Multitarget Polymerase Chain Reaction Testing for Diagnosis of Bacterial Vaginosis

Policy Number: 2.04.127  Last Review: 12/2018
Origination: 12/2014  Next Review: 12/2019

Policy
Blue Cross and Blue Shield of Kansas City (Blue KC) will not provide coverage for Multitarget Polymerase Chain Reaction Testing for Diagnosis of Bacterial Vaginosis. This is considered investigational.

When Policy Topic is covered
Not Applicable

When Policy Topic is not covered
Multitarget polymerase chain reaction (PCR) testing for diagnosis of bacterial vaginosis is considered investigational.

Considerations
The most common diagnostic approach to BV is use of the Amsel criteria. The Amsel criteria require 3 of the following 4 to be present in order for a diagnosis of BV to be confirmed:

- vaginal discharge that is homogeneous, thin and whitish gray discharge;
- presence of clue cells on microscopic examination. These are squamous epithelial cells that normally have a sharply defined cell border but in BV, have bacteria adherent to their surfaces and appear to be “peppered” with bacteria;
- pH of vaginal fluid greater than 4.5;
- a fishy odor of vaginal discharge before or after addition of 10% KOH

For patients who cannot be diagnosed by the Amsel criteria, there are other scoring systems used in conjunction with Gram stain for the laboratory diagnosis of BV:

Nugent and Ison and Hay Criteria:
Levels of 3 types of bacteria in vaginal discharge samples are estimated, Lactobacillus, Gardnerella/Bacteroides and Mobiluncus, Levels of Lactobacillus and Gardnerella/Bacteroides are rated on a scale of 0 to 4 based on the number of
cells per field at 100X magnification, and levels of Mobiluncus is rated on a scale from 0 to 2. A composite score is then calculated by summing the 3 subscores, as follows:

Not consistent with BV:
Score of 0-3; or
Score of 4-6 with clue cells not present

Consistent with BV:
Score of 4-6 with clue cells present; OR
Score of at least 7

Some clinicians include a third, middle category in Nugent scoring, with a total score of 0-3 considered normal, 4-6 as intermediate/equivocal and 7-10 as definite BV.

The simplified Ison and Hay criteria are as follows:

- Grade 1 (Normal): Lactobacillus morphotypes predominate;
- Grade 2 (Intermediate): Flora are mixed with some Lactobacillus morphotypes and some Gardnerella or Mobiluncus morphotypes present;
- Grade 3 (BV): Gardnerella and/or Mobiluncus morphotypes predominate. Lactobacilli morphotypes few or absent.

<table>
<thead>
<tr>
<th>Description of Procedure or Service</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Populations</strong></td>
</tr>
</tbody>
</table>
| Individuals:  
• With signs or symptoms of bacterial vaginosis | Interventions of interest are:  
• Multitarget polymerase chain reaction testing | Comparators of interest are:  
• Clinical and microscopic evaluation, including scoring systems such as the Nugent score | Relevant outcomes include:  
• Test accuracy  
• Test validity  
• Symptoms  
• Change in disease status |

Bacterial vaginosis (BV) is a common medical condition resulting from an imbalance in the normal vaginal flora. Although identification of Gardnerella vaginalis has traditionally been associated with BV, there is no single etiologic agent. Most cases are asymptomatic, and most symptomatic cases can be diagnosed using clinical and microscopic evaluation. Multitarget polymerase chain reaction (PCR) testing is proposed as an alternative to currently available laboratory tests to diagnosis BV. This test may improve outcomes if it is a more accurate and reliable method to diagnose BV, especially in symptomatic women with an indeterminate diagnosis.

In individuals who have signs or symptoms of BV who receive multitarget PCR testing, the evidence includes several prospective studies on technical performance and diagnostic accuracy. Relevant outcomes are test accuracy and validity, symptoms, and change in disease status. Several studies have evaluated the diagnostic accuracy of multitarget PCR tests for BV, including 2 studies evaluating commercially available tests. The studies found sensitivities between
90% and 95% and specificities between 85% and 90% compared with standard methods of diagnosis. Most studies used a combination of the Amsel criteria and Nugent scoring as the reference standard. There is a lack of direct evidence on the clinical utility of PCR testing for BV (ie, studies showing that testing leads to better patient management decisions and/or better health outcomes than current approaches). Moreover, a chain of evidence does not currently support multitarget testing because most symptomatic women can be diagnosed with a standard workup and/or a trial of empirical therapy, and it is not clear which subpopulations might benefit most from this test. Studies have not been conducted in the most clinically relevant target population: symptomatic women with indeterminate diagnoses after standard workup. The evidence is insufficient to determine the effects of the technology on health outcomes.

