PROTOCOL TITLE:

CLN-UP: ChLorhexidine gluconate versus povidoNe iodine for vaginal surgical preparation for Urogynecological Procedures

PRINCIPAL INVESTIGATOR:

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2

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REGULATORY FRAMEWORK:

Please indicate all that apply:

	DOD (Department of Defense)
	DOE (Department of Energy)
	DOJ (Department of Justice)
	ED (Department of Education)
	EPA (Environmental Protection Agency)
	FDA (Food and Drug Administration)
x	HHS (Department of Health and Human Services)
	VA
	Other:

Is this a clinical trial per the NIH definition of a Clinical Trial? x Yes ☐ No

NIH Definition of a Clinical Trial:

A research study in which one or more human subjects are prospectively assigned to one or more interventions. An "intervention" is defined as a manipulation of the subject or subject's environment for the purpose of modifying one or more health-related biomedical or behavioral processes and/or endpoints. Examples include: drugs/small molecules/compounds; biologics; devices; procedures (e.g., surgical techniques); delivery systems (e.g., telemedicine, face-to-face interviews); strategies to change health-related behavior (e.g., diet, cognitive therapy, exercise, development of new habits); treatment strategies;

prevention strategies; and, diagnostic strategies. (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.

If yes, please confirm that the research team is familiar with and agrees to comply with the investigator requirement to register the study on the ClinicalTrials.gov database. Additionally, the approved consent document(s) must be uploaded to the ClinicalTrials.gov database x *Yes* ☐ *No*

FUNDING: This is funded by an internal OB/GYN endowed research award.

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1. Objectives

The primary objective of this research study is to perform a single-blinded, non-inferiority randomized-controlled trial to compare the effectiveness of two pre-surgical vaginal antiseptic cleaning solutions prior to pelvic surgery (which may include a vaginal approach or surgery on the vagina). Our central hypothesis is that chlorhexidine gluconate will be non-inferior to povidone iodine and that both antiseptic solutions will equally prevent postoperative infections. The specific aims are:

Aim 1: To compare postoperative urinary tract infection (UTI) rates between women cleaned with chlorhexidine gluconate (CHG) versus povidone iodine (PI) preoperatively. For the purposes of this study, UTI will be defined as: 1) greater than 100,000 CFUs on culture, or 2) at least 10,000 colony forming units on urine culture, in a symptomatic patient, or 3) patient reported UTI symptoms empirically treated within 2 weeks after surgery. Our primary **hypothesis** is that chlorhexidine gluconate will be non-inferior to povidone iodine with respect to the number of UTIs identified and treated within 2 weeks of surgery.

Aim 2: To compare postoperative culture proven urinary tract infection (UTI) rates between women cleaned with chlorhexidine gluconate (CHG) versus povidone iodine (PI) preoperatively. For the purposes of this aim UTI will be defined as: 1) greater than 100,000 CFUs on culture, or 2) at least 10,000 colony forming units on urine culture, in a symptomatic patient. Our primary **hypothesis** is that chlorhexidine gluconate will be non-inferior to povidone iodine with respect to the number of UTIs identified and treated within 2 weeks of surgery.

Aim 3: To compare postoperative rates of surgical site infection (SSI) in women who receive chlorhexidine gluconate versus povidone iodine vaginal antiseptic preparation preoperatively, defined as per CDC guidelines (described below). **Hypothesis**: Chlorhexidine gluconate will demonstrate a non-inferior rate of postoperative SSI compared to povidone iodine.

Aim 4: evaluate vaginal and vulvar irritation for post groups on postop day 1 as measured by a 5-point vaginal irritation scale previously used in a safety and tolerability study examining vaginal chlorhexidine gluconate (Al Niaimi et al) **Hypothesis:** Chlorhexidine gluconate will demonstrate a non-inferior rate of postoperative vaginal and vulvar irritation for postop day 1.

2. Background

Steady improvements have been made in surgical infection control over the past century including improved instrument sterilization methods, operating room ventilation, surgical barriers including gowns and drapes, surgical technique, preoperative antimicrobial prophylaxis, and preoperative cleaning or prepping of the surgical site. Despite these advancements, UTIs and SSIs continue to be a common cause of postoperative morbidity.

Urinary Tract Infections are one of the most common post-operative complications associated with urogynecologic surgery. One study estimated that 33% of women develop UTIs in the 12 week period following surgical treatment for stress urinary incontinence (Anger et al). UTIs are associated with increased health care costs, antibiotic resistance, and morbidity and mortality for patients. Because UTIs are so common, they are used as a quality metric and tracked by the Joint Commission, the Centers for Medicare and Medicaid Services (CMS), and National Surgical Quality Improvement Program (NSQIP), among others.

Another concern following pelvic surgery (which may include a vaginal approach or surgery on the vagina) is development of surgical site infections (SSI). A recent study found that SSIs were among the most common healthcare-associated infection, accounting for 31% of all healthcare-associated infections (HAI) among hospitalized patients. (Magill 1) Vaginal surgery is classified as clean-contaminated procedures because of the natural bacterial flora of the vagina. This generally increases infection risk over clean procedures.

Several studies demonstrate decreased SSI rates when chlorhexidine gluconate is used for abdominal preoperative antisepsis. Common abdominal surgeries such as hysterectomy and cesarean section demonstrate 44% and 19% lower odds when chlorhexidine gluconate is used instead of povidone iodine for preoperative surgical site antiseptic preparation. (Uppal et al) (Elshamy et al).

