Title: Community-Based, Point-of-Care Sexually Transmitted Infection Screening

Among High-Risk Adolescents in Los Angeles and New Orleans: Study Protocol,

Adolescent Medicine Trials Network

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Abstract

Background: Sexually transmitted infection (STI) rates are increasing in the United States, with approximately half of new infections occurring among adolescents age 15-24 years. Gay, bisexual, and transgender youth (GBTY), homeless youth, and youth with histories of drug use, mental health disorders, and incarceration are all at uniquely high risk for STIs. However, these adolescents often lack access to sexual health services. In this study, we are using point-of-care STI tests in community-based settings to screen for and treat STIs in adolescents.

Methods: We are recruiting 1500 HIV-uninfected youth and 220 HIV-infected youth from homeless shelters, GBTY organizations, and community health centers in Los Angeles, California and New Orleans, Louisiana. Study participants receive STI screening every 4 months for 24 months. STI screening includes rapid HIV, syphilis, Chlamydia trachomatis (CT), Neisseria gonorrhoeae (NG), and Hepatitis C Virus testing. Trained paraprofessionals conduct all STI testing. When a participant screens positive for an STI, they are either linked to a partner medical clinic or provided with same-day antibiotic therapy and expedited partner therapy. We monitor STI prevalence among study participants, as well as point-of-care test performance, linkage-to-care, and treatment outcomes.

Discussion: As STI rates continue to rise, it is important to improve access to screening and treatment services, particularly for high-risk adolescents. In this study, we aim to evaluate the use of point-of-care STI diagnostic tests in community-based organizations. We hope to determine the prevalence of STIs among those adolescents and evaluate the effectiveness of community-based STI screening programs.
47**Trial registration:** ClinicalTrials.gov registration #NCT03134833, registered April 28, 2017.

49**Key Words:** sexually transmitted infections, adolescents, point-of-care testing
There are approximately 20 million new sexually transmitted infections (STIs) every year in the United States. Half of those infections occur among adolescents age 15-324 years [1]. STI rates have been steadily increasing over the past few years, with adolescent rates of *Chlamydia trachomatis* (CT) infection, *Neisseria gonorrhoeae* (NG) infection, and syphilis infection all on the rise (Figure 1) [2].

**Figure 1: Chlamydia trachomatis** (CT) and *Neisseria gonorrhoeae* (NG) Infection Rates Among Adolescents from 2007-2016 [2, 3]

Adolescents are at particularly high risk for STIs due to a combination of behavioral, biological, and social factors. Behaviorally, adolescents are more likely to engage in higher-risk sexual behaviors such as concurrent partners or sex without a condom. Biologically, adolescent females are often more susceptible to contracting an
infection if exposed [2, 4]. Socially, adolescents often lack access to sexual health services or do not pursue STI testing due to confidentiality concerns [5].

STI prevalence is highest in the southern and western United States, with black and Latino adolescents at particularly high risk [2]. Social and geographic differences in STI prevalence are likely due to disparate access to sexual health services [6]. Gay, bisexual, and transgender youth (GBTY) are at an increased risk for STIs due to a combination of risk factors, such as condomless sex, concurrent partners, and sex with older partners [2]. Their behaviors reflect that being GBTY may be associated with parental rejection, stigma, discrimination from peers, and increased stress associated with being a member of a minority, whether that minority status comes from race, ethnicity, socioeconomic status, or sexual orientation. Finally, several studies have shown that homelessness, history of incarceration, and illicit drug use are also associated with increased STI risk in adolescents [7-9].

It is critical to diagnose and treat adolescent STIs for a number of reasons. Left untreated, many STIs can lead to long-term health consequences. Bacterial STIs such as CT and NG may lead to reproductive system damage, while syphilis can cause serious neurological damage [10-12]. Viral STIs such as human papillomavirus, herpes simplex virus, and hepatitis C virus can cause cancer, genital blisters, and liver failure, respectively [13-15]. Furthermore, STIs increase the risk of acquiring human immunodeficiency virus (HIV) infection three-to-five fold [16].

Fortunately, diagnostic tests are available for many STIs. Specifically, rapid diagnostic tests create a new opportunity to screen for and treat STIs in community-based settings previously unequipped to offer testing services [17-19]. As those tests become
more readily available, it is important to understand their effectiveness in diagnosing and treating STIs in high-risk adolescent populations.

In this component of the Comprehensive Adolescent Research and Engagement Studies (CARES), part of the Adolescent Medicine Trials Network for HIV/AIDS Interventions Research Program Grant (NIH grant U19HD089886), we aim to evaluate the use of rapid STI testing among adolescents at community-based organizations in Los Angeles, CA and New Orleans, LA. Fifteen hundred high-risk HIV-uninfected youth and 220 HIV-infected youth will receive rapid STI testing every four months over the course of two years. We will monitor STI prevalence, test performance, linkage to care, and treatment outcomes.

