Cost-effectiveness Analysis of Chlamydia trachomatis Screening Via Internet-based Self-collected Swabs Compared With Clinic-based Sample Collection

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Background: Although the Centers for Disease Control and Prevention have recommended population-wide Chlamydia trachomatis screening of sexually active women less than 26 years of age, more than half of sexually active young women are not routinely screened. A Website (IWTK, www.iwantthekit.org), was developed in 2004 to promote home-based sample collection.

Methods: A decision tree was designed to model a hypothetical cohort of 10,000 women per year who order an internet-based C. trachomatis screening kit. We compared the incremental cost-effectiveness of 2 screening strategies: self-sampling via the IWTK website, and traditional, clinic-based screening by the same cohort of women who used IWTK. Probabilities and costs were estimated for each node in the decision tree. Estimates were derived from primary data, published data, and unpublished health data.

Results: The internet-based screening strategy prevented 35.5 more cases of pelvic inflammatory disease and saved an additional $41,000 in direct medical costs as compared with the clinic-based screening strategy.

Conclusion: Our model estimates demonstrated that an internet-based, self-swab screening strategy was cost-effective compared with the traditional, clinic-based screening strategy. Assuming that the popularity of the use of the internet as a resource for information about healthcare and sexually transmitted infections leads to an increased use of IWTK, the public health benefit of this cost-effective strategy will be even greater.

Chlamydia trachomatis (Ct) is the most common bacterial sexually transmitted infection (STI) in the United States: >2.8 million new cases are estimated to occur annually. Most Ct infections in women are asymptomatic. Untreated Ct infection can progress, giving rise to serious and costly sequelae for women, including pelvic inflammatory disease (PID), infertility, ectopic pregnancy, and chronic pelvic pain. With the advent of highly specific and sensitive nucleic acid amplification tests, noninvasive improved detection and treatment of Ct infection is possible.

The Centers for Disease Control and Prevention (CDC) have recommended population-wide screening of sexually active women aged <26 years. Although the annual Ct screening rate increased from 25.3% in 2000 to 41.6% in 2007, and many studies have shown that Ct screening in women is cost-effective, more than half of sexually active young women with a health insurance plan are not routinely screened in clinics. Moreover, many women who meet CDC guidelines are not screened at publicly funded clinics due to budgetary constraints, and screening is even less frequent in private practice settings. As adults and adolescents are increasingly using the internet to search for information about healthcare and STIs, this resource holds great promise as a means of increasing Ct screening. Many women prefer to screen for STIs at home, and when given this opportunity, are more likely to obtain screening as compared with those women whose only option is clinic-based screening (64.6% vs. 31.6%). Accordingly, the use of home-based sample collection may significantly increase Ct screening above that achievable with traditional, clinic-based screening alone.

A Website, www.iwantthekit.org (IWTK), was developed in 2004 to promote home-based sample collection. This Website offers both Ct screening and education as an innovative strategy to encourage young women to self-collect vaginal swabs and mail them to a laboratory for testing. We have evaluated the cost-effectiveness of this innovative, internet-based, self-sampling strategy compared with the traditional clinic-based screening strategy.

MATERIALS AND METHODS

Decision Analysis Model

A decision tree was designed to model a hypothetical cohort of 10,000 women per year who request a Ct screening kit through the internet. We compared the incremental cost-effectiveness of 2 screening strategies: self-sampling via the IWTK Website; and traditional clinic-based screening among the same hypothetical cohort of women who use IWTK. Probabilities and costs were estimated for each decision tree node. Estimates were derived from primary data, published data, and unpublished health data.

Medical outcomes included PID, chronic pelvic pain, ectopic pregnancy, and tubal infertility. The model incorporated programmatic screening, treatment costs, and medical

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Supported by Award Number U54EB007958 and 3U54EB007958-03S1, issued under the American Recovery and Reinvestment Act of 2009, from the National Institute of Biomedical Imaging and Bioengineering.

The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute of Biomedical Imaging and Bioengineering or the National Institutes of Health.

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Received for publication October 5, 2010, and accepted March 17, 2011.

