**A Clinical Decision Support Intervention to Optimize Adolescent HIV Screening and PrEP Delivery in Primary Care**

**A. BACKGROUND AND SIGNIFICANCE**

Despite the disproportionate burden HIV in adolescents and young adults, uptake of HIV testing and pre-exposure prophylaxis (PrEP) remain suboptimal. The United States Preventative Services Task Force (USPSTF) and Centers for Disease Control and Prevention (CDC) guidelines1 endorse universal HIV testing and PrEP counseling. However, only 9% of U.S. high school students have been HIV tested and <1% of PrEP prescriptions are for minor adolescents.2 HIV prevention service delivery also suffers from striking health inequities, with disparate rates of HIV testing and PrEP prescription by race, sex, and sexual orientation.3,4

Pediatric primary care visits are a window of opportunity for STI and HIV screening, and based on results, delivery of effective interventions such as PrEP. Yet sexual health service delivery in pediatric primary care is hampered by limited time and lack of pediatrician comfort with sexual health discussions. In these busy settings, high provider mental workload can also result in biased decision making. Developing strategies for pediatricians to equitably and efficiently follow existing guidelines for HIV prevention services could help address low screening rates and disparities in PrEP prescribing.

Clinical decision support (CDS) systems are “knowledge-driven interventions that can promote safety, education, workflow efficiency, equity, and quality of care.”5 These systems, ranging from one-time electronic health record (EHR) alerts to multicomponent systems that also include provider or patient education, harness behavioral economic theory and cognitive informatics to provide “nudges” toward evidence-based decision making and away from biased decisions. Within primary care, EHR-based CDS has been demonstrated to increase HPV vaccination and other preventive service uptake in adolescents.6 Clinical decisions support thus represents an untapped potential strategy for increasing pediatrician adherence to HIV testing and PrEP guidelines, decreasing biased decision making, and improving patient prevention-related outcomes.

In the proposed research, I will develop and pilot test a multi-component CDS system to improve equitable HIV screening and link youth at risk for HIV to evidence-based HIV prevention practices, including PrEP. In my NIMH-funded K23 research, I developed the “T.A.K.E. (Treat Act Know Engage) Steps” intervention, which uses motivational interviewing, communication skill building, and health navigation to prevent repeat STIs and HIV for youth with STIs in primary care.1 However, foundational research is needed to develop an efficient and effective strategy for implementing patient-centered interventions such as T.A.K.E. Steps in primary care. In this pilot research, I will leverage 1) the Children’s Hospital of Philadelphia (CHOP) 31-clinic primary care network and its EHR system (EPIC, Verona, WI); 2) the mentorship of Dr. Robert Gross, 3) the

Clinical Informatics Program of CHOP’s Department of Biostatistics and Health Informatics , and; 4) WoodLab, my computational science system which manages HIV testing and PrEP data, including visit note text. This pilot research will leave me well poised to apply for independent funding for widescale testing of a bundled intervention combining the clinician-focused CDS system with the patient-focused T.A.K.E. Steps intervention.

My **SPECIFIC AIMS** are:

Aim 1: To **build and iteratively refine a CDS system** to improve HIV screening and PrEP counseling in primary care. Approach: User-centered design process involving clinician, clinic staff, and adolescents.

Hypothesis 1 (H1): The final CDS system will be usable for pediatricians.

Aim 2: To **evaluate feasibility and acceptability of the multi-component CDS system**. Approach: We will deploy the CDS system for six-months at two CHOP primary care clinics and use survey and interview data to assess acceptability and feasibility.

H2: The system will be feasible for pediatricians and acceptable to pediatricians and adolescent patients.

Aim 3: To assess preliminary **efficacy of the CDS system** in improving **equity in HIV screening and PrEP counseling**. Approach: Pre/post interrupted time series design assessing associations between CDS implementation and HIV screening and PrEP counseling by race, sex, sexual orientation, and gender identity.

H3: CDS implementation will be associated with significant reductions in inequities in HIV screening and PrEP counseling.

**B. RELEVANCE:** This proposal addresses the Gilead Research Scholars Program priority of advancing cross-cutting HIV-related research which addresses **“unmet patient needs and health inequities in order to build a more inclusive research landscape.” This pilot research will combine behavioral economics theory, the science of human computer interaction, and pragmatic evaluation methods to generate critical** preliminary data for a multi-centered, hybrid effectiveness/implementation trial assessing the efficacy of a bundled intervention, combining the CDS system with the T.A.K.E. Steps intervention, to improve equitable and broad delivery of HIV prevention service in pediatric primary care.

