Reducing Perioperative S. aureus Transmission via use of an Evidence-Based, Multimodal Program Driven by an Innovative Software Platform (OR PathTrac)

PI: Randy Loftus
IRB ID #: 201802843

Project Details

I. Project Introduction

I.1 ***Project to be reviewed by:***
IRB-01

I.2 ***Project Title:***
Reducing Perioperative S. aureus Transmission via use of an Evidence-Based, Multimodal Program Driven by an Innovative Software Platform (OR PathTrac)

I.3 ***Short Title (optional):***

I.4 ***Provide a short summary of the purpose and procedures of the study proposed in this IRB application.***

- ***DO NOT include information on studies not proposed in this application.***
- ***Use LAY terminology only. This must be easily understandable by IRB community members and nonscientists.***
- ***DO NOT cut and paste technical abstracts from funding applications that may not be understood by a general audience.***

The purpose of this study is to prevent the spread of S. aureus, a dangerous bacterium, within the operating room and between patients undergoing surgery. We will combine several approaches in a "bundle" of activities to achieve this goal. The bundle will include removal of bacterial pathogens from patient skin sites before surgery, from provider hands before, during, and after surgery, from environmental surfaces before and after terminal cleaning, and from the injection ports of patient intravenous catheters. We will use a new surveillance system to evaluate how well the bundle, and each component of the bundle, is working. Surveillance will identify S. aureus transmission events, and movement of S. aureus between reservoirs before, during, and after surgery (perioperative). Surveillance will map transmission events to identify actionable steps to improve the bundle. An infection control perioperative team will act on the surveillance reports to proactively address the action items, and to measure the effect of their efforts for the treatment group. We will compare perioperative S. aureus transmission events for patients receiving the bundle to perioperative S. aureus transmission events for patients receiving usual care.

The goal of the study is to reduce S. aureus transmission from known reservoirs during the perioperative period. One known reservoir is patient skin sites. That is why we are decolonizing patients before surgery. Another known reservoir is provider hands. That is why we are providing a hand hygiene system that is located close to the anesthesia provider so they can wash their hands at every opportunity. Conventional hand washing devices on the wall or on the anesthesia machine do not facilitate hand washing during the fast-paced OR procedures. A third known reservoir is intravascular devices. That is why we are using the HubScrub and DOCit system that allows providers to scrub the hub at every opportunity with only 2 turns and within 10 seconds. A fourth known reservoir is the operating room environment itself. We are using surveillance to deploy strategic targeting of high risk environments as well as to continually optimize every component of the bundle over the 2 years. In summary, the study population is the perioperative period that includes patients, providers, equipment, environment, and even the air into which bacteria can be aerosolized for the patient and the patient to follow. The goal is to show that improved basic measures across the board in a dangerous environment like the OR can reduce high risk S. aureus transmission events.

Our primary outcome is S. aureus transmission events. The surveillance instrument as detailed in this proposal defines transmissions. Surveillance involves utilizing systematic reservoir collection kits (RDB Bioinformatics, Omaha, NE 68154) to collect S. aureus isolates from known reservoirs in perioperative environments. The OR PathTrac software (RDB Bioinformatics, Omaha, NE 68154) uses algorithms to guide analysis of the S. aureus isolates and to identify transmission events. Transmission stories are processed by the software to generate transmission maps that identify improvement successes and failures. It also identifies actionable steps to improve the bundle. The perioperative infection control team then uses this information to continually optimize the bundle, and the software to measure the effect.

The grant funding this research project will pay RDB Bioinformatics for the kits, for the analysis of the swabs for S. aureus, and for the OR PathTrac analysis on a fee-for-service basis. RDB Informatics is providing no funding for this study or in-kind support.

I.5 ***Specify your research question(s), study aims or hypotheses (do not indicate "see protocol")***

Surgical site infections are a subset of healthcare-associated infections (HAIs) that affect 3-5% of all patients undergoing surgery and are associated with a 2-fold increase in patient morbidity and mortality, a 2-fold increase in hospital duration, and a 66% increase in the risk of intensive care unit (ICU) admission (1-4). The Centers for Disease Control (CDC) and the World Health Organization (WHO) consider HAIs as a devastating issue tied to antibiotic resistance and have highlighted three major goals for HAI prevention including the following: 1) Prevention of infections in patients undergoing surgery, 2) Prevention of patient-to-patient bacterial transmission, and 3) improvement in antibiotic stewardship (5-7). These recommendations apply to the perioperative arena where the contribution of intraoperative bacterial reservoirs to bacterial transmission events and postoperative infection development has been confirmed (8-10). Indeed, a multicenter study recently demonstrated that stopcock contamination occurred in 23% of surgical cases, was associated with increased mortality, and was linked by molecular typing to postoperative infection (9). Intraoperative bacterial reservoir isolates have also been directly linked to the causative organism of infection for 30% of 30-day postoperative HAIs. Finally, transmission of S. aureus has been confirmed in up to 39% of surgical cases and has been directly linked to postoperative infection development(11). As such, attenuation of perioperative S. aureus transmission is an important target for HAI reduction. Therefore, our primary objective is to reduce perioperative S. aureus transmission. Our secondary objective is to examine the impact of reduced S. aureus transmission on the incidence of superficial and deep surgical site infections (SSIs).

I.6 ***Background and significance and/or Preliminary studies related to this project. (do not indicate "see protocol")***

We have demonstrated that intraoperative S. aureus transmission affects 39% of all-comers to the operating room and that transmitted pathogens can be directly linked to the development of SSIs (11). Individually, improvements in patient decolonization, provider hand hygiene, intravascular catheter design and handling, and environmental cleaning can reduce infection and consequently improve intraoperative patient safety. For example, we determined that bacterial contamination of intravenous stopcock sets is associated with increased patient mortality (8,9) and that anesthesia provider hands are an important vector for these high-risk events (10). At Dartmouth, this finding led to hand hygiene improvements that reduced stopcock contamination and postoperative HAIs (12, 13). We documented that an improved catheter design significantly reduced bacterial injection as compared to conventional open lumen devices (14), and that a novel disinfection approach can reduce stopcock contamination and postoperative infections and phlebitis (15). We have mapped intraoperative environmental contamination (16) which has led to the development of an improved intraoperative environmental cleaning procedure (17). Recently, we made the exciting finding that different clonal lineages (MLST) of S. aureus differ in their pathogenicity and risk of transmission (18). For example, among 22 different lineages that are frequently encountered in the OR, MLST 5 is associated with increased risk of strong biofilm formation, multidrug-resistance, transmission, and postoperative HAI development (18) This finding points to the importance of understanding the genotype of the infectious agent in order to drive genotype and patient-specific decolonization efforts. In addition, we found that methicillin-resistant S. aureus isolates are more transmissible than methicillin-sensitive isolates, indicating that S. aureus phenotype can be used to optimize perioperative preventive measures focused on attenuating high-risk S. aureus transmission and infection development (19). In this proposal, we plan to combine these activities into a single multi-modal program (or “bundle”) that will lead to further reductions in infection and improvements in intraoperative patient safety. These activities will be accompanied by a real-time surveillance program using OR PathTrac to track transmission among reservoirs (e.g. patient, provider hands, stopcock, environment and equipment)(18, 19, and 21). The surveillance program will drive optimization of the different components of the bundle and allow for assessment of relative effectiveness.

I.7 ***Literature cited / references (if attaching a grant or protocol enter N/A).***

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2. Koff MD, Brown JR, Marshall EJ, O’Malley AJ, Jensen JT, Heard SO, Longtine K, O’Neill M, Longtine J, Houston D, Robison C, Moulton E, Patel HM, Loftus RW. Frequency of Hand Decontamination of Intraoperative Providers and Reduction of Postoperative Healthcare-Associated Infections: A Randomized Clinical Trial of a Novel Hand Hygiene System. Infect Control Hosp Epidemiol 2016; 37: 888-95

3. Kirkland KB, Briggs JP, Trivette SL, Wilkinson WE, Sexton DJ. The impact of surgical site infections in the 1990s: attributable mortality, excess length of hospitalization, and extra costs. Infect Control Hosp Epidemiol 1999; 20:725-30

4. Boucher HW, Talbot GH, Bradley JS, Edwards JE, Gilbert D, Rice LB, Scheld M, Spellberg B, and Bartlett J. Bad Bugs, No Drugs: No ESKAPE! An Update from the Infectious Diseases Society of America. Clinical Infectious Diseases 2009; 48:1–12

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6. Centers for Disease Control and Prevention. Updated guidelines for evaluating public health surveillance systems: recommendations from the guidelines working group. MMWR 2001; 50:1-35

7. http://www.whitehouse.gov/the-press-office/2014/09/18/fact-sheet-obama-administration-takes-actions-combat-antibiotic-resistan

8. Loftus RW, Koff MD, Burchman CC, Schwartzman JD, Thorum V, Read ME, Wood TA, Beach ML. Transmission of pathogenic bacterial organisms in the

anesthesia work area. Anesthesiology 2008; 109: 399-407

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11. Loftus RW, Koff MD, Brown JR, Patel HM, Jensen JT, Reddy S, Ruoff KL, Heard SO, Yeager MP, Dodds TM. The epidemiology of Staphylococcus aureus transmission in the anesthesia work area. Anesth Analg 2015; 120: 807-18

12. Koff MD, Loftus RW, Burchman CC, Schwartzman JD, Read ME, Henry ES, Beach ML. Reduction in intraoperative bacterial contamination of peripheral intravenous tubing through the use of a novel device. Anesthesiology 2009; 110:978-85

13. Koff MD, Corwin HL, Beach ML, Surgenor SD, Loftus RW. Reduction in ventilator associated pneumonia in a mixed intensive care unit after initiation of a novel hand hygiene program. J Crit Care 2011; 26:489-95

