An Epidemiological Analysis of MDRO Acquisition in Critically Ill Burn Patients in Western Pennsylvania

by

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Abstract

Rationale: The growing public health concern of antibiotic resistance is becoming more critical and urgent. Multi-drug resistant organisms (MDROs) are becoming increasingly prevalent in healthcare settings and physicians are faced with the reality that treatment options are becoming scarcer. Burn patients are a special case within the hospitalized population as they are potentially exposed to pathogens internally through inhalation injury, effectively placing them at a higher risk for infection. As the first line of defense is compromised, burn injuries must be especially monitored as they are highly susceptible to subsequent infection. There is no set standard of infection prevention for burn patients currently. Identifying potential factors for acquiring an infection in a sample may allow healthcare workers to better prevent transmission among high-risk, densely populated healthcare settings. A thorough review and breakdown of a select group impacted with burn injuries will help elucidate factors behind population at increased risk.

Methods: Data was collected from burn patients admitted to the UPMC Mercy Burn ICU in 2018 that fit set inclusion criteria. Variables of interest include age, gender, total body surface area (TBSA) of burn, length of stay (LOS), previous history of MDRO, identified MDRO during hospitalization, and documented inhalational injury presence. The four MDROs of interest are

methicillin-resistant *Staphylococcus aureus* (MRSA), extended-spectrum beta-lactamase-producing bacteria (ESBL), Vancomycin-resistant enterococci (VRE) and carbapenem-resistant Enterobacteriaceae (CRE).

Results: Of the roughly three thousand burn patients evaluated for admission, 225 were admitted and 48 passed the exclusion criteria. There was a large disparity between gender, nine females and 39 males, in patients with critical burns. 12 of the 48 patients had a positive result for an MDRO during their stay and the majority (7) had a documented inhalation injury. Of the four evaluated MDROs, MRSA was present in nearly every case of a positive MDRO result. Patients with higher levels of burns were associated with having a longer LOS duration. There is also a statistically significant relationship between MDRO acquisition and LOS.

Conclusions: The results of this analysis reinforce previous findings regarding the epidemiology of burn patients, but also demonstrate the need for increased surveillance in healthcare settings to prevent the onset and spread of MDROs. The large proportion of MDROs are attributed to MRSA, supporting previous conclusions and indicating the high transmission potential as well as the need to focus on preventative measures.

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1.0 Introduction

Multi-drug Resistant Organisms (MDROs) are a rapidly growing concern in public health. Officials are warning against the use of antibiotics and antimicrobials without prior prescription and encouraging the public to only use as directed. MDROs are a major issue for healthcare facilities as they are highly transmissible and can survive standard cleaning regimens of rooms, linens, and handwashing. Additionally, treatment comes with a high price tag for both healthcare companies and patients.

1.1 Epidemiology and History

Burn injury severity varies greatly depending on a large number of factors including, but not limited to the amount of body surface area burned, critical areas burned, age, chemical exposure, immunosuppression, and depth of burn sustained. Burns are especially complicated injuries as they carry an enhanced risk for infection.

The American Burn Association estimates there are approximately 40,000 burn hospitalization admissions per year in the United States out of nearly 486,000 burn injuries that receive medical treatment. Of those, inhalation injury accompanies a conservative estimate of 2,000, equating to approximately 5% [1]. Inhalation injury occurs when the burns sustained are internalized and the airway becomes tainted with debris and allows the entry of toxins. While inhalation injury has a broad spectrum of severity, its most serious complications include secondary infections and systemic toxic effects from chemicals [1]. Combined with cutaneous

burns, inhalation injury increases the incidence of complications and overall mortality of thermal injury [2]. Inhalation injury is not common in burn patients, but those who present with this type of injury are at a higher risk for infection and complications. However, it appears that increasing burn size has a relationship with a rise in the incidence of inhalation injury [2].

When evaluating the severity of burns on a patient, it is imperative for physicians to identify if an inhalation injury has occurred through thorough examination. Delayed presentation contributes to the difficulty in quickly diagnosing and treating inhalation injuries. Heterogenous presentation of inhalation injury and lack of criteria complicates diagnoses and may prolong treatment, increasing the probability of infection [3]. Burn wound infections are important sources for serious complications and can drastically change a patient's outcome. As burn wound surfaces are immediately sterilized resulting from exposure and contact to high temperature, they can eventually become colonized with harmful organisms [4]. Consequently, the lack of normal organisms (flora) allows the presence and proliferation of dangerous organisms to colonize the injured area. The last several decades reveal that gram-negative infections are prevailing due to their virulence and emerging resistant nature [4]. Gram-positive MDRO infections include methicillin-resistant *Staphylococcus aureus* (MRSA) and Vancomycin-resistant enterococci (VRE). MDRO gram-negative infections include, but are not limited to, extended-spectrum beta-lactamase-producing bacteria (ESBL) and carbapenem-resistant Enterobacteriaceae (CRE).

The majority of burn injuries are avoidable and as such, emphasis is placed on preventative measures that include, but are not limited to ensuring there is a functional smoke detector, hot water monitoring, efficient fire evacuation plans and child-proof measures [5]. These campaigns are organized and promoted by national organizations including the American Burn Association (ABA), the Centers for Disease Control and Prevention (CDC) and the American Red Cross.

Moreover, groups that are considered to be at a higher risk for sustaining a burn injury includes children, the elderly and those with disabilities. For these populations, more specific preventative campaigns have been developed such as in-school or in-home demonstrations[6]. Furthermore, previous studies consistently have shown that there is a statistically significant difference in burn injury incidence rates between gender, tying males to a higher rate [7, 8].

As incredible medical advances have prevailed over the last fifty years, burns are no longer viewed as seriously critical conditions with radical treatment options and therefore, burn mortality has decreased since 1950 as evident in the drop of adjusted death rate in the US from 3.0 per 100,000 in 1981 to 1.2 per 100,000 in 2006 [9]. In addition to the decrease in mortality, incidence and severity have also decreased [5]. Newer treatment methods such as burn wound excision and grafting have emerged and replaced dated ones that are counterproductive, including immersion hydrotherapy [10]. Although developments have created significant strides in promoting healing, the threat of complications remains.