**C1. BACKGROUND**: Three key problems in HIV screening and prevention are addressed in this proposal.

**Problem 1: Inadequate adherence to clinical practice guidelines**: CDC guidelines recommend universal HIV screening, counseling on the existence of PrEP for all sexually active adolescents, and referral to start PrEP for youth with STIs.7 While >50% of incident STI and HIV diagnoses in the U.S. occur in youth, service delivery is both inadequate and inequitable. Young cisgender women have lower HIV screening rates than cisgender males, and PrEP uptake has been predominately in white men, although the most HIV diagnoses in the U.S. occur in Black and Latinx individuals.8 Compounding the problem is the challenge for health systems in measuring key equity-related metrics they might act upon. Gender identity and sexual orientation are not typically captured, and PrEP counseling is not easily identifiable as a discrete variable in EHRs. These data limitations further hamper measurement and achievement of quality service delivery.

**Problem 2: Implicit bias** **is a driver of health inequities in HIV screening and prevention**. Implicit bias-unintentionally held attitudes and beliefs that affect decisions in health care-worsens as mental workload increases.9 Busy pediatricians are vulnerable to shifting away from evidence-based and toward “gut” decision making as patient volume, complexity, and performance demands increase.9 At the 15-17-year-old well visit, there are five mandated health screenings, seven risk-based screenings, and 19 suggested topics for anticipatory guidance. These pressures lead clinicians to both leave HIV screening and PrEP behind, and creates vulnerability to biased decision making. Implementing CDS systems, such as electronic alerts and reminders, order sets, and easily accessible guidelines, uses behavioral economics theory to provide a “nudge” toward evidence-based decisions and away from flawed decisions that further health inequities.10

**Shape

Description automatically generatedProblem 3: Health systems must target earliest stages of the HIV prevention continuum.** The first steps in the HIV prevention care continuum are recognizing patients’ HIV risk and testing them.11 Given low rates of HIV testing in adolescents, all later stage interventions are relevant only for a small subset of the at-risk population. Therefore, we have focused on the critical first step in determining PrEP eligibility—that is, improving risk assessments and HIV testing (**Figure 1**). Our research aims to pilot test a multi-component CDS system which first targets HIV testing (Step 2), but also addresses later steps including counseling (Step 3), linkage (Step 5), and prescription (Step 6). We will use EHR data, patient-reported demographics and sexual behavior, and natural language processing methods to determinants of prevention care delivery across the continuum.

**C2. INNOVATION:** Our research is innovative in the following ways. First, we will utilize an **integrated approach** using user-centered mixed methods from clinical informatics, data science, and clinical effectiveness research**.** Second, we will incorporate adolescent perspectives into CDS design and evaluation to create an intervention that is not only usable, but **patient-centered**. Third, we will target multiple steps of the HIV prevention care continuum, both increasing **HIV screening** through the CDS system, and then utilizing test results to **raise PrEP awareness, and link patients to PrEP.** Fourth, we will evaluate our CDS system for impact on **screening inequities,** thereby targeting multiple Institute of Medicine quality domains.

**D. APPROACH**

**D1) Investigator Capabilities and Preliminary Data:** Our team has a rich set of resources to support our efforts including:

**Clinical Informatics Program:**  This programwithin CHOP’s Department of Biostatistics and Health Informatics, consisting of pediatricians, informaticians, and human systems engineers will collaborate on CDS design in Aim 1

**WoodLab:** My research lab centers on a data science platform that is continually updating with all primary care-based STI and HIV screening encounters (n>100,000), including test orders, test results, PrEP prescriptions, and visit note text.4,12,13 These data will be used in our Aim 3 outcome assessments.

**The Adolescent Health Questionnaire (AHQ):** In 2021, the primary care network deployed this electronic questionnaire for adolescents at well visits. The AHQ captures sexual activity which can be used to drive CDS alerts in Aim 1, and sexual orientation and gender identity data which will be used in Aim 3.