Background

**Bacterial Vaginosis**

Bacterial vaginosis (BV) is a condition caused by an imbalance in the normal bacteria vaginal flora. It is common, especially in women of reproductive age. While there is no single known etiologic agent, there is a shift in vaginal flora that involves a depletion of Lactobacillus species and overgrowth of other bacteria, including Gardnerella vaginalis, Mycoplasma hominis, Peptostreptococcus, Mobiluncus species, and other anaerobic gram-negative rods. Prevalence of the condition is high, and it is asymptomatic in most cases. According to data from a nationally representative sample of women surveyed in 2001 to 2004, the prevalence of BV among women ages 14 to 49 in the United States was 29%.

Additionally, BV is often confused with nonbacterial causes of vaginitis, including Candida (ie, yeast infection, caused by a fungus) and Trichomonas (caused by a parasite).

When symptomatic, BV is associated with characteristic signs and symptoms. The most common sign of BV is an abnormal grayish-white vaginal discharge, generally with an unpleasant, often “fishy” smell. Some women experience mild itching. Additionally, BV may be a risk factor for conditions such as preterm delivery and spontaneous abortion in pregnant women, pelvic inflammatory disease, as well as acquisition of HIV and other sexually transmitted infections. Because of potential risks during pregnancy, treatment of BV is indicated for symptomatic pregnant women. However, national organizations do not recommend routine screening for BV among pregnant women, and national guidelines do not address screening of nonpregnant women.

**Treatment**

Though BV resolves spontaneously in a high percentage of women, treatment for symptomatic BV is usually a course of oral antibiotics, either metronidazole or clindamycin. Antibiotic treatment results in a high rate of remission of symptoms, but recurrences are common within the first year after treatment. Probiotics, alone or in conjunction with antibiotics, are also used, but their efficacy in improving cure rates or preventing recurrences is not well-characterized.
Laboratory- and Examination-based methods of Diagnosis
BV can be diagnosed in the primary care setting based on patient-reported symptoms, clinical findings during vaginal examination and analysis of vaginal discharge. Office-based analysis of vaginal discharge includes a wet mount preparation using saline, an odor (“whiff”) test to detect amines before or after the addition of 10% potassium hydroxide (KOH) and a test of the pH level. Clinical diagnosis generally involves applying the Amsel criteria, which requires 3 of the following 4 to be present in order for a diagnosis of BV to be confirmed:
- vaginal discharge that is homogeneous, thin and whitish gray discharge;
- presence of clue cells on microscopic examination. These are squamous epithelial cells that normally have a sharply defined cell border but in BV, have bacteria adherent to their surfaces and appear to be “peppered” with bacteria;
- pH of vaginal fluid greater than 4.5;
- a fishy odor of vaginal discharge before or after addition of 10% KOH

In most cases of uncomplicated BV, clinical and microscopic examination of the discharge is sufficient to make a presumptive diagnosis using the Amsel criteria. For patients with a moderate to high probability of BV following clinical and microscopic exam, an empiric treatment trial can be prescribed. Patients who respond to empiric treatment do not require further workup.

A subset of women may require more definitive tests to determine whether BV is present. These include women with unusual or unexpected signs and symptoms and those in whom it is not possible to exclude other etiologies with certainty. In these cases, laboratory tests are available to assist with making a definitive diagnosis. Gram staining of vaginal discharge samples is the conventional laboratory method of BV diagnosis, and many experts consider it to be the criterion standard for diagnosing BV. Samples are analyzed using criteria such as the Nugent criteria, or a modified version by Ison and Hay (see Considerations).

A limitation of both of the above diagnostic methods (ie, clinical diagnosis using Amsel criteria and laboratory diagnosis using Nugent, or Ison and Hay criteria) is that they have subjective components and therefore may be imprecise. Gram stain examination, moreover, is time-consuming and requires substantial training, and it difficult to determine an appropriate clinical response for intermediate scores. The 2 methods of diagnosis can also be used in combination to increase diagnostic accuracy.

