Infections Caused by Multi-Drug Resistant Organisms Are Not Associated with Overall, All-Cause Mortality in the Surgical Intensive Care Unit: The 20,000 Foot View

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Abstract

Background—Resistant pathogens are increasingly common in the Intensive Care Unit (ICU), with controversy regarding their relationship to outcomes. We hypothesized that an increasing number of infections with resistant pathogens in our surgical ICU would not be associated with increased overall mortality.

Study Design—All ICU-acquired infections were prospectively identified between January 1st, 2000 and December 31st, 2009 in a single surgical ICU. Crude in-hospital, all-cause mortality data was obtained using a prospectively collected ICU database. Trends in rates were compared using linear regression.

Results—A total of 799 resistant pathogens were identified (257 gram-positive, 542 gram-negative) from a total of 3024 isolated pathogens associated with 2439 ICU-acquired infections. The most frequently identified resistant gram-positive and -negative pathogens (defined as resistant to at least one major class of antimicrobials) were methicillin-resistant *Staphylococcus aureus* and *Pseudomonas aeruginosa*, respectively. Pathogens were most commonly isolated from the lung, blood, and urine. Crude mortality rate declined steadily from 2000–2009 (9.4% to 5.4%; equation for trend y= −0.11x +8.26). Linear regression analysis of quarterly rates revealed a significant divergence in trends between increasing total resistant infections (equation for trend y=0.34x + 13.02) and percentage resistant infections (equation for trend y=0.36x + 18.66) when compared to a decreasing mortality ($p = 0.0003$, $p = <0.0001$, respectively).

Conclusions—Despite a steady rise in the proportion of resistant bacterial infections in the ICU, crude mortality rates have decreased over time. The rates of resistant infections do not appear to be a significant factor in overall mortality in our surgical ICU patients.

Introduction

Many studies over the last decade have revealed increasing rates of infections caused by multi-drug-resistant organisms (MDRO), including both gram-positive and –negative

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pathogens. (1–6) A higher prevalence of MDRO is found in the inpatient setting, specifically the intensive care unit (ICU), when compared to the outpatient setting. (7)

Rising rates of ICU-acquired infections have been attributed to an increase in the severity of disease of patients admitted over time. As hospitals are more frequently operating at capacity, patients previously managed in the ICU are being treated in step-down units and hospital wards, while some historically inpatient treatments are now provided at home. This is reflected in the Centers for Disease Control and Prevention's (CDC) National Nosocomial Infections Surveillance (NNIS) system/National Healthcare Safety Network (NHSN) data revealing rising number of ICU beds, with a slightly declining total hospital bed capacity. (8) As such, patients receiving care in the ICU are at higher risk for hospital-acquired infections due to increasing age, co-morbidities, severity of underlying disease, and more frequent operative interventions.

These MDRO infections have gained great public attention as they have been associated with significantly increased healthcare spending, primarily due to private isolation rooms, prolonged lengths of ICU and hospital stay, and increased utilization of expensive antimicrobials. (7, 9) It has been suggested that this association is also due to inadequate initial antimicrobial regimens, additional invasive interventions for infection control, and a higher underlying severity of disease. (10)

There has been much debate regarding the clinical significance and attributable outcomes for MDRO. Controversy exists regarding the attributable mortality due to a multitude of studies with conflicting data studying MDRO. While many studies have not demonstrated a significant association between resistant pathogens and mortality (11–16), many do conclude resistance is independently associated with increased mortality. (17–24) Quite a few of these reports have serious limitations due to small sample size, lack of a control group, failure to distinguish infections from colonization, analysis of multiple pathogens collectively, and a complete lack of adjustment for confounders of outcomes including severity of disease, comorbidities, ventilation status, and the use of invasive procedures or devices. No causal relationship can currently be absolutely asserted between resistance and clinical outcomes leaving us to continue to wonder if resistant infections are "simply a reflection of underlying severity of illness, associated comorbidities, or host physiologic/ immunologic compromise". (14)

We hypothesized that although there has been an increasing number of infections caused by MDRO at our institution, our overall ICU mortality rates have not noticeably increased over time. We therefore, sought to determine if a rising microorganism resistance pattern would be associated with an increase in overall, all-cause mortality in our ICU.

