KentuckyOne Health®
Saint Joseph Hospital

Impact of a Pharmacist-Led Antimicrobial Stewardship Initiative to Improve Clinical and Economic Outcomes in Patients with Complicated Infections

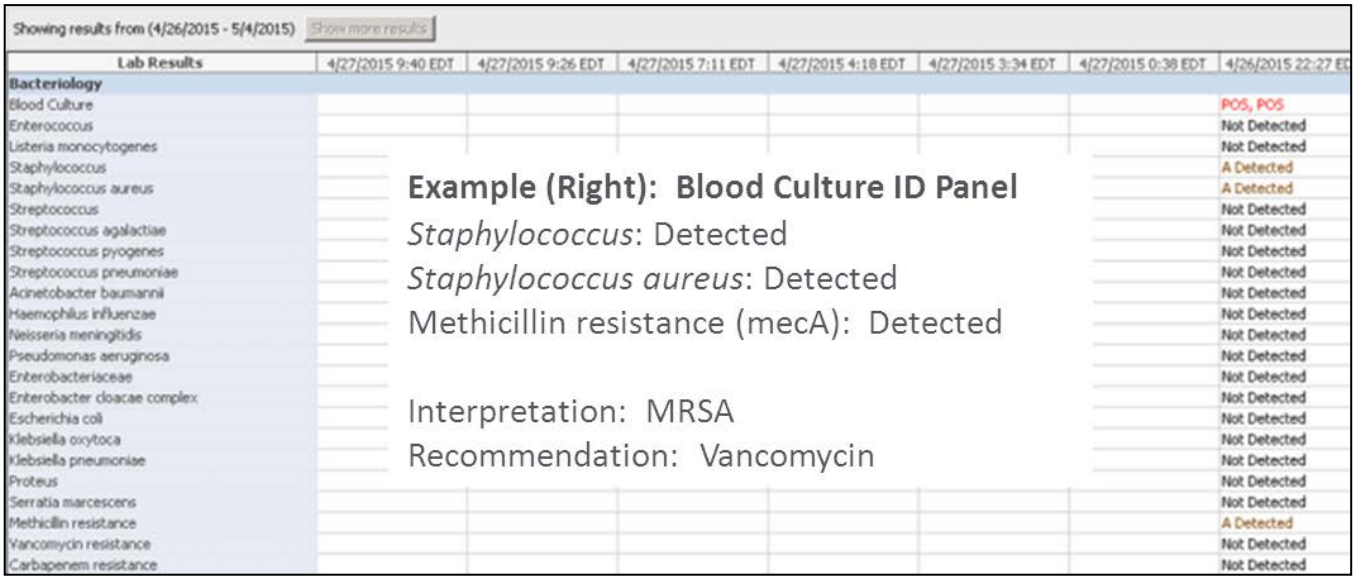
TIERS 1 & 2 of a multi-tiered approach to improve infection-related outcomes

Early diagnosis and prompt initiation of effective antimicrobial therapy are necessary to improve clinical outcomes in patients with severe or complicated infections. The use of rapid diagnostic tests, including polymerase-chain reaction (PCR)-based assays, has been shown to reduce the time required for pathogen identification. A growing body of evidence also suggests that mandatory Infectious Diseases (ID) consultation results in greater adherence to evidence-based treatment guidelines, reduced in-hospital mortality, and earlier discharge. Conditions such as bacteremia, candidemia, cardiovascular device-related infections, central nervous system (CNS) infections, and infective endocarditis are often associated with increased mortality and length of stay. A multi-tiered approach was developed by the antimicrobial stewardship team to improve clinical and economic outcomes among patients with these conditions.

In an effort to reduce the time required for identification of bloodstream infections, a blood culture PCR system was implemented at our facility in January 2015. Although blood cultures are generally considered the gold standard for diagnosis of bloodstream infections, incubation times of up to 96 hours may be required before an organism is identified. PCR-based technologies may be used to amplify DNA from pathogens that are commonly isolated in the blood. The FilmArray Blood Culture Identification (BCID) Panel is an FDA-approved multiplex PCR system that can detect up to 24 different bacterial and fungal pathogens and three antibiotic resistance genes (i.e., *mecA*, *vanA/B*, and KPC). A protocol was developed by our multidisciplinary antimicrobial stewardship team to ensure that rapid diagnostic testing was performed on all positive blood culture specimens.