Various commercial tests are also available to provide rapid and accurate pH evaluation and amine detection. For example automated devices that measure the volatile gases produced from vaginal samples and a colorimetric pH test are commercially available.

Vaginal culture is not an appropriate diagnostic method to identify BV because it is not caused by the presence of a particular bacterial species.
Nucleic Acid Probes
DNA probes have been developed and are now available to directly detect and quantify the bacteria in vaginal fluid samples. Bacterial DNA is extracted and amplified by PCR methods, using either universal or specific primers. Bacteria are then identified by characterizing their ribosomal DNA (rDNA) sequences. The specific target is typically the ribosomal subunit of the 16SrRNA gene, which is present in all bacteria. The 16SrRNA genes can be amplified by PCR using universal and/or specific primers. The amplified product is then quantified to give an assessment of how many microorganisms are present. In addition to being able to more accurately diagnose health conditions, use of these new techniques has resulted in the identification of previously unrecognized cultivation-resistant organisms in vaginal fluid.

Proposed multitarget PCR Test
Several commercially available tests measure multiple organisms using PCR technology for the diagnosis of BV. The tests and the organisms in the panels are shown in Table 1.

Table 1. Components of Commercially Available Multitarget PCR Tests
<table>
<thead>
<tr>
<th>Organism</th>
<th>SureSwab</th>
<th>BD Max</th>
<th>MDL Panel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atopobium vaginae</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Gardnerella vaginalis</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lactobacillus species</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Megasphaera (type 1, type 2, and/or species)</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BVAB (type 1 and/or type 2)</td>
<td>X</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

BVAB: bacterial vaginosis-associated bacteria; MDL: Medical Diagnostics Laboratory; PCR: polymerase chain reaction.

SureSwab (Quest Diagnostics) tests for Lactobacillus species, G. vaginalis, Atopobium vaginae, and Megasphaera species. A. vaginae is a bacterium species which, using molecular-based techniques, has been found to be more common in women with BV than women with normal flora.²

The SureSwab Total test involves obtaining vaginal swab specimens and extracting total DNA. Next, real-time PCR is used to quantitate the 4 types of bacteria. Results are reported as log cells per milliliter for each organism (concentrations of all Lactobacilli species are reported together). In addition, the company provides summary interpretive information based on the findings from all tests. Interpretive information accompanying test results classify findings into one of the following 3 categories: not supportive, equivocal, and supportive.

A classification of not supportive of BV diagnosis is based on:

- The presence of Lactobacillus species, G. vaginalis levels <6.0 log cells/mL, and absence of A. vaginae and Megasphaera species; or
- The absence of Lactobacillus species, G. vaginalis levels <6.0 log cells/mL, and absence of A. vaginae and Megasphaera species; or
- The absence of all targeted organisms.
A classification of equivocal is based on:

- The presence of *Lactobacillus* species, plus *G. vaginalis* at least 6.0 log cells/mL, and/or presence of *A. vaginae* and/or *Megasphaera* species.

A classification of supportive of BV diagnosis is based on the presence of Lactobacillus species, *G. vaginalis* levels at least 6.0 log cells/mL, and presence of *A. vaginae* and/or *Megasphaera* species.

Quest Diagnostics also offers a SureSwab® bacterial vaginosis/vaginitis test that includes the bacterial vaginosis test, previously described, and tests for *Trichomonas vaginalis* and 4 Candidiasis species.

Another product, the BD Max, tests for markers of BV and vaginitis. The test uses a similar process to that described for SureSwab. Vaginal swab specimens are collected, DNA is extracted, and real-time PCR is used to quantitate targeted organisms. Results of BV marker tests are not reported for individual organisms. Instead, qualitative BV results are reported based on the relative quantity of the various organisms. In addition to the BV markers, the BD Max also tests for the vaginitis markers *Candida glabrata*, *Candida krusei*, other Candida species, and *Trichomonas vaginalis*.

Medical Diagnostics Laboratory offers a Bacterial Vaginosis Panel. Four markers (shown above in Table 1) are assessed using real-time PCR and *Lactobacillus* is profiled using quantitative PCR.

