Protocol with Statistical Plan Cover Page

Title: **S**top Comm**u**nity MR**S**A Colonizat**i**on **A**mong Pat**ie**n**t**s (SUSTAIN)

Protocol Date: 6/10/2013

NCT: NCT02029872

Date: 6/10/13

Principal Investigator: Jason Farley, PhD, MPH, NP

Application Number: NA_00079147

1. Abstract

Methicillin resistant *Staphylococcus aureus* (MRSA) kills more patients in the United States (U.S.) than Acquired Immunodeficiency Syndrome (AIDS)[1]. Further, persons living with Human Immunodeficiency Virus (HIV) experience MRSA infection at significantly higher rates than the general population (12.3/ 1000 person years compared to 1 to 2/1000 person years)[2] and MRSA remains a substantial reason for hospital admission among this patient population[3]. Colonization with *Staphylococcus aureus* is a major risk factor for infection in persons living with HIV and AIDS (PLWHA)[4] and eradication of MRSA colonization reduces the occurrence of subsequent infection in patients[5]. Household contacts with MRSA colonization increase failure rates of decolonization[6]. The clinical practice guidelines for MRSA management from the Infectious Diseases Society of America (IDSA) recommend providing decolonization to persons with repeated skin and soft tissue infections as well as their household contacts; however, the guidelines report that evidence is limited in support of this recommendation[7]. Additionally, these recommendations do not include sexual partners outside the home and there is mounting evidence of MRSA transmission between sexual partners and sexual networks[8]. Strategies that reduce the spread of MRSA among people living with HIV/AIDS (PLWHA) are vitally needed[9] to reduce this disparity.

To assess colonization prevalence among PLWHA, we conducted an epidemiologic evaluation of MRSA among persons within the Johns Hopkins University AIDS Service (JHUAS). The study included 500 subjects (65.8 % male) along with the sexual partners of 35 subjects. The MRSA colonization prevalence was 16.8% among subjects and 37% (17/35) in their sexual partners (unpublished data). These findings demonstrate an exceptional difference in colonization prevalence in PLWHA compared to the US population[10] and supports the need for further research to understand decolonization regimens that evaluate outcomes for individual decolonization only compared to the inclusion household and/or sexual partner interventions. We propose a randomized controlled trial (RCT) among 100 PLWHA (50 per arm) within the JHUAS to evaluate an individual versus household/sexual partner decolonization intervention.

2. Objectives/Aims

The specific aims of the proposed RCT are:

1. To compare a MRSA decolonization protocol for the colonized individual (index) versus the index plus their household member and/or routine sexual partner(s).
   H0: Index plus household/sexual partner(s) decolonization will be associated with a lower occurrence of MRSA colonization at 6 months after completion of decolonization protocol.
2. To estimate the intervention effect size and develop an intervention fidelity assessment plan to scale the intervention into a larger multi-city R01 application.
3. To determine the molecular characteristics and antimicrobial susceptibilities of both the clinical and colonizing isolates among index patient as well as household members.

3. Background

Community-associated methicillin resistant *Staphylococcus aureus* (CA-MRSA) greatly impacts health outcomes among PLWHA. Outbreaks of CA-MRSA skin and soft tissue infections have occurred in metropolitan areas throughout the country including San Fransisco[11], Boston[12] and Dallas[13]. These outbreaks have identified key risk differences for CA-MRSA colonization and/or infection among this population

including substance abuse [14;15]; high risk sexual practices including men who have sex with men and heterosexual persons with multiple sexual partners[16] as well as a sexual partner with a known skin infection[16]. Risk for MRSA infection also includes lower CD4 counts[12;13;16]; high viral load[12;17]; recent hospital admission[18]; β-lactam antibiotics[11]; routine hands on contact with customers at work[16]; lack of cotrimoxazole prophylaxis[13;17]; and known MRSA infection in the last 12 months[11]. Due to routine interaction with the healthcare system, PLWHA who are colonized with MRSA may serve as a reservoir for fueling healthcare associated transmission. The identification of high risk community groups harboring MRSA is integral to the prevention of transmission within vulnerable populations.

A recent open-label randomized controlled trial among 183 HIV negative pediatric patients with community-onset *Staphylococcus aureus* skin infections compared decolonizing the entire household versus the index child with skin infection alone. The researchers found the intervention to be successful at prevention of skin infection, but it did not lead to greater *S. aureus* eradication in the colonized children. The team hypothesized this finding to be a result of MRSA contacts outside the home[19].

