

Enhanced SexHealth Intervention to Improve Adolescent Outcomes: A Clinical Trial
Project phase 3 = A Randomized Controlled Trial to Evaluate the Enhanced ED SexHealth
Intervention (with the revised CDS system) versus a Standard Information arm to Determine the
Effect Size of Rates of Health Service Uptake

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- Dr.s Satterwhite and E. Miller will help with protocol development, and data analysis.
They will not be engaged in human subject research for this trial and will only have
access to completely de-identified data completely void of all PHI.

Research Personnel:

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Study Sites:

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Protocol Version: (2.0)

Protocol Date: (Oct. 06, 2017))

1. STUDY OBJECTIVES/HYPOTHESIS

Primary Objective(s)

To enhance and test our ED SexHealth intervention that provides risk reduction counseling and point-of-care services as well as connections to sustainable, non-episodic sources of care.

Hypothesis 1: The enhanced ED SexHealth intervention will result in statistically significantly higher health service uptake rates versus a standard information arm.

Hypothesis 2: The enhanced ED SexHealth intervention will be feasible, as measured by qualitative and quantitative data from adolescents, health educators, ED providers and hospital administrators.

2. BACKGROUND and RATIONALE

Although highly preventable, STIs/HIV and unintended pregnancy are significant and costly public health problems that disproportionately impact adolescents, especially minority and uninsured youth.¹⁻³ While these disparities result from a complex convergence of patient, provider, and health systems factors, limited access to care directly contributes to these disparities, independent of race/ethnicity.⁴⁻⁸ Adolescents make 19 million Emergency Department (ED) visits each year and frequently report intercourse not protected against STI/HIV or pregnancy.⁹⁻¹⁰ Further, among these youths, rates of infection with chlamydia and gonorrhea are up to 7 times higher than the general population.¹¹⁻¹⁴

One non-traditional setting for targeted interventions is the ED. ED-based interventions are feasible because most adolescent visits are not urgent and, in fact, youth commonly present with sexual health concerns.¹⁰ For several million high-risk adolescents, the ED is their only or primary contact with health care.¹⁰ As such, there is growing support to use the ED to improve adolescent sexual health outcomes, specifically calling for contraception, behavioral counseling, and links to ongoing care.¹⁶⁻¹⁹ The ED has been used successfully to target aspects of adolescent health, but most sexual health efforts have focused only on *testing* for STIs/HIV.¹¹⁻¹³ Routine HIV testing in EDs has been well received by adolescents and guardians.²⁰⁻²⁴ Recently, a clinical decision support (CDS) system was used in two EDs to improve testing rates for STIs/HIV.^{12,22} Computerized CDS systems use patient characteristics to generate tailored recommendations, are a scalable strategy for health promotion, may increase patient disclosure of risk factors, and are effective at overcoming barriers such as time constraints and knowledge gaps.²⁵⁻²⁹ CDS systems may increase testing acceptance, but without the accompanying provision of behavioral counseling to increase preventive behaviors, their use is unlikely to lead to reductions in STIs/HIV or unintended pregnancy.

This proposal addresses a major gap in health care access for this vulnerable population and is consistent with Healthy People 2020 objectives, to “promote healthy sexual behaviors, strengthen community capacity, and increase access to quality services to prevent STIs.”¹⁵ It will lay the groundwork for a large-scale trial of the intervention. By connecting the highest-risk adolescents with point-of-care services and sources for care, this proposed work is significant because our ED SexHealth intervention has potential to reduce disparities in STIs/HIV and unintended pregnancy as well as risks for long-term sequelae including pelvic inflammatory disease, infertility, and cervical cancer. The prevention of STIs/HIV and unintended pregnancy, together with prevention of life-threatening illnesses and social consequences, could result in significant decreased costs for adolescents, families, and society.

Preliminary work

We have completed two small, open trials (CMH-IRB #'s 15090399 and 14060265) of the SexHealth intervention. In version 1, 20 sexually experienced patients aged 14-19 years presenting to our ED received motivational interviewing from a dedicated health educator to foster engagement in safer sex behaviors and completion of sexual health services. The intervention included agenda setting, exploration of behaviors, decisional balance exercises, tailored feedback and health service provision (i.e., condoms, emergency contraception [EC] prescription for future use, testing for pregnancy/sexually transmitted infections [STIs], and Adolescent Clinic referral). Mean intervention length was 15.7 minutes. Most (65%) participants completed ≥ 1 service. Most (78%) reported that the interventionist maintained high fidelity to intervention principles and most (80%) were very satisfied with the intervention.