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15. Loftus RW, Brindeiro BS, Kispert DP, Patel HM, Koff MD, Jensen JT, Dodds TM, Yeager MP, Ruoff KL, Gallagher JD, Beach ML, Brown JR. Reduction in intraoperative bacterial contamination of peripheral intravenous tubing through the use of a passive catheter care system. Anesth Analg 2012; 115:1315-23

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II. Research Team

II.1 ***Principal Investigator***

Name	E-mail	College
Randy Loftus	randy-loftus@uiowa.edu	Carver College of Medicine

II.2 ***Team Members***

UI Team Members

Name	E-mail	College	Contact	Key	UI	VAMC	Consent Process	Deactivated

				Prsn	COI	COI	Involvement	
Randy Loftus, MD	randy-loftus@uiowa.edu	Carver College of Medicine	Yes	Yes	Yes		No	No
Lauren Allan, DO, BA	lauren-allan@uiowa.edu	Carver College of Medicine	No	Yes	No		Yes	No
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Thomas Granchi, MD	thomas-granchi@uiowa.edu	Carver College of Medicine	No	Yes	No		Yes	Yes
Brent Hadder, MD	brent-hadder@uiowa.edu	Carver College of Medicine	Yes	Yes	No		Yes	No

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Yasmin Lyons, DO	yasmin-lyons@uiowa.edu	Carver College of Medicine	No	Yes	No	Yes	No
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Nicolas Noiseux, MD	nicolas-noiseux@uiowa.edu	Carver College of Medicine	No	Yes	No	Yes	No
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Denise Peck, ARNP/PA	denise-peck@uiowa.edu	University Hospitals	No	Yes	No	Yes	No
Deanna Persons, High School	deanna-persons@uiowa.edu	College of Liberal Arts and Sciences	No	Yes	No	Yes	No
Andrew Pugely, MD	andrew-pugely@uiowa.edu	Carver College of Medicine	No	Yes	No	Yes	No
Roseanne Rath, PA-C, MA	roseanne-rath@uiowa.edu	Carver College of Medicine	No	Yes	No	Yes	No

Joan Ricks-McGillin, BSN	joan-ricks@uiowa.edu	University Hospitals	No	Yes	No		Yes	No
Rebecca Rosenberg, PA	rebecca-a-rosenberg@uiowa.edu	Carver College of Medicine	No	Yes	No		Yes	No
Jonathan Rueter, PA-C	jonathan-rueter@uiowa.edu	Carver College of Medicine	No	Yes	No		Yes	No
Jennifer Shanklin, MD	jennifer-shanklin@uiowa.edu	Carver College of Medicine	No	Yes	No		Yes	Yes
Mel Sharafuddin, MD	mel-sharafuddin@uiowa.edu	Carver College of Medicine	No	Yes	No		Yes	No
John Sharp, MD	william-sharp@uiowa.edu	Carver College of Medicine	No	Yes	No		Yes	No
Zita Sibenaller, PHD	zita-sibenaller@uiowa.edu	Carver College of Medicine	Yes	Yes	No		Yes	No
Lori Stout, BSN, BSN	lori-stout@uiowa.edu	Carver College of Medicine	Yes	Yes	No		Yes	No
Judy Swafford, RN	judy-swafford@uiowa.edu	University Hospitals	No	Yes	No		No	No
Chad Tracy, MD	chad-tracy@uiowa.edu	Carver College of Medicine	No	Yes	No		Yes	No
Alicia Walter, ADN	alicia-walter@uiowa.edu	Carver College of Medicine	Yes	Yes	No		Yes	No

Non-UI Team Members

Name	Institution	Location	FWA	Role	DHHS	Contact	Key Prsn	UI COI	VAMC COI	Consent Process	Involvement	Email

Nothing found to display.

II.3 ***The Principal Investigator of this study is:***
Faculty

II.6 ***Identify the key personnel. The system will automatically designate the PI and all faculty members on the project as "key personnel." For information about other team members who should be designated as "key personnel" please click on the help information.***

Name	Is Key Personnel
Randy Loftus, MD	Yes
Lauren Allan, DO, BA	Yes
Kiran Annam, ARNP	Yes
Raven Brenneke, BA	No
Cheryl Byrnes, Advanced Registered Nurse Practioner	Yes
Nicholas Cardillo, MD	No
Brian Clark, PA-C	Yes
John Cromwell, MD	Yes
Megan Davis-de Geus, MSN	Yes
Sundar Durgempudi Tripura, MD, FRCA	Yes

Bradley Erickson, MD	Yes
Lance Evans, BA	Yes
Mark Fisher, MD	Yes
Luis Garcia, MD	Yes
Joshua Godding, BS	Yes
Michael Goodheart, MD	Yes
Thomas Granchi, MD	Yes
Brent Hadder, MD	Yes
Alexia Herber, High School	Yes
Jean Hogan, ARNP	Yes
JoAnne Hudachek, BSN	Yes
Gretchen Kass, ARNP	Yes
John Keech, MD	Yes
Prashant Khullar, MD	Yes
Susan Kloos, BSN, RN	Yes
Walter Lawrence, MD	Yes
Yasmin Lyons, DO	Yes
Megan McDonald, MD	Yes
Patrick McGonagill, MD	Yes
Nicole Miller, BA, PA-C, BS	Yes
Andreea Newtson, MD	Yes
Nicolas Noiseux, MD	Yes
Brittany Parchert, BSN	Yes
Denise Peck, ARNP/PA	Yes
Deanna Persons, High School	Yes
Andrew Pugely, MD	Yes
Roseanne Rath, PA-C, MA	Yes
Joan Ricks-McGillin, BSN	Yes
Rebecca Rosenberg, PA	Yes
Jonathan Rueter, PA-C	Yes
Jennifer Shanklin, MD	Yes
Mel Sharafuddin, MD	Yes
John Sharp, MD	Yes
Zita Sibenaller, PHD	Yes
Lori Stout, BSN, BSN	Yes
Judy Swafford, RN	Yes
Chad Tracy, MD	Yes
Alicia Walter, ADN	Yes

II.5 ***Select research team member who is the primary contact for study participants.***
Randy Loftus

III. Funding/Other Support

III.1 ***Funding Sources***

Type	Source	Grant Title	Name of PI on Grant
Private Foundation/Association	Anesthesia Patient Safety Foundation	Reducing Perioperative S. aureus Transmission via use of an Evidence-Based, Multimodal Program Continually	Randy W Loftus

		Optimized by Innovative Surveillance (OR PathTrac)	
* Private Foundation/Association	RDB Bioinformatics	Reducing Perioperative S. aureus Transmission via use of an Evidence-Based, Multimodal Program Continually Optimized by Innovative Surveillance (OR PathTrac)	Randy Loftus

Departmental / PI Discretionary

* new source name

III.2 ***What type of funding agreement would be completed?***
Corporate/Industry Funded Clinical Trial

III.3 ***Does any member of the research team have a financial conflict of interest related to this project according to the Conflict of Interest in Research policy? If yes, please indicate which members below.***

Name	Has Conflict of Interest
Randy Loftus, MD	Yes
Lauren Allan, DO, BA	No
Kiran Annam, ARNP	No
Raven Brenneke, BA	No
Cheryl Byrnes, Advanced Registered Nurse Practioner	No
Nicholas Cardillo, MD	No
Brian Clark, PA-C	No
John Cromwell, MD	No
Megan Davis-de Geus, MSN	No
Sundar Durgempudi Tripura, MD, FRCA	No
Bradley Erickson, MD	No
Lance Evans, BA	No
Mark Fisher, MD	No
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Joan Ricks-McGillin, BSN	No
Rebecca Rosenberg, PA	No
Jonathan Rueter, PA-C	No
Jennifer Shanklin, MD	No

Mel Sharafuddin, MD	No
John Sharp, MD	No
Zita Sibenaller, PHD	No
Lori Stout, BSN, BSN	No
Judy Swafford, RN	No
Chad Tracy, MD	No
Alicia Walter, ADN	No

III.5 ***What is the current status of this funding source?***

Source	Status	Other Status Description
Anesthesia Patient Safety Foundation	Awarded	
RDB Bioinformatics	Other	RDB is not providing funding. RDB is listed because they are providing kits that are paid for by the grant.

IV. Project Type

IV.1 ***Do you want the IRB to give this project***
Regular (expedited or full board) review

IV.2 ***Enter the date you will be ready to begin screening subjects/collecting data for this project. (If you do not have a specified date, add "upon IRB approval")***
4/01/18

IV.3 ***Are you requesting a waiver of informed consent/authorization (subjects will not be given any oral or written information about the study)?***
No

V. Other Committee Review

V.1 ***Does this project involve any substance ingested, injected, or applied to the body?***

- ***Do not answer yes, if the involvement includes a device, wire, or instrument***

Yes

V.1.a ***What is/are the substance(s):***
These are all currently used in care:
Nasal povidone iodine (Povidone-Iodine Solution 5%, 3MTM, St. Paul, MN 55144-1000)

2% Chlorhexidine Gluconate (CHG) Cloths, FDA-approved antiseptic solution (Sage Products LLC 2018 · 3909 Three Oaks Rd, Cary, IL 60013)

We will also be using a catheter care product (Catheter Care Station, HubScrubTM and DOCitTM, Mentor Ohio US 44060)that disinfects open or closed lumens with 62% isopropyl alcohol and includes a hand hygiene component with 62% alcohol.