In this proposed research, we plan to test whether a decolonization intervention has greater impact if applied to all members of an index patient's household and/or sexual partner network as compared to only the individual patient. In a prior HIV/MRSA prevalence study, we conducted whole body surveillance for MRSA. Through that study, we have identified high and low yield body sites and have reduced the total number of body sites that will be evaluated in this study. We have also modified the risk factor questionnaire previously approved in prior studies, to simplify the document and update it with the most recent MRSA and HIV literature.

4. Study Procedures

The applicant proposes a prospective, randomized controlled open-label trial known as SUSTAIN, or **S**top Comm**u**nity MR**S**A Coloniza**t**ion **a**mong Pat**i**e**n**ts. The SUSTAIN trial will evaluate MRSA decolonization and determine differences in the prevalence of MRSA colonization (main outcome) at 6 months. Patients with a known history of MRSA colonization will be recruited from the (JHUAS). After consent and baseline MRSA screening, index subjects (50 per arm), described below, will be randomized to a standardized decolonization protocol directed at both the individual and their household and/or sexual partner(s) or a decolonization for the individual alone. Each index (i.e. person living with HIV within the Johns Hopkins Moore Clinic) will be approached for enrollment in the study. Information flyers, study rotating digital kiosk and provider referral will be used for recruitment. We will also search the Johns Hopkins Hospital Epidemiology and Infection Control (HEIC) database for known MRSA colonized individuals and contact former study participants.

SUSTAIN Standardized Decolonization Regimen (intervention):

According to the IDSA clinical practice guideline[7], the standardized decolonization regimen for the nose and groin will include a 5-day course of nasal mupirocin calcium 2% cream applied inside the nose twice daily, plus a 4% chlorhexidine gluconate (soap) used in the shower/bath every day for 10 days[20],[19]. For individuals colonized within the throat we will add chlorhexidine gluconate oral rinse 0.12% used in a gargle and spit fashion twice daily for 7 days. A standardized educational session on use and accompanying CDC instructional frequently asked questions handout and an instructional medication sheet will be provided. For children < 7 years of age, we will provide decolonization using 4% chlorhexidine gluconate (soap) used in the shower/bath every day for 10 days. No antimicrobial cream or gargle will be utilized. If an adult household member or sexual partner is colonized at a single site, he or she will receive the soap, rinse and Mupiricin cream. If he/she is not colonized at any body site, no decolonization regimen will be provided.

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ENROLLMENT:

Patient Population/Setting:

The Johns Hopkins Hospital is located in Baltimore, Maryland, an urban area with a high incidence of HIV infection. Greater than 50% of our clients reside in East Baltimore; > 75% reside within the city limits. In 2010 we provided HIV primary and specialty services across all clinics to approximately 3200 patients. On average, 971 individual patients are seen monthly for HIV care alone. The Moore Clinic site is an outpatient clinic located in East Baltimore. The demographics of the patient population at this clinic parallels the HIV epidemic in Maryland: 37% women; 81% African American; mean age of 39 years; and self reported risk group of the following: 18% men who have sex with men (MSM); 4% MSM and intravenous drug user (IDU); 38% IDU; 33% heterosexual transmission; and 7% other/unknown. Dr. Farley's prior work in this clinic identified a 15.2% prevalence of MRSA colonization among 500 subjects in this clinic.

Eligibility: See inclusion/exclusion criteria below.

Adult Index Subject Consent: Subjects will be approached after they have been identified through one the methods described above in Study Procedures. The consent process will be completed in a private area of the Moore Clinic or CRU. The consent form will be read aloud to any participant that has difficulty with reading. The consent has been developed on a 5th grade reading level.

Adult Household and Sexual Partner Consent: Household members may be consented as individuals or as a group with a research assistant reviewing the protocol with the individual or household/family at their chosen location (i.e. at home or at the CRU). Each adult member of the household, 18 years of age and older, will be provided with a copy of the consent form and asked to read and sign. Sexual partners who may be outside the home will be consented separately at the location of his/her choosing. The consent has been developed on a 5th grade reading level.

Adolescent Consent: For eligible subjects 14-17 years old we will follow these procedures:

1. Adult consent, at a 5th grade reading level, will be used and we will follow the same pattern as the adults. For our purposes, the adolescent will be asked to identify a parent or legal guardian from whom permission for enrollment can be obtained.
2. After review of the trial (i.e. review the key elements of informed consent), if the adolescent remains interested in participation we will encourage the adolescent to discuss the study and decide together with their parent or legal guardian about enrollment.
3. Adolescent will sign the form with the parent or legal guardian signing as a witness.