DOI: 10.1097/OLQ.0b013e31821bf050

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costs averted through prevention of PID and its sequelae. The time horizons used for PID sequelae to occur were 10 years for infertility, 5 years for ectopic pregnancy, and 2 years for chronic pelvic pain. We did not consider transmission or time-to-treatment effects in our analysis. Costs were adjusted to 2010 US dollars and future costs were discounted at a rate of 3%. The analyses were conducted from a public healthcare perspective and included only direct medical costs.

Protocol

The IWTK protocol has been described previously. Briefly, women were mailed a home collection kit, consisting of a sample collection swab, a transport tube, directions, and a stamped, self-addressed mailer. Women were instructed to mail the sample to the STD laboratory for processing by Aptima Combo2 (Gen-Probe, Inc, San Diego, CA). All participants were notified of results, and infected participants were given assistance in making clinic appointments for treatment.

Data were collected from women presenting to the Baltimore STD and Family Planning Clinics for Ct testing using endocervical swabs for the AC2 assay. These women were all given 2-week follow-up appointments. If clinical findings suggested infection, women were treated presumptively for Ct on the day of their screening visit. Clinic staff attempted to contact all women whose Ct test was positive if they did not receive presumptive treatment or return for their follow-up visit.

Probability Estimates

The sample return rate for the internet strategy was based on data collected from July 2004 through June 2010 by IWTK. The estimate for the clinic-based screening rate among the same hypothetical cohort of women who used IWTK was calculated by applying data from the Detection Acceptability Intervention for STD’s in Young Women study (DAISY) to data from IWTK. In the DAISY study, the ratio of the home-based test return rate to the clinic-based screening rate was 1.38 among all participants for all tests. Therefore, we estimated the clinic attendance rate by dividing the internet sample return rate from IWTK by 1.38.

A modified meta-analysis was conducted to estimate the sensitivity and specificity of the vaginal and endocervical AC2 tests. A PubMed literature search on all fields using the terms “(chlamydia) AND (screening) AND (Aptima or TMA or NAAT) AND (sensitivity OR specificity)” retrieved 33 papers, including 1 review paper. Seven of these studies met our full inclusion and exclusion criteria: original study on Chlamydia screening among women; and vaginal swab or endocervical swab used for AC2 testing.

The Ct prevalence estimate for the hypothetical cohort was based on study results from IWTK activities between July 2004 and June 2010. The same prevalence was used for both screening strategies, as we assumed one hypothetical cohort.

The proportion of women with positive Ct test results who received treatment was based on tracking records from IWTK for the internet-based screening strategy and from Baltimore STD and Family Planning Clinics for the clinic-based screening strategy. On the basis of the internet staff experience, we estimated that an average of 1 hour of labor was required to contact each Ct-positive woman and assist with treatment for the internet-based screening strategy. On the basis of Disease Intervention Specialist experience (personal communication, Disease Intervention Specialist personnel, and Baltimore City Health Department), we estimated that an average of 1.25 hours of labor were required to contact each Ct-positive woman who did not return for results and assist with treatment for the clinic-based screening strategy.

We used published literature to derive the azithromycin treatment success rate, prevalence of PID among untreated Ct-positive cases, proportion of silent PID, proportion of inpatient PID treatment, and rates of key sequelae. The prevalence of PID among untreated Ct-positive cases was based on results from earlier classic studies, which used actual laparoscopic or histologic findings and reported asymptomatic and symptomatic PID. Probability estimates are provided in Table 1.

Cost Estimates

The average cost per Ct test performed as a result of an internet-based request was calculated using the annual Website maintenance cost divided by 10,000 annual requests, plus the labor and kit cost required to fulfill the request, and test performance costs for returned AC2 kits. The average cost of each Ct test in the clinic setting was calculated using direct clinician labor costs at Baltimore STD and Family Planning Clinics (40 minutes), supplies used during one clinic visit, and laboratory processing for each AC2 test. We did not include the capital costs of setting up the Website or the clinic in our analyses because the Website already exists, as do many STD and Family Planning Clinics.