All positive blood culture bottles are initially assessed via gram-stain. Reflex PCR testing of all positive blood culture specimens is performed automatically using the FilmArray BCID Panel. Standard microbiologic identification and antimicrobial susceptibility testing is performed in addition to PCR testing. Results are available within one hour of performing the test versus 72-96 hours with conventional testing. The electronic medical record was redesigned to accommodate the new test results (Figure 1). Guidelines were also developed by the ID Clinical Pharmacy Specialist to assist the medical staff with interpretation of PCR results and to facilitate rapid initiation of effective antimicrobial therapy (Figure 2). Medical staff education was provided by the pharmacist in charge of antimicrobial stewardship at our facility. This program highlights the impact of an ID Clinical Pharmacy Specialist within the health-system and demonstrates effective collaboration between pharmacists and other healthcare providers. The Clinical Triggers program has also helped to advance pharmacy practice by showcasing the pharmacist's role in disease-state management, in addition to being the medication expert. By working closing with other physician specialty groups, clinical pharmacy specialists can play a significant role in improving infection-related outcomes.

FIGURE 1.



Showing results from (4/26/2015 - 5/4/2015) Show more results

Lab Results	4/27/2015 9:40 EDT	4/27/2015 9:26 EDT	4/27/2015 7:11 EDT	4/27/2015 4:18 EDT	4/27/2015 3:34 EDT	4/27/2015 0:38 EDT	4/26/2015 22:27 ED
Bacteriology							
Blood Culture							POS, POS
Enterococcus							Not Detected
Listeria monocytogenes							Not Detected
Staphylococcus							A Detected
Staphylococcus aureus							A Detected
Streptococcus							Not Detected
Streptococcus agalactiae							Not Detected
Streptococcus pyogenes							Not Detected
Streptococcus pneumoniae							Not Detected
Acinetobacter baumannii							Not Detected
Haemophilus influenzae							Not Detected
Neisseria meningitidis							Not Detected
Pseudomonas aeruginosa							Not Detected
Enterobacteriaceae							Not Detected
Enterobacter cloacae complex							Not Detected
Escherichia coli							Not Detected
Klebsiella oxytoca							Not Detected
Klebsiella pneumoniae							Not Detected
Proteus							Not Detected
Serratia marcescens							Not Detected
Methicillin resistance							A Detected
Vancomycin resistance							Not Detected
Carbapenem resistance							Not Detected

Example (Right): Blood Culture ID Panel

Staphylococcus: Detected

Staphylococcus aureus: Detected

Methicillin resistance (mecA): Detected

Interpretation: MRSA

Recommendation: Vancomycin

FIGURE 2.

BioFire BLOOD CULTURE ID Multiplex PCR
Interpretive Guidelines (Saint Joseph Hospital)

PCR Result	First-Line Empiric Therapy	Comments
***Enterococcus* genus**		
vanA/B negative	Ampicillin 2g IV q4h	Vancomycin if history of severe beta-lactam allergy
vanA/B positive (VRE)	Linezolid 600mg IV/PO q12h	Daptomycin may also be used for treatment of VRE
Listeria monocytogenes	Ampicillin 2g IV q4h	Trimethoprim-sulfamethoxazole if severe beta-lactam allergy
Staphylococcus aureus		
mecA negative	Nafcillin 2g IV q4h	Target a vancomycin trough concentration of 15-20 mg/L.
mecA positive (MRSA)	Vancomycin 15mg/kg IV q12h	Consider daptomycin for MRSA with vanc MIC ≥2 mg/L
***Staphylococcus* genus (if *S. aureus* PCR is not detected)**		
mecA negative	Nafcillin 2g IV q4h	Consider withholding anti-Staphylococcal therapy if only one bottle is positive and no risk factors for endocarditis
mecA positive	Vancomycin 15mg/kg IV q12h	
***Streptococcus* genus**		
S. agalactiae (Group B)	Ampicillin 2g IV q4h	
S. pneumoniae	Ceftriaxone 2g IV q24h	For CNS infections, increase dose to 2g IV q12h & add vanc
S. pyogenes (Group A)	Penicillin G 3M.U. IV q4h PLUS Clindamycin 600mg IV q8h	
Antimicrobial Resistance Genes		
KPC	ID Consultation (± Colistin)	Carbapenem-resistance gene; Isolation precautions
mecA	Vancomycin 15mg/kg IV q12h	Methicillin-resistance gene; Isolation precautions
vanA/B	Linezolid 600mg IV/PO q12h	Vancomycin-resistance gene; Isolation precautions

