Point of Care Diagnosis of Vaginal Infections to Ensure Accurate Treatment: (PAT Study)

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Point of Care Diagnosis of Vaginal Infections to Ensure Accurate Treatment: (PAT Study)

Source of Support:
Cepheid

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LIST OF ABBREVIATIONS AND ACRONYMS

BV	Bacterial vaginosis
CLIA	Clinical Laboratory Improvement Amendments
CDC	Center for Disease Control
CRF	Case Report Form
DNA	Deoxyribonucleic acid
FDA	Food and Drug Administration
HIPAA	Health Insurance Portability and Accountability Act
IRB	Institutional Review Board
KOH	Potassium hydroxide
MWH	UPMC Magee Womens Hospital
MWRIF	Magee-Womens Research Institute and Foundation
NAAT	Nucleic Acid Amplification Test
OB/GYN	Obstetric/gynecology(ic)
PAT	Point of care for Accurate Treatment
PGIC	Patient Global Impression of Change
PGIS	Patient Global Impression of Severity
PHI	Protected Health Information
PTID	Participant identifier
POC	Point of Care
SDS	Sheehan Disability Scale
STI	Sexually transmitted infection
TV	*Trichomonas vaginalis*
UPMC	University of Pittsburgh Medical Center
US	United States
VVC	Vulvovaginal candidiasis

PROTOCOL SUMMARY

Short Title:	**PAT (Point of care for Accurate Treatment)**
Principal Investigator:	Sharon Hillier, PhD
Sample Size:	Approximately 300 participants
Study Population:	Individuals 14 years and older, assigned female sex at birth, who are seeking care at a UPMC Magee-Womens Hospital (MWH) participating PAT study office complaining of symptoms of vaginitis
Study Duration:	Approximately two weeks of follow-up per participant with a projected accrual period of approximately 12 months
Study Sites:	Obstetric/gynecologic (OB/GYN) practices/offices located within UPMC Magee-Womens Hospital (MWH) and outpatient centers affiliated with the Department of OB/GYN or MWH
Study Design:	Two arm, randomized, single center trial of usual care vs. Xpert® Xpress MVP (multiplex vaginal panel; Cepheid, Sunnyvale, CA) directed care for vaginitis diagnosis and treatment Individuals who are complaining of vaginitis symptoms and are seeking care at one of the PAT study participating offices/departments within or affiliated with MWH will be invited to participate. In this study, the office visit will serve as the enrollment (index) visit. Following informed consent, participants will complete a brief questionnaire and self-collect three vaginal swabs for three tests that are FDA-cleared for vaginitis diagnosis: Xpert® Xpress MVP, BD MAX™ Vaginal Panel (Becton-Dickinson, Franklin Lakes, NJ), and BD Affirm™ VPIII Microbial Identification Test (Affirm™ VPIII; Becton-Dickinson). Participants will be randomized (1:1) into one of two arms after collecting swabs. In Arm 1, vaginitis diagnosis and treatment will be based on usual provider evaluation and treatment during the office visit. The Xpert® Xpress MVP test will be batched with delayed results made available to the provider following the participant's 2-week study follow-up telephone contact. In Arm 2, the Xpert® Xpress MVP test will be run in real time as a point of care (POC) test at the time of the office visit and the results will be made available to the provider in approximately one hour. Providers will be asked to use the MVP test result for diagnosis and treatment of the participant.

All participants, regardless of arm, will complete a follow-up telephone contact approximately two weeks after their office/medical visit to assess symptom resolution and satisfaction.

The study will include review and collection of electronic medical record information related to the office/medical visit (i.e., evaluation, testing, diagnosis and treatment).

A Healthcare Provider Sub study will also be performed as part of the PAT study. The sub study will include a baseline questionnaire completed by clinicians at participating offices and then a follow-up questionnaire administered to clinicians who were involved in the PAT study as described below. The sub study will help investigators to understand how providers feel about POC testing for vaginitis.

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1. Background

Bacterial vaginosis (BV), *Trichomonas vaginalis* (TV) infection and vulvovaginal candidiasis (VVC) are common in reproductive age women. The prevalence of BV and TV in the US are 29% and 3%, respectively, but can vary depending on the study population[1,2]. Adverse sequelae associated with BV[3-5] and TV[7-9] include increased acquisition of sexually transmitted infections including HIV and pregnancy complications including preterm birth. While the prevalence of VVC cases is unknown, 20% of women are colonized by *Candida* species in the absence of signs and/or symptoms, and 70% are colonized over a year[10]. Approximately 75% of women will experience at least one episode of VVC infection requiring treatment during their lifetimes[11].

