Could Home Sexually Transmitted Infection Specimen Collection With e-Prescription Be a Cost-Effective Strategy for Clinical Trials and Clinical Care?

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Background: Results of a recent demonstration project evaluating feasibility, acceptability, and cost of a Web-based sexually transmitted infection (STI) testing and e-prescription treatment program (eSTI) suggest that this approach could be a feasible alternative to clinic-based testing and treatment, but the results need to be confirmed by a randomized comparative effectiveness trial.

Methods: We modeled a decision tree comparing (1) cost of eSTI screening using a home collection kit and an e-prescription for uncomplicated treatment versus (2) hypothetical costs derived from the literature for referral to standard clinic-based STI screening and treatment. Primary outcome was number of STIs detected. Analyses were conducted from the clinical trial perspective and the health care system perspective.

Results: The eSTI strategy detected 75 infections, and the clinic referral strategy detected 45 infections. Total cost of eSTI was $94,938 ($1266/STI detected) from the clinical trial perspective and $96,088 ($1281/STI detected) from the health care system perspective. Total cost of clinic referral was $87,367 ($1941/STI detected) from the clinical trial perspective and $71,668 ($1593/STI detected) from the health care system perspective.

Conclusions: Results indicate that eSTI will likely be more cost-effective (lower cost/STI detected) than clinic-based STI screening, both in the context of clinical trials and in routine clinical care. Although our results are promising, they are based on a demonstration project and estimates from other small studies. A comparative effectiveness research trial is needed to determine actual cost and impact of the eSTI system on identification and treatment of new infections and prevention of their sequelae.

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Curable sexually transmitted infections (STIs) are prevalent in the United States despite the availability of sensitive and noninvasive diagnostic screening tests.

Untreated *Chlamydia trachomatis* (*CT*) and *Neisseria gonorrhoeae* (*GC*) infections can lead to pelvic inflammatory disease (PID) with sequelae of ectopic pregnancy, infertility, and chronic pelvic pain.[1] Furthermore, prevalent *CT*, *GC*, and *Trichomonas vaginalis* (*TV*) infections all increase an individual's susceptibility to HIV acquisition.[2,3]

Because most STI infections are asymptomatic, many infected individuals are not diagnosed and treated in a timely manner. To expand access to screening services, groups have evaluated the use of home sampling kits that individuals request via the Internet and submit to a laboratory via the US postal service.[4,5] However, these evaluations did not collect longitudinal data to determine the impact on early detection and treatment of infection or include a standard care comparison group.

In 2012 to 2013, we conducted a demonstration project[6] to determine the feasibility of a full-scale trial on home STI sample collection and e-prescriptions and to collect preliminary data on study outcomes. The demonstration project established the potential feasibility and effectiveness of the eSTI system. Using data from the demonstration project, we modeled the potential cost impact that may be seen in a future comparative effectiveness trial of eSTI versus referral to standard clinical care that includes e-prescriptions for treatment in the model.

MATERIALS AND METHODS

Design

We constructed a decision tree (Supplemental Digital Content, http://links.lww.com/OLQ/A95) for a future comparative effectiveness research (CER) trial comparing 2 strategies for enrolling, testing, and treating women for *CT*, *GC*, and *TV* using nucleic acid amplification tests (NAATs): (1) eSTI with participants receiving a home collection kit for STI screening and an e-prescription for treatment versus (2) referral to standard clinic-based STI screening and treatment. The primary outcome was the number of STIs detected, and the secondary outcome was the number of STI tests completed.

In the planned comparative effectiveness trial, 2790 participants would be randomized to either the eSTI arm or the clinic referral arm. This number was chosen as the sample size required to show significant differences between arms given the findings of our demonstration project.[6] To ensure inclusion of low literacy populations, participants would either enroll through the Internet or receive assistance enrolling from community health workers. Those in the clinic referral arm would be directed to a local clinic for STI testing and treatment. To ensure comparability of testing outcomes between the 2 arms, participants in the clinic referral arm would also self-collect specimens in the clinic setting using the same kit

as those in the eSTI arm. Those in the eSTI arm would receive a home collection kit in the mail and would mail their sample to the laboratory for testing. They could access their test results from the eSTI online system or from community health workers by telephone and, if positive and asymptomatic, would have the option to have an electronic prescription sent to a local pharmacy or to receive a referral to a local clinic for treatment. Those with positive results who did not obtain their results within 3 days would be contacted by trial staff and assisted with obtaining treatment.

