PROTOCOL NAME

Preventing the Spread of Infection in Nursing Homes

CDC Contract Title: Implementation of a novel strategy to prevent *Staphylococcus aureus* (SA) Acquisition in Community-Based Nursing Homes to Prevent Invasive SA Infection - Feasibility and Pilot to Guide a Multicenter Stepped Wedge Cluster Trial

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GENERAL INFORMATION

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Commonly Used Abbreviations

SA	*Staphylococcus aureus*
MRSA	Methicillin-resistant *S. aureus*
MSSA	Methicillin-susceptible *S. aureus*
HCW	Health care worker
NH	Nursing home
LTCF	Long term care facility
CRISP	Chesapeake regional information system for our patients
ADL	Activities of daily living

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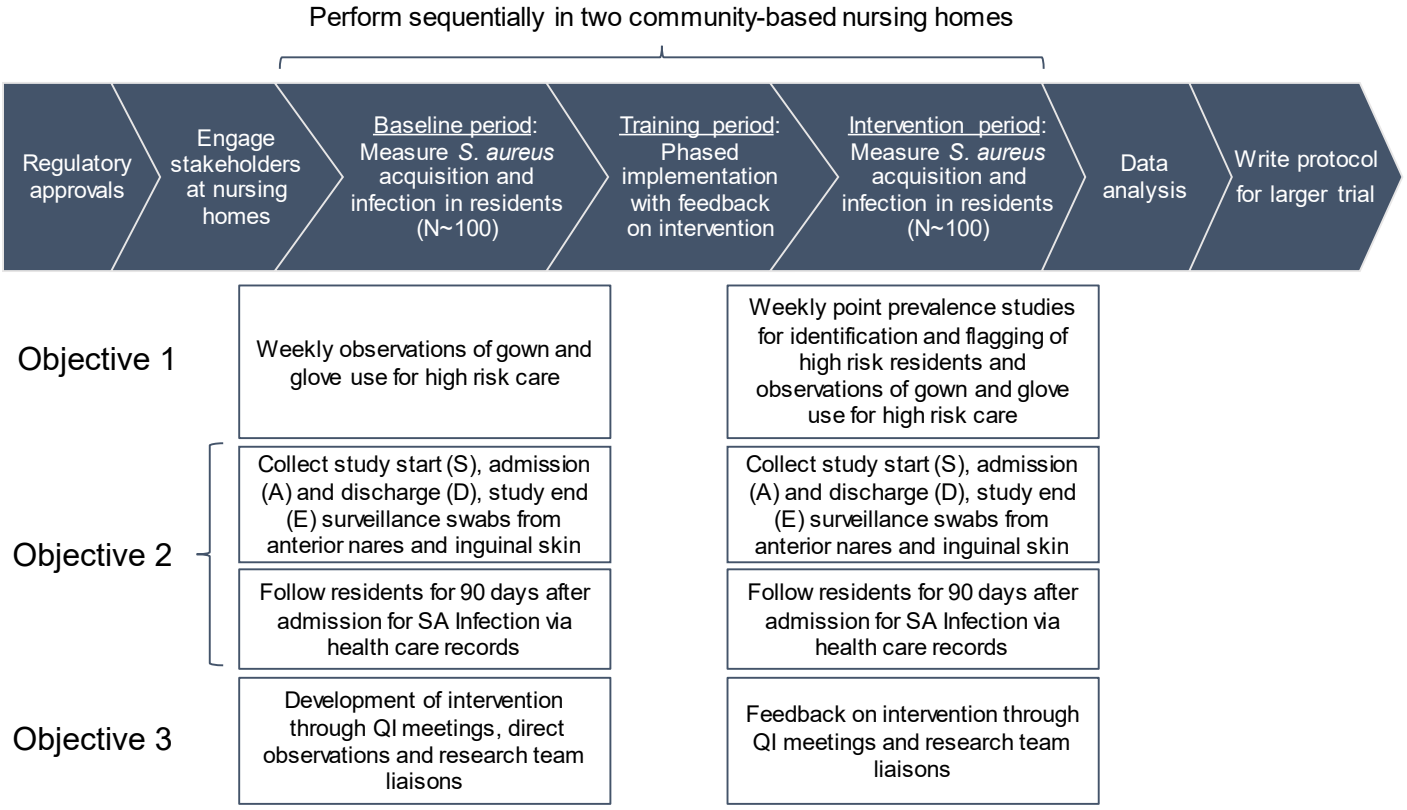
Abstract

Nursing homes are settings with a high rate of *Staphylococcus aureus* (SA) acquisition, which leads to infection, particularly for short stay residents. The current standard of care for preventing SA acquisition and SA infection in nursing homes is Standard Precautions (gowns and gloves for *anticipated* contact with blood, body fluids, skin breakdown or mucous membranes) for all residents.