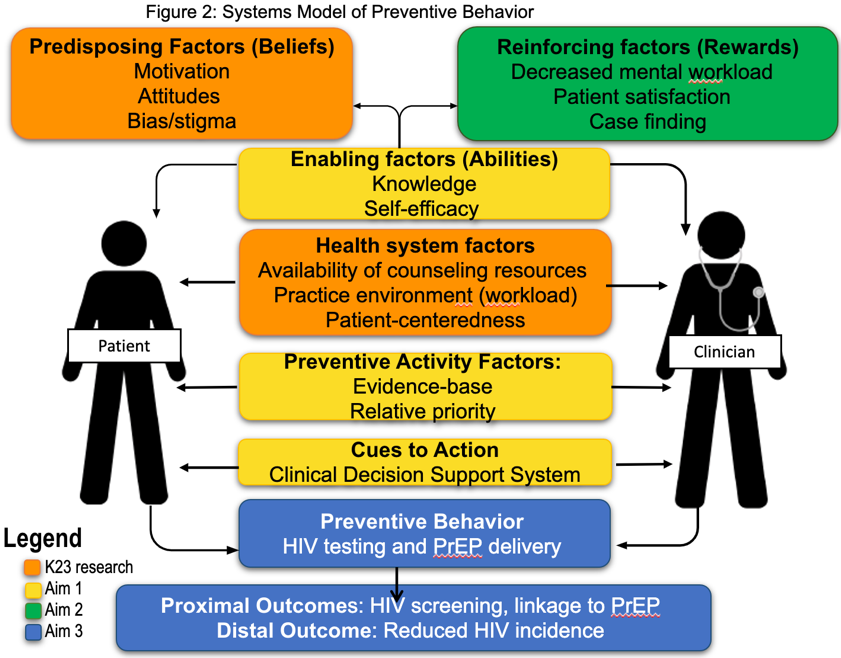
**Penn Center for AIDS Research (CFAR):** Mentor Dr. Gross is Co-Director of the Penn CFAR, and will contribute his extensive experience in HIV treatment and prevention intervention design and evaluation, and the CFAR will provide biostatistical and implementation science support.

**My prior research, and that of my mentors, also lays the foundation for this proposal:**

**A data-to-care pipeline can improve the quality sexual health service delivery:** My WoodLab efforts have informed STI screening improvement efforts, including a practice-led quality improvement intervention which led to a 22% increase in Chlamydia screening at one clinic.3 These data are now augmented by the AHQ data, capturing both EHR and patient-reported elements. Using these data, we identified that only 8% of adolescents have been screened for HIV and only 1 in 4 sexually active adolescents have received STI screening.

**Rigorous user-centered design of CDS systems can improve adolescent health outcomes:** My NIMH-funded K23 research demonstrated that CDS for HIV testing and PrEP delivery is highly appealing to pediatricians and perceived to be an appropriate and feasible future intervention.14 However, a CDS system for HIV prevention in pediatric primary care has not yet been designed or implemented.The CHOP informatics team has extensive experience in development and implementation of CDS in pediatric primary care and has used collaboratively designed CDS systems to improve HPV vaccination rates in adolescents.6

**Health inequities limit delivery of quality HIV prevention services in pediatric primary care:** STIs are a CDC indication for PrEP counseling and prescription, yet our research found that only 8% of youth with STIs in our network received PrEP counseling, all of whom were cisgender males, despite our 12% STI prevalence rate in cisgender females.4 My research has also demonstrated implicit bias in STI screening, finding that primary care providers were 88% more likely to screen their Black vs White patients for chlamydia.12 These findings support the need to develop and adapt prevention interventions for primary care that promote universal screening to decrease biased care, and measure equity as a key component of effectiveness.

**D2. Theoretical Model:** The **Systems Model of Clinical Preventive Care** frames our research.15 This model posits that preventive health interventions, in this case, HIV screening and PrEP delivery, must account for predisposing, enabling, and reinforcing factors the screening or prevention behavior for both clinicians and patients within the enveloping health systems. In **Figure 2,** *orange* elements are addressed in T.A.K.E Steps, my patient-oriented K23 intervention, *yellow* in this proposal’s Aim 1 (CDS design), *green* in Aim 2 (acceptability/feasibility), and *blue* in Aim 3 (equity assessment). I hypothesize that the CDS system will operate chiefly by providing effective **cues to action** to support HIV screening and prevention. These cues will be supported by additional actions of the CDS: **enabling** clinician knowledge and self-efficacy, **reinforcing** behavior through reducing mental workload and increasing patient satisfaction, augmenting **health systems factors** by incorporating modules that facilitate linkage to PrEP counseling, and enhancing clinician awareness of **preventive activity factors.**

**D3) SCIENTIFIC PLAN:**

Setting: All aims will occur in the CHOP primary care network which generates >100,000 visits annually. Over half of patient families live at/below the poverty line, >69% receive Medical Assistance and ~70% are Black. Two clinics provide Title X family planning services. None offer HIV point-of-care testing.