**Methods**

**Objectives**

We are conducting rapid HIV, CT, NG, syphilis, and hepatitis C virus (HCV) testing among adolescents age 15-24 years at community-based organizations in Los Angeles and New Orleans. Our partner community-based organizations cater to GBTY, homeless youth, youth with a history of mental health disorders, and youth with a history of incarceration. Study participants receive STI testing at 4-month intervals for 24 months, totaling one baseline visit and six follow up visits. When a participant receives a positive STI test result, they are linked to care at a nearby medical clinic and/or provided with antibiotic treatment by the interviewing staff. We hypothesize that by providing rapid STI testing among high-risk adolescent populations, we will find a high prevalence of STIs. We also expect that by providing same-day testing results, we will be able to
provide better linkage to care and treatment than with traditional lab-based testing. For objectives of other components of the ATN CARES study, refer to other ATN CARES protocol papers [20-24].

Research ethics and approval

The study protocol has been approved by the Institutional Review Board of the University of California Los Angeles (UCLA IRB #16-001674-AM-00006). Any protocol deviations or indications of adverse events are reported to the Institutional Review Board.

STI tests

Rapid STI tests were selected according to performance, availability, and cost. Sensitivity and specificity values of each test are shown in Table 1.

Table 1: Sensitivities and Specificities of STI Rapid Diagnostic Tests [25-29]

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
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<tbody>
<tr>
<td>Determine HIV-1/2 Ag/Ab Combo</td>
<td>100%</td>
<td>99.75%</td>
</tr>
<tr>
<td>Xpert HIV-1 Qual</td>
<td>98.7%</td>
<td>100%</td>
</tr>
<tr>
<td>Syphilis Health Check</td>
<td>71.4%</td>
<td>91.5%</td>
</tr>
<tr>
<td>HCV Rapid Antibody Test</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Xpert CT/NG Assay</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Vaginal swabs</td>
<td>Urine</td>
</tr>
<tr>
<td>CT</td>
<td>99.5%</td>
<td>100%</td>
</tr>
<tr>
<td>NG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CT</td>
<td>99.1%</td>
<td>99.9%</td>
</tr>
<tr>
<td>NG</td>
<td></td>
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</tbody>
</table>

HIV antigen and antibody screening is done using the Determine HIV-1/2 Ag/Ab Combo test (Alere Inc., Waltham, MA) (Figure 2). The test is a point-of-care lateral flow strip that detects both HIV-1/2 antibodies and the HIV-1 p24 antigen using 50 microliters
of fingerstick whole blood. The window period is 12-26 days, and results are ready in 20-
15040 minutes. The test is Clinical Laboratory Improvement Amendments (CLIA) waived
and FDA approved [25, 30].

153Figure 2: Determine HIV-1/2 Ag/Ab Combo test [31]

HIV RNA and DNA screening is performed with the Xpert HIV-1 Qual test
(Cepheid, Sunnyvale, CA) (Figure 3). The test is a point-of-care qualitative in vitro HIV
test, detecting HIV-1 RNA and DNA. The HIV-1 Qual test requires 100 microliters of
whole blood, and results are available in 90 minutes [26]. The test is approved for use in
the European Union and undergoing the approval process with the FDA. Our study is the
first in the United States to use the test, and results are available as research use only.
This test is done to detect acute HIV infections that may not be detected with the Alere
HIV test.

164Figure 3: GeneXpert machine used for HIV-1 Qual and CT/NG tests [32]

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Syphilis screening is done using the Syphilis Health Check, a rapid point-of-care treponemal antibody test (Diagnostics Direct, Cape May Court House, NJ) (Figure 4). The test uses 50 microliters of whole blood, and results are available in 10 minutes. The Syphilis Health Check is the only FDA-approved rapid syphilis test [27].

**Figure 4: Syphilis Health Check test [33]**

HCV screening is done with the HCV Rapid Antibody Test (OraSure Technologies, Bethlehem, PA), a rapid point-of-care assay used for the detection of
antibodies to the hepatitis C virus (Figure 5). The test uses whole blood and results can be read in 20-40 minutes. The test is CLIA-waived and FDA approved [28].

**Figure 5: HCV Rapid Antibody Test [34]**

Finally, CT/NG screening is performed using the Xpert CT/NG Assay (Cepheid, Sunnyvale, CA) (Figure 3). The test is a qualitative in vitro real-time PCR test for the detection of CT and NG. Results are available in 90 minutes [29]. The test is FDA approved using urine samples and vaginal swabs. However, it has also been verified in accordance with CLIA using pharyngeal and rectal swabs [35]. Male participants self-collect pharyngeal and rectal swabs as well as a urine sample, while female participants self-collect pharyngeal, rectal, and vaginal swabs.