CHG is also known to have a longer duration of action than PI. While iodine has a duration of action of 2 hours, CHG has been characterized as having a duration of action of 6 to 48 hours depending on the level of alcohol concentration in the antiseptic solution. (Hemani et al)

Because of this, chlorhexidine is the preferred antiseptic of choice prior to abdominal surgeries.

For vaginal surgery, povidone iodine is the only FDA approved antiseptic agent. Because of this, some institutions limit or restrict the use of chlorhexidine vaginally. However, chlorhexidine has been shown to be a safe and effective vaginal presurgical antiseptic. (Al-Niaimi) The American College of Obstetricians and Gynecologists (ACOG) recommend that either CHG or PI are acceptable antiseptic agents. We are not aware of any studies directly comparing perioperative infection rates between CHG and PI at the time of pelvic surgery (which may include a vaginal approach or surgery on the vagina). A recent systematic review evaluating preoperative antisepsis at the time of vaginal hysterectomy identified minimal data, although one study which used bacterial colonies as a surrogate of SSI showed fewer bacteria sampled serially during a vaginal hysterectomy with CHG versus PI (Culligan). This corroborates the notion that CHG has a longer residual effect at the site of application over PI.

There have been no studies to specifically determine non-inferiority of chlorhexidine gluconate to povidone iodine for preoperative vaginal preparation prior to urogynecologic procedures with regard to either urinary tract infection or surgical site infection rates. Therefore, the primary objective of this study is to perform a single-blinded, non-inferiority randomized controlled trial to compare the effectiveness of two pre-surgical vaginal antiseptic cleaning solutions prior to pelvic surgery.

3. Study Design

We will perform a single masked, non-inferiority randomized-controlled trial to compare the effectiveness of chlorhexidine gluconate and povidone iodine pre-surgical vaginal antiseptic cleaning preparations prior to pelvic surgery (which may include a vaginal approach or surgery on the vagina). The target population are those patients presenting for urogynecologic surgery in the University of New Mexico health system. Participants will be masked as they will not be informed regarding which intervention they receive while under anesthesia at the start of their scheduled procedure. All women will give written or verbal consent prior to enrollment. It is not feasible to mask the surgeon, as the two antiseptic preparations are colored differently which is evident throughout surgery.

4. Inclusion and Exclusion Criteria

We will recruit patients who present to the University of New Mexico (UNM Women's Care Eubank Clinic or Sandoval Regional Medical Center) with urogynecologic conditions requiring pelvic surgery (which may include a vaginal approach or surgery on the vagina). Patients will receive usual care including evaluation of prior medical history and physical exam, any necessary diagnostic studies and preoperative workup. All patients will be offered typical treatment options regardless of their desire to participate in the research study.

Patients will be enrolled if they meet the inclusion and do not meet the exclusion criteria.

The inclusion criteria are:

- Female Subjects >18 years of age
- English or Spanish speaking/reading
- Must be able to provide informed consent.
- Undergoing urogynecologic procedures or surgery at UNM, OSIS, or SRMC

Exclusion criteria:

- Pregnant - all patients are verified regarding pregnancy status prior to gynecologic surgical intervention at all sites of surgery within the UNM system –

for patients who are premenopausal and have a uterus, a urine pregnancy test is administered in the preoperative setting. Pregnancy status is also determined prior to this in the office setting by interview and patient provided history prior to offering surgery to the patient.

- Inability to return for follow-up visits
- No concurrent need for vaginal antisepsis, such as cases of sacral neuromodulation
- Lack of telephone
- Known allergy to either antiseptic agent
- Prisoners will not be eligible to participate in this study

5. Number of Subjects

The primary outcome of this study is to determine rates of urinary tract infections in the period 2 weeks post-surgery for both cohorts. For the purposes of this study, UTI has been defined in section 1 (objectives), aim 1. We have powered the study based on a 10% difference in UTI rates between groups within 2 weeks of surgery. Based on a non-inferiority study design and a between group difference of less than or equal to 10%, we need 58 patients per group (chlorhexidine gluconate versus povidone iodine) to detect no difference with an alpha =0.05 and with 80% power. Assuming a high dropout rate of 20%, we will enroll a total of up to 200 patients (100/group), or until we reach our primary endpoint of 2 week follow up for 116 patients, or 58 patients in each group. We have increased the numbers due to COVID-19 and loss to follow-up.

This is not a multi-center study. Data will be housed at the Eubank clinic.

6. Study Timelines

Timeline	**May 2019- April 2020**	**May 2020-Sept 2020**
Subject recruitment, therapy, through 3 month follow up	x	x
Data analysis		x
Manuscript preparation		x

Over the past 12 months, 318 urogynecology cases were performed at UNM and SRMC. Assuming a conservative estimate of 50% enrollment, recruitment of up to 200 patients would be feasible over the next 3 month period.. Since subjects will be followed for 6 weeks after surgery, it may take up to 14 months to collect 6 weeks of follow up data. We estimate that data analysis, manuscript preparation and publication will take an additional 10 months.

7. Study Endpoints

The **primary endpoint** of our study is to determine the incidence of urinary tract infections within weeks of surgery in women who undergo pelvic surgery (which may include a vaginal approach or surgery on the vagina) with either chlorhexidine gluconate or povidone iodine vaginal antiseptic preparation. Our **secondary endpoints** are to investigate SSI rates in the two groups at 6 weeks, and vaginal irritation on the first postoperative day.

Given the extremely low-risk nature of the therapeutic interventions, we do not have any **safety endpoints.** However, any patients noted to have an allergic response will be treated according to the normal standard of care depending on the severity of their allergic reaction.

