinded to the participants or the study team because of the nature of the intervention.

As mentioned in Section 3, if difficulty retaining coaching participants during the RCT generates a disparity in evaluable participants per arm, the RCT's randomization scheme will be changed to 2:1, intervention vs SOC, to balance numbers of evaluable participants per arm.

3.3 Study Duration, Enrollment and Number of Sites

3.3.1 Duration of Study Participation

Aim 1: Study duration for Aim 1 will be two days, as the first day participants will complete the CASI at time of consent, and the second day (scheduled based on participant availability, they will complete the virtual or in-person focus group or in-depth interview.

Aim 2: Study duration for Aim 2 will be one day for completing all the activities.

Aim 3:

Pilot phase: We will use pilot testing over a projected 3-month period to ensure that intervention critical steps are primed for implementation. Over one month, we aim to recruit n=10 participants. Pilot phase participants will follow the same study procedure timeline as participants randomized to the coaching intervention arm of the RCT, excluding the 6-month follow-up visit, and will not be followed in the RCT or contribute outcome data. At the end of every health coaching visit (the baseline, 1-week, 1-month and 3-month visits), pilot phase participants will complete a brief feedback interview to ensure face validity and identify areas needing refinement. Following this phase, we will systematically review

feedback and adapt the study design and strategy as needed prior to the RCT, with amendments submitted to the IRB as needed for modifications to study design.

Intervention phase: Study duration for Aim 3 will consist of data collection and health coaching visits over a 6-month period (see Table 1: Schedule of Study Procedures for Aim 3 RCT), with the baseline visit as the study's start. Visit windows, as described in Table 1, show that the 1 week visit window is +7/-5 days, the 1 month visit window is + 30/- 14 days, the 3-month visit window is + 30/- 14 days, and 6-month visit window is +/- 30 days.

3.3.2 Total Number of Study Sites/Total Number of Subjects Projected

The study, including all three aims, will be conducted at investigative sites in the United States. For Aim 1, participants will be recruited from two clinics affiliated with the Children's Hospital of Philadelphia (CHOP) that house Title X adolescent family planning clinics, Karabots Care Network and Cobbs Creek Care Network, from the Adolescent Specialty Clinic, and by word-of-mouth referral from existing participants. For Aim 2, participants will be recruited from two clinics affiliated with the Children's Hospital of Philadelphia (CHOP) that house Title X adolescent family planning clinics, Karabots Care Network and Cobbs Creek Care Network. For Aim 3, participants will be recruited from Children's Hospital of Philadelphia (CHOP) primary care clinics.

Analysis and study coordination will occur at the Roberts Center for Pediatric Research of the Children's Hospital of Philadelphia.

Aim 1: Recruitment goal for Aim 1 is 50 participants, recruited in groups of 5-8 for virtual or in-person focus groups or in-depth interviews. Once this number is reached, recruitment will stop.

Aim 2: Recruitment goal for Aim 2 is 25 clinicians, clinic staff, and administrators are recruited from the primary care clinics. Once this number is reached, no more providers will be recruited.

Aim 3: Recruitment goal for the pilot phase is 10 participants. Recruitment goal for the RCT is 150 participants, 75 for each arm (with the chance of more participants in the RCT's intervention arm than control arm if there are changes to the randomization scheme).

3.4 Study Population

3.4.1 Inclusion Criteria

Aim 1

1) Males or females age 13 to 19 years.

2) History of ≥1 STI

3) Able to speak and understand written English

4) Able to access internet, a mobile device or computer, and video conferencing using a HIPAA compliant CHOP approved vendor. During the COVID-19 Pandemic, study procedures must be conducted remotely to protect participant safety; this is only applicable to Aim 1 and will not apply to the remainder of the study.

Aim 2

1) Clinical providers (physicians, certified nurse practitioners, physician assistants, and registered nurses) who provide clinic care to ≥1 adolescent patient diagnosed with an STI in the past year.

2) Able to speak and understand written English

Aim 3

1) Males or females aged 13 to 19 years.

2) Seeking STI-related testing, treatment, prevention counseling, or follow-up care

3) History of ≥1 STI in the 30 days prior to recruitment

4) Confirmed treatment for a laboratory-confirmed diagnosis of Trichomonas vaginalis (via microscopy or nucleic acid amplification test [NAAT]), Neisseria gonorrhea (NAAT), Chlamydia trachomatis (NAAT), or Treponema pallidum (via new positive rapid plasmin reagin [RPR] assay) within the prior 30 days

5) Self-reported HIV negative status and/or HIV negative status as per medical record review

6) Able to speak and understand written English

7) If participating in remote visits, must be able to access internet, a mobile device or computer, and video conferencing using a HIPAA compliant CHOP approved vendor. If attending in-person visits, must be able to access a phone for scheduling in-person visits.

3.4.2 Exclusion Criteria

All aims

1) Unable to provide informed consent due to intoxication or severe psychological distress.

Subjects that do not meet all of the enrollment criteria may not be enrolled. Any violations of these criteria must be reported in accordance with IRB Policies and Procedures.

4 STUDY PROCEDURES

4.1 Screening/Baseline Visit

Aim 1

- Informed Consent
- Survey questionnaire
- Virtual or in-person focus group or in-depth interview: Given the sensitive nature of the topic, we recognize that some youth may not be comfortable in the group setting. At the time of informed consent, participants will have the ability to opt-out of the focus group and instead conduct an individual, audio or video recorded, in-depth interview. In addition, if participants who have opted for focus group participation are unable to attend the group at the scheduled time or no-show for the focus group, they will be offered the option of conducting an in-person, or if necessary, a telephone or video conferencing interview using a HIPAA compliant CHOP approved vendor.
- At the end of each focus group and in-depth interview, we will remind participants of where they can access sexual health and preventative care services and we will share the clinics' contact information.

Aim 2

- Informed consent
- Chart simulated recall
- In-depth interview
- CASIs measuring demographics acceptability, feasibility, and appropriateness of PrEP in pediatric care

Aim 3

- Informed Consent
- Randomization
- Computer assisted survey instruments (See Section 5.1.3.1)
- Health coaching
- Electronic medical record review

4.2 Study Intervention Phase

Aim 1: No intervention

Aim 2: No intervention

Aim 3: The discussion of the intervention phase is strictly for Aim 3 of the study project.

For the Aim 3 RCT phase, the participants randomized to the standard of care group will not undergo the health coaching intervention. The participants randomized to the health coaching group will attend health coaching sessions at the baseline, 1-week, 1-month and 3-month visits.

4.2.1 Follow up Visit 1

Aim 1: N/A
Aim 2: N/A
Aim 3: Both the health coaching group and the standard of care group will complete follow-up surveys at the 6-month follow-up visit.

4.3 Unscheduled Visits

Aim 1: There will be no unscheduled visits for the virtual or in-person focus groups or in-depth interviews.

Aim 2: There will be no unscheduled visits for the provider interviews.

