RESEARCH PROTOCOL

Date	7/20/20
Title	Is chlorhexidine vaginal preparation prior to hysterectomy superior to iodine in reducing bacterial count; a randomized controlled trial
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Purpose of Study

- To determine the influence of chlorhexidine gluconate surgical/topical antiseptic solutions on the bacterial environment of the vagina during hysterectomy and compare that to the effect of standard iodine-based preparations on the same.
  - ***Primary Aim:*** To determine if chlorhexidine gluconate surgical preparation maintains a lower rate of contamination to the surgical field, as determined by bacterial count at 90 minutes from initial preparation, when compared to iodine based preparation.
  - ***Secondary Aims:*** To investigate the difference between chlorhexidine gluconate and iodine-based preparations influence on:
    - Rate of contamination at both 30 and 60 minutes from initial preparation.
    - Reducing specific pathogens commonly causing post-operative infection throughout the 90-minute window from preparation.
    - Reducing those pathogens that commonly cause bacterial vaginosis.

Hypothesis or **Research Question**

- We hypothesize that the percent of samples considered contaminated by bacterial count at 90 minutes from preparation will be 20% lower in the group that receives chlorhexidine preparation vs povidone-iodine.

- We further hypothesize that this trend will be demonstrated throughout the 30-90 minute time window following vaginal preparation.
- Additionally, we hypothesize chlorhexidine will reduce bacterial counts of pathogens more commonly associated with post operative gynecologic infections better than povidone-iodine.
- Finally, we hypothesize chlorhexidine will clear the pathogens associated with bacterial vaginosis more effectively than povidone-iodine.

Background

Although the rate of hysterectomy is declining nationally, it remains the most commonly performed procedure in gynecology[1,2]. As such, postoperative infection remains the most common complication of surgical procedures in gynecology[3]. Historically, 30-40% of patients undergoing a hysterectomy develop a post-operative infection[4]. The initiation of antibiotic prophylaxis for appropriate surgical procedures was a significant advancement in the prevention of surgical site infection. More than 30 prospective randomized clinical trials demonstrated reduced risk of infection and morbidity following hysterectomy when receiving antibiotic prophylaxis[3].

Overall incidence of post operative infection remains relatively low, with a recent cross sectional analysis of NSQIP (National Surgical Quality Improvement Program) data reporting 2.7% occurrence for superficial, deep and organ space infections after hysterectomy[5]. Nonetheless, surgical site infections result in significant morbidity, loss of quality of life, higher risk of re-intervention, and increased costs to the patients affected by them[9]. Within gynecology oncology, the risk of post operative infection remains as high as 36%[10-13]. Therefore, initiatives sponsored by the Centers for Disease Control, National Health Service Network, Centers for Medicare and Medicaid Services and the Joint Commission have targeted preventing and ultimately eliminating postoperative surgical site infections as a priority in patient safety efforts[14].

Antibiotic prophylaxis has been standardized[3] and universally implemented. A remaining variable is the method of aseptic preparation of the vagina with substantial variation of technique being reported even within institutions[15]. This is concerning in light of the fact that most post-hysterectomy wound infections result from ascending spread of vaginal flora[24,25]. Removing variability and implementation of standardized protocols have shown infection rate reduction at large surgical centers[9,12]. Establishing which aseptic solution should be implemented within these protocols remains challenging. The most recent Committee Opinion by the American College of Obstetricians and Gynecologists concludes there is insufficient evidence to render a strong recommendation for either povidone-iodine or chlorhexidine as the ideal agent for surgical preparation of the vagina and that further evidence is necessary[16].