8. Research Setting

The study will be performed at the University of New Mexico Hospital (UNMH), Sandoval Regional Medical Center (SRMC) and University of New Mexico Outpatient Surgery and Imaging Services OSIS, and all associated urogynecology clinics. Potential subjects will be recruited in the UNM Eubank and SRMC clinics. All patients will have a complete history and physical taken. They will undergo a pelvic exam and will undergo typical preoperative diagnosis and workup performed as part of the standard of care for their respective urogynecologic diagnosis. After recruitment, they will undergo the consent process, and fill out initial questionnaires in the outpatient offices or by phone. All other follow-up will be performed in the above-mentioned outpatient clinics.

There are no laboratory tests in this trial other than what would routinely be collected for the workup of urogynecologic conditions or postoperative infections or complications. As we are essentially comparing two standard treatment options we do not think community advisory board is necessary. There will not be any research conducted outside of the UNM HSC and its affiliates.

9. Resources Available

Dr. Peter Jeppson is a board certified subspecialist in Urogynecology and will serve as the primary investigator (PI) for this study. In addition, Drs. Komesu and Dunivan will also help oversee and mentor Dr. Rockefeller with this study; they are both very experienced researchers. All have been PIs on multiple research trials and has successfully completed and published many studies. Dr. Nicholas F. Rockefeller is a Female pelvic medicine and reconstructive surgery (urogynecology) fellow. He has the time and resources including 12 months of protected research time, to complete this study.

The University of New Mexico (UNM) urogynecology division evaluates patients primarily in two outpatient clinics. *UNM Eubank Urogynecology Clinic* located in Northeast Albuquerque provides a full range of services for women with pelvic floor disorders. The Eubank clinic consists of 8 examination rooms, 2 treatment rooms, and 2 physical therapy rooms. Our second location is at *Sandoval Regional Medical Center (SRMC),* a community-based facility located in Rio Rancho, New Mexico, a large suburb located north of Albuquerque.

Research Staff**:** The Urogynecology Division employs a clinical research manager, 3 research coordinators and one student research assistant. Our research staff has extensive experience conducting multi-center investigations and recruiting patients to clinical studies, with special expertise in community-based research and quality of life studies.

Research Experience: The Urogynecology Division at UNM has a strong history of conducting high quality research and collaboration with other investigators in the US and abroad, and has consistently met or exceeded recruitment goals on time. We have been members of the NICHD-sponsored Pelvic Floor Disorders Network, and have met recruitment goals with high rates of follow-up and accurate data collection. In addition to PFDN research, Dr. Peter Jeppson has mentored and has been the PI on multiple clinical trials and contributes multiple publications in peer-reviewed journals. His Curriculum Vitae is attached.

Our group is well versed in the importance of adherence to protocols, timely completion of regulatory requirements, effective recruitment strategies, and the importance of the inclusion of minority subjects. Research is integral to all aspects of Divisional work; importantly, all members of the clinical team participate in research efforts. There are weekly research meetings to discuss the progress of the ongoing studies within the department, and it is an excellent forum to ensure that all involved are adequately informed of their duties, of the protocol, and of the procedures.

We do not anticipate that emergency care outside of normal operating protocol will be needed for this study; however the urogynecology physicians are available on a 24 hour basis, 7 days per week for any patients requiring emergency care.

10. Prior Approvals

This is a new study that has not been previously submitted for approval but Institutional Review Board approval for the University of New Mexico Health Sciences Center will be obtained prior to initiating the study.

This study has been approved by the Department Scientific Review Process for the Obstetrics and Gynecology Department by Dr. Lawrence Leeman.

This study does not include any ionizing radiation, or biological specimens. The drugs that are used in this study include Povidone Iodine and Chlorhexidine Gluconate.

11. Multi-Site Research

This is not a multi-site research study.

12. Study Procedures

This single masked, non-inferiority randomized controlled trial will be conducted at the UNM Eubank Clinic and SRMC Urogynecology clinic and associated operating rooms. We will recruit at least 200 participants between the sites. All collaborating investigators are members of the Urogynecology division at UNM.

The primary aim of our study is to determine if UTI rates are similar between typical preoperative vaginal antiseptic cleaning solutions (i.e. chlorhexidine gluconate vs. povidone iodine). The target population will be patients with urogynecologic conditions desiring surgical management that would require vaginal surgical preparation. If a patient decides during their clinic visit to proceed with surgical management that would require vaginal surgical preparation they will be considered for the study. If the patient is interested in surgical management and fulfills study inclusion criteria, we will then offer her the choice of participating in this study. Written or verbal consent will be obtained from all participants by research staff prior to enrollment. All participants will then complete baseline surveys including patient demographics, medical/surgical history, and contact information, which are attached as supporting documents. This information will be collected from the patient on the day of enrollment with information supplemented from their medical record as needed.

Randomization assignment will be generated by a computer based randomization table and assigned by a research coordinator. Assignments will be kept in sealed opaque envelopes

numbered sequentially. On the day of the patient's surgery, after previously signing or verbalizing consent and deciding to participate, the next envelope in the sequence will be opened, randomizing the patient to chlorhexidine gluconate or povidone iodine. The therapy allocation will then be carried out.

Patients randomized to chlorhexidine gluconate or povidone iodine will undergo standardized preoperative surgical site preparation by surgical staff. Abdominal cleaning will be done with chlorhexidine gluconate in 70% isopropyl alcohol as this is the standard antiseptic used throughout the institution. Vaginal antiseptic cleaning will be performed with either chlorhexidine or povidone based on the randomization scheme, this will be performed in a standardized fashion as described in supplemental vaginal preparation instruction document (included in appendix A).