Methods

This study was approved by the Institutional Review Board for Health Sciences Research at the University of Virginia (#15780). Due to the retrospective nature of the analysis the need for individual informed consent was waived.

All ICU-acquired infections were identified between January 1st, 2000 and December 31st, 2009 in a single, 16-bed surgical, trauma ICU (STICU). These infections were identified from a prospectively-collected database tracking all infectious complications from the general surgical, trauma, and transplantation services. This dataset is maintained by three times weekly chart review, direct patient examination, and a review of all daily laboratory, microbial, and pharmacy reports. Inclusion into this study required the patient to be located in the STICU at the time of infection acquisition.

This prospectively collected dataset has been previously described. (14) Variables recorded in this database include age, sex, race, body mass index, location at time of infection, primary diagnosis, primary operation, comorbidities, Acute Physiology and Chronic Health Evaluation (APACHE) II score (25), maximum temperature, white blood cell count within 24 hours of treatment initiation, sites of infection, pathogens isolated, antibiotics provided, antibiotic susceptibilities, duration of treatment, length of hospitalization, and all-cause, inhospital mortality. Documented comorbidities included diabetes mellitus (insulin dependent and non-dependent), hypertension, coronary artery disease, peripheral vascular disease, cerebrovascular disease, renal insufficiency (creatinine >2.0 mg/dL) prior to admission, hemodialysis dependence, pulmonary disease, mechanical ventilation (excluding immediate post-operative period), malignancy, hepatic dysfunction, chronic corticosteroids, and solid organ transplantation.

Infections were defined in accordance with the CDC definitions and diagnostic criteria. (26) A urinary tract infection was diagnosed following a positive urine culture, which had 10^5 microorganism per cm^3 or 10^4 microorganisms per cm^3 in a symptomatic patient. Pneumonia was defined as production of purulent sputum, isolation of a predominant organism from a properly collected specimen, a new or changed infiltrate on chest radiograph and a quantitative endotracheal suction specimen with 10^4 colony-forming units/mL. A blood stream infection was diagnosed when a recognized pathogen was cultured from a sterile collected blood specimen; *Staphylococcus epidermidis* or other coagulase-negative staphylococci required two separate positive specimens to be labeled as a bloodstream infection. The criteria for surgical site infections (SSI) were defined according to the definitions outlined by the Hospital Infection Control Practices Advisory Committee in their guideline for SSI prevention. (27)

Gram-positive antibiotic resistant pathogens were defined as oxacillin- or methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* spp. (VRE). Gram-negative antibiotic resistant pathogens were defined as such if the pathogen was resistant to all members of a single major class of antimicrobials by in vitro testing by the University of Virginia Clinical Microbiology Laboratory.

Crude in-hospital, all-cause mortality data was obtained using a prospectively-collected ICU admission-discharge database. This dataset recorded total number of ICU admissions, discharges, and deaths. Crude mortality for each quarter was determined by total deaths in the ICU out of the total ICU admissions.

Statistical analyses were performed using Student's t-test or Mann-Whitney test for continuous variables and Chi-square or Fisher's exact test for binomial categorical variables. All continuous data are reported as a mean ± standard error of the mean. All statistical tests were considered significant at an alpha level of 0.05. Trends in rates were compared using linear regression.

Results

During our study period we identified a total of 2439 consecutive ICU-acquired infections in a total of 880 patients. There were 3024 separate pathogens isolated from the ICU-acquired infections, of which 799 were considered to be antibiotic resistant (542 gram-negative, 257 gram-positive). Demographics and outcomes of patients with *completely* sensitive infections (those with sensitive organisms only) and infections with *any* resistant organism are found in Table 1. Annual data of resistant gram-negative and –positive organisms, total ICU-acquired organisms, resistant organisms, and percentage resistance can be seen in Table 2. Quarterly data of rising resistant gram-negative and -positive organisms, as well as the percent resistance can be seen in Figure 1 and Figure 2, respectively.

