"Effect of Prophylactic Negative Pressure Versus Silver Impregnated Silicone Bandage on Cesarean Section Surgical Site Infection Rate"

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PROTOCOL AND STATISTICAL ANALYSIS PLAN

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No Participant Contact (Data Only) Project Narrative

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1. ***Summary:***

This will be a prospective study using data that is already routinely collected through the HealthPartners system. Patients will not be affected by it, it is largely a chart abstraction and analysis in patients who have not centrally opted out of research.

Changes in patient care are not part of this study.

Post-operative infections are a serious cause of complication after surgery. Cesarean sections are unique because by definition they are contaminated by the vagina, as the uterus is contiguous with the vagina anatomically. When a surgical opening is created involving the uterus vaginal bacteria is unavoidably deposited into the abdominal space during delivery of the infant. Methods of procedure and sterile techniques are deployed throughout the procedure to minimize post c-section infections. Women with morbid obesity are at highest risk for development of surgical site infection. At Regions Hospital, post-operative surgical site wound care is addressed with the use of a prophylactic negative pressure wound therapy (NPWT) device (wound vacs) in lieu of traditional bandages after cesarean section in women at high risk for infection (BMI > or = 40). Alternatively many of the OB/GYNs have also started using a competing product called Mepilex Border Post-Op Ag for all patients. CMS (the dominant insurer of pregnant women in the US) has determined other types of pelvic surgery surgical site infections as a hospital acquired condition (HAC), which is tied directly to reimbursement. Though not currently affected by this policy, c-section surgical site infections may be considered in the future. So developing cutting edge practice now may avoid higher surgical site infection rates correlating directly to loss of reimbursable care to the hospital. Eliminating surgical site infections positively affects patient's well-being and the hospital's fiscal health. There is conflicting published data on benefits of surgical site dressing decisions for cesarean section. In our practice we have found it difficult to find a difference, however we have noted that our surgical site bundle (everything we do to prevent infections such as antibiotics, soaps, washes, etc) has dramatically reduced our surgical site infections. Recent studies demonstrate little benefit of the negative pressure wound therapy. However, published research, performed at Regions, and utilizing internal data suggests that negative pressure wound therapy lowers the incidence of surgical site infection rate in cesarean sections. We would like to evaluate the benefits of continuing the negative pressure wound therapy that some of our doctors use against using the Mepilex bandage that many of our other doctors use. It is not common practice to obtain consent prior to placing a bandage and is generally surgeon preference. In performing cesarean sections we currently place these bandages without informed consent (the surgery, is of course performed with informed consent). In our study we will compare the bandages selected based on surgeons' preferences and compare differences in infection rates over a 2 year period of time.

2. ***Study aims***

□ Our research question is which of our current practices of covering cesarean section incisions is 1) most clinically effective at eliminating surgical site infection and 2) is most cost effective. Patient safety is paramount and we would want to use the most effective form of surgical site infection prevention bandage/covering – however we do not know which of our practice is more effective. This question is unique to both high risk patients (BMI = or > 40), which uses one type of covering versus our normal risk patients (BMI < 40).
□ Our hypothesis is that a sterile silver impregnated silicone foam dressing (Mepiliex Border Post-Op Ag) will be effective in maintaining a low surgical site infection rate in both high risk patients (BMI = or > 40) as well as in normal risk patients (BMI < 40). We believe using the Mepilex bandage will be a more cost effective strategy.

□ Post-operative surgical site infections are uncommon in our practice (about 1%) they are clinically and financially significant complications of surgery. Strategies to minimize this known complication are essential. Our study is largely exploratory in that there aren't any adequate head-to-head studies that can help us guide our practice in selecting a wound-cover following cesarean.

□ The primary clinical aim of this project is to compare and differentiate infection rates between our current two practices. The first practice that many of our OB/GYNs have selected (as part of their clinical practice, not this study) is prophylactic negative pressure wound therapy dressing (wound vac) in high risk patients (BMI = or > 40) and a standard sterile dressing in women who are normal risk (BMI < 40). This change in addition to our surgical site bundle have shown dramatic decreases in surgical site infections and many of our doctors want to continue

on our success. Several other OB/GYNs have decided to switch to use a different approach (as part of their clinical practice, not this study) and use a silver impregnated silicone dressing (Mepiliex Border Post-Op Ag) regardless of BMI. The study will focus on women who have had a cesarean section at Regions Hospital. There have been conflicting data on whether the wound vac strategy is more effective or similarly effective to not using a wound vac; there have been a paucity of research studies that look at this data. There is only a single study that is prospective and it is inadequately powered; the rest are retrospective studies that have conflicting results. There have been no head-to-head comparisons in the class of Mepilex and Mepilex-related products versus prophylactic wound vacs. Our doctors are already using the two sets of products however it is not currently being studied.