We propose a feasibility study of a novel strategy, the *addition* of targeted gown and glove use, to prevent SA acquisition and SA infection in residents of community-based nursing homes. Our novel strategy is based on prior research on the risk of transmission from residents to healthcare workers' (HCWs) gowns and gloves, the first step in SA transmission. Rather than wearing gowns and gloves for all care activities to prevent transmission (as in Contact Precautions), gown and glove use can be targeted to specific high risk "moments" of care for specific high risk residents. High risk "moments" for gown and glove use are care activities most likely to transmit SA to HCW clothing and hands (in the absence of gown and glove use) based on prior research. (1, 2) Residents with chronic wounds and medical devices are: 1) most likely to be colonized with SA; 2) most likely to acquire SA; 3) most likely to transmit SA to HCW clothing and hands; and 4) most likely to develop a SA infection based on prior research (1-3) and thus would be considered high risk residents.

We will perform a quasi-experimental (before-after) study of this intervention, targeted gown and glove use, at two community-based nursing homes to demonstrate its feasibility and evaluate its effect on SA acquisition and SA infection rates. A quasi-experimental study design allows each nursing home to act as its own control, reducing variability. During a two month baseline period, we will measure SA acquisition and SA infection using surveillance cultures from residents and review of health care records. We will also assess gown and glove use for high risk care in high risk residents during the baseline period and begin to develop the intervention using a participatory human factor engineering informed approach. During a one month training period, we will begin phase implementation of the intervention in the nursing homes. During a two month intervention period, we will again measure SA acquisition and SA infection using surveillance cultures from residents and review of a state-wide electronic health information repository. We will also assess gown and glove use for high risk care in high risk residents during the intervention period and evaluate the intervention. SA acquisition is an excellent measure of resident-to-resident SA transmission, which our intervention is designed to decrease. It is also a more frequent outcome than SA infection, increasing the power of our study to detect a difference if one exists. We will assess adherence with all components of the intervention and the change in gown and glove use between baseline and intervention periods.

Figure 1. Overview of Project



1 Background

1.1 *Rationale*

Nursing homes are healthcare settings that house a high prevalence of people with both MRSA and MSSA colonization, creating a high risk for resident-to-resident transmission of *Staphylococcus aureus* (SA). There is a mingling of long term and short term stay residents in community-based nursing homes which mix a population recovering from acute illness with a chronically ill population which has high prevalence of SA colonization. For example, we found that short stay residents are at four-fold higher risk for MRSA acquisition than long stay residents. Once SA acquisition occurs, people are at higher risk for infection as colonization typically precedes infection. Up to 30% of MRSA colonized patients develop an infection contributing to community onset invasive SA infections. Nursing home stay was identified as a common risk factor for invasive MRSA infection after recent hospital discharge.

Nursing home staff are the most frequent vector for SA transmission as their clothing and hands become contaminated with SA during the care of SA colonized residents. In contrast to hospitals, where the standard of care for patients with MRSA is Contact Precautions (gowns and gloves for all patient contact), community-based nursing homes typically use Standard Precautions (gowns and gloves for anticipated contact with blood, body fluids, skin breakdown or mucous membranes) for residents with MRSA. Prior research demonstrating high rates of MRSA acquisition in nursing homes suggests that Standard Precautions do not adequately reduce the transmission of SA.

Contact Precautions have not been widely adopted by nursing homes for several reasons. Nursing homes are resource-limited settings without the level of professional staff and laboratory infrastructure of hospitals. In addition, nursing home staff have deeply rooted beliefs that Contact Precautions stigmatize residents. There is a clear need for a solution - tailored to the nursing home setting - to reduce the risk of SA (and other antibiotic resistant bacteria) acquisition and infection. Our goal in this project is to demonstrate the feasibility of a novel intervention, targeted gown and glove use, to decrease SA acquisition and SA infection as a precursor for a future multisite stepped wedge cluster trial.

1.2 *Population*

Study participants will be nursing home (NH) residents and staff in participating community-based NH study sites. All study activities will occur in the participating community-based NH study sites.

1.3 *Risk/Benefits*

The risks related to this study are minimal – the same as that encountered in daily life or at a routine doctor's visit. There are two types of participants, NH residents and staff. The two types of participants have different risks which we have minimized.

Potential risks to resident participants include those associated with non-invasive cultures (anterior nares and inguinal fold skin) and the loss of confidentiality of individual health information collected as part of the study.

We will minimize these risks as follows. Resident participants will be educated on how the cultures are performed at the time of enrollment to reduce any psychological discomfort. Study coordinators will have competencies in doing these procedures and will use gentle pressure to reduce possible irritation or discomfort during from the culture procedures.

Access to study records will be restricted to study staff, investigators and officials of the Office of Human Research Protections. Every effort will be made to keep the study records confidential through the use of locked briefcases for transport of paper records, assignments of unique participant identifiers, password protected databases and storage of paper records in locked filing cabinets in rooms that are locked when not in use (see **11. Data Handling and Record Keeping** for additional details).

There are few, if any potential risks to staff. Staff will be observed during routine care in order to estimate gown and glove use. A number of staff will be shadowed in order to determine how to best implement the intervention, targeted gown and glove use. A few staff will serve as liaisons to the project team. All staff will wear disposable gowns and non-latex gloves while providing specific care for specific residents during the intervention period. Wearing gowns and gloves are part of Standard (infection control) Precautions for certain care activities and pose no risk to the staff. We will not collect any identifiable data on any staff and thus there is no risk of loss of confidentiality.