If a patient demonstrates an allergic reaction to either antiseptic (povidone iodine or chlorhexidine gluconate), they will be routinely treated for allergic symptoms and informed of the antiseptic type, the allergy will also be added to their medical record.

Table 1: Outcomes collected at various time points

	Baseline	2 weeks	6 weeks
Demographic and medical history	X		
Follow up questionnaire	X	X	X
Vaginal irritation questionnaire	Postop day 1		

Our primary outcome is to report the rates of postoperative urinary tract infections for each cohort at 2 weeks postoperatively. It is our standard of care to see patients back at 2 weeks and 6 weeks following surgical management of urogynecological conditions.

If patients are unable to follow up in clinic as standard care, telephone communication may be used to ask patients if they have received care at an outside facility for urinary tract infection or other infection related to surgical treatment.

Outcome Measures:

1. **Urinary tract infection (UTI): Patients with >100k colony forming units on urine culture, symptomatic patients with >10k colony forming units on urine culture or reported UTI symptoms resulting in empiric treatment without urine culture.**
2. **Surgical Site Infection (SSI)**: Surgical site infection as defined by the below criteria in the 6 week postoperative period.

1) We will categorize SSI based on CDC criteria (ref) adapted from the CDC guidelines as referenced below. We will recorded SSI events 6 weeks after surgery.
    a. CDC Criterion: Surgical Site Infection (SSI)
        i. Superficial incisional SSI must meet the following criteria:
            1. Date of event for infection occurs within 6 weeks after any operative procedure (where day 0 is the procedure date)
            2. AND involves only skin and subcutaneous tissue of the incision
            3. AND patient has at least one of the following:

a. Purulent drainage from the superficial incision.
b. Organisms identified from an aseptically-obtained specimen from the superficial incision or subcutaneous tissue by a culture or non-culture based microbiologic testing method which is performed for purposes of clinical diagnosis or treatment (for example, not Active Surveillance Culture/Testing (ASC/AST).
c. Superficial incision that is deliberately opened by a surgeon, attending physician** or other designee and culture or non-culture based testing is not performed. AND patient has at least one of the following signs or symptoms: pain or tenderness; localized swelling; erythema; or heat.
d. Diagnosis of a superficial incisional SSI by the surgeon or attending physician** or other designee.

4. ** The term attending physician for the purposes of application of the SSI criteria may be interpreted to mean the surgeon(s), infectious disease, other physician on the case, emergency physician or physician's designee (nurse practitioner or physician's assistant or nurse midwife).
5. There are two specific types of superficial incisional SSIs:
6. Superficial Incisional Primary (SIP) - a superficial incisional SSI that is identified in the primary incision in a patient that has had an operation with one or more incisions (for example, C-section incision or chest incision for CBGB)
7. Superficial Incisional Secondary (SIS) - a superficial incisional SSI that is identified in the secondary incision in a patient that has had an operation with more than one incision (for example, donor site incision for CBGB)
8. The following do not qualify as criteria for meeting the definition of superficial SSI:

9. Diagnosis/treatment of cellulitis (redness/warmth/swelling), by itself, does not meet criterion "d" for superficial incisional SSI. Conversely, an incision that is draining or that has organisms identified by culture or non-culture based testing is not considered a cellulitis.
10. A stitch abscess alone (minimal inflammation and discharge confined to the points of suture penetration).
11. A localized stab wound or pin site infection- Such an infection might be considered either a skin (SKIN) or soft tissue (ST) infection, depending on its depth, but not an SSI Note: A laparoscopic trocar site for an operative procedure is not considered a stab wound.

ii. Procedure-associated Module SSI Deep incisional SSI Must meet the following criteria:
1. The date of event for infection occurs within 6 weeks after the operative procedure (where day 0 = the procedure date) according to the list in Table 2
2. AND involves deep soft tissues of the incision (for example, fascial and muscle layers)
3. AND patient has at least one of the following:

a. Purulent drainage from the deep incision.
b. A deep incision that spontaneously dehisces, or is deliberately opened or aspirated by a surgeon, attending physician** or other designee AND organism is identified by a culture or non-culture based microbiologic testing method which is performed for purposes of clinical diagnosis or treatment (for example, not Active Surveillance Culture/Testing (ASC/AST) or culture or non-culture based microbiologic testing method is not performed AND patient has at least one of the following signs or symptoms: fever (>38¬∞C); localized pain or tenderness. A culture or non-culture based test that has a negative finding does not meet this criterion.
c. An abscess or other evidence of infection involving the deep incision that is detected on gross anatomical or histopathologic exam, or imaging test.

4. ** The term attending physician for the purposes of application of the SSI criteria may be interpreted to mean the surgeon(s), infectious disease, other physician on the case, emergency physician or physician's designee (nurse practitioner or physician's assistant).
5. There are two specific types of deep incisional SSIs:

6. Deep Incisional Primary (DIP) - a deep incisional SSI that is identified in a primary incision in a patient that has had an operation with one or more incisions (for example, C-section incision or chest incision for CBGB)
7. Deep Incisional Secondary (DIS) - a deep incisional SSI that is identified in the secondary incision in a patient that has had an operation with more than one incision (for example, donor site incision for CBGB)
8. SSI Organ/Space SSI Must meet the following criteria:
9. Date of event for infection occurs within 6 weeks after the operative procedure (where day 0 = the procedure date) AND infection involves any part of the body deeper than the fascial/muscle layers, that is opened or manipulated during the operative procedure AND patient has at least one of the following:

a. purulent drainage from a drain that is placed into the organ/space (for example, closed suction drainage system, open drain, T-tube drain, CT guided drainage)
b. organisms are identified from fluid or tissue in the organ/space by a culture or non-culture based microbiologic testing method which is performed for purposes of clinical diagnosis or treatment (for example, not Active Surveillance Culture/Testing (ASC/AST).
c. an abscess or other evidence of infection involving the organ/space that is detected on gross anatomical or histopathologic exam, or imaging test evidence suggestive of infection. AND meets at least one criterion for a specific organ/space infection site.

