Published in final edited form as:
Sex Transm Dis. 2008 July ; 35(7): 649–655. doi:10.1097/OLQ.0b013e31816ddb9a.

Cost-Effectiveness of Screening Strategies for *Chlamydia trachomatis* Using Cervical Swabs, Urine, and Self-Obtained Vaginal Swabs in a Sexually Transmitted Disease Clinic Setting

Diane R. Blake, MD[*], **Nancy Maldeis, MPH**[†], **Mathilda R. Barnes, BS**[†], **Andrew Hardick, BS**[†], **Thomas C. Quinn, MD, SCD**[†,‡], and **Charlotte A. Gaydos, MS, MPH, DRPH**[†]

[*]Department of Pediatrics, Division of Adolescent Medicine; University of Massachusetts Medical School, Worcester, Massachusetts [†]Department of Medicine, Division of Infectious Diseases; Johns Hopkins University School of Medicine, Baltimore, Maryland [‡]National Institute of Allergy and Infectious Diseases, NIH, Bethesda, Maryland

Abstract

Background—We evaluated the cost-effectiveness of Chlamydia screening strategies that use different methods of specimen collection: cervical swabs, urines, and self-obtained vaginal swabs.

Methods—A decision analysis was modeled for a hypothetical cohort of 10,000 per year of women attending sexually transmitted disease (STD) clinics. Incremental cost-effectiveness of 4 screening strategies were compared: 1) Endocervical DNA probe test (PACE2, Gen-Probe), 2) Endocervical AC2 (Aptima Combo 2, Gen-Probe), 3) Self-Obtained Vaginal AC2, and 4) Urine AC2. Sensitivities of the vaginal, urine, and cervical AC2 tests were derived from 324 women attending STD clinics. The primary outcome was cases of pelvic inflammatory disease prevented. The model incorporated programmatic screening and treatment costs and medical cost savings from sequelae prevented.

Results—Chlamydia prevalence in the sampled population was 11.1%. Sensitivities of vaginal, urine, and cervical AC2 were 97.2%, 91.7%, and 91.7%, respectively. The sensitivity of the DNA probe was derived from the literature and estimated at 68.8%. The self-obtained vaginal AC2 strategy was the least expensive and the most cost-effective, preventing 17 more cases of pelvic inflammatory disease than the next least expensive strategy.

Conclusions—Use of a vaginal swab to detect Chlamydia in this STD clinic population was cost-saving and cost-effective.

It has been well established that *Chlamydia trachomatis* screening among women in most settings is cost-effective.[1–8] Populations studied have included women attending family planning clinics,[2–5] sexually transmitted disease (STD) clinics,[4] emergency departments,[1] youth clinics,[5] gynecology clinics,[5] student health centers,[3] and military recruits[6,7] and population based screening of 15- to 29-year-old women.[8] Most of the analyses assumed asymptomatic status of women.[3,5–8] Two analyses, however, compared several strategies, with some of the strategies taking symptom status into account and others screening everyone the same way regardless of symptom status.[1,2] Many analyses took the health care system

Correspondence: Diane R. Blake, MD, Department of Pediatrics, University of Massachusetts Medical School, 55 Lake Avenue North, Worcester, MA 01655. E-mail: E-mail: diane.blake@umassmed.edu.

Presented at the International Society for Sexually Transmitted Diseases Research meeting, July 10–14, 2005, Amsterdam, The Netherlands.

perspective.[1–3,5] However, 2 conducted analyses from the military perspective,[6,7] and 2 used the societal perspective.[4,8]

In most previous analyses, either an endocervical specimen was tested[4,5] or a urine specimen was tested.[1,3,6–8] Consequently, many previous analyses did not evaluate the impact of omitting the speculum examination on the cost-effectiveness outcome.[1,3–7]

The Aptima Combo 2 (AC2) test is among a new generation of tests that use nucleic acid amplification and is FDA-cleared for use on endocervical, urine, and vaginal specimens. Because most Chlamydia infections are asymptomatic,[9–12] many women who seek screening have no symptoms. Unless they are due for an annual Papanicolaou (Pap) smear, asymptomatic women who are screened with a vaginal or urine AC2 test do not require a speculum examination, omission of which can save time and money.

The objective of this study was to evaluate the cost-effectiveness of several Chlamydia screening strategies and to incorporate conditions where a speculum examination may not be necessary.

Methods

Design

A decision analysis was modeled for a hypothetical cohort of 10,000 women per year attending Baltimore STD clinics. Incremental cost-effectiveness of 4 Chlamydia screening strategies were compared: 1) Endocervical DNA Probe (PACE2, Gen- Probe), 2) Endocervical AC2 (Aptima Combo 2, Gen-Probe), 3) Self-Obtained Vaginal AC2, and 4) Urine AC2. Strategies 1 and 2 always required a speculum examination; strategies 3 and 4 only required a speculum examination for symptomatic patients or those due for a Pap smear.

The primary outcome measure was number of cases of pelvic inflammatory disease (PID) prevented. Secondary outcome measures were PID-related sequelae including infertility, ectopic pregnancy, and chronic pelvic pain. The model incorporated programmatic screening and treatment costs and medical costs averted through prevention of PID and its sequelae. The time horizon was 10 years to allow for all PID sequelae to occur. The analyses were conducted from the public health care perspective and included only direct medical costs.

Probability and Cost Estimates

Primary data, unpublished state and local data, and published literature were used to estimate probabilities and costs for the decision analysis. Sensitivities of the vaginal, urine, and endocervical AC2 tests were derived from 324 women (92.6% black) attending Baltimore STD clinics between April 5, 2004 and February 3, 2005. All positive tests were confirmed by retesting the sample using GenProbe's FDA cleared Aptima *C. trachomatis* (ACT; Gen-Probe), which has different target sequences than the AC2. Classification as a positive case required at least 1 of the samples (vaginal, urine, or endocervical) to test positive with confirmation. Each woman had all 3 samples collected. Following sample collection, women were asked to rate the 3 sample techniques in order of their preferred method. Written informed consent was obtained from all participants. The study was approved by the Western IRB, Seattle, WA, and the Baltimore City Health Department.

The prevalence of Chlamydia among these women, the proportion of infections that were symptomatic, the proportion of infections that were treated, and the proportion of women who required a Pap smear were all derived from this sample. The sensitivity of the DNA probe[13–20] and the estimated proportion of women with untreated *Chlamydia cervicitis* who

would develop PID[3,21–23] and its sequelae[24–27] were derived from the literature. See Table 1 for additional probability estimates.