There is no direct, individual benefit that can be guaranteed as a result of participation in this research study. There is societal benefit as this study will provide information about the transmission of *S. aureus* and other bacteria that could ultimately reduce the risk of infection for other nursing home residents. All residents and staff will be given the opportunity to have their questions answered by the study coordinators or investigators as needed. Given the minimal risks to the participants, the benefits outweigh the risks.

1.4 *Study Conduct*

This study will be conducted in compliance with the current protocol approved by the Institutional Review Board and according to Good Clinical Practice standards. All study documents will be posted on a secure document management site. No deviation from the protocol will be knowingly implemented without the prior review and approval of the IRB except where it may be necessary to eliminate an immediate hazard to a research subject. In such case, the deviation will be reported to the IRB as soon as possible.

2 Study Objective

Our goal in this project is to demonstrate the feasibility of a novel intervention, targeted gown and glove use, to decrease SA acquisition and SA infection as a precursor for a future multisite stepped wedge cluster trial. Our targeted intervention limits both cost and stigma while blocking the transmission and acquisition of multiple organisms.

Objective 1: To implement a targeted gown and glove intervention in two community-based nursing homes.

Expected Outcome 1: A targeted gown and glove intervention can be successfully implemented across two community-based nursing homes with >80% compliance with gown and glove use for high risk care in high risk residents.

Objective 2: To evaluate the impact of a targeted gown and glove intervention on SA acquisition and SA infection rates.

Expected Outcome 2a: The intervention will decrease SA acquisition and infection rates.

Expected Outcome 2b: We will determine the effect size to guide the design (including the sample size) of a future trial.

Objective 3: To develop an implementation “toolkit” that can be easily adapted and implemented at nursing homes in a future trial.

Expected Outcome 3: Barriers to and strategies for implementation of the targeted gown and glove intervention will be identified leading to modification of the pilot intervention and development of an implementation “toolkit” for a future trial.

3 Study Design

3.1 *Primary Study Endpoints/Secondary Endpoints*

Outcome 1: Compliance with each component of the intervention (identification and flagging of high risk residents, use of gowns and gloves for high risk care) based on 1) weekly point prevalence studies for high risk residents and 2) weekly observations of high risk care interactions with 5-10 residents over the 2-month intervention periods. There will also be weekly observations of high risk care interaction of 5-10 residents over the 2-month baseline period to assess the change in gown and glove use.

Outcome 2a: The primary outcome will be a change in SA acquisition rates comparing baseline and intervention periods. Residents in the nursing home will be swabbed at the start of the study period, or when they are admitted. Then they will all be re-swabbed at discharge or when the study ends. Acquisition will be defined as a positive culture for a new SA in a resident who was negative for that SA at the start of the study period or admission. Cultures will be performed in the research lab using well established methods. Specimens will be saved for future evaluation of other bacteria. The secondary outcome will be invasive SA infections and other infections within 90 days of nursing home admission in residents as detected through surveillance from health care records including but not limited to CRISP, a state-wide central repository of health care records including hospital and nursing home discharge summaries.

Outcome 2b: The observed SA acquisition rate reduction from this pilot study will be used to estimate the effect size that will inform the sample size for a larger trial.

Outcome 3: We will qualitatively examine the acceptability of, and any barriers to implementation using broad stakeholder feedback. Elements found to be infeasible or unacceptable will be modified at each stage and an implementation toolkit will be developed for the future trial.

3.2 *Study Design/Type*

Study Design

We will use a quasi-experimental study of a targeted gown and glove intervention (described below) with each nursing home acting as its own control to reduce between nursing home variability.

Intervention

Our novel strategy is based on extensive prior research on the risk of *S. aureus* (SA) transmission from residents to staff gown and gloves during care interactions, the first step in transmission. Our prior work suggests a novel, evidence-based approach to preventing SA transmission and SA acquisition: targeted gown and glove use. Rather than wearing gowns and gloves for all care activities, gown and glove use could be targeted at a) specific high risk "moments" while caring for b) high risk residents. The staff interactions targeted for gown and glove use are those most likely to transmit SA to staff clothing and hands based on prior research. The targeted gown and glove use is in addition to Standard Precautions for all residents. The residents targeted are both long and short stay residents and are: 1) most likely to be colonized with SA; 2) most likely to acquire SA; 3) most likely to transmit SA to staff clothing and hands; and 4) most likely to develop a SA infection based on prior research.

High risk "Moments" for Gown and Glove Use
- dressing the resident
- transferring the resident
- providing hygiene
- changing linens
- changing the resident's brief or diaper
- device care or use
- dressing wounds

High Risk Residents
- Chronic wounds
- Invasive medical devices
- Short stay
- Totally dependent on HCW

Implementation Strategy

We will use a participatory approach to develop, implement, and evaluate the intervention. In other words, we will actively involve multiple stakeholders, including front-line staff and nursing home leaders in all stages of the project, including design, implementation, and evaluation.

