MULTIDRUG-RESISTANT ORGANISMS (MDRO): COST-EFFECTIVE ANALYSIS OF HORIZONTAL VS. VERTICAL SURVEILLANCE

by

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ABSTRACT

Introduction: Multidrug-resistant organisms (MDRO) are still a serious public health problem in healthcare facilities and are a major cause for morbidity and mortality in hospitalized patients. There is currently no consensus for the most effective surveillance approach for MDRO management. The objective of this study is to compare focused enhanced surveillance for populations at high-risk for MDRO colonization to the current vertically oriented (organism focused) surveillance strategy. A cost-effective analysis will be performed to determine which approach is more economical.

Methods: Electronic medical record surveillance was performed to randomly identify 100 high-risk patients. Nursing staff in the UPMC-Mercy ICUs and infection control department gathered samples from patients for the following MDRO: *Methicillin-resistant Staph aureus (MRSA), Vancomycin resistant Enterococci (VRE), Carbapenem resistant enterobactericiae (CRE) and extended spectrum Beta lactamase producing organisms (ESBL).* Specimens were analyzed, and the results were recorded. Chart abstraction collected patient characteristics, severity index and comorbidity index. Stata SE 15.1 was used for data analysis to compare the current surveillance method to the horizontal approach. TreeAge software was used to conduct a cost-effective analysis to compare the two approaches.

Results: From Oct 1st, 2017 through Nov. 30th, 2017 there were total of 155 eligible patients identified through EMR surveillance. We screened 74 patients who met our clinical criteria and

26 patients who met our 7-day length of stay criterion. There were 52% men in our cohort, with an average age of 60.1 years. The mean severity index was 38.8 and the mean comorbidity index was 4.4. There was evidence of MDRO (CRE, ESBL, VRE & MRSA) in 30% of patients with high-risk clinical criteria and 27% in 7-day LOS patients, as compared to 10% MRSA captured using the current screening strategy. Horizontal surveillance was found to be the cost-effective approach.

Discussion: Clinical-based horizontal surveillance is a more effective way of identifying MDRO colonization and infection. The next step in our research is to include a larger patient sample to verify these data results.

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PREFACE

I would like to thank Dr. Frank and Dr. Kingsley for their help and guidance in the completion of this research and paper. I would like to thank Dr. Yassin for his guidance and continued support of this project, along with the UPMC-Mercy infection control department and the UPMC-Mercy Intensive Care Unit nursing staff. Finally, I would like to thank Kathleen Shutt for her guidance in statistical analysis.

1.0 INTRODUCTION

Antimicrobial resistance is a serious public health problem in the United States and globally. According to the CDC, at least 2,049,442 cases and 23,000 deaths are caused by resistance each year (About Antimicrobial Resistance, 2017). Antimicrobial resistance occurs when a microbe develops the ability to resist the effects of an antibiotic or a similar drug. Resistance spreads through the overuse and misuse of antibiotics, as well as poor prevention and infection control practices (Antimicrobial Resistance, 2018). If an organism becomes resistant, an infection caused by the organism becomes more difficult to treat since antimicrobial options are reduced or limited (About Antimicrobial Resistance, 2017). Without public health and clinical intervention, a range of infections, including HIV, pneumonia, tuberculosis and gonorrhea may become almost impossible to treat. Understanding how resistance occurs, how it is spread and how to prevent it has become a high priority in the public health and healthcare professionals, institutions, and communities.

There is growing concern regarding those microbes that are becoming resistant to multiple antimicrobials, which are called multidrug-resistant organisms (MDRO) or “superbugs.” In 2013, the CDC published a report of the 18 most concerning drug resistant threats in the United States. The threats were categorized as urgent, serious, or concerning. Some of those threats include carbapenem-resistant Enterobacteriaceae (CRE), methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant Enterococcus (VRE), all of which are MDRO (Biggest Threats,

2017). The prevalence of these organisms has steadily increased over the past several decades, which has prompted government officials to create guidelines and procedures to prevent their spread and stop resistance (Multidrug-resistant organisms (MDRO) management, 2015).

The CDC has highlighted "Four Core Actions" to fight antimicrobial resistance: "preventing infections and preventing the spread of resistance, tracking, improving antibiotic prescribing and stewardship, and developing new drugs and diagnostic tests" (About Antimicrobial Resistance, 2017). The focus of this study is aimed at preventing infections with MDRO and subsequently preventing their spread through enhanced surveillance methods in a hospital setting.

1.1 MDRO IN HEALTHCARE FACILITIES

Over the last several decades, the prevalence of MDRO in hospitals and healthcare facilities has increased (Siegel et al., 2017). In 1999, MRSA accounted for greater than 50% of *S. aureus* isolated in intensive care units (ICU) in National Nosocomial Infection Surveillance (NNIS). By 2003, that number had risen to about 60% (NNIS, 2003). A similar increase was seen in VRE, where between 1999 and 2003 there was an increase from 25% to about 28.5% respectively (NNIS, 2003 and Fridkin et al., 2001). This increase in prevalence is a serious public health concern because MDRO poses a significant risk to vulnerable hospitalized patients.

Hospitalized patients are more at risk for MDRO colonization and infection. Patients who are the most vulnerable include those with severe disease and underlying medical problems, those with compromised immune systems, recent surgical patients and patients with indwelling devices (Lautenbach et al., 2001 and Goetz et al., 1998). It has been shown that patients in an ICU have

the most risk factors for MDRO colonization and infection, and have the highest infection rates (Siegel et al., 2017). One study found that "the risk that an ICU patient will acquire VRE increases significantly once the proportion of ICU patients colonized with VRE exceeds 50%" (Bonten et al., 1998). Consequently, hospitalized patients have higher rates of morbidity and mortality when infected with MDRO.

According to the CDC, MRSA, CRE, and VRE alone are responsible for 13,185 deaths per year (About Antimicrobial Resistance, 2017). Patients with a MRSA infection are estimated to be 64% more likely to die than patients with a non-resistant form of the infection (Antimicrobial Resistance, 2018). An infection with a MDRO can increase a patient's length of stay and increase healthcare costs during admission (Giske et al., 2008, Wilson et al. 2004, Song et al., 2003 and Cosgrove et al., 2006). In a surveillance study conducted at the University of Pittsburgh Medical Center-Mercy (UPMC-Mercy), it was found that patients who screened positive for Acinetobacter baumannii (a common MDRO) had a longer length of stay than patients who screened negative, at an average of 10.4 days and 3.8 days respectively (Harvey et al., 2015). Another study at the same facility found the average length of stay for patients with carbapenem-resistant organisms (CRO) or CRE to be 21 days, which is alarmingly high (Bozich et al., 2017).

The transmission of MDRO represents a challenge to patient safety, outcomes and quality of care. It has been reported that MDRO can transmitted from person to person from the hands of healthcare providers or from contaminated surfaces near the patient (Siegel et al., 2017). It is critical to preventing the spread of MDRO and preventing infections to practice the best infection control practices. Significant research has been conducted on creating the best policies for preventing MDRO in healthcare facilities.

1.2 PREVENTION OF MDRO IN HEALTHCARE FACILITIES

The CDC has developed guidelines for controlling MDRO in healthcare facilities. Current recommendations call for contact precautions for patients colonized with MDRO in health care institutions. The CDC recommends contact precautions "for all patients infected with specific multidrug-resistant organisms (MDROs) and for patients that have been previously identified as being colonized with target MDROs" (Siegel et al., 2017). Contact precautions may include patient placement in a single room and health care staff and visitor gloving and gowning upon entry into patient room. In addition, other contact precautions include washing in and out upon entry and exit of patient room and appropriate cleaning performed after patient discharge.