In version 2, we developed a computerized clinical decision support (CDS) system to enhance service delivery from the dedicated health educator. The enhanced intervention, conducted by the same educator as version 1, included the same intervention components and the CDS system which used patient-entered behavioral data to create tailored, evidence-based service recommendations for educator use during the intervention. In this version, we also dispensed EC medication directly to patients (rather than prescriptions) for immediate and/or future use and provided medication for untreated, patient-reported STIs. For 32 participants in this open trial, the CDS system generated a total of 124 recommendations, 3.9 recommendations per participant. The educator discussed 77% of all recommendations. Most (75%) participants had uptake of ≥ 1 health service, which was an improvement from the pilot study (65%) but not statistically significant ($p > 0.05$). Nearly all (93%) were satisfied with their recommendations and 100% were satisfied with the counseling session. The educator rated the system-generated recommendations as “very” useful (94%) and “very” easy to use (91%).

In order to improve health service uptake and facilitate safer sex behaviors, we will again enhance our SexHealth intervention by including: 1) improved use of motivational techniques, 2) additional ED-based services (i.e., HIV testing, regular hormonal contraception), 3) condom skills training, and 4) an expanded clinical decision support system to generate tailored service recommendations (i.e., dynamically adaptive checklists) for use by the health educator.

3. STUDY DESIGN

This is an adaptive trial with an initial **Formative Revision Process** followed by a **Randomized Controlled Trial**. Up to 500 adolescents will be consented into this study to achieve 6 completed subjects for the formative process and 80 completed subjects (40 in each arm) for the RCT. Up to two Health Educators will be consented as secondary subjects who will complete post-intervention assessment survey's.

Formative Revision Process

Based on pilot feedback and relevant literature,¹⁹⁻²³ we made modifications to increase adolescents' motivation for service uptake and safer sex behaviors. To increase motivation, we will: 1) expand opportunities to increase receptiveness to change, 2) emphasize interpersonal skills for educators, 3) increase opportunities to develop discrepancy between behavior and risk, and 4) emphasize need for regular care and how to access it. We will incorporate CDS system-generated recommendations directly into the intervention to facilitate participant risk

comprehension and standardize service provision. We will add behavioral skills training and role play for condom use. The educator will deliver the revised SexHealth intervention with a formative group of 6 adolescents. We will gather feedback on intervention acceptability and feasibility using individual session analysis and in-depth interviews. Sessions will be audio-recorded and coded to provide educator feedback and evaluate fidelity to core MI skills. Each adolescent will also complete an in-depth post-intervention interview, with a separate team member. Interviews will be audio-recorded and written notes taken. Data from session analysis, interviews, and educator feedback will be incorporated into the final version with a targeted length of 30 minutes. Our intervention manual contains highlights of revisions, including tailoring for sexual minorities.

The study will then continue as a two-armed randomized controlled, parallel group design with 80 completed participants.

Randomized Controlled Trial

The **Control Group** will receive a printed health pamphlet and a list of local resources with the phone number for Adolescent Clinic. Participants will then be referred back to their ED provider, who will provide their standard care.

The **Intervention Group** will receive the same pamphlet as controls and the enhanced ED SexHealth intervention with the educator. Based on behaviors, CDS system recommendations (generated from screening survey responses only for intervention participants), and discussions, participants may be offered testing (for pregnancy, gonorrhea/chlamydia, and/or HIV), hormonal birth control, condoms, emergency contraception (for immediate or future use), treatment for previously diagnosed (yet untreated) infection with gonorrhea/chlamydia, and a scheduled appointment at Adolescent Clinic (for ongoing care, including repeat STI/HIV testing if needed). All services will be provided at point of care, costs will be covered by the study. We will use urine/swab specimens for STI testing (Gen-Probe Inc.) with results available within 7 days. We will contact those with an STI and advise them to seek care at the hospital-affiliated Adolescent Clinic or we can call in a prescription for treatment of Chlamydia. We will use fingerstick blood for HIV testing (Alere North America Inc.) and for those with a reactive screen, we will provide immediate, in-person counseling with a case manager from our community partner (see letter from KC CARE Clinic), obtain a confirmatory test, and arrange for rapid follow-up.