Parental Permission/Pediatric Assent: For subjects 7 to 13 years old we will follow these procedures:

1. The study will be discussed with the child including a demonstration of the cotton swab procedure as well as the intervention procedures, as applicable.
2. The child will be provided a Research Assent Form for Children and will be included in the discussion with the parent/guardian or legally authorized representative (LAR).
3. The child will sign the Research Assent Form.
4. Parent or LAR will provide permission/consent for the child's participation.

Parental Permission: For eligible subjects less than 7 years of age we will follow the following procedures:

1. We are requesting a consent waiver for all children up to 7 years of age.
2. Parent or LAR will provide permission/consent for the child's participation.

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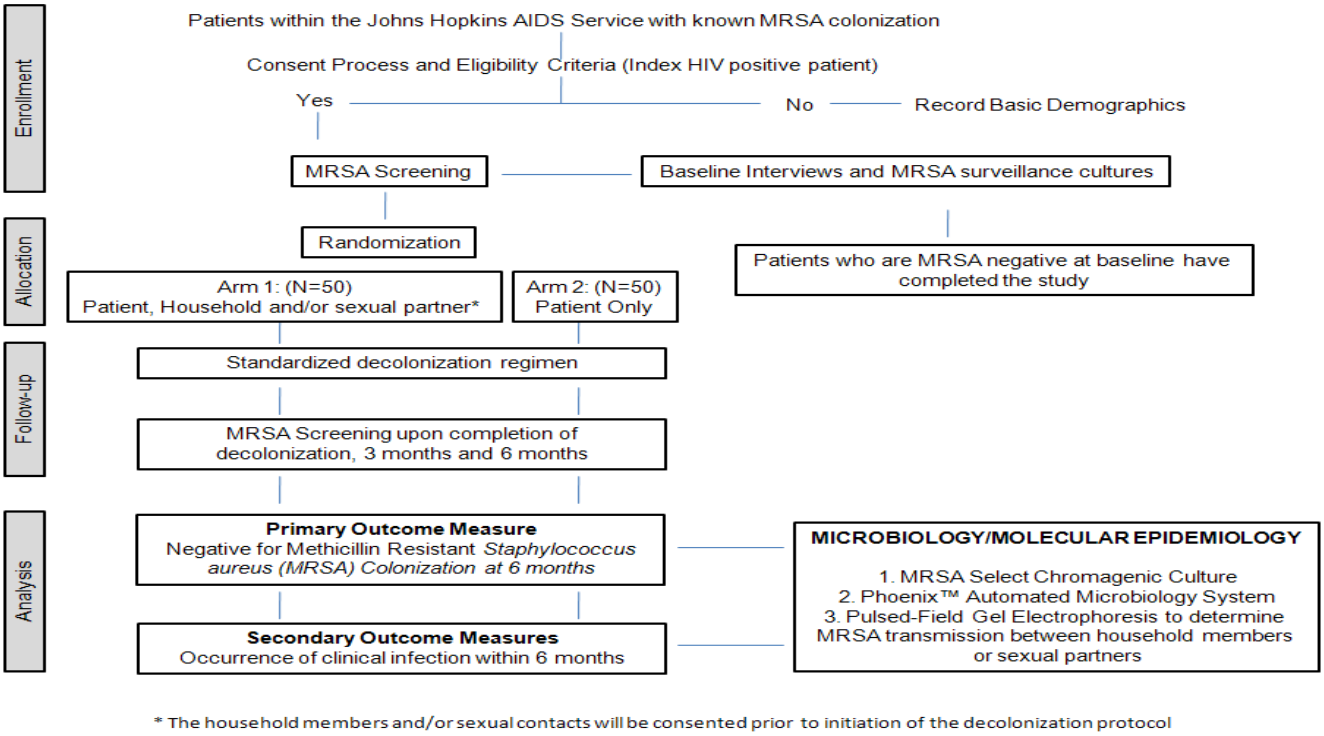
Assessment of Adult/Adolescent Protocol Comprehension Prior to Signing Consent: After the consent form is read, the RA will evaluate comprehension with three protocol specific questions: 1) what is the name of the bacteria or germ that we are trying to get rid of?; 2) How does this study plan to get rid of this bacteria or germ?; how will you be assigned to the different options in this study? We will deem the subject to have an acceptable level of comprehension based on their ability to answer those questions.