For the intervention, gown and gloves will be used for high risk care in high risk residents. Implementation will require the following steps: identification and flagging of high risk residents, then making acceptable gowns and gloves available at point of care. We will engage stakeholders including nursing home administrative and clinical staff, residents and family in these steps. We will develop separate human-factors engineering informed educational materials for staff, residents and family members, incorporating the feedback from our prior focus groups (4) and considering the well-known usability engineering (usefulness + ease of use) principles to increase acceptability and use. Phased assessment of the implementation of this intervention will be performed with modification at each step.

We will use the existing quality improvement infrastructure in each of the two nursing homes to actively involve and obtain input from multiple key stakeholders (nursing assistants, nurses, nurse manager, and other leaders) about the intervention and implementation toolkit. Each nursing home has regular quality improvement meetings attended by key stakeholders. The staff member responsible for infection control at the nursing home and a human factors expert from the research team will attend these meetings. In these meetings, we will first introduce the intervention idea and any evidence supporting the intervention and will seek input and active involvement of health care workers in detailing the intervention and implementation plan. We will use this same mechanism to conduct a qualitative evaluation of the intervention and implementation toolkit.

We will conduct direct observations of nursing assistants' and nurses' use of gowns and gloves for residents with wounds and/or devices before (for informing the intervention design and implementation process) and after implementing the intervention (for conducting qualitative evaluation of the intervention and how to improve the intervention/implementation package). Before implementation, we will conduct direct observations in order to: (1) understand the baseline process and workflow; (2) identify necessary changes in work system design and workflow to make it easy for HCWs to comply with the new targeted gown and glove

intervention; and (3) identify any potential barriers before implementation to take the necessary precautions. We will develop an observation instrument based existing literature, and input from multidisciplinary stakeholders. We will form two-person teams consisting of a team member with infection control certification and a human factors engineer who will shadow a HCW while taking care of high risk residents. Based on preliminary studies and our previous research experience using this type of methodology, we expect to reach theoretical saturation after observing five HCW, on different days and shifts, while they perform activities that require gowns and gloves (based on current standard of care), each for 2-4 times. After implementation, we will use a similar methodology to observe a comparable number of HCW to identify any barriers to compliance with the new targeted gown and glove intervention and any workarounds/strategies they developed to overcome the barriers. These findings and learnings will be key for improving our intervention and implementation toolkit for future large-scale implementation efforts.

In this participatory approach, we will identify 2-3 HCWs (e.g. 2 nursing assistants, 1 nurse) from each nursing home to be liaisons to our research team. Our research team member with infection control certification and human factors experts will work closely with these HCWs, through regular meetings, in every phase of the study, including design, implementation and evaluation. For example, before implementation, these HCWs will be asked to describe the nursing assistant workflow and provide input on how to redesign the "nursing home work system" (e.g., best locations to store gowns and gloves, alternatives approaches to flagging eligible patients, and design characteristics of effective visual cues to flag high risk patients) to ensure successful implementation of the intervention.

3.3 *Duration*

Each of two nursing homes will participate for a period of approximately 6 months. After an initial month of engagement, the next 2 months will be a baseline data collection period; the next 1 month, an intervention training period and the final 2 months, an intervention data collection period.

4 Selection and Withdrawal of Participants

All residents present in the two nursing homes during the project will be potential participants. HCWs can participate in a number of ways. HCWs will be observed during routine care in order to estimate gown and glove use. A number of HCWs will be shadowed in order to determine how to best implement the intervention, targeted gown and glove use. Up to 6 HCWs will serve as liaisons to the project team. All HCW will wear disposable gowns and non-latex gloves while providing specific care for specific residents during the intervention period.

4.1 *Inclusion Criteria for Residents*

- Age ≥18 years
- Reside in a participating NH

4.2 *Exclusion Criteria for Residents*

- Identified by NH staff as combative or with other behavioral problems which could lead to agitation if approached by project staff

4.3 *Inclusion Criteria for Staff (shadowing, team liaisons)*

- Staff at study site
- Willing to work with project team on intervention implementation

4.4 *Exclusion Criteria for Staff (shadowing, team liaisons)*

- None

4.5 *Subject Withdrawal*

Study residents or staff will be withdrawn from the study if found to have been initially ineligible or if they refuse to participate. No follow-up with withdrawn participants is required.

4.6 *Medication*

All medications are permitted during the study.

5 Facility Engagement

Within a month of project start at the NH, a meeting will occur with facility/unit administrators at each NH. We will then meet with the unit nurse managers to discuss the study procedures and develop solutions to anticipated problems.

6 Waiver of Informed Consent for Residents

6.1 *Waiver of Informed Consent*

We are requesting a waiver of informed consent for residents participating in this study. Under 45 CFR 46.116(d), the IRB "may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent" or waive the requirement to obtain consent all together, provided that:

1. The research involves no more than minimal risk to the participants;
2. The waiver or alteration will not adversely affect the rights and welfare of the participants;
3. The research could not practicably be carried out without the waiver or alteration; and
4. Whenever appropriate, the participants will be provided with additional pertinent information after participation; and
5. The research is not FDA-regulated.

