Title: Detection, Education, Research, and Decolonization without Isolation in Long-term Care (DERAIL MRSA)

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Abstract

Purpose: To create a model of Acute Care Hospital:Long-Term Care Facility (LTCF) infection control collaboration that reduces infection risk in the elderly using the prevention of MRSA disease as the program proof-of-concept model.
Scope: Three free-standing LTCFs and one acute care organization.
Methods: A prospective, cluster randomized trial in 12 nursing units. We first removed MRSA from the population in the intervention units and then tested and decolonized all new admissions to those units. All nursing unit personnel received education on the nature of pathogen transmission, the need for effective cleaning and disinfection of healthcare facility surfaces/equipment, and the importance of good hand hygiene.
Results: Because of frequent comingling between intervention and control unit patient residents during each day, the trial was changed to a quasi-experimental before:after trial in year 2. In year 1, there was a 30.2% reduction in colonization from baseline ($p=0.028$); in year 2, the reduction was 36.6% ($p<0.001$). There was a 47.7% reduction in MRSA infection during year 1 ($p=0.09$) that improved to 72.7% in year 2 ($p<0.001$). Two of the LTCFs joined in a long-term contract for management of their Infection Prevention program, thus developing a workable model for Acute Care Hospital:LTCF collaboration.

Key Words: Long-Term Care Facility (LTCF); Infection Prevention; methicillin-resistant *Staphylococcus aureus* (MRSA); nasal decolonization; mupirocin; retapamulin; cluster-randomized trial

The **Purpose** of this study, which was a **Research Demonstration Project**, was to create a model of Hospital:Long-Term Care Facility (LTCF) infection control collaboration by developing LTCF-tailored interventions that reduce infection risk in the elderly and to use the prevention of methicillin-resistant *Staphylococcus aureus* (MRSA) clinical disease as the program proof-of-concept model. Thus, the main goal was to use current literature-based knowledge, our considerable experience in infection control, and preliminary data we had collected to test a novel approach for controlling one of the most prevalent and important multidrug-resistant organism (MDRO) pathogens found in LTCFs, namely MRSA. Our hypothesis for the DERAIL MRSA program was that one can safely remove the colonization risk from nearly all residents (patients) in a way that does not interfere with the desired lifestyle for persons in these facilities and thereby reduce the risk of infection and lower the cost of care by avoiding preventable disease. Achieving this primary goal would also demonstrate two secondary goals that we sought to achieve: one, that a scientific, planned approach to the issue of specific healthcare-associated infections in LTCFs can solve these problems; the other, that a partnership between acute and long-term care is beneficial in dealing with patient safety and quality practices across the United States healthcare continuum.

The objectives that needed to be met in order to reach our goals were:

- To test the effectiveness of an admission testing and immediate decolonization of positive persons protocol for reducing MRSA colonization prevalence in LTCFs
    - Colonization prevalence and disease reduction were measured for this objective
    - Cost of the program was compared to the expense avoidance achieved by disease prevention
    - We also compared the effectiveness of using a molecular diagnostic test for nasal screening to culture-based testing of multiple body sites for detecting MRSA colonization as a secondary objective
- To further develop an Infection Control Outreach Program designed to provide expert guidance on infectious disease prevention specific to LTCFs
    - Interactions between the acute and long-term care infection control professionals were qualitatively monitored for this objective.
    - MRSA was be the concept pathogen evaluated.
- To create a model of a hospital:LTCF infection control collaboration
    - The final success of the intervention was a measurement of this objective – success would be achieved if the LTCFs involved adopt the successful program as part of their ongoing standard of care.
    - The adoption of this model by other healthcare organizations would be a demonstration that such collaborations are externally viewed as viable and beneficial.

The **Scope** of this study was the **Long-Term Care Facility** (LTCF) component of our healthcare system, which are often referred to as nursing homes. It is that part of the United States healthcare serving some of the most vulnerable citizens who are unable to manage independently in the community *and* it is the major healthcare component that has not been well studied regarding effective ways to minimize healthcare-associated infection risk while still maintaining the desired interactive lifestyle for its patient-residents. The LTCF is functionally the home for the resident, who is usually elderly, perhaps physically or mentally impaired, and having special healthcare needs; they may be in declining health and they often will stay as an inpatient for years as well as require end-of life care - hence, comfort, dignity, social interaction, and rights are paramount. The need for ongoing socialization precludes the use of typical kinds of barrier precautions that are applied for infection control in acute care facilities to limit the spread of potentially pathogenic microorganisms causing healthcare-associated infection (HAI).