The Centers for Disease Control (CDC) guidelines describes the point-of-care tests that can be performed as an adjunct to a clinical history and physical examination to support diagnosis of vaginal discharge syndromes[12]. These tests include: measurement of vaginal pH, “whiff” test [addition of potassium hydroxide (KOH) to vaginal fluid for assessment of amine odor], and microscopic examination of fresh samples of the discharge to identify presence of clue cells, motile trichomonads, and/or budding yeast/pseudohyphae. The sensitivity and specificity of microscopic detection of clue cells, yeast, and trichomonads by clinicians can vary considerably[13-14]. Despite these limitations, the low cost and convenience of point-of-care testing have contributed to their continued use. In a variety of studies conducted, laboratory testing (Nugent score, yeast culture, FDA-approved and independent molecular assays) performed better than clinician-diagnosed vaginitis[15-17]. CDC guidelines recommend use of alternative commercially available point-of-care tests or clinical laboratory testing in settings where pH paper, KOH, and wet prep evaluation by microscopy are not available[12].

In a published study of 290 women seeking health care for symptoms of vaginitis, more than half had a lab-diagnosed condition, with 30% of women having BV, 34% having VVC and 7% having TV based on laboratory testing[18]. This study documented that only one in five women having symptoms of vaginitis had CDC-recommended point-of-care testing, such as assessment of vaginal pH, microscopic examination of vaginal fluid, or the whiff test, is performed when women

present with vaginal symptoms in primary women's health care settings. Overall, four of 10 women seeking health care for symptoms of vaginitis in this study were prescribed inappropriate treatments. Return visits for symptoms of vaginitis were common, occurring over the next 3 months in 20% of the women. The frequency of return visits ranged from 17% of women with VVC, 35% of women having BV, and 42% of women with TV. Surprisingly, follow-up visits for vaginal symptoms were also common for women having no lab-diagnosed vaginitis at the index visit, with 12% of women returning with symptoms of vaginitis. The women who were prescribed unneeded treatment were significantly more likely to return with symptoms of vaginitis in the subsequent three months versus those who were not treated (22% versus 6%, p=0.02). Empiric treatment of women having symptoms of vaginitis is common and is perceived to cause no harm. However, these data suggest that empiric treatment of women having symptoms, but no infectious cause of vaginitis, may result in more symptom-triggered visits and a greater health care burden. Similarly, low rates of clinical evaluation of vaginitis have been reported among women referred for management of recurrent vaginitis[19].

Advances in highly sensitive nucleic acid amplification testing (NAAT) for the microorganisms associated with vaginal infections have provided an opportunity to employ more sensitive and specific methods for diagnosis of these infections. The BD MAX™ Vaginal Panel provides results by an algorithmic analysis of molecular DNA detection of *Lactobacillus* species (*L. crispatus* and *L. jensenii*) in addition to *Gardnerella vaginalis, Fannyhessea vaginae* (formerly *Atopobium vaginae)*, *Amygdalobacter indicum* (formerly BVAB2), and *Megasphaera lornae* (formerly *Megasphaera* type 1). This test has 90.5% sensitivity and 85.8% specificity for BV diagnosis, compared with Amsel criteria and Nugent score[20]. It also provides results for *Candida* species and *T. vaginalis*. The Aptima® BV (Hologic, Inc., San Diego, CA) detects *G. vaginalis, Fannyhessea vaginae (A. vaginae)*, and certain *Lactobacillus* species including *L. crispatus, L. jensenii,* and *L. gasseri*, with sensitivity and specificity ranging from 95.0% to 97.3% and 85.8% to 89.6%, respectively (using either clinician- or patient-collected vaginal swabs) [12].

The Xpert® Xpress MVP is a new on-demand NAAT developed by Cepheid, to aid in the diagnosis of vaginal infections in women with a clinical presentation of vaginitis/vaginosis. The test is simple to use and detects DNA targets from anaerobic bacteria associated with BV (*A. vaginae*, *A. indicum*, and *M. lornae*), *Candida* species and *T. vaginalis*. Cepheid has recently received 510(k) clearance and CLIA Waiver for Xpert® Xpress MVP. When compared to moderately complex nucleic acid amplification tests performed in a laboratory by trained technologists, the Xpert® Xpress MVP demonstrated high positive percent agreement ranging from 93.6 to 99.0%, and negative percent agreement ranging from 92.1% to 99.8% for both clinician-collected samples and patient-collected samples[21].
The overarching objective of the proposed study is to evaluate whether same day testing using the Xpert® Xpress MVP test in a patient care setting results in a higher degree of appropriate treatment of vaginitis compared to standard of care for women having vaginitis symptoms.