Health Educator

We will recruit a health educator with training in public health and health behavior change. They will receive training including in-depth Motivational Interviewing (MI) training supervised by expert team members. Training will include mock patients for hands-on practice and immediate feedback. Encounters will be audio-taped and coded using the Motivational Interviewing Treatment Integrity Coding system to provide objective feedback. The educator will receive instruction in adolescent sexual health including HIV/STIs, sexual minority issues, contraception, and HIV counseling and testing (in partnership with KC CARE Clinic and the Midwest AIDS Training and Education Center). The educator will discuss the first 6 trial participants with Drs. Catley and Miller and attend a one-day “booster” training halfway through the study (led by Drs. Catley and Miller). All sessions will be audio-recorded; 20% will be randomly selected and evaluated for MI fidelity using accepted techniques.¹⁰²⁻⁰³

Provision of health services

Participants may be offered testing (for pregnancy, gonorrhea/chlamydia, and/or HIV), hormonal birth control, condoms, emergency contraception (for immediate or future use), treatment for previously diagnosed (yet untreated) infection with gonorrhea/chlamydia, and a scheduled

appointment at Adolescent Clinic (for ongoing care, including repeat STI/HIV testing if needed). The participant then selects which (if any) of these recommendations s/he wants to receive/complete. Urine pregnancy testing will be conducted at the time of the ED visit. For STIs, urine specimen or swab (from throat, rectum, or vagina) will be collected, labeled with study ID number, and stored in the hospital laboratory. The nucleic acid amplification tests will be performed according to manufacturer's directions and testing will occur every few days (Aptima Combo-2; Gen-Probe Inc., San Diego, CA). Subjects with an STI will be contacted and advised to seek treatment, preferably at the Adolescent Clinic where treatment is free. We will use fingerstick blood for HIV testing (Alere North America Inc.) and for those with a reactive screen, we will provide immediate, in-person counseling with a case manager from our community partner (see letter from KC CARE Clinic), obtain a confirmatory test, ([Mayo \(test code HIVDI- HIV-1 and HIV-2 Antibody Confirmation and Differentiation, Serum\)](#)) and arrange for rapid follow-up. We will follow state statutes for reporting Chlamydia, gonorrhea and HIV infections.

Process for Medication Provision

The provision of medication will be a collaborative process involving the participant, the educator and the study team. For any prescription medication, the health educator will discuss the medication with an ED physician or nurse practitioner. That provider will review the medication(s) with the educator and place the order within Cerner. The ED provider may decide that a medication desired by the participant or recommended by the system is not appropriate and refuse provision (e.g., in case of drug allergy).

Data Collection /sources

We will collect immediate post-intervention survey data from all participants. The health educator will complete a survey following each intervention. We will collect data on health services (i.e., STI/pregnancy testing, condoms, emergency contraception, hormonal contraception, STI treatment, HIV testing, referral to clinic) offered, accepted, and completed as well as services provided as part of ED clinical care. When determining completion of sexual health services, services that are completed via a standing order or protocol (e.g., adolescent female receiving urine pregnancy test before radiographic imaging) will be noted and not included when determining our outcome measurement.

Incentives

Compensation for the formative group will be up to \$55.00.

Part 1	Part 2	Part 3
Take survey	Meet with the Health Educator	Take survey about meeting with the Health Educator
\$5.00	\$30.00	\$20.00

Compensation for the RCT will be up to \$80:

\$5 for completing the screening survey, if the subject does not qualify or decides not to continue in the study, their participation will be over and they will receive a \$5.00 Target® gift card.

If a subject qualifies to continue in the study and signs the written consent they will receive a Greenphire Clincard instead of the Target® card. If they continue in the study they will be randomized into study group. At the end of this visit they will receive the Greenphire Clincard gift card. It will be uploaded with \$5.00 for taking the computerized survey and \$30 for completing the randomization part of the visit for a total of \$35.00. An additional \$10-each will be loaded onto the Greenphire Clincard when month 2 and month 4 surveys are completed and final \$25 for month 6 survey completion. All surveys can be completed online or by telephone. All health services (e.g., STI testing, condoms) will be provided at no cost to participants in the intervention arm. Charges for any service for participants in the control arm will be billed by the ED provider according to their standard practice.

Visit 1 (screening)	Visit 1 (randomization)	2 mo.	4 mo.	6 mo.
Take computerized screening survey	Be randomized into study group and complete assigned arm procedures	Take survey online or by phone	Take survey online or by phone	Take survey online or by phone
\$5.00	\$30.00	\$10.00	\$10.00	\$25.00

4. TARGET STUDY POPULATION SPECIFICS

Recruitment procedures: We will use our electronic tracking system to identify potential participants who will be approached sequentially based on arrival and availability (e.g., we will not interrupt patient care). Patients may be approached in private areas of waiting rooms or treatment spaces. Interested patients will initially complete a screening survey. For subjects reporting no previous sexual activity, their involvement in the study will terminate upon screening survey completion.