**Training**

Interviewing staff conducts all STI and HIV rapid testing at community-based recruitment sites. Interviewers are typically BA level paraprofessionals with little prior experience related to rapid diagnostic testing. Some have previously received phlebotomy...
training, but most receive phlebotomy training upon hiring. Interviewers receive and are certified with state-specific HIV counselor training. HIV counselor training includes training on finger pricking, conducting different types of rapid HIV tests, interpreting results, and providing counseling regarding safe sex practices. Specific trainings were also coordinated in Los Angeles and New Orleans for each diagnostic test. Trainings were conducted by the respective diagnostic test companies (Alere, Cepheid, Diagnostics Direct, and Orasure). Interviewers were evaluated on their ability to properly collect finger prick blood and on their ability to correctly interpret results. Repeat diagnostic test trainings are conducted every six months to ensure interviewers continue to correctly perform tests. A binder with step-by-step test instructions is at every site in case any questions arise.

Interviewers are also trained on how to instruct participants to self-collect rectal swabs, pharyngeal swabs, vaginal swabs and/or a urine sample. For rectal swabs, an image is used to show the acceptable level of fecal contamination on the swab (Figure 6).

**Figure 6:** Instructions for self-collected rectal swabs

![Instructions for self-collected rectal swabs](image)

Fleshlite (Austin, Texas) models are used to demonstrate how to self-collect vaginal and rectal swabs (Figures 7 and 8), while a mirror is used to locate the tonsils and
demonstrate how to self-collect a pharyngeal swab. The figure, Fleshlite models, and mirror are used by the interviewer when instructing a participant about how to self-collect the specimen.

Finally, interviewers are trained on how to administer treatment for CT and NG infections. The antibiotics are prescribed by a physician, and interviewers are trained by the physician on how to properly deliver antibiotic therapy. Training includes information about antibiotics mechanisms, pharmacokinetics, potential adverse effects, partner therapy, retesting, and STI counseling. Interviewers practiced providing treatment using sample scenarios to demonstrate competence.
Testing flow

While HIV, CT, NG, and syphilis testing is performed at every recruitment site, HCV testing is only performed at sites with populations at higher risk of HCV (history of incarceration or drug use). Every study participant receives every STI test unless they specifically choose to opt out. Opting out does not affect eligibility or reimbursement.

At baseline, the rapid HIV test is done as part of the eligibility screening to determine if the participant is HIV-infected or uninfected. If eligible for the study, the participant is enrolled and receives the additional STI testing. An interviewer with phlebotomy certification draws blood, which is then used for the HIV RNA/DNA test, the syphilis test, and the HCV test at certain sites. The participant self-collects their own urine sample and / or pharyngeal, rectal, and vaginal swabs. Clients are encouraged to stay until their test results are available.

Appointments occur at four-month intervals for two years. However, if a patient reports potential STI exposure or STI symptoms, they will be invited for testing at any point during the study.

Linkage to care, treatment, and partner management

Participants receive their test results on the same-day they are tested. Whenever possible, they are told the results in person. If the participant needs to leave their appointment before their results are available, the interviewer asks the participant how they would like to receive results, and then communicates results with them through phone call, text, or email. When a patient receives a positive test result, they are either
referred to a partner medical clinic or their primary care provider to receive treatment, or
they are provided with treatment by the interviewing staff. All partner medical clinics
agreed to and signed an STI treatment protocol that is in accordance with CDC
recommendations.

If the participant elects to seek treatment at a clinic, the interviewer works with
the participant to find a clinic that is geographically convenient, and the study organizes
free transport to the clinic via the Uber application. Interviewers counsel participants on
the importance of partner treatment and safe sex practices. They also follow up with
study participants to ensure they were able to receive treatment, and study staff obtain
records of treatment from the clinic.

For CT and NG infections, participants can receive same-day treatment from the
interviewing staff. The interviewers treat vaginal, urethral, and pharyngeal CT infections
with 1 gm oral azithromycin [1]. They treat rectal CT infections with 100 mg oral
doxycycline twice daily x 7 days, as evidence shows doxycycline is more effective than
azithromycin in treating rectal CT [37-40]. NG infection, while often treated with an
injection, is treated with 1 gr oral azithromycin and 400 mg oral cefixime [1]. Concurrent
CT and NG infections are treated according to the type of CT infection. If there is a
vaginal, urethral, or pharyngeal CT infection in addition to an NG infection, treatment is
1 gr oral azithromycin and 400 mg oral cefixime. If there is a rectal CT infection in
addition to an NG infection, treatment is 100 mg oral doxycycline twice daily x 7 days
and 400 mg oral cefixime.