Cost estimates are presented in Table 2. All costs were converted to 2006$ using the medical care portion of the consumer price index. Maryland Medicaid reimbursement rates were used to estimate the cost of the AC2 and DNA Probe tests. Additional cost of a speculum examination was calculated by multiplying an STD clinician's hourly salary rate by the average amount of time required to perform a speculum examination and adding the cost of a plastic speculum to this estimate. Average time to perform a speculum examination (7 minutes) was calculated from a time-in-motion study of routine patient evaluations that required speculum examinations at the STD clinics. Cost to treat a Chlamydia infection included the Maryland Public Health rate for 1 g of azithromycin and 15 minutes of an STD clinician's time.

The cost to treat PID as an outpatient was calculated using the Maryland Medicaid reimbursement rate for a level 5 (40 minute) initial visit and a level 4 (25 minute) follow-up visit.[28] The inpatient costs to treat PID[29] and the costs associated with PID sequelae[4,6,24,29–33] were derived from the literature and the South region of the Health Care Utilization Project. All future costs were discounted at a rate of 3% and cost to charge ratios were used to estimate the costs when only charge data were available.

Analyses

Analyses were conducted using TreeAge Pro 2006 (TreeAge Software, Williamstown, MA) decision analysis software. Incremental cost savings, cases of PID prevented, and incremental cost effectiveness ratios (ICER) were calculated for each screening strategy using DNA probe screening as the comparator strategy. Because the most cost-effective strategy not only prevented more cases of PID but also saved money as compared with the DNA probe screening strategy, ICERs were expressed as negative values. Threshold prevalence was calculated for each strategy to determine at what Chlamydia prevalence the strategy would become the most cost-effective strategy.

Univariate and bivariate sensitivity analyses were conducted for parameters where estimates were uncertain. No published consensus exists on the societal value placed on preventing a case of PID. We, in consensus with other STD experts, decided to use $400 as a conservative estimate of the acceptable cost of preventing a case of PID. Therefore, when univariate sensitivity analyses identified parameter values that increased the cost of the most effective strategy, the parameter value at which the ICER exceeded $400 per case of PID prevented was calculated.

Results

Primary Data

The Chlamydia prevalence in the sampled population of 324 women was 11.1% (95% CI, 7.7%–14.5%). Sixty-six percent of the screened sample were symptomatic with reported genital complaints; however, only 18.8% had abdominal pain. The sensitivities of the vaginal, urine, and endocervical AC2 for detecting Chlamydia in this sample were 97.2%, 91.7%, and 91.7%, respectively. Ninety-four percent of the infected women were successfully treated with antibiotics. Thirty-eight percent of the women were due for a Pap smear on the day of their visit. Forty-six percent of participants preferred vaginal specimen collection, 29% endocervical collection, and 25% urine collection. Ease of vaginal self-collection was reported as "easy" by 80.9%, "OK" by 16.1%, and "hard" by 3.0% of women.

Cost-Effectiveness Analysis

Total costs of each screening strategy, number of cases of PID prevented, cost savings, and ICERs are listed in Table 3. The least expensive and most effective strategy was the self-obtained vaginal AC2 strategy, with programmatic costs savings of $64,000 compared with endocervical DNA probe screening and prevention of 88 additional cases of PID. The other two AC2 strategies prevented fewer cases of PID while costing more money than the self-obtained vaginal AC2 strategy and thus were dominated by the self-obtained vaginal AC2 strategy.

Prevalence Threshold

The urine AC2 and endocervical AC2 strategies never become the most cost-effective strategies regardless of the Chlamydia prevalence. This is because the cost to process AC2 is the same regardless of specimen used, the cost to obtain a urine or endocervical sample is never less than the cost to obtain a vaginal sample, and the sensitivity of the vaginal AC2 in this study is higher than the sensitivity of either the urine or endocervical AC2. The endocervical DNA probe strategy becomes less expensive than the self-obtained vaginal AC2 strategy when the prevalence is 7.6% or less.

Univariate Sensitivity Analyses

The only variable for which a change in parameter value would result in urine AC2 becoming the most cost saving strategy was a urine AC2 sensitivity greater than the self-obtained vaginal AC2 sensitivity. Similarly, the only variable for which a change in parameter value would result in endocervical AC2 becoming the most cost saving strategy was an endocervical sensitivity greater than 99% or both the urine AC2 and vaginal AC2 sensitivities less than 90%.

One-way sensitivity analyses, using the ranges listed in Table 1, demonstrated that changes in parameter estimates for the following variables were each capable of shifting the most cost-savings strategy from self-obtained vaginal AC2 toward endocervical DNA probe: successful treatment of fewer than 66% of infected women; presumptive treatment of at least 30% of infected women at screening visit; PID sequelae costs less than $1,210; endocervical DNA probe test cost less than $21.60; self-obtained vaginal AC2 test cost more than $49.80; or endocervical DNA probe sensitivity greater than 77.5%.

Given that the self-obtained vaginal AC2 strategy continued to prevent more cases of PID than the endocervical DNA probe strategy even when it costs more, the parameter values of variables at which the ICER for self-obtained vaginal AC2 strategy exceeded $400 were calculated and are presented in Table 4.

Bivariate Sensitivity Analyses

Figure 1 demonstrates the effect of varying both the vaginal AC2 sensitivity and the endocervical AC2 sensitivity. Likewise, Figure 2 demonstrates the effect of varying both the vaginal AC2 sensitivity and the endocervical DNA probe sensitivity. Figure 3 demonstrates the effect of varying both the cost of the AC2 and the cost of the DNA probe.

Effect of Reducing Speculum Examinations

If all patients were evaluated with a speculum examination regardless of lack of symptoms and need for Pap smear, then the self-obtained vaginal AC2 strategy saves less money, but is still cost saving. As compared with the endocervical DNA probe strategy, requiring a speculum examination for all patients in the self-obtained vaginal AC2 strategy reduces cost savings from $64,000 to $52,000.