Approximately 1.8 million United States residents live in the nation's 16,500 LTCFs, and the acuity of their disease(s) appears to be increasing. In Illinois alone, there are approximately 1,200 long-term care facilities serving more than 100,000 residents, from the young to the elderly. Almost as many healthcare-associated infections (HAIs) occur in LTCFs annually as in acute care hospitals in the US, with estimates somewhere between 1.6 and 3.8 million infections per year. The Study on the Efficacy of Nosocomial Infection Control (SENIC) documented the effectiveness of a hospital infection control program that applies standard surveillance and control measures, but there is no SENIC-equivalent study documenting the efficacy of infection control measures in LTCFs, and few controlled investigations have analyzed the efficacy or cost effectiveness of any specific control measures in that setting. Furthermore, LTCF residence has been frequently identified as a risk factor for antibiotic-resistant infection in hospitalized patients, and multi-drug-resistant bacteria are increasingly important causes of infection in LTCFs. Outbreaks, typically associated with unusual clustering of resistant bacterial infections, such as from MRSA, on a single nursing unit are now frequently reported. In this setting, infection with MDROs has been associated with increased morbidity, mortality, and healthcare cost. Thus, there is a great need to perform well-designed demonstration projects in the LTCF to *i*) begin solving the problem of HAI in this setting and *ii*) more fully integrate this critical component of our healthcare system with the acute care facility component for effective control of HAI and drug-resistant pathogens across the United States of America.

Why select MRSA as the target pathogen? One third of all adults carry *Staphylococcus aureus* in their anterior nares, where it generally causes no symptoms. Unlike most harmless bacteria that colonize our bodies, this one has high capacity to cause disease, often during a time when someone is compromised due to illness or surgery as well as in the very young and in elderly persons. *S. aureus* invades the body, causing illness ranging from common skin infection to less frequent, serious pneumonia, urinary infections, and disease of the blood and heart. The ability of *S. aureus* to exploit compromises in our bodily defenses has made it one of the leading causes of infectious disease in humans and a leading cause of healthcare-associated infection. The antibiotic resistant form of this organism is known as MRSA. Once colonized with MRSA, humans appear particularly prone to develop infection that causes critical disease and death. Importantly for our healthcare system, MRSA has seen more than a 10-fold increase in hospital stays for this infection since 1995. *S. aureus* resistant to most of the antibiotics developed to treat *S. aureus* infection, is called meticillin-(later methicillin)-resistant *S. aureus* (MRSA) and were first identified in the early 1960s; thus, this is a relatively new pathogen that has quickly disseminated. Though named after their ability to resist treatment by one class of antibiotics (methicillin – a penicillin-class drug), they are, in fact, resistant to treatment with most classes of antimicrobial agents and may be more virulent than sensitive strains. Many studies have demonstrated that infections caused by MRSA result in very high morbidity and much additional medical cost. For example, the mortality attributed to MRSA bloodstream infection has been estimated at 24%, and the median cost is reportedly as high as $51,492 per case, primarily due to prolonged length of hospital stay. One large prospective US study from the Centers for Disease Control and Prevention on invasive disease in 2005 found the mortality associated with invasive MRSA to be 20%. Others have reported even higher figures, with a 22% mortality associated with surgical site infection and >30% for bacteremia.

Over the past 15 years, there has been a marked increase in the prevalence of infections caused by MRSA. Because MRSA is resistant to many antibiotics, settings in which it has thrived are patient care environments in which antibiotics are widely used, particularly when persons remain in these settings for prolonged periods of time.

In such locations, the organism spreads from one individual to another, generally on the hands of caregivers. As a result, MRSA infections have become particularly common in hospitals, and they are now recognized as a problem among residents of long-term care. Delorme and colleagues recently reported a 183% increase of MRSA infections in LTCF residents between 2006 and 2007, with an overall rise in disease for inpatients and outpatients of 77%---a disease rate more than 100-fold higher than the U.S. national rate of tuberculosis. Clearly, now is the time for the development of effective control strategies to deal with MRSA in the LTCF setting; thus, this microbe seems ideal as a model for Acute Care Hospital:Long-Term Care Facility infection control collaboration.

To begin improving LTCF care likely requires the creation of a model for Acute Care Hospital:Long-Term Care Facility infection control collaboration by developing LTCF-tailored interventions that reduce infection risk in the elderly living there. HAIs in the LTCF are as diverse and complex as they are in the acute care hospital, but the approach for control needs to be different. As noted earlier, the LTCF is functionally the home for the resident, who is usually elderly, is perhaps physically or mentally impaired, and has special health care needs. Trying to solve all the HAI problems at one time, particularly without an evidence base to start from, is not practical or possible. However, targeting a particular and highly problematic pathogen, such as MRSA, can accomplish two important goals. A successful program will *i*) demonstrate that a strong Hospital:LTCF partnership is beneficial *and* it will *ii*) delineate a useful approach to controlling MRSA in the LTFC setting. Our plan was to demonstrate the benefit of such collaboration by working with three LTCFs that would care for approximately 5,000 persons over 3 years.

The overall **Methods** to the DERAIL MRSA intervention design were straightforward. We first removed the target pathogen (MRSA) from the population by decolonizing the intervention unit patients and then tested (using a rapid method) and decolonized all positive new admissions to those units. All nursing unit personnel received education on the nature of pathogen transmission, the need for effective cleaning and disinfection of healthcare facility surfaces/equipment, and the importance of good hand hygiene, which are considered standard practices for adequate MRSA control.

