Targeted versus Universal Decolonization to Prevent ICU Infection
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6-7-20XX

BACKGROUND	
• Background	• *S. aureus* causes the most health-care associated infections than any other pathogen. Common infections caused by *S. aureus* are: ventilator-associated pneumonia, surgical site infections, and central-catheter-associated bloodstream infections. Methicillin-resistant *S. aureus* (MRSA) is especially virulent and is of particular concern in the ICU, where patients are at high risk for infection • Since 2007, the previous standard of care in all hospitals has been nasal screening of patients for MRSA upon ICU admission and the use of contact precautions with carriers, per CDC guidelines • In addition to screening, some hospitals have employed decolonization strategies to reduce the incidence of *S. aureus* infections. ➢ Decolonization therapy usually involves use of mupirocin (Bactroban®) intranasal ointment and chlorhexidine bathing. ➢ Several studies have shown that daily chlorhexidine bathing of all patients in the ICU can reduce incidence of MRSA infection. • However, there are still questions about whether or not decolonization should be used, and if so, which specific patient populations should be targeted. For example, should only patients that are identified as carriers via nasal screening undergo decolonization therapy or should all patients be decolonized? Definitive answers to these questions may help to establish a new standard of care that is more effective at reducing hospital-acquired infections with MRSA.
STUDY OVERVIEW	
• Title/Citation	• Huang S, Septimus, E, Kleinman, K, et al. Targeted versus universal decolonization to prevent ICU infection. N Engl J Med. 2013; …??
• Funding	• Contract with the AHRX Healthcare-Associated Infections Program • Grant from the CDC Prevention Epicenters Program • Total cost of trial = $3 million ($40 per patient)
• Study Dates	• January 1 – December 31, 2009: 12-month baseline period • January 1 – April 7, 2010: Phase-In Period • April 8, 2010 – September 30, 2011: 18-month intervention period
• Trial Design	• A three-group cluster-randomized, comparative-effectiveness trial was conducted in adult ICUs within hospitals
• Objectives	• To determine what type of decolonization strategy works best to reduce MRSA and other pathogens in ICU's, and whether such a strategy would be appropriate to use on a routine basis.
METHODS	
• Inclusion Criteria	• Less than 30% of patients in the ICU receiving either intransal mupirocin ung or chlorhexidine bathing during the baseline collection period • Stable use of infection-prevention initiatives during the baseline period • Agreement to refrain from adoption of new initiatives during the trial
• Exclusion Criteria	• ---
• Interventions	• Participating Hospitals were assigned at random to be in one of three groups: o Group 1: MRSA screening and isolation ▪ The previous standard of care in all hospitals ▪ Bilateral screening of nares for MRSA performed on ICU admission ▪ Contact precautions taken for carriers of MRSA, per CDC guidelines o Group 2: MRSA screening, isolation, and decolonization (Targeted Decolonization) ▪ Same screening as above ▪ Decolonization therapy for MRSA+ pts: • Mupirocin, 2%, intranasal ointment, bid for 5 days AND • Chlorhexidine, 2%, bathing cloths, qd o Group 3: Decolonization of all patients (no screening) (Universal Decolonization) ▪ All patients received decolonization therapy above • Groupings were established as follows: o Hospitals placed into one of 6 groups based on ICU volume o Within each group of 6, the hospitals were again ranked according to prevalence of MRSA carriage in ICU according to baseline