Given that most patients with PID have lower abdominal pain[34] and the PID Evaluation and Clinical Health study only enrolled patients who were experiencing pelvic discomfort,[35] we looked at the effect of not requiring a speculum examination in patients who do not have abdominal pain. Symptomatic patients who do not have lower abdominal pain can be evaluated for Chlamydia and Gonorrhea with a vaginal or urine AC2 and can be diagnosed with trichomoniasis, vulvovaginal candidiasis, and bacterial vaginosis with a wet mount of a blindly obtained cotton swab vaginal specimen.[36] In the sample of 324 women evaluated in this study, 18.8% had abdominal pain. If patients evaluated with the urine AC2 or self-obtained vaginal AC2 strategy only received a speculum examination if they had abdominal pain or needed a Pap smear (50% of sample), then the self-obtained vaginal AC2 strategy savings would rise to $79,000 as compared with the DNA probe comparator strategy.

Discussion

In this population of women attending Baltimore STD clinics, self-obtained vaginal AC2 outperformed the other strategies for detection of Chlamydia infections. As a result, it was more effective than either the urine or endocervical AC2 tests in preventing PID. The additional cost of the AC2 test as compared with the DNA probe test was more than compensated for by the cost savings associated with preventing substantially more cases of PID. Additional savings were realized as a result of the ability to omit the speculum examination in many women tested with self-obtained vaginal AC2. Furthermore, of the 3 sampling techniques experienced by these women, vaginal sampling was preferred by the most women and over 80% reported it was “easy” to perform. Despite a relatively small sample size, the difference in acceptability between vaginal swabs and urine or cervical swabs was statistically significant ($P < 0.01$).

The role of the speculum and bimanual examinations in asymptomatic women, symptomatic women, and STD contacts was evaluated in a recent retrospective chart review of patients attending the same STD clinics where the primary data for this study were collected.[37] The investigators found that among symptomatic patients, 5.9% of the syphilis infections and 4.2% of the herpes infections were diagnosed during the speculum examination; however, they did not specify how many of these lesions were internal versus found on the external genitalia, which would require only an external visual inspection.[37] Among STD contacts and asymptomatic patients the percentages were lower: 1.7% and 0.6% respectively for syphilis diagnoses and 0.6% and 1.7% respectively for herpes diagnoses.[37] Furthermore, the investigators demonstrated that a low percentage of clinically relevant diagnoses (including syphilis, herpes, and PID) would be missed if all patients were screened with self-collected vaginal specimens and serologies for syphilis and herpes simplex virus: 9.3% in symptomatic patients, 3.3% in STD contacts, and 2.3% in asymptomatic patients.[37] Whether it is acceptable to miss 9.3% of clinically relevant diagnoses in symptomatic patients is a judgment call. However, the percentage of missed diagnoses would have been less if the symptomatic patients with abdominal pain had received bimanual examinations. It is not possible from the data provided to estimate the exact reduction that this would have led to.[37]

It is now well accepted that Chlamydia screening among women is cost-effective.[1–8] In our cost-effectiveness analysis of 3 AC2 screening strategies we have paid particular attention to the accrual of healthcare system savings when it is possible to omit the speculum examination. Our findings are consistent with those of Shafer et al. and Howell et al. who also concluded that when no other indication exists for a speculum examination, omitting the speculum examination increases the cost-effectiveness of Chlamydia screening.[2,38] In Howell’s study, urine specimens were used when there was no indication to perform a speculum examination, but endocervical specimens were used if a speculum examination was already being conducted for other reasons.[2] The test used in that study, ligase chain reaction, performed better on endocervical specimens than urine specimens.[2] Howell et al. [2] found that the urine test was

more cost-effective if there was no other indication to conduct a speculum examination and, not surprisingly, if a speculum examination was already indicated, use of the more sensitive endocervical specimen was more cost-effective. Shafer et al.[38] compared use of the urine ligase chain reaction to use of the endocervical ligase chain reaction in asymptomatic adolescents and concluded the same: in asymptomatic females who would not otherwise need a speculum examination, use of the urine specimen was more cost-effective, even though it was slightly less sensitive. In the population we studied, self-obtained vaginal AC2 prevented the most cases of PID, saved the most money, and was preferred by the most women.

Our results may not be generalizable beyond an STD clinic setting. Nevertheless, STD clinics serve women with diverse needs. Some women request only an STD screen and are otherwise healthy. Providing these women with noninvasive screening not only respects the desires of many patients but also saves money from the health care system perspective. Limiting speculum examinations to women who require a Pap smear or present with a gynecologic symptom increases the health care savings of the self-obtained vaginal AC2 screening program by 23%. If however, the speculum examination were limited to women who required a Pap smear or presented with abdominal pain, regardless of genital symptoms, then the health care savings would increase an additional 23% for a total health care savings of 46%.

Other studies have supported the accuracy and acceptability of self-obtained vaginal swabs, when tested by nucleic acid amplification tests, for the detection of Chlamydia infections.[39–50] Given rising health care costs and the epidemic of Chlamydia infections in the United States, the provision of an algorithm of using self-obtained vaginal swabs to screen women who do not require a Pap test and who deny having abdominal pain in clinic venues has the potential to be a cost-effective strategy. Vaginal swabs can also be used to diagnose other vaginal and cervical infections such as gonorrhea, trichomonas, yeast infections or bacterial vaginosis.[36,43,44,47] A limitation of this approach is that some clinically important conditions, such as primary syphilitic chancre, HSV lesions, or other medical conditions (i.e., tumor or pregnancy) may be missed. However, many of these other conditions can be diagnosed by alternative means, like serological tests or may be detected during external genital inspection. Future study of this algorithm will provide more information as to the worth of such an approach.

In summary, our results demonstrated that use of self-obtained vaginal swabs was more cost-effective than urine or cervical specimens and patient acceptability of self-obtained vaginal swabs was highest of the 3 specimens evaluated.

Acknowledgments

The authors greatly acknowledge the clinicians of the Baltimore City Health Department, particularly Dr. Emily Erbelding, Treza Salama, and Toni Ingram.

Funding for this study was provided by GenProbe, San Diego, CA, and the HIV Prevention Trials Network (HPTN), sponsored by the National Institute of Allergy and Infectious Diseases (NIAID), National Institute on Drug Abuse (NIDA), National Institute of Mental Health (NIMH), and Office of AIDS Research, of the NIH, DHHS (U01-AI-068613).