ALLOCATION:

Randomization: This study has taken into consideration the guidelines for reporting of clinical trials as recommended by the CONSORT report[21] to inform the study design (Figure 1). After recruitment and informed consent, patients will undergo pre-randomization screening. Patients who screen negative for MRSA at this point will have completed the protocol. Patients screening MRSA positive will then be randomized to the two possible open-label treatment arms. Arm 1 will include randomization to standardized decolonization protocol of the individual plus household and/or sexual partner(s). Arm 2 will include randomization to standardized decolonization protocol for the individual patient alone. Randomization will occur through computerized random number generation in Stata, version 11. A simple parallel randomization design will be utilized. Once developed, this randomization scheme will be placed in an individually concealed enveloped. The RA will not be aware of the randomization scheme of the individual envelopes until opened in front of the patient on the day of randomization.

Figure 1: SUSTAIN Study Design Overview



Data Collection Measures:

The risk factor questionnaire used in the proposed study has been thoroughly evaluated with over 1000 subjects (50% with HIV). Questions have been added or removed as applicable to this patient population. The

questions in the protocol can easily be administered by a study team member in 20 minutes. The questionnaire has been thoroughly evaluated by experts in the field of hospital epidemiology and infection control for content validity. In addition to the subject questionnaire, each instrument contains an additional section for the research team to interrogate the patient's medical record to verify specific pieces of the medical history such as CD4 count, medication history, viral load, etc. Adolescents will complete the questionnaire, but for children younger than 13, we will have the parent complete the risk factor questionnaire. Each document ends with a microbiology results page for the principle investigator (PI) to complete.

MRSA Screening Procedures:

Index patients will either 1) self refer by contacting the research assistant after seeing flyers or posted signs on the Moore Clinic revolving kiosk screen; 2) be referred from their HIV provider in clinic; or 3) be contacted by the research assistant (RA) based on known history of MRSA status from either prior participation in MRSA research studies directed by Dr. Farley or through the MRSA screening flag placed in the electronic patient record by hospital epidemiology and infection control. Screening will take place after the index patient has contacted our research team to schedule a time for an appointment within the Clinical Research Unit (CRU) or at their home based on individual preference. The PI and/or RA will provide information regarding the study, answer any questions and obtain informed consent. The PI will be available in person or via telephone to answer any questions when an RA is present for the consent. Once enrolled, the RA will assign a study identification number (SIN) to the subject. This will be the primary mode of identification throughout the study. The SIN will appear on the consent form, the questionnaire, as well as all MRSA cultures. As part of the informed consent document, the subject will receive information on how to contact the investigators to discuss culture results or any noted treatments that may be related to *S. aureus*.

During the study visit, the RA will provide the clinician with the necessary swabs for MRSA screening and will complete or assist with collection as needed. All patients presenting to the outpatient HIV clinic who are willing to undergo testing will be screened by obtaining a swab from the following anatomical sites: anterior nares, the throat, the groin/perineum, the vagina (for women) and rectum. The standardized check-list for obtaining and processing swabs has been outlined and is available for review in Appendix A.

All swabs will receive a study number pre-printed on a label. The SIN will not identify the patient's name, medical record number or other identifying information. The SIN will be used for data analysis purposes and will be recorded on the informed consent documents, the risk factor questionnaire and the surveillance swabs. Before sending the swabs, the RA will take a brief "time-out" to reassess that all paperwork is completed, swabs appropriately labeled with SIN and medical record #, as appropriate, and that all informed consent, questionnaire and swabs all contain the same SIN.

Screening of Adult Household Contacts and Sexual Partners:

All household contacts in both arms of the study will be offered MRSA screening. We will complete the same procedures for adult household contacts and sexual partners described above. Contacts will receive swabs of the same body sites with each swab labeled with the same study ID # as the index case, but with the addition of HC # and SP # to identify household contact and sexual partners respectively. This will assist us with identification and linkage during the molecular epidemiologic evaluation of the isolates.

Screening of Children/Adolescent Household Contacts:

For children/adolescents under 18, we would screen nares, throat and rectum only. All screening of the child up to 12 years of age would be conducted with the parent present. Adolescents will be asked whether or

not they wish for their parent to be present during the rectal swab. All swabs will be conducted in the presence of two adults (either RA and parent or two RAs). Adolescents between 18 years of age and 21 years of age will receive the adult screening protocol sites.