BioFire BLOOD CULTURE ID Multiplex PCR
Interpretive Guidelines (Saint Joseph Hospital)

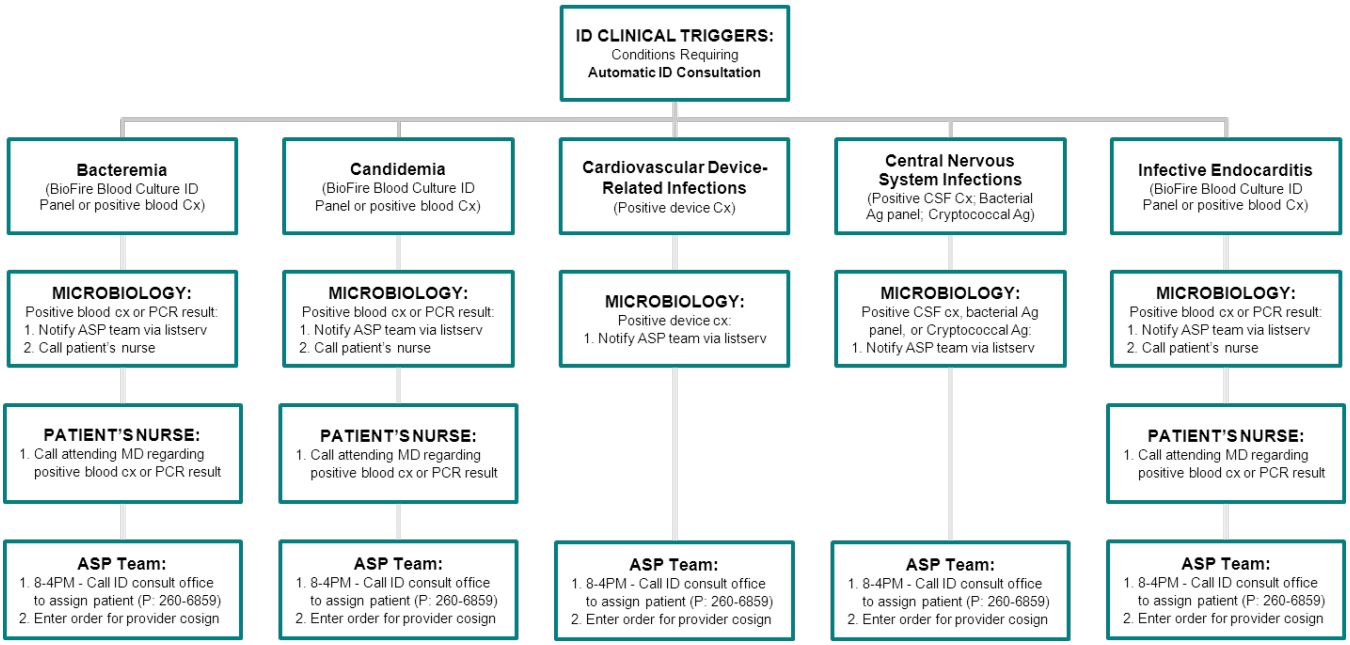
PCR Result	First-Line Empiric Therapy	Comments
Acinetobacter baumannii	Meropenem 2g IV q8h (+/- colistin OR tobramycin)	Consider isolation precautions
Enterobacteriaceae		
Enterobacter cloacae	Meropenem 500mg IV q6h	96% Susceptible (2014) (Zosyn - 79% Susceptible)
Escherichia coli	Zosyn 4.5g, then 3.375g IV q6h	93% Susceptible (2014) (Ceftriaxone - 91% Susceptible)
Klebsiella oxytoca	Ceftriaxone 2g IV q24h OR Zosyn 4.5g, then 3.375g IV q6h	91% Susceptible (2012) 93% Susceptible (2012)
Klebsiella pneumoniae	Meropenem 500mg IV q6h	100% Susceptible (2014) (Zosyn – 88% Susceptible)
Proteus	Zosyn 4.5g, then 3.375g IV q6h	99% Susceptible (2014) (Ceftriaxone - 90% Susceptible)
Serratia marcescens	Cefepime 1g IV q6h	97% Susceptible (2014) (Zosyn - 65% Susceptible)
Haemophilus influenzae	Ceftriaxone 2g IV q24h	
Neisseria meningitidis	Ceftriaxone 2g IV q24h	For CNS infections, increase dose to 2g IV q12h
Pseudomonas aeruginosa	Zosyn 4.5g, then 3.375g IV q6h	94% Susceptible (2014) (Meropenem - 88% Susceptible)
Yeast (*Candida* species)		
Candida albicans	Fluconazole 800mg loading dose, then 400mg IV/PO q24h	
Candida glabrata	Micafungin 100mg IV q24h	
Candida krusei	Micafungin 100mg IV q24h	
Candida parapsilosis	Fluconazole 800mg loading dose, then 400mg IV/PO q24h	
Candida tropicalis	Micafungin 100mg IV q24h	