The General Design was an IRB-approved, cluster randomized trial performed in 12 nursing units (approximately 650-700 beds in total) at three different LTCFs with a total of approximately 4,200 annual admissions. Nursing units each belonging to one of three categories---skilled nursing, rehabilitation, dementia care---were included in the cluster randomization. These 12 units were randomly assigned to intervention or control. Study duration was planned for 24 months, with a planned evaluation period at 12 months when a scheduled preliminary analysis was completed. At the time of this 12-month analysis, it was found that a cluster randomized design was not appropriate for LTCF, because there was too much socialization between all units each day; thus, the decision was made to make all units intervention units for year 2 in order to test if the original intervention plan would have an increased impact. The critical reason for continuing a second year was to demonstrate sustainability of the intervention for MRSA colonization reduction and to gather more data on the reduction of MRSA disease in the LTCFs (secondary endpoint). The onsite Infection Control Preventionist (ICP) working at each facility or one of the two research Infection Control Preventionists recorded all positive clinical cultures and all antimicrobial prescriptions for the patients (residents) on all units during the study and used standardized criteria designed for detecting infections in Long-Term Care.

All patients cared for on both the control and intervention units were tested for MRSA colonization on admission, *and* at 4-month intervals ("point prevalence surveys").

During the final quarter for each study year, all patients were tested for nasal MRSA colonization at the time of admission and discharge to assess transmission rates in the control and intervention units. Standardized environmental decontamination procedures for all rooms, common areas, and equipment with anti-staphylococcal detergents or bleach were conducted over a 1-week period at 4-month intervals on all units. An educational program on the importance of hand hygiene was given annually for all nursing units. Patients with active MRSA infection (disease) were placed in contact isolation; isolation was ***not*** used for MRSA carriage only. All patients were prospectively followed for infectious disease using standardized criteria as well as by monitoring of cultures and antibiotic use and the data recorded on a standard form.

Microbiologic Methods. A pre-moistened double swab of both nares was performed for nasal colonization testing, and a new single swab was used on any open wounds. Real-time PCR was performed at the LTCF using one of the nasal swabs and processed in the Cepheid GeneXpert® system using their FDA cleared Xpert® MRSA test. The testing was done onsite at each LTCF and processed either by the onsite nursing personnel working at each facility or by the research personnel hired as part of this funding. This testing has proven safe in over 500,000 patients who have received it at NorthShore since the beginning of our program to control MRSA that commenced on August 1, 2005. Subjects had the right to decline this testing should they desired to do so. The other nasal swab and any wound swabs was transferred to the research laboratory, where they were cultured. All MRSA isolates were tested for the presence of mupirocin (*mupA*) resistance and banked for later subspecies typing using pulsed-field gel electrophoresis (PFGE) of isolates detected during admission, at point prevalence surveys, and at discharge. During year 1 of the study, additional swabs for culture were collected from throat, axilla, inguinal areas, and the peri-rectum of patients providing written, informed consent to determine the efficiency of nasal PCR alone in comparison to routine culture from multiple body sites as a means of validating the utility of nasal swabs alone tested by PCR for MRSA surveillance.

PFGE was performed in the research laboratory to determine *i*) the clonality of MRSA strains introduced into the LTCFs, *ii*) the pattern of potential spread within the facilities, and *iii*) the association of any mupirocin resistance with specific MRSA clonal groups. We used standard methods that our laboratory is very familiar with and we have published on in the past. We analyzed this data to determine the risk of spread of the detected clones for residents in the intervention units as well as the control nursing units and then calculated the quantitative benefit of the intervention in limiting MRSA transmission.

Standard Decolonization Regimen (Intervention Units). A 5-day regimen of mupirocin calcium 2%, twice daily (applied to the nares and any open wounds), plus at least one chlorhexidine gluconate 4% wash, was the standard regimen used. Medications were applied by the patient, a caregiver, or one of the research ICPs. This regimen has proven safe in several thousand patients who have received it at NorthShore since the beginning of our program to control MRSA on August 1, 2005. Subjects had the right to decline this decolonization should they desire to do so.

Intensive Decolonization Regimen (Intervention units): This regimen consists of minocycline (100 mg orally twice daily for 5 days), rifampin (600 mg orally once daily for 5 days), 2% mupirocin ointment applied to the anterior nares twice per day for 7 days, and a bath or shower with 4% chlorhexidine once per week for 2 weeks. Because this is a more aggressive decolonization regimen with potential adverse events from the systemic medications, only those providing written informed consent were given this regimen.

Statistical Considerations: The primary outcome measure was MRSA colonization prevalence at the time of the point prevalence surveys. Secondary outcomes included the number of MRSA infections, positive MRSA clinical cultures, antimicrobial agent prescription episodes, and proportional mupirocin resistance. Nursing units were stratified into three groups: skilled nursing, rehabilitation, dementia care. Within each stratum, units were randomized to either the control or intervention arm prior to the initiation of patient recruitment. Generalized estimating equation (GEE) models were fit for all outcome variables to adjust for the cluster randomization. Models fit used SAS PROC GENMOD with an exchangeable correlation structure. Distributions and link functions were specified as appropriate for the scale of each outcome measure (e.g., binomial distribution and log link for dichotomous outcomes). Randomized intervention group and unit strata were included as independent variables in the models. Interim analyses were performed after 6 and 12 months elapsed.