Our decision tree incorporated costs of screening, result notification, and treatment of positives. The analyses were conducted from 2 perspectives: the clinical trial perspective (CTP), which included only direct medical costs incurred by a clinical trial and the health care system perspective (HSP), which included only direct medical costs incurred by the health care system. Patient costs, such as travel time to the clinic, were not included. Costs were adjusted to 2013 US dollars using the medical care component of the consumer price index. Published literature was also used to estimate probabilities and costs for the referral to standard clinical care arm.

Probabilities

Probability estimates are provided in Table 1. We derived our participant testing rate estimates of 67% for the eSTI arm and 40% for the clinic referral arm as well as the ranges for sensitivity analyses from our primary data[6] and the literature.[5,7,8]

Our STI prevalence estimate was derived from the Centers for Disease Control and Prevention chlamydia surveillance data from family planning clinics for the 3 regions that we plan to include in the future trial: 5.2% in California, 14.1% in Texas, and 8.3% in Maryland.[9] Although the average prevalence in these 3 regions is 9.2%, we cannot be sure that an equal proportion of participants will be recruited from each region. There may be some dilution of STI prevalence if participants who enroll are at lower risk than the overall population from which they are drawn. Therefore, we conservatively estimated an 8% STI prevalence for the potential future trial. We chose to use *CT* prevalence as the primary outcome of interest, as this STI is much more prevalent than *GC* and regional prevalence data for *TV* are not readily available.

Estimates for the proportion of eSTI arm participants obtaining test results online or receiving results from staff were derived from our primary data. As was done in the demonstration study, if a participant randomized to eSTI does not retrieve her positive result online within 3 days, the staff would make 3 telephone calls and send 3 e-mails to her to connect her to care. Infected participants with *CT* or *GC* that are unable to be reached would be referred to Disease Intervention Specialists (DISs) at health departments for assistance with treatment. All 8 of the infected women identified in the demonstration project were treated without DIS assistance. Given the small sample, estimates for the proportion of women who are successfully notified and treated were derived from the literature,[10] and we made the assumption that 10% would require DIS assistance.

It is assumed that all participants with positive results who are randomized to the clinic arm would receive their treatment in a clinic or through public health department DIS field–delivered therapy. However, those with positive *CT* and/or *TV* results who are randomized to eSTI would have the option of treatment in a clinic or eRx, which is an electronic prescription sent to their pharmacy of choice. For pregnant women or those with any symptom suggestive of PID in the eSTI arm, clinic treatment would be recommended. Women with *GC* would be required to receive treatment in clinic because current Centers for Disease Control and Prevention treatment guidelines recommend first-line therapy include ceftriaxone, which must be administered by injection.[11] Based on preliminary data[6] and weighting for expected prevalence of each infection (see Appendix http://links.lww.com/OLQ/A94), we estimated that 64.2% of women would choose eRx.