Developed by the SJH Antimicrobial Stewardship Program (Updated 2/2015)

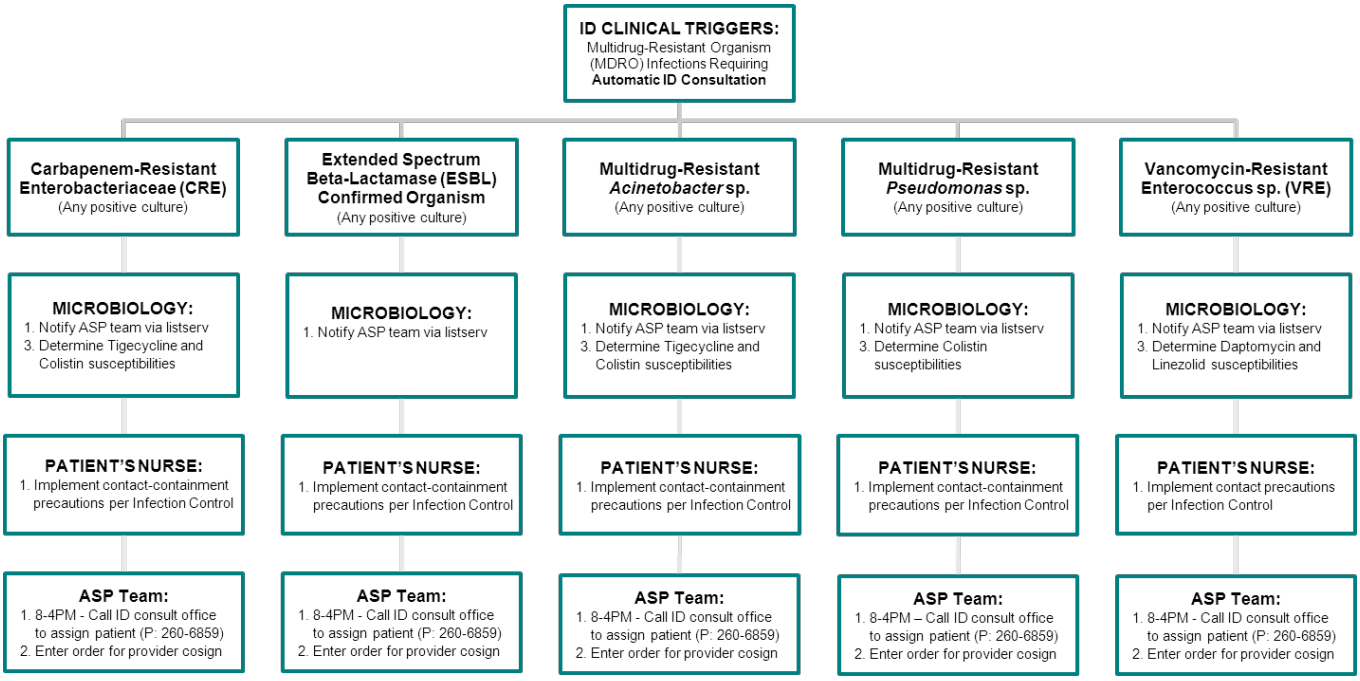
In June 2015, a 'Clinical Triggers' policy requiring automatic ID consultation was developed by the antimicrobial stewardship team and approved by the Medical Governing Council. ID consultation was required after initial pharmacist review for each of the following high-risk medical conditions: bacteremia, candidemia, cardiovascular device-related infections, central nervous system infections, and infective endocarditis. An ID consult was also required if any of the following multidrug-resistant organisms (MDROs) were identified: carbapenem-resistant Enterobacteriaceae (CRE), extended-spectrum beta-lactamase (ESBL) producing organisms, multidrug-resistant Acinteobacter or Pseudomonas species, or vancomycin-resistant Enterococcus (VRE).