□ The primary analytic goal of the project will be to look at the cost of the current practice and compare it to the cost of the proposed new practice/comparison practice both with and without incorporating the approximate costs of complications in the bullet point noted above. This is one of the most important points that our study will address, as it will help provide data to inform the fiduciary responsibility of obstetricians in caring for their patients. We will obtain national averages and multiple it by the number of additional patient encounters related to complications; additionally we will obtain billing information of patients with infectious complications to analyze actual differences in cost. We will also collect ICD-10 and CPT codes for hospital, lab and clinic bills during the hospitalization and the subsequent 30-day postoperative period. As part of the data abstraction, these items will be reviewed by two members of the study team to evaluate whether the costs are related to wound care and complications versus routine care. Toes will be broken by a third study team member. We will also analyze the total cost of care in the two groups.

□ The secondary clinical goal is to compare the location of the infections (cellulitis, which is easily treated and shallow, versus an abscess; the different locations result in dramatically different treatment intensities such as outpatient antibiotics for simple cellulitis versus invasive inpatient drainage procedures for a complex abscess).
□ An additional secondary clinical goal is to compare the cost of treating the infections by approximating the cost of inpatient stays, outpatient visits, hospital procedures and antibiotics given.
□ An additional secondary clinical goal will be to look for complications of the types of post-operative bandages (gauze bandage vs negative pressure wound therapy dressing vs silver impregnated silicone foam bandage).

3. ***Background, Rationale, Significance***

□ Post-operative wound infections are a clinically significant and sometimes life-threatening complication of abdominal surgery. Each type of surgery has different risk factors for infection. The vaginal space has its own colonization of bacteria that ascend through the cervix (the "birth canal") into the uterus and exit through the uterine incision into the abdomen. This causes a type of "contamination" that is inherent to cesarean sections not encountered in other types of surgery. Morbidity from cesarean section infections varies from minimal interference to life-threatening and costly. Some infections can be treated with opening up an abscess in the clinic, others with antibiotics and some with hospitalization, which can include IV antibiotics, invasive procedures to drain infectious material or surgery. Each infection costs hundreds to thousands of dollars depending on the type of treatment needed. Minimizing infection is imperative in all patients.
□ Obesity is a risk factor for abdominal incision infection, cesarean section is no different. Rates of obesity have been increasing for decades in the United States. As a major trauma hospital, Regions is a referral center for many patients with comorbid conditions too high risk for many community hospitals; obesity is no exception. We need to be vigilant in finding the safest surgical covering in our highest risk patients.
□ Our first of two strategies that our OB/GYNs use relies on negative pressure therapy (wound vacs) in high risk patients. We do not currently use it on obese patients (BMI > or = 30 and < 40), we do use it on patients with morbid obesity (BMI > or = 40). We use standard bandages for patients that are not morbidly obese (BMI <40), which generally is a sterile gauze. Recently our many of the OB/GYNs in our group have decided a more cost effective strategy based on high expenses from the wound vacs based on national trends with OB/GYNs as well as success in Regions Hospital with low post operative wound rates; the use the Mepilex Border Post-Op Ag dressing. The OB/GYNs who have continued with the wound-vac based strategy did not want to switch dressing types and are interested on building on our group's demonstrated improvement. In 2018 about half of our infections were in high-risk patients and half were in low-risk patients. Our infection rate is about 4-10 / 500 =

0.8=2% (annual volume is about 500 cesarean sections); we consider this to be good relative to national averages (5-10%). Our goal is 0%.

□ Because post-operative infections are relatively rare the effects of bandages cannot be easily determined without a research protocol to control for confounding variables. In our goal of doing no harm our goal post-operative infection rate is 0%. We would like to systematically approach methods to help us achieve this goal.

□ We use surgical site infection prevention bundles to help prevent infections including a preoperative wash, a surgical sterilization/prep, sterile technique, pre-operative antibiotics and sterile abdominal dressing. Our practices change with time and the only way to know the effect of one particular change in this overall uncommon (but clinically salient) complication is to study it; fortunately we are already practicing and collecting data in a way that studying these effects would not affect our patients.