Povidone-iodine solution has been considered the standard for aseptic surgical preparation of the vagina for decades[6-8] and is the only solution approved by the FDA for vaginal use[16]. There are however specific qualities of the solution that suggest it may be less than ideal for use in the vagina. First, the vagina is not protected by keratinized epithelium and therefore iodine can be absorbed systemically during vaginal preparation[17]. Second, iodine is less effective in low pH environments[18]. Considering the normal vaginal pH is 3.8-4.5, the aseptic properties of iodine are called into question as a vaginal solution. Finally, it has been shown that iodophores are inactived in the presence of blood[18]. Therefore, by performing surgery and contaminating the prepared field with some quantity of blood, some degree of the desired asepsis is lost. In light of these inadequacies, an alternative agent must be considered.

More contemporary efforts have begun to focus on chlorhexidine as a more ideal agent for aseptic efforts in surgical preparation of the vagina. In 2010, a large, multicentered, randomized trial of patients undergoing clean contaminated surgeries compared post surgical infection rates between those cleansed with chlorhexidine and those with povidine-iodine. They found that chlorhexidine decreased post-operative superficial wound infections by 50%[19]. Only 10% of the study population underwent non-abdominal gynecologic surgery, and the method of their vaginal preparation was not specified. Though this article cannot be sited as

setting the standard for vaginal preparation, it did change the general approach to skin preparation in the United States and helped support the superiority of chlorhexidine as an aseptic solution.

A recent prospective quality improvement study, performed at an academic tertiary care center on patients of the gynecology oncology service undergoing cytoreductive surgery, reported their results after implementing a surgical site infection prevention bundle that involved 5 steps throughout the surgical process from pre-op to wound care. One of these was vaginal preparation with 4% chlorhexidine. Their baseline infection rate was reported as being 20%. Through their efforts, they decreased the post-operative infection rate to 3%[9]. Due to the high baseline infection rate of their population as well as the multiple interventions employed within their bundle, the study provides further evidence of the likely superiority of chlorhexidine.

The only randomized controlled trial performed to date comparing 4% chlorhexidine to povidone-iodine as a vaginal preparation was reported in 2005. Discussing the true incidence of post-operative infection following hysterectomy and the exceedingly high number of participants that would be required to look at actual infection rates, the authors selected a surrogate marker of infection as their primary outcome. They showed that chlorhexidine decreased bacterial colony counts in the vagina 40% more effectively than povidone-iodine thirty minutes from initial aseptic preparation. The study was however underpowered at time points beyond 30 minutes and lacked specific information on pathogens within the reported cultures[19].

Therefore, the purpose of our study is to use a randomized controlled trial to determine whether chlorhexidine is superior to povidone-iodine as an aseptic solution in the vagina by comparing its affects on bacterial count, change in common pathogens responsible for postoperative infection and colony counts throughout the time course of a hysterectomy.

Research Plan

- **Study Design**
  - Randomized Controlled Trial

- **Setting for the study**
  - Patients of Cincinnati Urogynecology Associates and/or Tri-State Gynecology Oncology, TriHealth, Inc. undergoing total vaginal, laparoscopic assisted, total laparoscopic, or robotic hysterectomy at Good Samaritan Hospital or Bethesda North Hospital will be eligible for enrollment.

  - The study will be offered to those patients found to meet all inclusion criteria and none of the exclusion criteria via phone (see attached script), in office or prior to surgery in the preoperative holding area
  - Patient will sign Informed Consent and Authorization prior to surgery, but not to exceed 6 moths before surgery.
  - Following enrollment, a SNOSE (Sequentially-Numbered, Opaque, Sealed Envelopes) will reveal group allocation.
    - Intervention group:
      - Patients randomized to the chlorhexidine group will undergo presurgical vaginal aseptic preparation using 4% chlorhexidine solution.
      - Vaginal culture swabs will be collected following induction of general anesthetic, prior to their vaginal preparation.
      - Swabs will be collected subsequently at times marked 30 minutes, 60 minutes and 90 minutes following preparation allowing for +/- 5 minutes.
      - EPIC will be interrogated, looking at the time period from day of surgery to 30 days post operatively, for evidence of surgical site infections, including superficial incisional, deep incisional and organ space infections. Incidents of surgical site infection will be determined by CDC guidelines[44]. (**see Appendix A**)