We are requesting a waiver of consent for this study population for the following reasons:

1. *The study will involve no more than minimal risk of harm to participants*
   See ***1.3 Risks/Benefits***.
2. *The waiver will not adversely affect the rights and welfare of the subjects.*
   Current nursing home accreditation standards mandate that equal, high quality care be provided to all patients, whether or not they are on contact precautions. All residents will receive the same high quality care during the study.
3. *The research could not practicably be carried out without the waiver.*
   To adequately evaluate the study outcomes, it is important that all or nearly all residents are included in the study. Obtaining authorization from 100% of residents is not practical in a nursing home because many residents lack decision making capacity. Contacting 100% of legally authorized representatives to obtain proxy authorization would also not be possible within the time constraints of the study given residents should be cultured within 72 hours of admission or study start. Requiring authorization would bias the estimate of acquisition of SA since more ill patients will be less likely to provide authorization but may be more likely to acquire SA.
4. *Whenever appropriate, patients can be provided with additional pertinent information after participation*
   In the event that individual residents, family members or staff members request additional information about the study, each site will have readily available copies of a study information sheet for residents and families which describes the purpose of the study, the procedures involved in the study, and who to contact for further information.

6.2 *Enrollment Process for Residents*

The study information sheet for residents and families will be provided in admission materials and made available to other residents. Similar to any routine clinical procedure, we will briefly explain the procedure of obtaining the surveillance swabs and ask whether we can perform the cultures now. The resident or their family member can refuse to have the surveillance cultures performed. If during the surveillance cultures, a resident exhibits a negative response to specimen collection, the procedure will be stopped.

6.3 *Waiver of HIPAA Authorization*

This study meets the criteria for a waiver or alteration of HIPAA under 45 CFR 164.512(i)(2)(ii) as described below. The waiver for recruitment is to allow research staff to discuss the resident with NH staff to determine eligibility criteria. Residents who are identified by NH staff as combative or with other behavioral

problems which could lead to agitation if approached for the study will not be approached. Accessing this information from NH staff reduces the burden on the resident with regard to time and research procedures, increases the feasibility of the study, and does not confer any additional risk.

In addition, we will capture information from the medical records of all residents at participating facilities. This information includes: demographics (ex. age, gender, ethnic and racial category), length of stay, level of care, recent hospitalizations, activities of daily living, case mix index, facility characteristics, skin breakdown, medical devices, recent antibiotic use and co-morbidities. Resident identifiers will be collected on case report forms to facilitate collection; however, no resident identifiers will be entered into the study database for non-enrolled residents; instead, a unique identifier or code will be assigned to each resident.

This study meets the requirements for waiver or alteration of HIPAA under 45 CFR 164.512(i)(2)(ii):

A. *Use or disclosure involves no more than minimal risk to the privacy of individuals because of the presence of at least the following elements:*
    1. *An adequate plan to protect health information identifiers from improper use or disclosure,*
    2. *An adequate plan to destroy identifiers at the earliest opportunity absent a health or research justification or legal requirement to retain them, and*
    3. *Adequate written assurances that the PHI will not be used or disclosed to a third party except as required by law, for authorized oversight of the research study, or for other research uses and disclosures permitted by the Privacy Rule*

        Confidentiality will be maintained to the fullest extent permitted by law. All study data collected at the NHs will be recorded on case report forms. These case report forms will be entered into a password protected relational database which will be kept on a research server which has a level and scope of security that equals or exceeds that established by the HIPAA Security Rules. Clinical data on study participants will be obtained electronically from the participating NHs and uploaded into the study database. Data regarding *S. aureus* infections will be sourced from a state-wide electronic health information repository and entered into the study database. Paper records will be stored in locked filing cabinets in a protected space. Data will be maintained on a secure electronic central database on a research server. Data will be backed up according to the network backup schedule.

        A unique identifier or code will be assigned to each resident participant. Bacterial isolates and culture specimens and datasets used for analysis will be labeled with this code. Only the study personnel who directly interact with subject or manage the subject's clinical protocol data will have access to participant identifying information. Culture data will be entered directly into the relational database; however, microbiology laboratory personnel will not have access to participant identifiers in the database. Study personnel who leave the research team will have their access to study data removed.

        As soon as permitted and when all data analyses are complete and have been published, source documents containing identifiable information will be shredded and identifying information will be removed from the database. During the entire study, all data will be managed centrally at the primary site. There will be a single data table which maintains the link between the unique code and patient identifiers. This table containing the link between code and identifying information will be destroyed on the server and in any backups when it is time to de-identify the database. If any paper copies of the link have been made, they will be shredded. PHI will not be shared or disclosed unless required by law.

B. *Research could not practicably be conducted without the waiver or alteration*
    To adequately evaluation the study outcomes, it is critical that all or nearly all residents are included in the study. Obtaining authorization from 100% of residents is not practical in a nursing home due to many residents' lack of decision making capacity. Requiring authorization would bias the estimate of acquisition of SA since more ill residents will be less likely to provide authorization but may be more likely to acquire SA.
C. *Research could not practicably be conducted without access to and use of PHI*
    To adequately evaluate the study outcomes, it is critical that we include basic clinical information as described in **11 Data Collection, Handling and Storage**. This includes important data such as

whether residents are short stay or long stay which could affect the SA acquisition, an outcome variable and other data which will allow us to describe our population in aggregate.