2. Study Objectives

2.1 Primary Objective:

1. To compare the proportion of study participants who are prescribed appropriate treatment at index visit or within 24 hours of index visit based on the provider assessment conducted at the time of the office/medical visit (Arm 1) to the proportion of study participants who are prescribed appropriate treatment when Xpert® Xpress MVP testing is performed and reported on the day of the office visit (Arm 2).

    a. Appropriate treatment is defined as CDC recommended or FDA approved treatment based on diagnosis from the self-collected samples. A positive result from both FDA cleared molecular tests (Xpert® Xpress MVP; BD MAX™ Vaginal Panel) will be considered the gold standard for the diagnosis of vaginitis/vaginosis for data analysis.

2.2 Secondary Objectives:

1. To compare the accuracy of provider's diagnosis of vaginitis (usual care) to the diagnosis of vaginitis based on the results of the Xpert® Xpress MVP test at the office/medical visit.
2. To compare the proportion of women who experience resolution of vaginitis symptoms at the two week follow up contact after undergoing evaluation with a novel POC molecular test to the proportion of women with resolution of vaginitis symptoms after evaluation by their provider's usual care.
3. To evaluate participant satisfaction with usual care vs point of care testing for vaginitis. Questionnaires will be administered to all participants at the office visit and approximately two weeks after enrollment.
4. To compare the accuracy of a nonamplified probe-based platform (BD Affirm™ VPIII) that tests for *Candida, Trichomonas vaginalis* and *Gardnerella vaginalis* compared to the results of two FDA-cleared molecular tests for diagnosis of vaginitis/vaginosis: two NAAT platforms (Xpert® Xpress MVP; BD MAX™ Vaginal Panel).

2.3 Exploratory Objectives:

1. Assess the impact of vaginitis symptoms on patient quality of life and productivity through use of the Sheehan Disability Scale (SDS), which will be administered at enrollment. Results will be assessed overall and stratified by participant-reported severity based on the Patient Global Impression of Severity (PGIS) instrument.

2. To assess provider satisfaction/treatment confidence with usual care assessment vs Xpert® Xpress MVP testing through the Healthcare Provider Sub Study.

3. Study Population

The inclusion and exclusion criteria in this section will be utilized to ensure the appropriate selection of study participants.

3.1 Recruitment:

Approximately 300 individuals, 14 years and older, assigned female sex at birth, seeking care at a PAT study participating office/department with symptoms of vaginitis (i.e. vaginal discharge, vaginal odor, vulvar or vaginal itch, vulvar or vaginal discomfort such as irritation, burning, pain or vulvar edema) will be invited to participate. Pregnant participants who report vaginal discharge will be required to have at least one additional symptom of vaginitis to participate as physiologic vaginal discharge is common during pregnancy.

Participants will be recruited by research staff from participating gynecologic/obstetric practices and MWH outpatient centers located within/affiliated with UPMC MWH. Recruitment will be under the direction of Dr. Harold Wiesenfeld who serves as Vice Chair, Gynecologic Services at UPMC MWH. MWH is the sole teaching site for Obstetrics and Gynecology (OB/GYN) for the University of Pittsburgh School of Medicine. Care is provided by faculty physicians, advance practice providers and OB/GYN house staff.

Research staff may pre-screen electronic schedules/records to identify individuals seeking care for vaginitis symptoms. Potential participants may also be identified/referred by staff who is providing their clinical care. . Interested participants may be provided with a brief description of the study and/or may be provided with the informed consent document to review for further study details/information. Paper or electronic consent may be utilized, as IRB approved. If approved by the IRB, interested individuals can sign informed consent in advance of their appointment. Other participants might be identified on the day of their office visit. For instance, if an individual is not identified or reached prior to their appointment, or an individual presents for a medical visit and has vaginitis complaints, they could be introduced to the study and if interested, be consented and enrolled in person.

This recruitment strategy is likely to capture a diverse population as individuals visiting MWH practices for routine care are approximately 20-80% White, 20-80% African American and 20% other ethnicities including Hispanic, Asian, Indian and Native American.