The most frequently identified resistant gram-negative and -positive pathogens were *Pseudomonas aeruginosa* and *Staphylococcus aureus*, respectively. The number of isolated pathogens and frequency of resistance in the remaining gram-negative and -positive pathogens can be found in Tables 3 and 4, respectively. Pathogens were most commonly isolated from the lung, blood, and urine. The number, frequency and location of all ICU-acquired infections is seen in Table 5.

The mean percentage of appropriate initial antibiotic therapy throughout the study period was 62.0%. This percentage did not vary significantly from year to year, and was 63.5% in 2000 and 68.5% in 2010. The majority of organisms that did not receive coverage by our empiric antimicrobial therapy were yeasts and VRE.

The unadjusted mortality following an infection was, on average, higher for infections from resistant organisms when compared to sensitive ones. The trend of rising mortality following a resistant infection over time, ($y = 0.7455x - 1461.2$) was not statistically significant ($p = 0.74$). Similarly, the trend toward declining mortality following a sensitive infection over time ($y = -0.3685x + 756.57$) was also non-significant ($p = 0.61$). (Figure 3) When compared to each other, the trends in mortality over time from a sensitive versus a resistant infection are not significantly different ($p = 0.63$).

There were 6502 total admissions to the STICU during our study period, resulting in an approximate admission rate of 54 patients per month. The total number of deaths equaled 381, roughly three per month. Quarterly crude mortality declined steadily from 2000 through 2009 (9.4% to 5.4%; equation for trend $y = -0.11x + 8.26$) as can be seen in Figure 4. During this time period, total number of resistant organisms rose (equation for trend $y = 0.34x + 13.02$), as did the percentage of resistant organisms (equation for trend $y = 0.36x + 18.66$). Linear regression analysis of quarterly rates revealed a significant divergence in trends between increasing total resistant organisms and percentage resistant organisms when compared to a decreasing mortality ($p = 0.0003$, $p = <0.0001$, respectively). (Figure 4)

Discussion

Antimicrobial Resistance

Antimicrobial resistance is not a new public health concern, reported as far back as the early 1960s. Methicillin was first introduced in 1959 and merely two years later reports of methicillin-resistant *Staphylococcus aureus* were being published out of England. (28–30) The first hospital-associated, drug-resistant microorganism outbreak in the United States followed shortly thereafter, in 1968, at the Boston City Hospital, where 18 patients had MRSA isolates. (31) A multitude of pathogens emerged over the following few decades, resistant to progressively newer antimicrobials. Among gram-negative pathogens, many MDRO had appeared by 1983 including *Serratia marcescens*, extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* and *Klebsiella pneumoniae*, *Pseudomonas*, *Enterobacter*, and *Citrobacter* species. (32) The gram-positive microorganisms also continued to gain resistance, as *Enterococcus faecium* developed vancomycin-resistance in 1988. (33, 34)

A plethora of recent reports reveal the progressively increasing proportions of antibiotic resistance in both gram-positive and –negative pathogens. A 10-year study of *Staphylococcus aureus* resistance, (including nearly 1.8 million isolates), revealed MRSA prevalence had continuously increased from 32.7% to 53.8% during the study period. (6) The recent frequency of resistant *S. aureus* has been confirmed by reports from the SENTRY Antimicrobial Surveillance Program of North America and the NNIS/NHSN

system report, in which they identified 51.4% and 59.5% oxacillin and methicillin resistance rates among *S. aureus* isolated from ICUs, respectively. (1, 5)