TABLE 1. Probabilities

Variable	Probability Estimate	Range	Source
Proportion who enroll online (ENROLLONLINE)	92%	88%–95%	Primary data (95% CI)
Proportion who enroll with staff assistance (1 − ENROLLONLINE)	8%	5%–12%	Primary data (95% CI)
STI prevalence (STIPREV)	8%	5%–10%	Ref. [9]
Proportion of participants in eSTI strategy who return kit (KITRETURN)	67%	55%–72%	Primary data[5,7,8]
Proportion of participants in clinic strategy who visit clinic (CLINICVISIT)	40%	32%–48%	Refs. [7,8]
Positive result received by participant in eSTI arm (POSRESULTRECEIVEDeSTI)	100%	95%–100%	Primary data[10]
Receipt of positive result online (RESULTONLINEPOS)	88%	53%–98%	Primary data (95% CI)
Receipt of positive result from study staff (1 − RESULTONLINEPOS)	12%	22%–47%	Primary data (95% CI)
Positive result received by participant in clinic arm (POSRESULTRECEIVEDclinic)	95%	90%–100%	Ref. [10]
Negative result received by participant in eSTI arm (NEGRESULTRECEIVEDeSTI)	91%	85%–95%	Primary data (95% CI)
Proportion of eSTI negative results received online			
If enrolled online (RESULTONLINENEGONLINE)	100%	75%–100%	Assumption
If enrolled with staff (RESULTONLINENEGSTAFF)	86%	49%–97%	Primary data (95% CI)
Proportion of eSTI negative results received from study staff			
If enrolled online (1 − RESULTONLINENEGONLINE)	0%	0%–25%	Assumption
If enrolled with staff (1 − RESULTONLINENEGSTAFF)	14%	3%–51%	Primary data (95% CI)
Negative result received by participant in clinic arm (NEGRESULTRECEIVEDclinic)	60%	14%–91%	Personal communication, Primary data
Receive treatment for positive result			
eSTI arm (RXDeSTI)	99%	90%–100%	Ref. [10]
Clinic arm (RXDclinic)	95%	80%–100%	Ref. [10]
Proportion of women in eSTI arm who receive treatment via eRx (eRx)	64.2%	31%–86%	Primary data (95% CI)
Proportion of women in eSTI arm who receive treatment at clinic (1 − eRx)	35.8%	14%–69%	Primary data (95% CI)
Proportion of women with positive result who require DIS (DIS)	10%	0%–20%	Assumption

CI indicates confidence interval.

Participants who are assigned to the eSTI arm who have negative test results can log in to the Web site to retrieve their result or call the trial hotline. Staff would only assist with providing a negative result if the participant initiated a call to staff. We assumed that approximately 100% of those who enroll online and obtain their negative result would do so online, rather than choosing the telephone option. To be conservative, we estimated a lower bound of 75% for the sensitivity analysis range. In the demonstration study, 1 woman of 7 who enrolled with staff assistance and had a negative test result called staff for her result. The remaining 6 viewed their negative results online. Consequently, we estimated that 14% of those who enroll with staff in the eSTI arm would call staff to obtain their negative result.

We based our estimate for proportion of participants in the clinic arm who receive a negative result on the experience of a home testing program that did not offer online results, but attempted to contact all participants with results (negative as well as positive).[4] In that study, the proportion of women who called in for results before study staff contacted them was approximately 60% (M. R. Barnes, personal communication, July 22, 2013). The range for our estimate was derived from the proportion in our study that enrolled with a staff person and called in for result (14%) and the proportion in our study who obtained their negative result via telephone call or online (91%).[6]

We did not incorporate sensitivity and specificity of the STI tests into the model because both arms will use the same highly sensitive (≥90%) and highly specific (≥99%)[12] diagnostic test, but rather made the assumption that all infections would be detected if the test is completed. The primary goal of this decision analysis was to determine which strategy produces greater test completion and more STI diagnoses regardless of which diagnostic test is used.

Costs

All costs are provided in Table 2 as "per participant" costs in 2013 dollars. Estimates for the Web site server and maintenance costs were supplied by Zerolag and N-Tonic (D. Calebresi, personal communication, February, 8, 2013), the companies that provided these services for the demonstration study.[6] Staff time required to enroll participants was derived from primary data and then multiplied by the Bureau of Labor Statistics hourly wage for a community health worker plus fringe benefits ($23.53).[13,14]

Kit costs and STI test processing costs for the eSTI arm are based on estimates supplied by the Johns Hopkins University (JHU), International STD, Respiratory, and Biothreat Research Laboratory, the laboratory that provided the kits and testing for the demonstration study. The JHU kit and STI test processing cost were also used as a conservative estimate for the clinic referral arm because these costs are lower than the Medicaid reimbursement rates for commercial NAATs (C. A. Gaydos and M. R. Barnes, personal communication, February 1, 2013).[15] The upper limit for the range was based on the Medicaid reimbursement rate for HCPCS 87801: NAAT detection of multiple organisms ($96.49).[15] The lower limit was based on the JHU kit and STI processing cost for *CT* and *GC* testing only ($55; C. A. Gaydos and M. R. Barnes, personal communication, February 1, 2013) plus the Medicaid reimbursement rate for HCPCS 87210: wet mount microscopic examination ($5.87)[15] because most STD clinics still rely on saline microscopic detection for *TV* rather than a NAAT.

