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Impact of At-Home Versus Clinic-Based Services on Chlamydia and Gonorrhea Treatment Rates

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Abstract

Background: Chlamydia and gonorrhea are the 2 most commonly reported sexually transmitted infections (STIs) in the United States. Additionally, the number of reported cases is lower than the estimated total number of cases due to a variety of factors including: unawareness of infection, lack of symptoms, social stigma, and the fact that chlamydia and gonorrhea are still not routinely screened for in many clinical settings. Past studies suggest that individuals prefer at-home sampling and would even get tested more often if STI self-collection were available. Numerous studies investigating the effectiveness, screening uptake, and safety of at-home sampling have been performed. However, the question of treatment rates in relation to at-home sampling remains. Can the use of at-home STI screening for chlamydia and gonorrhea lead to increased rates of treatment compared to traditional STI screening methods in sexually active adults?

Methods: An extensive search was conducted using MEDLINE-PubMed, MEDLINE-Ovid, and TRIP with the keywords: ((home OR "internet access*" OR "specimen handling" OR "self-sampling") AND (screen* OR test*) AND (gonorrhea OR chlamydia) AND (treatment OR therapy)). The eligibility criterion was applied to the results and duplications were removed. References of selected studies were considered. Quality of included studies was assessed using GRADE.

Results: Two randomized controlled trials (RCTs) met the inclusion and exclusion criteria and were included in this systematic review. The first study recruited 2072 participants who were then randomly allocated to receive a text message with a link containing instructions to either complete at home screening (intervention) or clinic-based screening (control). The proportion of participants treated was 1.1% in the intervention group versus 0.7% in the control group. The second study conducted a population-based trial that included all people between ages 18-25. The intervention group, 10 000 individuals, received information on chlamydia and a mail-back urine sampling kit by post. The control group, 31 519 individuals, received nothing by mail and was not made aware of the study. The intervention led to 2.5 times more individuals receiving treatment.

Conclusion: At-home chlamydia and gonorrhea sampling may lead to increased rates of treatment.

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Impact of At-Home Versus Clinic-Based Services on Chlamydia and Gonorrhea Treatment Rates

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Biography

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To *my parents*: Thank you for the huckleberries and for always being a phone call away.

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List of Abbreviations

TRIP…Turning Research into Practice
RCT…Randomized Controlled Trial
GRADE… Grading Recommendations Assessment, Development and Evaluation
STD… Sexually Transmitted Diseases
CDC… Center for Disease Control and Prevention
PID… Pelvic Inflammatory Disease
USPSTF… United States Preventive Services Task Force
MSM… Men who have Sex with Men

Impact of At-Home Versus Clinic-Based Services on Chlamydia and Gonorrhea Treatment Rates

BACKGROUND

Chlamydia and gonorrhea are the most commonly reported sexually transmitted infections (STIs) in the United States with an estimated 2.86 million cases of chlamydia and 820 000 cases of gonorrhea occurring annually.[1] According to the Center for Disease Control and Prevention (CDC), "the number of reported cases is lower than the estimated total number because infected people are often unaware of, and do not seek treatment for, their infections and because screening for chlamydia is still not routine in many clinical settings."[1] Estimates of prevalence are further complicated by the fact that the majority of affected people are asymptomatic.[2] Research by Banerjee et al[3] suggests that "patients experiencing symptoms may have reservations about coming to sexual health clinics due to social stigma, work and family life restraints."