Aim 3: Research staff will attempt to be flexible with unscheduled visits and conduct a study visit if the participant is within the time frame for their next visit. If the participant is not within the time frame for their next visit, the study staff will reschedule the participant for another time.

4.4 Subject Completion/Withdrawal

Aims 1, 2, 3: Participant completion of the study will be closely monitored in both treatment arms. Our criteria for defining study completion, withdrawal, drop out, and attrition is defined below.

Multiple attempts will be made to retain participants in the study. Participants in either treatment group who do not attend a visit after 3 unsuccessful contact attempts will be considered a no-show for that visit.

Subjects may withdraw from the study at any time without prejudice to their care. They may also be discontinued from the study at the discretion of the Investigator for lack of adherence to visit schedules. The Investigator may also withdraw subjects who violate the study plan, or to protect the subject for reasons of safety or for administrative reasons. It will be documented whether or not each subject completes the study. If the Investigator becomes aware of any serious, related adverse events after the subject completes or withdraws from the study, they will be recorded on the CRF.

Participants will be asked to provide at least three forms of secure contact information (e.g., cell phone, email, social media). In addition, participants will be asked about preferred method of contact, and will be asked for consent to text message. At the end of each study visit, participants will be scheduled for their next visit. We will use flexible visit windows for each coaching visit. Before the window opens, participants will be contacted via their preferred method to confirm their next appointment. If a participant does not respond after 2--3 attempts using one strategy (i.e., texting, emailing, calling) then a new outreach strategy will be used to diversify the approach. If a participant does not respond after five unanswered attempts, we will stop trying. Study staff will provide reminder contact (text, call or email) prior to each visit based on the participants preferred method. To facilitate follow up, the coaching sessions will not be restricted to the clinic, and instead coaches will

be able to meet youth in the community or over a CHOP-approved HIPAA compliant platform.

4.4.1 Early Termination Study Visit

Aims 1, 2, 3: If a visit is interrupted due to external factors, attempts will be made to resume at the earliest possible time, and resultant data will be handled in the same fashion as survey collection and interviews completed in one sitting. Participants who withdraw from the survey or interview prior to completion will be offered the option of having their earlier responses redacted from the record. If they choose to do so, any data collected for that participant will be excluded from all analyses. If participants elect to end an interview early but allow use of data already collected or if interviews are truncated due to external factors and unable to be completed, responses will be collected and handled according to standard study procedures. Analysis of data from partial interviews will be included in the study for the questions or portions of the survey and/or interview which were completed.

5 STUDY EVALUATIONS AND MEASUREMENTS

5.1 Screening and Monitoring Evaluations and Measurements

5.1.1 Aim 1

5.1.1.1 Focus groups or In-depth interviews

Five audio recorded in-person, or video recorded virtual focus groups will be conducted ~50 participants, 5-8 per group.

Focus groups and in-depth interviews will identify HIV/STI prevention barriers and facilitators and preferences for an intervention format across different demographic populations of adolescents. We will conduct separate focus groups for the following populations: cisgender females, heterosexual males and YMSM/TW, and a mixed sex/sexual orientation group of adolescents with identified depression on their annual primary care screening. Participants will have the option to complete an in-depth interview if they wish to not participate in the focus group, as described in section 4.1. Identifying key content themes and delivery preferences among different demographic groups and youth with mental health conditions will allow for enhanced tailoring of content for different adolescent user groups. For example, if youth with depression are more likely to identify medication self-efficacy as a barrier to PrEP uptake, intervention content can be tailored for this population to emphasize PrEP adherence strategies.

Focus groups will occur in-person, or if necessary, via virtual video conferencing using a HIPAA compliant CHOP approved vendor. Focus groups will start with an informational session on HIV/STI prevention strategies (PrEP, condoms, HIV/STI testing, and partner notification). We will then facilitate the focus group to identify the most salient barriers/ facilitators for each prevention strategy within each focus group. In the second half of the focus groups, we will focus on adolescent preferences for the delivery of sexual health care, and delivery of the proposed intervention. Youth will then share their preferences. Focus groups will last 1-2 hours. The individual in-depth interviews will occur in-person, via

phone, or video conferencing using a HIPAA compliant CHOP approved vendor. These interviews will focus on youth preferences for sexual health care in primary care, using the participant's own prior sexual health encounters in primary care as the framework for the interview. Given the sensitive nature of the topic, youth have the option to opt out of any of the interview questions (see appendix). In-depth interviews will last 30-45 minutes.

5.1.1.2 Survey Questionnaire

Prior to focus group participation, participants will complete a brief survey in-person, or via an emailed REDCap link, which will take approximately 15 minutes and will be used to assess demographics and sexual health measures. This will include questions of hearing of, accessing, and plans to start PrEP. We will measure knowledge of prevention strategies like PrEP and targets, including demographics and sexual behavior via CASI in REDCap. For participants who consented in-person, they will have the option to complete the survey in-person at the time of informed consent. For those participants recruited via phone or email, they will complete the survey via a REDCap link emailed to them before the virtual or in-person focus group or interview.

5.1.1.3 Electronic Medical Record Review

As part of the study, the study team will review the CHOP medical record of the participants for particular variables:

- STI diagnoses (gonorrhea, chlamydia, syphilis, trichomonas)
- Mental health diagnoses: derived from the problem list in the general EPIC chart. No data will be accessed from protected mental health encounters.

This information will be taken through the CHOP EPIC system as well as our team's QlikView database. The QlikView data visualization platform contains STI diagnosis data that is derived from EPIC and relayed from the CHOP data warehouse. These data will be used to confirm STI and mental health diagnosis from screening.

5.1.2 Aim 2

5.1.2.1 Chart simulated recall

Prior to the CSR, providers will receive a brief educational session about health coaching and PrEP. The CSR will then provide data on clinician decision making around PrEP and comprehensive HIV prevention delivery. Chart-simulated recall is a well-validated method in which providers review charts of their own patient encounters to understand clinical decision making and rationale for clinical behavior. Study staff will randomly select 3-4 charts of visits where an STI diagnosis was made. Clinicians will be asked to give a 1-2 sentence summary of the encounter including the patient's age, sex, chief complaint, and mental health comorbidities. With the EHR available for reference, we will ask participants what factors facilitated or hindered delivery of HIV and STI prevention care, including PrEP counseling or initiation, HIV testing, discussion of partner notification. We will ask if and how mental health co-morbidities affected with delivery of prevention care. These data will be used to understand how and when clinicians may best refer to the coaching intervention.

5.1.2.2 In-depth interview

Additional interview questions will be grounded in the Consolidated Framework for Implementation Research (CFIR) which includes five core constructs associated with effective implementation: 1) characteristics of the intervention: acceptability of PrEP and coaching, and advantages to current care; 2) outer setting: perception of patient needs and impact of mental health comorbidities; 3) inner setting: characteristics of the primary care system and implementation climate for PrEP and coaching; 4) characteristics of individual provider: knowledge, beliefs, and self-efficacy for HIV/STI prevention care, including PrEP prescription; and 5) implementation process: attitudes toward integrating comprehensive HIV and STI prevention in primary care.

