Prior Authorization Review  
Panel MCO Policy Submission

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Type of Submission – Check all that apply:
- [x] Revised Policy*
- [ ] Annual Review – No Revisions

*All revisions to the policy must be highlighted using track changes throughout the document. Please provide any clarifying information for the policy below:

CPB 0433 Chlamydia Trachomatis - Screening and Diagnosis

Revision History since last PARP submission:
08/23/2018 - This CPB has been revised to state that Chlamydia screening is considered medically necessary for all pregnant women in the first trimester and re-testing is considered medically necessary in pregnant women who tested positive in the first trimester.
04/25/2019 – Next tentative scheduled review date by Corporate.

Name of Authorized Individual (Please type or print):  
Dr. Bernard Lewin, M.D.

Signature of Authorized Individual: 

www.aetnabetterhealth.com/pennsylvania

Revised 08/23/2018
Chlamydia Trachomatis - Screening and Diagnosis

Policy

I. Aetna considers Chlamydia trachomatis (C. trachomatis) screening a medically necessary preventive service according to the recommendations of the National Institute for Health and Clinical Excellence, United States Preventive Services Task Force (USPSTF) and the Centers for Disease Control and Prevention (CDC). Chlamydia screening is recommended for the following groups:

A. All pregnant women in the first trimester; and
B. All sexually active women aged 24 years and younger; and
C. Women 25 years and older with any of the following risk factors for C. trachomatis infection:

1. Having had C. trachomatis or other sexually transmitted diseases in the past; or
2. New or multiple sexual partners; or
3. Not using condoms consistently or correctly; or

*Please see amendment for Pennsylvania Medicaid at the end of this CPB.*
II. Aetna considers C. trachomatis screening experimental and investigational for asymptomatic men, and for women who do not meet the above criteria, because of insufficient evidence in the peer-reviewed literature.

III. Aetna considers C. trachomatis diagnostic testing medically necessary for members with signs or symptoms of C. trachomatis infection.

IV. Aetna considers C. trachomatis re-testing in pregnant women who tested positive in the first trimester medically necessary.

V. Aetna considers home testing for C. trachomatis experimental and investigational because of insufficient evidence in the peer-reviewed literature.

VI. Aetna considers antigen detection point-of-care tests experimental and investigational for screening asymptomatic persons for Chlamydia trachomatis because their effectiveness has not been established.

Background

In its updated recommendations on Chlamydia trachomatis (C. trachomatis) screening, the USPSTF strongly recommended that clinicians routinely screen all sexually active women aged 24 years and younger, and other asymptomatic women at increased risk for infection, for chlamydial infection (USPSTF, 2007). Other risk factors for chlamydial infection include a history of chlamydial or other sexually transmitted infection, new or multiple sexual partners, inconsistent condom use, and exchanging sex for money or drugs. The USPSTF also recommended that clinicians routinely screen all asymptomatic pregnant women aged 24 years and younger for chlamydial infection. The USPSTF made no recommendation for or against routinely screening asymptomatic low-risk women in the general population for chlamydial infection. The USPSTF found at least fair evidence that screening low-risk women could detect some additional cases of Chlamydia trachomatis, but concluded that the potential benefits of screening low-risk women may be small and may not justify the possible harms.
The USPSTF made no recommendation for or against routine screening of asymptomatic, low-risk pregnant women aged 25 years and older for chlamydial infection. The USPSTF found fair evidence that the benefits of screening low-risk pregnant women are small and may not justify the possible harms.

The USPSTF concluded that the evidence is insufficient to recommend for or against routinely screening asymptomatic men for chlamydial infection. The USPSTF found no direct evidence to determine whether screening asymptomatic men for chlamydial infection is effective for reducing the incidence of new infections in women.

The American College of Obstetricians and Gynecologists (ACOG, 2017) recommend that all pregnant women be tested for chlamydia early in pregnancy. Pregnant women who tested positive in the first trimester should be re-tested within approximately 3-6 months, preferably in the 3rd trimester. In non-pregnant females, ACOG recommends testing in all women under 25 years and in women 25 years and older who have risk factors.

Chlamydia screening among young women under the age of 26 is a measure that has been adopted by the National Committee for Quality Assurance (NCQA) for inclusion in the Health Plan Employer Data and Information Set (HEDIS). C. trachomatis infection is the most common sexually transmitted disease (STD) in the United States affecting an estimated 4 million people. Prevalence is highest in sexually active females under the age of 25 years.