References

1. Mehta SD, Bishai D, Howell MR, et al. Cost-effectiveness of five strategies for Gonorrhea and Chlamydia control among female and male emergency department patients. Sex Transm Dis 2002;29:83–91. [PubMed: 11818893]
2. Howell MR, Quinn TC, Brathwaite W, et al. Screening women for *Chlamydia trachomatis* in family planning clinics: The cost-effectiveness of DNA amplification assays. Sex Transm Dis 1998;25:108–117. [PubMed: 9518379]

3. Paavonen J, Puolakkainen M, Paukku M, et al. Cost-benefit analysis of first-void urine *Chlamydia trachomatis* screening program. Obstet Gynecol 1998;92:292–298. [PubMed: 9699769]
4. Marrazzo JM, Celum CL, Hillis SD, et al. Performance and cost-effectiveness of selective screening criteria for *Chlamydia trachomatis* in women: Implications for a national chlamydia control strategy. Sex Transm Dis 1997;24:131–141. [PubMed: 9132979]
5. Genc M, Mardh PA. A cost-effectiveness analysis of screening and treatment for *Chlamydia trachomatis* infection in asymptomatic women. Ann Intern Med 1996;124(1 pt 1):1–7. [PubMed: 7503471]
6. Howell MR, Gaydos JC, McKee KT Jr, et al. Control of *Chlamydia trachomatis* infections in female army recruits: Cost-effectiveness of screening and treatment in training cohorts to prevent pelvic inflammatory disease. Sex Transm Dis 1999;26:519–526. [PubMed: 10534206]
7. Howell MR, McKee KT Jr, Gaydos JC, et al. Point-of-entry screening for *C. trachomatis* in female army recruits. Who derives the cost savings? Am J Prev Med 2000;19:160–166. [PubMed: 11020592]
8. Hu D, Hook EW III, Goldie SJ. Screening for *Chlamydia trachomatis* in women 15 to 29 years of age: A cost-effectiveness analysis. Ann Intern Med 2004;141:501–513. [PubMed: 15466767]
9. Mertz KJ, Voigt RA, Hutchins K, et al. Jail STD Prevalence Monitoring Group. Findings from STD screening of adolescents and adults entering corrections facilities: Implications for STD control strategies. Sex Transm Dis 2002;29:834–839. [PubMed: 12466728]
10. Nsuami M, Cammarata CL, Brooks BN, et al. Chlamydia and Gonorrhea co-occurrence in a high school population. Sex Transm Dis 2004;31:424–427. [PubMed: 15215698]
11. Rogers SM, Miller HG, Miller WC, et al. NAAT-identified and self-reported Gonorrhea and Chlamydial infections: Different at-risk population subgroups? Sex Transm Dis 2002;29:588–596. [PubMed: 12370526]
12. Kahn R, Moseley K, Thilges J, et al. Community-based screening and treatment for STDs: Results from a mobile clinic initiative. Sex Transm Dis 2003;30:654–658. [PubMed: 12897689]
13. Semeniuk H, Zentner A, Read R, et al. Evaluation of sequential testing strategies using non-amplified and amplified methods for detection of *Chlamydia trachomatis* in endocervical and urine specimens from women. Diagn Microbiol Infect Dis 2002;42:43–51. [PubMed: 11821171]
14. Wylie JL, Moses S, Babcock R, et al. Comparative evaluation of Chlamydiazyme, PACE 2, and AMP-CT assays for detection of *Chlamydia trachomatis* in endocervical specimens. J Clin Microbiol 1998;36:3488–3491. [PubMed: 9817859]
15. Carroll KC, Aldeen WE, Morrison M, et al. Evaluation of the Abbott LCx ligase chain reaction assay for detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in urine and genital swab specimens from a sexually transmitted disease clinic population. J Clin Microbiol 1998;36:1630–1633. [PubMed: 9620391]
16. Lauderdale TL, Landers L, Thorneycroft I, et al. Comparison of the PACE 2 assay, two amplification assays, and Clearview EIA for detection of *Chlamydia trachomatis* in female endocervical and urine specimens. J Clin Microbiol 1999;37:2223–2229. [PubMed: 10364589]
17. Black CM, Marrazzo JM, Johnson RE, et al. Head-to-head multi-center comparison of DNA probe and nucleic acid amplification tests for *Chlamydia trachomatis* infection in women performed with an improved reference standard. J Clin Microbiol 2002;40:3757–3763. [PubMed: 12354877]
18. Pollara C, Terlenghi L, De Franscesco MA, et al. Comparative evaluation of BDProbeTec ET, LCx and PACE 2 assays for the detection of *Chlamydia trachomatis* in urogenital specimens. Eur J Clin Microbiol Infect Dis 2003;22:512–514. [PubMed: 12884065]
19. Modarress KJ, Cullen AP, Jaffurs WJ Sr, et al. Detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in swab specimens by the Hybrid Capture II and PACE 2 nucleic acid probe tests. Sex Transm Dis 1999;26:303–308. [PubMed: 10333286]
20. Pasternack R, Vuorinen P, Kuukankorpi A, et al. Detection of *Chlamydia trachomatis* infections in women by Amplicor PCR: Comparison of diagnostic performance with urine and cervical specimens. J Clin Microbiol 1996;34:995–998. [PubMed: 8815129]
21. Paavonen J, Kiviat N, Brunham RC, et al. Prevalence and manifestations of endometritis among women with cervicitis. Am J Obstet Gynecol 1985;152:280–286. [PubMed: 3923837]