For eligible youth who agree to participate during the iterative revision process, all youth will receive the intervention until six adolescents have been enrolled. After that time, all eligible and interested participants will be randomized to treatment or control arm.

Based on prior work demonstrating differences in STI and pregnancy testing due to presence of genito-urinary symptoms, we will ensure balanced allocation of participants reporting genitourinary complaints (i.e., concern for pregnancy/sexually transmitted infection, lower abdominal pain, urinary complaints, genital pain or discharge, or vomiting in a female patient) between treatment groups in a 1:1 ratio. We will generate our randomization sequence using REDCap, which will also host our computerized surveys. We will recruit participants during times when adolescents are more likely to visit the ED, using ED arrival data from the previous year to determine recruitment times and we will weight recruitment shifts based on the proportion of adolescents who presented during each block for weekdays (Monday-Thursday)

and weekends (Friday-Saturday). After survey completion, participants will be randomized to receive the intervention or control arm. Randomization will be assigned based on computer-generated algorithm and using numbered sealed envelopes.

Inclusion/Exclusion Criteria

Inclusion: Part 1 (BASELINE) Adolescents who present for care to the CMH Main ED for any reason who 1) are aged 14-19 years and 2) reside within 30 minutes travel time of CMH will be eligible to complete the computerized health behavior screening survey. We selected thirty minute travel time (per subject self-report) to facilitate potential clinic referral.

Part 2 (INTERVENTION) and (Part 3 Post-Intervention survey for Formative Group)

Adolescents who report previous sexual activity on screening survey will be eligible to participate as part of the formative group or within the randomized trial. For subjects reporting no previous sexual activity on the screening survey, their involvement in the study will terminate upon survey completion.

Exclusion: Subjects who are unable to provide consent (i.e., determined to be too ill by the ED team, have cognitive impairment due to chronic condition or acute medical concern), are in police custody, are seeking care due to sexual assault or psychiatric emergency, or do not speak English will be excluded. We will also exclude patients if they are under the clinical care of a study investigator working in the ED (i.e., Melissa Miller or Denise Dowd).

5. DATA COLLECTION

Surveys will be administered via REDCap, which enables administration of online surveys via a secure website utilizing a secure sockets layer (SSL) protocol. Electronic data will be stored in an encrypted format on hospital firewall-protected servers, written data will be stored in a locked office. Direct data entry provides a confidential means of survey administration, consistent delivery, and enhanced data accuracy.^{49,50} Data from clinical records will be electronically extracted from hospital databases. Participants will be assigned an anonymous study number. Surveys will be completed confidentially and will not contain identifying information. Contact information will be recorded separately, via a separate REDCap data collection tool, and will be used for notification of test results. This data will include medical record number, date of birth, address, and phone number. We do not plan on collecting social security number as we feel this study will qualify for exemption from Greenphire and have requested exemption. In order to better evaluate the over-all adolescent population in the Main ED we will be collecting refusal data from those potential subjects and their parents who decline to participate.

Secure Storage of Data

Records to be kept and Secure Storage of Data: Survey development, data collection and handling will be conducted through Children's Mercy's REDCap Research software. The Redcap database is protected by Gazzang's zNcrypt product. zNcrypt transparently encrypts and secures data at rest without any changes to your applications or database and ensures there is minimal performance lag in the encryption or decryption process. Advanced key management and process-based access controls enable organizations to meet compliance regulations and ensure unauthorized parties or malicious actors never gain access to the encrypted data. zNcrypt meets compliance for HIPAA, PCI-DSS, FISMA, EU Data Protection, and more.

Data will be exported from REDCap to statistical programs for analysis (i.e. SAS, SPSS, Excel.) All data will be securely stored on password-protected servers. Only personnel involved in the study will have access to the data. Data transfer between members of the study team will be conducted solely within the confines of the CMH network.

6. STUDY DURATION/STUDY TIMELINE

We expect to consent 500 subjects into this study in order to obtain 6 completed subjects in the Formative phase and 80 completed subjects into the RCT phase of this study.