Study initiation after screening:

After results for the index subject are obtained, a member of Dr. Farley's team will contact the subject to review the results and randomize the MRSA positive subject into the intervention or control arms. Subjects in the individual arm, will initiate after learning results at the clinic follow-up visit. For individuals assigned to the intervention group, we will schedule a time for a home visit to screen household members or a time in the CRU for evaluation. This screening visit will occur within 14 days of obtaining the original culture results. All household members will then initiate the intervention at the same time.

Microbiological Measures:

We will utilize the following microbiologic procedures: Following the current gold standard, each swab will be streaked onto CHROMagar-MRSA (BD Diagnostics, Inc.) a selective MRSA medium, and then placed in Trypticase soy broth (TSB) with 6.5% $NaCl^{22}$ to enhance Staphylococcal identification. CHROMagar-MRSA plates are incubated at 35˚C and reviewed at 24 hours. Mauve colored colonies on CHROM-MRSA will be confirmed as *S. aureus* (SA) by Gram stain and latex agglutination (Staphaurex Plus [Remel, Lenexa, KS]). All MRSA isolates will then undergo molecular characterization using pulse-field gel electrophoresis (PFGE), a molecular epidemiologic approach that facilitates identification of patterns in the genetic structure of bacteria to determine if transmission has occurred. Our team has extensive experience with this molecular typing mechanism.

FOLLOW-UP:

Patient Evaluation Time Points: After informed consent, each subject will undergo pre-randomization MRSA screening followed by completion of a risk factor screening questionnaire as part of the baseline visit. Results of these tests will be available in 24 hours. After culture results are available, the study team will randomize the subject and provide the required decolonization materials and schedule a start date. For individuals randomized to the arm including their household members/sexual partner, a date will be scheduled to visit the home or CRU. Once the decolonization protocol is complete, a follow-up MRSA screening assessment and adherence evaluation will occur (Visit #1). All subjects will be provided personal hygiene and household cleaning instructions. Based on this date, the research assistant will determine the date of the 3 (Visit #2) and 6 (Visit #3) month follow-up for subsequent risk factor and microbiologic evaluation. Study visits and variables collected at each visit are summarized in table 1.

Table 1: Timeline for Study Data Collection and Assessments for all participants

	Baseline	Visit 1	Phone	Visit 2	Phone	Visit 3
Data to be collected	**Pre-**	**Post-**		**3**		**6**

	Screening and Consent	decolonization MRSA Screening	check-in	month	check-in	month
Full ACASI Risk Factor Questionnaire	X					
Abbreviated ACASI Risk Factor Questionnaire				X		X
MRSA Screening	X	X		X		X
Molecular Evaluation	X					X
Telephone contact for appointment reminder			X		X	

5. Inclusion/Exclusion Criteria

Eligibility Criteria:

Individuals, 21 years of age and older, of all racial and ethnic groups, receiving care within the JHUAS who have a prior history of MRSA colonization are eligible to participate as the index HIV positive subject. This person should have at least two members in the household and/or a sexual partner. A post-consent pre-randomization screening phase will be completed to ensure subjects are MRSA colonized. In addition to these criteria subjects must be willing to be randomized to either arm of the study, including randomization to household and/or sexual partner evaluation. Sexual partners and/or household members will also be required to provide informed consent. Subjects and their contacts must have no documented or reported allergies to any agent used in the standardized decolonization regimen. Parental assent will be required for household members less than 7 years of age. Exclusion criteria include: allergy to any component of decolonization protocol; individuals who live alone and have no active sexual partners; individuals who are unable to provide written informed consent.

Recruitment Strategy:

Study team members will speak with JHUAS providers to discuss the study and seek patient referrals (i.e. index patient). A HIPAA waiver will be sought in order to obtain a list of patients with a known history of MRSA colonization from Johns Hopkins Hospital Epidemiology and Infection Control Department. In the HIPAA waiver, we are asking to contact the patient's provider in the Moore Clinic to inform of the patient's eligibility for the study prior to the subject seeing his or her provider in clinic. The provider could then inform the patient of their eligibility and ask if we can contact them about the study. Dr. Farley's previous work has already identified over 70 JHUAS patients with a known history of MRSA colonization. The patients in this prior study have agreed to be contacted for future studies when they signed informed consent. We have included details for a HIPPA waiver to evaluate this information in this IRB application. We have also

completed a HIPPA form 3 to document that we have permission to contact the index patient again for future studies on MRSA in this patient population. These index HIV positive patients will be approached for study screening during a clinic visit or via telephone to schedule a study visit. Index HIV positive patients will receive a $25.00 gift card on completion of the protocol. We will offer household members a single gift card of $50.00 regardless of the number of participants.