7 Informed Consent for Health Care Workers (HCWs)

HCWs will participate in a number of ways. 1) Up to 10 HCWs will be shadowed in order to determine how to best implement the intervention, targeted gown and glove use. 2) Up to 6 staff will serve as liaisons to the project team. 3) HCWs will be observed during routine care in order to estimate gown and glove use. 4) All staff will wear disposable gowns and non-latex gloves while providing specific care for specific residents during the intervention period.

We request a waiver of documentation of informed consent (verbal/oral consent) for healthcare workers who are involved as research team liaisons or in shadowing to help develop this infection control intervention. This is a minimal risk study in which staff are being asked to participate as stakeholders in the development of an infection control intervention. The information collected is anonymous. If we were to use a consent document, the signed document would be the only link between the healthcare worker and the information.

We will not obtain informed consent for our observations of gown and glove use or the routine use of gown and gloves for providing specific care for specific residents during the intervention period because this will be standard practice in the nursing home as agreed upon by the participating NH (see below, ***7.1 Recruitment Process***).

7.1 *Recruitment Process*

HCWs will be recruited through participating NHs. Prior to study commencement at a NH, a meeting will be scheduled with facility/unit administrators at each prospective NH. Upon confirming their agreement to participate, we will meet with unit nurse managers and medical providers, distribute a study information sheet for nursing home staff to all HCWs at that facility that interact with residents and provide a phone number for follow-up. We will also present at a staff meeting to explain study procedures, answer questions and address concerns.

7.2 *Informed Consent Process for Health Care Workers*

Prior to study start in the NH, research staff will describe the study at a staff meeting. Research staff will introduce themselves, briefly re-explain the study and ask the healthcare worker if he/she would like to participate in a research study being conducted by the PI by being shadowed or participating as a project team liaison. The staff member will make clear that participation is voluntary and there will be no repercussions for not participating. The staff member will explain the procedure of shadowing the HCW in order to determine the best way to implement this intervention or what will be involved in being a project team liaison. As part of being a project team liaison, meetings or discussion may be recorded. The staff member will also explain that we are not collecting any identifiable information and any results will not be linked to the individual staff member. The staff member will offer to answer any questions and will offer contact information for the investigator on request.

8 Study Procedures

8.1 *Study Schedule*

	Study Period Start or Resident Admission	**Study Period End or Resident Discharge**
	Day 0	Day 1-60
Obtain medical history for eligibility from electronic medical record (HIPAA waiver for study)	R	
Obtain permission from Resident (waiver of informed consent)	R	
Confirm permission from Resident		R
Collect anterior nares and inguinal skin specimens	R	R

	Study Period Start or Resident Admission	Study Period End or Resident Discharge
	Day 0	Day 1-60
Monitor for Adverse Events	R	R

8.2 *Study Period Start or Resident Admission*

Research staff will speak with NH staff to determine which residents are eligible. Eligible residents will be approached for permission to perform study procedures. At study period start or resident admission, subjects will have a specimen of the anterior nares and inguinal skin.

8.3 *Study Period End or Resident Discharge*

Research staff will confirm with NH staff to determine that the resident is eligible. Eligible residents will be approached for permission to perform study procedures. At study period end or resident discharge, subjects will have a specimen of the anterior nares and inguinal skin.

9 Adverse Events

9.1 *Adverse Events and their Grading*

We will collect data on SERIOUS ADVERSE EVENTS as defined by HRPO policy that occur while the study participants are enrolled.

9.2 *Attribution of Adverse Events*

The Principal Investigator will determine attribution of serious adverse events. The following scale will assess the relationship of AEs to the study procedures:

- Not related: no temporal association, or the cause of the event has been identified, or the study procedures cannot be implicated
- Possibly related: temporal association, but other etiologies are likely to be the cause; however involvement of the study procedures cannot be excluded
- Probably related: temporal association, other etiologies are possible but unlikely
- Related: established temporal or other association for event not reasonably explained by the patient's known clinical state or any other factor

9.3 *Adverse Event Reporting*

Serious Adverse Events that are more likely than not (probably or definitely) related to the research will be reported immediately of the site investigator becoming aware of the SAE to the local IRB according to established IRB policy. The principal investigator will evaluate the adverse event and determine whether the adverse event affects the Risk/Benefit ratio of the study and whether modification to the protocol is required.

The principal investigator will conduct a review of all serious adverse events annually. The principal investigator will evaluate the frequency and severity of the serious adverse events and determine if modifications to the protocol is required. A summary of the serious adverse events will be reported to the UMB IRB annually, when renewal is sought.

10 Statistical Plan

10.1 *Data Analysis, Sample Size, and Precision*

For objective 1, we will calculate point estimates and 95% confidence intervals for the rates of compliance with each component of the intervention (identification and flagging of high risk residents, use of gowns and gloves for high risk care) as well as the change in gown and glove use for high risk care during the baseline and intervention periods. We will observe 40-80 encounters per nursing home where gowns and glove should be used which will result an estimate of the rate of compliance that is accurate +/- 8-10 percentage points.