	○ For each group of 3 consecutive hospitals, a Group # was assigned randomly (1, 2, 3) • All adult ICUs within a given hospital were assigned to implement the same strategy • Patient notices about group-specific protocols were posted in each ICU room • The requirement for written informed consent was waived
• Major Outcomes	• Primary Outcome: MRSA-positive cultures (ICU-attributable) ○ Screening tests excluded from analysis b/c Group 3 did not screen ○ ICU attributable = sample collection occurred any time between 3rd day of ICU admittance to 2nd day after discharge • Secondary Outcome: MRSA-positive (or any other pathogen-positive) bloodstream infection ○ ICU attributable = same organism had to be isolated from 2 or more blood cultures obtained within 2 calendar days of one another • Data from phase-in period was excluded from analysis
• Statistical Analysis	• Statistical Power obtained based on rarest outcome → MRSA bloodstream infection • Designed to have 80% power to detect: ➢ a 40% reduction in rate of MRSA bloodstream infection in group 2 compared to group 1 ➢ a 60% reduction rate in group 3 compared to group 1 • Intention-to-treat analysis • Proportional-hazards models were used (difference in hazards based on baseline compared to intervention period) • Adjustment models accounted for age, sex, race, insurance type, coexisting conditions, and surgery during the hospital stay • SAS 9.3 software was used
RESULTS	
• Enrollment	• 55 hospitals (98 ICUs) were assessed for eligibility, but only 45 met inclusion criteria • 45 hospitals (78 ICUs) randomly assigned to be in one of three groups described above, but 2 reported not meeting inclusion criteria after being assigned • 43 hospitals (74 ICUs) underwent an intervention period, but 1 withdrew after intervention began • Hospitals were located across 16 different states
• Study Results	• MRSA screening occurred in: ○ 97.5% of pts in Group 1 ○ 98.6% of pts in Group 2 ○ 0.7% of pts in Group 3 • Intervention Periods were compared to baseline periods • Primary Outcome Hazard Ratios (infections that tested positive for MRSA) ○ Group 1 (Screening and Isolation): 0.92 ○ Group 2 (Screening, Decolonization): 0.75 ○ Group 3 (Universal Decolonization): 0.63 ○ Universal Decolonization significantly reduced the hazard ratio • Secondary Outcome Hazard Ratios (bloodstream infection that tested positive for MRSA) ○ Group 1: 1.23 ○ Group 2: 1.23 ○ Group 3: 0.72 ○ Universal Decolonization reduced the hazard ratio, even though no difference between group 1 & 2 • Secondary Outcome Hazard Ratios (bloodstream infection from any pathogen) ○ Group 1: 0.99 ○ Group 2: 0.78 ○ Group 3: 0.56 ○ Universal Decolonization significantly reduced the hazard ratio
AUTHORS' CONCLUSIONS	
• This study provides evidence that universal decolonization is the most effective strategy at reducing MRSA infections and bloodstream infections from any pathogen. Universal decolonization: ○ Reduced MRSA infections by 37% ○ Reduced bloodstream infections from any pathogen by 44% ○ Prevents 1 MRSA infection for every 181 pts decolonized ○ Prevents 1 bloodstream infection from any pathogen for every 54 pts decolonized • Factors that could have contributed to the finding that universal decolonization was the most effective strategy: ○ Chlorhexidine kills many pathogens, so it protects the patient against many microorganisms during a vulnerable time ○ Universal decolonization reduces # of microorganisms in the environment overall, thus decreasing chance for patient-to-patient transmission ○ Universal decolonization eliminated screening step, which requires a wait-time for results. Universal decolonization occurred on patient's first day in ICU.	

- Universal decolonization may reduce need for contact precautions, which can interfere with care
- Screening may still be useful to monitor drug resistances to mupirocin and chlorhexidine that could occur over time
- Since the study included community hospitals and not just academic institutions who are accustomed to participation in research studies, the authors have every reason to believe that universal decolonization is implementable at all hospitals
- This was not a blind study (hospital workers were aware of the intervention strategy being employed), which may have resulted in "un-measured behavior," but it is unlikely to have occurred to the extent of causing a 44% reduction in infections
- If universal decolonization is implemented, surveillance for drug resistances will be necessary

LIMITATIONS

- Cost-effectiveness of universal decolonization was not studied, which is a significant issue in the current health-care marketplace
- It is unknown whether universal decolonization completely eliminates need for contact precautions for MRSA carriers
- Effect of mupirocin alone was not studied, so it is unknown how much it contributed to the benefits of universal decolonization. Any reduction in S. aureus bloodstream infections must be attributed to chlorhexidine.

DISCUSSION

- Do the benefits of universal decolonization outweigh the risks of eventually introducing more drug-resistances (as resistant bacteria are "selected" through this process)?
  MRSA Mupirocin resistance has been reported in some studies
  Chlorhexidine resistances have been reported (via multi-drug efflux pump), but are rare in the United States
- What are the costs and time-involvement of universal decolonization versus screening and targeted decolonization?