**Regulatory Status**

In October 2016, the Food and Drug Administration completed a review of a de novo request for classification of the BD Max™ Vaginal Panel (Becton, Dickinson, Franklin Lakes NJ). The test was granted class II designation, marketing authorization, and is indicated for the direct detection of DNA targets from bacteria associated with bacterial vaginosis (DEN160001).

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests (LDTs) must meet the general regulatory standards of the Clinical Laboratory Improvement Act (CLIA). No multitarget quantitative polymerase chain reaction tests for bacterial vaginosis are available under the auspices of CLIA. Laboratories that offer LDTs must be licensed by CLIA for high-complexity testing. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of this test.

**Rationale**

The evidence review was created in October 2014 and has been updated regularly with searches of the MEDLINE database. The most recent literature review was performed through April 25, 2017.
Assessment of a diagnostic technology focuses on the following parameters: (1) technical performance; (2) diagnostic accuracy (sensitivity, specificity, positive predictive value [PPV], negative predictive value [NPV]) in relevant clinical populations; and (3) clinical utility (ie, demonstration that the diagnostic information can be used to improve patient outcomes). Following is a summary of the key literature to date.

**Individuals with Signs or Symptoms of Vaginal Vaginosis**

**Clinical Context and Test Purpose**
The purpose of multitarget polymerase chain reaction (PCR) testing in patients who have signs or symptoms of bacterial vaginosis (BV) is to confirm the diagnosis of BV so that appropriate treatment is selected and patient outcomes are improved.

This review evaluates whether multimarker PCR testing improves diagnostic accuracy and health outcomes compared with standardly used diagnostic tests. Most cases of BV can be identified using clinical examination and microscopic examination, and screening asymptomatic patients is not recommended by national organizations (see Practice Guidelines and Position Statements section).

Therefore, the most relevant potential target population for multitarget PCR testing is women with signs and symptoms of BV who have an indeterminate diagnosis after standard workup (ie, women in whom a Gram stain is currently indicated).

The questions addressed in this evidence review are: In individuals who have signs or symptoms of BV, does multitarget PCR testing have better diagnostic accuracy than standardly used approaches, does it change patient management decisions, especially choice of treatment, and does it lead to improvements in health outcomes?

The following PICOTS were used to select literature to inform this review.

**Patients**
The relevant population of interest is patients with signs or symptoms of BV.

**Interventions**
The intervention of interest is a multitarget PCR test for BV.

**Comparators**
The comparators of interest are standard diagnostic approaches such as clinical examination and microscopic examination of vaginal specimens.

**Outcomes**
The primary outcomes of interest are test accuracy and validity, symptom resolution, and cure rate (absence of symptoms and normal vaginal flora).
**Time**
The timing for measuring symptom resolution is 7 to 10 days (ie, the length of a course of antibiotics). Symptoms could be assessed in the longer term (eg, a month) to evaluate recurrence of BV.

**Setting**
The test would be used in the primary care or specialty care setting (ie, gynecology).

**Technical Performance**
The U.S. Food and Drug Administration (FDA) decision summary for the BD Max test includes a description of the results of technical performance evaluation.\(^3\) The document reported a high level of within-site and between-site of test findings.

**Section Summary: Technical Performance**
Evidence submitted to FDA indicates that the FDA-cleared test has acceptable technical performance and there is a lack of published studies on other tests.

**Diagnostic Accuracy**
There are no published studies on the diagnostic accuracy of the SureSwab test, but information is available on the diagnostic accuracy of the BD Max test and the BV PCR panel offered by Medical Diagnostics Laboratory (MDL). Additionally, several studies have been published on the diagnostic accuracy of tests that are not currently commercially available in the United States.

**BD Max Test**
The FDA decision summary for the BD Max test includes a description of a prospective clinical diagnostic accuracy study. The study included 1763 women with symptoms of BV or vaginitis. Both clinician-collected and self-collected vaginal swabs were obtained, and they were analyzed independently. A total of 1559 (88%) clinician-detected and 1582 (90%) self-detected samples were available for analysis.