In a recently published study of 290 women seeking health care within the UPMC system for symptoms of vaginitis, more than half had a lab-diagnosed condition, with 30% of women having BV, 34% having VVC and 7% having TV based on laboratory testing[18]. The distribution of vaginal infections is anticipated to be similar in the PAT study as we are enrolling participants from similar communities/offices.

Informed consent will be obtained prior to conducting any study procedures.

3.2 Inclusion Criteria:

(Individuals must meet all of the following criteria to qualify)

1. Individuals who are assigned female sex at birth, by participant report
2. At least 14 years of age
3. Complaining of at least one symptom of vaginitis: vaginal discharge, vaginal odor, vulvar or vaginal itch. Women having vulvar or vaginal discomfort such as irritation, burning, pain of less than 2 months duration are also eligible.
   Note: pregnant participants who complain of vaginal discharge will be required to have at least one additional vaginal symptom to be eligible.

4. Seeking care at one of the PAT participating offices and/or outpatient centers.
5. Able and willing to provide informed consent.
6. Willing to undergo all study-related assessments and procedures, including self-collection of vaginal swabs, answering questions/surveys, agreeing to the review and collection of information from their medical record from the office (enrollment/index) visit and up to 4 weeks after the office visit.

3.3 Exclusion Criteria:

(Individuals who meet any of the following criteria will be excluded)

1. Previous participation in the PAT study.
2. Any condition, that in the opinion of the investigator, would preclude provision of consent, make participation in the study unsafe, complicate interpretation of study outcome data, or otherwise interfere with achieving the study objectives

3.4 Potential Risks:

- No invasive procedures or investigational medications are involved, so potential risks of participation in this study are minimal.

- Answering questions may be uncomfortable or embarrassing

- Self-collection of vaginal swabs may cause some discomfort, but there is virtually no risk for the collection of swabs containing polyester or nylon fibers.

- Participants may be inconvenienced by participation in this study.

- There is a potential for a breach of confidentiality to occur. There is a possibility for people other than the researchers involved in this study to gain access to the participant's research information. Extensive measures are taken to prevent this from occurring.

4. Study Procedures

Participants may be identified through pre-screening of schedules/electronic medical records and may be contacted/consented in advance of a scheduled appointment as permitted by the University of Pittsburgh Institutional Review Board (IRB). IRB approved flyers may also be used to recruit participants. Consent may be obtained by paper or electronically as approved by the IRB. If the patient is not reached or identified in advance of the visit, the patient may be approached at the time of their visit by study personnel. Following written/electronic informed consent, participants will be assigned a unique participant study number for the questionnaire and associated specimens.

After providing informed consent and confirming eligibility, the participant will be asked to complete a baseline questionnaire and collect vaginal specimens; the order of specimen

collection and questionnaire is not important and will depend largely on office flow. Questions will include demographics, current symptoms, recent relevant treatment in past 30 days, history of recurrent vaginitis in past 12 months, and baseline validated symptom score (PGIS) and the Sheehan Disability Scale (SDS).

Upon arrival for the office/medical visit, the participant will be provided instructions to self-collect vaginal swabs for the following three kits:

- Xpert® Swab Specimen Collection kit for the Xpert® Xpress MVP on the GeneXpert Xpress Instrument System
- BD Molecular Swab Collection kit for the BD MAX Vaginal Panel on the BD MAX™ System
- BD Affirm™ Ambient Temperature Transport System (ATTS) for the BD Affirm™ VPIII on the B-D MicroProbe® Processor.

Kits will be preassembled by researchers with the appropriate collection kits and swabs. Collection order of the swabs will be randomized to prevent collection bias. Patients/participants who are reached in advance of their office appointment (i.e. the day before or within 24 hours of the scheduled appointment) may be asked to come to the research clinic to complete research activities (i.e. informed consent, collection of swabs, completion of questionnaire).

After swab collection, the participant will be randomly assigned to Arm 1 or Arm 2. The randomization will be assigned through REDCap. Participants will be made aware of which arm they were assigned to and will be handed a card to provide to their healthcare provider to make them aware they are in the PAT study and which arm they are assigned to (usual care vs. Xpert® Xpress MVP results). The card will also indicate what time the MVP results will be available (approximately one hour from the time of collection) for participants in Arm 2.