1.2 Complications

With any injury that involves open wounds, there is an increased risk for serious complications including infections, sepsis, multi-organ dysfunction syndrome (MODS) and death. Prevention and treatment of infection with burn patients are exceedingly difficult due to an impaired immune response [11]. Burn patients require special attention and precautions to prevent contracting a hard to treat hospital acquired infection (HAI), specifically, a multi-drug resistant organism (MDRO). Approximately 75% of burn mortality is tied to acquired infections, emphasizing the importance of minimizing infections [12]. The risk of acquiring an infection

appears proportionate to the severity and extensiveness of the burn sustained- the larger percentage total body surface area (TBSA) burned, the higher degree of risk. Additionally, several other risk factors exist including inhalation injury, flame burn, admission to the ICU and extended hospitalization all play a role increasing the probability of acquiring an infection [13]. The growing spread of the dangers stemming from antibiotic resistance coupled with an enhanced susceptibility to infections places burn patients at a potentially higher risk for acquiring an MDRO while in a healthcare setting.

2.0 Antibiotic Resistance

Antibiotic resistance is a public health concern growing at an alarming rate for a multitude of reasons. As of 2013, at least 2 million people become infected with antibiotic-resistant bacteria and 23,000 die each year as a direct result from their infection [14]. As the prevalence of drug-resistant bacteria is growing rapidly in recent years, it has become evident that strains that acquire resistance have an evolutionary advantage over those that do not. When confronted with an antibiotic, strains that underwent mutations and developed resistance will still be able to proliferate. In the same environment, strains that are untainted will succumb to the effect of antibiotics and eventually die out [15]. On a much larger scale, this demonstrates the effect of inappropriate antibiotic use in the world today. The most frequently considered explanations include lenient and prophylactic antibiotic prescribing habits of healthcare professionals, individuals obtaining unprescribed antibiotics through friends and family, and consuming of livestock given antibiotics when being raised. While difficult to quantify, the high-end estimate of animals affected by antibiotics is 70 percent [16]. These cohesively amalgamate to widespread resistance and culminates into a worldwide public health issue.

Pathogens can gain resistance to antibiotics through intrinsic or acquired mechanisms. The role of antibiotics is to dismantle the defense mechanisms of the infectious cell, but the manner of doing so varies on the class of antibiotic. Antibiotics function by inhibiting a specific, crucial structure within the cell, thereby triggering the entire structure to become ineffective. The areas that are targeted are the cell wall, including the cell membrane, the 30S and 50S subunit, and DNA gyrase and RNA polymerase [17]. Different antibiotics will target different structures.

Antimicrobial stewardship, a detail-ridden approach tailored to the individualized treatment of patients, was developed in the 1970s in response to growing resistance rates but has lost steam in recent years [18]. The goals of antimicrobial stewardship are to decrease costs for patients and healthcare facilities, optimize outcomes, and reduce antimicrobial resistance [19]. Prescribers are encouraged to focus on approaching treatment by finding a healthy medium between antibiotic prescription and the well-being of the patient. All systematic and meta-analyses that reviewed antimicrobial stewardship interventions find that these programs were effective in reducing nosocomial occurrence due to resistant strains [19]. Despite this movement, complications are constantly arising as newer, more resistant strains are emerging, so it becomes necessary to constantly update and adjust current protocols.

2.1 Multi-Drug Resistant Organisms (MDROs)

As MDROs are not easily treated by a common antibiotic regimen, they create situations where treatment is more costly and complex. Antibiotic resistance contributes to the difficulty of treatment in MDRO infections by eliminating the effectiveness of typical, less potent antibiotics. Antibiotic resistance is an urgent public health concern with a high growth rate in recent years, largely in part from increased inappropriate use of antibiotics and antimicrobials. MDROs of interest include methicillin-resistant *Staphylococcus aureus* (MRSA), extended-spectrum beta-lactamase-producing bacteria (ESBL), Vancomycin-resistant enterococci (VRE) and carbapenem-resistant Enterobacteriaceae (CRE). Most nosocomial pathogens, such as the aforementioned, can live on inanimate surfaces for weeks, posing a threat to the vulnerable population in the healthcare

setting [20]. MDRO prevalence continues to be on the rise in healthcare settings and the exact transmission pathways are still poorly understood [21].

2.1.1 Methicillin-Resistant *Staphylococcus aureus* (MRSA)

MRSA, a gram- positive species, is the leading cause of skin and soft tissue infections in the United States and consequently, one of the most common infections identified in burn patients [11, 13, 22]. The two types of MRSA, hospital- and community-acquired, reflect different strains. Since emerging, MRSA is also seen as one of the most serious threats to burn victims by opening the door to potentially aforementioned fatal conditions such as sepsis [13]. The most common site for MRSA colonization is the anterior nares but is frequently seen in more than one site such as throat, groin, and axilla [23, 24]. *S. aureus* bacterial infections that took place in the pre-antibiotic era possessed a mortality rate of over 80 percent. After penicillin was introduced with the reputation for improving prognosis, resistant strains were discovered less than two years later. The rate of resistance to penicillin today is now greater than 90 percent in human S. aureus isolates, demonstrating that penicillin is now useless as a treatment against MRSA infections [22].

The mechanism of resistance occurs in the alteration of the genes. *S. aureus* naturally contains four PBPs, penicillin-binding proteins, ranging in numbers one through four that are typically the targets of antibiotics [25]. These PBPs are the backbone of the cell wall, enhancing its integrity by synthesizing peptidoglycan. Resistance stems from the *mecA* gene that encodes PBP2a. Different from the other PBPs, PBP2a is a mutation that demonstrates strongly reduces affinity for beta-lactams, rendering these drugs nearly or completely inefficient. The presence of PBP2a results in resistance to all beta-lactam antibiotics [22]. This resistance from the *mecA* gene is broad spectrum, conferring resistance to the entire class of beta-lactam drugs [26]. Beta-lactams

are the most widely used class of antibiotics regarding infectious diseases and are known for their limited side effects and wide range of use, including narrow and broad-spectrum penicillins and cephalosporins. Beta-lactam antimicrobials aim to disable the defense mechanisms of both gram-positive and gram-negative bacteria by compromising the structure of the cell wall through degradation.

As MRSA is resistant to penicillin and beta-lactam antibiotics, the need for and use of Vancomycin has been high. In the instance of MRSA infections, Vancomycin is recommended by the Infectious Diseases Society of America (IDSA) as it is a potent antibiotic and usually reserved for cases where another antibiotic treatment is not feasible. Vancomycin is bactericidal against most gram-positive species [27]. While MRSA is typically known as a HAI, it can also be spread in the community, outside of a healthcare facility. Risk factors for MRSA acquisition include surgical procedures, an increased LOS in a healthcare facility and antibiotic use [13].