Formative Participant Involvement (n=6):

Timeline of assessments			
At initial ED visit			
	Part 1	Part 2	Part 3
	Baseline	Intervention	Post Intervention
Demographics	X		
Sexual health behaviors	X		
Theory Planned Behavior (TPB) measures (e.g., attitudes, risk perception, intentions)	X	X	
Health services offered, accepted		X	
Healthcare utilization*	X		
Satisfaction measures			X
Fidelity to motivational interviewing**			X
Readiness for safer sex/service uptake	X		
Current or incident HIV or STI #	X		
*Assessed via self-report and hospital medical record; **Intervention participants only; # Assessed via study testing, self-report, and/or hospital medical record			

RCT Participant Involvement (n=80):

Timeline of assessments						
	Part 1		Part 2			
	At initial ED visit		Time from initial visit			
	Baseline	Post-treatment	3 wk	2 mo	4 mo	6 mo
Demographics	X					
Sexual health behaviors	X			X	X	X
Theory Planned Behavior (TPB) measures (e.g., attitudes, risk perception, intentions)	X	X				X
Health services offered, accepted		X				
Healthcare utilization*	X		X	X	X	X
Satisfaction measures		X				
Fidelity to motivational interviewing**		X				
Readiness for safer sex/service uptake	X	X		X	X	X
Current or incident HIV or STI #	X					X

*Assessed via self-report and hospital medical record; **Intervention participants only; # Assessed via study testing, self-report, and/or hospital medical record

7. STATISTICAL CONSIDERATIONS

The **Primary Outcome Measure** is the proportion of participants in each arm who receive any health service (i.e., STI/pregnancy/HIV testing, condoms, emergency or other hormonal contraception, Adolescent Clinic referral/visit completion). Visit completion will be measured at 3 weeks; all others at initial ED visit.

Feasibility Measures: All participants: (1) proportion of eligible patients enrolled; (2) proportion rating screening survey as very/fairly satisfactory; and (3) proportion completing follow-up. Intervention arm: (1) proportion completing intervention; (2) proportion in which 75% of recommendations are discussed; (3) proportion rating intervention as very/fairly satisfactory; and (4) counseling session time. We will examine length of stay for participants vs. non-participants and costs.

We use items adapted from national surveys to assess risk behaviors. We will use an audio computer-assisted self-interview (ACASI) to reduce social desirability bias and literacy barriers. Follow-up will be completed via web-based surveys or telephone.

Sample size: In a review of 130 patients, we found the pre-intervention proportion of ≥ 1 service uptake was .08. Our pilot study provided an estimate of the post intervention proportion of .65. We used conservative estimates for differences in uptake rates between arms, inflating the control to .15 (vs. .08), deflating the intervention to .50 (vs. .65). With these estimates, an alpha of .05 and a sample size of 76 participants (38 each arm) we achieve a power of .94, well above the usual .80. Given that our primary outcome will be measured at 3 weeks, and our historical attrition rate has been low, we will recruit only four additional participants (N=80) to protect against attrition. Even with 25% attrition, we would still achieve .84/.91 power for two-tail and

one-tail tests respectively. To protect against self-selection or attrition biases, we will randomize arm assignments and analyze potential impacts of attrition.

Hypothesis: The enhanced ED SexHealth intervention will result in statistically significantly higher health service uptake rates versus a standard information arm.

We will compare rates of participants in each arm who complete ≥ 1 health service using tests of the differences between two sample proportions. We expect an effect size of .57 (i.e., .65-.08) which is much higher than used in the sample size estimate (.50-.15=.35). Because we will have power to detect differences as small as .21, we should have more than a sufficient sample size.

Descriptive statistics of the percentages, mean, median, range, as well as confidence intervals, will be used to describe feasibility and theory of planned behavior measures (e.g., attitudes, risk perception), behaviors, and demographics. Appropriate analyses will be performed to examine distributional characteristics of outcome measures and to model temporal changes as a function of group assignments. We will compare rates of condom use using bivariate and multivariate methods that capture arm differences and mediation and moderation covariate influences over time. Demographic characteristics and baseline assessment scores of the two arms will be compared using appropriate chi-square and t tests. Analyses will be done with SPSS Version 21 or SAS 9.3.

Retention Strategies: All youth provide contact methods to receive brief text/email messages, modeled on best practices to facilitate referral completion and study retention. To aid recall, we conduct surveys every 2 months. Compensation will be up to \$85: \$5 for completing the screening survey, \$25 for ED treatment; \$10-25/each telephone or on-line survey completed.

Expected results/outcomes

Upon successful project completion, we will determine if our enhanced ED SexHealth intervention results in increased service uptake rates compared to control and intervention feasibility. Results will provide necessary evidence (e.g., effect size estimates) to support a successful R01 application that proposes a multi-site clinical trial to evaluate efficacy. This trial may provide further justification that improved access to effective services is cost-effective and reduces the financial and social burden of HIV, STIs, and unintended pregnancy in the U.S.