Recruitment of Household Members/Sexual Contacts:

To avoid disclosure of personal health information (PHI), the index patient will be given the option for a home visit by the research team or they and their household members and sexual contacts can be screened at the Clinical Research Unit (CRU). We will work closely with the IRB/DSMB to protect subject's PHI. Recruitment of the primary sexual partner and or family members will occur by referral from the enrolled subject. During the risk factor evaluation, the subject will be asked, "In the last 6 months have you had sex?" We then ask several follow-up questions on sexual activity. The enrolled subject will be asked to refer his/her primary sexual partner, the person the subject most frequently engages in anal, vaginal or oral sex with, to the study. At no time will study data of either the primary subject or the subject's sex partner be shared by the research team to the other participant regardless of their awareness of the other partner's status. Neither the screening process, nor the questionnaire reveals any information about HIV status.

6. Drugs/Substances/Devices

According to the IDSA clinical practice guideline[7], the standardized decolonization regimen for the adult colonized in either the nose or groin will include a 5-day course of nasal mupirocin calcium 2% applied inside the nose twice daily, plus a 4% chlorhexidine gluconate (soap) used in the shower every second day for 10 days[20]. For individuals colonized within the throat we will add chlorhexidine gluconate oral rinse 0.12% used in a gargle and spit fashion twice daily for 7 days. A standardized educational session on use and accompanying instructional handout will be provided. Children under 6 months will not be included in the study. For children over 6 months and <7 years of age 4% chlorhexidine gluconate (soap) used daily for 10 days. For children over the age of 7, we will follow the same protocol as adults.

7. Study Statistics

ANALYSIS*:*

Dependent Variable (DV): The DV is a group of mutually exclusive, non-ordered outcomes which include: negative for *S. aureus,* positive for methicillin susceptible *S. aureus,* positive for methicillin resistant *S. aureus.*

Independent Variables: A thorough search of the available literature has been completed to develop the risk factor questionnaire designed for this study[23]. The questionnaire includes: demographic data, medical history, sexual history, substance abuse history, as well as healthcare associated and community-based MRSA risk factors.

Sample Size: Based on prior studies, it appears that the probability of MRSA colonization at 6 months after decolonization ranges from 60% to 80%. Although an exact effect size is not known for individuals with household/sexual partner decolonization, we have considered both feasibility and public health importance. We believe the intervention will achieve a 50% reduction in colonization at 6 months (i.e. 30% colonization [0.30]

in the arm with individual and household/sexual partner decolonization compared to 60% [0.60] colonization in individual alone arm). **Based on these figures and an alpha of 0.05, the total sample size required to achieve approximately 80% power is 41 per arm.** We anticipate 20% attrition and will oversample by 9 subjects per arm, bringing total sample size to 50 per arm.

Statistical Analysis Plan: Demographic variables will be evaluated using chi-square and Fisher's exact testing as appropriate. Fisher's exact will also be utilized to compare proportion of persons colonized at 6 months. Multinomial logistic regression will be used to determine the odds of subsequent MRSA colonization in the two arms and to determine the magnitude of the effect size between the arms.

LIMITATIONS AND PLAN TO ADDRESS:

As with any clinical trial, this study has possible limitations:

1. Confidentiality. In any study that includes recruitment of individuals with a specific disease process; careful discussion of these risks will be required within the informed consent process. At no time will the HIV status of the index patient be disclosed to the household member and/or sexual partner. Although persons living with HIV serve as the index patient group, the study is specific to MRSA decolonization and subsequent prevention of infection. The consent form does not mention HIV status to avoid disclosure of HIV status to potential family members.
2. Willingness of participants to participate. This study will require participants to be willing to undergo bacterial culture of private anatomical areas. In a prior JHUAS MRSA evaluation, Dr. Farley obtained these specimens in 100% of participants. The study team will work with providers within the JHUAS to recruit subjects with a history of MRSA colonization and/or infection.
3. Loss to follow-up. To ensure retention, the researchers have provided the subject with several possible methods of communication that the subject may select to best suit his/her individual needs. We will collect name, address and telephone number along with e-mail address as available for each subject. This communication will meet all necessary requirements for HIPAA to maintain confidentiality and privacy. As an incentive to encourage follow-up and participation, each subject will be offered a $25.00 a gift card, which they will receive upon completion of each follow-up visit. We have also built into our sample size calculation a 20% oversampling in case these methods fail. Research assistants will contact the patient daily during the decolonization phase of treatment to ensure fidelity with the prescribed treatment regimen and to monitor for adverse drug reactions associated with this treatment regimen.
4. Access to all community contacts. We will be unable to test and/or evaluate all possible contacts. This may present a potential for selection bias into the study for individuals who are less sexually active or persons whose sexual partner is within the household. We will encourage all participants to provide contact details of all known consistent sexual partners, but will not seek casual sex partners.