22. Jones RB, Mammel JB, Shepard MK, et al. Recovery of *Chlamydia trachomatis* from the endometrium of women at risk for chlamydial infection. Am J Obstet Gynecol 1986;155:35–39. [PubMed: 3755292]
23. Stamm WE, Guinan ME, Johnson C, et al. Effect of treatment regimens for *Neisseria gonorrhoeae* on simultaneous infection with *Chlamydia trachomatis*. N Engl J Med 1984;310:545–549. [PubMed: 6363935]
24. Haddix AC, Hillis SD, Kassler WJ. The cost effectiveness of azithromycin for *Chlamydia trachomatis* infections in women. Sex Transm Dis 1995;22:274–280. [PubMed: 7502180]
25. Westrom L. Incidence, prevalence, and trends of acute pelvic inflammatory disease and its consequences in industrialized countries. Am J Obstet Gynecol 1980;138:880–892. [PubMed: 7008604]
26. Westrom L, Bengtsson LP, Mardh PA. Incidence, trends, and risks of ectopic pregnancy in a population of women. Br Med J (Clin Res Ed) 1981;282:15–18.
27. Westrom L, Joesoef R, Reynolds G, et al. Pelvic inflammatory disease and fertility. A cohort study of 1,844 women with laparoscopically verified disease and 657 control women with normal laparoscopic results. Sex Transm Dis 1992;19:185–192. [PubMed: 1411832]
28. American Academy of Pediatrics. AAP Medicaid Reimbursement Survey Report. Elk Grove Village, IL: American Academy of Pediatrics; 20042005.
29. Washington AE, Katz P. Cost of and payment source for pelvic inflammatory disease. Trends and projections, 1983 through 2000. JAMA 1991;266:2565–2569. [PubMed: 1942401]
30. Rein DB, Kassler WJ, Irwin KL, et al. Direct medical cost of pelvic inflammatory disease and its sequelae: Decreasing, but still substantial. Obstet Gynecol 2000;95:397–402. [PubMed: 10711551]
31. VanderLaan B, Karande V, Krohm C, et al. Cost considerations with infertility therapy: Outcome and cost comparison between health maintenance organization and preferred provider organization care based on physician and facility cost. Hum Reprod 1998;13:1200–1205. [PubMed: 9647547]
32. van Valkengoed IGM, Postma MJ, Morre SA, et al. Cost effectiveness analysis of a population based screening programme for asymptomatic *Chlamydia trachomatis* infections in women by means of home obtained urine specimens. Sex Transm Infect 2001;77:276–282. [PubMed: 11463928]
33. Petitta A, Hart SM, Bailey EM. Economic evaluation of three methods of treating urogenital chlamydial infections in the emergency department. Pharmacotherapy 1999;19:648–654. [PubMed: 10331829]
34. Blake DR, Fletcher KE, Joshi N, et al. Identification of symptoms that indicate a pelvic examination is necessary to exclude PID in adolescent women. J Pediatr Adolesc Gynecol 2003;16:25–30. [PubMed: 12604142]
35. Ness RB, Soper DE, Peipert J, et al. Design of the PID evaluation and clinical health (PEACH) study. Control Clin Trials 1998;19:499–514. [PubMed: 9741869]
36. Blake DR, Duggan A, Quinn TC, et al. Evaluation of vaginal infections in adolescent women: Can it be done without a speculum? Pediatrics 1998;102:939–944. [PubMed: 9755269]
37. Singh RH, Erbelding EJ, Zenilman JM, et al. The role of speculum and bimanual examinations when evaluating attendees at a sexually transmitted diseases clinic. Sex Transm Infect 2007;83:206–210. [PubMed: 17108005]
38. Shafer MA, Pantell RH, Schachter J. Is the routine pelvic examination needed with the advent of urine-based screening for sexually transmitted diseases? Arch Pediatr Adolesc Med 1999;153:119–125. [PubMed: 9988241]
39. Gaydos CA, Dwyer K, Barnes M, et al. Internet based screening for *Chlamydia trachomatis* to reach non-clinic populations with mailed self-administered vaginal swabs. Sex Transm Dis 2006;33:451–457. [PubMed: 16652069]
40. Oakeshott P, Hay P, Hay S, et al. Detection of *Chlamydia trachomatis* infection in early pregnancy using self-administered vaginal swabs and first pass urines: A cross-sectional community-based survey. Br J Gen Pract 2002;52:830–832. [PubMed: 12392124]
41. Hsieh Y-H, Howell MR, Gaydos JC, et al. Preferency among female army recruits for use of self-administered vaginal swabs or urine to screen for *Chlamydia trachomatis* genital infections. Sex Transm Dis 2003;30:769–773. [PubMed: 14520176]

42. Newman SB, Nelson MB, Gaydos CA, et al. Female prisoners' preference of collection methods for testing for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* infection. Sex Transm Dis 2003;30:306–309. [PubMed: 12671549]
43. Chernesky MA, Hook EW III, Martin DH, et al. Women find it easy and prefer to collect their own vaginal swabs to diagnose *Chlamydia trachomatis* or *Neisseria gonorrhoeae* infections. Sex Transm Dis 2005;32:729–733. [PubMed: 16314768]
44. Holland-Hall CM, Wiesenfeld HC, Murray PJ. Self-collected vaginal swabs for the detection of multiple sexually transmited infections in adolescent girls. J Pediatr Adolesc Gynecol 2002;15:307–313. [PubMed: 12547662]
45. Richardson E, Sellers JW, Mackinnon S, et al. Prevalence of *Chlamydia trachomatis* infections and specimen collection preference among women, using self-collected vaginal swabs in community settings. Sex Transm Dis 2003;30:880–885. [PubMed: 14646634]
46. Hoebe CJPA, Rademaker CW, Brouwers EE, et al. Acceptability of self-taken vaginal swabs and first-catch urine samples for the diagnosis of urogenital *Chlamydia trachomatis* and *Neisseria gonorrhoeae* with an amplified DNA assay in young women attending a public health sexually transmitted disease clinic. Sex Transm Dis 2006;33:491–495. [PubMed: 16547452]
47. Wiesenfeld HC, Lowry DLB, Heine RP, et al. Self-collection of vaginal swabs for the detection of Chlamydia, gonorrhea, and trichomonas. Sex Transm Dis 2001;28:321–325. [PubMed: 11403188]
48. Shafer M-A, Moncada J, Boyer C, et al. Comparing first-void urine specimens, self-collected vaginal swabs, and endocervical specimens to detect *Chlamydia trachomatis* and *Neisseria gonorrhoeae* by a nucleic acid amplification test. J Clin Microbiol 2003;41:4395–4399. [PubMed: 12958275]
49. Schachter J, McCormack Wm, Chernesky MA, et al. Vaginal swabs are appropriate specimens for diagnosis of genital tract infection with *Chlamydia trachomatis*. J Clin Microbiol 2003;41:3784–3789. [PubMed: 12904390]
50. Schachter J, Chernesky MA, Willis DE, et al. Vaginal swabs are the specimens of choice when screening for *Chlamydia trachomatis* and *Neisseria gonorrhoeae*: Results from a multicenter evaluation of APTIMA assays for both infections. Sex Transm Dis 2005;32:725–728. [PubMed: 16314767]
51. Gaydos CA, Theodore M, Dalesio N, et al. Comparison of three nucleic acid amplification tests for detection of *Chlamydia trachomatis* in urine specimens. J Clin Microbiol 2004;42:3041–3045. [PubMed: 15243057]
52. Gaydos CA, Quinn TC, Willis D, et al. Performance of the APTIMA Combo 2 assay for detection of *Chlamydia trachomatis* and *Neisseria gonorrheae* in female urine and endocervical swab specimens. J Clin Microbiol 2003;41:304–309. [PubMed: 12517865]
53. Moncada J, Schachter J, Hook EW III, et al. The effect of urine testing in evaluations of the sensitivity of the Gen-Probe APTIMA Combo 2 assay on endocervical swabs for *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. Sex Transm Dis 2004;31:273–277. [PubMed: 15107628]
54. Westrom, L.; Eschenbach, DA. Pelvic inflammatory disease. In: Holmes, KK.; Sparling, PF.; Mardh, P-A., et al., editors. Sexually Transmitted Diseases. Vol. 3rd ed. New York: McGraw-Hill; 1999. p. 783-809.
55. Ness RB, Soper DE, Holley RL, et al. Effectiveness of inpatient and outpatient treatment strategies for women with pelvic inflammatory disease: Results from the Pelvic Inflammatory Disease Evaluation and Clinical Health (PEACH) randomized trial. Am J Obstet Gynecol 2002;186:929–937. [PubMed: 12015517]
56. Simonsen L, Conn L, Pinner RW, et al. Trends in infectious disease hospitalizations in the United States, 1980–1994. Arch Intern Med 1998;158:1923–1928. [PubMed: 9759689]
57. Hirsch MB, Mosher WD. Characteristics of infertile women in the United States and their use of infertility services. Fertil Steril 1987;47:618–625. [PubMed: 3569545]
58. Thompson Medical Economics. Drug Topics Redbook Update. 2002;Vo1. 21:10.
59. The Medical Letter. The choice of antibacterial drugs. Med Lett Drugs Ther 1999;41:95–104. [PubMed: 10548955]