13. Data Analysis

Data Analysis: Between and within group differences will be evaluated using Wilcoxon-Mann-Whitney test for categorical variables and t-tests for continuous variables. If there are any baseline differences between groups, a multivariate analysis will determine the contribution of these differences to observed differences (if any) between groups.

Power Analysis: Power analysis was performed based on previously reported rates of postoperative urinary tract infection after urogynecologic surgery as well as rates of relative reduction in infection with chlorhexidine presurgical preparations as opposed to povidone iodine. To achieve significance for a non-inferiority study using these assumptions we would need 116 patients, 58 per group to detect this difference with alpha =0.05 and with 80% power.

To allow for a dropout or loss to follow up of 20% due to the pandemic, we will enroll at least 200 patients.

Comparative Cost Analysis
The cost analysis will be conducted from patient and health system perspective and will be expressed as incremental cost required to prevent one episode of UTI.

Direct and indirect cost of health care utilization will be obtained when episodes of UTI occur, including the patient reported travel expenses and copays to obtain care, cost of UTI diagnosis with urine dipstick, urinalysis, and urine culture standardized to University of New Mexico Health Sciences Center institutional pricing as well as the cost of antibiotics for treatment.

14. Provisions to Monitor the Data to Ensure the Safety of Subjects

There is no DSMB that will be monitoring safety of these procedures. Both vaginal antiseptic preparations are routinely used preoperatively for surgery for urogynecologic conditions. Additionally, we will keep track of any adverse events and ask patients about adverse events on either the operative or postoperative day, as well as at the 2 week and 6 week follow up visits. Because neither of the studied treatments are experimental and are already widely used, we do not anticipate an above average risk of adverse events; overall risk is minimal. Participants will have access to a 24/7 phone number to reach research or clinical staff with any concerns. All adverse events will be recorded and reported to the study PI.

We do not anticipate any conditions that would trigger a suspension or termination of the research study.

15. Withdrawal of Subjects

Any participant may withdraw from the study at any time without penalty and will continue to receive the clinical standard of care. A subject may be withdrawn from the study without her consent at the discretion of the physician and study staff if they believe she no longer meets study inclusion criteria or if she meets exclusion criteria, or if they believe that it is not in her best interest to continue study participation. Investigators may withdraw a subject if the subject is not following the study protocol. If a participant is withdrawn from the study either at her own discretion or that of the research staff, she may continue with management of her urogynecologic condition in the usual fashion.

To minimize withdrawal from the study, patients will be randomized in the preoperative anesthesia care unit (PACU) on the day of surgery. We will follow CONSORT guidelines (Shultz 2010), and analyze all participants assessed for eligibility within the study. We will document reasons for withdrawal from the study including failure to meet eligibility criteria or participant

declining enrollment into the study. The withdrawal procedure is clearly documented in the study consent.

If a patient withdraws from the study, the research team will not be required to destroy or retrieve any health information that has already been used or shared prior to when withdrawal is received.

16. Data Management/Confidentiality

Randomization assignment will be generated by a computer based randomization table and assigned by a research coordinator. Assignments will be kept in sealed opaque envelopes numbered sequentially, and on the day of the patient's surgery a research coordinator will open the next envelope in the sequence. This de-identified study subject number will then be assigned to the patient. All data collection sheets and questionnaires will contain the subject number and day of the enrollment. No other patient identifiers will be collected on study forms. PHI including patient name, date of birth, phone number, and medical record number will be collected to track appointments and kept separate from participant study data in a locked cabinet in a locked secured office.

The data collection, HIPAA and consent forms will be maintained in a locked file cabinet in the locked Eubank research office. A separate folder will be designated for each participant. The offices have the additional security of being badge-access only for UNM OBGYN department employees. A key matching study number to subject's name will be stored on a password protected computer on a secure UNM OBGYN department server.

The only identifiers collected will be patient name, date of birth, and telephone number for site use only and to ensure patient follow up. This will not be entered into the database, but it will be kept with the other identifying information.

The data does not include sensitive information or information requiring additional protection.

All data will be kept in a locked file cabinet in the research administrative area. In order to further ensure patient confidentiality, the identifying information will be kept separately from the numbered study files in a locked cabinet.

Electronic data entry will be performed in the OBGYN administrative offices, using the de-identified subject study number. The electronic data will be encrypted, password protected, and stored on the secure UNM OBGYN department server. This server's electronic security is

monitored / maintained by the Health Sciences Library and Informatics Center (HSLIC). A REDCAP database will be created to collect, store and manage the data. REDCAP databases are reposed securely and all data entered is deidentified. The REDCAP database is only accessible using a individual unique login and password and access is only provided to co-investigators. Access is restricted to co-investigators and will be protected using the unique REDCAP login and password provided to each co-investigator.

Access to the files and REDCAP will be restricted to research personnel and Investigators and will be locked or protected using the unique REDCAP login and password provided to each co-investigator. The data will be stored for 5 years after completion of analysis and then will be destroyed. The data will not be publically available.