If left untreated, chlamydia and gonorrhea can cause serious complications. The CDC warns that, "untreated, about 10-15% of women with chlamydia will develop pelvic inflammatory disease (PID). PID and "silent" infection in the upper genital tract may cause permanent damage to the fallopian tubes, uterus, and surrounding tissues, which can lead to infertility and/or an increased risk of ectopic pregnancy."[1] Additional complications can include facilitation of HIV infection. In males, untreated infection can increase risk of epididymitis and prostatitis.[2]

"The current strategy of testing in the health care system includes clinically indicated (symptomatic) testing, partner tracing, and opportunistic screening." [4] This is the "clinic-based" or "traditional" model. The United States Preventive Services Task force (USPSTF) only recommends screening for chlamydia in sexually active women age 24 years and younger, and in older women who are at increased risk for infection. In men, the USPSTF states that current evidence is insufficient to assess the balance of benefits and harms of screening. [5]

With the advent of new technology, self-sampling and self-testing modalities are becoming increasingly available to deliver much needed sexual health interventions. Harding-Esch et al[6] makes an important distinction in that "self-testing differs from self-sampling". "Self-testing enables individuals to take a sample, perform a test, and interpret the results by themselves, without the need of a laboratory." Self-sampling allows patients to order a test kit from a virtual service (via an app or website), collect their own samples, return said samples to a laboratory, and be notified of their results by text message or telephone.[6] Self-sampling/self-collection was the modality investigated in this systematic review.

Recent studies[7] have indicated that some patient demographics prefer at-home sampling. Qualitative data collected by Gaydos et al[7] suggests that individuals who have undergone home-collected sampling prefer the simplicity, security, and privacy of self-collected specimens. In addition, "when questioned about preference; 94% of women answered that they would get tested more often for an STI if self-collection of a vaginal swab was available."[8] Numerous studies investigating the effectiveness, screening uptake, and safety of at-home sampling have been performed.[9]

Yet, there are still gaps in the research. These digital technologies, while offering at-home self-sampling, often require participants with positive test results to seek out a sexual health clinic for treatment. It is possible that these patients are lost to follow up. Few studies have addressed treatment rates as a primary outcome when comparing at-home sampling to traditional methods for STI screening. Can the use of at-home STI screening for chlamydia and gonorrhea lead to increased rates of treatment compared to traditional STI screening methods for sexually active adults?

METHODS

An extensive literature review was conducted using MEDLINE - PubMed, Evidence-Based Medicine Reviews Multifile-OVID, and the Turning Research into Practice (TRIP) databases. The following terms were used in each database to yield a comprehensive search: ((home OR "internet access*" OR "specimen handling" OR "self sampling") AND (screen* OR test*) AND (gonorrhea OR chlamydia) AND (treatment OR therapy)). The references of included articles were also reviewed. Inclusion criteria: studies conducted on humans within the last 10 years, randomized controlled trials, and studies published in the English language. Exclusion criteria: studies using at-home testing for follow up/retesting of previously positive patients instead of as the initial screening tool. Quality of the included studies was assessed using the Grading Recommendations Assessment, Development and Evaluation (GRADE) Working Group guidelines.[10]

RESULTS

An initial search of 3 databases yielded 177 articles for review. After 22 duplicates were removed the records were screened using eligibility criteria. The bibliographies of eligible articles were reviewed, but did not yield any additional studies. Two randomized controlled trials[11],[4] were ultimately considered for this review. See Figure 1 for a search summary. See Table 1 for the quality of reviewed studies.

Study 1 - Wilson et al:

This randomized, single blind, controlled trial[11] was published in 2017 and took place in London. The goals of the study were to assess the effectiveness of an e-STI testing and results service on testing uptake and number of STI cases diagnosed. A secondary outcome of the study, and the outcome evaluated in this systematic review, was the proportion of participants prescribed treatment for an STI.[11]

Researchers recruited 2072 participants, ages 16-30 years, in the boroughs of Lambeth and Southwark. Both face-to-face and online recruitment strategies were employed. Promotional locations included universities, market stalls, barbershops, bars, and nightclubs and via Facebook, Twitter, and Grindr (a dating application for gay and bisexual men). The study was promoted in conjunction with a health promotion message, to motivate participants to join the trial and consider taking an STI test. Participants were sent a £10 cash incentive on submission of self-reported data.[11]