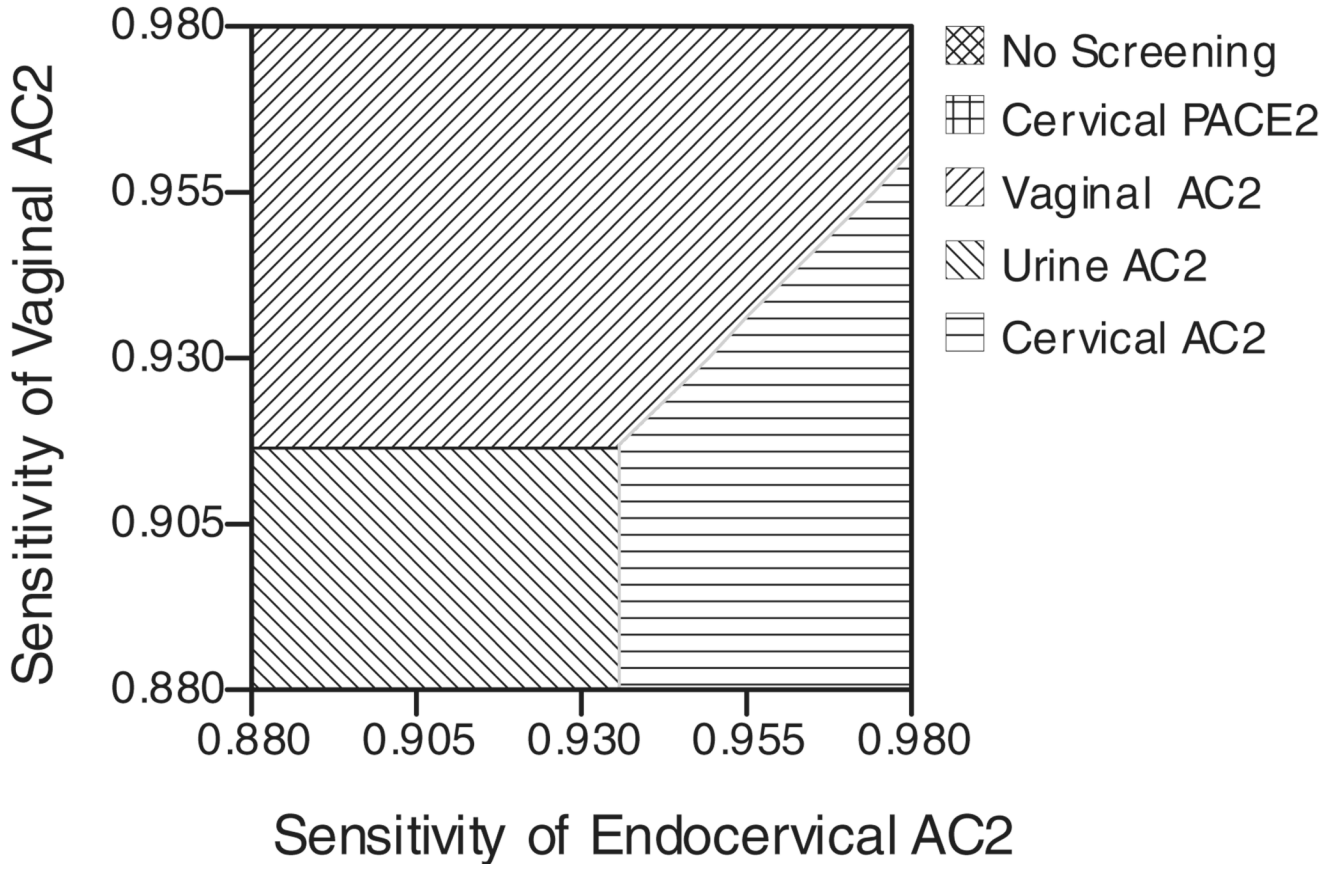

Fig. 1.
Two-way sensitivity analysis of endocervical AC2 sensitivity versus vaginal AC2 sensitivity. AC2 indicates Aptima Combo 2; PACE2, DNA probe.