- Control group:
    - Those patients randomized to the povidone-iodine group will have their presurgical vaginal aseptic preparation performed using 10% povidone-iodine solution.
    - They will have culture swabs collected following induction of general anesthetic, prior to their vaginal preparation.
    - Swabs will be collected subsequently at times marked 30 minutes, 60 minutes and 90 minutes from preparation allowing for +/- 5 minutes.
    - EPIC will be interrogated, looking at the time period from day of surgery to 30 days post operatively for evidence of surgical site infections, including superficial incisional, deep incisional and organ space infections. Incidents of true surgical site infection will be determined by CDC guidelines[44]. (**Appendix A**)

- **Participants**
    - Study population: All women 18 years of age or older, who plan to undergo total vaginal, laparoscopically assisted vaginal, total laparoscopic, or robotic-assisted laparoscopic hysterectomy, with or without additional concomitant procedures by a physician at Cincinnati Urogynecology Associates or Tri-State Gynecology Oncology, TriHealth Inc. and will be approached for recruitment in their office or in the pre-operative holding area.
    - Inclusion/Exclusion criteria:
        - Inclusion
            - Adults 18 years of age and older
            - English speaking
            - Undergoing total vaginal, laparoscopic assisted vaginal, total laparoscopic, or robotic-assisted laparoscopic hysterectomy by a physician at Cincinnati Urogynecology Associates or Tri-State Gynecology Oncology TriHealth Inc.

- Concomitant procedures such as vaginal vault suspension, suburethral sling, cystoscopy, enterocele repair, anterior or posterior colporrhaphy, bilateral salpingectomy or salpingooophorectomy, staging procedures, lymph node sampling and other indicated procedures will be included
- Ability to provide consent

- Exclusion
  - Unwillingness to participate in the study
  - Non English speaking
  - Patients that do not undergo a hysterectomy
  - Reported allergy to iodine or chlorhexidine preparation solutions
  - Patients undergoing planned debulking surgery for ovarian, fallopian tube or primary peritoneal cancers
  - Current infection necessitating hysterectomy
  - Active sepsis, pelvic abscess or pelvic inflammatory disease
  - Patient receiving Flagyl for treatment of vaginitis or for surgical prophylaxis during the perioperative period, including day of surgery.

- Sample Size

  - Given the incidence of infection following hysterectomy, a surrogate outcome was felt to be necessary in order to complete the study in a timely fashion. Therefore, using the only published randomized controlled trial, we selected contamination of the field as our outcome measure.
  - Contamination is defined as having >5000 bacteria within a culture[19].
  - The previous study suggested a 22% difference in bacteria contamination, therefore our sample size was calculated to be 71 patients per arm to

detect a 22% difference in cultures defined as contaminated at 90 minutes from surgical preparation.

- *Power Analysis*
  - Our calculation demonstrated need to enroll 60 patients in each arm based on the following:

- A difference of 22% in number of cultures found to have >5,000 bacteria growing 90 minutes from preparation
- Significance at 0.05
- Power at 80%
- Odds ratio was 0.289
- Assuming an estimated loss rate of 15%, the number of patient enrollment per arm was set to 71, for a total of 142 patients. [Attrition calculation: (60/0.85)]
  - Subjects will be randomized by using a random numbers table and sealed sequential envelopes prepared by an independent statistician. Patients of Cincinnati Urogynecology Associates and Tri-State Gynecology Oncology will have independent randomization schedules.