2.1.2 Vancomycin-Resistant Enterococci (VRE)

While VRE is not as commonly seen as MRSA, it appears VRE's highly virulent characteristic contributes to its pathogenicity [28]. Recent decades have shown a steep decline from 25 percent to 2 percent in death due to sepsis from infection with enterococci and the use of Vancomycin can be attributed to that [29]. However, with the increased use of Vancomycin, a new challenge is battling growing resistance. As Vancomycin is generally reserved as a last-resort antibiotic, its use is restricted for specific cases to reduce growing resistance in the population. However, the emergence and increase of Vancomycin-resistant strains allowed mortality to rates to pass those of MRSA [29]. Vancomycin use is tied back to the emergence and growth of MRSA in the 1960s, possibly where resistance began to develop. The latest data reports approximately 30

percent of Enterococcus species isolates from the United States are resistant to vancomycin, causing an estimated 1,300 deaths per year [14, 30]. As patients who present with more serious burn injuries typically require care in the intensive care unit for an extended period, they become susceptible to infection. It was discovered that while the percentage of TBSA alone is an independent risk factor for acquisition of VRE, the combination of the percentage of TBSA burnt and the percentage of third-degree burns sustained were significantly associated with VRE acquisition [31].

They are gram-positive anaerobes and opportunistic pathogens, living commensally in the gastrointestinal tract of humans and many other organisms. Despite the abundance and availability of anti-gram-positive agents, enterococci continue to exhibit their quick-adapting nature by demonstrating resistance to previous and newer agents, effectively posing a challenge in healthcare [32, 33]. Enterococci possess a far more diverse range of resistance mechanisms than *Staphylococcus*. The main mechanism for vancomycin resistance seen in enterococci comes from the alteration of the peptidoglycan pathway, changing the typical D-Alanine- D-Alanine to either D-Alanine-D-Lactate or D-Alanine-D-Serine. Alteration of the pathway greatly restricts a drug's effectiveness by decreasing binding affinity ~1000 fold and can occur by genes within enterococci [33, 34]. Resistance is proportional to the percent composition of D-Alanine-D-Lactate to D-Alanine-D-Alanine [30, 35]. Vancomycin operates by binding to D-Alanine- D-Alanine pentapeptides, resulting in the blockage of cell wall synthesis. Without cell wall synthesis, the cell will degrade. Operons are a crucial catalyst in changing the pathway. Within enterococci, operons are labeled vanA consecutively through vanG, then vanL, vanM, and vanN. Most VRE outbreaks in humans are attributed to vanA and vanB genes as they are the most globally widespread van-operons [33]. While they vary in structure and function, the modification of the peptidoglycan

pathway remains a constant outcome. Similar to Staphylococcus, Enterococci resistance to beta-lactams is acquired through the overproduction of PBPs with a low-binding affinity for these drugs, most notably PBP4 and PBP5 [30].

2.1.3 Extended-spectrum beta-lactamase-producing bacteria (ESBL)

Similar to other MDROs, ESBL has been credited with increasing prevalence in healthcare settings for over 30 years, despite infection control guidelines. This indicates that they are highly resistant and can endure numerous environments with implemented prevention strategies [20]. This increasingly resistant nature may be due in part to ESBL's gram-negative structure. ESBLs are a rapidly growing and evolving group of over 200 of beta-lactamases from more than 30 countries [44]. These beta-lactamases have intrinsic bacterial resistance to penicillins, third generation cephalosporins and aztreonam. Cephalosporins, at one point, were effective treatment options when resistance to beta-lactams first evolved and spread. Third-generation cephalosporins, including ceftriaxone and cefotaxime, were later developed to be stronger in the face of resistant strains than predecessors. However, mutated organisms began to demonstrate resistance to these third-generation cephalosporins [43]. This resistance can be attributed to the production of beta-lactamases, the production of which is the most common mechanism for enterococci resistance. While the most common cause for resistance in gram-positive organisms, such as MRSA and VRE is the change of normal PBPs, gram-negative infections such as ESBL acquire resistance through a combination of resistance to beta-lactams, genetic mutations and horizontal gene transfer [45]. Treatment options for infections of ESBL-producing organisms are severely limited as all beta-lactams are inefficient. Carbapenems are typically the treatment of choice, but professionals are

concerned the misuse of carbapenems will contribute to the growing crisis of carbapenem resistance [44].

Previous studies have shown that ESBL thrives in environments with water, such as sinks, showers and toilets (some citation). Thus, desiccation may be an option for preventing transfer to humans. Unlike other MDROs, ESBL-producing organisms display co-resistance to many other classes of antibiotics, posing a large challenge in treatment [44]. ESBL infections can range from urinary tract infections that are uncomplicated to life-threatening sepsis. Their unpredictable effects make them especially dangerous and should be treated promptly. Independent risk factors were identified as patient age greater than 60 years, previous hospital admission and current in-hospital vancomycin use [46]. Despite evolving infection control strategies, data from large surveillance networks report a steady rise of resistance to many treatment options, especially cephalosporins, for a decade. This increase can be attributed to the quick spread of ESBL-producing strains of bacteria [47].

2.1.4 Carbapenem-Resistant Enterobacteriaceae (CRE)

CRE is categorized as an extremely urgent threat to public health which desperately calls for immediate attention and action [14]. Enterobacteriaceae, a family of gram-negative bacteria, is the most abundant form of pathogenic bacteria for nosocomial infections [15, 36, 37]. As carbapenems are generally considered the last-resort treatment of choice, acquiring resistance is detrimental. CRE includes Enterobacteriaceae that are resistant to any carbapenem such as ertapenem, imipenem and meropenem. CRE can further be divided into two categories- carbapenemase-producing Enterobacteriaceae (CP-CRE) and non-carbapenemase Enterobacteriaceae [38]. In the case of resistance to carbapenems, colistin, an old antibiotic

previously stopped use because of neurotoxic side effects, has been used very scarcely as a treatment and has shown promising results. However, several countries recently report the emergence of resistance to colistin tracing back to rise in a transferrable gene, mcr-1, which was sourced back to farm animals, demonstrating the effect of antibiotic transfer from animals to humans [15, 36, 39]. Similar to other MDROs, risk factors include previous antibiotic treatment, prolonged hospitalization, care in a surgical or intensive care unit and invasive procedures [31, 40].

Resistance to Carbapenems is due to the production of beta-lactamases, namely carbapenemases, as well as other mechanisms including efflux pumps and modification of the active site. Carbapenemase, acting as antagonists to carbapenems, functions by hydrolyzing carbapenem antibiotics and rendering them ineffective [36, 41]. They are beta-lactamases that can also hydrolyze penicillins, cephalosporins and carbapenems [42]. While Carbapenemase-producing Enterobacteriaceae is fairly rare, there has been a rise in concerns regarding the growth and spread of these strains [43].