5.1.2.3 Computer Assisted Survey Instruments

Acceptability of the proposed coaching intervention in primary care will be measured via the Acceptability of the Intervention Measure (AIM). Feasibility, the extent to which the intervention could be successfully implemented within the setting, will be measured by the Feasibility of Intervention Measure (FIM). Appropriateness, the perceived fit of the intervention and relevance for the practice setting, will be measured with the Intervention Appropriateness Measure (IAM).

5.1.3 Aim 3

5.1.3.1 Computer Assisted Survey Instruments **(baseline, 3-month and 6-month visit)**

The CASI will take approximately 40 minutes. These data will be entered directly into the secure REDCap platform by participants, with the option of having the survey read aloud and entered by study staff if the participant prefers. We will measure theorized intervention predictors and targets including demographics, sexual behavior, health activation, stigma, and self-efficacy. Surveys are:

Background/Demographics

Current Prevention Practices

Intentions Questions

Self-Efficacy

Knowledge and Attitudes Survey

Confidence in Safer Sex Scale

CRAFFT

General Self Efficacy Scale (GSES)

HIV Knowledge and Attitude

Modified ACES Inventory

Modified Partner Communication

Parent Adolescent Communication

Sexual Self Efficacy Scale

Youth Pediatric Symptom Checklist

Interpersonal Reactivity Index (IRI)

Inventory of Parent and Peer Attachment (IPPA)

Coaching Satisfaction Survey

5.1.3.2 Health Coaching Session

Coaches will review the interview output with participants to collaboratively create a coaching plan prioritizing educational and skills-building topics for coaching sessions. At each coaching session, coaches will reassess barriers and facilitators of HIV/STI prevention and deliver indicated risk-reduction counseling. Coaching sessions will focus on generating skills to move participants toward prevention goal attainment by using MI to elicit participant perspectives on prevention needs (such as PrEP initiation) and challenges, and then using ACT to reframe barriers as recognizable dilemmas for which there are effective solutions. Each coaching session will include a brief psycho-educational module about an HIV/STI prevention topic according to the individualized educational plan. The Aim 2 data will determine the optimal method for coaches to communicate prevention goals to the PCP after each session, to ensure appropriate linkage to clinical care.

5.1.3.3 Electronic Medical Record Review

As part of the study, the study team will review the CHOP medical record of the participants for particular variables:

- STI test dates
- STI diagnoses
- STI medications including PrEP
- Mental health diagnoses: derived from the problem list in the general EPIC chart. No data will be accessed from protected mental health encounters.

5.2 Efficacy Evaluations

These are the measures that will be used to assess the efficacy of the study intervention

Aim 1: N/A

Aim 2: N/A

Aim 3: The primary efficacy outcome is the difference in change in self-efficacy between baseline and six-month visits for the intervention group versus control, as measured by the modified Generalized Self-Efficacy Scale.

5.2.1 Diagnostic Tests, Scales, Measures, etc.

See the list of CASIs in section 5.1.3.1 above.

5.3 Safety Evaluation

Subject safety will be monitored by adverse events surveillance, reporting and attention to continuous quality improvement to reduce the occurrence of adverse events.

Although the study is minimal risk, it still requires a high level of scrutiny and vigilance with respect to participant safety and data management, particularly given the sensitive nature of the data and enrollment of minor adolescents. At least once every three months, we will review data storage and integrity. We will jointly review and report any unanticipated or adverse events (i.e., breach of privacy) to the CHOP IRB and National Institute of Mental Health (NIMH) in accordance with the NIMH reportable events policy.

For Aim 1, the focus groups and individual interviews contain questions that may make some participants uncomfortable or contain sensitive information. At the beginning of the focus group, we will outline the rules of the group (see appendix), including a statement that participants can opt out of answering any question, that confidentiality will be upheld, and that all opinions will be respected, and that we will use pseudonyms (e.g. favorite superhero, cartoon character, or color) to refer to each other in the group. For the Aim 1 individual interviews, participants will be allowed to opt out of any questions, and the script has been designed to still glean important information about sexual health in primary care, even if a participant does not want to share their own testing experience. In addition, the study team will take additional precautions for those participants completing focus groups or in-depth interviews on a phone or via video conferencing using a HIPAA compliant CHOP approved vendor. We will have two research team members moderating each focus group. The virtual conference rooms will be password protected, and a study team member must admit each participant into the group. Before admitting them to the larger group, a study team member will individually and confidentially confirm the physical location of each participant and their best contact information. Participants will also choose a pseudonym (e.g. favorite superhero, cartoon character, or color) prior to entering the virtual focus group and the moderator will change their screen name to that pseudonym prior to entry.

For Aim 3, all participants will be patients of CHOP primary care clinics, and thus can be rapidly referred to clinicians and social workers in case there is a need to intervene for an identified mental health issue. Our mood rating instrument, the PSC-17, does not include any assessment of suicidal ideation. However, if a participant discloses suicidal ideation, homicidal ideation, or abuse during an intervention session, the PI will be notified immediately, as well as the clinic social worker. Based on clinician assessment, participants who report suicidal ideation will be referred to the local Emergency Department or psychiatric crisis center, as needed. Any reports of child abuse will be reported to the clinic social worker and reported to ChildLine in accordance with Pennsylvania State Law. All participants will be provided mental health resources at the end of the first session, irrespective of their score on the PSC-17.

Participants will complete a modified version of the Adverse Childhood Experiences survey. To minimize the risk to participants that may arise regarding fear of disclosing a specific form of adversity, the study will utilize a modified version of the ACES questionnaire that has been validated in middle and high school students. The modified inventory is presented in 7 items. Within each item, participants are presented with a diagram including 2-4 circles. Each circle contains the description of an ACE, with language adapted from the cited inventories. The wording has been modified to be appropriate for the reading and comprehension abilities of 14 to 18-year-olds. Participants are instructed to read the ACE description contained in each circle, to think back on their entire life, and to decide if the

ACE described within the circle applies to them. Youth respond to each item on the inventory by indicating how many circles (0- 4) in that item apply to them. The modified ACE inventory allows the investigators to calculate a conventional ACE score (in keeping with the extant literature). Because this is a validated scale, we must include all questions to come up with a composite score. However, participants do not have to answer any question they feel uncomfortable with. There is a great deal of literature about the connection between ACES and STI diagnoses.[25-29] The data from the ACES questionnaire will be used to determine whether the final health coaching intervention needs to be modified to contain trauma-focused elements. Lastly, substance abuse will be measured by the CRAFFT which contains opening questions frequency of substance use, followed by questions regarding specific negative consequences of substance abuse. A score >4 on the CRAFFT is suggests substance dependence. Participants with CRAFFT scores >4 will be given a list of resources for substance treatment and referred back to their PCP.