V.1.b ***Are any of these substances defined as a Schedule I - V Controlled Substance?***
No

V.2 ***Are any contrast agents used for any purpose in this study?***
No

V.4 ***Are all drugs or substances in this study being used within the FDA approved population (i.e., children, adults)?***
Yes

V.5 ***Are all drugs or substances in this study being used within the FDA approved indication (i.e., disease, condition)?***

Yes

V.6 ***Are <u>all drugs or substances</u> in this study being used within the FDA approved dose?***
Yes

V.7 ***Are <u>all drugs or substances</u> in this study being used within the FDA approved route of administration?***
Yes

V.9 ***Will any subject be asked to undergo a diagnostic radiation procedure (including radiographic, nuclear medicine, DEXA)?***
No

V.14 ***Will any subject be asked to undergo a radiation therapy procedure (including external beam therapy, brachytherapy, or nuclear medicine therapy)?***
No

V.20 ***Does this project involve the deliberate transfer of recombinant or synthetic nucleic acid molecules, or DNA or RNA derived from recombinant or synthetic nucleic acid molecules, into one or more human research participant?***
No

V.21 ***Will any portion of this project be conducted in the CRU, or does it use any CRU resources?***
No

V.22 ***Will this project use:***

- ***any resource/patients of the Holden Comprehensive Cancer Center***
- ***involve treatment, detection, supportive care, or prevention of cancer***

No

V.25.a ***Will the study involve <u>any</u> of the following activity at UI Health Care, even if subjects or their insurance will not be billed for the item or service, and regardless of the study funding source (including studies with departmental or no funding)?***

- ***Procedures, tests, examinations, hospitalizations, use of Pathology services, use of clinic facilities or clinical equipment, or any patient care services, including services conducted in the Clinical Research Unit; or***
- ***Physician services or services provided by non-physicians who are credentialed to bill (ARNPs, Physician Assistants, etc.)***

Yes

V.25.b ***Will there be any procedures or services that may happen as part of a subject's regular medical care and as part of the study?***
Yes, but all procedures/services will be paid for by the sponsor, even if the service is standard care

V.25.c ***Will any study equipment or devices be supplied by a study sponsor?***
No

V.25.e ***Is there or will there be an internal budget for this study?***
Yes

V.25.f ***Is there or will there be an external budget for this study?***
Yes

V.26 ***The study involves Department of Nursing Services and Patient Care nursing, nursing resources or evaluates nursing practices at UI Health Care.***
Yes

VI. Subjects

VI.1 ***How many adult subjects do you expect to consent or enroll for this project?***
2800

VI.2 ***What is the age of the youngest adult subject?***
18.0

VI.3 ***What is the age of the oldest adult subject?***
120.0

VI.4 ***What is the percentage of adult male subjects?***
50

VI.5 ***What is the percentage of adult female subjects?***
50

VI.6 ***How many minor subjects do you expect to consent or enroll for this project?***
0

VI.13 ***Describe EACH of your subject populations***

- ***Include description of any control group(s)***
- ***Specify the Inclusion/Exclusion criteria for EACH group***
- ***Studies under IRB-03 enrolling non veterans as part of the subject population must present a compelling argument to the IRB for the inclusion of non-Veterans (e.g., insufficient number of Veterans; survey of VA employees; study of active duty military; study involving Veterans' family members), and the research is relevant to the care of Veterans or active duty military personnel.***

This study will involve treatment (bundle) and usual care groups.

Surgical service lines will include orthopedic total joint, orthopedic spine, gynecology/oncology, thoracic, general, hernia, colorectal, open vascular, plastic, and open urological procedures. These lines will be randomized 1:1 to either the bundle of activities or usual care. The unit of randomization is the service line. The perioperative environment (the patient, the patient to follow, and all providers caring for the patient and the patient to follow) for the randomized service line (treatment or usual care) will be involved in surveillance. This means that all patients, all providers caring for those patients (changes day by day), and care environments (equipment and stopcock sets) will be involved in surveillance. Surveillance from treatment and control groups will yield S. aureus transmission events that will be processed to guide proactive improvements in the treatment bundle.

Treatment group (bundle) inclusion/exclusion criteria:

Inclusion criteria: Patients seen at UIHC who are scheduled to undergo surgery from providers in one of the service lines above, documentation of informed, written consent, >18 years of age, procedure requiring general/regional anesthesia.

Exclusion criteria: Lack of documented informed, written consent, patients <18 years of age, procedures outside of the surgical service lines listed above, not requiring general/regional anesthesia, patients not seen in the UIHC clinics, and an allergy to iodine/shellfish or chlorhexidine.

Usual care group (existing practice at UIHC) inclusion/exclusion criteria:

Inclusion criteria: Patients seen at UIHC who are scheduled to undergo surgery from providers in one of the service lines above, documentation of informed, written consent, >18 years of age, procedure requiring general/regional anesthesia.

Exclusion criteria: Lack of documented informed, written consent, patients <18 years of age, procedures outside of the surgical service lines listed above, not requiring general/regional anesthesia, patients not seen at UIHC, and an allergy to iodine/shellfish or chlorhexidine.

VI.14 ***Provide an estimate of the total number of subjects that would be eligible for inclusion in each of your study populations (include your control population if applicable)***
We anticipate that >80% of all patients undergoing surgery in the surgical service lines above will be eligible for the study.

We do not know what the service line will be for the treatment and control until we randomize. We do not know exactly how many patients each line will see over the next 2 years. There are 24,000 patients that undergo adult surgery at UIHC each year. Over two years, that is 48,000 patients. The lines selected in total represent >80%, at least 38,400. That is 3840 per line, or roughly 1500 patients each year per line. Thus, we expect that 80%, or roughly 1200 patients, will be

eligible for the study for each line over the 2 year period. In terms of providers, approximately 10 providers will be involved in the care of each patient in the OR and discharge area combined. Thus, over two years, there will be 12,000 providers (not exclusive; as providers may be repeatedly sampled over the two year period).

Treatment group (bundle): 80% of all patients in the randomized service lines are expected to be eligible, N=1200 for each service line. We expect participation from the majority (>80%) of providers in the OR and in the discharge area, N=12,000 providers for each line.

Usual care group: 80% of all patients in the randomized service lines are expected to be eligible, N=1200 for each service line. We expect participation from the majority (>80%) of providers in the OR and in the discharge area, N=12,000 providers for each line.

VI.15 ***Describe how you will have access to each of your study populations in sufficient number to meet your recruitment goals.***
We will be attempting to capture all patients that meet inclusion criteria which could include patients seen and consented in the clinic, seen and consented on the hospital floor, intensive care units (inpatient surgery), or pre-anesthesia testing (PAT). Any patient meeting inclusion criteria that the surgeon obtains surgical consent for could be captured. Poster reminders will be placed in the clinics, on the ward, and PAT. The study consent forms will be attached to the surgical consent forms. Surgical providers obtaining surgical consent will obtain study consent when possible. This will otherwise be executed via our research team via pager. Preoperative kit orders will be completed by surgical providers or physician study team members when needed. The signed and held order will populate a list in EPIC for the PI (Loftus)that will be filtered by type of surgery, surgeon, and date of surgery within 10 days. It will include the patient medical record number, address/phone number, and an icon indicating the POC signed and held order. Loftus will work the list to send ordered kits to patients. Loftus will enter a new signed and held order for the kit and will associate the assigned kit number with the order, which will create a new ICON indicating ordered kit sent to patient. This will also update the Clarity report in EPIC with the kit number in addition to the other previously mentioned fields. The patient will receive the kit along with a reminder for why they received the kit (see attached in miscellaneous), use the kit (up to 3 reminders will be provided by Loftus study team), and RDB will receive and process the kits. Patients will use a prepaid mailer to send the kits to RDB which will have the RDB address in the send and return fields so that patients are not revealing their identity to RDB (process okay per USPS). RDB will send returned kit numbers to Loftus daily. Loftus will complete the signed and held orders for patients in the Clarity report that returned kits for processing. The completed POC will generate another ICON indicating received and processed and will again update the Clarity report. The research assistants will work the list to select 2 patients with completed POC orders, treatment and control, for OR PathTrac Observation each day. The assistants will confirm 1st patient consent. Once confirmed, an OR PathTrac Kit will be ordered in EPIC which creates an ICON indicating consent confirmed, a consent confirmed box checked in the RDB microEMR will be placed (3 ways for tracking consents, the written document and two electronic confirmations), and the preoperative swab and OR PathTrac kit numbers entered into the microEMR along with baseline patient demographic information (OR room number and case number, surgery duration, date and time). Informed, written consent will be obtained from the second patient on the day of surgery (see attached consent for patient 2),an OR PathTrac Kit ordered, demographic information (see previous) entered into the microEMR, and surveillance completed. If the second patient does not provide consent for their samples, the pair will be excluded and recruitment continued to reach 1,000 pairs. Our prior experience and recent experience at the University of Iowa strongly suggests that patient refusal to provide written consent for intraoperative cultures will be a rare event. The assistant will then follow the 1st patient to the recovery area for sampling as previously described using the Ward Environment Surveillance (WES) kits. The WES kit number will be associated by the micro EMR to the other kit units. This will allow RDB processing, tracking, and reporting of S.aureus transmission during the entire perioperative period.

VI.16 ***Do you <u>plan</u> to recruit/enroll non-English speaking people?***
No

VI.18 ***Do you propose to enroll any of the following in this study as subjects?***

- ***Employee of the PI or employee of a research team member***
- ***Individual supervised by PI or supervised by member of research team***
- ***Individual subordinate to the PI or subordinate to any member of the research team***
- ***Student or trainee under the direction of the PI or under the direction of a member of the research team***

No

VI.20 ***Will subjects provide any information about their relatives?***
No

VI.23 ***Will anyone (other than the subject) provide you with information about the subject (e.g. proxy interviews)?***
No

VI.26 ***Is this project <u>about</u> pregnant women?***
No

VI.27 ***Will this project involve fetuses?***

No

VI.28 ***Does this project involve adult subjects who may be incompetent or have limited decision-making capacity on initial enrollment into the study?***
No

VI.32 ***Does this project involve subjects whose capacity to consent may change over the course of the study?***
No

VI.37 ***Does this project involve prisoners as subjects?***
No

VII.A. Project Description (A)

VII.A.1 ***Where will project procedures take place (check all that apply)?***

- UIHC - Preanesthesia testing, surgical clinics, postanesthesia care unit, hospital floors (wards).
- Other UI campus site - RDB Bioinformatics at the University of Iowa Bioventures Center.