3.0 Previous Findings

A thorough review of relevant literature showed similar findings and the conclusions presented were similar regarding the purpose and effectiveness of surveillance. Previous studies demonstrate and reinforce the need for implementation of surveillance to reduce the incidence of patients acquiring an MDRO during their LOS. An important previous conclusion acknowledges MRSA acquisition rates declined in a statistically significant manner over time, most likely due to stricter infection control policies and surveillances [13]. Previous evidence indicates that screening patients for MRSA upon admission has been successful in reducing MRSA incidence and could pave the way for the prevention of other organisms, including CRE and VRE [30]. After review of relevant literature, a common conclusion drawn states and emphasizes the need for enhanced screening and infection control to prevent and reduce MDRO incidence, but the ideal approach can differ among pathogens. There is no current agreed upon, standard method of prevention of infection for burn patients.

Each institution has unique policies, practices, and patients so fluctuation and variation of MDRO incidence among healthcare environments is to be expected. Several studies agree that MRSA is of the highest prevalence among the most common MDROs and acquisition of any MDRO results in extended hospitalization.

3.1 Public Health Significance and Impact

The public health significance of this study is boundless. The contraction of MDROs is preventable in many circumstances. MDRO infections are associated with increased mortality and morbidity, increased complication of care as well as significantly prolonging the length of stay (LOS) for patients, consequently increasing their financial burden. Furthermore, the additional costs for laboratory tests, imaging and pharmacy services may not be covered by insurance. On average, hospitals spend up to an additional 40,000 dollars treating patients infected by an MDRO [48]. From a financial standpoint, after 18 consecutive days of hospitalization, the income for a hospital is lower since the cost of hospitalization is lower for patients [49]. Furthermore, the treatment of HAIs is no longer reimbursable for hospitals, putting them at a loss [30]. In serious cases, entire units or wards require decontamination and are shut down completely, costing hospitals hundreds of thousands of dollars [48].

The reduction of MDRO presence in healthcare settings promotes a more cost-efficient and productive style of care. A quicker patient turn-around allows more beds to be available and healthcare workers (HCW) to devote their attention and care to other cases. There are significant differences in MRSA colonization rates among hospitals which can be attributed to possible understaffing and an increased workload due to MDROs, despite infection control methods [13]. An extended LOS is thought to be a contributing factor as an increased duration augments chances for the contraction of an infection, therefore MDRO minimization is necessary for more efficient utilization of resources. A previous study found that the length of stay increased from 6.5 to 13 days for those who had a resistant infection [50].

By design, hospitals are a top location to acquire an MDRO. Screenings for MDROs vary among institutions but are typically ordered some point after admission. Since there is a lack of

consistency regarding the proper time to screen for an MDRO, it is beneficial to epidemiologically analyze certain variables and their impact on MDRO acquisition. This analysis aims to identify factors that appear to influence MDRO acquisition. It is hypothesized that this data set will follow the trends of previous studies, reflecting a higher prevalence of MRSA than other MDROs and impact about less than 10 percent of the sample.

4.0 Methods

This study is of retrospective design, containing analyses within a single center. The structure of this study will help clarify the relationship of different variables in regard to MDRO acquisition. UPMC Mercy, the only Burn Intensive Care Unit (ICU) in Western Pennsylvania, is also the only center in Western Pennsylvania to an American Burn Association-verified burn center and Level I Trauma Center. The University Institutional Board Review (IRB) approved the study as a Quality Improvement project (1908).

4.1 Inclusion Criteria

To maintain consistency and limit the data pool, certain inclusion criteria in the selection of the patients were set and followed. Patients must have been admitted to a UPMC Mercy Burn Unit in Western PA between January 1st- December 31st, 2018, sustained a TBSA burned of 11 percent or higher and been alive at the time of discharge. Burn location was not a determining factor in eligibility. The reasoning behind creating the inclusion criteria of 11 percent or higher comes from recommendations from the American Burn Association, stating the burn injuries that are typically more serious and should be referred to a burn specialty center are ones that are have greater than 11 percent of TBSA in patients under 10 or over 50 years of age. Additionally, burns that are chemical or electrical in nature of any degree should be referred [31, 32]. Since burn causes are unknown, the cut-off of 11 percent of higher ensures a data set that encompasses serious, critical burns.

4.2 Statistics

Descriptive variables of interest will be investigated for potential patterns and relationships. This includes inhalation injury, MDRO presence and identification, LOS, gender and age. Data will be analyzed and compared through counts of different patient outcomes. In order to quantify a relationship between LOS and MDRO status, a logistic regression will be performed and analyzed through SAS Studio to identify if a statistically significant relationship exists. Tables will be created through Microsoft Excel.

4.3 Procedure

Roughly three thousand burn patients were evaluated in 2018 for admission at the burn center. Out of these, 225 were admitted to the burn unit and were documented and sorted by total body surface area (TBSA) of the burn sustained in ascending order. Those with a TBSA of 11 percent or higher were included in the study, yielding a total of fifty patients. Data collected for these patients include age, gender, LOS, TBSA, history of MDRO, presence of inhalation injury and presence and identification of MDRO after clinical culture and standard screening, if applicable. For this study, LOS is defined as the time between the date of admission and date of discharge. History of MDRO was determined by documented presence of MDRO within the last three years. PowerChart was used for the collection of all data and review of individual medical charts. Each patient's Lund-Browder chart was examined to determine two factors- TBSA magnitude of burn, and whether inhalation injury was suspected or identified. Clinical cultures are samples ordered for overall care purposes and are not infection prevention surveillance. Any

bodily fluid is acceptable for this. Standard screening definition varies by institution. This location defines standard screening as assessing for nasal MRSA and axillary multi-drug resistant *Acinetobacter*.

All variables were recorded with assigned numerical values to all possible conditions. Patient gender was assigned based on medical records and dichotomized with a 0 for males or a 1 for females. Clinical culture and standard screening results were coded to follow the included key.

5.0 Results

5.1 Data

Nearly three thousand individuals sustained burns and were evaluated for admission in 2018 to the Burn Intensive Care Unit. Out of these, 225 were admitted. Of the 56 patients who met the inclusion criteria with TBSA burns of 11 percent or higher, 48 were alive at time at discharge. This group of 48 was composed of nine females and 39 males, demonstrating a distinct difference in gender breakdown as males composed over 81% of the sample. For all 225 patients, the average TBSA was 9.13 percent and the average LOS was 11.15 days.