The criterion standard for BV status was a combination of the Nugent score and Amsel criteria. The Nugent score was calculated first; the Amsel criteria were only calculated for samples with intermediate findings on the Nugent score. For these intermediate samples, those with 2 of 3 of the following criteria were considered positive for BV: vaginal pH greater than 4.5, the presence of clue cells, and positive whiff test. The document reported the diagnostic accuracy of the multitarget test, compared with the above reference test. However, it did not detail how the relative levels of the organisms in the panel were combined to determine whether the multitarget test was positive or negative for BV.

Compared with the above criterion standard, the sensitivity and specificity of the multitarget test were 90.5% and 85.8% for clinician-collected samples, and 90.7% and 84.5% for self-collected samples, all respectively. PPVs of 89.0% and 88.1% and NPVs were 87.7%, and 87.8% were found for clinician-collected and self-collected samples, all respectively.
**BV PCR Panel**
In 2016, Hilbert et al reported on a quantitative real-time PCR test. The study was funded through MDL and evaluated markers in that laboratory’s BV Panel. The study included 400 samples from 149 premenopausal women ages 18 and older who presented with vaginitis. Fifteen samples were excluded, including 8 samples with discordant findings using the Amsel criteria and the Nugent score, leaving 385 samples from 146 women in the analysis. Samples were obtained at the initial and at follow-up clinic visits. Participants were evaluated for BV using the Amsel criteria, and vaginal smears were evaluated by Nugent score. Additionally, vaginal samples were sent to MDL and tested for multiple organisms. In multivariate analysis, the model that best predicted BV included *A. vaginae*, *G. vaginalis*, *Megasphaera* type 1, and *Megasphaera* type 2. The selected model incorporating these 4 markers had a sensitivity of 92% and a specificity of 95% for predicting BV. When only samples from the first visit were analyzed, for which 84% were from BV-positive women, the model had a sensitivity of 91% and a specificity of 96%. At the second visit, when 94% of samples were from BV-negative women, the sensitivity was 100% and specificity was 96%.

**Tests Not Commercially Available in the United States**
Several studies have reported on the validation of multitarget PCR tests not currently commercially available in the United States. For example, in 2012, Cartwright et al published data on a multitarget semi-quantitative PCR test including 3 organisms: *A. vaginae*, *Megasphaera* type 1, and *BVAB2*. The investigators used separate samples for the development and validation phases, and compared the diagnostic accuracy of the multitarget panel with an accepted reference standard. The patient population consisted of 402 women presenting at a clinic for sexually transmitted infections (n=299) or a personal health clinic (n=103). The reference standard was a combination of the Nugent and Amsel criteria. First, Nugent scores were generated, and samples were categorized as BV positive, BV negative, or intermediate. Then, samples with intermediate Nugent scores were reanalyzed using the Amsel criteria. The intermediate samples that met the Amsel criteria were considered positive for BV and those that did not were considered negative for BV.

Samples from 169 women were included in the development phase, of which 108 (64%) were positive for BV and 61 (36%) were negative for BV. The sensitivity and specificity of this PCR test were 93.3% and 92.9% for diagnosing BV, respectively, compared with the reference standard. The investigators also calculated a composite score based on the levels of these 3 organisms in the sample. The composite score (sum of the 3 individual scores) was categorized as 0 to 1: BV negative; 2: indeterminate: 3 to 6: BV positive.

In the validation phase, the multitarget PCR test was assessed using an additional 227 samples. Compared with the samples used in the development phase, more were collected from the lower prevalence general health clinic. According to the reference test, 100 (48.5%) of 227 cases were positive for BV and 107 (51.5%) negative. Using the composite score generated in the developmental phase, 14
(6.2%) of the 227 samples yielded a composite score of 2 and were categorized as indeterminate (this included 5 BV-positive and 9 BV-negative samples). Of the 213 evaluable samples, 104 (99.05) of 105 BV-positive samples had a positive composite score and 98 (90.7%) of 108 BV-negative samples had a negative composite score. When the entire study population was analyzed, the multitarget PCR assay had a sensitivity of 96.7%, a specificity of 92.2%, a PPV of 94.0%, and a NPV of 95.6%, with an indeterminate rate of 5.3%.