For objective 2, we will estimate and compare the rates of transmission in the baseline and intervention periods in each nursing home. To estimate the rates from binary data, we note that the risk that a person acquires the infection in the interval between swabs can be written as 1-exp(-λt) where “t” is the number of days between swabs and λ is interpretable as the daily rate of acquisition. We will estimate λ in the baseline and intervention periods using maximum likelihood estimation and compare the two rates. Likelihood methods will be used to calculate a confidence interval for the ratio of the rates. This will be done for each nursing home separately. We will test 100 residents per nursing home per period which will result an estimate of the rate of acquisition that is accurate +/- 4-6 percentage points. These estimates will give us insight into the effect size of the intervention and the variation between nursing homes for future planning.

For objective 3, primary data will be notes and transcribed audio recordings from quality improvement meetings, regular meetings with the research team liaisons, and direct observation. No identifiable information or PHI will be collected. All qualitative data will be transferred to the qualitative software package, NVivo©. Data will be organized so that the setting and the method of collection can be traceable. We will use an iterative data analysis approach; after some data are collected, these will be analyzed to inform future qualitative data collection efforts

11 Data Collection, Handling and Storage

The Principal Investigator is responsible to ensure the accuracy, completeness, legibility, and timeliness of the data reported. Data collection is the responsibility of the study staff.

Paper records or case report forms will be filled out at the participating community-based NHs. Copies of the paper records or case report forms will serve as source documents and maintained for recording data for each subject enrolled in the study. All source documents will be completed in a legible manner to ensure accurate interpretation of data. Black ink is required to ensure clarity of reproduced copies. When making changes or corrections, the original entry will be crossed out with a single line, and the change initialed and dated. Erasing, overwriting, or use of correction fluid or tape will not be done.

All available source documents and laboratory reports will be reviewed by the clinical team and data entry staff, who will ensure that they are accurate and complete. AEs must be graded, assessed for severity and causality, and reviewed by the site PI or designee.

Confidentiality will be maintained to the fullest extent permitted by law. All study data collected at the NHs will be recorded on case report forms. These case report forms will be entered into a password protected relational database which will be kept on a research server which has a level and scope of security that equals or exceeds that established by the HIPAA Security Rules. Clinical data on study participants will be obtained electronically from the participating NHs and uploaded into the study database. Data regarding S. aureus infections will be sourced from a state-wide electronic health information repository and entered into the study database. Paper records will be stored in locked filing cabinets in a protected space. Data will be maintained on a secure electronic central database on a research server. Data will be backed up according to the network backup schedule.

A unique identifier or code will be assigned to each resident participant. Bacterial isolates and culture specimens and datasets used for analysis will be labeled with this code. Only the study personnel who directly interact with subject or manage the subject’s clinical protocol data will have access to participant identifying information. Culture data will be entered directly into the relational database; however, microbiology laboratory personnel will not have access to participant identifiers in the database. Study personnel who leave the research team will have their access to study data removed.

As soon as permitted and when all data analyses are complete and have been published, source documents containing identifiable information will be shredded and identifying information will be removed from the database. During the entire study, all data will be managed centrally at the primary site. There will be a single data table which maintains the link between the unique code and patient identifiers. This table containing the link between code and identifying information will be destroyed on the server and in any backups when it is time to de-identify the database. If any paper copies of the link have been made, they will be shredded.

Selected discussions and meetings with research team liaisons will be audio-recorded on a case-by-case basis. To protect the privacy of participants, they will be referred to by a letter or number only. These anonymous identifiers will only be used to track the statements of each participant throughout the meetings. Audio recordings will be kept on a secure password-protected server with access only by research team

members. The audio recordings of the meetings/discussions will be held until completion of analyses in case questions arise regarding the transcripts and then they will be destroyed.

Shadowing observations of healthcare workers will be conducted using an observation form. The use of gowns and gloves will be recorded. No identifiable information will be recorded during the shadowing observations.

12 Study Management Plan

12.1 *Study Coordination*

The University of Maryland, Baltimore will be the coordinating site for this study under the direction of the PI, Dr. Roghmann. It will also implement the protocol in community-based NHs in Maryland. It will coordinate study operations and be the central repository for data entry into a centralized database and perform all of the microbiology testing.

It is also responsible for training study personnel and monitoring study progress and performance. The PI and project manager will visit the NHs for a one day study start up meeting in which we review the study protocol, informed consent procedures and study procedures. In addition, the project manager will visit the NHs for study monitoring as needed during the study. We will have weekly meetings with study staff during enrollment to review performance (see below), protocol deviations and adverse events.

12.2 *Performance monitoring*

Study performance will be monitored via the centralized study database. The monitoring period will begin soon after enrollment begins and continue through data collection closeout. Monitoring will focus on timing, frequency and quality of study recruitment, follow-up, and data collection. Reports will be generated on a regular basis related to recruitment and data completeness. Components of the reports will include number of participants screened, number of participants enrolled, number of participants lost to follow-up, key demographics of enrolled participants, number of missing or deficient forms and summaries of data audits and edits.