Antimicrobial stewardship team members are contacted via a secure email listserv when clinical triggers are identified. Antimicrobial therapy is reviewed by the ID Clinical Pharmacy Specialist to ensure that effective antimicrobial therapy has been initiated based on culture and/or PCR results. The attending physician is also contacted regarding positive blood culture results and other critical lab values if present. During normal hours of operation, the antimicrobial stewardship team will contact the ID consult office after receiving a notification from the lab (Figure 4).

FIGURE 4.



Abbreviations: Ag = Antigen; ASP = Antimicrobial Stewardship Program; CSF = cerebrospinal fluid; Cx = culture; ID = Infectious Diseases; MD = medical doctor (or provider); PCR = polymerase chain reaction



A follow-up study was conducted to determine the clinical and economic impact of this pharmacist-led initiative in patients with bacteremia. Among patients with microbiologically documented gram-negative bacteremia, in-hospital mortality was reduced from 12% to 7% when compared to an historical cohort (Table 1). Overall and ICU length of stay were reduced by 1.6 and 2.4 days, respectively. The average time from blood culture collection to pathogen identification was reduced from 67.9 hours to 18.7 hours ($p<0.001$). The study also demonstrated a significant economic benefit to the hospital. The average total cost per case was reduced from $12,559 to $9,032.

Table 1. Impact of Multiplex PCR Testing and Automatic ID Consultation

	HISTORICAL Cohort	PROSPECTIVE Cohort
PRIMARY/SECONDARY ENDPOINTS	n = 69	n = 42
All-Cause In-Hospital Mortality, %	12%	7%
Overall Length-of-Stay, days (SD)	8.5 (5.8)	6.9 (5.0)
ICU Length-of-Stay, days (SD)	6.8 (4.6)	4.4 (4.2)
Total Cost Per Case	$12,559	$9,032
Time to speciation, hours (SD)	67.9 (17.1)	18.7 (6.8)

*Saint Joseph Hospital, KentuckyOne Health (Preliminary Data)

Demonstration of the Sustained Impact of Antimicrobial Stewardship Activities on the Incidence of Multidrug-Resistant Organisms (MDROs)

TIER 3 of a multi-tiered approach to improve infection-related outcomes

The role of a clinical pharmacist is not limited to medication therapy management. Rather, it encompasses all aspects of antimicrobial stewardship and infection control that directly impact patient care. Our multidisciplinary team has focused on prevention *and* treatment of MDROs and other complicated infections. These data are included in order to demonstrate the sustained impact of antimicrobial stewardship activities at our facility.