This same rising proportion of resistant pathogens is also recognized in gram-negative microorganisms. In 2003, nosocomial pathogens isolated from ICU patients, including *Escherichia coli*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae*, all had increased antimicrobial resistance when compared to the previous five years. *K. pneumoniae* had a staggering 47% increase in resistance. (1) The Intensive Care Antimicrobial Resistance Epidemiology Project found increasing antimicrobial resistance in almost all identified nosocomial microorganisms, consistent with numerous other reports of rising antibiotic resistance, specifically in the ICU. (2–4, 7)

Attributable Mortality

Despite an abundance of literature demonstration rising resistance patterns, there is a paucity of compelling data from which to draw conclusions. As previously stated, few studies have adequate sample size, control for clinically relevant confounders, distinguish between infection and colonization, and analyze the data based on isolated pathogen.

There are a number of studies that suggest resistant pathogens are "opportunistic" in that they preferentially infect those with the highest severity of illness. This observation has been previously reported out of our institution's data by Raymond et al (14), in which they found resistant gram-negative infections were associated with higher APACHE II scores and multiple comorbidities (including hemodialysis and ventilator dependence, as well as liver disease). After controlling for these variables by matching, antibiotic resistance was not associated with increased mortality. (14) This pattern of higher severity of illness in patients with resistant organisms has also been seen by a number of additional studies. (17, 19, 35, 36)

Pena and colleagues (11) compared ESBL- and non-ESBL-producing *Klebsiella pneumoniae* bacteremia. This prospective cohort study found resistant *K. pneumoniae* was isolated significantly more frequently from those in the ICU, with underlying diseases, previous operations, antibiotics, and urinary catheters. They found no significant overall or attributable mortality differences. (11)

Bhavnani and colleagues (12), as well as Skippen and colleagues (13) also evaluated ESBL- and non-ESBL-producing *K. pneumoniae* and *E. coli*. Bhavnani (12) found resistant organisms were more frequently isolated from ICU patients, those with ventilator dependence and supplemental nutrition requirements via gastrostomy or jejunostomy tubes. Skippen (13) reported a significantly higher proportion of patients with ESBL-infections having prior antibiotic exposure, prior admission to the ICU, and overall longer length of hospital stay. The outcomes of those with resistant infections in both studies were similar to the sensitive organisms in clinical success, attributable mortality, and all-cause mortality. (12, 13)

Suarez and colleagues (15) reported a study regarding carbapenem-resistant *P. aeruginosa*. Similarly, they found carbapenem-resistance was higher in those with extended lengths of stay, previous antimicrobial exposure, and inappropriate empiric or definitive antimicrobial treatment. (15) Despite this, they too did not find a significant difference in 30-day or attributable mortality.

A systematic review was conducted by Athanassa and colleagues (16) to determine the significance of methicillin resistance on *S. aureus* ventilator associated pneumonia (VAP) outcomes. This review included eight articles and found MRSA was associated with higher

crude- and ICU-mortality. However, the studies that adjusted for potential confounding factors (severity of illness, adequate empiric antimicrobial treatment), found no difference in mortality. The authors noted that patients with MRSA infections tend to be older, have terminal illnesses, be mechanically ventilated, have prolonged hospitalizations, and receive inappropriate antimicrobials. They conclude MRSA VAP has been associated with higher mortality in the past, however, adjustment for risk factors reveals this association may not be causal since it disappears when adjusted for confounders. (16)

While many of these studies did not find significant differences in mortality, even without matching, a number of studies did. Aloush and colleagues (17) found cases of multi-drug-resistant *P. aeruginosa* were significantly more likely to be transferred from another institution, have previous antibiotic exposure, have been in the ICU, have a foley catheter, central venous catheter, mechanical ventilation, be bedridden, and have vasopressor therapy. Despite significant differences in cases and controls, the authors only matched on hospital ward (during the same time period) and length of stay. (17) Similarly, Lautenbach and colleagues (35) found the cases of ESBL-producing *E. coli* and *K. pneumoniae* had significantly higher APACHE II scores, more frequent central venous catheter and foley catheter use, and longer duration of hospital stay. Despite this, the authors only matched based on organism, site of infection and date of organism isolation, again failing to control for significant confounders.