4.1 Arm 1:

For Arm 1 (usual care), the Xpert® Xpress MVP testing will be stored at room temperature and tested within 17 days of receiving the sample, as permitted, per manufacturer test instructions. The results of the MVP test will be entered into the electronic medical record as determined by the MWH Point of Care (POC) Committee AFTER the participant's two-week telephone contact. MVP test results will be available to the provider and participant through the EMR. The other two swab samples (BD Affirm™ ATTS and BD Molecular Swab Collection Kit) from participants in Arm 1 will be transported to the MWRI Lab for processing. The results of these tests are for research purposes only and will not be given to providers or entered into the medical record.

4.2 Arm 2:

For Arm 2, the Xpert® Xpress MVP test will be performed in real time (using the self-collected swab) in clinical areas at UPMC MWH by clinical non-laboratory research staff. GeneXpert Xpress Instrument Systems, provided by the sponsor, will be placed strategically in or near appropriate clinical space as determined by available space and in consultation with the hospital/office staff. The Xpert® Xpress MVP test takes approximately one hour to result.

Research staff will place the result the EMR once resulted. The other two swab samples (BD Affirm™ ATTS and BD Molecular Swab Collection Kit) from participants in Arm 2 will be transported to the MWRI Lab for processing. The results of these tests are for research purposes only and will not be given to providers or entered into the medical record.

For participants randomized to Arm 2, healthcare providers will be aware they are in the study. The provider will be reminded that they will receive the Xpert® Xpress MVP test result within approximately an hour of collection. The provider will be asked to use the Xpert® Xpress MVP result to diagnose and treat the participant but will not be required to do so. Results will be entered into the electronic medical record/made available to the provider and participant as determined by the MWH Point of Care (POC) Committee. To simulate real world practice and to allow flexibility, providing the test result and treatment to the participant may vary among providers. For instance, in some practices, the provider may choose to have the patient wait in the office/center until the Xpert® Xpress MVP result is available and then discuss the diagnosis and provide treatment in person, while other providers may allow the patient to leave the office/center, review the result once available, and contact the patient with the diagnosis and treatment later that day.

Data will be abstracted from the EMR by a researcher. The data collected will include items such as demographics, chief complaint, assessment of vaginal discharge, provider impression and treatment, as applicable. Any additional testing done by the provider will also be collected including wet mount microscopy, vaginal pH, whiff test, cultures, and sexually transmitted infection (STI) testing. Data will be entered into the PAT REDCap (Research Electronic Data Capture) database by unique PTID by a researcher.

In both arms, the two additional swabs will be tested in the MWRI Lab for *Trichomonas vaginalis*, *Candida* species and *Gardnerella vaginalis* using the BD Affirm™ VPIII and for *Candida*, *Trichomonas vaginalis* and bacterial vaginosis using the BD MAX™ Vaginal Panel. The results from the BD Affirm™ VPIII and BD MAX™ Vaginal Panel will be used for research purposes only and will not be shared with the provider or participant, regardless of the arm of the study. The BD MAX™ result will be used to evaluate the Primary Objective, as appropriate treatment is defined as CDC recommended or FDA approved treatment based on diagnosis from concordant NAAT (Xpert® Xpress MVP and BD MAX™ Vaginal Panel) results from the self-collected enrollment swabs. The results from the Xpert® Xpress MVP and BD MAX™ Vaginal Panel will be compared to the Affirm VPIII results as a secondary objective to assess the accuracy of this testing system.

Participants will be contacted approximately two weeks (14-day target with window of 10-21 days) following the visit to complete a follow-up questionnaire including questions such as current (or resolution of) symptoms, compliance with treatment, additional care or treatment, and satisfaction/comfort with self-collection of swabs, satisfaction with diagnosis and treatment, and a validated symptom score (PGIC). The questionnaires will take less than ten minutes to complete; answers will be entered into the PAT Study REDCap database by research staff.

For participants in Arm 1, following the 2-week follow-up contact, the researcher will share the Xpert® Xpress MVP results with the office staff, and enter the results into the electronic medical

record as determined by the MWH Point of Care (POC) Committee. It will be the responsibility of the provider to provide additional treatment if needed.

Up to four weeks following enrollment, a researcher will perform an EMR chart review to include but not limited to the following:

- Collection of data from the office/medical (enrollment/index) visit, including provider information, assessment and treatment prescribed
- Review/collection of tests performed/ordered at the office/medical visit and associated results, to include STI testing
- Subsequent contact, testing and/or vaginitis treatment following enrollment and/or based on delayed Xpert® Xpress MVP results.
- Treatment switches

4.3 HEALTHCARE PROVIDER SUB STUDY:

The PAT study will also include a sub study to collect data from providers at UPMC MWH to better understand how providers feel about POC testing for vaginitis.