Institutional guidelines were developed by the antimicrobial stewardship team to prevent environmental cross-contamination with resistant microorganisms. A 3-Tiered Patient Care Cleaning (PCC) Program was previously developed in 2011 for all patient care areas. Direct observation of environmental cleaning procedures occurred during Tier I. During Tier II, fluorescent markers were applied to high-touch patient surface areas prior to terminal cleaning, and follow-up monitoring was performed by either the Environmental Services Director or Infection Preventionist. Finally, bacterial ATP bioluminescence monitoring of patient care surfaces and equipment was performed during Tier III. The system detected ATP from bacteria or other organic substances and allowed for real-time objective monitoring of environmental cleaning procedures.

Targeted interventions such as implementation of enhanced dosing strategies were also employed to improve clinical outcomes in patients receiving ant-infective agents. Outcomes were re-assessed at the end of 2015 to determine the impact of these interventions on the incidence of multidrug-resistant organisms. The following outcomes were observed after implementing targeted stewardship interventions and enhanced cleaning practices:

- Carbapenem resistance rates among patients with *Acinetobacter* and *P. aeruginosa* infections fell by 61% and 6%, respectively (**Figure 5**).
- The total number of *Acinetobacter* sp. infections was reduced from 61 (0.7 / 1000 patient days) to 19 (0.26 / 1000 patient days) (**Figure 6**).
- The total number of *P. areuginosa* infections was reduced from 274 (3.2 / 1000 patient days) to 137 (1.9 / 1000 patient days) (**Figure 7**).

FIGURE 5.