A Certificate of Confidentiality will not be used to protect data from forced release. No identifying or study related data will be transported to outside locations. There will be no audio or video recordings or photographs taken.

17. Data and Specimen Banking

As stated above, the data collection, HIPAA and consent forms will be maintained in a locked file cabinet in the Eubank research office. A separate folder will be designated for each participant. A key matching study number to subject's name will be stored on a password protected computer on a secure UNM OBGYN department server. In order to further ensure patient confidentiality, the identifying information will be kept separately from the numbered study files in a locked cabinet. The data will be maintained for 5 years after completion of the study and then destroyed.

No specimens will be archived for future use.

18. Risks to Subjects

Risks of enrollment in the study include loss of confidentiality. We will take every measure to try to ensure the security and confidentiality of participants. Participants will be recruited in a private room and will have ample time to consider whether they want to participate in the study. Also, locked filing cabinets will be used to protect patient consent information and collected data. The link identifying patients and their study numbers will be stored on a password protected computer on a secure UNM OBGYN department server.

Additionally, each patient who will be offered enrollment will already have agreed to surgical treatment for their pelvic organ prolapse. Risks would include allergic reaction to either type of preparation. Currently if patients are allergic to povidone iodine, chlorhexidine gluconate is used. Any patients noted to have an allergic response will be treated according to the normal standard of care depending on the severity of their allergic reaction.

Pregnant women will not be included in the study. Patients with childbearing potential are routinely tested for pregnancy on the day of surgery prior to their case. If they are pregnant, the patient meets exclusion criteria and will be ineligible to participate.

There are no risks to those who are not subjects.

19. Potential Benefits to Subjects

The patients enrolled are already opting for surgical treatment of their urogynecologic conditions. Participation in this study may help to improve an individual participant's condition, but it is also possible that the condition may not improve. There is no guarantee that any individual will personally benefit by participating in this research study.

20. Recruitment Methods

We will recruit women from our urogynecology clinical practice and we do not plan to advertise for this study.

The urogynecology clinics at UNM Eubank, and SRMC have a large referral population of patients with pelvic floor conditions and SUI. Subjects will be identified in the clinics at UNM Eubank clinic, and SRMC by investigators. The patients will be counseled about possible treatment options for urogynecological conditions including non-surgical and surgical techniques as according to standard of care. If the patients elect surgical management, they will be introduced to the study and provided with written information that may help them decide if participation in the study is right for them. Subjects are encouraged to consult with family, friends, and primary health care providers, as well as communicate any questions they may have before beginning the consent process. We will request a waiver of HIPAA authorization for recruitment purposes.

If a woman declines to participate or is withdrawn from the study either by her desire or that of the research staff, she will be offered the same treatment options. Her follow up appointments will be the same regardless of participation in the study.

If a patient indicates by initialing on their consent form or verbalizing, "Yes, you may contact me in the future regarding research projects," they may be contacted in the future using their provided information for future research projects.

21. Provisions to Protect the Privacy Interests of Subjects

Privacy concerns are taken into account with every patient seen at the UNM and SRMC clinics. Participants approached and/or interviewed in the clinic setting will be in private offices or examination rooms in the UNM Eubank, or SRMC clinics or in the preoperative areas of UNM Main Hospital or SRMC Hospital, where all staff, including research staff, are well-versed in sensitive health care discussions and procedures. Telephone interviews for recruitment and study data gathering are conducted in the research staff area or private physician offices, where all staff have received CITI Training. The office area designated for the entire urogynecology research staff is isolated from the clinical administrative staff area, providing protection for participants and potential participants during screening, recruitment, study-designated calls, and data entry. All study sheets used to collect patient information will be de-identified.

At all times throughout the clinical investigation, confidentiality will be observed by all parties involved. All data will be secured against unauthorized access. Privacy and confidentiality of information about each subject will be preserved in study reports and in any publication. Each subject participating in this study will be assigned a unique identifier. An IRB-approved HIPAA authorization is required to be signed. All documents containing personal health information (screening logs, consent documents, data forms) are maintained in locked file cabinets with access available only to research staff and investigators. Data is entered into a password protected system. No individual identifiers are entered into the system. The sole link with personal information is maintained by the research team on a password protected computer on a secure UNM OBGYN department server with access limited to authorized research staff and investigators. This information is only to be used at the study center.

22. Economic Burden to Subjects

There are no study related costs to the participant outside of what would be recommended for standard care. Whether enrolled in the chlorhexidine gluconate or povidone iodine, participants will not be billed outside of standard operating procedure for their surgical care.

23. Compensation

There will be no monetary compensation for involvement in the study.

24. Compensation for Research-Related Injury

If participants are injured or become sick as a result of this study, UNMHSC will provide emergency treatment at the study participant's cost. No commitment is made by the University of New Mexico Health Sciences Center to provide free medical care or money for injuries to

participants of the study. Reimbursement for treatment for all related costs of care will be sought from the participant insurer, managed care plan, or other benefits program. The participant will be responsible for any associated co-payments or deductibles required by the insurance. Participants will be encouraged to report any illness or injury they believe to be related to the study to the investigator or research staff. Participants will be given telephone contact information for the urogynecology office for the purpose of asking any questions or stating any concerns about the study or treatment as a research subject. They may also be directed toward the HRPO. This language will be stated in the written consent document, and reviewed during the informed consent process

25. Consent Process

Patients will be approached about the research study at the urogynecology clinic at UNM Eubank and at SRMC or the associated hospitals at UNM Hospital or SRMC Hospital during a discussion for the management of their urogynecologic condition. Each patient undergoes counseling in a private room with a closed door to ensure privacy. The physicians in the urogynecology division and research staff will be able to obtain consent after the participants have been counseled about their condition. Our division routinely treats this condition and are highly qualified to counsel patient regarding the risks, benefits, alternatives for the treatment. Those recruited will have already decided to undergo surgical management for their urogynecologic conditions. Hence, they will not be coerced into performance of any "extra" treatments. Additionally, care will not be withheld if they decide not to participate.