Most C. trachomatis infections cause no symptoms. Left untreated, C. trachomatis infection can lead to complications such as pelvic inflammatory disease in the female, which has emerged as a major cause of tubal factor infertility and ectopic pregnancy in women of childbearing age. Chlamydia infection can be passed to the newborn during delivery through the birth canal with a manifestation of neonatal eye infection or pneumonia. These sequelae are unfortunate because C. trachomatis infection is effectively treated with antibiotics.

Diagnosis is based on the detection of the microorganism itself, its antigens, or genetic material collected from the lower genital tract, or in some instances, a urine sample. The sensitivity of tissue culture ranges from 65 to 80%. More available non-culture tests, such as the direct fluorescent antibody (DFA) and the enzyme immunoassay (EIA), which detect chlamydial antigens in clinical specimens have
specificities from 96 to 99%. However, these tests with high specificity yield a large number of false-positives in a population with a low disease prevalence. DNA amplified hybridization tests are both highly specific and sensitive and are proving to be the best tests in large scale screening. Additionally, the LCR and the PCR can be performed on urine specimens. New DNA amplified hybridization techniques such as transcription mediated amplification (TMA), Q-B replicase amplified hybridization, and nucleic acid sequence-based amplification (NASBA) are currently being investigated and appear to be very promising.

Rietmeijer et al (2008) assessed the recent U.S. literature on chlamydia positivity in chlamydia screening programs among asymptomatic men in non-sexually transmitted disease clinic settings. These investigators reviewed published articles between 1995 and June 2007, using PubMed as the primary search tool. Articles were abstracted and positivity rates summarized by type of venue, race/ethnicity, age group, and U.S. region. The overall median positivity rate was 5.1%. The highest rates were observed among men tested in juvenile (7.9%) and adult (6.8%) detention facilities, among blacks (6.7%), the 15 to 19 years old (6.1%) and 20 to 24 years old (6.5%) age groups, and among men screened in the southern United States (6.4%). Chlamydia rates among men are high in certain venues, particularly correctional settings, but also depend on the demographical composition of the target population and location. The authors concluded that programs considering male chlamydia screening programs should conduct pilot programs to assess chlamydia positivity as well as feasibility and cost in target venues.

Gift and colleagues (2008) reviewed the literature on the cost-effectiveness of screening men for chlamydia. The reviewed studies examined both proactive and opportunistic screening and included screening of risk groups and of the general population. Some older studies included enzyme immunoassays; more recent studies featured nucleic acid amplification assays. Six studies used dynamic transmission models; 14 studies analyzed male and female chlamydia screening interventions. Several contained sufficient data to examine the cost-effectiveness of male screening compared with female screening. Male screening was preferred to expanded female screening in 1 study. In other studies, combined male and female screening programs were cost-saving. The authors concluded that studies comparing chlamydia screening in men with chlamydia screening in women may be the most useful for guidance to programs. The studies which compared the 2 generally have found that screening men from the general population is not
preferred to screening women from the general population, although 1 study found that screening of men from risk groups can be cost-effective compared with screening women from the general population.

Michel and colleagues (2009) assessed the performance of a Conformité Européenne (CE)-marked home test for chlamydia trachomatis (CT) that is available over the Internet. A total of 231 eligible women attending the Social Hygiene Clinic (SHC) or Obstetrics-Gynecology (OB-GYN) Clinic in Iloilo City, Philippines were recruited to an evaluation of the HandiLab-C chlamydia home test (HandiLab-C). One vaginal swab was tested with HandiLab-C on-site and the second in Cambridge, United Kingdom with 2 nucleic acid amplification tests (NAAT), the Roche Amplicor and Abbott m2000. The organism load of NAAT-positive swabs was quantified. Concordance between the NAATs was high (kappa agreement: 0.984). Using the Abbott assay as the gold standard, the sensitivity and specificity of the Roche assay were 97.4 % and 100 %, respectively. The prevalence of CT by Abbott was 8.0 % (8/100) in the OB-GYN Clinic and 23.7 % (31/131) at SHC. The sensitivity of HandiLab-C was 12.5 % (1/8) and 19.4 % (6/31) in OB-GYN and SHC, respectively; with specificities of 93.5 % (86/92) and 88 % (88/100), respectively. Overall positive and negative predictive values of HandiLab-C were 28 % and 84.5 % respectively. No correlation between HandiLab-C performance and organism load (range of 1.3 x 10(2) to 1.4 x 10(7) bacteria/swab) was observed. The authors concluded that the performance of HandiLab-C is very poor, with the test yielding more false-positive (18/193) than true-positive (7/38) results. It remains accessible via the Internet under various brand names and has retained its CE mark. This situation raises serious concerns about the regulation of diagnostic products available via the Internet and the standards of certain Notified Bodies that issue the CE mark.