Higher severity of illness (measured directly or indirectly) in the cases of resistant infections can be seen in a number of other studies where the analysis failed to control or match based on these factors. (19, 36) A meta-analysis by Schwaber and colleagues (22) included 16 studies examining ESBL-producing Enterobacteriaceae. Only a single study in this series adjusted for confounders and, thus, conclusions regarding causality cannot be drawn.

A common thread seen throughout the vast majority of these studies is a higher severity of disease in the patients with resistant organisms when compared to those with sensitive ones. Thus, we believe resistance is "a reflection of underlying severity of illness, associated comorbidities, or host physiologic/immunologic compromise" as was first stated by our colleague in 2003. (14)

We acknowledge the "20,000 foot view" presented here does not control for confounders. We also have found higher severity of disease seen in patients with resistant infections when compared to those with sensitive ones. We have also demonstrated that mortality following an infection, including those with resistant organisms, has not increased over time. Despite this lack of change in mortality associated with resistant infections, overall mortality in the ICU has declined during our study period. The declining mortality in the ICU reveals improvements in general critical care have outweighed the rising number of MDRO and any possible increase in mortality from these infections.

Controversy continues to exist regarding the attributable mortality of resistant infections due to the multitude of studies with conflicting data. Far less controversial is the improvements in critical care over the last decade or so and the improved outcomes of these critically ill patients.

Improved Critical Care

Over the past decade there have been many noteworthy developments in ICU diagnostics, monitoring, supportive treatment, emergency medical care, and technology, which has led to improved outcomes in critical care. Marked progress has been made in organ support systems and their interface with the patient, allowing better tolerated interventions, as described by Vincent and Singer. (37) Stott (38), as well as Vincent and Singer (37)

described numerous developments in critical care over the last decade, a selection of which we will review here.

Great advancements were made in pulmonary critical care, including a multicenter, randomized trial comparing traditional ventilation management with low tidal volume and decreased plateau pressures for patients with acute lung injury and ARDS. (39) They found lower mortality and fewer ventilation days in the low tidal volume group. (39) A major literature review in 2005 confirmed strong evidence for the use of both volume- and pressure-limited ventilation as lung-protective strategies of ventilator support for acute lung injury and ARDS patients. (40)

Another development leading to improved outcomes in pulmonary critical care included the widespread use of daily sedation holidays. Daily interruption of sedative infusions reduced the total days of mechanical ventilation and subsequently days in the ICU in a randomized, controlled trial by Kress and colleagues. (41)

Hebert and colleagues (42) found a restrictive strategy of red-cell transfusion (for hemoglobin < 7.0 g/dL) was equivalent to a liberal strategy (<9.0 g/dL) and found to be superior in less acutely ill patients and those younger than 55 years. (42) In 2002, Bernard (43) and the Hypothermia after Cardiac Arrest Study Group (44) found overall reduced mortality and improve neurological outcomes following hypothermia after ventricular fibrillation-related cardiac arrest. A final process measure is the "FASTHUG" for daily assessment of critically ill patients including a quick review of each patient's Feeding, Analgesia, Sedation, Thromboembolic prevention, whether the Head of the bed is elevated, Ulcer prophylaxis, and Glucose control and its adequacy. [CE: Please query author to confirm that ref 45 is cited in the right place.]