VII.A.2 ***Is this project also being conducted by other researchers at their own sites (e.g. a multi-site collaborative project)?***
No

VII.B. Project Description (B)

VII.B.1 ***Does this project involve any of the following (Check all that apply):***

- ☐ **Registry** – The collection and maintenance of data (not including biologic samples) in which: (1) the individuals in the registry have a common or related condition(s), and/or (2) the individuals in the registry are interested in being contacted for future studies by investigators other than those listed in Section II of this project.(UI Guide)
- ☑ **Repository** – The collection, storage, and distribution of human biologic samples and/or data materials for research purposes. Repository activities involve three components: (i) the collection of data and/or specimens such as blood, tissue, saliva, etc.; (ii) the storage of data or specimens, and data management function; and (iii) the sharing of data/specimens with recipient investigators other than the original investigators. (paraphrased from OHRP)
- ☐ **Expanded Access** – A process regulated by the Food and Drug Administration (FDA) that allows manufacturers to provide investigational new drugs to patients with serious diseases or conditions who cannot participate in a clinical trial. Examples of expanded access include non-protocol access to experimental treatments, including protocol exception, single-patient IND, treatment IND, compassionate use, emergency use, continued access to investigational drug, and parallel track (ClinicalTrials.gov & FDA).
- ☑ **Clinical (or Treatment) trial** – A prospective biomedical or behavioral research study of new treatments, new drug or combinations of drugs, new devices, or new approaches to surgery or radiation therapy. (NIH and ClinicalTrials.gov & FDA)
- ☑ **Physiology intervention/study** – A pharmacologic or measurement study aimed at understanding basic mechanisms of disease and/or of normal human physiology, often without any therapeutic intent (though a clinical trial could include such components, often labeled as “translational” or “basic science” aims.) Measurements in such studies could include, but are not limited to, a blood draw, EKG, EEG, MRI, auditory or sensory testing, checking vital signs, DEXA scans, eye tracking, specimen collection, exercise, fasting, special diets, etc.
- ☐ **Behavioral intervention/study** – May be used to refer to studies of individual or group behavior. This option does not include drugs, biologics, or devices but could include psychotherapy, lifestyle counseling, behavior modification, etc.
- ☐ **Diagnostic trial** – Protocol designed to evaluate one or more interventions aimed at identifying a disease or health condition (ClinicalTrials.gov & FDA)
- ☐ **Non-clinical** – any college/department that would regularly submit to IRB-02
- ☐ **Other**

VII.B.1.a ***Does this project involve any of the following (Check all that apply):***

- ☐ **Phase I trials** – include initial studies to determine the metabolism and pharmacologic actions of drugs in humans, the side effects associated with increasing doses, and to gain early evidence of effectiveness; may include healthy participants and/or patients (ClinicalTrials.gov & FDA)

- [x] **Phase II trials** – include controlled clinical studies conducted to evaluate the effectiveness of the drug for a particular indication or indications in patients with the disease or condition under study and to determine the common short-term side effects and risks(ClinicalTrials.gov & FDA)
- [ ] **Phase III trials** – include expanded controlled and uncontrolled trials after preliminary evidence suggesting effectiveness of the drug has been obtained, and are intended to gather additional information to evaluate the overall benefit-risk relationship of the drug and provide an adequate basis for physician labeling(ClinicalTrials.gov & FDA)
- [ ] **Phase IV trials** – studies of FDA-approved drugs to delineate additional information including the drug's risks, benefits, and optimal use(ClinicalTrials.gov & FDA)

VII.B.1.b ***Provide the NCT (National ClinicalTrials.gov Identifier) number***
NCT03638947

VII.B.2 ***Does this project involve a drug washout (asking subject to stop taking any drugs s/he is currently taking)?***
No

VII.B.6 ***Will any subjects receive a placebo in this study when, if they were not participating, they could be receiving an FDA-approved treatment for their condition?***
No

VII.B.11 ***Is there a separate, written protocol that will be submitted in addition to this IRB New Project form? (Note: a grant application is not considered to be a protocol)***
No

VII.B.18 ***Does this project involve testing the safety and/or efficacy of a medical device?***
Yes

VII.B.19 ***Describe in detail procedures in place for maintaining device shipment and receipt records:***
The medical device utilized in this study is a software program (RDB Bioinformatics, Omaha, NE 68154) designed for bacterial differentiation. All devices, equipment, culture supplies and media used for the purpose of bacterial differentiation are considered exempt for FDA regulations (like the MALDI-Toff used at Iowa for culture specimens). This is a cloud-based device, so procedures for maintaining device shipment and receipt records to not apply.

VII.B.20 ***Who will be responsible for maintaining these shipment and receipt records?***
This is a cloud-based device, so procedures for maintaining device shipment and receipt records to not apply.

VII.B.21 ***Describe in detail procedures in place for tracking use and disposition of devices described in this study:***
This is a cloud-based device, so procedures for maintaining device shipment and receipt records to not apply.

VII.B.22 ***Who will be responsible for maintaining these use and disposition tracking records?***
This is a cloud-based device, so procedures for maintaining device shipment and receipt records to not apply.

VII.B.23 ***Describe in detail procedures in place to limit access to authorized study personnel for the storage, control, and dispensing of the investigational devices. (For example, investigational devices are kept in a locked area away from approved devices or have a keyed interlock, and only study personnel authorized to dispense the device have the keys)***
Two-factor authentication is required for access to the software. Only study personnel and the infection control perioperative team will be granted access. Access will be limited based on participation. For example, laboratory personnel will only have access to the laboratory component of the software, clinical research assistants will only have access to the data entry fields, and the infection control perioperative team will only have access to the reporting platform. The study personnel will have complete access. A signed data management plan with UIHC is in place.

VII.B.24 ***Is the device FDA-approved for the way it will be used in this study?***
No

VII.B.25 ***Is there an IDE (Investigational Device Exemption) for this device in this research project?***
No

VII.B.29 ***Indicate the appropriate FDA status you and/or the sponsor are requesting for the use of this device in this study.***

Non-Significant Risk (NSR) device/software

VII.B.31 ***Provide a detailed rationale for why this device meets the FDA definition of a Non-Significant Risk Device (NSR)***
This software program is indicated for bacterial differentiation and is therefore considered exempt from FDA regulations. It is not an implanted device purported to preserve or sustain human life, is not intended to diagnose, cure, or mitigate human disease, does not impair usual practice or provide any risk to the patient. The device serves to differentiate bacterial specimens collected from the perioperative care environment into hyper transmissible, resistant, and virulent pathogens. Once identified, the system maps those "super bugs" so that healthcare environments can understand where their gaps in basic preventive measures are. For example, where the gaps in hand hygiene are. Once identified, the institution can use the information to design, measure, analyze, improve, and control the super bug spread. We hypothesize that this can help to reduce infections. As this device does not meet the FDA definition of a significant risk device (SRD), it is a NSR.

VII.B.32 ***Provide a summary of prior investigations with this device.***
This device was tested in a beta project at UIHC where bacterial traffic in the operating room was catalogued.

VII.B.33 ***Have there been any prior IRB reviews (at UI or elsewhere) and/or determinations made with regard to this device?***
Yes

VII.B.34 ***Provide a discussion of these reviews/determinations.***
I have not seen Dr. Reddy's IRB determinations, but they are on file with the IRB. The device and study were determined to be of no significant risk to patients.

VII.B.35 ***Has the FDA made an assessment of risk with regard to this device?***
No

VII.B.36 ***Has this device/software been approved by the FDA for another indication or in another form from its use in this project?***
No

VII.C. Project Description (C)

VII.C.1 ***Does this project involve any research on genes or genetic testing/research?***
No

VII.D. Project Description (D)

VII.D.1 ***Check all materials/methods that will be used in recruiting subjects (you will need to attach copies of all materials at the end of the application):***

- Pictures/diagrams/models -
- Posters -
- Use of any information available to the researchers or their colleagues because this person is a patient OR use of any information considered to be Protected Health Information (PHI) OR review of patient/clinic records - We will use the EPIC lists as previously described to send kits, track receipt, and guide surveillance. Email will be used to communicate with surgeons regarding subjects meeting inclusion criteria.
- Letter -

VII.D.2 ***List the individual data elements you will need to access/use from the patient or clinic records to identify potential subjects for recruitment***
Age >18 (this will be differentiated by the order in EPIC where only patients age >18 have the order included in preoperative order sets)
Surgical clinic visit (involving orthopedic total joint, orthopedic spine, gynecology/oncology, cardiothoracic, general abdominal, colorectal, open vascular, general breast, and open urological procedures). Also documented allergies.

VII.D.3 ***Describe why you could not practicably recruit subjects without access to and use of the information described above***
We cannot approach every patient in the clinic without this information.

VII.D.4 ***Describe why you could not practicably obtain authorization from potential subjects to review their patient or clinic records for recruitment purposes.***
It is impractical for us to approach every patient in the clinic to get authorization to review their medical record.

VII.D.5 ***Describe plans to protect the identifiers from improper use or disclosure***
The patients are protected by the HIPAA policy at the University of Iowa Hospitals and Clinics. PHI will be stored in EPIC. EPIC protects this data based on UIHC policy. Patient demographic factors entered into the RDB Bioinformatics will be de-identified, only associated to kit numbers. This information will be protected by 2-factor authentication and encrypted. A data safety plan signed by RDB and UIHC affiliates is in place.