ACES questionnaire

There are some questions included in the ACES questionnaire that probe about sensitive information related to prior childhood trauma. While participants are informed that they may refuse to answer any questions at any time, responses or reactions to certain questions may indicate potential distress on the part of the participants. If at any time during the assessment or completion of the questionnaires, a participant divulges to any study staff that he or she is at risk for harm, including but not limited to being abused or experiencing violence, if harm is suspected or likely, or if the participant indicates he or she is suicidal/homicidal, a member of the subject's primary care team or a study physician will be notified. This primary care team member or study physician will come speak directly in-person or over the phone with the subject at that time. They will determine clinical risk and follow up, which may include referral to one of the onsite primary care social workers or a local crisis center.

6 STATISTICAL CONSIDERATIONS

6.1 Primary Endpoint

Aim1: Identification of barriers and facilitators to HIV/STI prevention behavior to be addressed in the intervention and determine preferences for intervention format and delivery strategy.

Aim 2:

- Acceptability of PrEP in primary care will be measured with the Acceptability of the Intervention Measure (AIM).
- Feasibility, the extent to which the intervention could be successfully implemented within the setting, will be measured by the Feasibility of Intervention Measure (FIM).
- Appropriateness, the perceived fit of the intervention and relevance for the practice setting, will be measured with the Intervention Appropriateness Measure (IAM)

Aim 3: Prevention self-efficacy, an intermediate behavioral target in our theoretical model. This construct will be measured at baseline, intermediate, and final follow up visit using a

modified Generalized Self-Efficacy Scale (GSES) assessing HIV and STI prevention self-efficacy.

6.2 Secondary Endpoints

Aim 1: None

Aim 2: None

Aim 3:

- Referral feasibility: # potential participants referred/# eligible.
- Recruitment feasibility: # enrolled/# patients referred.
- Retention feasibility: # completing all sessions/# enrolled.
- Acceptability: Assessed at the final visit by a Coaching Satisfaction Survey
- Secondary outcomes:
    - a) Repeat STI test results at three-months and six-months.
    - b) Prevention behavior, including uptake of PrEP, condom use, HIV testing, and partner notification of positive STI results

6.3 Statistical Methods

6.3.1 Baseline Data

Aim 1: Study information will be gathered through focus group and in-depth interview data. Themes from the focus groups and in-depth interviews will be reported and will be used to inform aims 2 and 3. Data from the baseline CASI summarized by standard descriptive summaries (e.g. means and standard deviations for continuous variables such as age and percentages for categorical variables such as gender). These data will be used to help identify whether different themes emerge from different populations of youth by sex, gender, and sexual orientation.

Aim 2: Baseline and demographic characteristics will be summarized by standard descriptive summaries (e.g. means and standard deviations for continuous variables such as age and percentages for categorical variables such as gender). Themes from the individual interviews and results from the chart simulated recall will be reported and be used to inform aim 3.

Aim 3: Baseline and demographic characteristics will be summarized by standard descriptive summaries (e.g. means and standard deviations for continuous variables such as age and percentages for categorical variables such as gender). We will also report baseline data from the multiple scale instruments, such as sexual behavior, substance use, risk perception and stigma scales, etc. (See section 5.1.3.1 for list of instruments.)

6.3.2 Analysis

Aim 1: We will conduct a deductive qualitative analysis of focus group transcripts and in-depth interview transcripts with our theoretical model guiding the coding process. Codes related to model constructs will be assigned to interview segments to organize the data, using the software NVivo, with two study team members separately reviewing the first 10 transcripts line by line, assigning codes as concepts become apparent. We will compare text segments to those that have been previously assigned the same code, and to segments coded separately by each analyst, to decide whether they reflect the same concept. We will use this process to generate a coding scheme, then apply it to all transcripts. Once coding is complete, we will review the data to document emerging themes-general insights gleaned from the entirety of the data- which may inform intervention content.

Aim 2: Survey data will be summarized via descriptive statistics. We will set a >80% threshold for high acceptability, feasibility and appropriateness. The interview coding process will parallel that described in Aim 1. We will use an integrated deductive and inductive coding approach. Transcripts will be reviewed using deductive methodology, where CFIR determinants will be used as the coding framework. After completion, the transcripts will be re-reviewed using inductive methodology where codes identifying novel barriers and facilitators of implementation that do not map onto the CFIR will be identified and used to develop a coding framework that is then applied to all transcripts. We will integrate the qualitative and quantitative data by merging findings through a comparative coding analysis. The AIM and FIM scores will be dichotomized (completely disagree/disagree vs completely agree/agree). We will compare the distribution of content themes between providers with high vs low acceptability and, separately, high vs low feasibility ratings. Data will then be used as a starting point in which to build an optimized PrEP-inclusive coaching implementation strategy to be tested in the subsequent RCT.

Aim 3: The primary analysis will be based on an intention to treat approach and will include all subjects randomized at Visit 1.

The primary outcome for the RCT is the change in prevention self-efficacy between intervention and control conditions between the baseline and six-month (final) visits. We will compare the exposure variable of treatment group with the outcome variable of continuous score on the modified Generalized Self-Efficacy Scale at baseline, intermediate (e.g. three month), and six-month visits using mixed effects logistic regression models with a random intercept for patient and a random slope for time. In exploratory analyses, to determine if the mental health predictors impact the self--efficacy outcome, we will create separate mixed effects regression models to compare self-efficacy score for those with and without mood ratings consistent with depression on the PSC-17, high trauma (Adverse Childhood Experiences Scale score >4 vs not), and substance abuse (CRAFFT score >4) adjusting for treatment group and demographic characteristics including sex. In order to assess the impact of STI timing on the primary outcome of prevention self--efficacy, we will use linear regression models and days between STI diagnosis and the first coaching visit in the intervention group, adjusting for demographic covariates including sex and sexual orientation. Finally, we will assess if coaching may have a significant effect on other domains in the self--efficacy pathway of our model, by repeating the primary analysis above with scores for the Patient Activation Measure [PAM], and Confidence in Safer Sex Scale.

There will be no adjustment of p value for multiple comparisons given the exploratory nature of these analyses.

Secondary outcome analyses:

- Referral feasibility: Calculated as the number of potential participants referred to study staff over the number of patients with bacterial STI at the clinics during the study period. This denominator will be identified using the CHOP STI dataset.

- Recruitment feasibility: Calculated as the number of patients enrolled over the number of patients referred.

- Retention feasibility: Calculated as the proportion of participants who completed each follow--up coaching session over the total number of scheduled coaching visits. To determine if the mental health is associated with retention, I will use logistic regression to compare proportions of subjects retained between the following participant groups: high depressive symptoms, high trauma score, and substance abuse (see definitions in exploratory analysis section above), adjusting for demographic characteristics such as race and sex.