Table 1 Patients Sustaining Critical Burns

Age	Gender	TBSA	LOS	Standard Screening	Inhalation injury presence	Clinical Culture
49	0	11	6	.	.	.
38	0	11.5	2	0	1	0
5	1	11.5	12	0	0	0
26	1	12	11	0	0	0
75	0	12	26	0	1	0
38	0	12.5	17	0	0	0
19	0	12.75	15	0	1	0
18	0	12.75	36	0	0	0
*	.	13	1	.	.	.
23	0	13	29	0	1	0
8	0	13.5	11	0	0	0
58	0	13.5	28	2	1	2
30	0	13.5	35	0	0	0
47	1	14	17	0	0	10
66	0	14	31	0	0	0
66	0	14.5	5	0	0	0

Table 1 Continued

49	1	14.75	37	0	0	0
1.5	0	15.75	31	0	0	0
51	0	16.5	32	0	1	0
41	0	16.5	32	0	.	0
3	0	17	16	0	1	0
28	0	18.45	17	0	1	0
11	1	20	13	0	0	0
82	0	20.5	35	0	1	0
40	0	21	12	0	1	0
33	0	21.25	26	2	0	2
34	0	22	20	0	.	4
81	0	22	40	2	1	2
60	0	23	8	0	1	0
38	0	24	34	0	1	0
48	1	24	38	0	1	0
36	0	25	17	0	1	0
50	1	27	28	0	1	0
39	0	27.6	27	0	1	0
20	0	28.5	30	2	.	2
71	0	30	48	0	0	0
28	0	30.75	32	2	1	2
18	0	32	37	2	1	2
82	1	34.5	19	0	.	0
48	0	34.75	30	0	1	0
36	0	38	16	0	1	0
4	0	41.5	2	0	1	0
70	0	41.5	28	2	1	2
29	0	43	34	2	1	0
84	0	45.5	15	0	1	0
58	0	52	88	0	1	9
43	1	54	108	0	1	5
*	.	54.5	4	0	.	0
45	0	58	73	0	0	2
64	0	61	76	0	1	0
*	.	66.25	5	0	.	0
*	.	77	18	0	.	0
*	.	86	1	.	.	.
*	.	91	8	.	.	.
*	.	unknown	6	0	.	0

Complete data set of patients with TBSA of 11 percent or higher

Table 1. Patient Sustaining Critical Burns. This table encompasses variables of interest on all patients analyzed. Asterisks indicate patients who were not alive at discharge.

Table 2 Clinical Culture Key

Value	Identification	Percent	Count
1	VRE	0	0
2	MRSA	66.67 0	8 0
3	CRE	0	0
4	ESBL	8.33	1
5	Other gram-negative rod	8.33	1
6	1 & 2	0	0
7	3 & 4	0	0
8	3 & 5	0	0
9	1 & 5	8.33	1
10	2 & 5	8.33	1
Total			12

Table 2 shows the possible outcomes recorded for clinical cultures performed. Clinical cultures are taken through any patient body fluid, including, but not limited to, sputum, urine, and blood. They are taken at any time during hospitalization and are not necessarily ordered for solely for infection control purposes.

Table 3 Standard Screening Key

Value	Identification	Percent	Count
1	VRE	0	0
2	MRSA	100	8
3	Acinetobacter	0	0
Total			8

Table 3 defines the possible outcomes recorded for standard screens performed. Standard screen definitions vary by institution. The standard screen at this location is defined as surveillance that occurs by different location every seven days. For MRSA, presence is evaluated through a nasal sample, as nares are a common location for colonization. For Acinetobacter, a sample from the axilla is acquired.

Table 4 Patients with Positive MDRO Results

Age	Gender	Admission Date	Discharge Date	TBSA	LOS	Inhalation injury	Standard Screening	Clinical Culture
58	0	1/18/18	2/15/18	13.5	28	1	2	2
47	1	8/28/18	9/14/18	14	17	0	0	10
33	0	12/2/18	12/28/18	21.25	26	0	2	2
34	0	8/3/18	8/23/18	22	20	.	0	4
81	0	4/15/18	5/25/18	22	40	1	2	2
20	0	9/5/18	10/5/18	28.5	30	.	2	2
28	0	1/18/18	2/19/18	30.75	32	1	2	2
18	0	10/3/18	11/9/18	32	37	1	2	2
70	0	5/9/18	6/6/18	41.5	28	1	2	2
29	0	9/5/18	10/9/18	43	34	1	2	0
58	0	5/5/18	8/1/18	52	88	1	0	9
43	1	12/8/18	3/26/19	54	108	1	0	5
45	0	12/4/18	2/15/19	58	73	0	0	2

A total of 12 patients reflected positive MDRO results either through screen, culture or both. Six patients had positive screenings and cultures while the remaining six demonstrated colonization through just one method of testing. Eight of these were identified as MRSA. Of the remaining four, there was a combination of MRSA and another gram-negative resistant organism, a combination of another gram-negative bacteria and VRE, another gram-negative bacterium, and ESBL alone. Standard screening results on the 48 patients reflected 8 positive screens, all of which

were determined to be MRSA. Those with a positive MDRO screen, culture or both had an average LOS of 43.2 days, while those with no identified MDRO presence had an average of LOS of 24.2 days. History of MDRO did not appear to play a role as only one patient had a reported history of MRSA and they did not contract an infection during their 2018 hospitalization.

Of potential interest are the patients with the same resulted MDRO that appear to be related to one another with similar admission dates, prompting the question if transmission occurred. There are three identified instances where admission and discharge dates overlapped, and patients sustained the same MDRO. Two patients admitted in the same day in January both had positive screens and cultures for MRSA. With the same admission date in September, another two patients showed positive screening results for MRSA. In December, two patients admitted two days apart were both documented with positive cultures of MRSA.

Table 5 Deceased Patients

Patient number	Admission date	Date of death	TBSA	LOS
24	8/4/18	8/23/18	34.5	19
33	2/1/18	2/5/18	54.5	4
36	12/13/18	12/18/18	66.25	5
37	5/25/18	6/12/18	77	18
38	5/25/18	5/26/18	86	1
39	2/7/18	2/15/18	91	8
40	12/11/18	12/17/18	unknown	6
49	11/22/18	11/22/18	13	1

The eight patients who died during their hospitalization had an average TBSA of burns of 60.32 percent and an average LOS of 7.75 days. In comparison, of the 48 patients who were discharged, there was an average TBSA of 24.66 percent and a hospitalization of 28.75 days. The large incongruity in average LOS between patients who did and did not make it to discharge

effectively demonstrates the speed at which high TBSA levels can impact a patient's life. While gender and age information were not readily available on these patients, the large TBSA in each of them speaks to the severity of their condition.