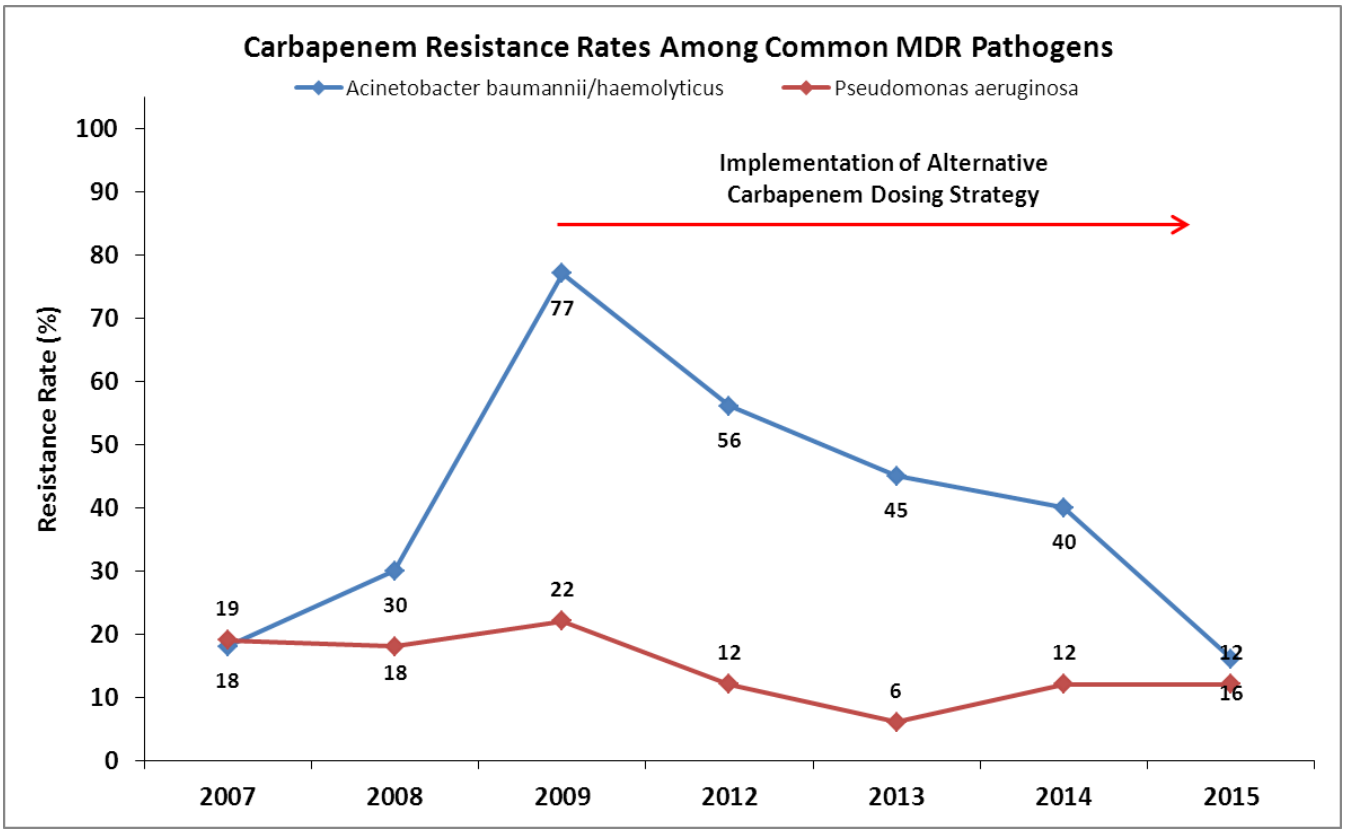


FIGURE 6.