Source documents (RDB kit inserts for reservoir collection, printed screen shots of the OR PathTrac microEMR,and patient demographic factor collection documents (see attached documents)will be kept in a binder that will be stored in a locked cabinet in the locked office of the PI.

Only research team members will have access to the EPIC lists of patient information linked to preoperative kit orders.

VII.D.6 ***Describe plans to destroy identifiers at the earliest opportunity consistent with conduct of the research***
We will not be collecting patient identifiers except on consent forms that will be stored as records and in EPIC lists. OR numbers and dates in the microEMR will only be associated with kit numbers and basic demographic information, not patient MRN or other identifiers. Once the study is complete with all primary and secondary endpoints collected, the EPIC lists will be deleted if possible by HCIS.

VII.D.7 ***Does the research team agree that the requested information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the study, or for other research for which the use or disclosure of the requested information would be permitted by the HIPAA Privacy Rule***
Yes

VII.D.8 ***Will a member of the research team discuss the study with the subject in person prior to the subject agreeing to participate?***
Yes

VII.D.9 ***Describe the physical location where the consent process will take place:***
Surgical clinic, preanesthesia testing (PAT), on the surgical floor if inpatient surgery.

VII.D.10 ***Will a member of the research team discuss the study with the subject by phone prior to the subject agreeing to participate?***
No

VII.D.12 ***Who will be involved in the consent process (including review of consent document, answering subjects' questions)?***

Name	Consent Process Involvement
Randy Loftus, MD	No
Lauren Allan, DO, BA	Yes
Kiran Annam, ARNP	Yes
Raven Brenneke, BA	Yes
Cheryl Byrnes, Advanced Registered Nurse Practioner	Yes
Nicholas Cardillo, MD	Yes
Brian Clark, PA-C	Yes
John Cromwell, MD	Yes
Megan Davis-de Geus, MSN	Yes
Sundar Durgempudi Tripura, MD, FRCA	Yes
Bradley Erickson, MD	Yes
Lance Evans, BA	Yes
Mark Fisher, MD	Yes
Luis Garcia, MD	Yes
Joshua Godding, BS	Yes
Michael Goodheart, MD	Yes
Thomas Granchi, MD	Yes
Brent Hadder, MD	Yes
Alexia Herber, High School	Yes
Jean Hogan, ARNP	Yes

JoAnne Hudachek, BSN	No
Gretchen Kass, ARNP	Yes
John Keech, MD	Yes
Prashant Khullar, MD	Yes
Susan Kloos, BSN, RN	No
Walter Lawrence, MD	Yes
Yasmin Lyons, DO	Yes
Megan McDonald, MD	Yes
Patrick McGonagill, MD	Yes
Nicole Miller, BA, PA-C, BS	Yes
Andreea Newtson, MD	Yes
Nicolas Noiseux, MD	Yes
Brittany Parchert, BSN	No
Denise Peck, ARNP/PA	Yes
Deanna Persons, High School	Yes
Andrew Pugely, MD	Yes
Roseanne Rath, PA-C, MA	Yes
Joan Ricks-McGillin, BSN	Yes
Rebecca Rosenberg, PA	Yes
Jonathan Rueter, PA-C	Yes
Jennifer Shanklin, MD	Yes
Mel Sharafuddin, MD	Yes
John Sharp, MD	Yes
Zita Sibenaller, PHD	Yes
Lori Stout, BSN, BSN	Yes
Judy Swafford, RN	No
Chad Tracy, MD	Yes
Alicia Walter, ADN	Yes

VII.D.15 ***Check all materials that will be used to obtain/document informed consent:***

- Other - The attached poster which summarizes elements of the study consent will be made available as a visual aide/reminder for both the surgical team and the patients.
- Consent Document

VII.D.16 ***Are you requesting a waiver of documentation of consent (either no subject signature or no written document)?***
Yes

VII.D.17 ***Choose one of the following to indicate why you are requesting that the IRB waive the requirement to obtain a subject signature as documentation of consent:***
A. The research presents no more than minimal risk (minimal risk means the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests)

AND

The study involves no procedures for which consent is normally required ouside of a research context. *(This type of waiver is often permitted for a minimal risk mail-out survey that includes a cover letter with all elements of consent, and returning the survey indicates consent. You cannot request this waiver if the study also involves the use of any protected health information (PHI).)*

VII.D.18 ***Explain why this meets the chosen criteria in A. or B. above:***
This applies only to the clinician subjects, and, this is minimal risk. We are not collecting provider identifiers. All bacteria collected from providers will

receive a unique barcode that will not be linked to the specific provider, only to the type of provider (anesthesia attending or anesthesia assistant).

VII.D.19 ***Before the subject gives consent to participate are there any screening questions that you need to directly ask the potential subject to determine eligibility for the study?***
Yes

VII.D.20 ***List any screening questions you will directly ask the potential subject to determine eligibility.***
Are you allergic to iodine, shellfish, or chlorhexidine? If the answer is yes, they will not be enrolled

VII.D.21 ***Will you keep a screening log or other record that would include information on people who do not enroll in the study?***
Yes

VII.D.22 ***Describe the information being collected and the purpose for keeping this information.***
For each service line, we will collect age and sex for those patients so that we can assess for biases, such as selection bias.
We will also track patients who did not send the kits in (via EPIC reports). These patients will not undergo surveillance because they will not have completed the required screening component. If three calls are made and they do not use the kits, they will be considered lost to f/u. This will be important information when results are reported.

VII.D.23 ***Will this information be shared with anyone outside the UI research team members?***
No

VII.D.25 ***After the subject agrees to participate (signs consent), are there any screening procedures, tests, or studies that need to be done to determine if the subject is eligible to continue participating?***
Yes

VII.D.26 ***List and describe screening***
As described in VII.D.22, the patient must use and return the preoperative swab kits. Three reminders will be provided. If they do not complete the initial screening process, they will be considered lost to f/u. Information required to meet inclusion criteria will be self evident (age which is in the chart, surgical service line which is already known...they are in the randomized line, and need for general/regional anesthesia (this is decided by the procedure).

VII.D.27 ***Discuss how much time a potential subject will have to agree to consider participation and whether or not they will be able to discuss the study with family/friends before deciding on participation.***
The patient will be seen in clinic, PAT, or on the floor/ICU as part of their visit. The initial time to decide will be limited by the study visit, as a preoperative order must be placed. However, they will be able to decline at any point down the road as previously described, including simply deciding not to use and return the ordered kit.

VII.D.28 ***How long after the subject agrees to participate do study procedures begin?***
Our goal is to focus on a 10-day window prior to surgery so that the kit can be shipped (two days), received (two days), processed (up to 2 days), and in the treatment group, treated for 2-4 days.

VII.D.29 ***Provide a description of the enrollment and consent process for adult subjects***

- ***Describe each study population separately including control population***
- ***Include when recruitment and consent materials are used***
- ***Use 3rd person active voice "The Principal Investigator will identify subjects. For example, the principal investigator will identify potential subjects, the study coordinator will discuss the study with subjects over the telephone and schedule the first study visit, etc..."***
- ***Describe the steps that will be taken by the research team to minimize the possibility of coercion or undue influence during the consent process***

We will be attempting to capture all patients that meet inclusion criteria which could include patients seen and consented in the clinic, seen and consented on the hospital floor, intensive care units (inpatient surgery), or pre-anesthesia testing (PAT). Any patient meeting inclusion criteria that the surgeon obtains surgical consent for could be captured and tracked by the preoperative order.

Preoperative signed and held orders for preoperative swab kits will populate a list in EPIC for the PI (Loftus). This list will be filtered by type of surgery, surgeon, and date of surgery within 10 days. Members of the research team will send out the kits after approval from the PI. Either treatment or control kits will be sent based on the service line, which will be linked by the kit number, and this will determine delivery of usual care or the treatment bundle on the day of surgery.

Before a kit is sent to the patient, a new signed and held order will be placed and associated with the kit number (specific to the kit sent to the patient) which will update the EPIC list with the kit number. The kits sent by the patient to RDB will be accomplished by a prepaid mailer. Patients will use and return the kits to RDB.

RDB will receive and process the kits. RDB will track the returned kit numbers and provide a list to Loftus. Loftus will complete the signed and held orders for patients in the Clarity report that returned kits for processing.

The completed POC will again update the Clarity report. The research assistants will work the list to select 2 patients with completed POC orders, treatment and control, for OR PathTrac Observation each day.

The assistants will confirm 1st patient consent. Once confirmed, an OR PathTrac Kit will be ordered in EPIC, a consent confirmed box checked in the RDB microEMR, and the preoperative swab and OR PathTrac kit numbers entered along with baseline patient demographic information.

Informed, written consent will be obtained from the second patient and the process repeated. If the second patient does not provide consent for their samples, the pair will be excluded and recruitment continued to reach a total of 1,000 complete pairs. Our prior experience at multiple centers and recent experience at the University of Iowa strongly suggests that patient refusal to provide written, signed consent for intraoperative samples will be a rare event. The assistant will then follow the 1st patient to the recovery area for sampling as previously described.