In 2015, Kusters et al reported on a semi-quantitative multiplex PCR assay for the diagnosis of BV. The research was conducted in the Netherlands and investigators did not report any affiliation with any company marketing a multitarget PCR test in the United States. The study included 159 women at least 18 years or older who presented with complaints of abnormal vaginal discharge. Women underwent examination and had a vaginal swab for PCR testing and a vaginal smear for microscopy. Eight (5%) women had missing data and were not selected for analysis. The investigators tested for 5 bacterial species, A. vaginae, G. vaginalis, Megasphaera type 1, and 2 Lactobacillus species (L. crispatus, Lactobacillus iners). They also calculated a lactobacillus index based on the relative presence of the 2 species. An index score less than 1 indicated a shift to disturbed vaginal microflora when there was a higher load of L. crispatus.

In the analysis, 83 (55%) of 151 women had normal vaginal microflora, 13 (9%) had intermediate vaginal microflora, and 55 (36%) had BV using the Nugent score. In women with a Nugent score indicating BV (score range, 7-10), G. vaginalis, A. vaginae, and Megasphaera type 1 were present in 96%, 87%, and 60% of the vaginal specimens, respectively. In women with normal vaginal microflora (Nugent score range, 0-3), these proportions were 27%, 6%, and 2%, respectively. The investigators also evaluated the diagnostic accuracy of the multiplex quantitative PCR assay compared with the Nugent score as the reference standard. The multiplex quantitative PCR test was considered positive when at least 2 BV-associated bacteria were detected and indeterminate when 1 BV-associated bacterium was detected and the lactobacillus index score was less than 1. In the remaining situations, the test was scored negative. Fifty-five samples were scored by PCR as BV-positive, 10 as BV-indeterminate, and 86 as BV-negative. The sensitivity and specificity of the multiplex BV-PCR test were 92% and 96%, respectively.

**Section Summary: Diagnostic Accuracy**

Several studies have evaluated the diagnostic accuracy of multitarget PCR tests for BV, including 2 studies evaluating commercially available tests. The studies found sensitivities of 90% to 95% and specificities of 85% to 90% compared with standard methods of diagnosis. As the reference standard, most tests used a combination of the Amsel criteria and Nugent score. The studies generally included symptomatic women, but none focused on women with an indeterminate diagnosis.

**Clinical Utility**
Direct Evidence
Direct evidence of clinical utility is provided by studies comparing health outcomes for patients managed with and without the test. Preferred evidence comes from randomized controlled trials. No published studies were identified that evaluated changes in patient management and/or health outcomes when a multitarget PCR test was used to diagnose BV compared with standard methods of diagnosis.

Indirect Evidence
Several diagnostic accuracy studies have found that multitarget PCR tests for BV have relatively high sensitivity and specificity compared with standard testing methods (ie, the Amsel criteria and Nugent score). However, test results are not as high as the other methods, and it is not clear which women might benefit because many can be diagnosed clinically. Data are lacking on use of the tests in women with an indeterminate clinical diagnosis. Additionally, tests use different markers and calculate composite scores differently.

Section Summary: Clinical Utility
There is insufficient direct and indirect evidence to establish the clinical utility of multitarget PCR tests.

Summary of Evidence
In individuals who have signs or symptoms of bacterial vaginosis (BV) who receive multitarget polymerase chain reaction (PCR) testing, the evidence includes several prospective studies on technical performance and diagnostic accuracy. Relevant outcomes are test accuracy and validity, symptoms, and change in disease status. Several studies have evaluated the diagnostic accuracy of multitarget PCR tests for BV, including 2 studies evaluating commercially available tests. The studies found sensitivities between 90% and 95% and specificities between 85% and 90% compared with standard methods of diagnosis. Most studies used a combination of the Amsel criteria and Nugent scoring as the reference standard. There is a lack of direct evidence on the clinical utility of PCR testing for BV (ie, studies showing that testing leads to better patient management decisions and/or better health outcomes than current approaches). Moreover, a chain of evidence does not currently support multitarget testing because most symptomatic women can be diagnosed with a standard workup and/or a trial of empirical therapy, and it is not clear which subpopulations might benefit most from this test. Studies have not been conducted in the most clinically relevant target population: symptomatic women with indeterminate diagnoses after standard workup. The evidence is insufficient to determine the effects of the technology on health outcomes.