The cost of a clinic screening visit for HSP was estimated using Bureau of Labor Statistics hourly wage plus fringe benefits for a clinician (physician assistant or nurse practitioner) for a 30- minute visit.[14,16,17] We used a lower range of 20 minutes and an upper range of 40 minutes for the visit. For CTP, we used the mean Medicaid E&M reimbursement rate for a level 2 initial visit ($59) in the 3 states, where the future comparative effectiveness trial is proposed. The Medicaid reimbursement rate was used as an estimate of what the trial would be expected to reimburse a participating clinic for providing the screening services. The upper end of the range was based on the E&M rate for a level 3 ($85) initial visit, and the lower end was based on the typical public STD clinic charge ($25), where the demonstration project was conducted (V. Levy, personal communication, July, 30, 2014).

Staff time required to provide participants with their positive test results (10 minutes) is based on data from one study participant and from personal experience of one of the authors (F.S.). We estimated that 3 unsuccessful telephone call attempts to notify an infected participant would require 5 minutes and that a telephone call to provide negative test results would require 2 minutes. Staff time to assure treatment of positives or refer to DISs was estimated at 15 minutes. We estimated that DIS involvement in treatment would require 1 hour.[10]

The cost of a clinic treatment visit for the HSP was estimated using clinician salary plus fringe benefits for a 30-minute visit if the participant was screened via eSTI and a 15-minute visit if the participant was screened in the clinic.[14,16,17] We assumed that a return clinic visit for treatment would require less time than an initial visit for treatment. The medication costs to treat *CT*, *TV*, and *GC* were estimated using the wholesale acquisition costs,[18] California formulary pricing,[19] 340B pricing, and the San Mateo Medical Center costs to purchase (G. Horne, personal communication, August 17, 2012). The costs from these 3 sources were averaged and weighted for expected prevalence of each infection (see Appendix http://links.lww.com/OLQ/A94). For the CTP, we incorporated only the costs of assisting participants with obtaining treatment, but not the cost of treatment itself because medication was self-pay in the demonstration project for participants who chose eRx and otherwise was provided through publicly funded clinics.

Analyses

Analyses were conducted using TreeAge Pro decision analysis software (TreeAge Software, Williamstown, MA). Incremental costs and incremental cases of STIs detected were calculated using clinic referral STI screening as the comparator strategy. With few exceptions, incremental cost-effectiveness ratios were not calculated because the clinic strategy was either weakly or strongly dominated by the eSTI strategy for almost all cases. One-way and best-case/worst-case sensitivity analyses were conducted, using ranges presented in Tables 1 and 2, for parameter estimates that were less certain.

RESULTS

Baseline Cost Analysis

Table 3 displays results of the baseline cost analysis. The eSTI strategy detected 75 infections and the Clinic referral strategy detected 45 infections

Health Care System Perspective

The total cost of the eSTI strategy was $96,088 ($1281 per STI detected), and total cost of the clinic referral strategy was $71,668 ($1593 per STI detected).

Clinical Trial Perspective

The total cost of the eSTI strategy was $94,938 ($1266 per STI detected), and total cost of the clinic referral strategy was $87,367 ($1941 per STI detected. Results for the secondary outcome (STI tests completed) are included in Table 3.

TABLE 2. Costs (Per Participant in 2013 Dollars)