Providers: We will send out an email to all providers (anesthesia attending physicians, anesthesia residents, and circulating nurse anesthetists) that describes the study. A sample email has been attached which was based on that used for the OR PathTrac study. Providers will be given the opportunity to opt out. If they email a statement that they would not like to be involved, they will not be approached on the study day. If they do not provide a written response, they will be approached, but they can still opt out. This will be explained. If they opt out at that time, their name will be added to the list of providers who are not to be approached. This is to avoid coercion. When providers are approached in the case that they have not opted out, they will simply be reminded of the study, the purpose of the study, and they will be asked to dip their hand in a bag of sterile, balanced electrolyte solution. They will also be asked to use provided hand hygiene and catheter disinfection systems (treatment bundle). The hand hygiene solution was previously used in the OR PathTrac study, and providers are familiar with this solution. There were no issues previously. If they opt out, other providers will be sampled in the case that they do not opt out so as to maximize the efforts put forth by patient participation prior to the OR date and provider assignment to the patient's surgery.

VII.D.37 ***Does the study include any form of deception (e.g., providing participants with false information, misleading information, or withholding information about certain study procedures)?***

Examples:

- ***Procedure includes a cover story that provides a plausible but inaccurate account of the purposes of the research.***
- ***Participants will be provided with false information regarding the particular behaviors of interest in the research.***
- ***Procedures include a confederate pretending to be another participant in the study.***
- ***Participants will be told that the research includes completion of a particular task, when in fact, that task will not be administered.***
- ***Study is designed to introduce a new procedure (or task) that participants are not initially told about.***
- ***If yes, a waiver of informed consent must be requested under question IV.3.***

No

VII.E. Project Description (E)

VII.E.1 ***Will subjects be randomized?***
Yes

VII.E.1.a ***Will any subjects be blinded to which study arm they have been assigned?***
Yes

VII.E.1.b ***Does the protocol permit telling subjects their treatment assignment at the end of the entire study?***
No

VII.E.1.d ***Justify why subjects cannot be told what study arm they have been assigned. You will need to disclose to subjects in the***

consent document that they cannot receive this information.
This is a quality improvement project protected by quality assurance.

VII.E.2 ***Describe randomization scheme/assignment including ratio such as 1:1, 2:1 etc.***
The service lines have been previously described. These lines will be randomized 1:1 to treatment (bundle) and usual care. This randomization will be computer generated by RDB software.

VII.E.3 ***Will any questionnaires, surveys, or written assessments be used to obtain data directly from subjects in this study?***
No

VII.E.5 ***Does this project involve creating any audiotapes, videotapes, or photographs?***
No

VII.E.6 ***Provide a detailed description in sequential order of the study procedures following the consent process - DO NOT cut and paste from the Consent Document.***

Describe study populations separately if they will be participating in different procedures - include CONTROL population if applicable.

DESCRIBE:

- ***What subjects will be asked to do/what happens in the study (in sequential order)***
- ***The time period over which procedures will occur***
- ***The time commitment for the subject for individual visits/procedures***
- ***Long-term followup and how it occurs***

Preoperative swab kit orders will track informed, written consent and will populate a list in EPIC for the PI (Loftus) that will be sorted by type of surgery and filtered (at the top of the list) by patients with orders for the kit that are actually booked for surgery within 10 days of the current date. That list will be used by Loftus to send kits to patients for preoperative swabbing and if in the treatment group, decolonization with Povidone iodine. Before sending, a new signed and held POC preoperative swab kit order will be placed and associated with the kit number. The kits will be sent by the research team to the patient along with a prepaid mailer. The kit will include 3 swabs (nasal, axillary, and groin), preprinted instructions for use, and an insert briefly summarizing the study for a reminder (see attached documents). The patient will follow the kit instructions and send the kit to RDB for processing.

RDB will process the samples and enter the results into the software platform. RDB will send a list of kit numbers received to Loftus. Loftus will complete the signed and held order in EPIC for those received. This will create an ICON indicating complete. The complete ICON will guide OR PathTrac Surveillance, where a treatment and control patient are selected each day, as geographically dispersed as possible in the OR.

Patients in treatment lines with completed orders who are selected for surveillance will receive the treatment bundle (see below). Patients in usual care lines with completed orders who are selected for surveillance will receive usual care. All second patients in the observational pairs described below will receive usual care. Only the first patient in a treatment pair will receive the bundle (The goal is to examine the impact of an evidence-based bundle in preventing spread of bacteria from one patient to another).

For surveillance in the OR for both treatment and control patients selected for observation, the observational unit will be a case pair. The first patient will have been previously consented. This will be confirmed by the research assistants. An OR PathTrac Kit will be ordered by Loftus or another physician research team member once consent is confirmed. The OR PathTrac and preoperative swab kit numbers will be entered into the RDB microEMR along with patient demographic information. Source documents will include a screen shot of the microEMR page with kit numbers and demographics and the kit insert. The OR surveillance as directed by the OR PathTrac kit will be conducted. The kits will be transported to RDB by the research team for processing. RDB will enter the results into the software platform.

The second patient will be approached for informed, written consent by the research team. This document is distinct from the first patient consent, as the second patient will not receive Povidone iodine, will not be asked to use the preoperative swab kit, and will not undergo postoperative surveillance. Only the OR PathTrac kit surveillance (while they are in the OR) will be conducted for the second patient. Once written consent is obtained, an OR PathTrac Kit will be ordered by Loftus or another physician research team member, the kit number associated with the first patient's preoperative swab kit and OR PathTrac kit numbers in the microEMR, and the demographic information entered into the microEMR as well. Source documents will include a screen shot of the microEMR page with kit numbers and demographics and the kit insert. The OR surveillance as directed by the OR PathTrac kit will be conducted. Kits will be transferred to RDB by the research team. RDB will process the kits and enter the results into the software platform. OR PathTrac kit orders electronically confirm obtained written consent.

The first patient will be followed to the recovery period. A ward environment surveillance (WES) kit will be used for surveillance. The kit will be associated to the above information in the microEMR as previously described. Ward (this is the recovery area, could be the intensive care unit, post anesthesia care unit, second stage recovery, a hospital floor, etc)surveillance will be conducted as directed by the kit. Kits will be transferred to RDB by the research team. RDB will process

the kits and enter the results into the software platform.

The treatment bundle will continue with the first patient for up to 48 hours into their recovery period. Usual care patients, and all second patients in a pair, will continue with usual care.

Treatment and control patients will be followed for up to 90 postoperative days to identify the occurrence of one or more healthcare-associated infections according to National Healthcare Safety Network (NHSN) definitions and will be called at the 90 day mark (up to 3 attempts will be made) to determine if they developed an infection. A research assistant will review the patient's electronic medical record via EPIC for bacteriology results for urine, sputum, wound, sterile sites and blood. If a positive culture is identified, the RA will provide the UIHC Clinical Lab with an accession number so that the isolate can be saved. Samples will be sent to RDB for analysis in order to determine if the organism was clonally-related to an organism isolated from one or more reservoirs during the pre/peri/post-operative period. At no point will personal ID information be attached to isolate(s).

All microbiological data will be entered into the RDB software platform. The platform will identify transmission events. This information will be graphically displayed, continually updated, and will bring genomic analysis to the bedside by providing a mechanism for the research team to continually optimize treatment bundle delivery.

The above process is summarized in the diagrams attached in the misc. documents. These diagrams, along with bullet points of the study in poster format, will be placed on the wall of physician offices where consent will be taking place to remind providers of the study and to serve as a visual aide for the patient during the consent process. The information on the posters will simply state the purpose of the study and participation requirements as outlined in the consent. Please see the poster attached in miscellaneous.

Procedures:

Preoperative, Intraoperative, and Postoperative Patient Culture Procedures:

This will involve use of a sterile ESwab to obtain nasal, axillary, and inguinal swabs. Nasal: the swab is to be inserted into each nares no more than 3/4 of an inch and rotated 360 degrees 10 times. Axillary: the swab will be applied to the middle of the armpit, pressed firmly against the skin, and rotated 10 times. Inguinal: the swab will be applied to the inguinal crease, pressed firmly against the skin, and rotated 10 times. After collection, each swab will be inserted into the collection medium (Aimes transport medium), the applicator stick snapped off as directed, and the cap placed on the tube to seal the contents.

Treatment Bundle:

Decolonization: Each patient in the treatment group will receive Povidone iodine treatment for their nose and potentially their surgical site on the day of surgery in the Day of Surgery Admissions(DOSA) area. The surgical team will approve and guide the application of the povidone iodine to the likely surgical incision site(s) or it will not be placed. The application of the povidone iodine to the inside of the nose will be guided by a member of the research team. 2% Chlorhexidine body Wipes are currently used in UIHC Day of Surgery Admission (DOSA) to help disinfect patient skin before surgery and we will make sure that treatment patients are properly administered these wipes and educated on their use.

Vascular care: Each patient in the treatment group will receive the Ultraport zero (BBraun Medical) closed, disinfectable stopcock set and the DOCit and HubScrub disinfection system (Saxa Medical). The DOCit is a cap that providers in the OR will insert syringes into to keep them free of environmental contamination, organized, and sterile given the 62% isopropyl alcohol in each cap. This is a FDA approved device that is on the market. It has been shown to reduce infections with a number needed to treat of 16. The HubScrub is a cap with the same disinfectant that providers will use to scrub the injection ports, or stopcock sets. This cap contains 62% alcohol and brushes for mechanical disruption of biofilms. The cap disinfects the port in 10 seconds, maintains disinfection for >72 hours when covered, and only needs to be turned 2 times to disrupt any biofilm. It is also evidence based and proven to reduce infections. It is also FDA approved and on the market. The DOCit and HubScrub systems will be provided in the preoperative area, affixed to the IV pole for easy access by the anesthesia provider in the OR, and transported with the patient to the recovery unit.

Hand Hygiene: The Saxa system also contains a single-handed hand hygiene device that allows the provider to disinfect their hands at every opportunity. It is affixed to the IV pole and will be used preoperatively, intraoperatively, and postoperatively.