Supplemental Information

Practice Guidelines and Position Statements

Centers for Disease Control and Prevention
In 2015, the Centers for Disease Control and Prevention updated its guidelines on sexually transmitted diseases. Regarding diagnosis of bacterial vaginosis (BV), the guidelines stated:
“BV can be diagnosed by ... clinical criteria (i.e., Amsel’s Diagnostic Criteria) or Gram stain. A Gram stain (considered the gold standard laboratory method for diagnosing BV) is used to determine the relative concentration of lactobacilli ... PCR [polymerase chain reaction] has been used in research settings for the detection of ... organisms associated with BV, but evaluation of its clinical utility is still underway. Detection of specific organisms might be predictive of BV by PCR. Additional validation is needed....”

**American College of Obstetricians and Gynecologists**
Published in 2012 and reaffirmed in 2016, the American College of Obstetricians and Gynecologists has produced a practice bulletin on the prediction of preterm birth. The bulletin stated that BV testing is not recommended as a screening strategy in asymptomatic pregnant women at increased risk of preterm birth.  

**U.S. Preventive Services Task Force Recommendations**
The U.S. Preventive Services Task Force’s (USPSTF) 2008 recommendations on screening for BV in pregnancy have stated that:

“The USPSTF recommends against screening for bacterial vaginosis in asymptomatic pregnant women at low risk for preterm delivery.” (Grade D recommendation)

“The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for bacterial vaginosis in asymptomatic pregnant women at high risk for preterm delivery.” (I statement)

**Medicare National Coverage**
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

**Ongoing and Unpublished Clinical Trials**
A search of ClinicalTrials.gov in May 2017 did not identify any ongoing or unpublished trials that would likely influence this review.

**References**

Billing Coding/Physician Documentation Information
There is no one CPT code for this testing. It would be reported with CPT codes for the various infectious agents for which testing was performed. Below is an example of a possible list of codes:

87491  Infectious agent detection by nucleic acid (DNA or RNA); Chlamydia trachomatis, amplified probe technique
87591  Infectious agent detection by nucleic acid (DNA or RNA); Neisseria gonorrhoeae, amplified probe technique
87481  Infectious agent detection by nucleic acid (DNA or RNA); Candida species, amplified probe technique
87512  Infectious agent detection by nucleic acid (DNA or RNA); Gardnerella vaginalis, quantification
87661  Infectious agent detection by nucleic acid (DNA or RNA); Trichomonas vaginalis, amplified probe technique
87798  Infectious agent detection by nucleic acid (DNA or RNA), not otherwise specified; amplified probe technique, each organism
87799  Infectious agent detection by nucleic acid (DNA or RNA), not otherwise specified; quantification, each organism

ICD-10 Codes
A54.02  Gonococcal vulvovaginitis
A56.02  Chlamydial vulvovaginitis
B37.03  Candidal vulvovaginitis
N76.0-  Acute, subacute and chronic vaginitis code range
N76.1   
There is no single CPT code for BV testing. It would be reported with CPT codes for the various infectious agents for which testing was performed. Below is an example of a possible list of codes:

87491: Infectious agent detection by nucleic acid (DNA or RNA); Chlamydia trachomatis, amplified probe technique
87591: Neisseria gonorrhoeae, amplified probe technique
87481: Candida species, amplified probe technique (3 units reported using the modifier -59 on 2 of them to indicate testing for different subspecies of Candida was performed)
87512: Gardnerella vaginalis, quantification
87661: Trichomonas vaginalis, amplified probe technique
87999: Unlisted microbiology procedure (4 units reported using modifier -59 on 3 of them to report different subspecies testing of Megasphaera was performed. This is incorrect coding because unlisted codes are only reported once since they do not have an assigned value.).

Additional Policy Key Words
N/A

Policy Implementation/Update Information

12/1/2014 New Policy. Multitarget polymerase chain reaction (PCR) testing for diagnosis of bacterial vaginosis is considered investigational.
2/1/2016 No policy statement changes
12/1/16 No policy statement changes.
12/1/17 No policy statement changes.
12/1/18 No policy statement changes.

State and Federal mandates and health plan contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. The medical policies contained herein are for informational purposes. The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents Blue KC and are solely responsible for diagnosis, treatment and medical advice. No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any form or by any means, electronic, photocopying, or otherwise, without permission from Blue KC.