There is limited evidence showing the effectiveness of contact precautions on preventing MDRO infections (Morgan et al., 2014). Huskins et al. conducted a large cluster-randomized trial and found that active surveillance for MRSA and VRE doubled the number of patients receiving contact precautions but did not reduce the rates of transmission for either MDRO (Huskins et al., 2011). In Harris et al., they found that universal gloving and gowning in the ICU did not prevent acquisition of MRSA and VRE (Harris et al., 2013). Additionally, there is evidence showing negative outcomes associated with contact precautions. It has been hypothesized that the reason for this could be less times spent with patients, which result in delays in care (Morgan et al., 2009). Previous research found that the more patients under contact isolation resulted in decreased compliance with the contact precaution guidelines (Morgan et al., 2014). Lastly, the implementation of contact precautions has been associated with adverse events. In Abad et al, researchers performed a systematic review of the literature and found data showing negative impacts on patient wellbeing, specifically increases in patients' depression scores (Abad et al., 2010). Other negative effects found were a decrease in time spent with the patient and a decrease

in patient satisfaction. Furthermore, studies have shown that contact precautions also burden healthcare workers (Stelfox et al., 2003). In a study conducted at UPMC-Mercy, healthcare workers were surveyed about their perceptions about contact precautions. It was reported that 60% of healthcare workers responded that contact precautions delay their work and 56% responded that contact precautions affect the time they had to interact with a patient (Jain et al., 2017). Therefore, healthcare facilities need to strategize beyond contact precautions as a way to manage MDRO in the hospital, such as through surveillance strategies.

1.3 SURVEILLANCE

Surveillance is a critical tool in controlling MDRO in healthcare settings. Surveillance is defined as continuous supervision or a systemic collection and interpretation of data (Principles of Epidemiology in Public Health Practice, 2012 and WHO Public Health Surveillance). The goals of surveillance are to identify the prevalence of a disease, detect any change and monitor the efficacy of prevention programs (Calfee et al., 2014). Since 1980, after the "Study on the Efficacy of Nosocomial Infection Control" showed that surveillance for nosocomial infections and infection control practices could prevent HAIs, surveillance has been seen as a necessary tool and has been implemented in many healthcare facilities (Haley et al., 1980, Sydnor et al., 2011 and Huskins et al., 2011). Surveillance for MDRO in healthcare facilities is recommended by the CDC (Siegel et al., 2017). Additionally, the Pennsylvania Department of Health has mandated that hospitals perform surveillance for MDRO (Medical Care availability & reduction of error (MCCARE) Act, 2007).

Surveillance is either passive or active. Passive surveillance uses already clinically available data, such as clinical microbial cultures or molecular testing, such as a respiratory viral panel. Active surveillance is the systematic collection and analysis of data. Historically, surveillance was clinically-based (horizontal), however it moved into pathogen-based (vertical) due to the automated nature and ease of use (Siegel et al., 2017).

Past research has shown the positive effect surveillance has had on controlling MDRO infections and decreasing nosocomial infections in the hospital (Robicsek et al., 2008 and Huang et al., 2007 and Lucet et al., 2005 and Ostrowsky et al., 2001). In a 2011 study by Jain et al., the authors implemented a "MRSA bundle" which included universal nasal surveillance, contact precautions for patients colonized or infected, hand hygiene and a change in responsibility that implemented a policy that all persons in contact with the patient was involved in infection control. Overall, they found a 62% decrease in MRSA infections after the implementation of these procedures (Jain et al., 2011). This study illustrates the importance of surveillance, but additional research findings have emphasized the need to further investigate the most effective surveillance approach (Diekema et al., 2007 and McKinnell et al., 2015). Current research is exploring the effectiveness of vertical and horizontal surveillance in capturing MDRO in the hospital.

1.3.1 Vertical Surveillance

Vertical surveillance is defined as a narrow-based approach focused on a particular pathogen. For MDRO, this means screening patients to identify specific pathogens, like MRSA or VRE. Many studies have shown positive effects of implementing this method of surveillance, as shown by the Jain et al article. Additionally, the CDC recommends focusing on the most epidemiologically important pathogens in using vertical surveillance to curb the overwhelming

increase in MDRO within healthcare facilities (Sydnor and Perl, 2011 and CDC Guidelines for Isolation Precautions, 2007). However, there is new evidence suggesting vertical surveillance may not be as effective at capturing MDRO in a hospital setting.

Recent research has explored the effectiveness of vertical surveillance and found that it may not be the best approach. In recent studies, researchers found that although the use of vertical surveillance based on certain pathogens was effective during outbreaks, it had little effect on endemic levels (Huskins et al., 2011 and Morgan et al., 2014). There is substantial need for a surveillance approach to be effective at capturing MDRO at endemic levels within a hospital setting.

Recent research has illustrated the economic burden of vertical surveillance. Vertical surveillance is costly and can be a burden on healthcare facilities. One study estimated that the cost of MRSA screening and contact precautions outweighed the benefits of preventing infections and resulted in economic costs of $104,000 per 10,000 admissions (McKinnell et al., 2015). Given the pressure on healthcare facilities to reduce costs, emphasis has been placed on developing effective surveillance measures that are more efficient at capturing MDRO.

1.3.2 Horizontal Surveillance

Horizontal surveillance is defined as an enhanced surveillance approach focused on high-risk populations. While vertical surveillance means screening everyone for a particular pathogen, horizontal surveillance focuses on certain populations to screen. Recent research has found that horizontal surveillance may be just as effective at capturing MDRO as vertical surveillance.

The focus of horizontal surveillance is the clinical risk factors that have been shown to be associated with MDRO colonization. Data has shown patients who are readmitted to the hospital

within 90 days and/or patients who have been admitted from an outside facility (like a Skilled Nursing Facility) are more likely to be colonized with MDRO (Fukuta et al., 2013). In addition, patients with an open wound, indwelling catheter or have a tracheostomy are more likely to be colonized. Finally, patients with a long length of stay are also more likely to be colonized with MDRO (Fukuta et al., 2013 and Mody et al., 2015 and Vasudevan et al., 2014). Focusing on these populations with evidence showing increased risk for colonization may be a more efficient approach for capturing MDRO in the hospital.

Two preliminary studies conducted at UPMC-Mercy investigated the risk factors associated with MDRO colonization. In Harvey et al., they found that all horizontal criteria investigated was more likely associated with a positive Acinetobacter patient. These criteria included patient admission from a long-term care facility, readmission within 30 and 90 days and patients with a chronic wound (Harvey et al., 2016). In Boznich et al., they found that three of the six horizontal criteria were associated with MDRO colonization and infection and concluded that horizontal surveillance may be a more effective approach to managing MDRO in their facility (Boznich et al., 2017).

The major benefit of horizontal surveillance over vertical is the decrease cost associated with horizontal surveillance. As stated, vertical surveillance is extremely costly and horizontal surveillance as a targeted population approach does not expend as many resources. If horizontal surveillance is shown to be just as effective as vertical surveillance in capturing MDRO, then it could be a cost-effective approach for healthcare facilities.

The objective of this study is to compare horizontal surveillance to vertical surveillance for MDRO in a hospital setting. The first step involves prospectively investigating if certain clinical criteria are associated with MDRO colonization and infection. This will ascertain patient clinical

characteristics which may predispose specific patients at a higher risk for MDRO colonization and infection. Next, we will compare the rates of MDRO captured in vertical surveillance verses horizontal surveillance. In addition, we will examine if use of a groin sponge is as effective as rectal swabs in capturing MDRO and examine the effect MDRO have on length of hospital stay. Finally, a comparison of cost will be determined for both approaches.

2.0 METHODS

The objective of this study was to compare focused enhanced surveillance for populations at high-risk for MDRO colonization to the current vertically oriented surveillance strategy. For this study, MDRO will be defined as microorganisms that are resistant to one or more classes of antimicrobial agents (Siegel et al., 2017). This study was approved by the University of Pittsburgh Internal Review Board as quality improvement on February 17, 2017 (Project ID: 915).

2.1 DESIGN

A prospective cohort study was conducted at a 500-bed, tertiary, university affiliated healthcare facility. Electronic medical record surveillance was performed to randomly identify 100 high-risk patients between October 2017 through November 2017. Vertical surveillance and horizontal surveillance was performed on these selected patients and a cost-effectiveness analysis was performed comparing the two approaches. MDRO included in the study were MRSA, VRE and MDRO-GNR (extended spectrum Beta lactamase (ESBL) and carbapenem resistant Gram-negative bacteria). Rates also included a history of MDRO, isolation status related to MDRO and length of stay. Figure 1 is a diagram depicting the study design.