Additional interventions continued to improve outcomes such as the implementation of evidence-based guidelines and process measures. The "Golden Hour and the Silver Day" found that by implementing a regimented protocol including measurements of serum lactic acid levels, aggressive resuscitation and cardiovascular support resulted in improved survival. (46) A second protocol-driven trial was early goal-directed therapy in treatment of severe sepsis and septic shock. (47) This study randomized septic patients to receive at least six hours of goal-directed critical care therapy in the emergency department prior to admission to the ICU. They found the early goal-directed therapy group had reduced in-hospital, 28-day, and 60-day mortality. (47)

The Surviving Sepsis Campaign introduced in 2004, and revised in 2008, provided comprehensive criteria and guidelines for the management of critically ill patients with severe sepsis and septic shock. (48, 49) These guidelines included recommendations regarding initial resuscitation, diagnosis, antibiotic therapy, source control, fluid and vasoactive drug therapy, as well as a number of additional interventions. These evidence-based guidelines were intended to increase recognition and improve outcomes in critically ill patients. (48, 49)

Lastly, intensive care unit teams are now also utilizing specialized input from a multitude of providers. Our STICU utilizes a number of essential consultant services including a surgical nutrition service, ICU-specific respiratory therapists and pharmacists, all of whom conduct rounds within their service and in conjunction with the STICU team improving overall communication and ICU care. Over time we will continue to develop technology, discover new therapies and interventions to improve patient outcomes in the critically ill population.

Conclusion

Patients receiving care in the ICU are progressively at higher risk of infection due to increased age, co-morbidities, and severity of underlying disease. A steady rise in total number of infections and resistant bacterial infections has occurred in conjunction with this rise in severity of illness in the ICU. Despite a rise in the proportion of resistant bacterial infections, crude mortality rates have steadily decreased over time. This finding is likely due to significant advances in technology and critical care. The rising rates of resistant infections do not appear to be a significant factor in the overall mortality in our surgical ICU patients as the impact of that resistant infection provides only a small contribution toward overall mortality.

Acknowledgments

Abbreviations

MDRO	Multi-Drug Resistant Organisms
ICU	Intensive Care Unit
CDC	Centers for Disease Control and Prevention
NNIS	National Nosocomial Infections Surveillance
NHSN	National Healthcare Safety Network
STICU	Surgical Trauma Intensive Care Unit
APACHE	Acute Physiology and Chronic Health Evaluation
SSI	Surgical Site Infection
MRSA	Methicillin-resistant *Staphylococcus aureus*
VRE	Vancomycin-resistant *Enterococcus* spp.
ESBL	Extended-spectrum beta-lactamase
VAP	Ventilator Associated Pneumonia
ARDS	Acute Respiratory Distress Syndrome
TRICC	Transfusion Requirements in Critical Care

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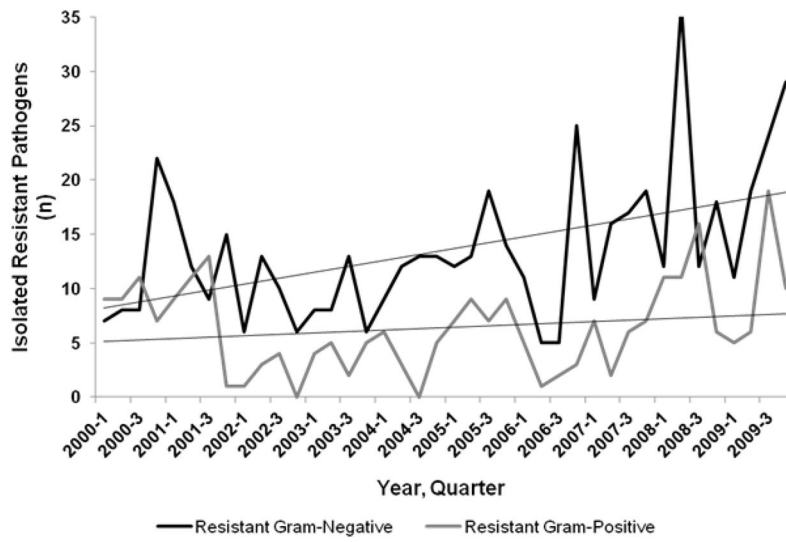
Figure 1.
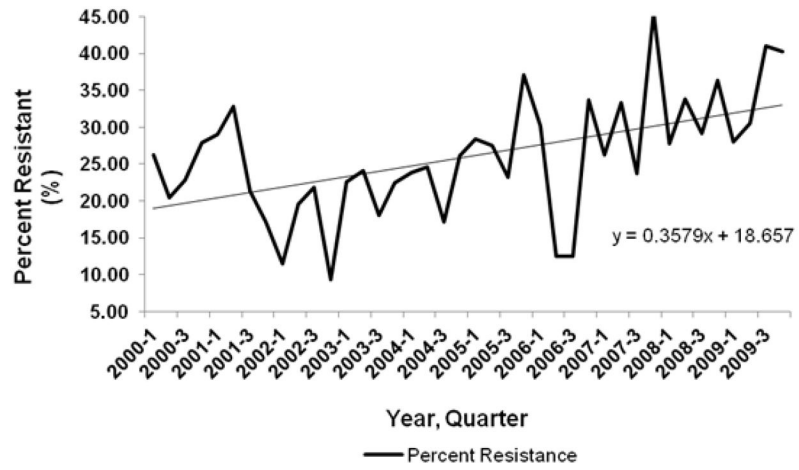Resistant gram-negative and –positive ICU-acquired pathogens.