- **Data Collection**
  - *Primary outcome*:
    - The percent of samples considered contaminated at 90 minutes from preparation between groups.
  - *Secondary Outcomes:*
    - The percent of samples considered contaminated at 30 and 60 minutes from preparation between groups.
    - Number of samples reaching a bacterial load of 100,000 following vaginal preparation at any of the specified time points.
    - The change in bacterial count over time. Specific attention will be given to investigate the following bacteria, most commonly identified in assocation with postoperative infections[22,23]:

- *Streptococcus Agalactiae*
- *Staphylococcus aureus*
- *Escherichia Coli*
- *Gardnerella Vaginalis*
- *Enterococcus Faecalis*
- *Bacteroides Fragilis*
- Also included, specific bacteria associated with the condition of bacterial vaginosis[22]:
    - *Gardnerella*
    - *Mobiluncus species*
    - *Prevotella*
    - *Bacteroides*
    - *Peptostreptococcus*

- The number of postoperative infections in each group

- *General Demographic Data*
    - Age, BMI, race, past medical history, home medications, allergies , smoking history, prolapse stage, cancer stage, procedures performed, length of stay, surgical and postoperative complications, and estimated blood loss
- *Data Collection tool*
    - A data collection tool will be utilized
- Please see **Appendix B** for evidence regarding outcome measures

- **Intervention or experimental aspect of the study**
    - *Vaginal preparation*
        - The vaginal scrub will be performed by the OR team according to standard procedures for asepsis within the TriHealth System
        - Solutions:
            - 4% chlorhexidine

- 10% povidone-iodine

- *Sample Collection*
  - Samples will be collected in a standard fashion in the operating room after the patient has been anesthetized
    - The ESwab liquid amies collection and transport system will be utilized.
    - The swab will be thoroughly rubbed along the vaginal surface in a circumferential pattern, careful to sample the entire surface of the vagina, beginning at the fornix and traveling towards the introitus for 10 seconds. The sample will avoid the cervical os or peritoneum.
    - A sample will be collected prior to any vaginal preparation, at 30 minutes, 60 minutes and 90 minutes from preparation (This last sample may be collected at end of surgery if prior to 90 minutes)
    - The samples will be labeled with the participant's study ID, name, and time of collection, annotated as time 0, 30, 60, or 90.
    - The samples may be collected +/- 5 minutes around the determined time to allow for surgical flow and circumstantial adjustment.
    - Swabs will then be sent to the laboratory for analysis
    - An in-service will be provided to teach all participating physicians the standard method of collecting swabs as described above.
  - *Laboratory Procedure Outline*
    - Samples will be handled by a single technician within the laboratory. This technician will be paid through study funds while they perform these duties.
    - The laboratory personnel will be blinded to the participants group assignment

- Sterile calibrated loops will be used to inoculate the specimen onto specific agar for cultures:
    - *Blood Agar*
    - *MacKonkey Agar*
    - *CAN Agar*
    - *Anaerobic Agars*
        - *Brucella*
        - *BBE/KUL*
        - *PEA*
- The inoculate will be streaked according to techniques commonly utilized in urine culture to facilitate analysis

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- The cultures will be read approximately 48-72hrs from inoculation
- A colony count will be performed on each sample
- Individual strains will be isolated and identified
- The individual pathogens will be identified using the MALDI (Matrix Assisted Laser Desorption/Ionization-Time of Flight*)* test, by Bruker Daltonics.
    - An affordable & reliable bacterial identification method. Based on mass spectrometry, using qualitative in vitro diagnostics, ribosomal proteins are analyzed and compared to two proprietary libraries for a match and identity verification.
    - Capable of identifying more than 200 organisms
    - *http://www.midilabs.com/maldi-tof*
- Bacterial Vaginosis will be identified through a modified Nugent[36] method.