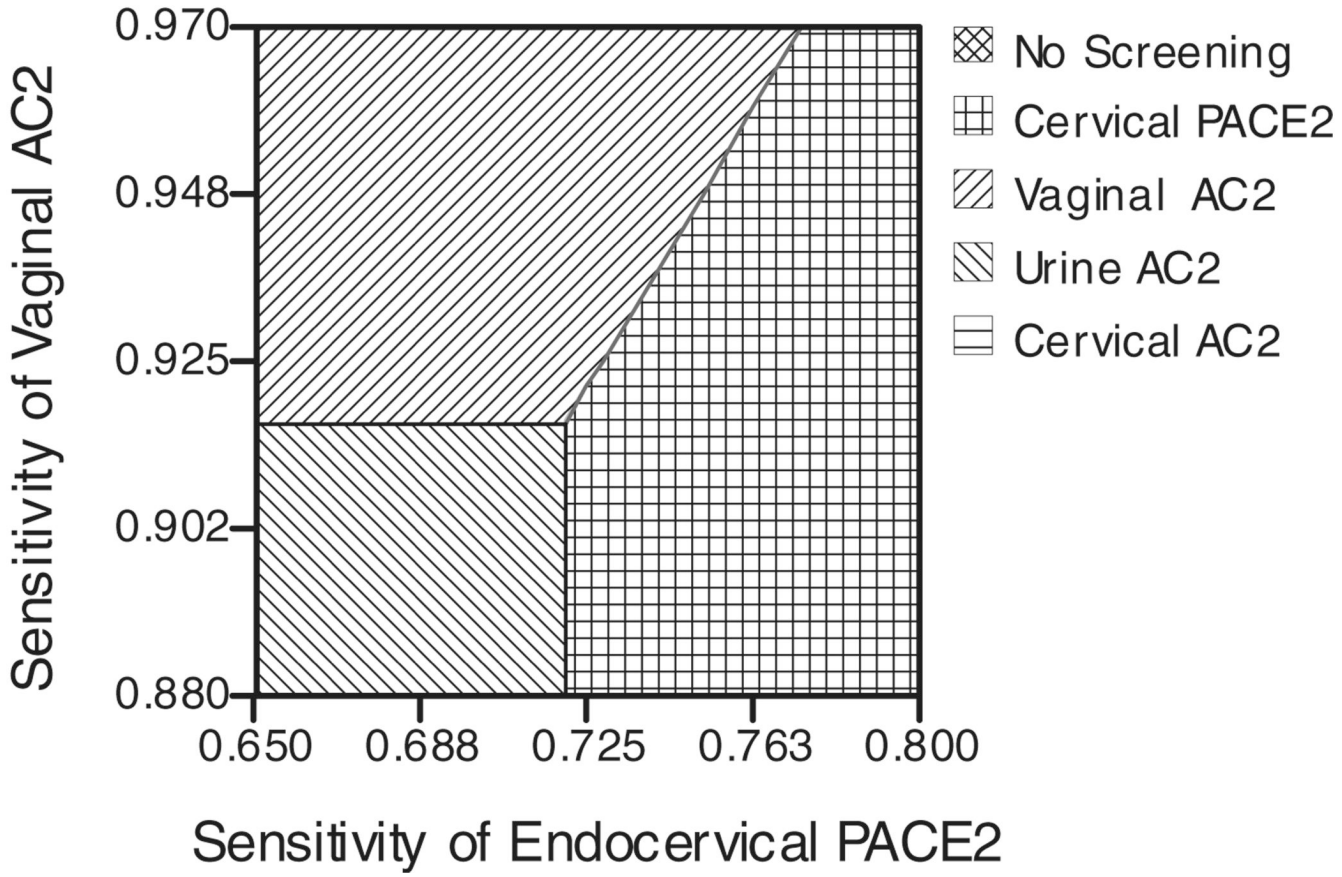

Fig. 2.
Two-way sensitivity analysis of endocervical PACE2 sensitivity versus vaginal AC2 sensitivity. PACE2 indicates DNA probe; AC2, Aptima Combo 2.