Figure 2.
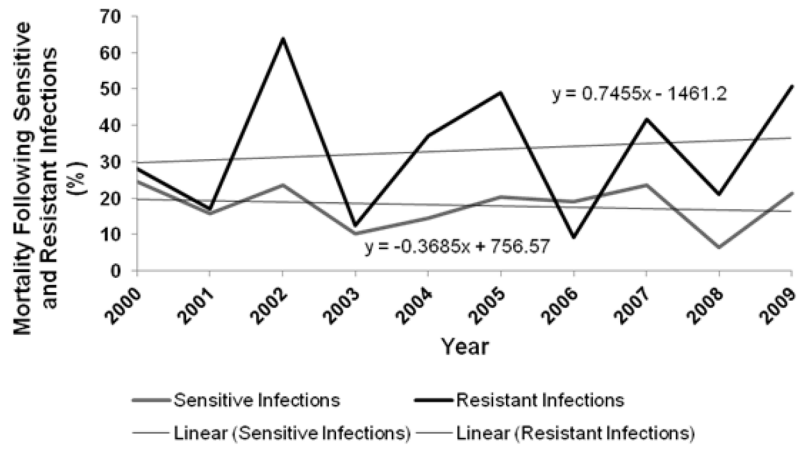Increasing overall ICU-acquired organism percentage resistance.

Figure 3.
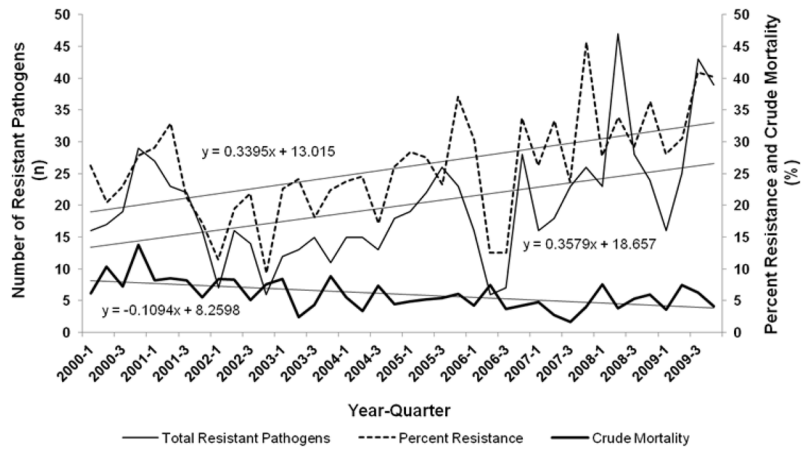Mortality Following a Sensitive and Resistant Infection

Figure 4.
Intensive care unit resistant pathogens, percent resistance, and crude mortality.