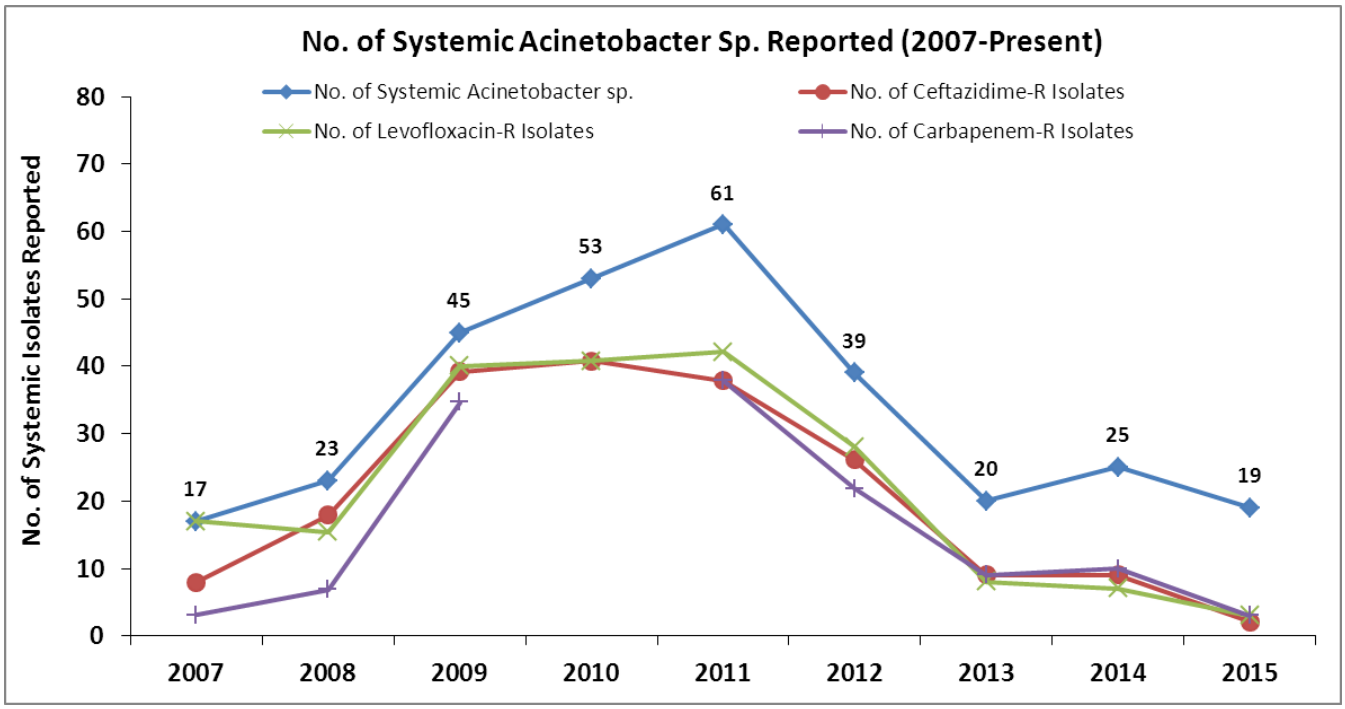
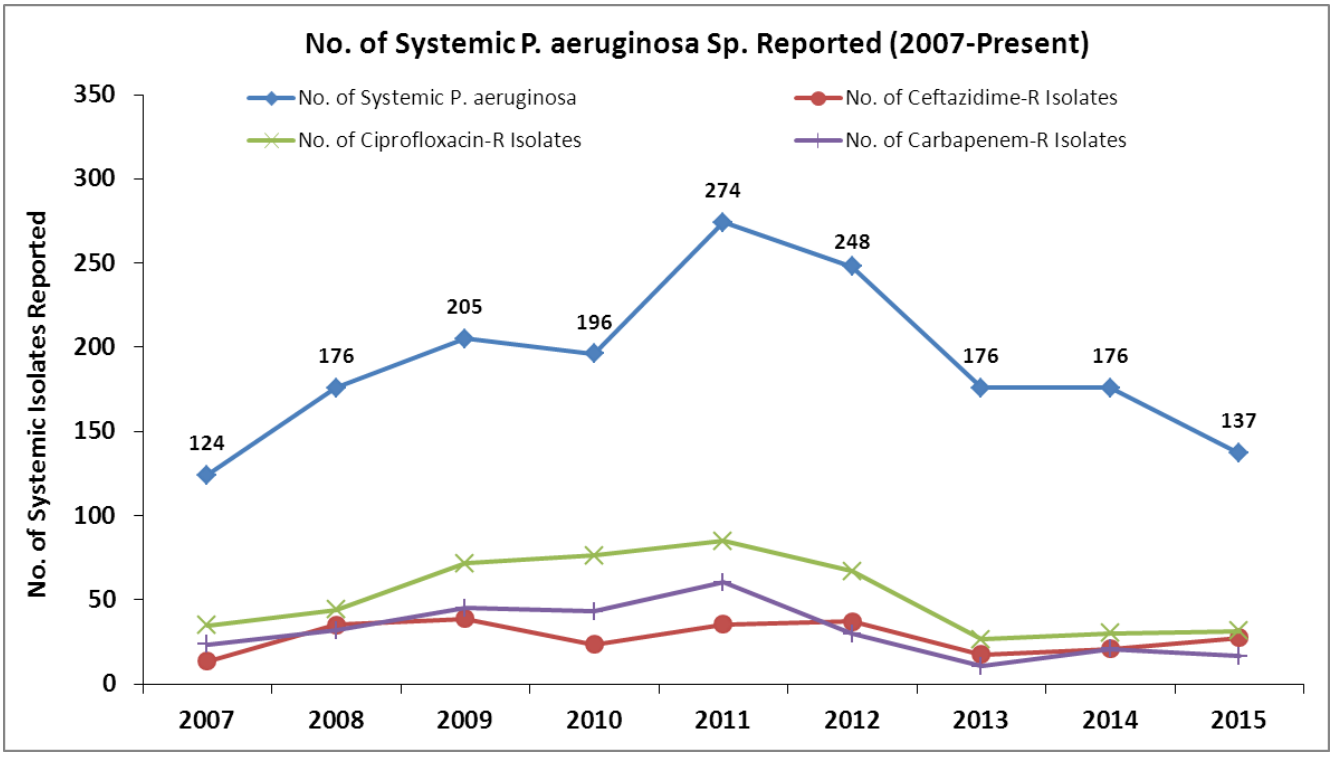


FIGURE 7.


No. of Systemic P. aeruginosa Sp. Reported (2007-Present)
No. of Systemic P. aeruginosa
No. of Ceftazidime-R Isolates
No. of Ciprofloxacin-R Isolates
No. of Carbapenem-R Isolates
No. of Systemic Isolates Reported
350
300
250
200
150
100
50
0
124
176
205
196
274
248
176
176
137
2007
2008
2009
2010
2011
2012
2013
2014
2015