**D3.1. Aim 1: Design and optimization of CDS**

Study Design: Mixed methods cross-sectional study developing the multi-component CDS system. We will apply user-centered design processes in three phases: 1) Requirements 2) Formative, 3) Summative.16

Participants: We will include three stakeholder groups: pediatricians, clinic staff, and adolescents.

Requirements Phase: We will engage in a collaborative design session with the CHOP Informatics Program to to identify the user and system requirements of a multi-component CDS system targeting multiple stages of the HIV prevention continuum (**Figure 1**). The first component will target universal STI and HIV screening (see example **Figure 3**), with supporting components more narrowly focusing on PrEP counseling, referral, and prescription (Steps 3, 5, and 6) for adolescents identified as high risk for HIV. First, we will define clinical scenarios representing when, where, and how CDS tools will be used. For example, scenarios will address how clinicians are prompted to test (e.g. alerts, default orders), under what circumstances they are prompted, and how the CDS can support PrEP counseling and/or linkage to prevention programs such as T.A.K.E. Steps (e.g. embedded provider education, automated messaging to counselors). We will then develop multiple interactive scenario-based multi-component CDS prototypes. The designs will apply existing CDS usability design principles.17 We will generate at least 3-10 iterative prototypes for testing in the formative phase.

**Graphical user interface, text, application, email

Description automatically generated**Formative Phase: We will engage the three cohorts (n=30 participants/cohort) in user-centered design interview sessions. For pediatricians and clinical staff, we will audio-record a “think aloud cognitive walkthrough interview introducing CDS prototypes using the clinical scenarios of adolescents presenting to primary care developed in the previous phase. Participants will be asked to verbalize thoughts regarding usability, goodness-of-fit of the CDS for the clinical scenario provided, technical issues, and general feedback while they engage with the prototypes. Survey and interview questions will determine the participant’s perception of: 1) impact on screening and counseling, 2) impact on equity, and 3) workflow burden. For adolescents, interviews will focus on how each prototype creates new or impacts existing patient-facing workflows, including confidentiality protection and result delivery. We will analyze data after every five visits and apply findings to narrow candidate designs and iterate design elements before moving into the summative phase with a final prototype of all components.

Summative phase: We will validate system usability and utility by testing the CDS system with pediatricians (n=30). Participants will interact with the CDS components with audio and screen-video recording to allow for identification of timing and location of system errors, user comments, or other events of interest while simultaneously collecting data for time on task, mouse clicks, and screen counts. We will assess usability via validated metrics of task completion, error rate, and appropriateness of participants’ decision-making (e.g. ordering HIV test). Subjective metrics will be collected via Likert-scale survey questions based on the Technology Acceptance Model (TAM) and will be supplemented by open-ended questions and comments from the Think-Aloud protocol.17

Sample size: ~30 participants can identify >95% of problems with a CDS system.18

Analysis: Data from each phase will be used to iteratively optimize the CDS design. Formative: Think aloud interview transcripts will be qualitatively deductively coded identify key usability themes across stakeholder groups, using Nvivo software for support. Themes will be applied to refine the CDS and workflows. Summative: Each usability metric will be assessed using pre-determined thresholds for effectiveness of the mockup design, including task completion rate of 90%, error rate less than 20% and survey responses of 80% agreement. Result data will be entered into the Research Electronic Data Capture (REDCap) system and analyzed using Stata 17 (STATA Corp, College Station, TX) to assess achievement of usability thresholds. Identified usability issues will be compiled in order to systematically prioritize and address any system redesign efforts. At the end of the analysis, we expect to have a single multi-component CDS system ready for implementation in Aim 2.

**D3.2. Aim 2:** **Acceptability and feasibility of the CDS system**.

Study design: Prospective single arm cohort study. The multicomponent CDS system developed in Aim 1 will be deployed at two high-volume CHOP primary care practices for six-months.

Setting: We will implement at one urban clinic with an embedded Title X family planning program and one suburban clinic providing general pediatric care only.

Intervention: The multi-component CDS system will be delivered at the clinic-level. The first component, targeting HIV screening, will deploy for all patients ages 13+. The cohort for the PrEP delivery modules will be developed in Aim 1, likely including adolescents endorsing high risk behavior on the AHQ and those with STIs.

Participants and recruitment strategy: We will enroll 30 pediatricians and 30 adolescents. Procedures will occur within a week of using (pediatricians) or receiving HIV prevention services through the CDS (adolescents).