Prior to starting the PAT study, all providers from participating offices will be invited to complete a baseline survey that will include questions about current practices of diagnosing vaginitis, perceived need and interest in POC vaginitis testing, participant vs provider collected swabs, etc. The questionnaire will take approximately five minutes to complete, will be anonymous and will be done either by paper or directly through REDCap.

Following completion of the PAT study, providers who have had patients participate in the PAT study will be eligible to participate in the Healthcare Provider Sub Study. Interested providers will be invited to sign an informed consent and then will be provided with a (paper/electronic REDCap) survey to complete. The survey will include questions that are similar to the baseline questionnaire with additional questions regarding demographics (i.e. gender, age, practice years) their experience in the study, such as getting test results in the same day and confidence in accuracy of results.

Providers who cared for patients participating in the PAT Study are under no obligation to consent to the sub study. The risks of participating in the sub study are minimal and include inconvenience and breach of confidentiality. The data collected from providers will be entered into REDCap by provider type (i.e. MD, NP, PA, CNM) but not by provider name to protect the (provider) participant's confidentiality.

Providers who consent and complete the final survey will be compensated for their time, as approved by the IRB.

4.3.1 Inclusion Criteria:

1. Able and willing to provide informed consent
2. Provided clinical care to at least one PAT study participant on the date of their study enrollment
3. Willing to undergo all study-related assessments including answering questions/surveys

4.4 Electronic Medical Record Abstraction:

A researcher who is familiar with/has access to the EMR will abstract information from the participant's chart from the office (enrollment/index) visit and up to approximately one month following the enrollment visit. The data abstracted will be information from the office visit for vaginitis including but not limited to demographics, chief complaint, length of symptoms, assessment of discharge, associated testing, impression and treatment. Any subsequent visits or encounters over approximately one month will be reviewed by a researcher to capture test results, prescribed treatment, treatment switches, etc. Information may also be reviewed/collected on subsequent contacts and treatment.

The abstracted data may be documented on a paper case report form and then entered into the PAT study REDCap database or may be directly entered into the database. The REDCap system is housed at the University of Pittsburgh; the database will be built and maintained by the data management team in Pittsburgh and will be used to enter and manage study data. REDCap is a secure, web-based application designed for clinical trial data collection. REDCap employs various methods to protect the data stored in the software application's backend database against data breaches.

5. Specimen Processing and Testing

The sites will adhere to the standards of good clinical laboratory practice and standard operating procedures for proper collection, processing, labeling, handling, transport, and storage of specimens.

- Laboratory Test Procedures
    - Cepheid Xpert® Xpress MVP: Immediately upon collection, the vaginal swab will be transferred to the Xpert® Swab Specimen Collection Kit and stored at ambient temperature (15-28°C). Specimen collection, storage and transport will be according to the manufacturer's instructions.
        - Arm 1: The sample will be tested within 17 days of collection. The clinical research staff will provide the result to the provider after completion of the participant's two week follow-up telephone contact.
        - Arm 2: The sample will be run by a clinical researcher as a point of care test in/near one of the PAT study participating offices. The result will immediately be given to the provider/entered into the EMR. Providers who agree to participate in this study will be asked to use the result of the FDA cleared test for diagnosis and treatment, but they will not be required to do so.

- BD MAX™ Vaginal Panel swab: Immediately upon collection, the vaginal swab will be transferred to the BD sample buffer tube, capped tightly, and stored at 15-30ºC until transport to the MWRI Lab. Specimen collection, storage and transport will be according to the manufacturer's instructions.
    - The sample will be processed and tested by MWRI Lab. Results will be for research purposes only and will not be given to providers or participants.

- BD Affirm™ VPIII: Immediately upon collection, the vaginal swab will be transferred to the BD Affirm™ VPIII ATTS and stored at ambient temperature (15-30°C) until transport to the MWRI Lab. Specimen collection, storage and transport will be according to the manufacturer's instructions.
    - The samples will be processed and tested by MWRI Lab. Results will be for research purposes only and will not be shared with providers or participants.

5.1 Biohazard Containment

As the transmission of HIV and other blood-borne pathogens can occur through contact with biological specimens, appropriate blood and secretion precautions and training will be employed by all personnel in collection, handling and processing of all specimens for this study. Biohazardous waste will be contained according to institutional, and all other applicable regulations.