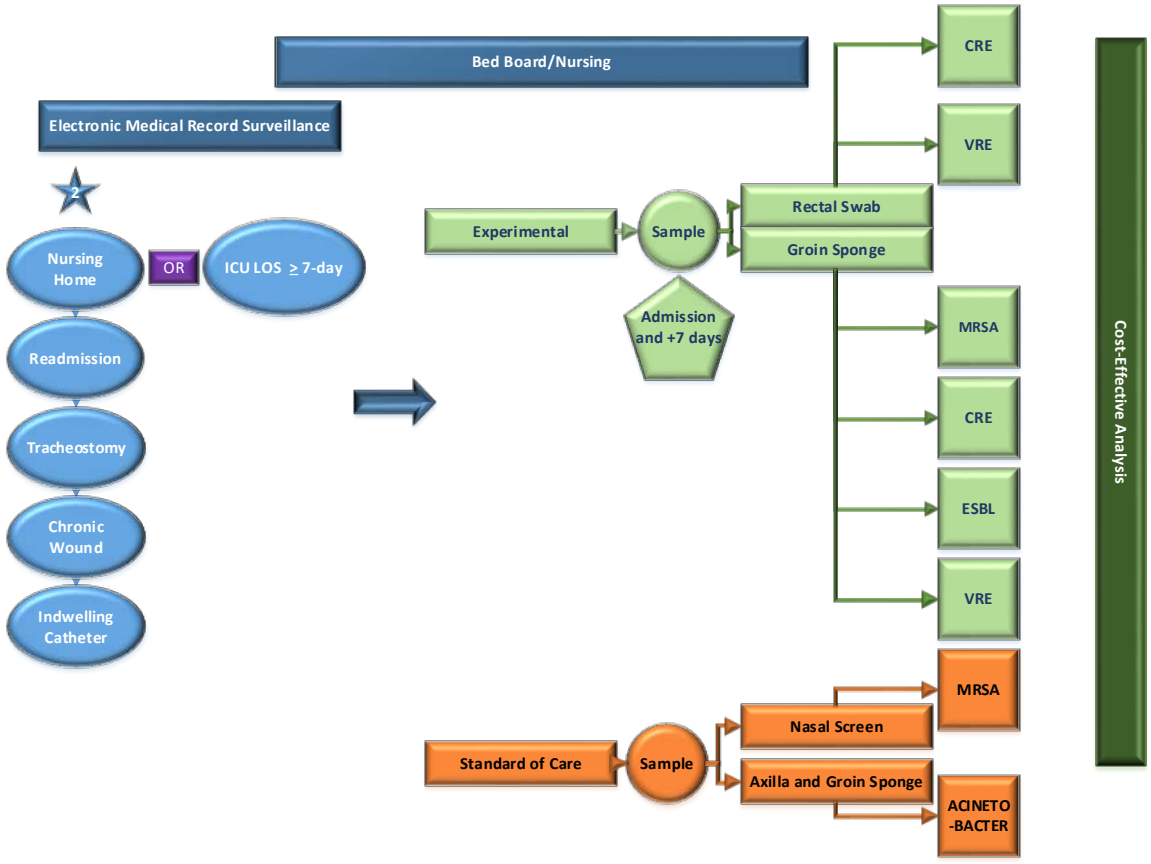

Figure 1. Study design

2.2 POPULATION

A total of 100 high-risk patients were included in the study. Patients were selected from Intensive Care Units (ICU). Patients in the behavioral, neonatal and rehabilitation units were excluded. Patients selected were considered high-risk for MDRO by having at least two out of five criteria on admission or if their length of stay met or exceeded seven days. The high-risk criteria include: admission from nursing home (or long-term care facilities), hospital readmission (within 90 days), the presence of chronic open wounds (more than 30 days), tracheostomy or chronic indwelling catheters. Indwelling catheters include: feeding tubes (e.g. percutaneous gastrostomy

(PEG) and jejunostomy), urinary catheters (urethral and supra public), intravenous catheters (e.g. hemodialysis catheters, peripherally inserted central venous catheters (PICC) and midline catheters) bowel diversion (e.g. colostomy, ileostomy and illeal conduit).

2.1 DATA COLLECTION

MDRO samples from patients were taken as follows. For the horizontal approach we used a rectal swab for CRE and VRE; we used a sponge to test for GNR-MDRO (ESBL & carbapenem resistant GNR), MRSA and VRE. For vertical surveillance we used the standard of care in our facility, a nasal swab for MRSA and an axilla and groin sponge for MDR-Acinetobacter. Figure 2 illustrates the axilla and groin sponge and rectal swab. The yield of the sponge was used as a comparison to the standard method of a rectal swab for VRE & nasal swab for MRSA. All patient samples were de-identified, transported, and analyzed in the laboratory and the results were recorded.

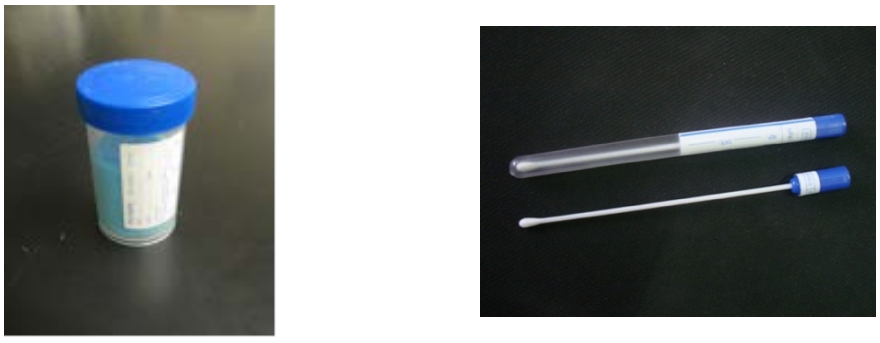

Figure 2. Groin sponge and rectal swab

Patient samples were collected as follows. A healthcare worker removed the blue sponge from the container and wiped down the patients' axilla (either side) and then the groin (Figure 3). If this area is not available to swab (i.e. due to burn or amputation) it was indicated as such on requisition. The soiled sponge was placed back into the container, closed and labeled. Next, to collect rectal swab, the container was opened and the swab was untwisted and removed from its case. A healthcare worker either turned the patient on their side or lifted their leg to locate the rectum. The rectum was swabbed 2 to 3 times in a circular motion. Finally, the swab was inserted back into container. Both patient samples were then placed in a labeled biohazard bag with the corresponding study ID number. Figure 4 shows the "study kits," which include the rectal swab, groin sponge and biohazard bag all labeled with the appropriate study ID.

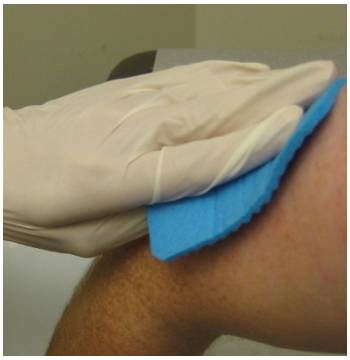

Figure 3. Groin sponge collection

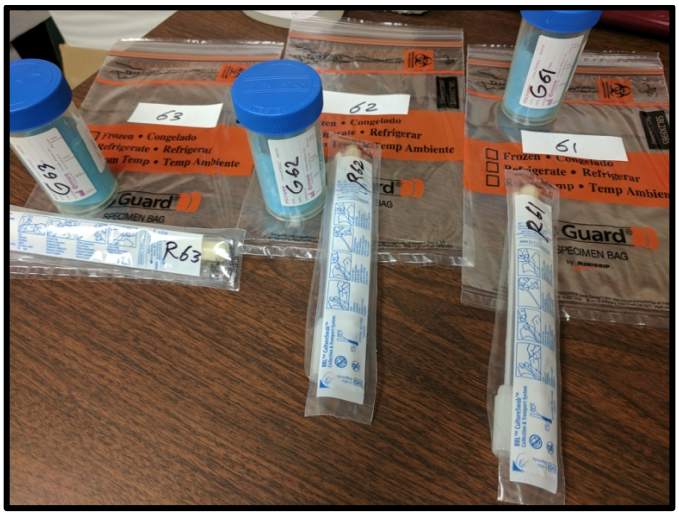

Figure 4. Groin sponge and rectal swab study kits

Processing of samples in the lab are as follows. On Day 1, the sponges and swab arrived in the lab and they were logged on the study spreadsheet as “00X”R for rectal swab and “00X”G for groin swab. Approximately 10 mL of nutrient broth was poured into a container and the sponge was soaked by rotating and vortex. Next, 1 mL of nutrient broth was poured into a cryotube and the swab was gently vortexed for 10 seconds. The container and cryotube were then incubated at 37°C without CO_2 for four hours. Next, a new cotton swab was soaked in approximately 100 µl of broth. Then 4 selective plates were inoculated with a new swab, half of the plate from the sponge sample and half of the plate from the swab sample. A fresh swab for every inoculation was used to avoid contamination. Next, the remaining broth was frozen down with glycerol; for the swab 250 µl of glycerol was added and the cryotube was frozen down and for the sponge 750µl of broth from the container was transferred to a fresh cryotube and 250µl of glycerol was added and frozen down. Next, the plates were incubated at 37°C without CO_2 overnight.