Cost-Benefit Analysis: The cost of healthcare-associated infection and the benefit of preventing those that are avoidable have been addressed by the Centers for Disease Control and Prevention. This report points out that for nearly all interventions that the benefit outweighs the cost. Scott calculated that the overall annual direct medical costs of HAI to US hospitals ranges from $28.4 to $33.8 billion (in 2007 dollars using the CPI for all urban consumers) and $35.7 billion to $45 billion (after adjusting to 2007 dollars using the Consumer Price Index for inpatient hospital services). Incorporating a range of effectiveness calculation for possible infection control interventions, the benefits of prevention range from $5.7 to $6.8 billion (20% of infections preventable, CPI for all urban consumers) to a high of $25.0 to $31.5 billion (70% of infections preventable, CPI for inpatient hospital services). Our data on prevention of MRSA infection in acute care demonstrates that 60% of these infections are preventable within 1 year. The cost:benefit of controlling MRSA as a target pathogen has been assessed, with a similar conclusion. This report analyzed 10 years of data on screening, surveillance, and outbreaks at the University Medical Center Utrecht. The costs associated with the policy in place were also calculated, including those for additional (disposable) material, cultures, specific medication, decontamination, and closing of nursing wards. Over the course of 10 years, the total cost reached €2,800,000. The financial consequences were compared to those in a hypothetical situation without the "search and destroy" policy of the Netherlands, which revealed that the cost of care would have been at least twice as high as the costs expended in the actual prevention program. Additionally, the cost of healthcare-associated MRSA infection, as opposed to a susceptible *S. aureus* (MSSA) infection, in long-term care was the subject of investigation by Capitano and colleagues. They compared the cost of care for 49 MSSA and 41 MRSA patients. Though they found that a significantly higher number of patients in the MRSA group had an indwelling device ($p<0.001$), pressure ulcer ($p=0.028$), or diabetes mellitus ($p=0.007$), there were no differences in the primary infection site ($p=0.297$) or the incidence of patients with more than two comorbidities ($p=0.509$). Importantly, because the majority of patients (82%) developed infection at least 30 days after their LTCF admission, the infections would be considered to have been largely LTCF acquired. The median direct infection management cost for MRSA was six times greater than that of a MSSA infection ($p<0.001$), and the median associated nursing care cost alone was two times greater ($p=0.001$). The median overall cost associated with MRSA-infected patients was 1.95 times greater than that with MSSA: median (range) for MSSA was $1,332 ($268-$7,265) versus $2,607 ($849-$8,895) for MRSA ($p<0.001$). Thus, from all perspectives, the prevention of MRSA in LTCF patients should be both medically and economically beneficial to the US health care system.

Our approach to assessing the economic aspect of the DERAIL MRSA program was straightforward. We used our past data on MRSA infection cost to estimate the resources saved by preventing MRSA infection and compared this benefit to the directly measured additional care expense of two cycles of decolonization of all facility residents, the expense of thorough

cleaning of LTCFs every 4 months, and the cost of admission testing and decolonization (personnel time and materials) of those found to harbor MRSA as a routine practice. We are also in the process of measuring the expense of antibiotic treatment directed toward possible MRSA infection on the intervention and control nursing units and will compare the data collected. However, the use of antibiotics to treat potential MRSA infection is unlikely to offset the cost of the program. Thus, in order to determine if the DERAIL MRSA proposal can be financially viable, we are determining the cost to US healthcare for residents needing to be sent to acute care hospitals for treatment of MRSA infection. Two of the three LTCFs in this program admit their residents almost exclusively to the NorthShore healthcare system, and we are capturing their total healthcare cost for these admissions as well as CMS billing and reimbursement so that we can determine precisely the cost of care in our facilities as well as the medical expense borne by the Medicare/Medicaid (CMS) program. As an example of the importance of this assessment, we investigated this type of results as part of our MRSA control program in the NorthShore system. We found that preventable MRSA infection had an excess cost of $23,783. Of this total, $13,304 was reimbursed by CMS; this illustrates that both the acute care provider as well as the US governmental-provided healthcare system(s) can benefit from control of MRSA infection.

The main limitation of the initial design was the unanticipated failure of a cluster randomized study approach to perform adequately. Although we had realized the daily community gathering of patients, we have not anticipated the magnitude of this daily mingling and its impact on separating outcome measures between intervention and control units. However, this was recognized at the end of year 1, and, after consultation with the involved LTCFs and our Project Officer (Dr. Hall), we all agreed that changing the study design to a before:after demonstration project was appropriate, as it would permit the assessment of the proposed MRSA intervention at three distinct LTCFs. Also, if successful, this would further support the likelihood that a successful Acute Care:LTCF cooperation design could be developed by demonstrating that such a collaboration could be successful even when an initial intervention does not have the full desired outcome.