After recruitment, research assistants assessed eligibility based upon participant willingness to take an STI test, access to the Internet, and sexual history of at least one partner in the last 12 months. An independent computer-based randomization program allocated participants to the intervention (n = 1031) or control groups (n = 1032) and

participants were sent text messages with differing URLs depending upon their allocation. Laboratory and research staff members were also blinded.[11]

The URL of the intervention group directed patients to a website that offered free postal self-sampling test kits for chlamydia, gonorrhea, HIV, and syphilis. For chlamydia and gonorrhea, women were sent vaginal swabs and men were sent a container for first-catch urine samples. Test kits for men who have sex with men (MSM) also contained swabs to take pharyngeal and rectal samples. Tests kits included pictorial leaflets with guidance on how to collect the specimens to ensure accuracy of collection. Test results were relayed via text. Patients with positive results were directed to local clinics for confirmatory testing and treatment as necessary.[11]

Participants in the control group were sent the URL of a website with the contact details, and locations of local sexual health clinics. These clinics provided care via walk-in services free of charge.[11]

Researchers collected self-report data about STI diagnosis and treatment, and later objectively verified this information in the patient health databases. A statistical analysis determined that the proportion of participants treated was 1.1% in the intervention group versus 0.7% in the control group (RR 1.72, 95% CI 0.71 to 4.16, $P = 0.231$). Of note, researchers were unable to recruit to target and therefore lacked power.[11]

Study 2 - Klovstat et al:

This population based randomized controlled trial[4] was published in 2013 and took place in Norway. The goals of the study were to determine whether screening with information and home sampling resulted in more young people getting tested, diagnosed, and treated for chlamydia in the three months following the intervention compared to the

current strategy of testing in the health care system. Treatment rates are the primary outcome addressed in this systematic review.[4]

A third party randomized everyone between the ages of 18-25 that were listed in the population register in Rogaland county, Norway. Unique personal identity numbers generated by the national population register were used instead of patient names. The total population at this time was 41 793 people. 10 000 people were randomized to the intervention group. Individuals in this group were aware of the study and their group assignment. The control group received no information about the study. Laboratory personnel were aware that mailed urine containers came from participants in the intervention group.[4]

"People assigned to the intervention group (10 000) received a mail package at their home address consisting of: information on the importance of testing and treating chlamydia, an invitation to take a home test free of charge, a urine container, a water-tight plastic container, instructions on how to obtain a first void urine sample, a prepaid return envelope, and a questionnaire (socio-demographic details, sexual behavior, symptoms (discharge, endocervical bleeding, pelvic pain, urethral itching, dysuria) and history of STI)." Participants were instructed to mail the urine samples by post in the provided container directly to the laboratory within three months after receiving the invitation. No reminders were given. The intervention group was divided into four subgroups according to municipality of residence to avoid overloading the lab with samples. Letters containing the test result and a contact phone number for support was provided to all participants from the diagnosing laboratory. If the test result was positive, the participant was requested to visit a clinic for treatment and partner tracing at no cost.[4]

"Participants assigned to the control group (31 519) received no intervention and were not informed about the trial and thus continued with the current strategy of testing in the health care system. Samples obtained in clinics included either cervical or urethral swabs or first void urine samples. Patients with positive test results were, as per current routines, contacted by a health professional for treatment and partner tracing. Test and treatment services were free of charge. The control group was also followed for 3 months and divided into four subgroups according to municipality. An observation period of three months was kept consistent between the control and intervention groups.[4]

A participant was defined as having been treated for chlamydia if they had filled a prescription for a drug against chlamydia within 30 days following a positive test result. Information was obtained from the Norwegian Prescription Database (NorPD). The study dataset was encrypted, made pseudonymous (by a third party) and merged with NorPD. Pseudonyms were removed prior to analysis and no personal identifiers were available to researchers. Overall, the intervention led to 2.5 (CI 1.9-3.4) times as many individuals receiving treatment for chlamydia compared to the control during the study period.[4]

DISCUSSION

Both studies[4,11] included in this review show that the use of at-home STI screening for chlamydia and gonorrhea lead to increased rates of treatment in the intervention group compared to traditional STI screening methods in sexually active adults. This information is clinically relevant because it suggests that at-home or internet accessed methods of screening may help decrease the overall prevalence of gonorrhea and chlamydia as well as the potential complications from these infections. A summary

of the following information and a description of the overall quality of each study can be seen in Table 1.