On Day 2, the plates were inspected. MRSA and ESBL were interpreted and the results were reported out. Biochemical identification and susceptibility testing was performed for

suspected ESBL and CRE colonies. On Day 3, the results of the growth were logged. The unique colonies were sub-cultured on an LB plate and frozen down. Finally, the specimen information and type of screening plate were indicated.

Medical records of 100 patients who were identified as high-risk were analyzed via Cerner PowerChart. Patient characteristics were abstracted and included: age, sex, year and month of birth, admission date, severity index, comorbidity index, length of stay, and mortality within admission. All data abstracted and reported were within 24 hours of ICU admission. Duplicate admissions and patients who did not meet our criteria were excluded from the study. SAPS II Calculator was used to determine hospital mortality related to their admission (Appendix A). Charlson Comorbidity Index was used to calculate comorbidity (Appendix B).

Results of MDRO clinical culture, history of MDRO, isolation status and standard screening were abstracted from the medical chart and recorded. History of MDRO was recorded if noted in the banner of the patient chart. Isolation status was recorded if any MDRO were noted in the banner of the patient chart. Clinical culture was recorded if there was a positive culture at any point during the patient's admission. A positive standard screening was recorded if there was a positive screen at any point during their admission.

2.2 DATA ANALYSIS

Statistical analysis was completed using STATA SE 15.1. Fisher's Exact tests were used to test associations between clinical criteria and MDRO colonization and infection. Fisher's Exact and Wilcoxon Rank-Sum tests were used to compare the clinical criteria group to the LOS group. Fisher's Exact tests were also used to compare horizontal and vertical surveillance data.

TreeAge Healthcare Pro 2017 software was used to perform a cost-effective analysis between both surveillance strategies. The costs and effectiveness of surveillance were calculated from the health care perspective.

3.0 RESULTS

3.1 BASELINE PATIENT CHARACTERISTICS

There was a total of 100 high-risk patients in our cohort that were analyzed, 74 who met the clinical criteria and 26 who were screened after 7-day LOS. There were 52 males and the average age was 60.1 years. The mean severity index was 38.8 and the mean comorbidity index was 4.4. The average length of stay for all 100 patients was 13.2 days.

Patients who met our high-risk clinical criteria were compared to patients who had a LOS that met or exceeded seven days. The average LOS in our high-risk clinical criteria group was 11.4 days verse 15.8 days in our 7-day LOS group and this was found to be significant, with a p-value of 0.001. There were no other statistically significant differences found between the two groups. The results are shown in Table 1.

Table 1. Patient characteristics: high-risk clinical criteria patients verse 7-day length of stay patients

	High-Risk Clinical Criteria Patients n=74	7-Day LOS Patients n=26	p-value
Age (Average)	60.8	58	0.46
LOS (# of days)	11.4	15.8	0.001
Sex (% males)	50%	57.70%	0.33
Severity Index	38.1	40.8	0.64
Comorbidity Index	4.5	3.8	0.25
Medicine vs. Surgery (# of Surgery Pts.)	13	7	0.23
Clinical Culture (% positive patients for any MDRO)	6/74=8%	4/26=15.4%	0.24
History of MDRO (% positive patients for any MDRO)	13/74=17.6%	5/26=19.2%	0.53
Vertical Screening (% positive patients for any MDRO)	5/74=6.8%	5/26=19.2%	0.07
Horizontal Screening (% positive patients for any MDRO)	22/74=30%	7/26=27%	0.5

3.2 CLINICAL CRITERIA

Of the 100 patients in our cohort, 74 met our high-risk clinical criteria on admission. The percent of patients with each clinical criterion is shown in Figure 5. It was found that 90.5% of patients had an indwelling catheter, while only 5.4% had a tracheostomy. 70.4% of patients were admitted from an outside facility.

The total number of high-risk criteria a patient had was not found to be associated with any of our MDRO indicators. It was found that an open wound was associated with CRE colonization/infection, with a p-value of 0.04. All other associations between clinical criteria and MDRO indicators were not found to be statistically significant. These results are reported in Table 2.

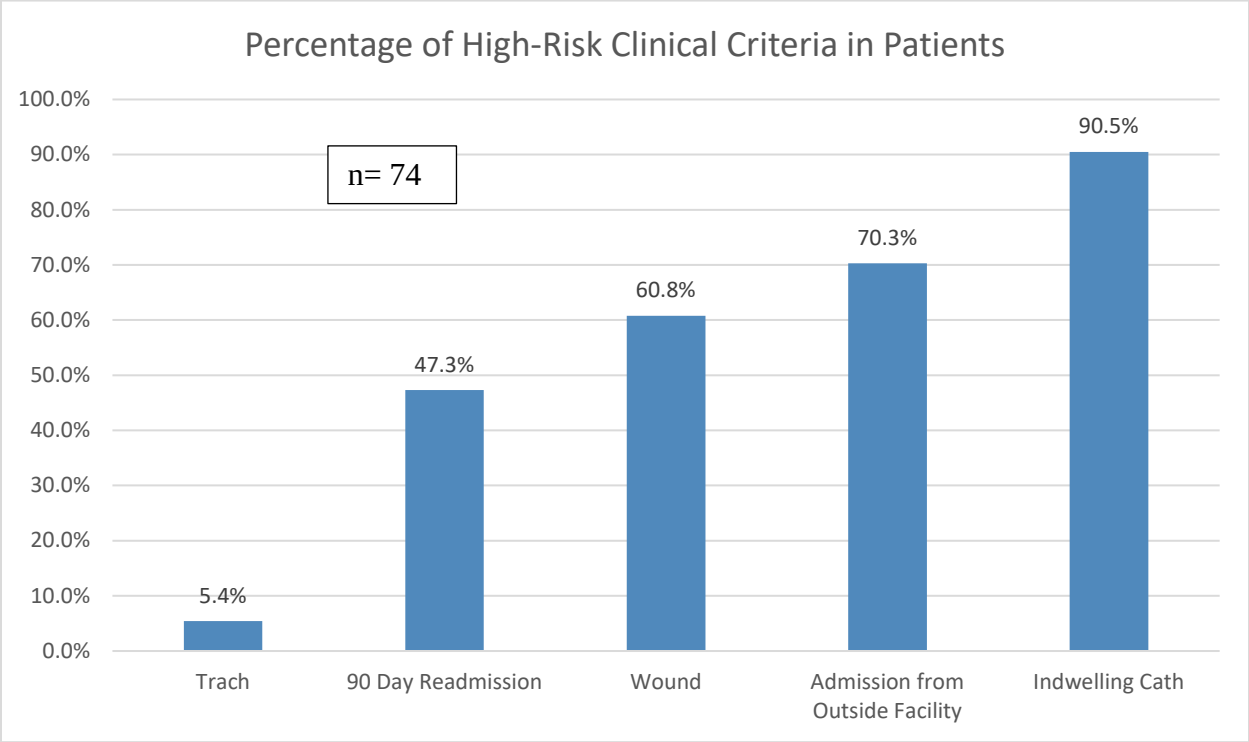

Figure 5. Percentage of patients with high-risk clinical criteria

Table 2. Associations between high-risk clinical criteria and MDRO indicators: number of patients, percent of patients and p-value