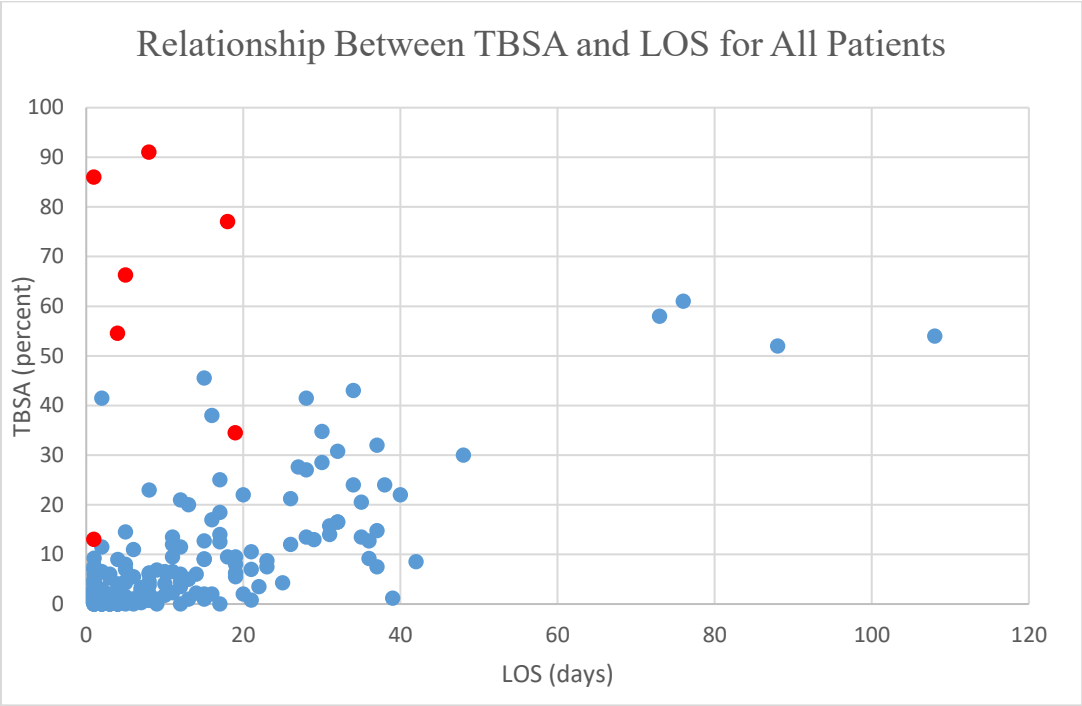

Figure 1 Relationship Between TBSA and LOS for All Patients

The highest LOS, over 40 days, belongs to patients with TBSA amounts that are not extremely high. Rather, their TBSA lies around 50 to 60 percent. This demonstrates treatment for the extensive wounds sustained requires an extended period. In contrast, patients with the highest TBSA values, 60 percent and higher, have relatively low LOS values, ranging from 1-15 days. This indicates that the extensive injuries sustained were not able to be treated and these patients did not get discharged. The highest TBSA amounts are related to extremely short LOS durations. The red dots indicate patients who passed away while the blue dots represent the remainder of the patients who were alive at discharge.

Table 6 Summary of Gender Distribution

Gender	Frequency	Percent
0	39	81.25
1	9	18.75
Total	48	100

The gender distribution displays a large disparity between males and females who sustained critical burns. Over 80 percent of the sample was male and less than 20 percent was female. The median age for males was 38 and 49 for females. Most of the injuries were sustained around age 42 to 49, however there were several instances of young children, 5 years and younger, and older adults, 75 years and older.

Table 7 Inhalation Injury Summary

	Frequency	Percent
Present	28	58.33
Not Present	15	31.25
No Data	5	10.42
Total	48	100

Inhalation injury was determined by an anatomical graphic of each patient indicating where burns were sustained. If there was injury to the face or neck, inhalation injury was counted. Five patients did not have a graphic in their file and therefore were not counted in the inhalation injury

statistics. 0 indicates no present inhalation injury and 1 denotes a documented inhalation injury. Roughly two-thirds of the patients analyzed presented with an inhalation injury. Since those with inhalation injury are known to be at higher risk for infection, the positive group may have an increased probability of complications.