Limitations

Potential bias: Wilson et al[11] addressed the potential for performance bias and states "participants were informed at the time of recruitment that they would be invited via text to use one type of sexual health service. The types were not specified outright." The potential for self-reporting bias was present but addressed with objective verification of electronic health records. The incentive bias was likewise addressed here: "Participants were instructed upon enrollment that the £10 cash incentive was for completing follow up. Given that both control and intervention groups were informed, the impact for incentivisation should be non-differential and would not explain the result."[11]

Klovstad et al[4] risked potential for detection bias because laboratory personnel were not blinded to the intervention group. The sample kits mailed to the lab for testing were the only at-home kits received throughout the study duration. The randomization also produced an imbalance between the groups in regards to municipality of residence. However, according to the study "adjustment for municipality in the analysis had minimal effects on the risk ratio estimates." Klovstad et al[4] also disclosed the potential for contamination in this statement: "with such a large intervention affecting a fourth of the population in the target age group, there is bound to have been some "leakage" of information to the control group."

Methodological limitations: Wilson et al[11] used community and social media based recruitment strategies then text messaging to deliver screening options to the intervention and control groups. Klovstad et al[4] attempted to "recruit" every sexually

active adult within a target age range and mailed testing kits to the intervention group only. These different delivery methods for promoting at-home sampling cannot be compared directly.

In addition, both studies[4,11] used a health promotion message in their intervention groups to motivate participants to join the trial and consider taking an STI test. It is impossible to determine whether the participants completed testing due to the intervention or due to the additional health education received. To further complicate causality, Wilson et al[11] incentivized their participants and all were free to use any other sexual health services or interventions during the trial period.

Wilson et al[11] included chlamydia, gonorrhea, HIV, and syphilis in their research. Study 2 only addressed chlamydia. For the purposes of this systematic review, the results of Klovstad et al[4] cannot be extended to include rates of gonorrhea treatment.

As mentioned previously, Wilson et al[11] researchers fell short of their recruitment target of 3000 participants. As a result, the study lacked power to detect differences in STI cases treated. Participants were free to use any other services or intervention during the study period, which introduced potential for contamination.

Suggestions for Future Research

Both studies[4,11] showed that the proportion of patients treated in the intervention group was greater than in the control. However, both studies required participants to seek out a traditional clinic for treatment of their positive test result. Wilson et al[11] recognizes that “it is plausible that whilst the intervention removed the barrier of having to attend a clinical service for testing in both studies, the subsequent requirement to attend clinic for

treatment may have deterred some participants." Further investigation and research is needed to determine this connection.

Another important factor requiring exploration is a cost analysis of home-based sampling methods/electronically accessed sexual health care compared to traditional clinic methods. In both studies, services for at-home and control groups were free. This is not an accurate depiction of how care is accessed in many other health care systems. Further research is needed to determine the cost effectiveness of these modalities before results can be applied to other countries like the United States.

CONCLUSION

At-home chlamydia and gonorrhea sampling may lead to increased rates of STI treatment. Both studies included in this review showed that the option of at-home sampling lead to increased uptake of screening, and that the proportion of patients treated in the intervention group was greater than in the control. However, both studies required participants to seek out a traditional clinic for treatment of their positive test result. Overall study quality was assessed using GRADE and determined to be "High". Yet, further research is required to determine the overall effectiveness and cost benefit of using digital modalities over traditional methods for STI screening.