Hadgu and Sternberg (2009) stated that Commercial NAATs have become one of the most frequently used tests for detecting CT. However, published studies have raised important concerns regarding the NAAT evaluation process in general and their reproducibility and clinical specificity in particular. This is because for many infectious diseases including chlamydia, a true gold standard simply does not exist and, as a result, estimation of test performance parameters in the absence of a gold standard is a difficult and challenging task.
Moncada et al (2009) stated that self-collected glans and rectal swab specimens from men who have sex with men (MSM) may be appropriate, convenient specimens for testing. These researchers evaluated the use of self-collected swabs for the detection of CT and neisseria gonorrhoeae by a transcription-mediated amplification test (AC2; Aptima Combo 2; Gen-Probe Inc.) and a strand displacement amplification test (SDA; ProbeTec; Becton Dickinson Co.) in MSM seen at the city STD clinic in San Francisco, CA. For the glans swab specimen, subjects enrolled early in the study rolled a Dacron swab across the meatus 3 times (method 1). A slightly more invasive procedure was performed later in the study: the subjects inserted the swab 1/4 inch into the urethra, rotated the swab, and then withdrew the swab (method 2). MSM self-collected a rectal swab specimen and also provided first-catch urine (FCU). Additional rectal swab samples were then obtained by the clinician. For the detection of CT and N. gonorrhoeae, all swabs were evaluated by AC2 and SDA, FCU was tested by AC2, and the clinician-collected rectal swabs were cultured. A rectal true-positive (TP) result was defined as a culture-positive result for CT or N. gonorrhoeae, 2 or more positive NAAT results, or a single NAAT-positive result confirmed by an alternate amplification method (the Aptima CT or N. gonorrhoeae test). A glans TP result was defined as a positive result for FCU, positive results for both glans specimens (one tested by AC2 and one tested by SDA), or a positive result for a single glans specimen confirmed by an alternate amplification method. The prevalence rates of CT and N. gonorrhoeae by testing of FCU were 6.8 % (60/882 specimens) and 12.2 % (108/882 specimens), respectively. Mixed results were obtained with the glans swab: N. gonorrhoeae detection by AC2 and SDA (method 1) had the best performance (sensitivities, greater than 92 %) with samples from a population with a higher prevalence of infection, but their performance for the detection of CT was poor and varied by collection method (sensitivities, 56 % to 68 %). The prevalence rates of CT and N. gonorrhoeae in the rectum were 7.3 % (66/907 specimens) and 9.4 % (83/882 specimens), respectively. The sensitivities of the tests with self-collected and clinician-collected rectal swab specimens were comparable (for CT, 41 % and 44 %, respectively, by SDA and 82 % and 71 %, respectively, by AC2; for N. gonorrhoeae, 77 % and 68 %, respectively, by SDA and 84 % and 78 %, respectively, by AC2). AC2 and SDA were far superior to culture for the detection of CT and N. gonorrhoeae in the rectum, with both tests detecting at least twice as many infections. While these investigators found self-collected rectal swabs from MSM to be valid specimens for testing, the sensitivities of the tests with glans swab specimens were disappointing except for those from patients with symptomatic N. gonorrhoeae infections. The authors stated that self-collected glans swab
specimens may not be appropriate for the detection of CT or for the detection of N. gonorrhoeae in low-risk or asymptomatic patients by AC2 and SDA, and they would not recommend their use; further studies are needed.

Cameron et al (2009) examined if postal testing kits (PTKs) or patient-delivered partner therapy (PDPT) for partners of women with CT reduce re-infection rates in women, compared with partner notification by patient referral. A total of 330 testing positive for chlamydia, at clinics for genito-urinary medicine, family planning and termination of pregnancy in Edinburgh, were randomized to 1 of 3 partner interventions: (i) patient referral, (ii) PTK (partners post urine for testing), or (iii) PDPT (1 g azithromycin for partners). Women submitted urine for chlamydia testing every 3 months. The primary outcome was re-infection assessed as time to first positive result by the Cox proportional hazard regression. The proportion of partners tested or treated with each intervention was determined. Out of 330 women, 215 (65 %) were re-tested over 12 months. There were 32 of 215 women (15 %) who re-tested positive (7, 15 and 10 women from the patient referral, PTK and PDPT groups, respectively). There was no significant difference in re-infection between PDPT versus patient referral (hazard ratio [HR] 1.32, 95 % confidence interval [CI]: 0.50 to 3.56), PTK versus patient referral (HR 2.35, 95 % CI: 0.94 to 5.88) or PDPT versus PTK (HR 0.55, 95 % CI: 0.24 to 1.24). There was no significant difference in the proportion of partners confirmed tested/treated between the patient referral (34 %) and PTK (41 %, p = 0.32) or PDPT (42 %, p = 0.28) groups. The authors concluded that PTK and PDPT do not reduce re-infection rates in women with chlamydia compared with patient referral. However, PDPT may offer other advantages such as simplicity and cost compared with patient referral.