Variable	Cost Estimate	Range	Reference
Server and Web site maintenance (WEBCOST)	$2		Personal communication
Staff labor to enroll participants (STAFFENROLLCOST)	14.7 min × $23.53/h = $5.76		Primary data[13,14]
eSTI kit cost (KITCOST)	$15		Personal communication
eSTI testing cost (PROCESSCOST)	$75		Personal communication
Clinic office visit cost (CLINICCOST)			
Clinical trial perspective	$59	$25–$85	Medicaid E&M reimbursement rates, personal communication, and Refs.
Health care perspective	$58.50/h × 30 min = $29.25	$19.50 (20 min)–$39 (40 min)	
Clinic STI test cost (CLINICSTICOST)[14,16.17]			
Clinical trial perspective	$90		Personal communication
Health care perspective	$90	$60.87–$96.49	Personal communication and Ref. [13]
Staff labor to notify positives (PHONERESULTCOSTPOS)	10 min × $23.53/h = $3.92		Planned Parenthood & County STI clinic estimates and Refs. [13,14]
Staff labor to unsuccessfully attempt notification of positives (NOTIFYCOST)	5 min × $23.53/h = $1.96		Assumption[13,14]
Staff labor to notify negatives (PHONERESULTCOSTNEG)	2 min × $23.53/h = $0.78		Assumption[13,14]
Staff labor to assure treatment of positives or refer to DIS (TRACKINGCOST)	15 min × $23.53/h = $5.88		Primary data[13,14]
DIS labor to treat positives (DISCOST)	1 h = $9.98	$4.99–$19.96	Ref. [10]
Medication treatment cost for chlamydia	1 g of azithromycin: $4.63		Refs. [18,19], personal communication
Medication treatment cost for trichomonas	2 g of metronidazole: $1.36		Refs. [18,19], personal communication
Medication treatment cost for gonorrhea	250 mg of ceftriaxone: $2.08 + 1 g of azithromycin: $4.63 = $6.71		Refs. [18,19], personal communication
Average STI treatment medication cost eRx (eRxMED)	$3.81	$1.36*–$5.99†	Appendix
Average STI treatment medication cost clinic (CLINICMED)	$4.97	$1.36*– $8.07‡	Appendix
Clinic visit to treat STI diagnosed in clinic (CLINICTREATCLINIC)	15 min × $58.50/h = $14.62	$9.75–$19.50	Refs. [14,16,17]
Clinic visit to treat STI diagnosed by eSTI (CLINICTREATeSTI)	30 min × $58.50/h = $29.25	$19.50–$39	Refs. [14,16,17]

*Least expensive treatment would be for trichomonas infection.

†Most expensive eRx treatment would be for both *TV* and *CT* infections.

‡Most expensive clinic treatment would be for all 3 infections.

TABLE 3. Cost-Effectiveness Analyses

Primary Outcome: STIs Detected

			Health Care System Perspective		Clinical Trial Perspective	
Scenario	**Strategy**	**STIs Detected**	**Total Costs**	**Cost/STI**	**Total Costs**	**Cost/STI**
A*	eSTI	75	$96,088	$1281	$94,938	$1266
	Clinic	45	$71,668	$1593	$87,367	$1941
B+	eSTI	100	$101,877	$1019	$100,333	$1003
	Clinic	45	$65,521	$1456	$82,286	$1829
C#	eSTI	38	$82,741	$2177*	$82,151	$2161
	Clinic	33	$57,563	$1744	$79,627	$2413

Secondary Outcome: Tests Completed

			Health Care System Perspective		Clinical Trial Perspective	
Scenario	**Strategy**	**Tests Completed**	**Total Costs**	**Cost/Test**	**Total Costs**	**Cost/Test**
A*	eSTI	935	$96,088	$103	$94,938	$102
	Clinic	558	$71,668	$128	$87,367	$157
B+	eSTI	1004	$101,877	$101	$100,333	$100
	Clinic	446	$65,521	$147	$82,286	$184
C#	eSTI	767	$82,741	$108†	$82,151	$107
	Clinic	656	$57,563	$88	$79,627	$121

ICERs were not calculated because the clinic strategy was either weakly or strongly dominated by the eSTI strategy for most cases.

A* base case: prevalence, 8%; kit return, 67%; clinic visit rate, 40%; office visit cost, $29.25 (HSP) and $58.95 (CTP); clinic STI test cost, $90.

B + eSTI best case: prevalence, 10%; kit return, 72%; clinic visit rate, 32%; office visit cost, $39 (HSP) and $85 (CTP); clinic STI test cost, $96.49 (HSP) and $90 (CTP).

C # eSTI worst case: prevalence, 5%; kit return, 55%; clinic visit rate, 47%; office visit cost, $19.50 (HSP) and $25 (CTP); clinic STI test cost, $60.87 (HSP) and $90 (CTP).