Study Timeline:

The following 3-year study timeline provides an overview of the study preparation period, enrollment and follow-up (Table 2).

Table 2: Timeline

Year	First 6 months	Second 6 months	Year 2	Year 3

Date: 6/10/13

Principal Investigator: Jason Farley, PhD, MPH, NP

Application Number: NA_00079147

Task	Preparation	Enrollment	Enrollment	Follow-Up
IRB Process				
Identify/Train Research and Lab Assistants				
Recruitment/Informed Consent/Screening				
Decolonization and Study Visits				
Surveillance for Clinical Infection				
Microbiologic Evaluations				
Data Entry and Statistical Analysis				
Present at Meetings and Publish Data				
Preparation of application for R01				

8. Risks

Potential Risks:

The risks for this study are minimal. There is a very small risk of bleeding associated with swabbing mucosal membranes; however, our institution has a long standing history of obtaining nares surveillance cultures for MRSA without any reported adverse events. Standard precautions will be applied for protection of the RA and/or clinician during specimen collection. All swabs will be collected in a private exam room. A clinic gown will be provided for the patient to protect modesty and privacy during collection. A female chaperone will be present at all times when specimens are being obtained from a female patient by a male clinician as is standard in our clinic during gynecologic evaluations.

Allergic reactions to mupiricin and/or chlorhexidine are rare. Patients with known allergy will be excluded from the study. All agents are FDA approved for the purposes used in this study.

Mupiricin Cream Possible Adverse Effects:

Local adverse effects may be associated with mupirocin application. Mupirocin ointment or cream may commonly cause itching, pain, stinging, and burning. Local effects from the nasal formulation have included epistaxis, rhinitis, taste perversion, pharyngitis, burning, and cough. Gastrointestinal side effects have included nausea (1.1%), abdominal pain (<1%), and diarrhea (<1%). Dry mouth has been reported with mupirocin nasal (<1%). Nervous system side effects associated with intranasal mupirocin have included headache (9%). Dizziness has been reported with mupirocin ointment (<1%). Ocular side effects associated with mupirocin nasal ointment have included blepharitis (<1%).

Chlorhexidine gluconate Oral Rinse Possible Adverse Effects:

Oral irritation and local allergy-type symptoms have been spontaneously reported as side effects associated with use of Chlorhexidine gluconate rinse. The following oral mucosal side effects were reported during placebo-controlled adult clinical trails: aphthous ulcer, grossly obvious gingivitis, trauma, ulceration, erythema, desquamation, coated tongue, keratinization, geographic tongue, mucocele, and short frenum. Each occurred at a frequency of less than 1.0%. Among post marketing reports, the most frequently reported oral mucosal symptoms associated with Chlorhexidine gluconate oral rinse are stomatitis, gingivits, glossitis, ulcer,

dry mouth, hypesthesia, glossal edema, and paresthesia. Minor irritation and superficial desquamation of the oral mucosa have been noted in patients using Chlorhexidine gluconate oral rinse. There have been cases of parotid gland swelling and inflammation of the salivary glands (sialadenitis) reported in patients using Chlorhexidine gluconate oral rinse.

Chlorhexidine gluconate Topical Soap:

The soap may cause burning and dryness of the skin. It may cause burning of the eyes. Skin erythema and roughness, dryness, sensitization, allergic reactions are possible, but rare.

Protection against Risks:

The study team recognizes that subjects may seek advice about issues beyond the scope of this study and will refer all non-study related health issues to the patient treating clinician. Any acute, previously undiagnosed, infection or any infection that appears to be worsening by a study team member will follow the standard procedure of evaluation by either referring the patient to the Johns Hopkins Adult emergency room or the Moore Clinic's acute evaluation clinic after the study team member has contacted the PI and the PI has notified the subject's primary HIV/AIDS clinician about this referral. For skin and soft tissue infections, the RA will accompany the patient to the site of clinical evaluation (i.e. Adult emergency room) in an effort to obtain wound cultures from the site. All other specimens will be obtained through consultation with microbiology upon their receipt of the subject's clinical specimen.