Fidelity will be assessed by reviewing baseline visit transcripts for the first ten participants and reviewing a random sample of 2 visits per week for ongoing supervision

- We will use the Motivational Interviewing Assessment-Supervisory Tools for Enhancing Proficiency (MIA-STEP) cut offs for fidelity: interventionist will have to demonstrate in the first ten sessions the use of at least half of the MI consistent items three to four times, namely, receive a “Somewhat” (4) frequency and extensiveness rating and at least an “Adequate” (4) skill level rating. In other words, the interventionist has to show capacity to use a moderate amount of MI strategies and skills and show an adequate level of performance when implementing them.

- On random sample, if three successive sessions occur in which they fall below proficiency standards, the interventionist will receive additional training, feedback, and coaching until he or she demonstrated again the minimal MI proficiency standards. Supervisors may elect to use the protocol’s MI proficiency standards as a supervisory benchmark for their clinicians. The MIA-Step MI rating worksheet tool (see below) will be used to assist in this task (https://motivationalinterviewing.org/sites/default/files/mia-step.pdf)

- In addition, the interventionist will complete the content checklist after each visit to assure each psychoeducation content domain (e.g. condoms, partner notification) was addressed in the session.

- Acceptability: I will calculate the proportion of participants who endorse each item on the Coaching Satisfaction Survey in the "agree" or "strongly agree" range.

Exploratory outcome analyses: Utilization of prevention behavior at the six-month time point. I will calculate the proportion of participants who:

- Initiate PrEP
- Do not develop repeat sexually transmitted infection (STI)
- Report 100% condom use
- Receive HIV testing
- Report partner notification of their initial STI

6.3.3 Safety Analysis

At least once every three months, we will review data storage and integrity. We will jointly review and report any unanticipated or adverse events (i.e. breach of privacy) to the CHOP IRB and NIMH in accordance with the NIMH reportable events policy. The frequencies of AEs will be summarized, although because this study is minimal risk, few are expected.

6.4 Sample Size and Power

Aim 1: The individual focus group size of 5-8 is informed by consensus methods literature. The goal of the pooled focus group size of ~50 is thematic saturation. The goal of the in-depth interviews is thematic saturation, which could be reach at ~15 participants. If we do not reach saturation at this sample size, or if key themes emerge among subgroups of participants which we wish to further explore, we will continue focus groups and in-depth interviews until saturation is met.

Aim 2: Previous studies demonstrate that 3-6 charts per clinician are sufficient for reliable and valid assessment in CSRs. We propose to interview 25 clinicians and nurses with the goal of achieving saturation of themes, for which this sample size should be sufficient, and will continue if saturation is not met.

Aim 3: We propose a sample size of 150 participants (75 intervention, 75 control – with the possibility of a greater number of intervention than control if we shift to 2:1 randomization) based on the aim of detecting a moderate effect size score difference in the change in modified GSES scores between intervention and control. Given this sample size, and assuming a range of intra--subject correlations across subjects ranging from (0.01 to 0.3), we will have 80% power and a two--sided alpha of 0.05 to detect a 0.7-0.9 standard deviation difference change in GSES scores from baseline and six months by treatment group. And be protected from and up to 10% lost-to-follow-up rate.

7 STUDY MEDICATION (AIM 3 STUDY INTERVENTION)

7.1 Description

Interventionist training: The health coach will be a masters level interventionist with expertise in HIV/STI prevention. The interventionist will complete a 2-day MI training. The Coach training will be reinforced in monthly meetings with the PI throughout the RCT to review session recordings for fidelity and boost MI skills.

Iterative pilot phase: Pilot testing will occur over a 3-month period to ensure that intervention critical steps are primed for implementation, with the aim of recruiting n=10 pilot participants. Pilot phase participants will follow the same study procedure timeline as participants randomized to the coaching intervention arm of the RCT, excluding the 6-month follow-up visit. Pilot participants will not be followed in the RCT or contribute outcome data. At the end of every health coaching visit (the baseline, 1-week, 1-month and 3-month visits), pilot phase participants will complete a brief feedback interview to ensure face validity and identify areas needing refinement. Feedback will be incorporated into the study design, with amendments submitted to the IRB as needed.

Intervention:

The intervention focuses on improving three specific domains related to STI and HIV risk: 1) knowledge, 2) activation (the motivation to manage one's own health) and 3) self-efficacy (the belief that a person can successfully carry out behavior change. With respect to health behaviors, the intervention aims to improve uptake of specific prevention practices based on the participants' preferences.

The format of the intervention is designed to have an intensive first session encompassing 1) psychoeducation about STI and HIV prevention; 2) motivational interviewing (MI-based) counseling to identify top prevention problems and goals, enhance commitment to behavior change, and develop an individualized prevention plan; and 3) Referral to the evidence-based components of their prevention plan: for example, connecting to a PrEP navigator to facilitate PrEP start, getting an HIV test, (which may include health management steps like learning how to message their provider to ask for test orders), or learning evidence-based skills to improve interpersonal communication that can be applied to condom negotiation or partner notification. Much of the format for the intervention draws on the MI literature, and many of the skills are adapted from Interpersonal Psychotherapy-Adolescent Skills Training (IPT-AST), an evidence-based depression prevention program. The interventionist has been trained in MI through a two-day intensive online training through the Motivational Interviewing Network of Trainers.

After the first session, the interventionist will follow up with the participant in one week to review the goals and prevention plan, and then in one month to check on progress and use MI to troubleshoot roadblocks. Participants in both the intervention and in the standard of care arm will follow up again in 3 months at clinic for repeat STI testing, as indicated by CDC. Participants in the intervention arm will have a final wrap up MI session at that time, however they will be able to reach out to the interventionist for an additional 3 months until the end of the study with questions or to access support around their prevention goals. At the

end of the 3-month health coaching visit, a sample of RCT phase participants assigned to the intervention arm will complete a brief feedback interview to ensure face validity and identify areas needing refinement for future studies.

The SOC group will receive treatment as usual. After their baseline visit, they will be referred to their PCP for management of any clinical issues that arise. Their clinic visit schedule will follow their clinical needs and recommendations of their provider. They will complete the 3-month and 6-month research visits. After completing the study, SOC participants will be offered one coaching session.

8 SAFETY MANAGEMENT

8.1 Clinical Adverse Events

Clinical adverse events (AEs) will be monitored throughout the study.

8.2 Adverse Event Reporting

Since the study procedures are not greater than minimal risk, SAEs are not expected. If any unanticipated problems related to the research involving risks to subjects or others happen during the course of this study (including SAEs) they will be reported to the IRB in accordance with CHOP IRB SOP 408: Unanticipated Problems Involving Risks to Subjects. AEs that are not serious but that are notable and could involve risks to subjects will be summarized in narrative or other format and submitted to the IRB at the time of continuing review.