□ The negative pressure therapy costs $300-500 per patient. A standard bandage is <$4. A silver impregnated silicone post-op dressing costs $20. This study would help address whether using a silver impregnated silicone foam would be cost effective in all patients or just in the high-risk population. If used universally savings in the high risk group could offset increased costs in the low risk group; costs are generally incurred by the hospital and not billed to the patient.

□ There is only 1 randomized control trial of negative pressure therapy; its limitation is that it is underpowered at about 160 patients in the final pool with 300 in the study. Its findings do not demonstrate a difference in negative pressure therapy however there are limitations in the study – it is underpowered and dressings are not kept on in both treatment groups for the same amount of time, which is a confounding factor. Also the study does not address a strategy for low-risk groups (1).There are no studies on the silver-impregnated bandage for comparison despite being commonly used. Just as benefit has not been clearly demonstrated, harm has also not been demonstrated (or suggested, aside from cost).

□ A retrospective study comparing negative pressure therapy in obese women was conducted at Regions Hospital, it demonstrates benefit in this type of dressing in high-risk (BMI > or = 40) patients (2). Meta analyses of several retrospective studies demonstrate heterogeneous but overall beneficial effects of negative pressure therapy versus "standard" dressing, but they are not compared to silver-impregnated bandages such as proposed in the current IRB request.

□ Silver has antibiotic properties and has been used anecdotally by several services within our hospital with good effects (including in the principal investigator's prior practice). In other words, using silver impregnated bandages is considered a routine practice in many practices following cesarean section.

□ Our study will fill the gap in that it will have more power than previously conducted research in the field. It will also compare a bandage that is thought to have antibiotic properties (the "silver" component of the silver impregnated silicone foam dressing). The silver impregnated silicone foam dressing is significantly less expensive than negative pressure therapy and slightly more expensive than a standard gauze dressing. This study will help us fill the knowledge-gap in whether there are significant differences in 2 arms of our study: negative pressure therapy vs silver impregnated silicone dressings in high risk patients (BMI > or = 40) and also standard gauze dressing vs silver impregnated silicone dressing in normal risk patients (BMI < 40). This will help us find a clinically prudent method to achieve zero surgical site infections while maintaining our fiduciary responsibility to our patients.

4. *Approach*

a. Study design

□ Study design will be in a prospective cohort trial. The first cohort will be patients who are having a cesarean section with OB/GYNs that prefer using paper bandages in patients with BMI <40 and prophylactic wound vacuum therapy in patients with BMI > or = 40. The second cohort will be patients who are having a cesarean section with OB/GYNs that prefer using Mepilex Border Post-Op Ag regardless of BMI.

□ This will be a pilot study as infection rates are low enough that a full study would take several years. However, if difference between methods are large enough then the study would be able to reveal this (see sample size section for details)

□ There will be two cohorts:

1) Cohort 1 - Normal risk (BMI < 40) – standard dressing (sterile gauze dressing)
High risk (BMI > or = 40) – negative pressure wound therapy / "wound vac"
2) Cohort 2- Normal risk (BMI < 40) – silver impregnated silicone dressing
High risk (BMI > or = 40) – silver impregnated silicone dressing

b. Population

i. Inclusion/Exclusion Criteria [See Human Subjects items to be moved here]

□ Inclusion/exclusion criteria: pregnant women who have a cesarean section; as the bandage will be applied when women are no longer pregnant (after fetus is delivered) they will technically not be pregnant at the time of inclusion in the study

□ Women will be excluded from the study if their bandage / BMI are not compatible with the cohort scheme noted above (for example if the patient's OB/GYN uses a bandage that is different than a wound vac, paper bandage or Mepilex dressing).

□ Specific diagnosis & procedure codes – pregnancy, cesarean section not having other abdominal surgery (example: concomitant hernia repair) except for with concomitant bilateral tubal ligation, which is often done with cesarean sections

□ Specific demographic inclusion/exclusion criteria – women of child bearing age having cesarean section at Regions Hospital

□ We will compare patients to a database of patients who have asked to be excluded from research, we will exclude patients who requested this. This information is kept in central HealthPartners databases.