Mania-Pramanik et al (2012) noted that in India, the impact of current C. trachomatis in reproductive health remains a neglected area of investigation. These investigators examined if current chlamydia infection is associated with any clinical complication that needs the attention of clinical investigators. In this cross-sectional study, these researchers enrolled 896 women attending the Gynecology Out Patient for the detection of C. trachomatis infection. Polymerase chain reaction (PCR) was used to diagnose current C. trachomatis infection and ELISA for past infections. Bacterial vaginosis, candida and trichomonas were screened. The results of symptomatic and asymptomatic groups were compared. The data was analyzed using Epi Info version 6 and "Z" test. A probability value of p ≤ 0.05 was considered as significant. Statistical analysis revealed significant association
between current C. trachomatis infection with infertility when comparing infected fertile (18.6 % versus 9.4 %, odds ratio: 2.19, p< 0.0005) and uninfected infertile women (45.6 % versus 27.3%, odds ratio: 2.24, p < 0.0001). Average infection rate was 12.1 %, highest in women with infertility (18.6 %) or with ectopic pregnancy (25 %). Significant proportions of infected women with infertility (p < 0.01) or with recent pregnancy (p < 0.001) were asymptomatic. Follow-up of infected women who became negative after treatment [28 women from infertility group and 9 women with recurrent spontaneous abortion (RSA)] revealed live-birth in 8 (21.6 %) women within 1 year, 4 with infertility and 4 with RSA. The authors concluded that the findings of this study suggested association between current C. trachomatis infection and infertility. Absence of signs and symptoms associated with this infection highlights its diagnosis in women with a history of infertility and RSA for their better management, as revealed by live-births with 1 year of follow-up.

Naderi et al (2012) stated that damage of the fallopian tube after sexually transmitted diseases like C. trachomatis, is an important risk factor for ectopic pregnancy (EP). These researchers evaluated the prevalence of C. trachomatis infection in patients with EP in the southeastern part of Iran. Polymerase chain reaction on fallopian tube tissue was applied to detect Chlamydia DNA in 42 patients with EP (EP group) and 87 patients without EP (control group) who underwent tubal ligation. The same protocol was performed with urine samples taken from the husbands in both groups. Out of all studied females, 5 patients in the EP group were PCR-positive for C. trachomatis and none of the control group subjects was PCR-positive for C. trachomatis infection (p < 0.05). Among the husbands, the PCR result was positive in the urine of 19 males (9 in the EP group and 10 in the control group). All PCR-positive women had husbands with PCR-positive urine samples. No significant difference was found between chlamydia infection in the EP and the control groups regarding age, duration of marriage, contraceptive method and history of infertility surgery and pelvic pain. There was no significant difference between prevalence of EP in women based on the PCR outcome in the husbands. The chlamydia infection in men did not show any relation to the number of marriages. The authors concluded that based on these findings, it can be concluded that chlamydia infection is an important risk factor of the fallopian tube damage and EP. Thus, screening programs and treatment of chlamydia infection are recommended in young women and high-risk women and men.
Kamel et al (2013) stated that *C. trachomatis* infection is a worldwide-distributed sexually transmitted infection that may lead to infertility. These researchers reported the prevalence of *C. trachomatis* infection among infertile women in Saudi Arabia. A community-based study was carried out at the obstetrics and gynecology clinic at Jazan General Hospital, Saudi Arabia. The study group included 640 Saudi infertile women aged between 18 and 40 years and who attended the gynecology clinic for infertility examination throughout 1 year of study (from July 1, 2011 to June 30, 2012). The randomized control group included 100 Saudi fertile women who attended the obstetrics clinic for routine antenatal care. All recruited women were screened for chlamydia infection by enzyme-linked immunosorbent assay (ELISA) for detection of serum-specific antibodies and then re-tested by the McCoy cell culture technique. The prevalence of *C. trachomatis* infection among infertile women was high, at 15.0 %. The rate of chlamydia infection detected by ELISA was 9.84 %, and it was 12.03 % by the culture method (p = 0.2443). The authors concluded that high prevalence of *C. trachomatis* infection among Saudi infertile women demands a national screening program for early detection among infertile couples.