12.3 *Data audits*

A list of completed forms for specific participants will be randomly selected from the study database on a regular basis (approximately quarterly). Hard-copies of these forms will be compared with the study database. Forms will also be inspected for proper tracking of modifications and completion of fields not captured in the study database. Discrepancies between the study forms and database and any errors found on the forms will be reported to study staff and resolution required.

12.4 *Data edits*

The data entry process will be guided by range and logic checks built into the study database. However, the entry of inappropriate data is still possible, so data edits will be run on the study database on a regular basis (approximately quarterly). Data edit reports will be generated for missing, out-of-range, unusual and inconsistent values. Study staff must respond to each data edit and make modifications to the study form and database as needed.

References

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5. Katz S. Multidisciplinary studies of illness in aged persons II. A new classification of functional status in activities of daily living. *J Chron Dis.* 1959; 9(1): 55-62.

APPENDIX: Study Variables

Table: Study Variables

	Ascertained			
Variables	**When**	**How**	**Purpose**	**Format**
RESIDENT CHARACTERISTICS (measured once on each subject)				
Identifying information- Name as appears in existing medical record at LTCF	Enrollment	Existing medical record at LTCF (MR)	Looking up information in MR	Nominal
Medical record number	Enrollment	MR	Looking up information in MR	Ordinal
SSN	Enrollment	MR	Looking up information in MR	Nominal
Demographics				
Level of Care	Enrollment	MR	Study variable	Nominal: Rehabilitation, Skilled Nursing, Maintenance
Short Stay	Enrollment	MR	Study variable	Yes/no
Unit in Facility	Enrollment	MR	Descriptive	Nominal: from list of units in participating LTCFs
Age	Enrollment	MR	Descriptive	Interval
Sex	Enrollment	MR	Descriptive	Nominal
Race	Enrollment	MR	Descriptive	per OMB Directive 15 definitions
Ethnicity	Enrollment	MR	Descriptive	per OMB Directive 15 definitions
Length of Stay in LTCF prior to Enrollment	Enrollment	MR	Descriptive	Interval
Charlson Co-morbidity Index	Enrollment	MR	Descriptive	Ordinal: 0-37
Dependence with ADLs	Enrollment	MR	Descriptive	Ordinal: 1 - minimal assistance, 2 - moderate assistance, 3 - requires assistance with most ADLs
Katz ADL (5)	Enrollment	MR/MDS	Descriptive	
History of colonization or infection with Multidrug Resistant Organism	Enrollment	MR	Descriptive	Yes/no
Types of Medical Devices:				
Urinary catheter	Enrollment	MR	Study variable	Yes/no
Venous catheter for parenteral medications	Enrollment	MR	Study variable	Yes/no
Gastro or jejunostomy tube for enteral nutrition	Enrollment	MR	Study variable	Yes/no
Other	Enrollment	MR	Study variable	Nominal
Type of skin breakdown:			Study variable	

	Ascertained			
Variables	**When**	**How**	**Purpose**	**Format**
Pressure ulcer	Enrollment	MR	Study variable	Yes/no
Unhealed surgical incision	Enrollment	MR	Study variable	Yes/no
Percutaneous medical device	Enrollment	MR	Study variable	Yes/no
Tracheostomy	Enrollment	MR	Study variable	Yes/no
GI Ostomy	Enrollment	MR	Study variable	Yes/no
Other	Enrollment	MR	Study variable	Nominal
HEALTHCARE SETTING FACTORS (measured once per facility)				
Facility (Study Site)	Facility Start-up		Descriptive	Nominal: from list of participating NHs
Number of Licensed beds	Facility Start-up	Administrator	Descriptive	Interval
Number of current beds	Facility Start-up	Administrator	Descriptive	Interval
Units	Facility Start-up	Administrator	Descriptive	Nominal: from list of units
Proportion of Beds- Rehab or Skilled nursing	Facility Start-up	Administrator	Descriptive	Ratio
Proportion of Beds- Short stay	Facility Start-up	Administrator	Descriptive	Ratio
Resident to staff ratio by Type of HCW and Shift	Facility Start-up	Administrator	Descriptive	Ratio
Staff Infection Control Training	Facility Start-up	Administrator	Descriptive	Yes/no; record policy
Full time employees for Infection Prevention in Facility	Facility Start-up	Administrator	Descriptive	Interval
OUTCOME VARIABLES				
SA or other Infection	Within 90 days of at admission or study period start	MR	Outcome variable	Yes/no
SA colonization of Anterior nares	At admission or study period start/discharge or study period end	Culture	Outcome variable	Yes/no
SA colonization of Inguinal skin	At admission or study period start/discharge or study period end	Culture	Outcome variable	Yes/no
STAFF/HCW OBSERVATIONS (weekly for 5-10 high risk care activities in each nursing home during both the baseline period and the intervention period)				
Gown use	Observation visits	Observation	Study variable	Yes/no
Glove use	Observation visits	Observation	Study variable	Yes/no