The **Results** of our study, particularly relating to **Principal Findings** and **Outcomes**, focused on *i*) measuring the reduction in MRSA colonization prevalence in LTCFs that we hypothesized would lead to less MRSA clinical disease and *ii*) further developing an Infection Control Outreach Program designed to provide expert guidance on infectious disease prevention specific to LTCFs, resulting in a model of a Hospital:LTCF infection control collaboration with success demonstrated if the LTCFs involved adopted the successful program as part of their ongoing standard of care. A third goal was to demonstrate that this project (e.g., MRSA control) was cost effective.

Our first focus was to reduce MRSA colonization, because that is the greatest risk leading to clinical infection. In total, 16,773 swabs were collected and tested through May, 2013, which provided an outstanding data set for analysis. Importantly, we had virtually 100% compliance with the nasal swabbing/surveillance protocol at all three nursing homes and thus are confident that the data generated from this study is reliable and broadly applicable regardless of the results. Tangentially, we also assessed the accuracy of our real time PCR test using 1,149 samples that were cultured using broth enrichment. We found that the sensitivity was 92.8%, specificity was 98.9%, positive predictive value was 84.4%, and negative predictive value was 99.5%. Thus, our chosen PCR test performed adequately for the needs of this study. The PCR testing is complete on all samples, and all PCR-positive swabs were cultured as well as had PFGE typing completed in our microbiology research laboratory.

As part of the proposal, MRSA-positive residents were decolonized and then retested 1 month after decolonization. Those patients remaining MRSA positive were given further treatment. All proposed point prevalence surveys scheduled to date are completed. This data gave us the opportunity to study the reliability of using nasal swabs as a determination of MRSA colonization status as well as documentation of an alternate agent (retapamulin) to mupirocin for nasal MRSA decolonization when a MRSA strain resistant to mupirocin was encountered. For assessment as to the utility of nasal screening to detect MRSA colonization, 302 residents were enrolled in a multiple body site testing protocol, and 291 qualified for analysis. Twenty-six (8.9%) residents had at least one body site that was culture positive for MRSA, with a total number of 63 culture positive body sites. More than two thirds (69%) of the 26 culture-positive residents were positive at $\geq$2 body sites. Importantly, 21 of the 26 (81%) culture-positive residents were MRSA nasal PCR positive. Of the five who were not PCR positive, three were culture positive in the perianal region, two were positive from the throat, and two were positive from the perineum; none of the five patients had a positive axilla culture. Culture of MRSA from any of the five body sites sampled was used as the reference standard for a positive patient. The sensitivity, specificity, PPV, and NPV for the nasal MRSA PCR tests were 81%, 87%, 38%, and 98%, respectively. The difference between culture and PCR performance was not significant (p=0.42).

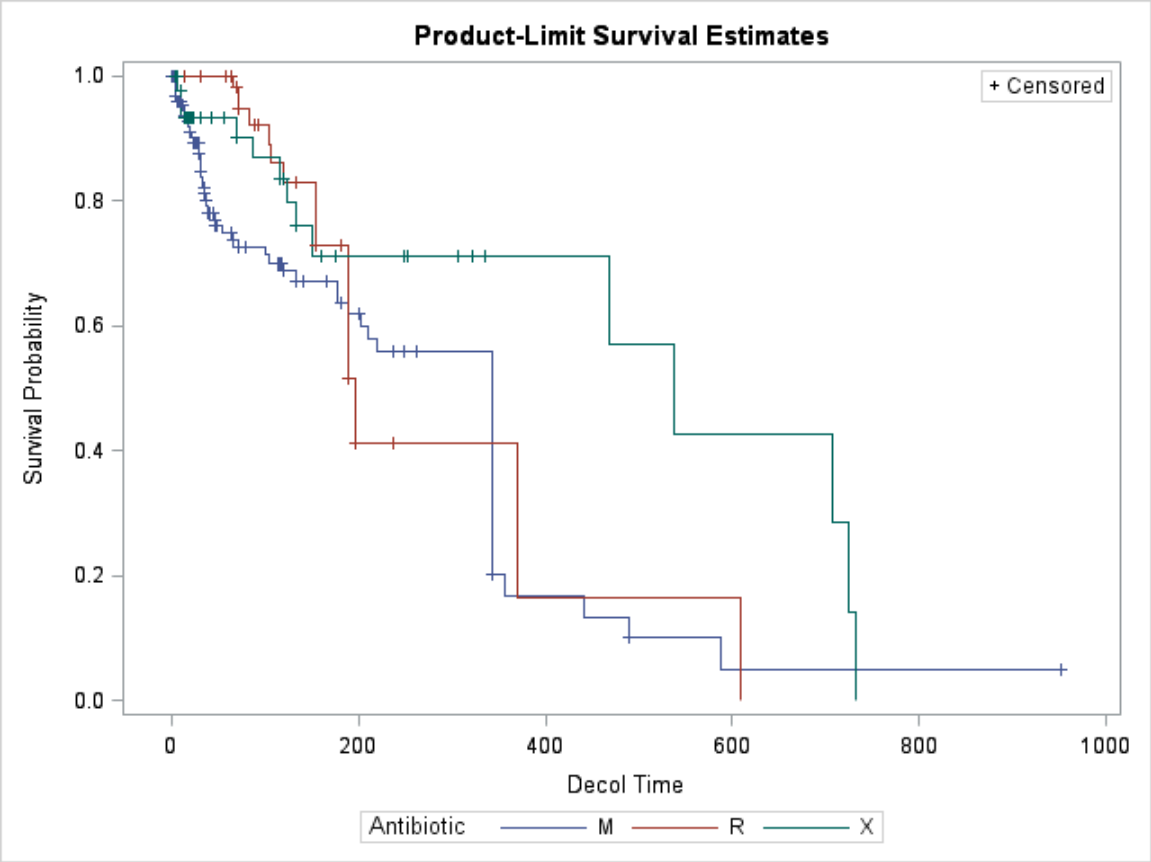
For the evaluation of retapamulin efficacy, 132 patients were treated with mupirocin, and 65 were treated with retapamulin. Forty-eight control patients were also included in the data set. A greater proportion of patients were successfully decolonized at retest in the mupirocin group (44.7%) than in the retapamulin group (33.8%), although the difference was not statistically significant (p=0.146). As shown in Table 1, mupirocin decolonized significantly more patients than was the observed loss of colonization in the untreated patients, for whom 22.9% did not remain MRSA colonized (p=0.008 for mupirocin; p=0.207 for retapamulin).