The National Institute for Health and Clinical Excellence's guideline on “Fertility: Assessment and treatment for people with fertility problems” (NICE, 2013) recommended that “Before undergoing uterine instrumentation women should be offered screening for Chlamydia trachomatis using an appropriately sensitive technique”.

**Home Testing:**

Rotblatt et al (2013) noted that in response to high chlamydia and gonorrhea morbidity, particularly among young African American and Latina women, the Los Angeles County Department of Public Health launched a free home testing program for chlamydia trachomatis (CT) and neisseria gonorrhoeae (NG). The primary objectives were to increase chlamydia and gonorrhea testing by removing key barriers and to motivate young women to screen routinely for these STDs. The program was promoted with a social marketing campaign urging women to order home collection kits online or by telephone. In the program's first year, 2,927 kits were ordered and 1,543 testable specimens returned; 131 women (8.5 %) had a positive test result. The authors concluded that the strong response, high morbidity, and program scalability indicated strong potential as a new tool for STD control.
Jamil et al (2013) systematically reviewed the strategies and outcomes of home-based CT/NG screening programs. Electronic databases were searched for home-based CT and/or NG screening studies published since January 2005. Screening information (e.g., target group, recruitment and specimen-collection method) and quantitative outcomes (e.g., number of participants, tests and positivity) were extracted. The screening programs were classified into 7 groups on the basis of strategies used. These researchers found 29 eligible papers describing 32 home-based screening programs. In 7 outreach programs, people were approached in their homes: a median of 97% participants provided specimens and 76% were tested overall (13,717 tests). In 7 programs, people were invited to receive postal test-kits (PTKs) at their homes: a median of 37% accepted PTKs, 79% returned specimens and 19% were tested (46,225 tests). Postal test-kits were sent along with invitation letters in 5 programs: a median of 33% returned specimens and 29% of those invited were tested (15,126 tests). Postal test-kits were requested through the Internet or phone without invitations in 4 programs and a median of 32% returned specimens (2,666 tests). Four programs involved study personnel directly inviting people to receive PTKs: a median of 46% accepted PTKs, 21% returned specimens and 9.1% were tested (341 tests). Postal test-kits were picked-up from designated locations in 3 programs: a total of 6,765 kits were picked-up and 1,167 (17%) specimens were returned for screening. Two programs used a combination of above strategies (2,395 tests) but the outcomes were not reported separately. The overall median CT positivity was 3.6% (interquartile range of 1.7 to 7.3%). The authors concluded that a variety of strategies have been used in home-based CT/NG screening programs. The screening strategies and their feasibility in the local context need to be carefully considered to maximize the effectiveness of home-based screening programs.

Smith et al (2014) stated that repeat infection with CT is common and increases the risk of sequelae in women and HIV sero-conversion in men who have sex with men (MSM). Despite guidelines recommending chlamydia re-testing 3 months after treatment, re-testing rates are low. These researchers are conducting the first randomized controlled trial (RCT) to evaluate the effectiveness of home collection combined with short message service (SMS) reminders on chlamydia re-testing and re-infection rates in 3 risk groups. The REACT (re-test after CT) trial involves 600 patients diagnosed with chlamydia: 200 MSM, 200 women and 200 heterosexual men recruited from 2 Australian sexual health clinics where SMS reminders for re-testing are routine practice. Participants will be randomized to the home group (3-month SMS reminder and home-collection) or the clinic group.
Participants in the home group will be given the choice of attending the clinic if they prefer. The mailed home-collection kit includes a self-collected vaginal swab (women), UriSWAB (Copan) for urine collection (heterosexual men), and UriSWAB plus rectal swab (MSM). The primary outcome is the re-test rate at 1 to 4 months after a chlamydia diagnosis, and the secondary outcomes are: the repeat positive test rate; the re-infection rate; the acceptability of home testing with SMS reminders; and the cost-effectiveness of home testing. Sexual behavior data collected via an online survey at 4 to 5 months, and genotyping of repeat infections, will be used to discriminate re-infections from treatment failures. The trial will be conducted over 2 years. An intention-to-treat analysis will be conducted. The authors concluded that this study will provide evidence about the effectiveness of home-collection combined with SMS reminders on chlamydia re-testing, repeat infection and re-infection rates in 3 risk groups. The trial will determine client acceptability and cost-effectiveness of this strategy.