The patients who would like to participate in the study will be consented during their new or return visit in the urogynecology clinic or by phone due to the current pandemic. Verbal consent will be noted on the updated consent form with a space to also sign. Due to the pandemic, research coordinators are mainly working from home and going through the consent with participants by phone for the safety of everyone. Privacy is still maintained as the coordinator ensures they have a place they can talk privately by phone. They will have these multiple opportunities to ask any questions that they may have, and they will also be provided with the clinic's contact information to get in touch with research investigators to address any additional questions or concerns. If they decide to participate at the next visit, they will be allowed to join as long as their surgical procedure has not been completed.

Subjects will be reassured that participation is completely voluntary and does not affect their treatment, their relationship with their providers, or the university to minimize the possibility of coercion or undue influence. The patients will be asked that they understand the opportunity to participate and their complete freedom to decline. This will also be asked if they understand and if they have any questions. There is no minimum time period needed between informing

the patient of the study and time of consent. Subjects will be encouraged to take as much time as they need.

This study will obtain HIPAA authorization prior to enrollment. HIPAA authorization is imbedded within the study consent form, which will be reviewed with all participants by the physician or research staff obtaining consent. Specific information that will be obtained includes prior medical history, surgical history, reproductive health history including child bearing, drug allergies, age, and ethnicity. This information will obtained by health care providers, not research coordinators, as deemed necessary for a more complete and accurate medical history of the patient.

The HIPAA form is included in the consent attached.

Subjects not fluent in English

Spanish speaking patients will be included in the study, and fully translated consents will be available in Spanish. Consent process for Spanish speaking patients will be conducted through a Spanish interpreter or with a research protocol member fluent in Spanish.

Cognitively Impaired Adults/Adults Unable to Consent/Use of a Legally Authorized Representative

NA. Cognitively impaired subjects will not be included in this study.

Subjects who are not yet adults (infants, children, teenagers)

NA. Only subjects ≥ 18 years of age will be included in this study.

Waiver or Alteration of Consent Process (consent will not be obtained, required element of consent will not be included, or one or more required elements of consent will be altered)

NA. There will be no waiver or alteration of the consent process.

26. Documentation of Consent

We plan to document consent, and the Consent form is attached. We do not plan on collecting/storing tissue samples.

27. Study Test Results/Incidental Findings

We do not intend to share study test or procedure results with study participants. Additionally, we do not anticipate that the research being conducted will result in incidental findings. Every patient will receive the practice's standard of care regarding workup and treatment of urogynecologic conditions, which may include different laboratory tests, urine culture or

urodynamic testing if unclear cause of incontinence, prolapse, or other urogynecologic condition, or imaging studies, as determined by their other active medical issues. These results are not directly a part of the research being conducted and will hence be disclosed to the patient. They will not, however, affect randomization.

28. Sharing Study Progress or Results with Subjects

We do not intend to share study progress with participants while the study is underway as not to introduce bias. We do not intend to seek out study participants to disseminate information once the study is complete. Women who are interested in the results will be provided the information where to read the manuscript once it is published. Study results for individual participants will not be shared.

29. Inclusion of Vulnerable Populations

There will not be any vulnerable populations included in this study. Those electing for treatment of urogynecologic conditions will not be coerced into doing so, nor will they be coerced into participating in this trial.

30. Community-Based Participatory Research

N/A. There will be no involvement of the community in this research.

31. Research Involving American Indian/Native Populations

NA. This research does not specifically target this population. If an American Indian woman is a candidate for this study she will be offered participation

32. Transnational Research

NA. This study is not transnational.

33. Drugs or Devices

Surgical preparations including chlorhexidine gluconate 4% solution as well as povidone iodine will be used for surgical preparation. According the American College of Obstetricians and Gynecologists (ACOG):

> "Vaginal cleansing with either 4% chlorhexidine gluconate or povidone–iodine should be performed before hysterectomy or vaginal surgery. Currently, only povidone–iodine preparations are approved by the U.S. Food and Drug Administration (FDA) for vaginal surgical site antisepsis. The CDC (Berrios-Torres SI) recommended alcohol-based preparations, which typically include

chlorhexidine, for external perioperative skin preparation, based on studies that suggest superiority over aqueous povidone–iodine preparations, raising the question of chlorhexidine use for vaginal surgical site antisepsis. In the United States, 4% chlorhexidine gluconate soap (containing 4% isopropyl alcohol) is often used off-label to prepare the vagina in women with iodine allergy, and some U.S. institutions prefer it for routine cases. To avoid irritation, chlorhexidine gluconate with high concentrations of alcohol (eg, 70% isopropyl alcohol, commonly used for skin preparation) is contraindicated for surgical preparation of the vagina. However, solutions that contain lower concentrations, such as the commonly used 4% chlorhexidine gluconate soap containing 4% alcohol, are usually well tolerated and may be used for vaginal surgical preparation as an alternative to iodine-based preparations in cases of allergy or when preferred by the surgeon."