Limitations, barriers, and responsive solutions

We considered these potential limitations. 1) This plan may be difficult to execute. However, our experiences and the literature demonstrate that ED-based interventions can work. 2) To protect against difficulty achieving sample size or higher than anticipated dropout rates, we planned incentives and used a conservative estimate for follow-up. 3) We use ACASI to reduce social desirability bias and literacy barriers. 4) Contamination threat is minimal as the intervention is conducted by personnel not available for control or non-study participants.

8. HUMAN SUBJECTS

Consent of Participants

We will use our electronic tracking system to identify potential participants to complete the computerized health behavior screening survey.

Consent/assent will be completed in two phases: 1) screening for eligibility and GU complaints with the health survey (see "health screening survey") and 2) formative group/randomized trial.

Subjects aged 14-17 years: For phase 1 (screening), potential subjects and parents will be given study information sheet ("info sheet"). Adolescents will independently provide verbal assent, which mirrors the clinical and legal standard for care. For phase 2, study details will be explained in private and written assent obtained from eligible adolescents who agree to

participate. We will request a waiver of parental permission from the institutional review board (IRB) because adolescents 14 years of age or older can seek reproductive care independently in Missouri and Kansas.

Subjects aged 14-17 years seeking ED care for medically emancipated condition: Since many of this subgroup of patients will likely be unaccompanied by a parent, and since they are able to consent for this type of care independently, we will request a waiver of parental permission for both phases from the IRB. For phase 1, potential subjects will be given study information (“info sheet”) and will independently provide verbal assent. For phase 2, the study will be explained in private and written assent obtained from those who agree to participate (“minor written assent”).

Subjects aged 18-19 years: For both phases, the study will be explained in private (“info sheet”). Subjects will provide verbal consent for phase 1 and written consent for phase 2 (“adult written consent”).

Institutional Review Board (IRB) Review and Informed Consent

This protocol, and any subsequent modifications, will be reviewed and approved by the Pediatric IRB at The Children’s Mercy Hospital & Clinics.

Subject Confidentiality

The planned procedures for protecting against or minimizing potential risks are described here.

Risk to confidentiality: All data will be managed in accordance with hospital institutional review board and HIPAA requirements to ensure confidentiality and protection of research participants. The Investigator and other site personnel will not use such data and records for any purpose other than for conducting the study. Only researchers involved in this study will have access to the collected specimens and data. All records will be kept in a locked file cabinet. Human subject’s names will be kept on a password protected database and will be linked only with a study identification number for this research. There are no patient identifiers recorded in the research record. All computer entry and networking programs will be done using study identification only. All data will be entered into a computer that is password protected. Clinical information will not be released without written permission of the subject, except as necessary for monitoring by IRB, the FDA, the OHRP, the Sponsor, or the Sponsor’s designee. Data will be stored in a locked office of the investigators and maintained for a minimum of three years after the completion of the study.

The electronic data will be subject to the routine security of the CMH system. Urine and blood samples will be stored in a refrigerator that is located in a badge secured area of our institution and will not be stored beyond the completion of the study.

Name, study number, medical record, and contact information will be recorded on a contact sheet separate from the data collection/research record and will be used for the sole purpose of participant contact for follow-up and to inform participants of positive test results. The contact sheet will be destroyed after study completion and not linked to the data collection/research record.

If a participant elects to have a pregnancy test, and the result is positive, we will encourage (but not require) involving family for medical decision-making, which follows standard of clinical care. Infections with Chlamydia or gonorrhea will be reported to the local health department, as

mandated by the state. Participants will be informed of these stipulations during the consent process.

Study Modification/Discontinuation

The study may be modified or discontinued at any time by the IRB, the Sponsor, the OHRP, the FDA or other Government agencies as part of their duties to ensure that research subjects are protected.

VIII. Medications and Risks

There may be risks to each medication offered in this study, if a subject chooses to take one. Risk of serious adverse event from medication: We do not anticipate any serious adverse events from medications. The Fertility and Maternal Health Drugs Advisory Committee has reviewed the use of hormonal contraceptives by adolescents and advises that “with the exception of oral contraceptive users 35 and older who smoke, and 40 and older who do not smoke, mortality associated with all methods of birth control is low and below that associated with childbirth.”