To protect against breaches of confidentiality regarding the patient's HIV status we will hold all sexual partner evaluations in the CRU in a location outside but adjacent to the Moore Clinic. Each study team member is explicitly aware that we will not disclose HIV status of the referring subject at anytime. Further, we have worded the questionnaire in a manner that does not lead on or disclose HIV status in the document.

Adverse drug reactions will be recorded for each patient and any ADR that results in breach of study protocol will be reported to the IRB within 7 days of the event. None of the agents used in this protocol are experimental and each has proven efficacy for use consistent with the intended use in this protocol.

Home Visit Safety Measures for Study Team:

All home-based study visits will occur with two research assistants. These RA's will carry a cell phone at all times. The RA will communicate with the PI before completing a home visit through a home visit screening log maintained separately from study materials. This log will identify the subject name and address and the time expected to arrive and depart the home. The RAs will send a text message on arrival and departure from the home to the PI or his designee. Any witnessed child or elder abuse in the home will be reported to appropriate authorities once the RA is in a safe place to do so.

Data Management and Security:

Study data will be collected and managed using REDCap (http://www.project-redcap.org) which is a secure, web-based application designed exclusively to support data capture for research. The Johns Hopkins University is a member of the REDCap consortium and this application is freely available to consortium members. REDCap provides: 1) an intuitive interface for data entry (with data validation); 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages (SPSS, SAS, Stata, R); 4) procedures for importing data from external sources; and 5) advanced features, such as branching logic and calculated fields. To maximize quality control, staff will be trained by the PI in all data collection and entry procedures. The PI will have access to all data upon entry

into REDCap. The research coordinator will monitor data collection by checking completed questionnaires for completeness. Study team members will have the access codes to enter and retrieve these data based on pre-determined job requirements.

Development of Data Safety Monitoring Board:

Although not required by the funding agency, the PI and his study team have developed a DSMB to monitor the conduct and safety of participants within the trial. The goals of this DSMB will be review of research protocol and study activities, review of data quality and completeness, fidelity to study protocol, review of participant recruitment and retention, adverse events. The board will make recommendations to the IRB and the investigative team concerning trial continuation, modification or conclusion. The DSMB will consist of the following members:

- Jackie Campbell, PhD, RN, FAAN: Dr. Campbell is a Professor within the JHU Schools of Nursing/Medicine/Public Health, a researcher and clinician in women's health. She is the co-director of the Johns Hopkins Center for AIDS Research (CFAR) Development Corp.
- Sarah Szanton, PhD, CRNP: Dr. Szanton is an Associate Professor within the JHU School of Nursing, a researcher and clinician in the geriatric population. She served on the JHU School of Medicine IRB for 3 years.
- Jennifer Stewart, PhD, RN: Dr. Stewart is an Assistant Professor within the JHU School of Nursing and a researcher whose work focuses on HIV prevention in the African American community.

Plan for Persons Testing Positive for MRSA:

Upon enrollment, all subjects will be provided a brief structured orientation and education session regarding *S. aureus* and MRSA by the RA. All patient questions will be answered and educational handouts developed by the Centers for Disease Control and Prevention (CDC) will be provided to the patient for additional information (available on-line at: http://www.cdc.gov/mrsa/pdf/SHEA-mrsa_tagged.pdf).

Each subject will be given information on how to obtain the results of their cultures. To avoid disclosure of results, the study team will not contact subjects directly to provide MRSA results. The subject will call, e-mail or schedule an appointment with either the RA or PI to receive the results. Information about what a positive test result means will be explained to the patient at that time or the patient may choose to discuss in greater detail at the next study visit.

9. Benefits

Potential Benefit of the Proposed Research to the Subject and Others: There may be no direct benefit to the subjects in this study; however, information obtained in this research may lead to a better understanding of risk associated with MRSA colonization and infection among persons with HIV and HIV/AIDS. Given the intensive monitoring of subjects, it is possible that a subject may benefit from more timely treatment of an infection.

10. Payment and Remuneration

Index HIV positive patients will receive a $25.00 gift card on completion of the protocol. We will offer household members a single gift card of $50.00 regardless of the number of participants.

11. Costs

There are no direct costs to the patient in this study. All subjects will be provided mupiricin, the chlorhexidine soap and oral rinse, as applicable.

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