High-risk Clinical Criteria	Positive Clinical Culture	History of MDRO	Positive Standard Screening (MRSA)	Horizontal Surveillance			
				MRSA	VRE	CRE	ESBL
Indwelling Catheter	5/74 (6.8%) (0.46)	13/74 (17.6%) (0.24)	4/74 (5.4%) (0.40)	1/74 (1.4%) (0.91)	9/74 (12.2%) (0.65)	5/74 (6.8%) (0.46)	13/74 (17.6%) (0.24)
Wound	3/74 (4.1%) (0.44)	7/74 (9.5%) (0.40)	4/74 (5.4%) (0.34)	1/74 (1.4%) (0.61)	7/74 (9.5%) (0.40)	6/74 (8.1%) (0.04)	7/74 (9.5%) (0.40)
Trach	0/74 (0%) (0.71)	1/74 (1.4%) (0.54)	0/74 (0%) (0.75)	1/74 (1.4%) (0.94)	1/74 (1.4%) (0.44)	0/74 (0%) (0.71)	1/74 (1.4%) (0.54)
Admission from Outside Facility	5/74 (6.8%) (0.42)	9/74 (12.2%) (0.58)	4/74 (5.4%) (0.53)	0/74 (0%) (0.29)	8/74 (10.8%) (0.38)	2/74 (2.7%) (0.06)	7/74 (9.5%) (0.138)
90 Day Readmit	5/74 (6.8%) (0.08)	8/74 (10.8%) (0.20)	3/74 (4.1%) (0.45)	0/74 (0%) (0.53)	6/74 (8.1%) (0.30)	3/74 (4.1%) (0.61)	7/74 (9.5%) (0.41)

3.3 VERTICAL VS. HORIZONTAL SURVEILLANCE

3.3.1 Vertical Surveillance

For vertical surveillance we collected information on a patient's clinical culture, history of MDRO, their isolation status and vertical standard screening results. Clinical cultures showed 10% of patients were positive for any MDRO. MDRO history showed 6% of patients had a history of MRSA and 6% had a history of VRE. Standard screenings results showed no patients screened positive for MDR-Acinetobacter, while 10% screened positive for MRSA. 18% of patients had a positive MDRO history and 10% of patients had positive standard screen and this was found to be significant at p= 0.035. These results are reported in Table 3.

Table 3. Vertical surveillance: percent of patients positive for clinical culture, history of MDRO, isolation status and vertical screening

	MDRO	Proportion	95% Confidence Interval
Clinical Culture	Any MDRO	10%	(0.054-0.178)
	MRSA	7%	(0.033-0.141)
	VRE	1%	(0.001-0.069)
	GNR	1%	(0.001-0.069)
	CRE + GNR	1%	(0.001-0.069)
History of MDRO	Any MDRO	18%	(0.116-0.269)
	MRSA	6%	(0.026-0.128)
	VRE	6%	(0.026-0.128)
	GNR	1%	(0.001-0.069)
	MRSA + VRE	3%	(0.009-0.090)
	CRE + ESBL	1%	(0.001-0.069)
	CRE + GNR	1%	(0.001-0.069)
Isolation Status	Yes	17%	(0.107-0.258)
Standard Screening	MRSA Nasal Screen	10%	(0.054-0.177)

3.3.2 Horizontal Surveillance

For horizontal surveillance, rectal swabs and groin sponges were collected for VRE, MRSA, CRE, and ESBL. The vertical surveillance method was compared to the horizontal approach. Using the vertical method, 10% of patients screened positive for MRSA verses 1% and 2% screened positive using the rectal and groin horizontal methods. 10% of patients had a positive clinical culture and 9% of patients had a positive history for any MDRO plus a positive horizontal screen and this was found to be significant at p=0.03. We compared MDRO captured using rectal swabs to MDRO captured using a groin sponge to determine if using a groin sponge was just as effective at capturing MDRO. A difference was found between both approaches for capturing CRE. These results are reported in Table 4.

Table 4. Horizontal surveillance: percent of patients positive for VRE, MRSA, CRE, and ESBL using rectal swab verses groin sponge

MDRO	Groin vs. Rectal	Positive Proportion	95% Confidence Interval
VRE	G	9%	(0.046-0.165)
	R	10%	(0.054-0.177)
MRSA	G	1%	(0.001-0.069)
	R	2%	(0.004-0.078)
CRE	G	3%	(0.009-0.090)
	R	7%	(0.033-0.141)
ESBL	G	12%	(0.068-0.201)
	R	10%	(0.054-0.177)

3.4 COST-EFFECTIVE ANALYSIS

Cost-effective analysis (CEA) was performed using TreeAge Health Care Pro 2018. The model was built on a base case and was varied using one-way sensitivity analysis (1-WSA) (McKinnell et al., 2015). Table 5 shows the variables included in the model.

Table 5. Variables used in CEA model

Abbreviation	Full name	Base Case	Min	Max
cClinInf	Cost of Clinical Infection	50000	20000	60000
cSCH	Cost of Horizontal Screening	200	100	300
cScV	Cost of Vertical Screening	50	30	70
pColtoINf	Probability of colonization to Infection	0.03	0.01	0.05
pScHpos	Probability of HS positive	0.15	0.1	0.2
pSchVpos	Probability of VS positive	0.06	0.05	0.1

The tree diagram is shown with horizontal surveillance as the favored strategy at the base case (Figure 6). Multiple 1-WSA were consistent showing that horizontal surveillance is the favored strategy, and this is shown in Figures 7, 8, 9, 10 and 11. Horizontal surveillance was the dominant strategy when the cost of vertical surveillance is greater than $37.50 (Figure 7). In addition, horizontal surveillance was the dominant strategy once the probability of positive screening using horizontal surveillance crosses 7.5% (Figure 8). Finally, Figure 11 shows the threshold of cost-effectiveness using 1-WSA comparing horizontal surveillance (blue) verses vertical surveillance (red). Horizontal surveillance becomes the favored cost-effective strategy with clear monetary benefit when the cost reaches just above $25.

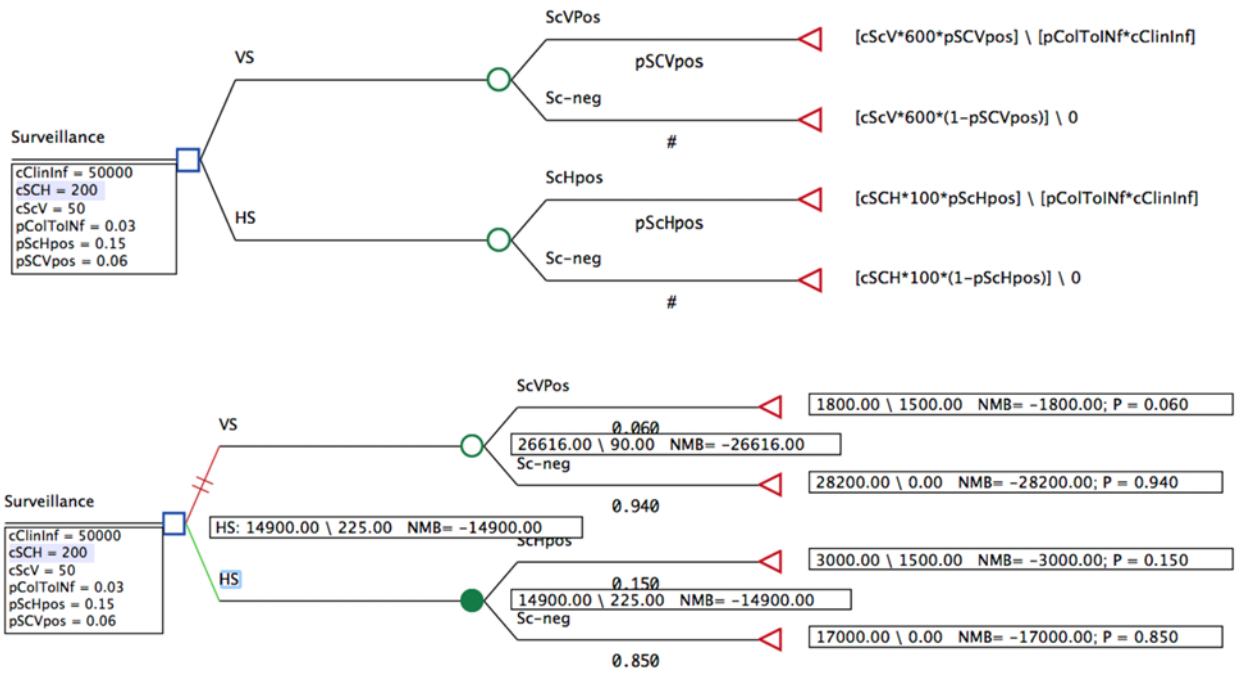

Figure 6. Tree diagram of cost-effective analysis comparing vertical vs. horizontal strategies

The diagram indicates horizontal surveillance is more cost-effective (green circle) and saves roughly $225 per patient.