Table 1. Decolonization results for mupirocin and retapamulin comparisons

	Mupirocin	Retapamulin	Controls
N	132	65	48
Decolonized at next retest	59 (44.7%)	22 (33.8%)	11 (22.9%)
p-value vs retapamulin	0.146		
p-value vs control	0.008	0.207	
Median time to decolonization from Kaplan-Meier estimation (95% confidence limit)	343 days (202, 343)	196 days (189, 371)	537 days (469, 725)
p-value vs retapamulin	0.123		
p-value vs control	0.034	0.132	

Figure 1 demonstrates this decolonization efficacy in a Kaplan-Meier curve.

Figure 1. Kaplan-Meier curve showing mupirocin and retapamulin decolonization rates compared to the control group



During the baseline period of our study, the colonization rate in tested cultures was 16.64% (Table 2). Interestingly, the three LTCF sites had substantially different rates at baseline (Table 2, $p<0.05$ for all three pairwise comparisons). During year 1 of the study, the colonization rate was reduced to 11.61% in the intervention units ($p=0.028$) but, as expected, remained steady at 17.85% in the intervention units ($p=0.613$ compared to baseline). The difference in rate between intervention and control units was statistically significant ($p=0.001$). During year 2, when all units received the intervention, the colonization rate was 10.55%. The difference between Baseline and year 2 rates was statistically significant ($p<0.001$) for the sample overall. Within each site, the reduction in colonization rate was statistically significant only for LTCF #2 ($p<0.001$).

Table 2. Colonization prevalence in each time period overall and by site

	Baseline		Year 1		Year 2	
	Int	Con	Int	Con	Int	Con
Total						
Number of cultures tested	315	358	715	762	1044	1230
Positive Confirmed MRSA tests	53	59	83	136	134	106
Culture prevalence	16.83%	16.48%	11.61%	17.85%	12.84%	8.62%
LTCF #1						
Number of cultures tested	63	84	145	171	198	256
Positive Confirmed MRSA tests	4	9	10	15	15	18
Culture prevalence	6.35%	10.71%	6.90%	8.77%	7.58%	7.03%
LTCF #2						
Number of cultures tested	137	98	308	195	462	305
Positive Confirmed MRSA tests	34	16	37	29	60	14
Culture prevalence	24.82%	16.33%	12.01%	14.87%	12.99%	4.59%
LTCF #3						
Number of cultures tested	115	176	262	396	384	669
Positive Confirmed MRSA tests	15	34	36	92	59	74
Culture prevalence	13.04%	19.32%	13.7%	23.2%	15.4%	11.1%

We also looked at conversion rates during one quarter for year 1 and year 2 of the study. Conversion rates are based upon paired admission and discharge testing samples for which the admission screen test was negative and the discharge screen was a PCR-positive, culture-positive test. Table 3 describes the number of conversions and demonstrates that there was an increase in conversions/transmissions during year 2. Interestingly, the admission prevalence rose between years 1 and 2 at two of the LTCFs, which may have contributed to an increased colonization prevalence that led to a modest increase in transmission.