ii. Sample size

□ Sample size of records to be obtained – enrollment will be 2 years, 1000 women
□ Sample size for the main analysis – anticipated follow-up of 75%, which would net 750 women
□ A rationale for selecting the sample size is provided and is summarized as due to a 0.5-3% post-operative infection rate in order to adequately power a study to find a difference – the records to be obtained would include all patient who satisfy the inclusion criteria, approximately 500 per year. Based on this study population and anticipated surgical site infection rate of 0.5% in best case scenario and 3% (both better than the national mean) with a power of 80% and alpha 0.05 we would need a study size of 862. As this is the first study of its kind in the comparison groups it would be clinically salient to find significance or not find it as both results would be clinically helpful in guiding obstetricians.
□ Follow-up in the postpartum period is notoriously low, approximately 50%. After cesarean most women tend to at least follow-up for an incision check in the clinics or go to the emergency room and thus it would be reasonable to expect 75% follow-up based on author prior clinical experience.
□ Counts of patients expected to be study-eligible are approximately 500 / year based on our standard variation in annual cesarean rates
□ Our two cohorts should be of similar size. Approximately half of the OB's have chosen each closure method as their methos of choice. All surgeons have similar obstetric volume and so the total group sizes will likely be similar in size. There are no anticipated changes to the current practice over the next two years.

c. Data collection process

i. Process steps for identification of patients or records

□ We will use obstetric logs (paper log), MIDAS (electronic log) and hospital/clinic EMR to identify any women who have a cesarean section at Regions hospital in the date window of interest.

□ The PI and co-investigators will review the patient records in the bullet points above for surgical site infection. Currently the Infection Prevention department already does this; the charts of the patients identified will be abstracted. All patients in the study will have their charts abstracted as

well by the PI for suggestion of surgical site infection or for any potential complications related to the surgical site coverings (standard gauze bandage, silver impregnated silicone dressing or negative pressure wound therapy device). Any question will be reviewed by an additional co-investigator obstetrician; if there is a discrepancy then the third co-investigator will make a final determination.

□ In the patients who have identified clinically identified infections (based on process identified above via chart abstraction) we will also obtain billing data and insurance payment information to identify the financial implications of the complications. This information will be obtained primarily by the HealthPartners Research Foundation Epic team, who will build an EMR database query to obtain this information.

□ All data sources needed for the study are named (e.g., chart review, patient survey, data pull from HP electronic medical record) – all data will be abstracted from clinical EMR / Regions charts. We will also use a log from labor & delivery (all births are written down in a paper register and electronic log [MIDAS]) and compare it to our data to make sure patients are included. The Infection Prevention department also keeps a register of all post-operative infections and we will use this information that is already obtained to make sure our records are accurate (this information is readily made available to our department as it is). Additionally, billing data will be obtained for those patients in whom an infection or surgical site complication occurs to analyze complications.

□ The person or job title obtaining each data source:

-Investigators will review each chart for evidence of surgical site infection or bandage-related complications

-The investigators in the Infection Prevention department will provide records that they already collect to the investigators to make sure data are accurate and complete

-HealthPartners Research Institute will use Epic data queries to obtain billing and reimbursement data for patients with surgical site infections / complications. The Research Institute calls the individuals who create these queries programmers and they will work with the PI. They will also compare patients that meet inclusion criteria that have requested to not be included in research to allow us to remove those patients.

ii. Process steps for data acquisition

□ All patient contact events involving data collection are described in the order they occur.

-Patients who enter an operating room at Regions Hospital and have a cesarean section will have the cesarean section as per routine. Part of the routine, obviously, includes that the surgery will conclude and a bandage will be placed.

-The circulator OR nurses will document the type of bandage placed, which is part of the routine already.

-The patient will have routine cares at Regions Hospital. At time of discharge or earlier the incisional covering will be removed as part of routine care. The patients at this time will all be instructed to take care of their incisions/wounds in the same manner regardless of which group they are in.

-The patient will have routine post-operative care in the clinics after discharge home

-The study investigators will do a preliminary review at 6 months to look for any potential harm or unintended complications; if there are any concerns the study may be halted and appropriate paperless-work will be filed with the IRB. If there are no unintended complications then the study will complete. If any of the patients' clinical providers request a review prior to the 2 year mark based on concern for patient harm the investigators will initiate up to 1 additional review.

-The study investigators will abstract patient charts to look for clinical concerns related to primary / secondary outcomes, which includes evidence of infection, bandage related problems, admission/readmission. Information that is routinely obtained from the infection-prevention department will be included into the abstraction. Data unrelated to primary outcomes that will be included will include basic patient demographic data such as payer type (Medicaid vs commercial insurance), BMI, race, comorbid conditions (diabetes, in particular), evidence of immune suppression (steroids, HIV, immune modulators).