In a Cochrane review, Fajardo-Bernal et al (2015) evaluated the safety and effectiveness of home-based specimen collection as part of the management strategy for CT and NG infections compared with clinic-based specimen collection in sexually-active people. These investigators searched the Cochrane Sexually Transmitted Infections Group Specialized Register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE and LILACS on May 27, 2015, together with the World Health Organization International Clinical Trials Registry (ICTRP) and ClinicalTrials.gov. They also hand-searched conference proceedings, contacted trial authors and reviewed the reference lists of retrieved studies. Randomized controlled trials of home-based compared with clinic-based specimen collection in the management of CT and NG infections were selected for analysis. Three review authors independently assessed trials for inclusion, extracted data and assessed risk of bias. They contacted study authors for additional information, and resolved any disagreements through consensus. These researchers used standard methodological procedures recommended by Cochrane. The primary outcome was index case management, defined as the number of subjects tested, diagnosed and treated, if test positive. A total of 10 trials involving 10,479 participants were included. There was inconclusive evidence of an effect on the proportion of participants with index case management (defined as individuals tested, diagnosed and treated for CT or NG, or both) in the group with home-based (45/778, 5.8 %) compared with clinic-based (51/788, 6.5 %) specimen collection (risk ratio (RR) 0.88, 95 % CI: 0.60 to 1.29; 3 trials, I² = 0 %, 1,566 participants, moderate quality). Harms of home-based specimen collection...
were not evaluated in any trial. All 10 trials compared the proportions of individuals tested. The results for the proportion of participants completing testing had high heterogeneity ($I^2 = 100\%$) and were not pooled. These investigators could not combine data from individual studies looking at the number of participants tested because the proportions varied widely across the studies, ranging from 30\% to 96\% in home group and 6\% to 97\% in clinic group (low-quality evidence). The number of participants with positive test was lower in the home-based specimen collection group (240/2074, 11.6\%) compared with the clinic-based group (179/967, 18.5\%) (RR 0.72, 95\% CI: 0.61 to 0.86; 9 trials, $I^2 = 0\%$, 3,041 participants, moderate quality). The authors concluded that home-based specimen collection could result in similar levels of index case management for CT or NG infection when compared with clinic-based specimen collection. Increases in the proportion of individuals tested as a result of home-based, compared with clinic-based, specimen collection were offset by a lower proportion of positive results. The harms of home-based specimen collection compared with clinic-based specimen collection have not been evaluated. They stated that future RCTs to examine the effectiveness of home-based specimen collection should be designed to measure biological outcomes of sexually transmitted infections (STI) case management (e.g., proportion of subjects with negative tests for the relevant STI at follow-up).

Furthermore, an UpToDate review on “Clinical manifestations and diagnosis of Chlamydia trachomatis infections” (Marrazzo, 2016) does not mention home testing as a diagnostic tool.

Salow and associates (2017) evaluated the concordance between clinic-collected extra-genital specimens and self-collected mailed-in extra-genital specimens among participants seeking sexually transmitted infection testing at a free clinic in Hollywood, CA. A convenience sample of 210 men who have sex with men were enrolled between February 29, 2016 and December 21, 2016 and received mail-in testing kits for CT and NG. All testing was performed using the GeneXpert CT/NG (Cepheid, Sunnyvale, CA). From the 210 mail-in kits distributed, 149 mail-in kits (71.0\%) were returned to the laboratory, resulting in 145 pairs (clinic-collected and mail-in) of rectal test results and 148 pairs of pharyngeal test results for both CT and NG detection. The concordance was 95.0\% for all CT rectal tests, 99.3\% for all CT pharyngeal tests, 95.7\% for all NG rectal tests, and 97.2\% for all NG pharyngeal tests. The authors concluded that roughly 2/3 of mail-in test kits were returned and concordance was generally high, however more than 1/3 of positive
results were missed in mail-in samples. They stated that the prevalence of potential false-negative results among mail-in samples warrants caution when implementing mail-in sexually transmitted infections (STI) testing strategies.

Moreover, these investigators stated that while the present study indicated that mail-in STI testing may not be a viable alternative to clinic-based STI testing, focus groups suggested people prefer having the option to test in the comfort of their own homes. Their research suggested that mail-in collection strategies may reach a greater number of individuals for screening that otherwise would not access testing services. They noted that future research should analyze the cost-effectiveness of mail-in samples versus clinic-collected samples due to the low cost of mailing specimens. In addition, providing easy-to-use in-home self-collected test kits may address access, confidentiality, and stigma-related barriers to STI clinic-based services.