Table 3. Conversion Rates according to Discharge Testing during One Quarter per Study Year

	Year 1	Year 2	p value
No. residents sampled	725	767	
Conversions*	12	27	
Conversion rate (%)	1.66%	3.52%	0.034

*Culture negative upon admission and positive at discharge

Most importantly, a critical goal was to actually reduce clinical disease, which was accomplished even more dramatically than was decolonization. During the baseline period, there were 44 MRSA infections and 365,809 patient-days, for an infection rate of 1.20 per 10,000 patient days. As with colonization, the three sites had significantly different clinical disease rates at baseline (Table 4, $p<0.05$ for all three pairwise comparisons). During year 1 of the study, there were nine infections in the control units (165,052 patient days, 0.55 infections per 10,000 patient-days) and 14 infections in the intervention units (129,113 patient days, 1.08 infections per 10,000 patient-days).The difference in rate between intervention and control units was statistically significant ($p<0.001$). During year 2, when all units received the intervention, there were 12 MRSA infections and 287,847 patient-days, for an infection rate or 0.42 per 10,000 patient-days. The difference between baseline and year 2 rates was statistically significant ($p<0.001$) for the sample overall.

Within each site, the reduction in infection rate was statistically significant for all individual sites, with LTCF #1 ($p=0.022$), LTCF #2 ($p<0.001$), and LTCF #3 ($p=0.009$).

Table 4. MRSA infection rates in each time period, overall and by site

	Baseline	Year 1		Year 2
		Control	Intervention	Decolonize All
Total				
Total # of Patient Days	365,809	165,052	129,113	287,847
Total Number of MRSA Infections	44	9	14	12
MRSA Infections per 10,000 patient-days	1.20	0.55	1.08	0.42
LTCF #1				
Total # of Patient Days	73,836	23,060‡	36,067‡	57,679
Total Number of MRSA Infections	16	2	5	4
MRSA Infections per 10,000 patient-days	2.17	0.87	1.39	0.69
LTCF #2				
Total # of Patient Days	128,287	56,518‡	44,407‡	97,371
Total Number of MRSA Infections	18	2	6	7
MRSA Infections per 10,000 patient-days	1.40	0.35	1.35	0.72
LTCF #3				
Total # of Patient Days	163,686	85,474	48,639	132,797
Total Number of MRSA Infections	10	5	3	1
MRSA Infections per 10,000 patient-days	0.61	0.58	0.62	0.08

‡Estimated based on relative distribution of beds between intervention and control units.

The preliminary financial impact on the overall healthcare system resulting from preventing MRSA infection was estimated from our past analysis of MRSA nosocomial infection cost ($23,783 per infected patient). The LTCF-wide intervention prevented 32 infections in year 2 (compared to baseline) for a total of $761,056. The cost of testing all patient at the time of admission, based on manufacturer's suggested retail price, would be no more than $100,000, and the cost of decolonizing 5% of the admissions (using mupirocin) would be $1,500. Thus, the net financial benefit to the healthcare system for these three LTCFs and the acute care hospitals serving them would be in excess of $650,000.

Our global goal with this study was to create a model of a Hospital:LTCF infection control collaboration for which the final success of the intervention was a measurement of this objective – overall success would be achieved if the LTCFs involved adopt the successful program as part of their ongoing standard of care. In early 2014, we signed a long-term contract with two of the LTCFs (all those within 10 miles of the acute care facility) to manage their infection control and thus were successful in this overarching objective of the funding request.

Discussion and Conclusions

As can be seen from our presented evaluation, the anticipated initial sustained disease reduction for the intervention units did not occur in year 1 (compared to control). Therefore, we performed systematic observations of patient behavior on the LTCF nursing units. We observed that, though the randomized nursing unit clusters were indeed separated, the residents gathered together in common areas for most of each day so that there was complete comingling of all intervention and control unit patients. Our conclusion from this observation, and the data collected, is that a cluster randomized trial is not always suitable for the LTCF setting. Our insights from the first 12 months were that a different study design was needed – more appropriate would be a quasi-experimental, before-and-after trial in our three LTCFs. Importantly, nasal MRSA screening was adequate, and we also learned that decolonization is not always effective, so follow-up testing with repeated decolonization attempts is needed. Overall, we conclude that active MRSA surveillance with targeted decolonization resulted in a significant decrease in the rate of clinical MRSA infections among LTCF residents without limiting socialization or activities of daily living (ADL). Furthermore, developing a formal relationship between our acute care hospital system and the LTCFs has led to an ongoing infection prevention interaction beyond control of MRSA.

The Principal Investigator met with Leadership at all three LTCFs during early 2012 and 2013 to update study progress and discuss the final outcome; more meetings are planned for 2014 once the final analysis is complete. As part of the ongoing program, the LTCF Infection Preventionists (IPs) are attending weekly meetings with our acute care hospital team, and this has provided an exceptional opportunity to exchange ideas and assist the LTCF IPs in their ongoing challenges faced within the long-term care setting. This has also facilitated them contacting their acute care colleagues as needed whenever issues arise that need discussion. The monthly phone conferences with study team for this research project highly facilitated the exceptional compliance with all aspects of this research program. Finally, as noted, a comprehensive management contract has been signed with two of the three LTCFs that will permit us to manage their Infection Control and Prevention program going forward and establish the long-term interaction that was this overarching goal of this Demonstration Project.