        - Utilizing colony counts obtained from culture plate reading and correlating this with specific identities found in the MALDI test, a Nugent score will be reported.
    - Nugent Score
        - Points will be awarded based on three morphotypes:
            - Medium to large gram positive rods
            - Small gram negative or variable rods
            - Curved gram negative or variable rods
        - Each of these morphotypes will be assigned a score based on their initial count:
            - 0 = No morphotypes
            - 1 = Less than 1,000
            - 2 = 1,000 – 4,000
            - 3 = 5,000 – 30,000
            - 4 = >30,000
        - The score for the three morphotypes is then added, and any score >7 is consistent bacterial vaginsosis, and a score <3 is normal flora.
        - Scores will be generated for each specific time point to allow trending following vaginal preparation.
- *Safety Considerations*
    - Povidone-iodine is FDA approved for use as a vaginal scrub solution and is considered to be safe[16].
    - Though this application would represent an off-label use, 4% chlorhexidine is considered a safe alternative to povidone-iodine for use as a surgical scrub of the vagina by the American College

of Obstetricians and Gynecologists[16]. TriHealth also includes chlorhexidine as a part of the standard surgical bundle. (**Appendix C**)

- **Statistical Analysis**

The primary outcome is the proportion of contamination (defined as having >5000 bacteria within a culture) at 90 minutes from initial preparation. Logistic regression will be implemented to compare the odds ratio between two groups. Furthermore, multiple logistic regression will be utilized to test for confounding variables. For continuous variable, descriptive statistics will be reported with mean and standard deviation (or median and interquartile range). Difference between two groups will be evaluated in each time point by independent Student's t-test or nonparametric equivalent (Mann Whitney-U test). Alpha < 0.05 will be considered statistically significant.

Ethical Considerations

- **Informed consent**
    - Patients who agree to participate in the study will sign a written informed consent. They will be consented by one of the stated investigators or trained study staff and they will receive a copy of the signed informed consent statements (ICS). A copy will be put in their medical file.

- **Privacy information**
    - Extensive efforts will be made to ensure participant confidentiality and prevent unauthorized release of personal information. Electronic study documents will be stored on a secure drive and hard copy documents stored in a locked area. Thereby, all identifying and protected health information will be maintained in a secure area at all times, accessible by authorized personnel only.

- Study documentation, both electronic and hard copy will be stored securely per TriHealth's Medical Records Retention Policy.

- **When and how will results be disseminated?**
  - We plan for the results to be disseminated at a national meeting in the form of a poster or oral presentation. We also plan for the results to be published.

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Appendix A
CDC Guidelines on Diagnosis of Postoperative Infections[44]

Superficial incisional SSI

- Date of event for infection occurs within 30 days
  (where day 1 = the procedure date)

- Involves only skin and subcutaneous tissue of the incision

- patient has at least one of the following:
  - purulent drainage from the superficial incision
  - organism identified from wound sampling
  - superficial incision that is deliberately opened
    - AND
      - patient has at least one of the following signs or symptoms:
        - pain or tenderness;
        - localized swelling;
        - erythema; or heat.

  - Diagnosis of a superficial incisional SSI by the surgeon, attending* physician or other designee.

*The term attending physician for the purposes of application of the NHSN SSI criteria may be interpreted to mean the surgeon(s), infectious disease, other physician on the case, emergency physician or physician's designee.

Deep Incisional SSI

- Date of event for infection occurs within 30 days
  (where day 1 = the procedure date)

- Involves the deep tissues of the incision (muscle/fascia)

- The patient has *one* of the following:
  - Purulent drainage from a deep incision
  - A deep incision that spontaneously dehisces, or is deliberately opened or aspirated by a surgeon or attending physician* **AND** an organism is identified by sampling **AND** the patient has at least *one*:
    - Fever (>38C)
    - Localized pain
    - Localized tenderness

- An abscess or other evidence of infection involving the deep incision that is detected on gross anatomical or histopathologic exam, or imaging test.

*The term attending physician for the purposes of application of the NHSN SSI criteria may be interpreted to mean the surgeon(s), infectious disease, other physician on the case, emergency physician or physician's designee.