-Data will be abstracted into either a password protected Microsoft Excel spreadsheet or password protected Microsoft Access database. Data will be kept under electronic-"lock and key" either on a HealthPartners server or on a password protected computer with encrypted hard drive, consistent with HealthPartners policy to make sure that any identifying information is protected.

-Data will analyzed by the PI and shared with a statistician (HealthPartners Institute statistics core), aggregate data will be shared with the co-investigators (they will have access to the non-aggregated data if needed)

Enrollment & Consent

How will subjects be enrolled: the EMR will be abstracted to find women who have had a cesarean section at Regions Hospital.

□ What types of recruitment tools will be used: the patients will be enrolled by reviewing their charts. Data that is part of Regions Hospital routine is already collected thus no additional data would be needed from patients.

□ Who will be the initial contact with potential subjects: there will be no contact with the patients or physicians performing services.

□ What steps will be taken to avoid coercion or undue influence in the recruitment of subjects: Bandages will be selected by the patients' OB/GYN surgeon as part of routine surgery. The patient will not experience anything different from routine care as a part of this study. When patients are admitted to the hospital we will however let them know that we are completing a study and that they may opt out of our data analysis by informing their nurse or surgeon that they wish to opt out of the data collection. Women who do not have a c-section (aka those who are excluded) will not receive this information as they are already not part of the study.

□ We do not anticipate any conflicts with other studies being completed on our patient population

We will request a waiver of informed consent as we are not contacting the patients, collecting additional information about patients or modifying care for these patients. We are comparing the outcomes that patients have based on their surgeon's practices.

□ Who will obtain consent? We believe that a chart-review type study such as this should be exempt from obtaining consent.

□ Why are we requesting a waiver?

- Our hypothesis is that infection rates will be similar in both arms of the comparison groups and thus we believe that this study will pose minimal risk. The study itself does not impart a particular bandage on the patient but looks to see whether there are differences in outcomes over a 30-day post-operative period; thus we do not anticipate any harm. Data will be collected presented in aggregate and protected health information will not be analyzed, which also demonstrates minimal risk.
- We believe that patients should be given the opportunity to exclude themselves from the study analysis and thus we will not include patient's that have asked HealthPartners to not be part of research.
- Consent is obtained for non-research procedures (the surgical procedure), the surgical procedure does include having a sterile dressing. It is up to the OB/GYN surgeon to

decide on the bandage to place. This would be done by any of the nursing staff or clinical providers who see patients; this is our current practice and would not change.

□ How will patients be notified:

- Patient's will be informed via standard HealthPartners methods, which includes potential inclusion in research unless they request to be excluded.

□ Who will provide consent? We will ask for a waiver of informed consent.

□ How will you ensure that the subject understands the consent? We will apply for a consent waiver. In an opt-out manner if a patient requests to not be included we will respect the patient's privacy in making this decision as part of standard HealthPartners policies.

d. Outcome/endpoint and other variable definitions, and instruments used

Definitions: superficial surgical site infection- defined according to Centers for Disease Control and Prevention criteria as infection involving only the skin or subcutaneous tissue occurring within 30 days of surgery with at least one of the following: 1) purulent drainage from the wound or 2) organism identified by culture or wound deliberately opened by the surgeon. Cellulitis will be evaluated as 1) erythema noted in clinical progress notes with antibiotics administered or 2) diagnosis of cellulitis with antibiotics administered. Our secondary outcome was a composite wound complication, including superficial, deep, or organ-space surgical site infection; wound dehiscence; seroma; or hematoma that occurred within 30 days of surgery. Other secondary outcomes included 30-day readmission, 30-day reoperation, and need for antibiotic treatment for any indication. The chart will be evaluated for nursing of provider notes that indicate problems with the bandage. Chart abstraction will be completed to look for other salient complications or factors that were not predicted. Primary and secondary outcomes will be binary with comments possible. Number of clinical visits for complications, enrollment in home healthcare for wound care and length of hospital visits will be noted.
□ Chart review form will be electronic, it will have the following elements (there will be 3 charts to protect PHI and to blind the analyst from the intervention), all participants will have a study enrollment number to link the data for appropriate analysis:

First form:

MRN	From EMR
Study enrollment #	From 1-1000

Second form:

Study enrollment #	From 1-1000
Intervention	Binary: cohort 1 vs cohort 2
BMI	BMI rounded to the tenths spot

Third form:

Study enrollment #	From 1-1000
Age	#
Enrolled	Yes / no
Follow-up after discharge from home	Yes / no
Complication noted	Yes / no
Date complication noted	Date
Comment complication	Comment (superficial surgical site infection, abscess, seroma, deep infection, organ-space surgical site infection, wound dehiscence, seroma, hematoma) and pertinent notes
Comment complication labs	Pertinent lab data (culture data, white blood counts)

Hospital readmission days	0 or more
Emergency room visits	0 or more
Clinic visits	0 or more
Home healthcare	Yes / no
Insurer type	Medicaid, Commercial
Diabetes	No / pre-existing type 2 / pre-existing type 1 / gestational well controlled / gestational poorly controlled
If diabetes – fasting glucose following day	Null or #
Hemoglobin a1c within 1 year prior or 3 months after cesarean section – highest	Null or #
Comorbid conditions	Pertinent per reviewer discretion including history of surgical site infection
MRSA carrier	Yes / no / unknown
GBS status (group B step)	Yes / no / unknown
Gestational age at delivery	#
Indication for cesarean	Comment
Planned cesarean	Yes / no
Stat cesarean	Yes / no
Patient received antibiotics	Yes / no
Surgical start time	Time
Surgical stop time	Time
Antibiotics given pre-operatively per SCIP protocol	Yes / no
Antibiotics given pre-operatively	Type of antibiotic noted
Antibiotics given after discharge 30-days	Yes / no
Antibiotics given after discharge 30-days – indication	Indication
Antibiotics given after discharge 30-days - type	Type
Patient had triple-I (infection diagnosed during surgery)	Yes / no
If patient had triple-I were antibiotics given pre-surgically	Yes / no
Patient is GBS carrier	Yes / no
Patient adequately treated for GBS	Yes / no
Fevers post operatively during hospital stay	Yes / no
Gravida	#
Parity	#
Number of prior cesareans	#
Number of prior post-operative cesarean infections	#
Pre-operative hemoglobin	#
Post-operative hemoglobin	#
Tobacco use	Yes / no
Hypertension	No / chronic HTN / gestational HTN / pre-eclampsia not severe / pre-eclampsia severe
Twin+ pregnancy	Yes / no
Race	Black / white / other
Ethnicity	Hispanic / not-hispanic
Interpreter use	Language spoken
Labor	Planned c-section / spontaneous labor / induction
Duration membranes ruptured (minutes)	#
Type of anesthesia	Spinal / epidural / general

Skin incision	Vertical / Pfannenstiel / other
Skin closure	Subcuticular / staples
Estimate blood loss (mL)	#
Additional procedures	Sterilization / hysterectomy / Bakri / compression sutures / other

e. Statistical analysis plan

Descriptive statistics generally as mean or total; chi-squared, Students t-test, Fisher exact tests as appropriate. Regression may be difficult with low infection rates.

□ Anticipate roughly 300-600 participants per cohort (after accounting for patient follow-up)

□ Variables per section "E" above

□ Silver impregnated silicone dressing versus wound vac/paper dressing will be 1 study analysis. Then stratification by arm will be completed

□ Infection rate will be reported as number (proportion). Clinical significance will be P<0.05. Dichotomous/categorical data will be reported as a proportion. Continuous variables may be dichotomized versus kept as a scale depending on the analysis (for example in our BMI > or = 40 versus BMI <40 would be one example of dichotomized data). Hemoglobin a1c (a measure of diabetic control) would likely be dichotomized into <7 (preferred in pregnancy) versus >7.

□ Missing data will be analyzed on a per-participant basis—for example if there is a recent BMI and not one done the day of surgery that may be used. Missing data that is used will be reviewed by a second investigator for appropriateness, if not certain then a third investigator will opine as to the appropriateness as a tie-breaker.

□ We will obtain hospital / practice billing data averages (for patient care in general) to multiply by the additional visits (ER, home healthcare or clinic), admissions, procedures and surgeries to increase the clinical salience of our analysis.

□ Dr. Goldenberg wrote the analysis plan and will complete the analysis plan. SPSS v25 or similar will be used. A statistician from the HealthPartners Institute Research Methodology Group will be used for post hoc analysis for additional insight. Dr. Goldenberg is confident he can complete descriptive as well as analytic statistics based on prior studies. He has generally performed his own statistical analysis when performing original research; post hoc statistician analysis has been consistent with his findings in these studies.

f. Power analysis or statement of precision

The following study parameters were used to find an appropriate sample size:

Study Parameters:

Incidence, group 1:	0.5%
Incidence, group 2:	3%
Alpha:	0.05
Beta:	0.2
Power:	0.8

The following sample sizes would be needed to have adequate power with a dichotomous endpoint, two independent sample study:

Sample Size:

Cohort 1	431 (silver impregnated silicone bandage)
Cohort 2	431 (negative pressure therapy, sterile gauze bandage – composite)
Total	862

The study might be underpowered to demonstrate the hypothesis when comparing the cohorts. Unlike certain interventions a positive or negative difference would be clinically salient as the groups have significantly different costs. Thus regardless of outcome this study could help our group modify practice.

g. Strengths and limitations

A strength of the study is the relatively homogenous environment in which the study will be conducted. While this also would decrease applicability to the general field of obstetrics it increases power to find differences where they might be too difficult to find otherwise. This includes a single hospital with a group of obstetricians that are all willing to participate in conducting this study (based on administrative meetings where we committed to studying a change in our practice prior to completely implementing it). Additional strengths include that this will be the largest trial of its kind and rather than studying an intervention against an outdated method we are comparing three specific interventions in a head-to-head trial (in two cohorts). An additional strength of this study is that our Infection Prevention co-investigators already collect much of the information in this study and have a robust system to detect surgical site infections that are noted outside of our system. A final benefit of this study is that it is able to incorporate two state-of-the-art interventions already being done that are low-risk and demonstrate which has the lowest complication rate to help inform our practice and the field of obstetrics in clinical care. In adding cost data to this analysis we will also help providers and hospitals maintain their fiduciary duties.

□ Limitations are primarily related to our sample size; unfortunately it is not possible in our practice to increase enrollment numbers without extending the study by several years; while this could be done it would not anticipated. Another limitation (despite being a strength) is that our practice is rather homogenous and so generalizability to other practices may be limited; as this would be the only data of its kind, this should at least help spur further research.

□ Possible biases include that while our study may not be powered to detect a difference, that does not inherently mean that a study does not exist if $p>0.05$. While we may draw conclusion based on this it may be a false negative. Selection bias may occur as our patient population has a tendency to be higher risk in terms of maternal morbidity than in many community hospitals. There may be ascertainment bias by the nursing staff reporting on patient complications and the obstetric team taking care of the patient in the hospital, but after the patient leaves that bias should be significantly decreased as it would take effort from the providers in the clinic to check which study group the patient is in (either accessing data or asking the patient).

5. Setting/Environment/Organizational feasibility

□ The study will be conducted at Regions Hospital and otherwise by chart abstraction/review
□ Cesarean section are done in the hospital-setting, thus the location is appropriate. We selected Regions Hospital as hospital leadership has already committed to using the incisional coverings despite their costs, thus the study can be completed over a long time course and over an anticipated 1000 patients. Other hospitals have not been systematically willing to use these coverings due to concern for cost; Regions pays for it due to the benefits that we believe have been demonstrated by our organization, which impacts reimbursement and thus this will be overall revenue neutral. Leadership is motivated to have the lowest overall surgical site infection. The Infection Prevention department collects much of the information we are studying and thus with minimal effort the organization will be providing much of the data abstraction.
□ The study will fit in with HealthPartners Triple Aim in the following ways. It will improve the health by allowing us to study a change in our practice pattern in a systematic manner and apply the changes to our practice. This will also improve the experience of each new family as complications decrease so the time spent recovering from child birth can be focused on the new family. Finally it will help us improve our fiduciary goals by not just looking at whether infection rates are different but also if there is a significantly different cost-burden with the infections that may be conferred by the different types of incisional coverings.

6. **Risks and Benefits**

□ Identify any reasonably foreseeable risks for subjects – the risk (even with an informed consent waiver) are minimal. All of the interventions clinically are not part of this study. This is not research on pregnant women, per se, as the patient is no longer pregnant at the time she is randomized and the incisional bandage is placed. Thus there will be no risk to the developing fetus. There is no effect on lactation and thus there is no risk to the newborn.

□ We minimize risks to patients as a matter of surgical principal by using typical sterile technique. We also minimize risks by removing all the bandages by the time the patient leaves the hospital so that way each incision is evaluated prior to the patient leaving. The alternative would be to wait until a clinic visit 1 week later (except for the gauze bandage), however we felt we would standardize and protect our patients best by removing the bandages prior to leaving. In our practice we found that many patients were non-compliant with care of 1-week bandages (bandages that go home with the patient and are removed after 1 week) and thus we do not want to keep the proposed bandages on for 1 week.