Table 1

Demographics and Outcomes of Sensitive Versus Resistant ICU-Acquired Infections

Demographics and outcomes	Sensitive	Resistant	p Value
n	1669	739	-
Age, y	52.8 ± 0.4	53.7 ± 0.5	0.16
Male sex	61.5%	61.5%	1.00
Body mass index	30.4 ± 0.2	31.4 ± 0.3	0.007
APACHE II score	19.2 ± 0.1	20.2 ± 0.2	<0.001
WBC, maximum	15.7 ± 0.2	15.0 ± 0.3	0.06
Trauma	49.4%	35.9%	<0.001
Transplant recipient	12.3%	21.9%	<0.001
Transfused	82.8%	93.2%	<0.001
Hemodialysis	17.1%	28.1%	<0.001
Ventilator dependence	68.8%	73.2%	0.01
Diabetes mellitus (I or II)	17.1%	19.0%	0.18
Antibiotic therapy, d	13.7 ± 0.2	15.2 ± 0.3	<0.001
Length of stay, d	35.0 ± 0.7	42.6 ± 1.4	<0.001
Crude mortality	23.0%	32.9%	<0.001

Table 2

Resistant Pathogens, Total Isolated Pathogens, and Percent Resistance of ICU-Acquired Organisms

Years	Resistant gram-negatives	Resistant gram-positives	Total resistant pathogens	Total pathogens	Percent resistance
2000	45	36	81	331	24.5
2001	54	34	88	359	24.5
2002	35	8	43	271	15.9
2003	35	16	51	239	21.3
2004	47	14	61	269	22.7
2005	58	32	90	321	28.0
2006	46	11	57	240	23.8
2007	61	22	83	269	30.9
2008	78	44	122	384	31.8
2009	83	40	123	341	36.1
	542	257	799	3024	

Table 3

Frequency of Isolated Gram-Negative Organisms and Resistance Pattern

Organism	Isolated organisms	Resistant isolates	Organism percent resistant	Percent of total resistant organisms
Pseudomonas aeruginosa	298	141	47.3	26.7
Stenotrophomonas maltophilia	85	78	91.8	14.8
Enterobacter cloacae	157	59	37.6	11.2
Serratia marcescens	113	46	40.1	8.7
Acinetobacter baumannii	101	45	44.6	8.5
Klebsiella pneumoniae	126	42	33.3	8.0
Escherichia coli	128	38	29.7	7.2
Klebsiella oxytoca	61	32	52.5	6.1
Enterobacter aerogenes	55	15	27.3	2.8
Citrobacter freundii	33	13	39.4	2.5
Burkholderia (pseudomonas) cepacia	13	9	69.2	1.7
Proteus mirabilis	32	4	12.5	0.8
Alcaligenes xylosoxidans	7	4	57.1	0.8
Pseudomonas fluorescens	5	2	40.0	0.4

Table 4

Frequency of Isolated Gram-Positive Organisms and Resistance Pattern

Organism	Isolated organisms	Resistant isolates	Organism percent resistant	Percent of total resistant organisms
Staphylococcus aureus	250	142	56.8	55.3
Enterococcus faecium	148	115	77.7	44.7
Enterococcus faecalis	131	0	0	0.0

Table 5

Sites of Resistant Pathogen Infections

Site	Resistant GNR infections	Most Common rGNR (N)	Resistant GPC infections	Most Common rGPC (N)
Lung	233	*P. aeruginosa* (93)	120	*S. aureus* (80)
Blood	70	*P. aeruginosa* (12)	86	*E. faecium* (31)
Urine	60	*P. aeruginosa* (20)	49	*E. faecium* (15)
Abdomen	43	*E. coli* (13)	44	*E. faecium* (31)
Wound	39	*P. aeruginosa* (17)	30	*E. faecium* (15)
Line	20	*S. maltophilia* (5)	37	*S. aureus* (14)
Pleura	8	*P. aeruginosa* (4)	8	*S. aureus* (4)
Skin/Skin Structure	3	*E. cloacae* (2)	5	*S. aureus* (1)