Study procedures: Participants will complete modified versions of the Acceptability (AIM), Feasibility (FIM) and Appropriateness (IAM) of the Intervention Measures and brief audio-recorded interviews.19 The interview guide will be grounded in our theoretical model (Figure 2) and designed to assess the CDS systems’ impact on predisposing, reinforcing, enabling, and health system factors to identify areas for further optimization.

Analysis: We will assess mean scores and standard deviations from the AIM, FIM, and IAM instruments. For interviews, we will use rapid qualitative analysis, also known as the “sort and sift, think and shift” approach, to efficiently yield action-oriented findings.20 We will first develop coding template forms including theoretical model constructs listed above, with additional open text areas to record observations not mapping onto these constructs. Two study team members will review each transcript, including relevant content into the templates to create a condensed inventory of each transcript. We will then use a matrix approach, creating two data grids (clinician and patient) where each study visit is a column and each construct or additional domain on the templates a row. This approach allows rapid visualization of the entirety of the data and identification of key themes that may be used to further modify the CDS.

Sample size: Thirty participants for each group should be sufficient for thematic saturation. If we do not reach saturation, we will continue interviews until it is met.

**D3.3. Aim 3:** **Assess preliminary** **efficacy of the CDS system** to improve **equity in HIV screening and PrEP delivery**.

Study design and setting:See Aim 2 above.

Participants: All patients aged 13+ years at the two clinics, six months before after CDS implementation.

Exposure measures: Primary: Intervention period. Secondary Patient race, ethnicity, age, sex, insurance, gender identity, and sexual orientation.

Outcome measures:

* Primary: Proportion of adolescent preventive visits with an HIV test order placed during the encounter.

Secondary: Proportion of adolescents with STIs receiving 1) PrEP counseling within three months of STI diagnosis, 2) PrEP prescriptions (tenofovir-emtricitabine, tenofovir-alefenamide, cabotegravir).

Data sources for evaluation:

* WoodLab: Patient race, ethnicity, sex, HIV test orders, and PrEP prescriptions. To assess for PrEP counseling during encounters, we use a natural language processing algorithm within the visit note data.
* Adolescent Health Questionnaire: Sexual orientation, gender identity.

Statistical Analysis: We will use a quasi-experimental interrupted time series (ITS) design. We will conduct separate logistic regression models for each outcome (HIV screening, PrEP counseling, and PrEP prescription), including a fixed effect for clinic to account for non-independence of observations within clinical settings. Regression models will include the time (months) elapsed since the start of the study, a binary indicator variable for intervention period, and the outcome at each visit, including interaction terms for each of our patient demographic characteristics: race, ethnicity, sex, gender, and sexual orientation. Given the exploratory nature of this study, we will focus on effect sizes of change rather than precision of estimates.

Sample size: Given a combined average of 600 patients per month at the clinics, we will have 88% power to detect even a 5% difference in HIV screening from our 8% baseline with a two-sided 0.01 significance level.

Table

Description automatically generated**E. CHALLENGES AND ALTERNATE APPROACHES** *What if the CDS system fails to increase equity?* Our efforts will be augmented by ongoing provider education and implicit bias training in the CHOP network. If we fail to find an effect, we will engage in targeted optimization research with the CHOP Center for Health Equity, and the CFAR Implementation Science Working Group*. What if HIV screening increases but PrEP outcomes do not?* We know HIV screening alone will not lead to PrEP uptake. The CDS will contain components such as facilitated linkage to prevention counselors and embedded PrEP education resources I have already developed for providers including educational videos and podcasts. *Why not do a definitive cluster RCT t?* We estimate needing ≥eight clusters to have sufficient power to detect efficacy **across varied and generalizable settings**. We aim to first optimize design and deployment in the proposed pilot testing before progressing to widescale efficacy testing, in accordance with general usability design principles.

**F. Project Timeline:** See Table 1

**G. FUTURE DIRECTIONS:** At conclusion of the research, the final data will be used to further refine the CDS and surround workflows, with a goal of then developing a clinical research program combining the CDS system with the T.A.K.E. Steps behavioral intervention. I will use these preliminary data to apply for my first R01-- a hybrid effectiveness-implementation cluster randomized trial combining the patient-centered T.A.K.E. Steps intervention with the clinician-centered CDS system, with the additional 29 CHOP clinics serving as trial sites.

**REFERENCES**

1. Centers for Disease Control and Prevention. Preexposure Prophylaxis for the Prevention of HIV Infection in the United States- 2021 Update. Department of Health and Human Services, Centers for Disease Prevention and Control. https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf. Published 2021. Accessed 2022.