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Figure 1: Study Search and Selection

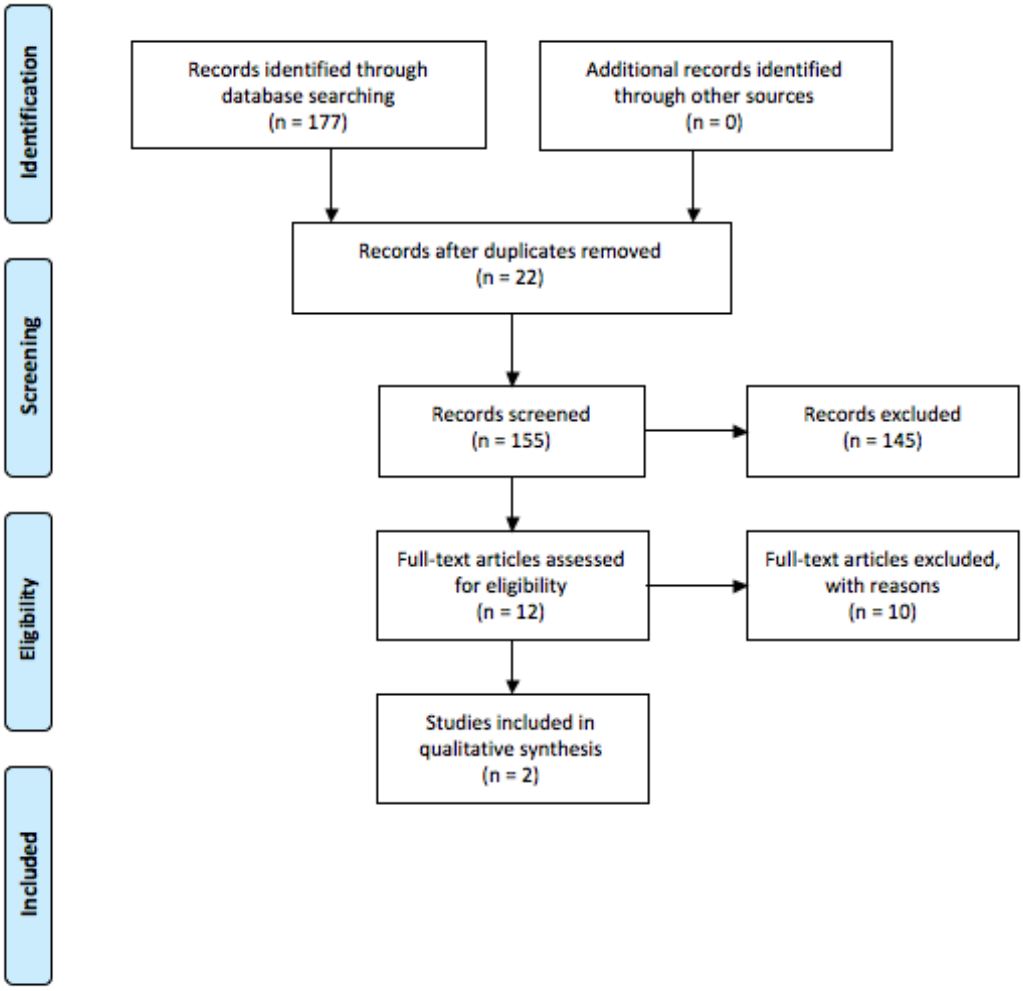

Table 1: Quality Assessment of Reviewed Articles

Study	Design	Downgrade Criteria					Upgrade Criteria	Quality
		Limitations	Indirectness	Inconsistency	Imprecision	Publication bias		
Wilson et al[11]	RCT	Not serious	Not Serious	Not Serious	Not Serious	Unlikely	Large Magnitude of effect RR = 2.5	High
Klovstad et al[4]	RCT	Not Serious	Not Serious	Not Serious	Not Serious	Unlikely	N/A	High