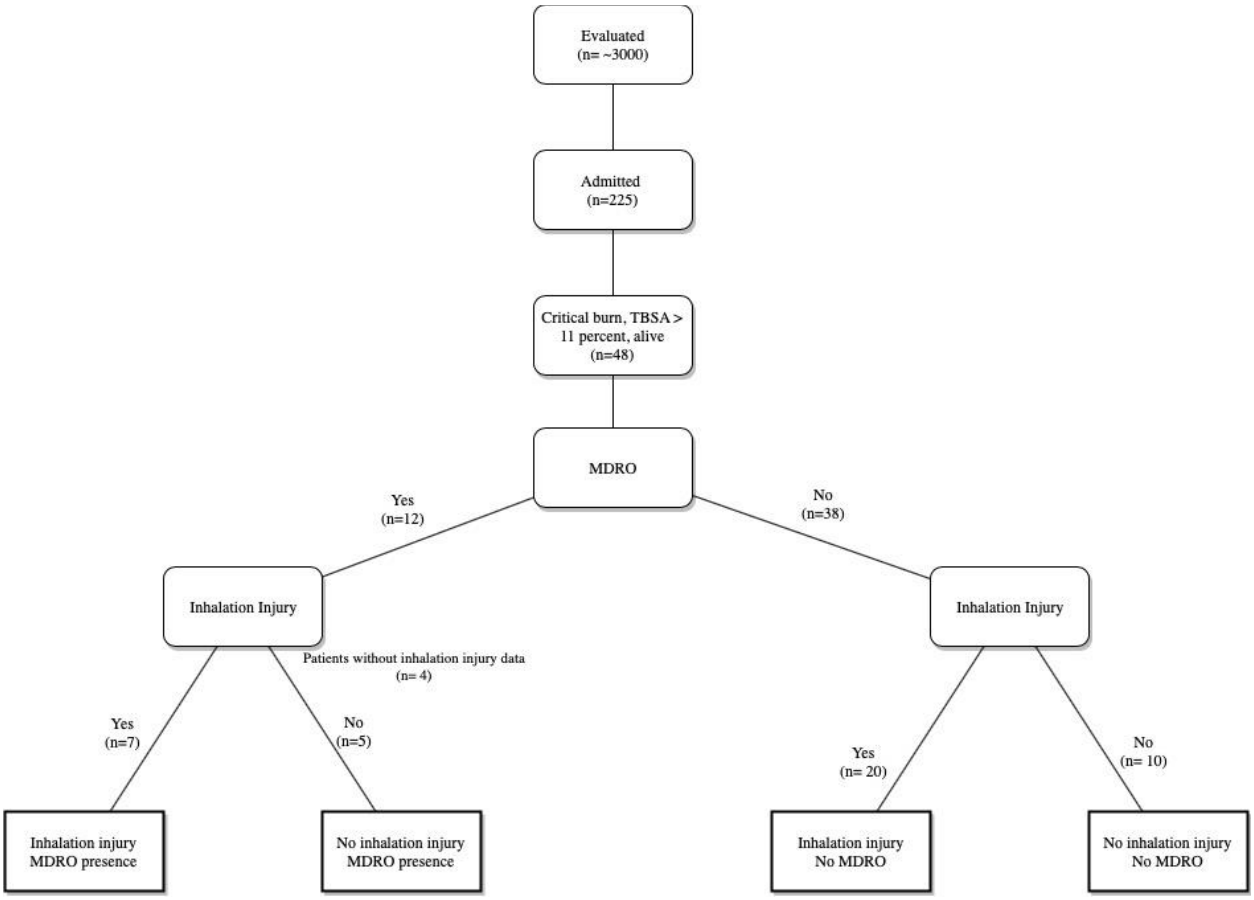

Figure 2 Burn Patient Outcomes

Four possible outcomes were assessed for each patient- inhalation injury with MDRO presence, no inhalation injury with MDRO presence, inhalation injury with no MDRO presence and neither inhalation injury nor MDRO presence.

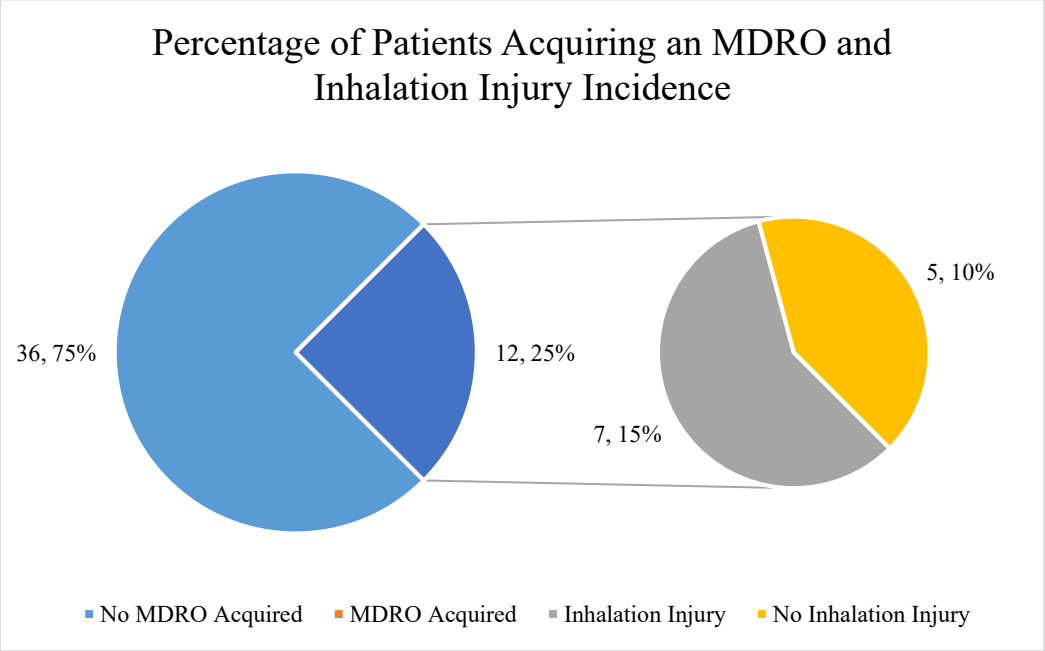

Figure 3 Percentage of Patients Acquiring an MDRO and Inhalation Injury Incidence

Of the 48 patients with clinical culture results in their charts, 36 (75 percent) had a negative MDRO result and 12 (25 percent) had a positive MDRO result. The 12 who had a positive MDRO result were then divided into two categories: no inhalation injury reported (5 patients), and an inhalation injury reported (7 patients). These findings support a previous conclusion where inhalation injury occurrence leads to higher risk of infection [2]. Conclusively, the rate of MDRO acquisition for the patients who fit all inclusion criteria is 25 percent.