Organ Space SSI

- Date of event for infection occurs within 30 days
  (where day 1 = the procedure date)

- Infection involves any part of the body deeper than the fascial/muscle layers, that is opened or manipulated during the operative procedure

- The patient has at least *one* of the following:
  - Purulent drainage from a drain that is placed into the organ/space (e.g., closed suction drainage system, open drain, T-tube drain, CT guided drainage).
  - Organisms identified from fluid or tissue in organ space
  - Abscess or other evidence of infection within the organ space detected grossly, from pathology or by imaging
  - Meets at least one criteria for the specific organ/space:

    - ***Intrabominal infections:***

      Intraabdominal infections must meet at least one of the following criteria:

      1. Patient has organism(s) identified from an abscess or from purulent material from intraabdominal space by a culture or non-culture based microbiologic testing method which is performed for purposes of clinical diagnosis or treatment (e.g., not Active Surveillance Culture/Testing (ASC/AST).

      2. Patient has at least one of the following:

         a. abscess or other evidence of intraabdominal infection on gross anatomic or histopathologic exam

         b. abscess or other evidence of intraabdominal infection on gross anatomic or histopathologic exam

AND

organism(s) identified from blood by a culture or non-culture based microbiologic testing method, which is performed for purposes of clinical diagnosis or treatment (e.g., not Active Surveillance Culture/Testing (ASC/AST). The organism(s) identified in the blood must contain at least one MBI organism. See Appendix A of the BSI protocol:

3. Patient has at least ***two*** of the following: fever (>38.0°C), nausea*, vomiting*, abdominal pain*, or jaundice*

And at least one of the following:

a. organism(s) seen on Gram stain or identified from fluid or tissue obtained during invasive procedure or from an aseptically-placed drain (e.g., closed suction drainage system, open drain, T-tube drain, CT guided drainage)by a culture or non-culture based microbiologic testing method which is performed for purposes of clinical diagnosis or treatment (e.g., not Active Surveillance Culture/Testing (ASC/AST).

b. organism(s) identified from blood by a culture or non-culture based microbiologic testing method which is performed for purposes of clinical diagnosis or treatment (e.g., not Active Surveillance Culture/Testing (ASC/AST). The organism(s) identified in the blood must contain at least one MBI organism(See Appendix A of the BSI protocol)

AND

imaging test evidence suggestive of infection (e.g., ultrasound, CT scan, MRI, ERCP, radiolabel scans [gallium, technetium, etc.] or on abdominal x-ray), which if equivocal is supported by clinical correlation (i.e., physician documentation of antimicrobial treatment for intraabdominal infection).

- **Vaginal Cuff Infections**

- Vaginal cuff infections must meet at least one of the following criteria:

1. Post hysterectomy patient has purulent drainage from the vaginal cuff on gross anatomic exam.

2. Post hysterectomy patient has an abscess or other evidence of infection at the vaginal cuff on gross anatomic exam.

3. Post hysterectomy patient has organism(s) identified from fluid or tissue obtained from the vaginal cuff by a culture or non-culture based microbiologic testing method which is performed for purposes of clinical diagnosis or treatment (e.g., not Active Surveillance Culture/Testing (ASC/AST).

For further organ sites, or further details, the CDC site can be accessed for clarification.

Appendix B

Rationale for Outcome Measures

- *Selecting Bacterial Count >5000 as cutoff*
  - A pilot study[26] completed by Culligan et al prior to their randomized trial[19] describes their selection of >5000 bacteria or colony forming units (CFU) because it correlated with common cutoffs in other laboratory tests for bacterial contamination, specifically urinalysis[26].
  - Earliest reports of the selection of 5000 colony forming units being used as a contaminate marker are found in literature from WWI, where soldiers being delivered to the field hospital who had a culture showing fewer than 5000 bacteria would have their wounds primarly closed[27].
  - Some studies in both military and civilian literature reveal that a bacterial contaminant load of 10^5 is required within the wound site in order to lead to an infection following antibiotics and closure[29,30]
  - However, it has been shown that the presence of a foreign body within the wound can dramatically decrease the inoculate required to lead to infection, these studies are outlined below:
    - One of these was performed by Elek and Conen in the late 1950's in an effort to determine the minimum dose of staphylococcus needed to cause wound infection. They showed that the inoculate required dropped from 10^6 to 10^2 with the addition of suture[27].
    - James built on their initial study with a robust animal model in 1961. They collected a total of 39 strains of staphylococci, then soaked suture material in broth with specific, different concentrations of staph. They placed the suture through the skin of mice and watched for pus formation. The tissues were harvested, slides prepared and actual inoculating dose of bacteria