* ICER: $5036.

† ICER: $227.

ICER indicates incremental cost-effectiveness ratios.

One-Way Sensitivity Analyses

Table 4 displays results of the 1-way sensitivity analyses.

Proportion in Clinic Referral Strategy Visiting STD Clinic for Testing

For both HSP and CTP, at a clinic visit rate of 32%, the clinic strategy cost less than the eSTI strategy, but detected half as many infections. For HSP, at a clinic visit rate of 48%, the clinic strategy cost less but detected fewer infections than the eSTI strategy. However, for CTP at a clinic visit rate of 48%, the clinic strategy cost more and detected fewer infections than the eSTI strategy.

Proportion of Kits Returned in eSTI Strategy

For HSP at a kit return rate of 55%, eSTI costs more than the clinic strategy, but the cost/STI was lower. For CTP, eSTI costs less and detects more infections than the clinic strategy. At a kit return rate of 72%, for both perspectives, the eSTI strategy cost more than the clinic referral strategy, but the cost/STI was lower.

STD Prevalence

Throughout this range for both perspectives, the eSTI strategy cost less while detecting more infections than the clinic referral strategy. The higher the prevalence, the lower the cost per STD detected.

Clinic Office Visit Cost

Throughout the range of $19.50 to $39 for HSP, the clinic strategy cost less, but the cost/STI was lower for eSTI. For CTP, at an office visit cost of $25, the eSTI strategy cost more than the clinic strategy, whereas at the $85 visit cost, the clinic strategy cost more. Throughout the range, the cost/STI detected was lower for eSTI.

Clinic STI Test Cost

For HSP at a clinic STI test cost of $60.87, the eSTI strategy cost more than the clinic strategy, but detected more infections. However, the cost/STI detected was slightly lower for the clinic strategy with an incremental cost per effect ratio of $1356 for eSTI. At a test cost of $96.49, eSTI cost more than the clinic strategy but the cost/STI detected was lower for eSTI. For CTP, the clinic STI test cost would remain constant at $90, the same cost as for eSTI.

Best-Case/Worst-Case Sensitivity Analysis

The 5 parameters that have the most influence in 1-way sensitivity analyses (STI prevalence, kit return rate, clinic visit rate, office visit cost, and clinic STI test cost) were varied simultaneously along the ranges found in Tables 1 and 2. The eSTI best-case and worst-case cost-effectiveness results for both perspectives are shown in Table 3.

DISCUSSION

Our model suggests that an eSTI strategy of self-sampling with a home collection kit and e-prescription for treatment of uncomplicated infections would be likely to detect more STIs and cost less per STI detected than a standard clinic referral screening and treatment strategy.

TABLE 4. One-Way Sensitivity Analyses

Variable	Lower Limit / Upper Limit	Strategy	STIs Detected	Health Care System Perspective		Clinical Trial Perspective	
				Total Costs	Cost/STI	Total Costs	Cost/STI
Proportion visiting clinic for testing	32%	eSTI	75	$96,088	$1,281	$94,938	$1,266
		Clinic	36	$58,021	$1,612	$70,580	$1,961
	48%	eSTI	75	$96,088	$1,281	$94,938	$1,266
		Clinic	54	$85,315	$1,580	$104,154	$1,929
Proportion of kits returned	55%	eSTI	61	$83,241	$1,365	$82,297	$1,349
		Clinic	45	$71,688	$1,593	$87,367	$1,941
	72%	eSTI	80	$101,441	$1,268	$100,205	$1,253
		Clinic	45	$71,688	$1,593	$87,367	$1,941
STD prevalence	5%	eSTI	47	$95,479	$2,031	$94,760	$2,016
		Clinic	28	$71,196	$2,543	$87,223	$3,115
	10%	eSTI	93	$96,494	$1,038	$95,057	$1,022
		Clinic	56	$71,982	$1,285	$87,464	$1,562
Clinic office visit cost health care perspective	$19.50	eSTI	75	$96,088	$1,281	—	—
		Clinic	45	$66,227	$1,472	—	—
	$39	eSTI	75	$96,088	$1,281	—	—
		Clinic	45	$77,108	$1,714	—	—
Clinic office Visit cost CTP	$25	eSTI	75	—	—	$94,938	$1,266
		Clinic	45	—	—	$68,423	$1,521
	$85	eSTI	75	—	—	$94,938	$1,266
		Clinic	45	—	—	$101,903	$2,265
Clinic STI test cost	$60.87*	eSTI	75	$96,088	$1,281	—	—
		Clinic	45	$55,413	$1,231	—	—
	$96.49	eSTI	75	$96,088	$1,281	—	—
		Clinic	45	$75,289	$1,673	—	—