The cost associated with Ct treatment for both strategies was estimated by using a 20-minute clinician visit, the State of Maryland Public Health cost for 1 g of azithromycin, and labor costs to track and treat a Ct-positive participant.
The cost associated with inpatient PID treatment was based on hospital direct costs and 1 level-4 outpatient follow-up visit. The cost associated with outpatient PID treatment was based on 1 level-5 initial visit, 1 level-4 follow-up visit, and medication costs. To calculate the cost associated with treatment of PID-related sequelae, we summed the proportion of women estimated to develop each sequela multiplied by the cost to treat the sequela and discounted by 3% for each year of delay in developing the sequela. Additional details have been published.\(^7\) Cost estimates are presented in Table 2.

**Analyses**

Analyses were conducted using TreeAge Pro 2009 decision analysis software (TreeAge Software, Williamstown, MA). The primary outcome measure was number of episodes of PID averted. Secondary outcome measures comprise PID-related sequelae prevented, including infertility, ectopic pregnancy, and chronic pelvic pain. Incremental cost savings, cases of PID averted, and incremental cost-effectiveness ratios were calculated using the clinic-based screening strategy as comparator.

A threshold analysis (parameter value at which recommendations would change) was conducted to determine the number of women who would request screening kits via the internet to make this strategy cost-effective. A similar approach was used to determine the Ct prevalence threshold levels. Univariate and bivariate sensitivity analyses were conducted for parameters where estimates were uncertain.

**RESULTS**

**Primary Data**

Between July 2004 and June 2010, the overall IWTK sample return rate was 35.9% (annual range: 30.6%–43%). This rate was used for our internet-based screening strategy estimate. We estimated that the clinic attendance rate for our hypothetical cohort would be 26% (0.359/1.38).\(^1\) Treatment was received by 99.9% of the Ct-positive women using IWTK and 90% of Ct-positive women cared for at clinics. Of clinic users who did not return for their follow-up clinic visit but subsequently received Ct treatment, 81.6% required assistance by Disease Intervention Specialist.

**Cost-effectiveness Analysis**

Results of cost-effectiveness analysis are listed in Table 3. For the hypothetical cohort of 10,000 women requesting a screening kit through the internet, the internet-based screening strategy would prevent 35.5 more cases of PID and save an additional $41,000 in direct medical costs versus the clinic-based screening strategy.

**Sensitivity Analysis**

We included the annual Website maintenance cost in our analyses and divided the cost equally among women who use the internet to request a screening kit: the more women requesting a kit, the lower the maintenance cost per request. Therefore, the number of women using the website affects the cost-effectiveness of the internet-based strategy. The threshold analysis showed that when the number of women requesting a kit through the internet reaches 200 annually, the internet-based screening strategy starts to prevent more PID cases than the clinic-based screening strategy, but without cost savings. When the number of women using the website reaches 1435 annually, the internet-based screening strategy also saves money.

For the base case scenario, the threshold analysis for Ct prevalence demonstrated that the internet-based screening strategy will always prevent more PID cases, regardless of how low the Ct prevalence is (given that sample return rate is higher than clinic attendance rate), but will not start to save money until the Ct prevalence reaches 6%. Two-way sensitivity analysis represented by Figure 1 illustrates the relationship between these key parameters.

One-way sensitivity analyses on remaining variables found in Tables 1 and 2 demonstrated that changes in parameter estimates would not change the direction of our findings, only the relative cost savings of the internet-based strategy. Results of 1-way sensitivity analyses for key parameters are reported in Table 4. The 2-way sensitivity analysis on internet-based...
screening kit return rate and clinic-based screening rate is illustrated in Figure 2.

**DISCUSSION**

Our analyses demonstrated that the innovative internet-based self-swab screening strategy is not only more effective, but also saves money compared with the traditional, clinic-based screening strategy for this hypothetical cohort of 10,000 women. Our results are consistent with the cost comparison between home- and clinic-based testing from the DAISY study,13 which also showed that the home-testing program could be cost saving.

We chose not to include initial capital costs associated with building the IWTK Website or building a new STD or Family Planning Clinic because both already exist. However, if they had been included, it is likely that the internet-based strategy would have been even more cost-effective than the clinic-based strategy, as the $31,251 capital cost spent on building the IWTK website is far less than the typical capital cost needed to build a new clinic. Assuming that the IWTK website can be used for 10 years, the annualized capital cost would be $3663 with a 3% annual discount rate. Even if the website annualized capital cost is added to the website annual maintenance cost, the internet-based screening strategy is still dominant in one-way sensitivity analysis. We also included internet annual maintenance costs but not clinic annual maintenance costs in the analyses because regardless of the number of women obtaining clinic-based Ct screening, the clinic will still provide care to symptomatic patients, patients with other STIs, and those needing Ct treatment.