6. ASSESSMENT OF SAFETY AND CLINICAL MANAGEMENT

6.1 Risk Management

Participants will be encouraged to ask questions to ensure they understand the research study and procedures. No adverse events are expected to occur from collection of multiple vaginal swabs, therefore no adverse events will be collected for this study.

When feasible, electronic case report forms (eCRFs) will be the first point of data entry for this protocol and will also serve as the source documents.

This study will be conducted in compliance with the protocol and applicable regulatory requirements. All paper research charts are maintained in locked files in a locked room. The research staff, under the direction of the primary investigator, may create and maintain electronic logs on password-protected computers connected to the UPMC/Magee-Womens Research Institute network in the Reproductive Infectious Diseases research offices.

7. Biostatistical Data and Analysis

7.1 Sample size calculations

The primary endpoint is the proportion of study participants prescribed appropriate treatment at index visit or within 24 hours of index as defined by use of a CDC recommended treatment regimen and/or a treatment approved for that indication by the US FDA for vaginitis/vaginosis. A previous study found that 40% of women received inappropriate treatment for vaginitis in community practice settings (18). We anticipate a higher proportion of women are being treated appropriately at the proposed study site since UPMC MWH is a teaching hospital that specializes

in healthcare for women. For the present study, we are making the assumption that 75% of women will receive appropriate treatment in the standard of care arm. We hypothesize that women in the study arm in which study clinicians and patients are provided with same day access to Xpert® Xpress MVP will have a higher proportion of women receiving appropriate treatment. A sample size of 150 participants in each arm will have 91% power to detect a difference of at least 15 percentage points in each arm of the study based on a Fishers exact test evaluated at the 2-sided .05 significance level.

7.2 Primary Endpoint Analysis

The proportion of women prescribed appropriate treatment at index visit or within 24 hours of index between the two arms (usual care versus Xpert® Xpress MVP testing) will be assessed using Fisher's exact test.

7.3 Secondary and Exploratory Endpoint Analyses

Patient and Provider satisfaction with usual care versus point of care testing will be evaluated on a 5-point Likert scale with 1 being very satisfied to 5 being very dissatisfied. Responses will be dichotomized for analyses (very satisfied and satisfied versus all others). Differences in patient and provider satisfaction with and the proportion of women who experience resolution of vaginitis symptoms after treatment based on usual care and point of care testing will be evaluated using Fisher's exact test.

A positive result from both of the two FDA cleared molecular tests (Xpert® Xpress MVP; BD MAX™ Vaginal Panel) will be considered the gold standard for the diagnosis of vaginitis/vaginosis for analysis. Samples yielding discordant results will be retested using the reserve sample. Samples which are discordant after retesting will be evaluated separately.

Fisher's exact test will be used to compare the provider's diagnosis of vaginitis based on usual care to the diagnosis based on the results of point of care testing. The sensitivity, specificity, negative and positive predictive values of the BD Affirm™ VPIII test for *Candida, Trichomonas vaginalis* and *Gardnerella vaginalis* will be calculated and compared to those of the two FDA-cleared tests using the test for equality of proportions.

Patient quality of life and productivity will be assessed using the Sheehan Disability Scale (SDS) where 0 indicates no functional impairment and 30 high functional impairment. Descriptive statistics will be used to assess overall SDS scores. Differences in SDS scores by participant-reported severity will be evaluated using Kruskal-Wallis (continuous SDS score) and Fisher's exact (categorized SDS score) tests.