Environmental cleaning: Surveillance will map ORs affected by residual contamination with hyper transmissible, resistant, and virulent organisms. This information will be communicated to the environmental cleaning service in the OR electronically, automatically updated each day, in order to guide improved routine and terminal cleaning for affected ORs. Improved routine cleaning will involve use of the conventional quaternary ammonium compound with a microfiber cloth followed by a surface disinfection wipe. Improved terminal cleaning will involve robotic cleaning using UV robots (using UV light in the OR for under an hour) at night/morning if not being used, or will involve increased duration of application of the previously described cleaning procedure.

Surveillance will be used to identify gaps in each of the above components in order that they can be addressed. For example, a particular service line may not be

facile at achieving effective decolonization. This would be addressed with patient outreach to that service line. All steps will be determined by a dedicated infection control perioperative team that will use surveillance to guide proactive, evidence-based, plan-do- study-act cycles.

OR PathTrac surveillance procedures: Research assistants will culture the baseline anesthesia environment (adjustable pressure-limiting valve and agent dial of the anesthesia machine)using environmental swabs, anesthesia attending hands on entry to the OR but after an opportunity to wash their hands using the wall-mounted devices using a modified glove juice technique that is simply dipping the dominant hand in a sterile bag containing a sterile, balanced salt solution, the same procedure for resident hands at baseline, the patient nasopharynx, axilla, and inguinal regions following induction of anesthesia and patient stabilization using patient Eswabs as described above, the same provider hand, patient, and environmental cultures at case end, and the patient intravenous stopcock at case end that will be cultured using an environmental swab. All cultures in the OR will be obtained using aseptic practice where the research assistant will be wearing a hat, a mask, and will wash their hands prior to dawning gloves. These same procedures will be applied to the patient to follow (the patient undergoing surgery in the same OR after the patient above.

Postoperative Surveillance Cultures: The first patient will be followed to recovery in same day: postanesthesia care unit (PACU), intensive care unit (ICU), hospital floor, or other units. Patients, provider hands, and environmental surfaces will be sampled using the procedures as described above within. A sample proximal to the surgical wound, but outside of the dressing, will be sampled. Patient samples and samples from the patient's recovery room environment will be collected within 48 hours prior to discharge.

Sample Processing: All samples will be sent to RDB Bioinformatics for processing. Results will be entered into the software. The software will guide testing to identify S. aureus transmission events. S. aureus transmission events will be processed to identify transmission stories, and transmission stories will be reported in the software platform to guide proactive improvements in the bundle.

Infection Tracking: The patient will be followed for 90 days postoperatively to identify and infection. Initial screening criteria will include an elevated white blood cell count, fever (T>38 degrees), anti-infection order, culture, or office documentation of infection. If one or more criteria are present, the patient will undergo a full chart review to determine if they developed a healthcare-associated infection (HAI) as determined by National Healthcare Safety Network (NHSN) definitions. All patient cultures obtained for infectious workup by the usual healthcare teams will be saved by the clinical microbiology laboratory. Samples will be sent to RDB for analysis in order to determine if the organism was clonally-related to an organism isolated from one or more reservoirs during the perioperative period.

Confounding Factor Analysis: Information from the patient medical record will be collected by the study team: date and time of surgery, diagnosis, ASA status (a system for assessing the fitness of patients before surgery), age, comorbidities (the presence of one or more additional diseases or disorders co-occurring with (that is, concomitant or concurrent with) a primary disease or disorder), surgery type and duration, type of anesthesia provided, operating room number, gender, dirty or infected surgery (yes/no), preoperative location, postoperative location, and duration of anesthesia. Data will password protected and kept in microEMR.

All patients will be called at 90 days (Up to 3 attempts will be made) to determine if they developed an infection.

VII.E.7 ***Will you attempt to recontact subjects who are lost to follow-up?***
No - those lost to followup will not be recontacted

VII.E.9 ***Will subjects be provided any compensation for participating in this study?***
No

VIII. Risks

VIII.1 ***What are the risks to subjects including***
- emotional or psychological
- financial
- legal or social
- physical?
Patients: Possible anxiety about properly following instructions on how to decolonize with povidone iodine. There is a rare but possible risk of topical hypersensitivity with topical iodine or chlorhexidine antiseptic solutions.

Providers: None apparent.

VIII.2 ***What have you done to minimize the risks?***

- ***If applicable to this study ALSO include:***
  - ***How you (members of your research team at Iowa) will monitor the safety of individual subjects.***
  - ***Include a description of the availability of medical or psychological resources that subjects might require as a consequence of participating in this research and how referral will occur if necessary (e.g. availability of emergency medical care, psychological counseling, etc.)***

Patients will be consented. Patients will receive thorough instructions for proper use of swab kits, Povidone iodine, and chlorhexidine. The consent process will require confirmation that there are no known allergies to shellfish, Povidone iodine, or chlorhexidine. The rare possibility of a hypersensitivity reaction to the topical Povidone or chlorhexidine antiseptic agents will be communicated. It will be recommended that they call their primary care doctor if they do develop a rash.

Providers will also have an opportunity to decline. Emails will be sent out to providers initially and the day before, and providers will have the opportunity to decline at any point the day of.

VIII.3 ***Does this study have a plan to have an individual or committee review combined data from all subjects on a periodic basis (such as summary or aggregate safety and/or efficacy data)?***
No

IX. Benefits

IX.1 ***What are the direct benefits to the subject (do not include compensation or hypothesized results)?***
None

IX.2 ***What are the potential benefits to society in terms of knowledge to be gained as a result of this project?***
Successful implementation of this study will provide an organized, cost-effective pathway to reduce patient harm for up to 7% of patients undergoing surgery and could be extended hospital-wide to improve quality of care delivered to thousands of patients each year, save the hospital system billions of dollars, and address the issue of antibiotic resistance.

X. Privacy & Confidentiality

X.1 ***What are you doing to protect the privacy interests of the subjects?***
Subjects are consented in a private location. The team member obtaining consent waits until medical personnel have completed their business with the subject and have left the room before beginning the consent procedures.

X.2 ***Are you collecting the Social Security Number of any subjects for any purpose?***
No

X.4 ***How will information/data be collected and stored for this study (check all that apply):***

- Paper/hard copy records (hard copy surveys, questionnaires, case report forms, pictures, etc.) - EPIC lists will remain in EPIC. No PHI will be transferred from UIHC to RDB. Each face sheet of the microEMR (the patient demographic entry sheet) for OR PathTrac and Postoperative observational units will be printed by the research assistant each day, placed into a binder, and the binder stored in the locked office of the PI. Consents will be maintained in a study binder and stored in the locked office of the PI.
- Electronic records (computer files, electronic databases, etc.) - Preoperative orders will be protected within EPIC. For OR and postoperative surveillance, we will be using the RDB Bioinformatics (University of Iowa Research Park, 2500 Crosspark Rd. E133 Coralville, IA 52241, United States) surveillance system. This system is comprised of an encrypted laptop that contains a micro electronic medical record (EMR) into which patient identification and kit identification numbers are entered as well as surgical clinic testing, ward anesthesia surveillance, and OR PathTrac system modules. The micro EMR and OR PathTrac systems have already undergone beta implementation at Iowa. They are protected by 2-factor authentication and are only accessible to research team members. The clinic and ward surveillance systems will be linked to these systems in the current study. RDB and UIHC have a signed data security plan. It is planned that long term storage of data will be with RDB Bioinformatics at UI Bioventures. This will be discussed in the BAA.
  - Name - Brandon Gordon
  - Title - Affiliate
  - University Job Classification - PZ01
- Biologic samples (blood draws, check swabs, saliva samples, tissue samples, etc.) - We will use IATA methods for bacterial transport/transfer. Patient swab samples will be stored and identified solely by the kit identification number used to obtain the swab. In the event that a patient subsequently develops an infection, patient cultures will be managed initially by the UIHC clinical lab in accordance with usual care. In addition, samples will later be transferred to

RDB Bioinformatics. It is planned that long term storage of biological materials will be with RDB Bioinformatics at UI Bioventures.

- Name - Randy Loftus
- Title - Associate Professor
- University Job Classification - FS12

X.5 ***Do the confidentiality protections indicated above allow only members of the research team to access the data/specimens?***
No

X.6 ***Describe***
RDB Bioinformatics is at UI Bioventures. Bacterial cultures will be de-identified (barcode) and demographic data linked to the barcode. Only bacterial culture data, OR date, surgical duration, OR room and case number, and kit numbers will be shared with RDB.

X.7 ***Does your study meet the NIH criteria for a Certificate of Confidentiality or will you be applying for Certificate of Confidentiality?***
No

XI. Data Analysis

XI.1 ***Describe the analysis methods you will use, including, if applicable, the variables you will analyze***
Enrollment/Randomization: Randomization is by the surgical line to treatment or control. The treatment bundle will include the improved RDB Bioinformatics S. aureus decolonization and screening processes described as above, as well as the previously described hand hygiene, environmental cleaning, and vascular care interventions. Active surveillance of bacterial transmission in the perioperative setting for both bundle and usual care groups will be used to drive activities that should further reduce the incidence of bacterial transmission. We will not disrupt processes that are already in place, and results will be entered into the medical record via standard laboratory resulting processes.

Patients that undergo S. aureus screening in treatment and control groups will be tracked via the RDB system (OR PathTrac) when the kits are employed as previously described. The bundle will be implemented in the treatment service lines. Usual care will occur in usual care lines. Transmission data will be used by an infection control perioperative team to continually optimize bundle interventions through plan-do-study-act cycles. The infection control perioperative team will consist of Drs. Cromwell, Goodheart, McGonagill, Noiseux, Tripura, Tracy, Garcia, Fisher, Keech, Pugely, Sharafuddin,Brent Hadder,Dr. Erikson, and Loftus and Michelle Mathias and another circulating nurse (TBD). The surveillance team will include a research assistant at 1.0 FTE and an assistant at 0.5 FTE whose responsibility will be to sample all reservoirs at the start of each case, the end of each case, and the post-operative area. All patients will be followed for 90 days by the research assistants.