With the growth in the number of women using the internet to acquire information about healthcare and STIs,11 an internet-based Ct screening program has the potential to reach a wide population of women at risk for STIs. Threshold analysis demonstrated that the internet-based screening strategy becomes dominant once the number of internet requests exceeds 1435 annually. IWTK is currently only available in a few states, but is already receiving >1500 annual requests, as well as an average of 86,829 website hits per month for 2010. With increasing awareness and availability of the internet-based Ct screening program in more geographical areas, the potential for detecting and treating Ct among women less likely to access clinic services will expand.

**TABLE 3.** Cost-effectiveness Analysis

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Ct+ Cases Detected</th>
<th>Total Cost</th>
<th>Incremental Cost</th>
<th>Cases of PID Expected</th>
<th>Incremental Cases of PID Averted</th>
<th>Incremental Cost/Case of PID Averted (ICER)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Internet screening</td>
<td>303</td>
<td>$860 K</td>
<td>—</td>
<td>179.9</td>
<td>35.5</td>
<td>—</td>
</tr>
<tr>
<td>Clinic screening</td>
<td>232</td>
<td>$902 K</td>
<td>$41 K</td>
<td>215.4</td>
<td>—</td>
<td>$1155*</td>
</tr>
</tbody>
</table>

*Internet strategy saves $1155 per each additional case of PID averted.
ICER indicates incremental cost-effectiveness ratio; PID, pelvic inflammatory disease.

**TABLE 4.** Univariate Sensitivity Analyses

<table>
<thead>
<tr>
<th>Variable</th>
<th>Alternate Value</th>
<th>Incremental Cost/Case of PID Averted (ICER)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High1</td>
<td>10.7%</td>
<td>Internet dominant</td>
</tr>
<tr>
<td>Low2</td>
<td>4.6%</td>
<td>$1012</td>
</tr>
<tr>
<td>Threshold§</td>
<td>5.97%</td>
<td>$1</td>
</tr>
<tr>
<td>Internet-based screening</td>
<td></td>
<td></td>
</tr>
<tr>
<td>kit return rate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>43.3%</td>
<td>Internet dominant</td>
</tr>
<tr>
<td>Low</td>
<td>30.6%</td>
<td>Internet dominant</td>
</tr>
<tr>
<td>Threshold</td>
<td>28.68%</td>
<td>$1</td>
</tr>
<tr>
<td>Clinic-based screening rate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>35.9%</td>
<td>Internet dominant</td>
</tr>
<tr>
<td>Low</td>
<td>13.9%</td>
<td>Internet dominant</td>
</tr>
<tr>
<td>Threshold</td>
<td>49.5%</td>
<td>$10</td>
</tr>
<tr>
<td>Cost for PID sequelae¶ treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>$5370.43</td>
<td>Internet dominant</td>
</tr>
<tr>
<td>Low</td>
<td>$ 646.42</td>
<td>$1087</td>
</tr>
<tr>
<td>Threshold</td>
<td>$1732.94</td>
<td>$1</td>
</tr>
</tbody>
</table>

*Using clinic-based strategy as the comparator.
1High range from Table 1.
2Low range from Table 1.
3The value of variables at which the internet-based strategy was no longer the dominant strategy (i.e., no longer saving money while preventing PID).
4Calculated based on rate of infertility, ectopic pregnancy, and chronic pelvic pain caused by PID, and cost associated with treatment for each complication after discounting by 3% for each year of delay.
ICER indicates incremental cost-effectiveness ratio; PID, pelvic inflammatory disease.
Although the overall Ct prevalence rate of 9.1% used in our analyses may be different in other areas of the United States, the threshold analysis for Ct prevalence demonstrated that for the base case scenario, the internet-based screening strategy will always prevent more PID cases, regardless of how low the Ct prevalence is, but will not start to save money until it reaches 6%. The CDC 2009 STD Surveillance report (http://cdc.gov/std/stats09/slides.htm) showed that Ct prevalence among women aged 15 to 24 years tested in family planning clinics was 6.7% in 2009 nationwide, with a steady annual increase since 2000, and that 45 states had Ct prevalence rates of ≥6%. If the internet-based screening test is available among these high-risk patients, it has great potential not only to prevent many cases of PID, but also to save a considerable amount of money due to costs averted during screening and treatment as well as through prevention of PID and its sequelae compared with the traditional, clinic-based Ct screening strategy. Nevertheless, patients with symptoms, especially if suggestive of PID or other concerning processes, should always still visit a clinic or private doctor for a complete medical evaluation.