□ There is a risk that patient data may be lost or viewed by others, however it is quite low as data will be password protected and encrypted as noted above. Furthermore patient identifiers will not be part of the data analysis and will be kept in a separate log. See Data Confidentiality and Privacy section.

□ The direct benefit of the research is we can implement the lowest risk infection prevention bundle possible for cesarean sections; if there is no observable clinical difference then we can take into account the cost differences. Recently we tried switching the type of negative pressure wound therapy device we used (from a 3-day version to a 7-day version that is less expensive and smaller); our infection rate changed and we do not know if it is due to confounding or due to the device change – in hind sight we wish that we studied in the same way as proposed here to control for confounding variables.

□ The benefit to society is it will identify a way to help bring surgical site infections to zero; while this seem unattainable at times, with each incremental change we get closer to providing that. Additionally this study would help decrease the cost of healthcare by helping obstetricians select the most effective but lowest-cost (short term at time of application) device. If the study demonstrates that a more expensive option is most effective then it can help obstetricians make the case to their hospitals that the extra expense might be revenue neutral or save money in terms of preventing complications.

7. **Data Confidentiality and Privacy**

□ Identifiable PHI will be kept in a data table separate from the remainder of the analyzed data. Additionally it will be maintained in the same PHI-protective required ways that HealthPartners requires. This includes using encrypted hard drives (in case of theft), password protected operating systems (in case of unauthorized access), and on HealthPartners computers whenever possible. We plan to partner with HealthPartners institute for data analysis so when sending email with the non-PHI containing data tables the information will stay within HealthPartners secure email system. Patient information will also be aggregated in the analysis, which will help maintain patient confidentiality when it comes to presenting our data in public for poster presentation and research papers. A study ID will be used on most of the spreadsheets / databases in order to help protect patient MRN from being divulged.

□ Since the patient's name and DOB will not be stored it will be difficult to cause harm with to a patient if data is somehow divulged. Since the only patient identifiable information would be stored in a table with only a study ID. If the MRN were released then somehow people would have to have access to HealthPartners systems to compromise that data. This still should not happen.

□ Study identifiers would be destroyed upon publication in compliance with a peer-reviewed journal's policy. PHI/study identifiable information would be easy to destroy as it would be kept in a different spreadsheet / database from the main study data. It would also be electronic so it could be destroyed with just a few buttons being pressed and without a trail.

8. Timeline

□ The study data should be collected over 2 years. There will be a preliminary 6-month (after the start) analysis to look for any detrimental effects/harm. Data should take about 1-2 months to abstract and 2 weeks to analyze. A poster abstract for presentation should take 1-2 months. A research paper or series of papers would probably take about another 1-3 months. As an obstetric practice, we would probably be ready to implement our changes within weeks of our data analysis being complete.

Enrollment: 6/1/2019 through 5/31/2021

Abstraction: 7/1/2019 through 6/30/2021

Analysis: 7/01/2021 through 7/15/2021

Poster/Paper/Presentations: 7/16/2021 through 12/31/2021

9. Dissemination/Sharing Results/Integration and Impact

□ We plan to publish probably at a Society of Maternal Fetal Medicine (SMFM), American College of Obstetrics and Gynecology (ACOG) or Society of Wound, Ostomy & Continence national conference. I anticipate 1-3 posters ready for publication. I would also be optimistic of an oral presentation as well. From these posters / oral presentation I would anticipate 1-3 manuscripts for publication.

□ We plan to implement our results in our practice (and that was the impetus for this study). Additionally, most of the hospitals in the HealthPartners family tend to defer to Regions when it comes to quality improvement and they would likely follow our lead if we can present clinically meaningful quantifiable data such as in this study. Many hospitals outside of HealthPartners also are interested in following our lead and we would be eager to share with them our results. Regardless of positive or negative results the data would be clinically salient and help us make financially responsible decisions in terms of using our healthcare resources.

□ We plan to disseminate data in our manuscript following STROBE guidelines.

10. References

1.) Prophylactic Negative Pressure Wound Therapy and Wound Complication After Cesarean Delivery in Women With Class II or III Obesity: A Randomized Controlled Trial. Wihbey et al. Obstetrics & Gynecology, 2018.

2.) Prophylactic Negative Pressure Wound Therapy in Obese Patients Following Cesarean Delivery. Looby et al. Surgical Innovation, 2018.

3.) Prophylactic negative-pressure wound therapy after cesarean is associated with reduced risk of surgical site infection: a systematic review and meta-analysis. Yu et al. American Journal of Obstetrics & Gynecology, 2018.