Treatment packs are pre-packaged and include antibiotic instructions, antibiotics,
physician contact information, water, and a snack. Treatment packs are available at every
We also offer participants with a positive CT and/or NG result up to 10 expedited partner therapy packets according to the number of partners reported in the past 90 days [41].

**Quality Control**

STI prevalence is monitored by the study team to ensure that prevalence falls within the expected range. Monthly quality control testing is performed at every testing site to confirm that all tests are functioning properly. Quality control testing is also performed whenever a new interviewer is conducting the tests, a new test lot number is received, or if the storage temperature falls outside of the recommended range.

**Data collection and analysis**

STI lab results are recorded on a paper lab form as well as through CommCare, a mobile data collection platform created by Dimagi (Cambridge, MA). Documentation of STI treatment is obtained from medical clinics. Using those data, we will evaluate STI prevalence, risk factors, and HIV seroconversion rates throughout the study period. We will also evaluate successful linkage to care and treatment of positive STI cases.

**Moving forward**

At the time of manuscript submission, we are in the process of making one change to our study protocol. Due to the high prevalence of a history of syphilis in our study population and the low specificity of the Syphilis Health Check, a participant with
A positive Syphilis Health Check result requires additional laboratory testing. Therefore, we will obtain rapid plasma reagin (RPR) titers and treponema pallidum particle agglutination (TP-PA) testing when a participant has a reactive Syphilis Health Check result. RPR and TP-PA tests will be performed through Quest Diagnostics. We anticipate that this change will significantly improve our ability to properly diagnose syphilis infections.

Discussion

As STI prevalence in the United States continues to rise, it is critical to improve access to STI screening and treatment, particularly among our country’s highest risk populations. In this study, we use point-of-care rapid diagnostic STI tests to screen adolescents for HIV, CT/NG, syphilis, and HCV. We are recruiting and enrolling participants at local community-based organizations in Los Angeles and New Orleans that cater to homeless youth and GBTY as well as youth with histories of drug use, mental health disorders, and incarceration. By targeting that traditionally tough-to-reach, high-risk group, we hope to determine the prevalence of STIs in the population and demonstrate the effectiveness of rapid STI testing programs in community-based settings. More broadly, we hope to help link those adolescents to health care and sexual health services that fit their specific needs.

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Conflicts of Interest

The authors declare no conflicts of interest.

References


371https://www.cdc.gov/std/herpes/stdfact-herpes.htm


374at: http://www.webcitation.org/6yklx8XuJ

37516. Galvin SR, Cohen MS. The role of sexually transmitted diseases in HIV


37717. Herbst de Cortina S, Bristow CC, Joseph Davey D, Klausner JD. A systematic
378review of point of care testing for Chlamydia trachomatis, Neisseria gonorrhoeae,
379and Trichomonas vaginalis. Infect Dis Obstet Gynecol 2016;

3802016:4386127. PMID: 27313440

38118. Kelly H, et al. Systematic reviews of point-of-care tests for the diagnosis of
383PMID: 29223960

38419. Guy RJ, et al. Performance and operational characteristics of point-of-care tests for
385the diagnosis of urogenital gonococcal infections. Sex Transm Infect 93.S4 (2017): S16-
386S21. PMID: 29223959

388Adolescent Trials Network 147 Comprehensive Adolescent Research and Engagement

39021. Rotheram-Borus, et al. (In print). Moving Toward a Cure: Integrating the Care and
391Prevention Continua to Stop HIV in the United States for Adolescents and Young Adults.
392J Med Internet Res.
39322. Swendeman D, et al. (In print). What strategies are enough to protect youth from HIV: Automated messaging, weekly behavioral monitoring, peer social media networks, or interpersonal coaching? J Med Internet Res.

39623. Arnold E, et al. (In print). Stepped Care Intervention to Suppress Viral Load Among Youth Living with HIV. J Med Internet Res.


40125. Alere Medical Co., Ltd. Determine™ HIV-1/2 Ag/Ab Combo.


403 Archived at: http://www.webcitation.org/6ykmXqSPf


40627. Diagnostics Direct, LLC. Syphilis Health Check.


41028. OraQuick. HCV Rapid Antibody Test.


412 Archived at: http://www.webcitation.org/6ykmuMT81


PMID: 16918168


39. Hathorn E, Opie C, Goold P. What is the appropriate treatment for the
management of rectal Chlamydia trachomatis in men and women? Sex
Transm Infect 2012; 88:352–354. PMID: 22517887

and doxycycline for the treatment of rectal chlamydial infection: a retrospective
cohort study. Sex Transm Dis 2014; 41:79–85. PMID: 24413484

management of sexually transmitted diseases. Centers for Disease Control
Archived at: http://www.webcitation.org/6ykmQCl8o