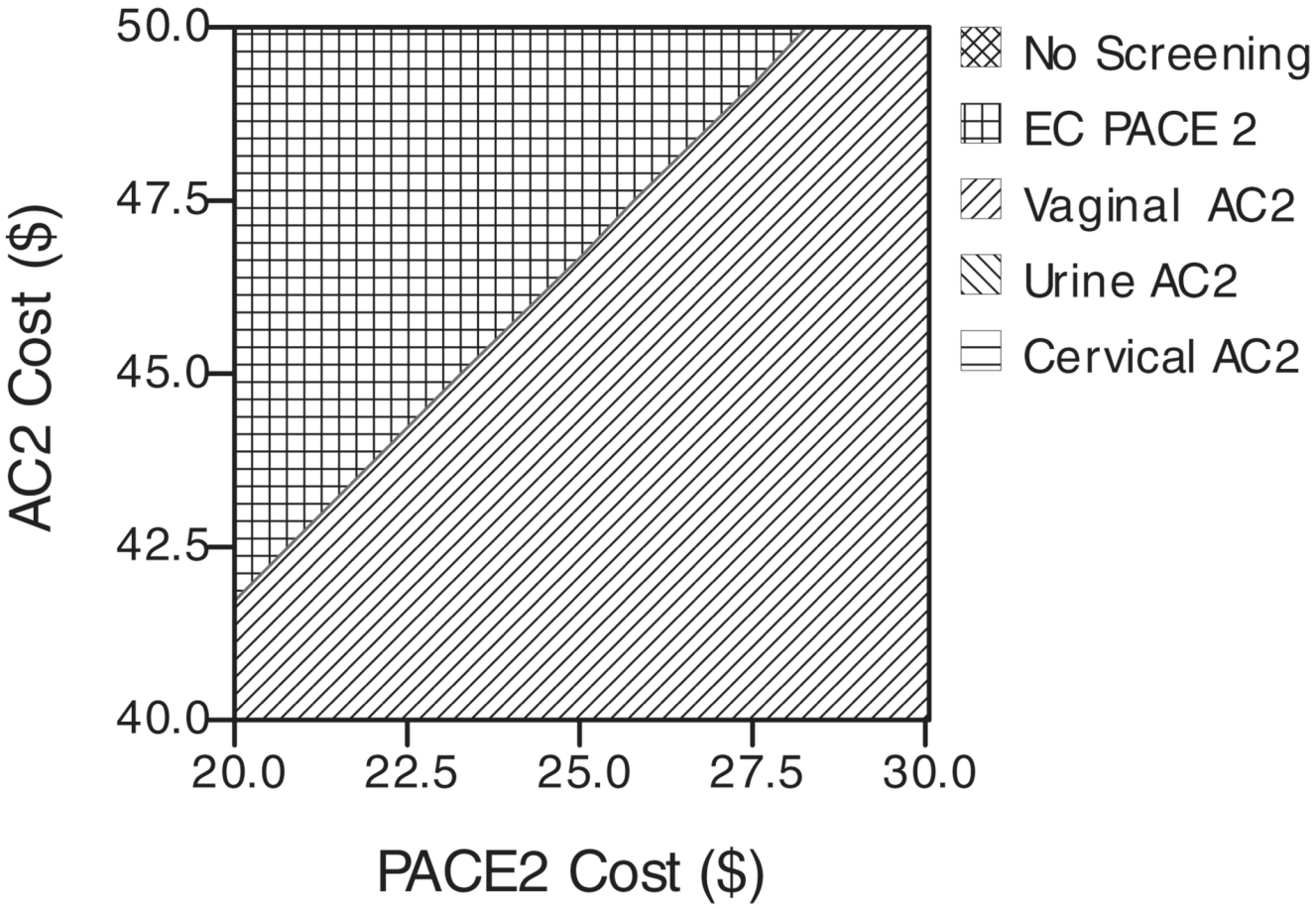

Fig. 3.
Two-way sensitivity analysis of AC2 cost versus PACE2 cost. AC2 indicates Aptima Combo 2; PACE2, DNA probe; EC, endocervical.

Table 1

Probability Estimates

Variable	Probability Estimate (%)	Range (%)	Reference
Chlamydia prevalence	11.1	7.7–14.5	Primary data and 95% CI
Sensitivity AC2			
Vaginal	97.2	85.5–99.9	Primary data and 95% CI
First catch urine	91.7	77.5–98.2	
Endocervical	91.7	77.5–98.2	
Specificity AC2			
Vaginal	99.5	97.1–99.7	50
First catch urine	99.3	98.8–99.3	50–52
Endocervical	98.3	97.6–98.3	50,52,53
Sensitivity DNA probe* (endocervical)	68.8	40–86.5	13–20
Specificity DNA probe* (endocervical)	99.8	95.6–100	13–20
PID	30	30–41	3,21–23
Proportion of PID that is silent	60	—	3,54
Proportion of PID that is overt	40	—	3,54
Inpatient treatment of PID	12.1	5–25	24,29,30,38,55,56
Chronic pelvic pain	18	—	24
Ectopic pregnancy	6	3.6–9.1	24–27
Infertility	9	7.7–20	24,25,27
Infertile women seeking fertility services	22.4	—	57
Proportion of women requiring a Pap smear and/or symptomatic and requiring a pelvic exam to rule out PID	79.0	71.3–86.8	Primary data and 95% CI
Proportion of women requiring a Pap smear and/or reporting abdominal pain and requiring a pelvic exam to rule out PID	50.5	40.9–60.0	Primary data and CI

* DNA probe was PACE2.

AC2 indicates Aptima Combo 2; PID, pelvic inflammatory disease.

Table 2

Cost Estimates (2006$)

Variable	Cost Estimate	Range	Reference
AC2*	$43.42	—	Maryland State Medicaid reimbursement rate
Endocervical DNA probe† cost	$28.02	—	Maryland State Medicaid reimbursement rate reimbursement STD clicnc
Cost to perform pelvic	Speculum, $0.68	—	Baltimore City STD clinic
examination at Baltimore	Clinician time, $4.72	—	
City STD clinic	Total: $5.40	—	
Cost of cervicitis treatment visit at Baltimore City STD clinic	Clinician visit, $10.12	—	Baltimore City STD clinic
Cost of treatment medication for cervicitis	Azithromycin 1 g, $15.84	—	Maryland public health price
Inpatient cost for PID treatment	$8900	$4277–$13,583	29 (HCUP 2003–South region)
Outpatient visit cost for PID treatment	Level 5 initial Office visit, $103 Level 4 F/U Office visit, $70	—	Maryland Medicaid rate
Cost of treatment medication	Ceftriaxone 250 mg, $20	—	58
for PID	Injection admin, $5	—	Estimate
	Doxycycline 100 mg BID × 14 d, $3	—	59
Cost for infertility treatment‡	$5091	$3915–$13,397	29–31 (HCUP 2003–South region)
Cost for ectopic pregnancy treatment§	$6294	$6294–$7947	29,30 (HCUP 2003–South region)
Cost for chronic pelvic pain treatment‖	$8997	$655–$16,694	4,6,24,30,32,33

*AC2 indicates Aptima Combo 2.

†DNA Probe was PACE2.

‡Estimated delay of 10 years before cost realized.

§Estimated delay of 5 years before cost realized.

‖Estimated delay of 2 years before cost realized.

Table 3

Cost Effectiveness Analysis

Screening Strategy	Total Cost	Cases of PID Expected	Incremental Costs	Incremental Cases of PID Prevented	Incremental Cost-Effectiveness Ratio (ICER)
Endocervical DNA probe*	$636,913	115	—	—	—
Endocervical AC2	$627,204	44	−$9709	71	−$137
First catch urine AC2	$613,732	44	−$13,472	0	−$13,472†
Self obtained vaginal AC2	$573,205	27	−$40,527	17	−$2384

*DNA Probe was PACE2 Assay.

†Division by 0 results in infinity, therefore, divided −$13,472 by 1.

AC2 indicates Aptima Combo 2.

Sex Transm Dis. Author manuscript; available in PMC 2009 July 16.

Table 4

Univariate Sensitivity Analyses

Variable	Alternate Value	Incremental Cost/Case of PID Prevented (ICER)
Prevalence	7.6%	$27
	6.5%	$425
Proportion treated	65%	$21
	56%	$406
Treated day of visit	30%	$6
	40%	$440
Cost of PID sequelae	$1210	$2
	$800	$404
Cost of endocervical	$21.60	$5
probe	$18.00	$410
Cost of self obtained	$49.80	$1
vaginal AC2	$53.40	$406
Sensitivity of endocervical	77.5%	$5
probe	80.5%	$415
Sensitivity of self obtained	88.5%	Break even
vaginal AC2	85.5%	$415

PID indicates pelvic inflammatory disease; ICER, incremental cost effectiveness ratio (compares self-obtained vaginal AC2 with endo-cervical DNA probe); AC2, Aptima Combo 2.