*ICER: $1356.

We are aware of only 2 other cost analyses of home collection screening versus clinic screening.[10,20] In one, clinician time and STI test costs for clinic screening were compared with test kit, packaging, and postage costs for home screening.[20] Screening rates in the 2 strategies were assumed to be equal. Time required to notify and assist with treatment was not incorporated, nor was the cost of a clinic visit beyond the clinician's time. The authors concluded that home screening could be cost-effective, but only if it resulted in less utilization of clinic services. Another study included not only the costs of testing and treatment but also the theoretical cost savings from prevention of PID.[10] Rates of screening in the Internet sampling group were estimated to be higher than in the clinic group based on the authors' primary data and the literature. The authors concluded that an Internet-based self-swab screening strategy led to more PID prevented at a lower cost than clinic screening. Although our study did not collect data on PID prevention, we were able to collect prospective data on the proportion of participants enrolling with staff assistance (and associated labor cost), proportion receiving positive and negative results online (and associated labor costs), and the proportion treated using eRx (and associated reduction in labor costs).

There are a few published studies that we can look to for estimates of clinic-based treatment rates for STIs that are detected via home screening and/or Internet methods.[5,10,21] However, the availability of eRx in a Web-based system has not been evaluated, except in our demonstration study,[6] and requires validation in a larger comparative effectiveness trial. If the overall study prevalence of STIs (*CT* + *GC* + *TV*) is greater than our estimate of 8%, cost per STI detected in a future trial may be lower than results of this cost analysis suggest.

There are limitations to our analysis. Results of cost-effectiveness analyses must be interpreted with caution, especially when parameter estimates that heavily influence the results are uncertain. The results of this analysis are strongly influenced by the home collection kit return rate estimate and the clinic visit rate estimate. We do not have data on the proportion of symptomatic versus asymptomatic participants who return kits and visit the clinic, and our estimates are limited because prospective randomized trials that directly compare these strategies have not been conducted. Furthermore, our estimates for trial staff labor costs are based primarily on investigator assumptions. Nevertheless, we have provided results of sensitivity analyses that were conducted to explore the influence of a range of estimates for these parameters. Lastly, this analysis is a static analysis in that it only considered the potential impact on the individual participants, but did not consider transmission. As part of a future scaled up comparative effectiveness study, we intend to include dynamic modeling to evaluate the cost-effectiveness of primary prevention for women who will not become infected due to decreased incidence in the population in addition to the secondary prevention of index women who are screened and treated.

A scaled CER trial will permit us to collect the following data for a more robust cost-effectiveness analysis: (1) rates of symptomatic participants in the clinic referral group that visit the clinic and in the eSTI group that return an STI kit; (2) rates of partner notification, partner treatment, and associated staff labor costs for each strategy; and (3) proportion of infections requiring DISs and associated labor costs for each strategy. Furthermore, we will be able to incorporate cases of PID and costs of PID sequelae prevented by each screening strategy as additional and important outcomes of a comprehensive cost-effectiveness analysis. If in the larger analysis the clinic referral strategy has a higher infection detection rate and/or treatment rate, then even if it costs more per STI detected, it may actually prevent more sequelae and lead to cost savings.

Our analysis indicates that eSTI is likely to be more effective and cost less per infection detected than clinic referral for STI screening in the context of a clinical trial as well as for clinical

care. If confirmed, our findings would support the routine use of eSTI in clinical trials where longitudinal STI testing is required as well as the development of national scale-up and financing strategies for online STI testing and treatment programs in the context of routine clinical care.

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