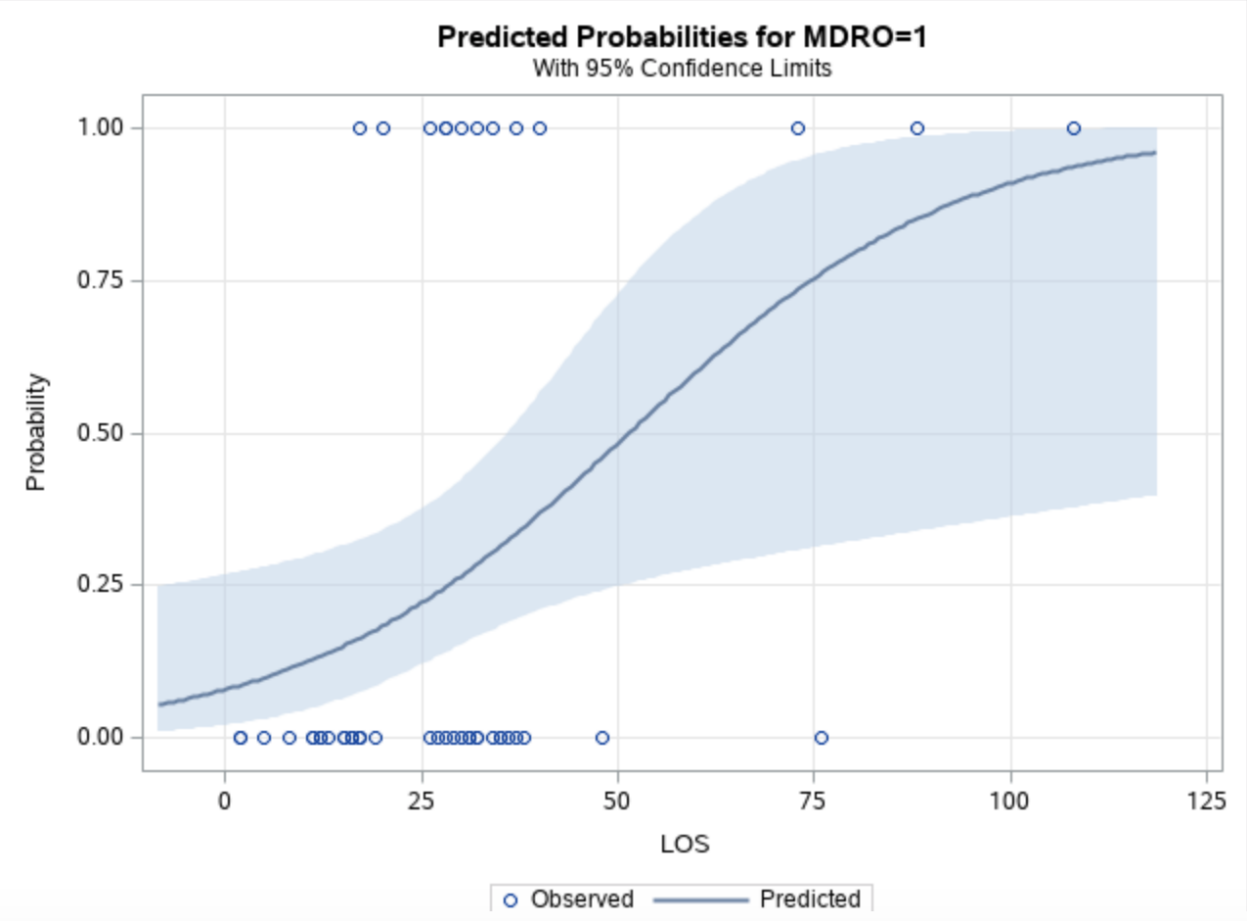

Figure 4 Logistic Regression of MDRO Acquisition and LOS

MDRO is dichotomized where 1= MDRO acquisition and 0= no acquisition. To assess the relationship between MDRO acquisition and LOS, a logistic regression model was used. This model was created on SAS Studio. In this population, a single day increase in LOS is associated with 4.9 percent greater odds of acquiring an MDRO (Odds ratio= 1.049, 95% CI= 1.007-1.092, p-value= 0.0210). A statistically significant relationship is assessed (p-value< 0.05).

6.0 Discussion

Overall, the data supports previous conclusions. The confirmed presence of an MDRO lengthened hospitalization for the patients in this sample by an average of nearly 20 days. The mean LOS for those with a documented MDRO was 43.2 days and 24.2 days for those without. Furthermore,inhalation injury may play a role in MDRO acquisition. The majority of those who became colonized with an MDRO during their stay had a reported inhalation injury (7 out of 12). The data also reflect a large amount of the MDROs as MRSA.

MRSA is the most prevalent over other MDROs in the Burn ICU at this facility as MRSA accounted for over 80 of the positive clinical cultures and 100 percent of the standard screens completed on the 48 patients who met inclusion criteria. High rates of MRSA isolates have been noticed worldwide, indicating a global concern [51]. Prevalence of MDROs vary on a number of factors, including geographic location, facility income, type of healthcare setting or temporal trends, so it is difficult to quantify a national or worldwide rate that accurately encompasses all healthcare settings. However, growing prevalence of MDROs has been identified in US hospitals and medical centers since introduction.

In 2018, there were over eight thousand MRSA infections reported. Pennsylvania acute care hospitals reported a significant decrease in MRSA bacteremia by 34 percent between 2017 and 2018 and presented a Standardized Infection Rate (SIR) for 0.66. The SIR for all general acute care hospitals with enough data in the United States in 2018 was 0.84. As Pennsylvania has a lower SIR than the national value, it demonstrates effective infection prevention methods in acute care settings in Pennsylvania [52]. The SIR is a summary measure used to track hospital-acquired infections and adjusts for facility and patient-level factors that contribute to risk. It is calculated

by dividing observed HAIs by predicted HAIs [53]. Currently, MRSA is the only MDRO for which an SIR is calculated.

6.1 Limitations

The findings conclusions drawn from this study prove useful in analyzing epidemiological and demographic factors concerning critically ill burn patients, however, limitations do exist. This study followed a single-center style and thus had a very small patient pool, potentially engendering external validity concerns. To account for this, future studies should include a much larger patient collection. This can be accomplished by expanding the inclusion criteria through analyzing years outside of 2018 and lowering the cut-off point for TBSA. To isolate the data to only the most severe cases identified, strict patient criteria were set and followed. By limiting patients to those with TBSA of 11 percent or higher, data regarding MDRO acquisition was not collected for those with less extensive burns.

Although a statistically significant relationship exists between LOS and MDRO presence, the population size is fairly small and may require additional data in the future. Another limitation to this analysis is the lack of evaluated patient medical history, comorbidities and conditions that may impact the findings. Patients who are immunocompromised, such as those previously diagnosed with HIV or cancer, are at an even higher risk for acquiring an MDRO during hospitalization but were not specifically identified during analysis.

6.2 Future Directions

The results of this analysis can be expanded and used as a baseline for future directions. Surveillance, defined as screenings and cultures that can determine the absence or presence of an MDRO, can be implemented at additional predesignated time points to evaluate patient status regarding MDRO acquisition. By applying stricter surveillance, it can assist in narrowing a more specific time point of when a patient contracted an MDRO and potentially identify areas of highest transmission, effectively reducing MDRO acquisition and transmission in a healthcare setting. Developments in surveillance of MDROs have the ability set the precedent for healthcare standards going forward. To further improve the external validity of this analysis, future directions should include expanding the patient pool to additional healthcare settings as well as screening for additional MDROs. The importance of proactive MDRO screening carries many benefits to both patients and healthcare institutions. Additionally, implementing surveillance in a larger group of patients, including those with all types of wounds, such as lacerations and surgery incisions, can prove beneficial in analyzing the impact of surveillance in a larger variety of injuries. Surveillance can also be lengthened into additional time points in attempt to narrow down when the patient contracted an MDRO. Learning precisely when and where an MDRO is acquired can assist healthcare professionals in focusing prevention efforts. By investing in proactive MDRO screening, healthcare locations can reduce excess treatment costs by focusing firsthand on prevention.

Current infection prevention control measures should also be reevaluated for their efficacy. This includes precautions such as current disinfectant regimens, adherence to handwashing by healthcare workers, and isolation of confirmed infectious patients. As there are currently no set standards on best practice of care for burn patients, it is imperative to practice isolation and

thorough decontamination techniques when possible [12]. Disinfectant methods have proven successful. Xenon-UV light by itself or with typical cleaning supplies has been shown to decrease the presence of MRSA and other pathogens by up to 99 percent [23]. Antibiotic resistance stewardship effectiveness can also be reassessed to account for newly identified resistance patterns. As newer, more resistant strains are emerging, it is imperative to reevaluate methods to best tackle the global issue of antibiotic resistance.

Inhalation injury has also been estimated to heighten the risk of infections and complications. The difficulty of detection lies in the various manifestations from patient to patient. To account for this, healthcare professionals must understand the importance of prompt detection and diagnosis of an inhalation injury. A thorough examination of the patient must occur and treatment on the side of caution should always be encouraged.

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