Sensitivity Cost Effectiveness Analysis

cScV	Strategy	Cost	Incr cost	Eff	Incr Eff	ICER	NMB	C/E	Dominance
▼0.0									
	VS	0.00	0.00	90.00	0.00	0.00	0.00	0.00	
	HS	14900.00	14900.00	225.00	135.00	110.37	-14900.00	66.22	
▼12.5									
	VS	6654.00	0.00	90.00	0.00	0.00	-6654.00	73.93	
	HS	14900.00	8246.00	225.00	135.00	61.08	-14900.00	66.22	
▼25.0									
	VS	13308.00	0.00	90.00	0.00	0.00	-13308.00	147.87	
	HS	14900.00	1592.00	225.00	135.00	11.79	-14900.00	66.22	
▼37.5									
	HS	14900.00	0.00	225.00	0.00	0.00	-14900.00	66.22	
	VS	19962.00	5062.00	90.00	-135.00	-37.50	-19962.00	221.80	(Dominated)
▼50.0									
	HS	14900.00	0.00	225.00	0.00	0.00	-14900.00	66.22	
	VS	26616.00	11716.00	90.00	-135.00	-86.79	-26616.00	295.73	(Dominated)

Figure 7. One-way sensitivity analysis comparing horizontal surveillance to vertical surveillance

When variating the cost of vertical screening, horizontal surveillance becomes the dominate approach when the cost of vertical surveillance is $37.50.

Sensitivity Cost Effectiveness Analysis

pScHpos	Strategy	Cost	Incr cost	Eff	Incr Eff	ICER	NMB	C/E	Dominance
▼0.0									
	HS	20000.00	0.00	0.00	0.00	0.00	-20000.00	20000.00	
	VS	26616.00	6616.00	90.00	90.00	73.51	-26616.00	295.73	
▼0.0375									
	HS	18556.25	0.00	56.25	0.00	0.00	-18556.25	329.89	
	VS	26616.00	8059.75	90.00	33.75	238.81	-26616.00	295.73	
▼0.075									
	HS	17225.00	0.00	112.50	0.00	0.00	-17225.00	153.11	
	VS	26616.00	9391.00	90.00	-22.50	-417.38	-26616.00	295.73	(Dominated)
▼0.1125									
	HS	16006.25	0.00	168.75	0.00	0.00	-16006.25	94.85	
	VS	26616.00	10609.75	90.00	-78.75	-134.73	-26616.00	295.73	(Dominated)
▼0.15									
	HS	14900.00	0.00	225.00	0.00	0.00	-14900.00	66.22	
	VS	26616.00	11716.00	90.00	-135.00	-86.79	-26616.00	295.73	(Dominated)

Figure 8. Sensitivity analysis comparing horizontal surveillance to vertical surveillance

When variating the probability of screening positive using horizontal screening, horizontal surveillance becomes the dominate approach when the probability reaches 7.5%.

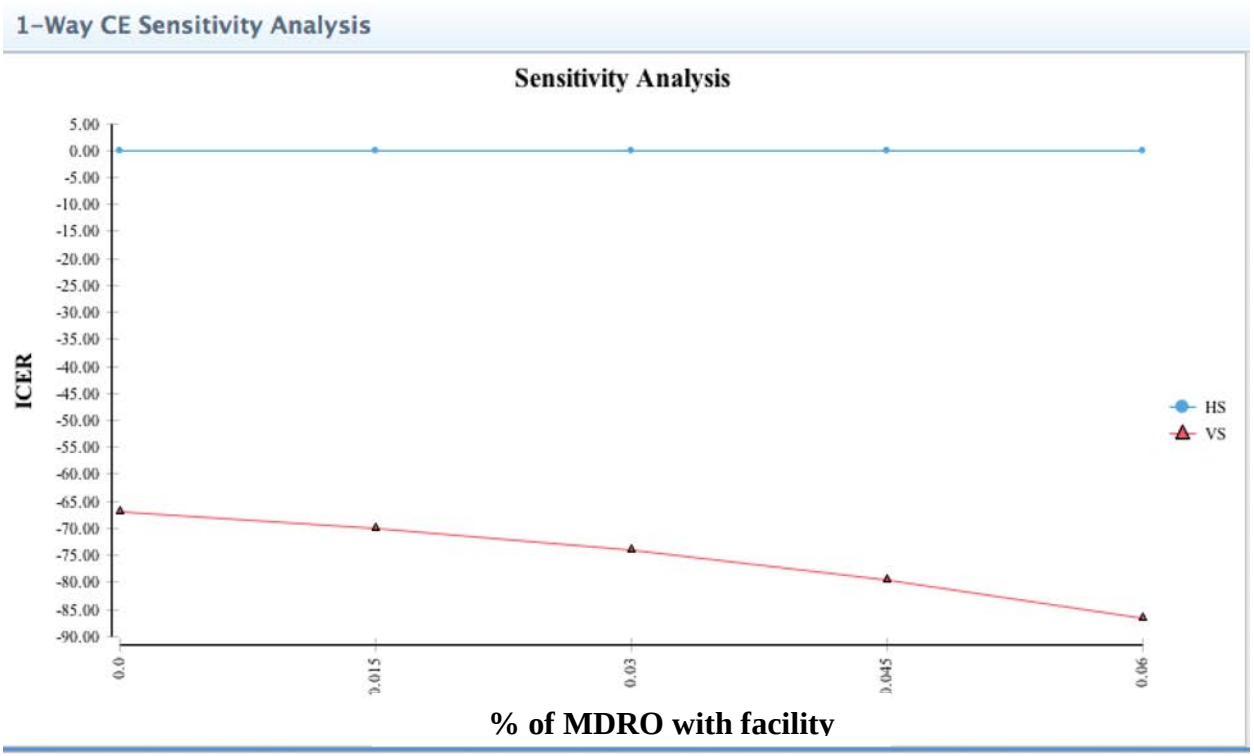

Figure 9. Sensitivity analysis comparing horizontal surveillance to vertical surveillance

When variating the percentage of any MDRO within a facility, horizontal surveillance is the more cost-effective approach.

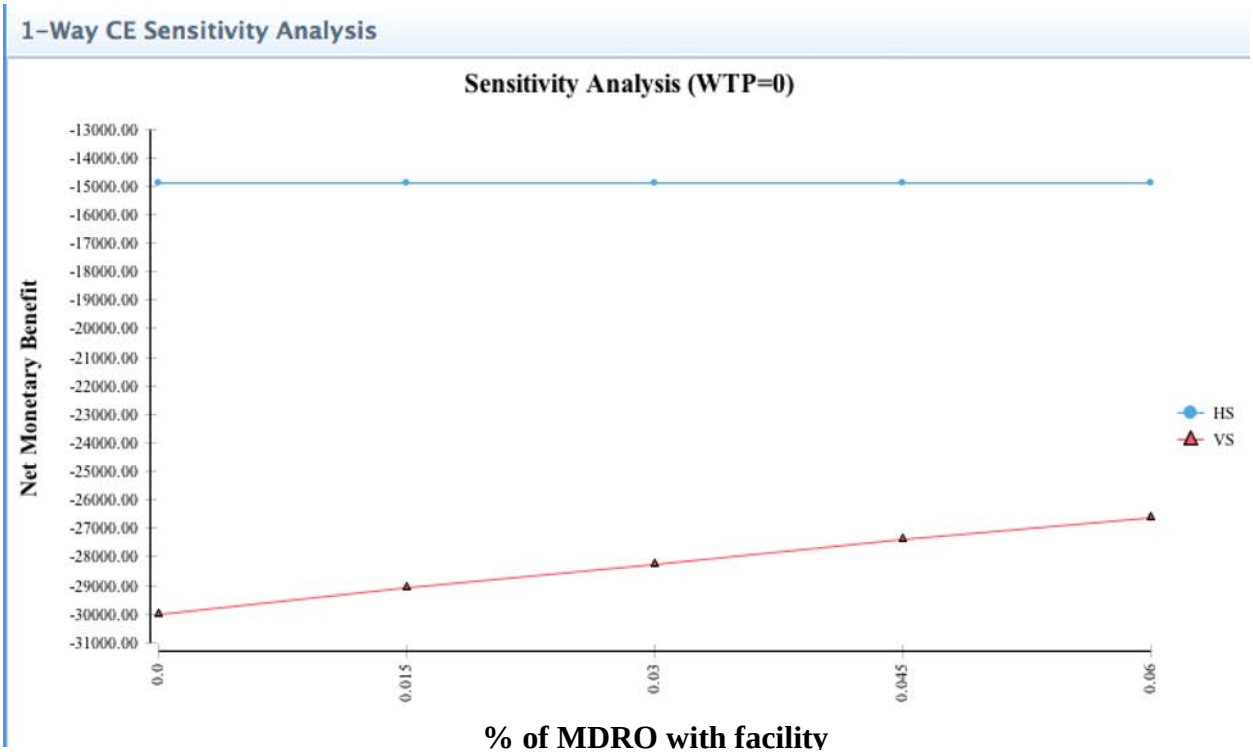

Figure 10. Sensitivity analysis comparing horizontal surveillance to vertical surveillance

When variating the percentage of any MDRO within a facility, horizontal surveillance is the more cost-effective approach.