To decrease risk of serious adverse events, we will follow regulations and recommendations in accordance with the Food and Drug Administration. We will prescribe the dosage regimen which contains the least amount of estrogen and progesterone that is compatible with a low failure rate and the needs of the individual patient. We will screen participants for predisposing conditions and duration of previous DMPA use. Women with these conditions should not use hormonal contraceptives: women with stroke or blood clot, circulation problems (especially if caused by diabetes), a hormone-related cancer such as breast or uterine cancer, abnormal vaginal bleeding, liver disease or liver cancer, severe high blood pressure, migraine headaches, or a heart valve disorder. Further, DMPA should not be used as a long-term method (i.e., longer than 2 years) unless other methods are considered inadequate.

Participants will be advised of all potential adverse events and instructed to seek care if symptoms develop or they have concern about such an event. In the case of illness or injury resulting from this study, treatment is available at The Children’s Mercy Hospital, and can be provided at the usual charge. Participants may also see care at the hospital-affiliated Title X Adolescent Clinic, which provides reproductive care at no or reduced cost.

For emergency contraception

- Plan B (also called levonorgestrel) is taken by mouth by a woman to prevent pregnancy after she has already had unprotected sex. It is available over-the-counter for any person to buy. Plan B has no serious or lasting side-effects and leaves the body within a few days. Some women (fewer than one in five) have mild and short-term side-effects, including irregular bleeding from the vagina, belly pain, being tired, nausea (feeling like you might throw up).
- Ella (also called ulipristal) is taken by mouth by a woman to prevent pregnancy after she has already had unprotected sex. A prescription is required to get Ella. Because the risks to a fetus (unborn baby) are not known, a woman should not take Ella if she is pregnant. Some women (fewer than one in five) have mild and short-term side-effects, including headache, belly pain, nausea, and irregular bleeding from the vagina.

For hormonal contraception

- Sprintec (ethinyl estradiol and norgestimate) Many formulations of hormonal contraception exist including those with estrogen and progesterone combined (e.g., Sprintec, Ortho-Evra) The most common side effects from combination hormonal contraception are mild and include: irregular vaginal bleeding, breast tenderness, nausea, and mood changes. Serious adverse events may occur. Older women who smoke are at increased risk of myocardial infarction or stroke. There is no increased risk of myocardial infarction or stroke among healthy nonsmoking women who use the pill. Blood clots in the legs and elsewhere are slightly more frequent with contraceptive use, but the risk is very low, and lower than the increased risk of clotting that occurs with pregnancy. There is no increased risk of birth defects in babies born to women who have taken hormonal contraception while pregnant, but a woman should not use hormonal contraception if she is pregnant.
- medroxyprogesterone acetate: The most common side effects from DMPA are mild and include: irregular menstrual cycles, cessation of menstrual periods, headache, and weight gain. Serious adverse events may occur. Use of DMPA may cause loss of bone mineral density, which may lead to an increased risk of developing osteoporosis. The decrease in bone calcium is most concerning if the patient has bone disease, family history of osteoporosis, or anorexia nervosa. Older women who smoke are at increased risk of myocardial infarction or stroke. There is no increased risk of myocardial infarction or stroke among healthy nonsmoking women who use the pill. Blood clots in the legs and elsewhere are slightly more frequent with contraceptives, but the risk is very low, and lower than the increased risk of clotting that occurs with pregnancy. There is no increased risk of birth defects in babies born to women who have taken hormonal contraception while pregnant, but a woman should not use hormonal contraception if she is pregnant.
- Ortho Evra and Xulane (Norelgestromin/ethinyl estradiol) is birth control patch that works by stopping ovulation. It may also change cervical mucus to prevent the sperm from reaching the egg and change the lining of the uterus to prevent a fertilized egg from implanting in the uterus. Side effects can include: breast tenderness or enlargement; headache; menstrual cramps; mild fluid retention or weight gain; mild skin irritation at the application site; nausea; stomach pain, cramps, or bloating; vaginal spotting or breakthrough bleeding; vomiting.
- NuvaRing (ethinyl estradiol and etonogestrel) is a birth control vaginal ring that contains female hormones that stop ovulation (the release of an egg from an ovary). This medicine also causes changes in the cervical mucus and uterine lining, making it harder for sperm to reach the uterus and harder for a fertilized egg to attach to the uterus. Side effects may include: headache; vaginal irritation or discharge, cervical pain; menstrual cramps; mood changes, decreased sex drive; nausea, vomiting, stomach pain; breast pain or tenderness; acne; or weight gain.

To treat an STD, a subject may be given an antibiotic.