Additionally chlorhexidine gluconate has been shown to be safe and effective as a vaginal presurgical preparation in a pre-post study. (Al-Niaimi A). The 53 patients receiving chlorhexidine gluconate in that trial actually experienced less vaginal irritation than those receiving povidone iodine, and did not have any serious adverse events.

34.Principal Investigator's Assurance

By submitting this study in the Click IRB system, the principal investigator of this study confirms that:

☐ The information supplied in this form and attachments are complete and correct.

☐ The PI has read the Investigator's Manual and will conduct this research in accordance with these requirements.

☐ Data will be collected, maintained and archived or destroyed per HSC Data Security Best Practices, including:

1. **Best Practice for data collection** is for it to be directly entered onto a data collection form that is in a secured access folder on an HS drive behind a firewall, or in a secure UNM Data Security approved system such as RedCap.
2. **Data collection of de-identified data**, if done in a clinical setting or other setting that does not allow direct entry into a secured system, may be done temporarily using a personal or university owned electronic storage device or hard copy document. **The important security safeguard is that no identifiers be include if the data is entered or stored using an untrusted device or storage.**
3. **Permanent (during data analysis, after study closure**) storage must reside on HSC central IT managed storage. Processing of data (aggregation, etc.) are to be carried out in such a way as to avoid creating/retaining files on untrusted storage devices/computers. Trusted devices are HSC managed and provide one or more of following safeguards: access logs, encryption keys, backups, business continuity and disaster recovery capabilities.

4. **Alternate storage media** must be approve by HSC IT Security as meeting or exceeding HSC central IT provided security safeguards.

Checklist Section

This section contains checklists to provide information on a variety of topics that require special determinations by the IRB. Please complete all checklists relevant to your research.

I. Waivers or Alterations of Consent, Assent, and HIPAA Authorization

NA. We are not requesting alterations of consent, assent, nor HIPAA Authorization

A. Partial Waiver of Consent for Screening/Recruitment

NA. We are not requesting a partial waiver of consent for screening/recruitment.

B. Partial Waiver of HIPAA Authorization for Screening/Recruitment

We are requesting a partial waiver of HIPAA authorization for screening/recruitment. We will review medical records of participants who have any missing questionnaire data, such as medical history, physical examination and demographic data. Consent will be obtained from patients to review this information.

C. Waiver of Documentation of Consent

NA. We are not requesting a waiver of documentation of consent

D. Alteration of Consent

NA. We are not requesting an alteration of consent.

E. Full Waiver of Consent/Parental Permission

NA. We are not requesting a full waiver of consent/parental permission.

F. Full Waiver of Consent/Parental Permission (Public Benefit or Service Programs)

NA. We are not requesting a full waiver of consent/parental permission..

G. Full Waiver of HIPAA Authorization

NA. We are not requesting a full waiver of HIPAA authorization.

H. Other Waiver Types

NA. We are not requesting other waiver types.

II. Vulnerable Populations

A. Adults with Cognitive Impairments

NA. Adults with cognitive impairments will not be included in this study.

B. Children

NA. Children will not be included in this study.

C. Pregnant Women and Fetuses

NA. Neither pregnant women nor fetuses will be included in this study.

D. Neonates of Uncertain Viability or Nonviable Neonates

NA. Neither neonates of uncertain viability nor nonviable neonates will be included in this study.

E. Nonviable Neonates

NA. Nonviable neonates will not be included in this study.

F. Biomedical and Behavioral Research Involving Prisoners

NA. Prisoners will not be enrolled in this study.

III. Medical Devices

None

IV. Export Control

There are no export control concerns with this study as there will be no select agents or toxins involved in the project, and no collaboration with foreign institutions, foreign nationals, publication restrictions, or foreign travel.

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ACOG Practice Bulletin No. 195: Prevention of Infection After Gynecologic Procedures. Obstet Gynecol 131, e172–e189 (2018).
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Awad, S. S. Adherence to surgical care improvement project measures and post-operative surgical site infections. Surg Infect (Larchmt) 13, 234–237 (2012).
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Uppal, S. et al. Chlorhexidine-Alcohol Compared With Povidone-Iodine for Preoperative Topical Antisepsis for Abdominal Hysterectomy. Obstet Gynecol 130, 319–327 (2017).
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Elshamy, E., Ali, Y. Z. A., Khalafallah, M. & Soliman, A. Chlorhexidine-alcohol versus povidone-iodine for skin preparation before elective cesarean section: a prospective observational study. J. Matern. Fetal. Neonatal. Med. 1–5 (2018). doi:10.1080/14767058.2018.1489533
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Anger, J. T., Litwin, M. S., Wang, Q., Pashos, C. L. & Rodríguez, L. V. Complications of sling surgery among female Medicare beneficiaries. Obstet Gynecol 109, 707–714 (2007).
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Schulz, K. F., Altman, D. G., Moher, D. & CONSORT Group. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. BMJ 340, c332 (2010).
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Magill, S. S. et al. Multistate point-prevalence survey of health care-associated infections. N. Engl. J. Med. 370, 1198–1208 (2014).
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Magill, S. S. et al. Prevalence of healthcare-associated infections in acute care hospitals in Jacksonville, Florida. Infect Control Hosp Epidemiol 33, 283–291 (2012).
12.
Al-Niaimi, A. et al. Safety and tolerability of chlorhexidine gluconate (2%) as a vaginal operative preparation in patients undergoing gynecologic surgery. Am J Infect Control 44, 996–998 (2016).
13.
Hemani, M. L. & Lepor, H. Skin preparation for the prevention of surgical site infection: which agent is best? Rev Urol 11, 190–195 (2009).