If a participant volunteers information that she or another minor is experiencing abuse or that she has thoughts of harming herself or others, we will notify CHOP social work and the appropriate authorities as needed. In addition, if the participant discloses potentially harmful side effects of the birth control method, we may make a clinical referral to the CHOP emergency department, ASC, and/or their primary care provider, depending on the severity of the side effect. We will track any referrals and/or mandatory reports that are made in REDCap.

9 STUDY ADMINISTRATION

9.1 Treatment Assignment Methods

9.1.1 Randomization

Aim 3: Simple 1:1 randomization will occur at baseline using the REDCap randomization tool. The randomization tables will be created by a statistician that is not a part of the study team. The study team will not take part in randomization. Participants will complete the baseline CASI before being randomized. The study team will not be able to change randomization after it is applied in REDCap.

As mentioned in Section 3, if difficulty retaining coaching participants during the RCT generates a disparity in evaluable participants per arm, the RCT's randomization scheme will be changed to 2:1, intervention vs SOC, to balance numbers of evaluable participants per arm.

9.1.2 Blinding

There will be no patient or study team blinding. Due to the nature of the intervention, there could not be blinding to which study arm the participants are in.

9.1.3 Unblinding

N/A

9.2 Data Collection and Management

All study data will be kept in compliance with CHOP procedures. Electronic data will be stored on CHOP supported REDCap platforms, databases created will be password-protected and stored on a CHOP SAN research drive and coded or de-identified at the earliest convenience of the study. Interview audio and focus group audio or video files and paper copies of surveys will be kept in a locked file cabinet in a locked office until recordings can be transcribed into electronic files and stored in the CHOP SAN network drive. Paper survey forms will be entered into REDCap as soon as possible. Paper survey forms will only be used if there are problems connecting to the internet for survey completion on a tablet or laptop computer since REDCap is web-based.

1. Confidentiality. Participants will be given unique study IDs to ensure that data cannot be linked to PHI. The study data will be recorded in REDCap whenever possible. Paper copy forms will be recorded in REDCap at the earliest possible convenience by study staff. All efforts will be made to enter paper form information into REDCap immediately following the participant visit completion, but if the paper copy cannot be entered into REDCap immediately due to internet connection errors, the paper copies will be stored in a locked file cabinet in the PI's locked office until a study team member can record the information in REDCap at the earliest possible moment. Paper surveys will be eliminated per CHOP's policy once information is entered and confirmed in REDCap. Data downloaded from REDCap will be password-protected, stored on a CHOP SAN network drive, and stored in a folder that only study staff have access to. Participants will use pseudonyms (favorite superhero, cartoon

character, or color) to refer to each other during the focus groups. The interview files will also be kept in a locked file cabinet in the PI's office. The audio or video recordings of focus groups and interviews will be transcribed, and electronic files will be kept on a CHOP SAN network drive in a folder that only study staff has access to. Once the files are transcribed, the original recording files will be destroyed. The audio or video recordings will be sent to a CHOP-approved audio or video transcription agency specializing in health-related research. They will be anonymized and not include the participant's name. In addition, the study team will take additional precautions for those participants completing focus groups or in-depth interviews on a phone or via video conferencing using a HIPAA compliant CHOP approved vendor. We will have two research team members moderating each focus group. The virtual conference rooms will be password protected, and a study team member must admit each participant into the group. Before admitting them to the larger group, a study team member will individually and confidentially confirm the physical location of each participant and their best contact information. Participants will also choose a pseudonym (e.g., favorite superhero, cartoon character, or color) prior to entering the virtual focus group and the moderator will change their screen name to that pseudonym prior to entry. Urine assays will be collected into specimen cups labeled with study ID number, date of collection, type of specimen (urine) and storage conditions prior to shipment. Urine assay results will be sent to CHOP at the Center for Clinical Pharmacology Laboratory. Once received, results will be entered into REDCap. After REDCap entry, the original excel file will be deleted.

2. Security. Upon completion of the data collection and data cleaning, a finalized copy of the data will be used for data analysis and stored on a private CHOP-supported research SAN drive. The file will also be password protected and PHI will be replaced with non-identifiers. If the finalized copy of the data becomes corrupted, data will be downloaded from REDCap and procedures used to clean the data will be carried out again

3. Anonymization, de-identification or destruction. PHI will be coded at the earliest possible moment in data cleaning processes. PHI will be replaced with non-identifiers (e.g., Date of birth will be replaced with age at study visit). As all data with be recorded on REDCap, a separate master list will not be created. Contact information will be stored in a separate database on the secure SAN network drive and will not be linked to study identification numbers. However, if they chose not to have their information used in future studies, once data is cleaned, all information is verified, and investigators successfully publish findings from the study, their PHI will be removed rendering all data deidentified. Electronic data will be retained and later destroyed in accordance with CHOP retention and destruction procedures.

9.3 Confidentiality

Data records collected during this study will be kept confidential in accordance with Institutional policies and HIPAA on subject privacy and that the Investigator and other site personnel will not use such data and records for any purpose other than conducting the study. PHI will be coded, de-identified, or removed at the earliest convenience of the study. No PHI will be shared outside of the primary research team. Due to the sensitive nature of

study data, a certificate of confidentiality will be obtained from the NIH prior to initiation of any study procedures.

No identifiable data will be used for future study without first obtaining IRB approval. The investigator will obtain a data use agreement between the provider (the PI) of the data and any recipient researchers (including others at CHOP) before sharing a limited dataset (PHI limited to dates and zip codes).

9.4 Regulatory and Ethical Considerations

9.4.1 Data and Safety Monitoring Plan

This research project has no more than minimal risk to the participants. Throughout the study, risks (loss of confidentiality, psychologic distress etc.) to the participants will be monitored by the co-investigators with oversight and monitoring responsibility falling primarily on the PI of the research team. All study information will be stored be stored on CHOP SAN drives, CHOP managed REDCap web application, password protected, and for paper copies and interview tapes in a locked cabinet in a locked office until information can be entered into electronic form.

Safety of research participants will be ensured through a Data and Safety Monitoring Plan consistent with NIMH guidelines. The PI will be responsible for ensuring that research adheres to this plan. We will train all research staff consenting participants to ensure all elements of informed consent are being performed. We will conduct routine monitoring of data throughout the study to ensure data is collected and recorded in adherence to the research plan, and that confidentiality of participants is maintained. Although the study is minimal risk, it still requires a high level of scrutiny and vigilance with respect to participant safety and data management, particularly given the sensitive nature of the data and enrollment of minor adolescents. At least once every three months, we will review data storage and integrity at the CHOP Roberts Center for Pediatric Research where the study team and the study data will reside. In addition, we will jointly review and report any unanticipated or adverse events (i.e. breach of privacy) to the CHOP IRB and NIMH in accordance with the NIMH reportable events policy.