- Azithromycin (also called Zithromax) is a medicine you take by mouth to treat Chlamydia (a common STD that often doesn't have symptoms). Most people taking this medicine have no side effects. Some people have mild and short-term side-

effects including diarrhea/loose stools (4%), vomiting (5%), abdominal pain (1%), rash (1%). Very rarely, this medicine can cause liver problems, severe allergy (swelling of the face or mouth, trouble breathing, or peeling skin), or a problem with heart rhythm (called prolonged QT) so people with these types of problems should not take azithromycin.

- Ceftriaxone (also called Rocephin) is a medicine given in a shot to treat Gonorrhea (another common STD). Most people taking this medicine have no side effects. Some people have mild and short-term side-effects including pain/redness where they get the shot (17%), diarrhea/loose stools (3%), changes in blood cells found in the body like high platelets (help the body make blood clots) or low white blood cells (help the body fight infections) (7%). Rare, but more serious side effects can include anemia (low hemoglobin) and severe allergy (swelling of the face or mouth, trouble breathing, or peeling skin). People who have had severe allergy to penicillin or other antibiotics in the family of drugs called cephalosporins should not take ceftriaxone.

Risk from fingerstick blood draw: To minimize the risk of infection, correct aseptic techniques will be used. To minimize discomfort, blood will be drawn by trained personnel.

Risk of emotional distress: Participants may experience increased stress over the sensitive survey questions. However, we feel this risk is minimal and we have included information in the consent process that reminds participants that they are not required to answer questions that make them feel uncomfortable. In the emergency department, there are always advocates available for patients and families, if needed, including health care providers, social workers, and patient advocates. In this study setting, if a participant expresses a concern or need that is outside of the scope of this project (e.g., sexual assault), we will refer those participants back to their ED treating team, as is our standard practice. During the consent process, we will inform participants that most of the information they share during the study will be kept confidential except in rare cases where their safety is at risk or mandated reporting is in effect

9. PUBLICATION OF RESEARCH FINDINGS

List any meetings or conferences where you will be presenting the data and the results of your study. This can be general. Please provide timeline for finalizing manuscript and when and where you plan to submit for publication.

Results will be disseminated via 1) publication in a peer-reviewed journal and 2) presentation at national meetings for pediatric medical research. These results will provide necessary evidence (e.g., effect size estimates) to support a successful NIH R01 application that proposes a multi-site clinical trial to evaluate efficacy. This trial may provide further justification that improved access to effective services is cost-effective and reduces the financial and social burden of HIV, STIs, and unintended pregnancy in the U.S.

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APPENDIX 1.

STUDY SCHEMA

FORMATIVE GROUP

PROCEDURE	Part 1 BASELINE Survey	Part 2 INTERVENTION	Part 3 POST-INTERVENTION Survey
Adolescents who meet Part 1 Base-line Inclusion criteria and have no exclusion criteria will be approached and invited to participate in the research study. Research Study Information FORMATIVE GROUP given to parent	X		
Obtain permission to interview teen alone	X		
Obtain verbal consent for FORMATIVE GROUP baseline screening from teen	X		
Teen completes computerized baseline screening survey	X		
Teen meets Part 2 INTERVENTION inclusion criteria	X		
FORMATIVE GROUP Written Consent Obtained		X	
Meets with Health Educator for Part 2 INTERVENTION including Health services offered and		X	
Post-intervention Survey to assess satisfaction with intervention			X

RANDOMIZED CONTROL TRIAL STUDY SCHEMA

PROCEDURE	At Initial ED Visit			3 weeks post ED visit	2 and 4 months post ED visit	6 months post ED visit
	BASELINE Survey	INTERVENTION	Post INTERVENTION Survey			
Adolescents who meet Part 1 Base-line Inclusion criteria and have no exclusion criteria will be approached and invited to participate in the research study. RCT Information given to parent	X					
Obtain permission to interview teen alone	X					
Obtain verbal consent for RCT baseline screening from teen	X					
Teen completes computerized baseline screening survey	X					
Teen meets Part 2 INTERVENTION inclusion criteria	X					
Teen is randomized to either the CONTROL ARM or the INTERVENTION ARM and consented with the appropriate consent form		X				
Meets with Health Educator for Part 2 INTERVENTION		X				
Teen takes post-intervention satisfaction survey			X			
Health Educator fills out post intervention assessment			X			
Medical Chart reviewed for health services utilization by study team				X		
Teen completes brief survey on: sex health behaviors, healthcare utilization, readiness for safer sex					X	X
Assessment of new occurrence of STD or HIV During survey						X