**Chlamydia Trachomatis Infection-Associated Risk of Cervical Cancer:**

Zhu and colleagues (2016) stated that as whether chlamydia trachomatis infection increases the risk of cervical cancer is controversial in the literature, these investigators performed a meta-analysis. Based on a comprehensive search of publications in the Medline, Cochrane, and Embase databases, these researchers identified and extracted data from all relevant articles examining C. trachomatis infection and the risk of cervical cancer. The quality of each included study was assessed according to the 9-star Newcastle-Ottawa scale. The strength of association between the C. trachomatis and risk of cervical cancer was estimated by odds ratio (OR) and 95 % CIs. A total of 22 studies with 4,291 cervical cancer cases and 7,628 controls were identified. Overall, C. trachomatis was significantly linked to increased cervical cancer risk in prospective studies (OR = 2.21, 95 % CI: 1.88 to 2.61, p < 0.001), as well as in retrospective studies (OR = 2.19, 95 % CI: 1.74 to 2.74, p < 0.001). Additionally, with a multi-variate logistic regression analysis adjusted for HPV and age, C. trachomatis infection was identified as an independent predictor of cervical cancer in 11 studies (OR = 1.76, 95 % CI: 1.03 to 3.01, p = 0.04). Co-infection of human papilloma virus (HPV) and C. trachomatis has a higher risk of cervical cancer (OR = 4.03, 95 % CI: 3.15 to 5.16, p < 0.001). A subgroup analysis based on histological type indicated an elevated risk for both squamous cell carcinoma (OR = 2.21, 95 % CI: 2.00 to 2.45, p < 0.001), and adenocarcinoma (OR = 1.61, 95 % CI: 1.21 to 2.15, p = 0.001), in associated with C. trachomatis. Subgroup analysis by where C. trachomatis infection was detected showed a significantly higher risk of cervical cancer associated with C. trachomatis
infection detected in serum (OR=2.20, 95 % CI: 2.01 to 2.42, p<0.001), cervical tissue blocks (OR=2.88, 95 % CI: 1.21 to 6.83, p=0.02), and cervical secretion (OR =2.71, 95 % CI: 1.41 to 5.20, p=0.003), especially in serum with no obvious heterogeneity. The authors concluded that these novel data demonstrated that individuals infected with C. trachomatis have a higher risk of cervical cancer. Thus, it is necessary to expand C. trachomatis infection screening and treat women with C. trachomatis promptly, particularly those with HPV infections. They stated that this approach will not only protect against pelvic inflammatory disease (PID) and infertility, but may also prevent cervical cancer. Moreover, these researchers stated that the underlying interaction between C. trachomatis and cervical cancer risk needs to be confirmed in longitudinal studies. Thus, the findings of this study called for further investigation in more prospective studies to provide more definitive evidence concerning the role of this pathogen as a promoter of HPV-mediated cervical carcinogenesis.

This study had several drawbacks: (i) most of the quantitative assessment studies were based on case-control studies where data on prevalence of C. trachomatis and cervical cancers were acquired simultaneously, rather than longitudinally. None of the studies had taken into account the association between the duration of C. trachomatis infection and the risk of cervical cancer, (ii) a meta-analysis is impossible to tackle the problems of confounding factors that could be inherent in the included studies. Inadequate control for confounders may bias the results in over-estimation or under-estimation of risk estimates, and (iii) heterogeneity may be introduced because of methodological differences among studies, including different specimen sources. Although there was low possibility of bias on visualization of funnel plots in this meta-analysis, the retrieved literature might potentially not be comprehensive enough. Studies with a statistically significant effect are more likely to be published and to be cited by other authors, while the results showed no association between C. trachomatis and cervical cancer may be unpublished.

Point-of-Care Tests for Screening of C. Trachomatis:

Kelly and colleagues (2017) summarized systematic reviews of the performance characteristics of commercially available point-of-care tests (POCT) for screening and diagnosis of urogenital CT infection. Two separate systematic reviews covering the periods 2004 to 2013 and 2010 to 2015 were conducted on rapid CT POCTs. Studies were included if tests were evaluated against a valid reference
standard. In the 1st review, a total of 635 articles were identified, of which 11 were included; 9 studies evaluated the performance of 8 antigen detection rapid POCTs on 10,280 patients and 2 studies evaluated a near-patient nucleic acid amplification test (NAAT) on 3,518 patients. Pooled sensitivity of antigen detection tests was 53 %, 37 % and 63 % for cervical swabs, vaginal swabs and male urine, and specificity was 99 %, 97 % and 98 %, respectively. The pooled sensitivity and specificity of the near-patient NAAT for all specimen types were greater than 98 % and 99.4 %, respectively. The 2nd review identified 2 additional studies on 4 antigen detection POCTs with sensitivities and specificities of 22.7 % to 37.7 % and 99.4 % to 100 %, respectively. A new 2-step, 15-min rapid POCT using fluorescent nanoparticles showed performance comparable to that of near-patient NAATs. The authors concluded that the findings of these 2 systematic reviews showed that antigen detection POCTs for CT, although easy to use, lacked sufficient sensitivity to be recommended as a screening test. They noted that near-patient NAAT showed acceptable performance as a screening or diagnostic test but requires electricity, takes 90 mins and is costly; more affordable POCTs are in development.