Surveillance Instruments: For the primary outcome of S. aureus transmission events, the surveillance instrument will include the perioperative environment for the randomly selected patient. This will include the preoperative cultures, the intraoperative cultures, and the postoperative cultures. These samples will be collected via use of ordered bacterial reservoir collection kits.

Reservoir sampling: These include the Clinical Arena in which the patient nasopharynx is sampled, the OR Arena case pair where 13 sites are sampled per case for a total of 26 sites that include anesthesia attending hands prior to surgery, anesthesia assistant (resident, student nurse anesthetist, Certified-Registered Nurse Anesthetist) hands prior to surgery, anesthesia machine adjustable pressure-limiting valve and agent dial (1 swab) at baseline, patient nasopharynx, axilla, and groin after patient induction and stabilization, the same provider groups case end, the same environmental sites at case end, and the stopcock case end. Finally the Postoperative Arena will entail surveillance any of these areas to which patients are transported such as day of surgery second stage, postanesthesia care unit, intensive care unit, floor (ward). Sites sampled will include primary nurse hands (one measurement), same patient sites (N=3), environmental sites (bed rail, side table, sink---same swab), surgeon attending hands (if present), and resident attending hands (if present).

Kits will be transported to RDB Bioinformatics laboratory for processing following sample acquisition. The dynamic surveillance software platform will guide proven, systematic phenotypic and genomic processing of collected samples in order to identify clonal transmission events occurring within and between operating room reservoirs in the observational unit (case pair). Guidance will be based on the strength of epidemiological-relatedness as follows: A transmission event will be defined as the presence of one or more isolates in a measured reservoir that was not present at case start. Transmission events within an observational unit will be further analyzed as directed by the RDB platform to identify clonally-related S. aureus transmission events.

The RDB Bioinformatics software platform will process transmission dynamics in order to continually summarize the epidemiology of S. aureus transmission. This information will be continually displayed in order to identify the most common reservoir of origin, the most common transmission locations (vectors), the most common mode of transmission (vertical or horizontal), and involvement of key portals of entry (stopcocks). To address strain characteristics, reports will focus on more pathogenic strains defined by the top 5 most transmissible, resistant, and virulent strain characteristics.

Automated analysis reports for overall transmission and for transmission of more pathogenic strains will be used by the infection control perioperative team to continually optimize the interventions affecting all patients in the treatment clusters as described further below. The platform will automatically quantify

transmission events occurring in treatment and control clusters such that involved in data collection and data entry will be blinded to the primary outcome.

All data will be analyzed by the statistician (Dr. Todd MacKenzie) at Dartmouth Hitchcock Medical Center who will not be involved in data collection.

Work flow: Monday-Friday only. Limited to patients that are seen in UIHC clinics. 1,000 case pairs: (500 treatment and 500 usual care) will be studied during the 2-year study period. This corresponds to one case pair in the "bundle" group and one case pair in the usual care group each day (5 days a week for 50 weeks each year). All patients will be followed for 90 days for infection development.

Data Handling: A multidisciplinary infection control perioperative team (the team) comprised of surgical, nursing, anesthesia and infectious disease providers will manage the information provided by the S. aureus transmission surveillance instruments to proactively optimize the multimodal program outlined below.

Treatment Interventions: The following applies only to 500 patients in the "bundle" treatment group (500 patients will be sampled in the clinic and will receive the bundle. The case to follow the screened patient in the OR will be included in order to determine whether the optimized bundle for the first patient can prevent transmission of S. aureus to the second patient. The second patient will not receive the bundle. They will receive usual care. Both patients in the 500 treatment pairs (1000 total patients) will undergo surveillance). The 500 patients that are screened in the clinic in the control group will undergo usual care as will the patient to follow. Both patients in the 500 control pairs(1000 total patients) will undergo surveillance.
• Improved patient decolonization: The additional decolonization with povidone-iodine addresses antibiotic stewardship because S. aureus is becoming more resistant to topical antibiotics as a result of widespread use.
• Improved vascular care and hand hygiene: All patients in the "bundle" treatment will receive closed, disinfectable stopcock sets (Ultraport Zero, BBraun Medical Inc, Bethlehem, PA 18018-3524), and catheter disinfection will be optimized with HubScrub and DOCit disinfection caps that address both the injection port and syringe tips (Saxa Medical Solutions, Mentor, OH 44060-4862) and leverage desiccation and mechanical disruption. Perioperative stopcock contamination rates will be monitored by surveillance reports filtered by stopcock involvement, and monthly reports of contamination will be used by the team to optimize catheter care via individual and group feedback. The vascular care system also contains a hand hygiene unit designed to link hand decontamination events with vascular care via proximity.
• Improved environmental cleaning: Environments (OR and ward) affected by high-risk S. aureus transmission events will be mapped by surveillance and addressed by automated reporting to the anesthesia workroom supervisor. This will trigger improvements in routine (standard cleaning using quaternary ammonium compound and micro cloth followed by a surface disinfection wipe) and terminal [improved routine technique followed by employment of robotic cleaning (Ultraviolet light)] cleaning. Fatigue mitigation: The team will use surveillance to continually monitor the impact and fatigue of the proposed interventions as conveyed by failure mode analysis of transmission dynamics involved clonal S. aureus transmission.

XI.2 ***Provide the rationale or power analysis to support the number of subjects proposed to complete this study.***

Statistical Analysis: The unadjusted primary intention to treat analysis will compare the proportion of clonally-related S. aureus transmission events occurring in treatment vs. control perioperative (preoperative, intraoperative case pair, and postoperative) observational units across the 6 randomized service lines using the Chi squared test. We will assess for balance for variables known to be associated with intraoperative transmission (case, duration > 2 hours, and discharge location). In the case of imbalance, we will use multivariate techniques to further explore the treatment effect using a generalized linear models approach.

Initial Power Analysis (see amendment below based on reviewer concerns): We intend to screen a total of 1000 patients for up to 10 surgical service lines. Service lines will be randomized 1:1, yielding 500 patients in each treatment arm. Each patient will provide 4 observational units that include preoperative to intraoperative, intraoperative case 1 to intraoperative case 2, intraoperative case 1 to postoperative, and preoperative to postoperative opportunities for detection of S. aureus transmission. Thus, 500 patients in each arm will provide 2,000 observational units for a total of 4,000 observational units during the two-year study period. We originally calculated that this provided 90% power to detect a 30% relative reduction in the primary outcome (10.58% down to 7.41%). The estimated clonally related S. aureus transmission rate was based on a previously reported detection rate of 58 events in 548 observational units for all-comers to the operating room at 3 major academic medical centers in the United States. To address service line variation, we supposed that the logit-frequencies of the primary outcome for each service line were distributed as a normal distribution with a mean of -0.41 and standard deviation of 0.20. This amount of between-line variation corresponds to an intra-cluster correlation (ICC) of approximately 1%. It can also be interpreted as the amount of variation in which service lines in the top quartile of rates would have an average frequency (after removing within subjection binomial variation) of 46% while service lines in the lowest quartile have an average frequency of 33%. These calculations were accomplished using Monte Carlo simulations written in R 3.3, and using in part the following approximation for the ICC when rates are logit-normal, 1/(1+1/[pa(1-pa)s2 (which can be readily derived using the delta theorem) where pa is the average frequency across centers and s is the standard deviation on the logit scale. We calculated that this provides 85% power to detect a 30% relative reduction in the primary outcome (40% down to 28%) if there is significant variation between service lines. If indeed there is no variation between service lines, the power is 98%.

We expect to lose some patients that are consented and enrolled in this study to non-compliance with study protocol. There may also be instances where the first OR case consented to the study but the following OR case does not consent on the day of surgery, making it an ineffective pairing for the study. Patients may also consent to the study when in the surgical clinic but change their mind and not consent to the study on the day of their operation. It is the patient's right to be able to exit the study at any time. In anticipation of patients who are consented but are not able to be used in the study we will need to consent more than the minimum 2000 total patients to reach the needed power. We estimate that consenting 2800 patients will give us enough room after drop-out/ineligibility due to a number of causes to generate a final amount of 2000 (as detailed above) successful patients that generate data for out study.

We have completed a pilot study at UIHC to evaluate the above power analyses. The pilot involved bacterial surveillance in approximately 40 observational units, or 80 cases. A total of 81 cases were enrolled because there was an unexpected cancellation. The primary outcome was intraoperative S. aureus transmission events. For the pilot, transmission events were defined as possible epidemiologically-related events, not yet clonal-additional testing required.

Below is a summary of the case-pairs observed stratified by service line.

Case Type # of Cases
Colorectal 10
Cardiothoracic 2
Gyn/onc 24
Orthopedics 44
Vascular 2
Total Cases 81

As orthopedic and gyn/onc procedures represented the majority of randomized units, we considered that those cases would serve as the best estimates for service line variation in S. aureus transmission detection. The incidence of S. aureus transmission detection ranged from 28% (orthopedic cases) to 58% (gyn/onc) cases. These results support our prior assumptions of anticipated service line variation, power calculations, and study design, and the variation is likely to be less with additional genomic analysis. Our hope is that this additional work and discussion can alleviate the reviewer concerns regarding study design.

XII. Future Research

XII.1 ***Do you wish to keep any information about subjects involved with this research project so that members of the current research team may contact them in the future for your own research projects?***
No

XII.2 ***Do you wish to keep any information about subjects involved with this research project so that other researchers may contact them for future research?***
No

XII.4 ***Does this project involve storing any data, tissues or specimens for future research?***
Yes – contribution for future use is mandatory for participation in the study