2. Magnuson DH, T.; Mera, R. Adolescent Use of Truvada (FTC/TDF) for HIV Pre-Exposure Prophylaxis (PrEP) in the United States: (2012-2017). 22nd International AIDS Conference; 2018; Amsterdam, Netherlands.

3. Petsis D, Min J, Huang YV, Akers AY, Wood S. HIV Testing Among Adolescents With Acute Sexually Transmitted Infections. *Pediatrics.* 2020;145(4).

4. Watson DL, Shaw PA, Petsis DT, et al. A retrospective study of HIV pre-exposure prophylaxis counselling among non-Hispanic Black youth diagnosed with bacterial sexually transmitted infections in the United States, 2014-2019. *J Int AIDS Soc.* 2022;25(2):e25867.

5. Teich JM, Osheroff JA, Pifer EA, Sittig DF, Jenders RA. Clinical decision support in electronic prescribing: recommendations and an action plan: report of the joint clinical decision support workgroup. *J Am Med Inform Assoc.* 2005;12(4):365-376.

6. Fiks AG, Grundmeier RW, Mayne S, et al. Effectiveness of decision support for families, clinicians, or both on HPV vaccine receipt. *Pediatrics.* 2013;131(6):1114-1124.

7. Weinstock HS, Kreisel KM, Spicknall IH, Chesson HW, Miller WC. STI Prevalence, Incidence, and Costs in the United States: New Estimates, New Approach. *Sex Transm Dis.* 2021;48(4):207.

8. Baugher AR, Trujillo L, Kanny D, et al. Racial, Ethnic, and Gender Disparities in Awareness of Preexposure Prophylaxis Among HIV-Negative Heterosexually Active Adults at Increased Risk for HIV Infection - 23 Urban Areas, United States, 2019. *MMWR Morb Mortal Wkly Rep.* 2021;70(47):1635-1639.

9. Hall WJ, Chapman MV, Lee KM, et al. Implicit Racial/Ethnic Bias Among Health Care Professionals and Its Influence on Health Care Outcomes: A Systematic Review. *Am J Public Health.* 2015;105(12):e60-76.

10. Holden RJ, Karsh BT. The technology acceptance model: its past and its future in health care. *J Biomed Inform.* 2010;43(1):159-172.

11. Nunn AS, Brinkley-Rubinstein L, Oldenburg CE, et al. Defining the HIV pre-exposure prophylaxis care continuum. *AIDS.* 2017;31(5):731-734.

12. Wood S, Min J, Tam V, Pickel J, Petsis D, Campbell K. Inequities in Chlamydia trachomatis Screening Between Black and White Adolescents in a Large Pediatric Primary Care Network, 2015-2019. *Am J Public Health.* 2022;112(1):135-143.

13. Wood SM, McGeary A, Wilson M, et al. Effectiveness of a Quality Improvement Intervention to Improve Rates of Routine Chlamydia Trachomatis Screening in Female Adolescents Seeking Primary Preventive Care. *J Pediatr Adolesc Gynecol.* 2019;32(1):32-38.

14. Petsis D, Pickel J, Dowshen N, Wood SM. Attitudes and barriers toward integrating PrEP in pediatric primary care. In: Centers for Disease Control STD Prevention Virtual Conference; September 2020.

15. Walsh JM, McPhee SJ. A systems model of clinical preventive care: an analysis of factors influencing patient and physician. *Health Educ Q.* 1992;19(2):157-175.

16. Johnson CM, Johnson TR, Zhang J. A user-centered framework for redesigning health care interfaces. *J Biomed Inform.* 2005;38(1):75-87.

17. Russ AL, Zillich AJ, Melton BL, et al. Applying human factors principles to alert design increases efficiency and reduces prescribing errors in a scenario-based simulation. *J Am Med Inform Assoc.* 2014;21(e2):e287-296.

18. Faulkner L. Beyond the five-user assumption: benefits of increased sample sizes in usability testing. *Behav Res Methods Instrum Comput.* 2003;35(3):379-383.

19. Weiner BJ, Lewis CC, Stanick C, et al. Psychometric assessment of three newly developed implementation outcome measures. *Implement Sci.* 2017;12(1):108.

20. Lewinski AA, Crowley MJ, Miller C, et al. Applied Rapid Qualitative Analysis to Develop a Contextually Appropriate Intervention and Increase the Likelihood of Uptake. *Med Care.* 2021;59(Suppl 3):S242-S251.