We will establish protocols to address potential disclosure of sensitive information to study team members (i.e. depression, substance abuse or intimate partner violence). In addition, protocols will be established to address any psychological distress on the part of participants during the course of data collection, involving existing clinical providers and social workers to evaluate and provide appropriate resources to the participant as appropriate. During the course of the study, research data will be stored in password protected files on secure servers in accordance with CHOP policy. We will be responsible for ensuring that all study team members understand the requirements for data storage and protection. All completed study documents will be stored in locked cabinets, and all computer-entered data will be stored and analyzed on password-protected computers at CHOP. Access to documents and data will be limited to myself and members of my research team. We will be responsible for ensuring that all those with access to the information understand the requirements for use of the data on password protected computers and servers. Any transfer of data between members of the research team will be done through CHOP's encrypted file sharing system.

In addition, during the randomized controlled trial in Aim 3, we will conduct routine monitoring of data throughout the study to ensure data is collected and recorded in adherence to the research plan, and that confidentiality of participants is maintained. As this is an experimental study, it requires a high level of scrutiny and vigilance with respect to participant safety and data management, particularly given the sensitive nature of the data and enrollment of minor adolescents. At least once per month during Aim 3 data collection and analysis, we will review data storage and integrity and jointly review and report any unanticipated or adverse events (i.e. breach of privacy) to the CHOP IRB and NIMH in accordance with the NIMH reportable events policy.

9.4.2 Risk Assessment

Aim 1: Risks to participants are anticipated to be minimal. There is a minor risk of unauthorized disclosure of PHI, which will be made known to participants. There is a risk of loss of confidentiality due to using video conferencing, however, the study team will take additional precautions for those participants completing focus groups or in-depth interviews on a phone or via video conferencing using a HIPAA compliant CHOP approved vendor. We will have two research team members moderating each focus group. The virtual conference rooms will be password protected, and a study team member must admit each participant into the group. Before admitting them to the larger group, a study team member will individually and confidentially confirm the physical location of each participant and their best contact information. Participants will also choose a pseudonym (e.g. favorite superhero, cartoon character, or color) prior to entering the virtual focus group and the moderator will change their screen name to that pseudonym prior to entry. Risks will be greatly reduced by the data protection procedures in section 8.2 above.

Aim 2: There is a minor risk of unauthorized disclosure of confidential information, which will be made known to participants.

Aim 3: Risks to participants are anticipated to be minimal. Coaching sessions will be administered by trained coaches in a confidential setting to avoid emotional discomfort to participants when discussing sensitive matters. There is minor risk of variance in the quality of coaching content, but this will be avoided due to extensive training provided to the coaches in accordance with the Motivational Interviewing Network of Trainers training system. Coaching sessions will be continuously reviewed for quality and fidelity to the treatment protocol. There is the minor risk that the CASIs may uncover previously undiagnosed depression or substance abuse. There is a minor risk of unauthorized disclosure of confidential information, which will be made known to participants.

Aim 1, 2, 3: Participants will be informed that their participation in all aspects of the proposed research is entirely voluntary, and that they are free to withdraw at any time. Strict measures will be taken to ensure participant privacy and confidentiality. All data will be de--identified then stored in the secure REDCap database, and all participants will be assigned a unique identification number. All personally identifiable information will be kept strictly confidential and stored in an encrypted document, on a dedicated research server only accessible by myself and the designated study staff. Original, signed and dated consent forms will be stored in a locked file cabinet, separate from study data, only accessible by myself and the designated study staff. Contact information for the PI will be included on

consent forms to allow participants to ask questions or raise concerns about the study. Should any specific concerns arise, the study team would intervene to address problems including, if needed, a change or discontinuation of study procedures. The IRB will be informed of any concerns, and the IRB and NIMH will be informed of any adverse events.

9.4.3 Potential Benefits of Trial Participation

There will be no direct benefit to participants from study participation. However, the proposed study could provide significant insights in the field of adolescent HIV prevention, increasing potential for adolescents to achieve better health outcomes and receive the sexual health care they need in their primary care physician's office. In the long term, the findings of this study could contribute to increased PrEP delivery in pediatric primary care and increased healthy sexual behavior. Those in the intervention arm of Aim 3 could directly benefit if the intervention helps subjects to achieve better health outcomes and receive sexual healthcare. The minimal risks of participation are reasonable in relation to these generalizable benefits.

9.4.4 Risk-Benefit Assessment

This study consists of surveys, interviews and focus groups, and health coaching intervention, and is no more than minimal risk for study subjects. The information gathered in this study will inform development of interventions to improve STI and HIV prevention care delivery to participants. The potential benefit of enhanced care to a disproportionately burdened population outweighs the unlikely, yet potential, risk of loss of confidentiality or psychological distress. Safeguards will be put in place to protect all patient study information and limit any disclosure in the limited and coded dataset and in the final de-identified dataset.

9.5 Recruitment Strategy

Aim 1: Recruitment for Aim 1 will occur on site at the proposed clinics when possible, or by phone or email. Existing participants may also refer friends or individuals from their social networks by sharing the study phone number and an electronic copy of the IRB-approved study flyer with them. On a regular basis, study staff will cross-reference adolescents scheduled for clinic visits with the CHOP STI database to identify patients who may be eligible for the study based on age criteria and history of at least one STI. The password-protected dataset application is only accessible to the PI and the study team. In the case of in-person recruitment, study staff will confirm with the visit provider whether they can approach the adolescent about study participation. If permitted, study staff will meet with potential participants, present information about the study, and if interested, participants can consent for study participation. A potential participant list will also be provided by the Pediatrics Research Consortium (PeRC). Study staff will confirm participant eligibility criteria through the electronic health record (EHR). For those youth who may express interest in the study to their provider, but are unable to stay to screen for inclusion, provider's may relay the best contact information for individuals to the study team and the team will contact them with information about the study. If in-person recruitment is not possible, study staff will contact youth from the STI database by their phone or email information listed in their EPIC record. For any recruitment or retention contact via phone, email or online, no information about the nature or the study or sexual health will be

included in email subject lines or on voicemail due to the sensitive nature of the content, and instead the study will be identified as "the coaching study." When potential participants are reached by phone or email, the study staff will provide a brief description of the study and inquire regarding interest in participation. For participants who screened for this study remotely, the study team will obtain verbal HIPAA authorization for screening. Study staff will go over the verbal HIPAA authorization for screening via telephone. The verbal HIPAA authorization for screening for has been uploaded to the eIRB application for approval. After HIPAA authorization, study staff will confirm the inclusion criteria for screening, including their prior STI status. It they are interested in participating and are eligible, study team will then email them a link of the currently approved Aim 1 written HIPAA authorization/consent form to complete via REDCap. The Aim 1 written HIPAA authorization/Consent form is in its final format and uploaded to REDCap. Study staff will go over the REDCap HIPAA authorization/consent form with participants via telephone as they complete the form. For participants recruited in person, an analogous process will occur with written HIPAA authorization prior to screening, and written informed consent/HIPAA authorization prior to enrollment if eligible. Participants will be offered the option of receiving a copy of the consent/assent form via email, postal mail, or at the time of their enrollment visit. In Cobbs Creek, Karabots, and Adolescent Specialty Clinic (ASC) we will have flyers to provide adolescents with information about the study. This sample flyer is provided in the application within eIRB.