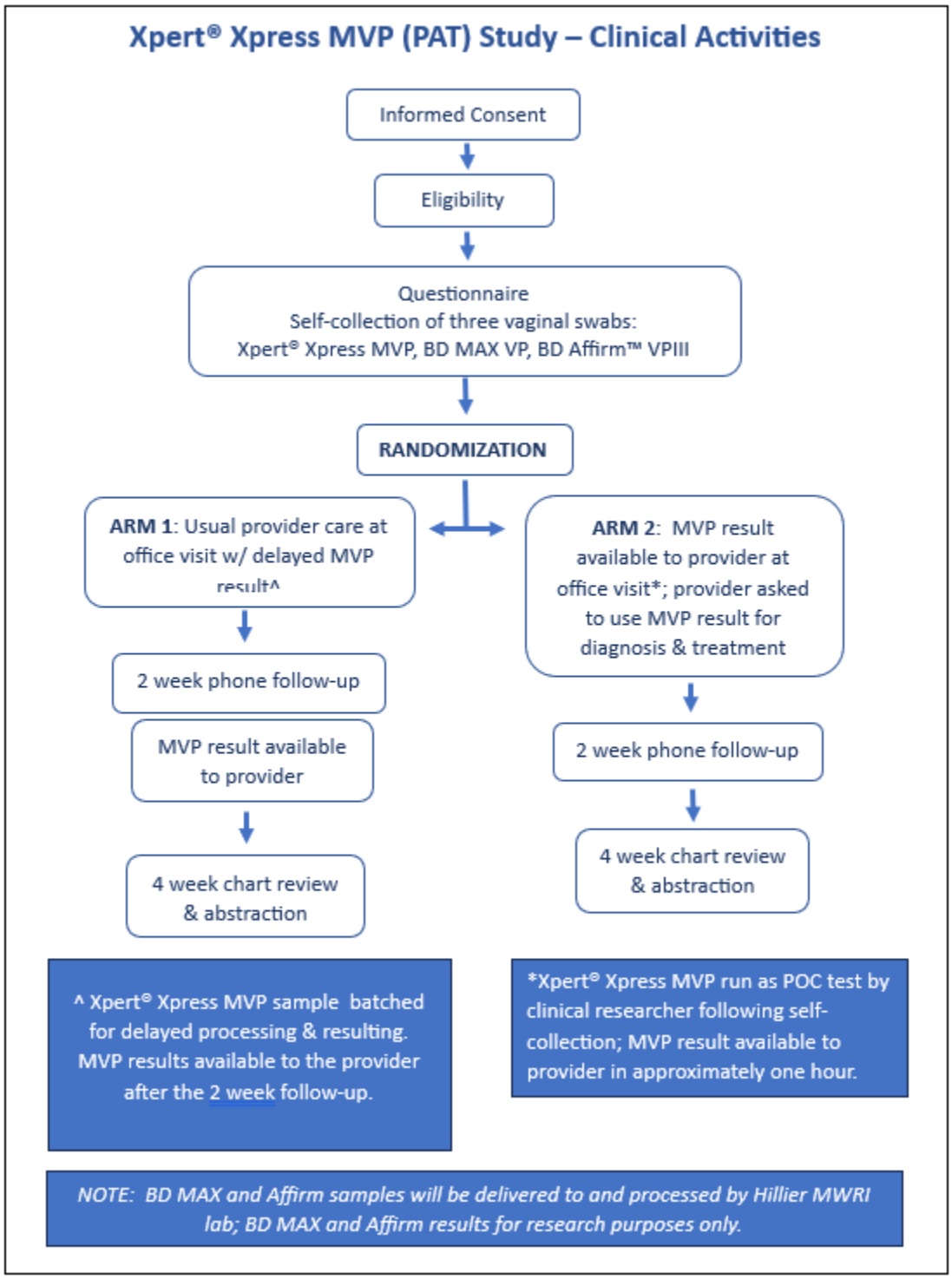
8. Costs and Payments:

The cost for the testing for vaginitis using the self-collected molecular methods will be covered by the study in both arms of the study. The cost of routine clinical care visits, which may include other diagnostic testing will not be covered by the study. Treatment may be prescribed by the healthcare provider according to usual care; the cost of this treatment will not be covered by the study.

Participants who complete the study will be compensated as approved by the University of Pittsburgh IRB. Participants may also be offered MWH garage parking passes for the office visit. Healthcare providers who participate in the sub study will be compensated for survey completion, as approved by the University of Pittsburgh IRB.

8.1 FUNDING

Funding for this investigator-initiated study is being provided by Cepheid.



Schedule of Participant Study Visits and Evaluations:

Study Procedures	**Visit 1**	**Visit 2**
Visit type	Enrollment	Follow-Up Telephone Contact
Time	0	2 weeks
Length of Visit	20 min	10 min
Informed consent	x	
Eligibility	x	
PGIS (Symptom severity)	x	
PGIC (Symptom severity – change)		x
Sheehan-disability-scale (Productivity; daily activity)	x	
Self-collect three vaginal swabs	x	
Randomization	x	
Provide Xpert® Xpress MVP results to provider – Arm 1		x
Provide Xpert® Xpress MVP results to provider – Arm 2	x	
Diagnosis based on usual care at time of visit – Arm 1	x	
Diagnosis based on Xpert® Xpress MVP result at time/day of visit – Arm 2	x	
Participant Compensation		x
Collect/update/review contact/locator information	x	
Chart review to extract visit details, diagnosis, tx and results*	x	x

*May occur up to 4 weeks following office (enrollment/index) visit

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