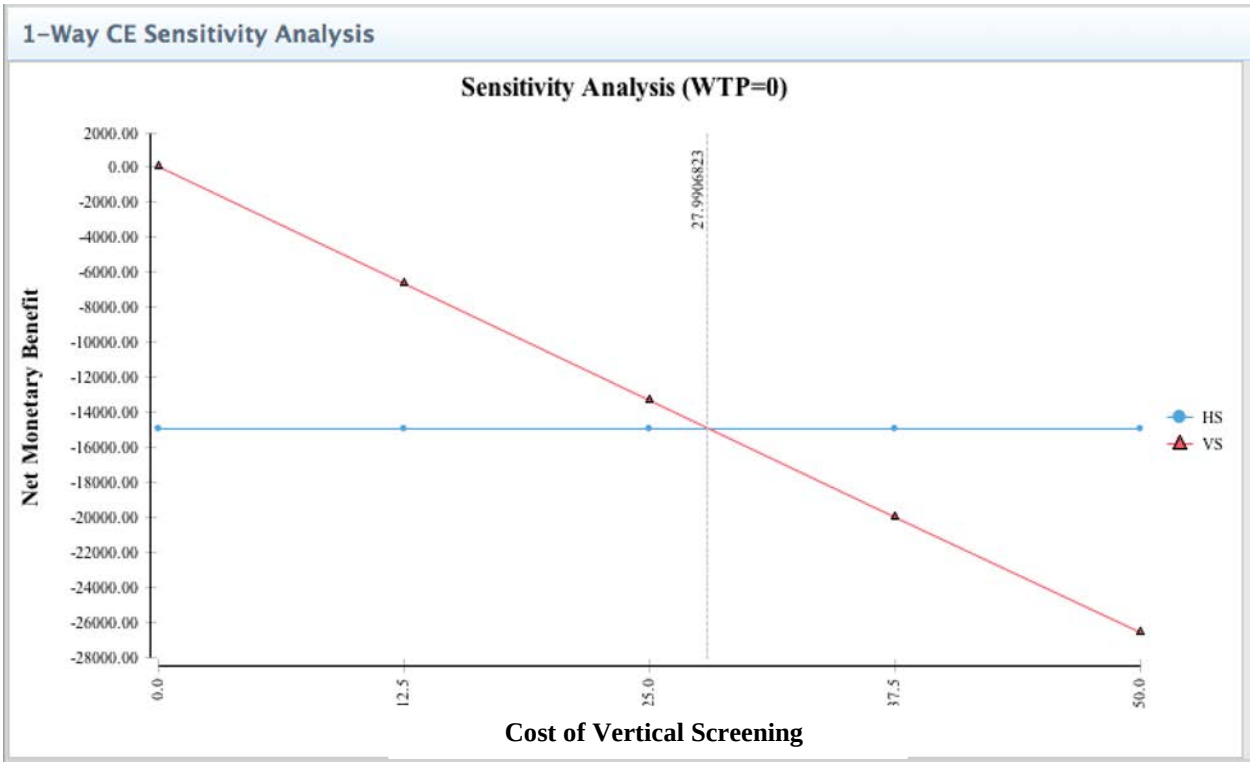

Figure 11. Sensitivity analysis comparing horizontal surveillance to vertical surveillance

When variating the cost of vertical screening, horizontal surveillance is the more cost-effective approach at roughly $28.

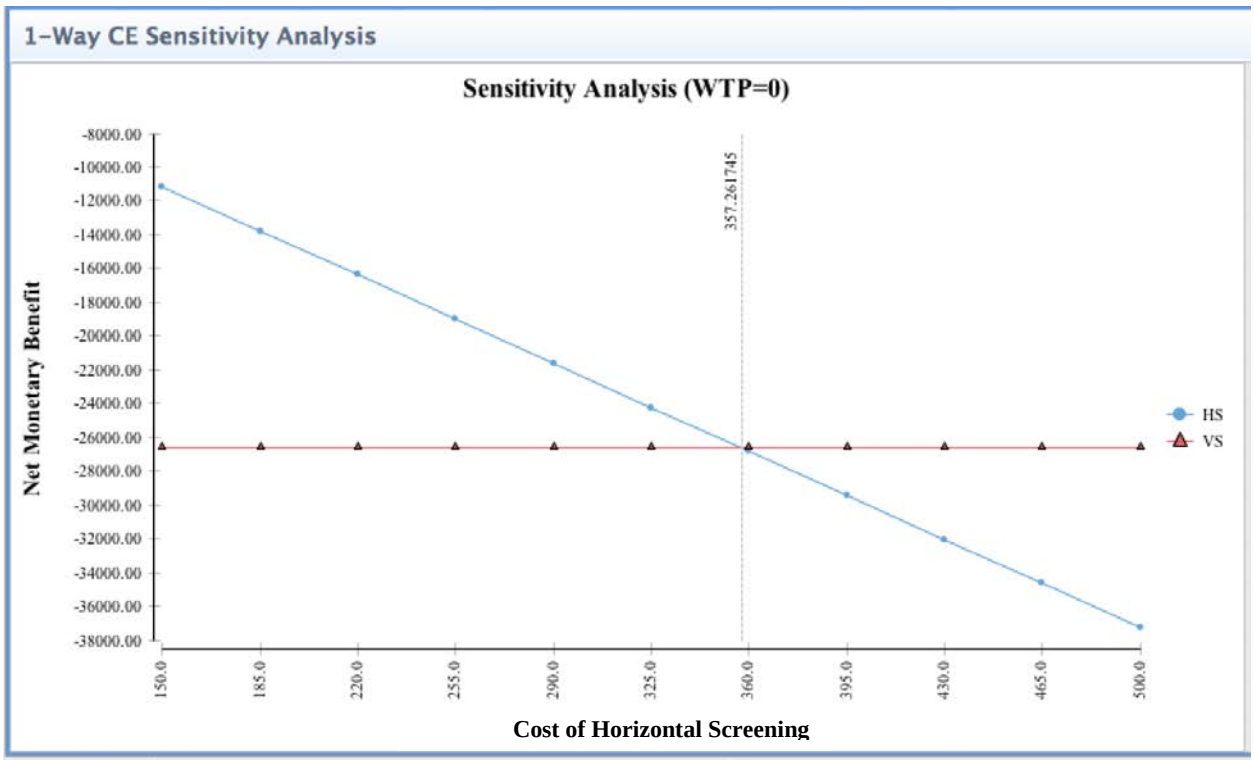

Figure 12. Sensitivity analysis comparing horizontal surveillance to vertical surveillance

When variating the cost of horizontal surveillance, vertical surveillance becomes the cost-effective approach when horizontal costs roughly $358.

4.0 DISCUSSION

MDRO is a serious public health problem and the prevalence of these organisms continues to rise within healthcare facilities. It is critical to patient safety and quality of care to explore better ways to prevent infections with these organisms. This study looked to compare the current surveillance strategy for MDRO to an enhanced method that focuses on high-risk patient populations. The aims of the research were to compare vertical and horizontal surveillance, to investigate the impact of length of stay on MDRO colonization and infection, and to perform a cost-effective analysis to determine which method was the most economical.