determined. They reported that a minimum bacterial count of 1000-1500 was required to induce a wound infection in the setting of a foreign body, such as suture. They further reported that their average true bacterial load introduced that lead to wound infection was between 3,200 and 4,800 bacteria[28].

- Further evidence of lower inoculate required for infection, specifically within the vagina is found in the symbiotic relationship rendered by mixed pathogens. Facultative organisms, when combined with anaerobes, can create favorable conditions for overgrowth and lead to abscesses more readily than either alone[31].
- Therefore, the level of 5,000 is considered a reasonable threshold to utilize as one of contamination.

- *Selection of time window for culture collection*
  - In the original pilot study reported by Culligan[26], samples were collected prior to preparation, then at 30, 90, 150 and 210 minutes. Growth of bacteria dramatically dropped off following the 90 minute cultures. Peak colony counts were identified between 30 and 90 minutes following preparation, suggesting a "weakest link" in standard infection prophylaxis.
  - In the randomized trial reported by Culligan[19] the same trend was reported. Highest contamination levels were seen at within the 30-90 minute window.
  - Literature reporting on the average length of time required to complete a hysterectomy for benign indications varies in reported results[32-35]:

Study	***TVH***	***TAH***	***LAVH***	***TLH***	***RTLH***
Chang	80	*XX*	*118*	*XX*	*XX*
Johns	*63*	*XX*	*102*	*XX*	*XX*

Shashoua	*XX*	*XX*	*XX*	*122*	*142*
Ribeiro	*78*	*109*	*XX*	*118*	*XX*

- Based on these average times, the window of highest contamination remains within the average length of most benign hysterectomies and therefore provides relevant clinical implication.

- *Rationale for Inclusion of BV analysis*
  - A prospective case series detailing vaginal cultures from women undergoing benign gynecologic, urogynecologic and gynecology oncology surgeries. The cultures were collected pre-operatively and were anylized using Nugent criteria. 27% of the women in this study were found to have bacterial vaginosis (BV) at presentation and 36% of these women developed a post-operative infection[37].
  - Soper, one of the most quoted authors when discussing the relationship of BV and cuff cellulitis reported that patients with BV have a 3x higher risk of developing cuff cellulitis or abscess after abdominal hysterectomy compared to those with healthy vaginal flora[38].
  - Another large series from the late eighties reported on patients with and without BV undergoing abdominal hysterectomy, and within this population, 35% of women with BV developed a postoperative cuff infection compared with 8% of women without BV[39].
  - Finally, The American College of Obstetricians and Gynecologists recommends screening for BV prior to performing a hysterectomy to prevent postoperative cuff infections[3].

Appendix C

Safety Considerations

- In a large prospective trial performed in Kenya, women in labor had vaginal lavage with chlorhexidine on average 2 times during labor in an effort to decrease HIV transmission. A total of 898 women underwent lavage with no adverse events[40].
- A large Swedish study compared chlorhexidine to placebo for vaginal lavage during labor. 2,238 women underwent vaginal lavage with chlorhexidine without adverse event contributed to the lavage[41].
- Another large, placebo-controlled randomized trial from Alabama, reported on vaginal lavage with chlorhexidine with over 500 women undergoing lavage without any maternal reactions to the solution[42].
- A review of the Swedish National Register for Gynecologic Surgery revealed that of the 43 hospitals included, none of them preferred povidone-iodine as a vaginal surgical scrub solution and the preferred solution was chlorhexidine[43].
- The only randomized trial comparing chlorhexidine to povidone-iodine for vaginal scrub reported zero adverse events[19].