Eligible participants will complete informed consent and the CASI prior to the focus group session, which will be scheduled once 9-12 participants have been recruited. If participants opt for doing an in-depth interview, the interview will be scheduled at their convenience. We will attempt to conduct all focus groups and interviews in-person, however given structural barriers with transportation that youth may face and concerns about safety during the COVID-19 pandemic, we will allow for phone or video conferencing focus groups and interviews as needed using a HIPAA compliant CHOP approved vendor. If a potential participant indicates they are not interested in participating in the study, this will be noted in a recruitment database and they will not be re-approached. Participants who complete Aim 1 may be eligible for the Aim 3 trial and will have the option at the time of informed consent of consenting for future contact.

Aim 2: Recruitment: We will recruit and enroll clinicians, clinical staff and coaches who referred patients to or participated in the pilot intervention, or who cared for youth with STIs during the study period. Potential clinician and staff participants will be identified by querying the CHOP STI database for all providers who cared for youth with STIs during the study period. All potential participants will be sent an email through the secure CHOP system asking if they are interested in participating in a research study and detailing brief study information. From an email survey link, potential participants can access the secure Research Electronic Data Capture (REDCap) screening survey to determine eligibility. Eligible individuals will be contacted by the study team, who will obtain informed consent in-person or by phone. Study staff will also be available on site at the two clinics and will approach clinicians and staff directly about the study.

Aim 3: Potential clinical trial participants will be identified and referred for recruitment by any of three strategies: 1) when nurses or clinical providers call with positive STI results,

they will provide adolescent patients with information about the study; 2) the STI database will be checked daily by the study team to identify new STI diagnoses and obtain the confidential contact information for potential participants to contact them directly by phone; and 3) potential participants will be approached in-person at the time of STI testing or treatment. Potential participants approached in-person can be provided with a recruitment flyer by a clinician or study team member. Screening for the study will occur via a REDCap form and can occur in person or by phone.

9.6 Informed Consent/Assent and HIPAA Authorization

Informed consent or assent (with parental permission) will be obtained from participants by phone or in-person (see section 8.5 above) before any study-related procedures are performed. Participants under age 18 years may consent for studies related to reproductive health services that adolescents legally can access without parental permission in the state of Pennsylvania. Those who wish to involve a parental caregiver in the decision to participate will complete an assent form (verbal or written and their parental caregiver will complete a parental permission form. All subjects will be recruited from primary care settings where they are seeking sexual health services for diagnosis, treatment, or prevention of STIs and HIV.

For participants who screened for this study remotely, the study team will obtain verbal HIPAA authorization for screening. Study staff will go over the verbal HIPAA authorization for screening via telephone. The verbal HIPAA authorization for screening for has been uploaded to the eIRB application for approval. After HIPAA authorization, study staff will confirm the inclusion criteria for screening, including their prior STI status. It they are interested in participating and are eligible, study team will then email them a link of the currently approved Aim 1 written HIPAA authorization/consent form to complete via REDCap. The Aim 1 written HIPAA authorization/Consent form is in its final format and uploaded to REDCap. Study staff will go over the REDCap HIPAA authorization/consent form with participants via telephone as they complete the form. For participants recruited in person, an analogous process will occur with written HIPAA authorization prior to screening and written informed consent/HIPAA authorization prior to enrollment if eligible.

Research staff will document the consent process via an electronic consent form in REDCap by indicating in the name and digital signature of the person obtaining consent who will attest that they have explained the study procedures and that the subject's participation in the study is voluntary. Participants will be offered the option of receiving a copy of the consent/assent form via e-mail, via postal mail, or at the time of their enrollment visit (for those who are eligible and agree to move forward with study procedures).

The text of the electronic consent form will be identical to that of the in-person consent form and will follow the CHOP Clinical Research Support Office "General Guidance on e-consent in REDCap" document. Electronic signature will be obtained within a signature field in the REDCap form and dated in a date field.

Research staff will complete the Documentation of Informed Consent (DOIC) to assess for completeness, as well as update additional information regarding the consent process. A copy of the signed informed consent document will be provided to each participant, if they want a copy.

When obtaining informed consent, all study staff must:

- Deliver comprehensive information about the study including its rationale and risks.
- Ensure that potential participants and their parent(s)/legal guardian, if applicable, understand the information provided and can ask any questions they may have regarding the study.
- Allow potential participants and their parent(s)/legal guardian, if applicable, to ask questions at the end of each section of the informed consent document.
- Assess potential participants' and their parent(s)/legal guardians' comprehension of the details in the consent, assent, and/or parental permission documents.
- Assure potential participants that participation is completely voluntary and that their regular care will not be affected should they choose to not participate in this study.
- Review the informed consent process to check for completeness and update additional information (DOIC).

All participants will be provided with a copy of their signed consent form in-person, via email, or via US mail.

9.7 Payment to Subjects/Families

Aim 1: The participants in Aim 1 will receive $40 in total for their participation in the study. After completing the CASI at time of enrollment, they will receive $10 and then will receive $30 once they complete the focus group or in-depth interview.

Aim 2: The participants in Aim 2 will receive $20 for their participation in the study.

Aim 3: Participants in both arms of the RCT will receive $40 each at the baseline visit, the three-month visit and the six-month follow up visit. Participants who complete baseline surveys within 3 business days of link receipt will receive $10. Participants in the health coaching arm of the RCT will receive an additional $5 if they complete a feedback survey in REDCap after the 1-week coaching session, and they will receive an additional $5 if they complete a feedback survey in REDCap or a feedback interview after the 3-month coaching session. At the 3-month time point, participants in the health coaching arm who completed a baseline coaching session but have missed subsequent visits, including a missed 3-month coaching session, will be offered $15 compensation for completing a feedback survey in REDCap.

Compensation will be paid using the ClinCard system. As per CHOP guidelines, all subjects will need to provide their contact information in order to process their ClinCard. They will also need to sign and date the ClinCard Compensation Receipt (CCR) as proof of receipt of their ClinCard as study payment, except for those participants who complete a visit by phone. Participants who complete a visit by phone or video conferencing will receive a ClinCard via mail. A member of the research team will contact them to confirm receipt of the ClinCard before loading any funds onto their card.

10 PUBLICATION

We will disseminate the findings of the RCT in peer reviewed scholarly publications and presentations at national and international academic meetings. The findings of the RCT will be used to build an R01 funding application for a multi-site, fully powered randomized controlled trial of the intervention, if successful. We will work with PolicyLab at CHOP to develop dissemination plans, as well. PolicyLab has extensive experience distilling research findings into policy relevant summaries and disseminating research findings to end users.

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