Appendix

The following tests are considered medically necessary for screening or diagnosis of *C. trachomatis* infection:

1. Cell culture
2. Enzyme immunoassay (EIA)
3. Direct fluorescent antibody (DFA)
4. DNA hybridization (DNA probe)
5. DNA amplified hybridization (nucleic acid amplification) which includes any of the following:
   - Ligase chain reaction (LCR); or
   - Polymerase chain reaction (PCR); or
   - Self-sustaining sequence replication (SSR); or
   - Strand displacement amplification (SDA).

CPT Codes / HCPCS Codes / ICD-10 Codes

Information in the [brackets] below has been added for clarification
purposes. Codes requiring a 7th character are represented by "+":

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>CPT codes covered if selection criteria are met (not covered for screening of</strong></td>
</tr>
<tr>
<td></td>
<td><strong>asymptomatic men):</strong></td>
</tr>
<tr>
<td>86631</td>
<td>Antibody; Chlamydia</td>
</tr>
<tr>
<td>86632</td>
<td>Chlamydia, IgM</td>
</tr>
<tr>
<td>87110</td>
<td>Culture, Chlamydia, any source</td>
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<tr>
<td>87270</td>
<td>Infectious agent antigen detection by immunofluorescent technique;</td>
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<td></td>
<td>Chlamydia trachomatis</td>
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<tr>
<td>87320</td>
<td>Infectious agent antigen detection by immunoassay technique, (eg,</td>
</tr>
<tr>
<td></td>
<td>enzyme immunoassay [EIA], enzyme-linked immunosorbent assay [ELISA],</td>
</tr>
<tr>
<td></td>
<td>immunochemiluminometric assay [IMCA]) qualitative or semiquantitative,</td>
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<tr>
<td></td>
<td>multiple-step method; Chlamydia trachomatis</td>
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<tr>
<td>87490</td>
<td>Infectious agent detection by nucleic acid (DNA or RNA); Chlamydia trachomatis,</td>
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<td></td>
<td>direct probe technique</td>
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<td>87491</td>
<td>Chlamydia trachomatis, amplified probe technique</td>
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<tr>
<td>87492</td>
<td>Chlamydia trachomatis, quantification</td>
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<td>87798</td>
<td>Infectious agent detection by nucleic acid (DNA or RNA), not otherwise specified;</td>
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<td></td>
<td>amplified probe technique, each organism</td>
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<td>87801</td>
<td>Infectious agent detection by nucleic acid (DNA or RNA), multiple organisms;</td>
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<tr>
<td></td>
<td>amplified probe(s) technique</td>
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<tr>
<td>87810</td>
<td>Infectious agent detection by immunoassay with direct optical observation;</td>
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<tr>
<td></td>
<td>Chlamydia trachomatis</td>
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<tr>
<td></td>
<td><strong>ICD-10 codes covered if selection criteria are met:</strong></td>
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<tr>
<td>N97.0</td>
<td>Female infertility</td>
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<tr>
<td>N97.9</td>
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<td>Z11.3</td>
<td>Encounter for screening for infections with a predominantly sexual mode of</td>
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<tr>
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<td>transmission</td>
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<td>Z11.8</td>
<td>Encounter for screening for other infectious and parasitic diseases [chlamydia]</td>
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<td>Z22.4</td>
<td>Carrier of infections with a predominantly sexual mode of transmission</td>
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<tr>
<td>Z31.41</td>
<td>Encounter for fertility testing</td>
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<td>Z72.51</td>
<td>High-risk sexual behavior</td>
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<td>Z72.53</td>
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The above policy is based on the following references:


43. Adelaide Health Technology Assessment on behalf of National Horizon Scanning Unit (HealthPACT and MSAC). Rapid point-of-care test for the detection of chlamydia; Horizon scanning prioritising summary - volume 13. Adelaide, SA: Adelaide Health Technology Assessment on behalf of National Horizon Scanning Unit (HealthPACT and MSAC); 2006.


to increase chlamydia retesting and detect repeat positive tests. BMC Infect Dis. 2014;14:223.


70. Marrazzo J. Clinical manifestations and diagnosis of Chlamydia trachomatis infections. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed February 2016.


Amendment to
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0433 Chlamydia Trachomatis - Screening and Diagnosis

There are no amendments for Medicaid.

www.aetnabetterhealth.com/pennsylvania
Revised 08/23/2018