This study first looked to prospectively examine if high-risk clinical criteria were associated with MDRO colonization and infection. It was found that a chronic wound was associated with CRE colonization and infection. This adds to existing evidence from previous studies in the same facility that found high-risk criteria was associated with MDRO colonization and infection. The specific high-risk criteria that were found to be associated with MDRO were the presence of a chronic wound and the history of tracheostomy or ventilator. Increasing our sample size would be beneficial to determine if other criteria were associated with MDRO colonization or infection. In addition, it was found that 10% of patients screened positive for MRSA, while MRSA screening rates in our facility are typically around 5-8%. These results indicate that our selected high-risk criteria are correct, as we are screening the patient population at highest risk for MDRO colonization and infection.

Next, the study looked to compare vertical surveillance to horizontal surveillance. The study showed that horizontal surveillance captured more MDRO than vertical surveillance. Vertical screening in our facility captures MRSA and MDR-Acinetobacter, while the horizontal

method captures MRSA, VRE, CRE and ESBL. In addition, it was found that a positive clinical culture was associated with a positive history of any MDRO plus a positive horizontal screen. This was not surprising, as history of MDRO has been found to be indicative of future MDRO colonization and infection (Connecticut State Department of Health). More research is needed with a larger sample size to comprehensively examine the effectiveness of horizontal surveillance compared to vertical surveillance.

Our MRSA screening results comparing both surveillance approaches were surprising. Using vertical surveillance, 10% of patients screened positive for MRSA, while with the horizontal approach only 2% of patients screened positive using a rectal swab and 1% of patients screened positive using a groin sponge. We hypothesize the difference in these numbers are attributed to how and where the samples were collected. The standard screening method uses a nasal swab, while the horizontal approach uses a rectal swab and/or groin sponge. Our results suggest that nasal swabs for MRSA screening may be the more effective approach. However, these results contradict a previous study in the same facility that found using a groin sponge significantly improves MRSA screening (Lee et al., 2015). More research with a larger sample size is necessary to investigate these results further and determine which sampling strategy is best. Possibly screening using a groin sponge and a nasal swab may best capture MRSA, however this expends more resources.

Additionally, this study looked to compare a rectal swab or groin sponge for MDRO collection. The results showed a difference between rectal swab and groin sponge for collecting CRE, at 7% verses 3% respectively. However, no conclusions can be made about which approach is most effective for sampling MDRO due to the small sample size. A larger sample size is

necessary to determine if there are statistically significant differences between the two sampling methods.

Finally, it was found that horizontal surveillance was the cost-effective approach in multiple one-way sensitivity analyses. At the base case, horizontal surveillance was more cost-effective compared to vertical surveillance and saves roughly $225 per patient. In addition, we calculated the thresholds for cost for each of the approaches. For vertical surveillance, at around $28 horizontal surveillance becomes the cost-effective approach. For horizontal surveillance, at roughly $358 vertical surveillance becomes the cost-effective approach. This indicates that the cost of horizontal surveillance would have to be higher than we predicted for our base case for vertical surveillance to be the more cost-effective approach. Furthermore, horizontal surveillance works better and is less costly compared to vertical surveillance.

There were some limitations to this study. The first is the small sample size, which was 100 patients. The small sample size resulted in an insufficient power for our analysis. In addition, the small size makes this research less generalizable to all hospitalized ICU patients. The second limitation in the study was the lack of a control group. It would have been beneficial to construct a case control study, instead of using patients as both cases and controls. The next step in research will be to increase our sample size and include a control group. The control group will consist of ICU patients who have not met any of our high-risk criteria and receive horizontal surveillance testing. By doing this, we can better compare the effectiveness of horizontal verses vertical surveillance strategies.

Additional limitations include EMR surveillance and methods of surveillance testing. First, there was a limitation with our generated patient list from the EMR system. The list was inaccurately generated, pulling patients with two criteria instead of three we initially wanted to

test. It was decided that investigating patients with two criteria for this study was sufficient, however this was remedied for future research to more carefully investigate specific high-risk criteria and their association with MDRO colonization/infection. Finally, there were limitations with surveillance testing techniques, including human error with lab techniques, data collection and analysis.

This research has implications for hospital infection control policy. Sufficient evidence supports surveillance as an effective way to management MDRO in a hospital setting (Robicsek et al., 2008 and Huang et al., 2007 and Lucet et al., 2005 and Ostrowsky et al., 2001). However, the focus has now shifted on ways surveillance can be more effective and less costly (Diekema et al., 2007 and McKinnell et al., 2015). This research found that horizontal surveillance captured more MDRO than the current vertical method. Additionally, we found that horizontal surveillance is the more cost-effective strategy. This research is preliminary evidence that supports horizontal surveillance as a more effective method for MDRO management in the hospital.

As it stands today, MDRO will continue to be a problem in hospitals and threatens patient safety and quality of care. Both the public health and healthcare communities need to continue to work to develop the best techniques for managing these organisms. This study is the first step in research to determine if horizontal surveillance is more effective and less costly. This new innovative infection control approach could reduce morbidity and mortality within hospitalized patients and save hundreds of thousands of healthcare dollars.

5.0 CONCLUSION

The presence of a chronic wound was found to be associated with CRE colonization. This supports existing data that found high-risk clinical criteria could be used as a more effective surveillance approach.

The rates of MDRO captured using the horizontal approach were greater than the rates captured using the vertical approach. This suggests that horizontal surveillance is a more effective approach than vertical surveillance. MRSA screening using a nasal swab technique captured more than when a rectal swab and groin sponge was used. This suggests that nasal swabbing for MRSA is the more effective technique.

It was found that horizontal surveillance was the more cost-effective surveillance approach. We conclude that this data supports horizontal surveillance as a more effective and less costly approach compared to current vertical surveillance.

Future research with a larger sample size and a control group are needed to verify these results. More research investigating surveillance approaches for MDRO is important for patient safety and quality of care.

APPENDIX A: SIMPLIFIED ACUTE PHYSIOLOGY SCORE (SAPS) II CALCULATOR

Purpose: To predict hospital mortality.

Scoring

1. Age (years)
Vitals
2. Heart Rate (bpm)
3. Systolic BP (mmHg)
4. Temperature (C or F)
5. Glasgow Coma Score
Oxygenation
6. Mechanical ventilation or CPAP (Yes or No)
7. PaO_2 (mmHg)
8. FiO_2 (%)
Renal
9. Urine Output mL per hour
10. BUN (mg/dL)
Chemistry
11. Sodium (mEq/L)
12. Potassium (mEq/L)
13. Bicarbonate (mEq/L)
14. Bilirubin (mg/dL)
Other
15. WBC ($x10^9$/L)
16. Chronic Diseases (Metastatic cancer, Hematologic malignancy and/or AIDS)
17. Type of Admission (Scheduled surgical, Unscheduled surgical, Medical)

APPENDIX B: CHARLSON COMORBIDITY INDEX SCORING

Purpose: To assess whether a patient will live long enough to benefit from a specific screening measure or medical intervention

Scoring: Comorbidity Component (Apply 1 point to each unless otherwise noted)
1. Myocardial Infarction
2. Congestive Heart Failure
3. Peripheral Vascular Disease
4. Cerebrovascular Disease
5. Dementia
6. COPD
7. Connective Tissue Disease
8. Peptic Ulcer Disease
9. Diabetes Mellitus (1 point uncomplicated, 2 points if end-organ damage)
10. Moderate to Severe Chronic Kidney Disease (2 points)
11. Hemiplegia (2 points)
12. Leukemia (2 points)
13. Malignant Lymphoma (2 points)
14. Solid Tumor (2 points, 6 points if metastatic)
15. Liver Disease (1 point mild, 3 points if moderate to severe)
16. AIDS (6 points)

Scoring: Age
1. Age <40 years: 0 points
2. Age 41-50 years: 1 points
3. Age 51-60 years: 2 points
4. Age 61-70 years: 3 points
5. Age 71-80 years: 4 points

Interpretation: Calculate Charlson Score or Index (i)
1. Add Comorbidity score to age score
2. Total denoted as 'i' below
2. Calculate Charlson Probablity (10 year mortality)
1. Calculate Y = e^(i * 0.9)
2. Calculate Z = 0.983^Y
3. Where Z is the 10 year survival

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