Significance

The Long-Term Care Facility (LTCF) component of our healthcare system, often referred to as nursing homes, is that part of the United States healthcare serving some of the most vulnerable citizens who are unable to manage independently in the community, and it is the major healthcare component that has not been well studied regarding effective ways to minimize healthcare-associated infection risk while still maintaining the desired interactive lifestyle for its residents. There is a great need to perform well-designed demonstration projects in the LTCF, such as this one just completed, to *i*) begin solving the problem of healthcare-associated infection (HAI) in this setting and *ii*) more fully integrate this critical component of our healthcare system with the acute care facility sector for effective control of HAI and drug-resistant pathogens across the United States of America. The importance of the knowledge gained from this project is great for future patients in our United States healthcare systems. We developed a successful approach for controlling MRSA in LTCFs that has improved the health of residents and lowered the cost of healthcare. For our program, a successful outcome demonstrated that a strong Acute Care Hospital:LTCF partnership is beneficial, *and* it demonstrated a useful approach to controlling MRSA in the LTFC setting. The result of our Demonstration Project documented that such a program is very possible.

Implications

The implications of this demonstration study project are far reaching and highly important. We have demonstrated that it is possible to reduce infection from an important pathogen such as MRSA in the LTCF setting while not interfering with the daily activities of the residents/patients at these facilities. The strategy for doing so rests on two premises: one, that MRSA can be removed from the patients in a facility, which is achievable at minimal cost; the other, that MRSA needs to be kept out of the facility once it is eradicated. This can be accomplished by screening at admission followed by rapid decolonization of those found positive, *OR* the LTCFs can require screening prior to admission and then complete decolonization of those known to be positive at the time of admission. Because entrance to a LTCF is not an emergent situation, this latter approach could minimize the economic burden on the facilities while at the same time maintain MRSA control. From the MRSA perspective, this study provides insight that MRSA infection can be prevented by decolonization even in the absence of contact isolation – which is less expensive and lowers the time burden placed on healthcare workers (by avoiding the need for isolation facilities and garments) when caring for patients. It is reasonable to expect that this would be similarly effective in acute care as it was in LTCF. We also contributed to the understanding of study design in LTCFs by demonstrating that a cluster randomized trial is not suitable for the LTCF setting. Our insights from the first 12 months are that a different study design may be needed – a more appropriate approach would be a quasi-experimental, before-and-after trial such as we undertook in year 2 at our three LTCFs – or, alternatively, a trial design in which each LTCF has a quality improvement/infection prevention intervention applied throughout the entire facility so that comingling of LTCF residents does not confound the intervention impact. Finally, this project demonstrates the benefits of formal Acute Care:LTCF collaboration and cooperation – both for improving patient safety and for avoiding unnecessary healthcare cost.

Publications

In Print
Das S, Anderson CJ, Grayes A, Mendoza K, Harazin M, Schora DM, Peterson LR. Nasal Carriage of Epidemic Methicillin-Resistant *Staphylococcus aureus*-15 (EMRSA-15) Observed in Three Chicago-Area Long Term Care Facilities. *Antimicrob Agents Chemother* 2013 Jun 24; [Epub ahead of print]: PMID:23796939

In Press
Detection of Methicillin-Resistant *Staphylococcus aureus* (MRSA) from Multiple Body Sites of Residents at Long Term Care Facilities. Schora DM, Boehm S, Das S, Patel PA, Schora K, Peterson KE, Grayes A, Hines C, Burdsall D, Robicsek A, Peterson LR. A manuscript detailing this work has been submitted and accepted for publication in AHRQ's Special Advances publication.

In Preparation
Impact of Detection, Education, Research and Decolonization without Isolation in Long Term Care (DERAIL) on MRSA Colonization and Transmission at Three Long Term Care Facilities. Donna Schora, Susan Boehm, Deborah Burdsall, Carolyn Hines, Parul Patel, Jennifer O'Brien, Sanchita Das, Jennifer L. Beaumont, Lance R. Peterson. A manuscript detailing this work has been submitted for publication in AHRQ's special supplement to Infection Control and Hospital Epidemiology.

Methicillin-Resistant *Staphylococcus aureus* Decolonization comparing Retapamulin and Mupirocin in Three Long-Term Care Facilities. Anna De La Peña, Becky Smith, Jennifer L. Beaumont, Donna Schora, Susan Boehm, Parul Patel, Jennifer O'Brien, Sanchita Das, Lance R. Peterson. Plan is to submit this to Clinical Infectious Diseases.

Planned

Molecular Epidemiology of MRSA spread in Long-Term Care Facilities
Plan is to submit this to Infection Control and Hospital Epidemiology.

A successful intervention to lower MRSA clinical disease in Long-Term Care
Plan is to submit this to Annals of Internal Medicine.

Comparison of Real-time PCR test performance in a Long-Term Care population
Plan is to submit this to Diagnostic Microbiology and Infectious Diseases.

Total Anticipated publications from this funding opportunity = 7