Our goal was not to compare clinic-based screening head-to-head with internet-based screening, but to evaluate the cost-effectiveness of the internet-based screening strategy for a hypothetical cohort of women who may be unwilling to attend a clinic. Consequently, we began with the assumption that a proportion of women who are willing to use the internet for Ct testing will be unwilling to attend a clinic, such that clinic attendance rate would never exceed internet sample return rate. We used the DAISY study results (1.38 overall ratio of home vs. clinic) to estimate the clinic-based screening rate. However, because of study design and resources available in a typical research study, this ratio could be higher in a real-world setting. If we had used the study result from only the DAISY neighborhood cohort, the ratio would be 2.2. Conversely, it is possible that the clinic-based screening rate could be equivalent to the internet-based screening kit return rate. Nevertheless, sensitivity analysis demonstrated that the internet-based strategy remained cost-effective even if the clinic-based screening rate was as high as the internet-based screening kit return rate (35.9%). Figure 2 illustrates the relationship between these two parameters.

The proportion of women with positive Ct tests who received treatment was >90% for both strategies. We accounted for the labor cost needed to achieve such a high treatment rate for both strategies. Sensitivity analyses demonstrated that the internet-based screening strategy was still more cost-effective even if we used the same treatment rate for both strategies.

There has been considerable disagreement recently among experts about the true PID rate among women with untreated Ct infection. We agree with the conclusion in the review by Haggerty et al that it is challenging to assess the true PID incidence.38 We have conservatively chosen to use in our analyses, results from older studies that assessed PID among asymptomatic and symptomatic women, rather than from newer studies that looked primarily at symptomatic PID. In addition, the older studies diagnosed PID based on laparoscopic or histologic findings, while many newer studies used clinical criteria alone, which have notoriously poor sensitivity and specificity for PID compared with laparoscopic or histologic findings. The best new data on asymptomatic PID were presented by Wiesenfeld et al25 and demonstrated that 23% of women with Ct infection had subclinical PID defined by ≥5 neutrophils in the superficial endometrium per 400× field. Given that an estimated 60% of PID is silent, the true PID rate (including asymptomatic and symptomatic PID) would be much higher than that reported in recent studies, which looked only at symptomatic PID rates.

We used the same estimates for the probability of PID and its sequelae among untreated Ct-positive women for both strategies because our analyses were based on the same 10,000 hypothetical women. In addition, a recent study has shown that demographic and microbiologic characteristics of women with subclinical and acute PID are similar, and suggested that the pathophysiological mechanisms of acute and subclinical PID are also similar.39 Sensitivity analysis demonstrated that changes in these parameters did not alter the direction of our findings.

Limitations

Some of the estimates used were derived from other studies rather than from our primary data collection. There is inherent uncertainty of the estimates for some variables, although we have conducted sensitivity analyses to explore their higher and lower estimates. In addition, our model does not consider transmission or time-to-treatment effects, and our data may not be generalizable to other geographic areas where differences in internet usage and use of clinical services may exist. Nonetheless, we have shown that use of the internet to reach individuals at risk for Ct infection who may not seek clinical services is cost effective.

Summary

Our model demonstrated that an internet-based, self-swab strategy is cost-effective compared with the conventional, clinic-based screening strategy. Assuming that the popularity of the internet as a tool for finding information about healthcare and STIs will continue to increase, the cost associated with each internet-based Ct screening test will decrease, and the public-health benefit of this cost-effective strategy will be even greater.
REFERENCES