ANTIMICROBIAL RESISTANCE SURVEILLANCE PROGRAM 2013 DATA SUMMARY REPORT

ANTIMCROBIAL RESISTANCE SURVEILLANCE REFERENCE LABORATORY

ANTIMICROBIAL RESISTANCE SURVEILLANCE PROGRAM 2013 ANNUAL REPORT

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Acronyms & Abbreviations

Acronyms & Abbreviations	Definition
AMR	Antimicrobial resistance
ARSP	Antimicrobial Resistance Surveillance Program
ARSRL	Antimicrobial Resistance Surveillance Reference Laboratory
AST	Antimicrobial susceptibility test
CA-MRSA	Community-associated methicillin-resistant *S. aureus*
CAR	Cordillera Autonomous Region
CLSI	Clinical Laboratory Standards Institute
CRE	Carbapenem-resistant *Enterobacteriaceae*
CSF	Cerebrospinal fluid
DMU	Data Management Unit
DOH	Department of Health
EQAS	External quality assessment
ER	Emergency room
ESBL	Extended-spectrum-beta-lactamase
HA-MRSA	Healthcare-associated methicillin-resistant *S. aureus*
MDR	Multi- Drug Resistance : *Resistance of the organism to at least 1 or more agents in 3 or more classes of antimicrobial categories*
MRSA	Methicillin-resistant *Staphylococcus aureus*
NCR	National Capital Region
NDM-1	New Delhi Metallo-beta-lactamase 1
OPD	Outpatient department
PDR	Pan Drug Resistance: *Non-susceptibility to all agents in all antimicrobial categories*
PRSP	Penicillin-resistant *Streptococcus pneumoniae*
WHO	World Health Organization
WHONET	Windows-based database software developed by the WHO Collaborating Centre for Surveillance of Antimicrobial Resistance based at the Brigham and Women's Hospital in Boston for the management and analysis of microbiology laboratory data with a special focus on the analysis of antimicrobial susceptibility test results
XDR	Extensively Drug Resistance: *Resistance to at least 1 agent in all but 2 or fewer antimicrobial categories*

1. INTRODUCTION 1

1. Introduction

Antimicrobial resistance (AMR), which refers to the ability of microorganisms that cause disease to withstand attack by antimicrobial medicines[1], is a serious public health threat to which the health authorities locally and globally has called attention to more urgently in the past 3 years.

AMR has far reaching and serious implications in health care as well as economies. Infections caused by resistant microorganisms often fail to respond to standard treatment, resulting in prolonged illness and greater risk of death[2]. AMR hampers the control of infectious diseases because patients remain infectious for a longer time, thus the risk of spreading resistant microorganisms to others is increased. AMR likewise increases the cost of health care as more expensive therapies must be used when infections become resistant to first-line medicines. Infections due to resistant microorganisms also increases health care costs and economic burden to families and societies as it often results in longer duration of illness and treatment, often in hospitals.

When we lose antimicrobials to resistance, the achievements of modern medicine such as organ transplant, cancer chemotherapy and major surgery would be compromised as these would not be possible without effective antimicrobials for prevention and treatment of infections. Losing antimicrobials to resistance can result in many infectious diseases becoming untreatable and uncontrollable. This can bring us back to the pre-antibiotic era.

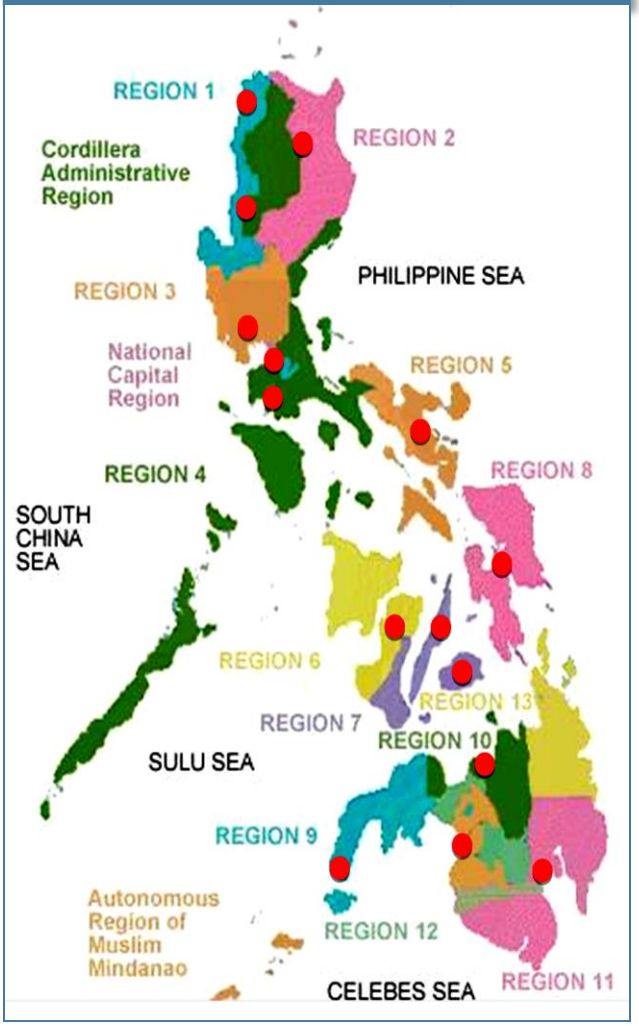
It is recognized that the issue of AMR must be addressed by concerted efforts of government agencies, health providers, drug industry, professional organizations, academe and civil society.

Surveillance is a fundamental part of an effective response to AMR problem.[3] It is needed to detect resistant microorganisms, enable correct decisions to be made about treatment options, and guide policy recommendations.[1]

Department of Health's Antimicrobial Resistance Surveillance Program (ARSP)

As the country's response to the recommendation of the World Health Organization (WHO) Working Group on the Regional Information Network on Antimicrobial Resistance that a surveillance program be initiated among member states of the Western Pacific Region to contain and prevent resistance to antimicrobials, the Philippine Committee on Antimicrobial Resistance Surveillance Program was created in 1988 by virtue of Department Of Health's Department Order 339-J.

Figure 1.1 ARSP Sentinel sites by region, 2013



The program aims to provide critical inputs to the Department of Health's effort to promote rational drug use by determining the current status and developing trends of antimicrobial resistance of selected bacteria to specific antimicrobials. Participating in the program are 22 sentinel sites representing 14 of the 17 regions of the country (Figure 1.1, Table 1.1).

Data Collection

The DOH-ARSP implements surveillance of AMR of clinical aerobic bacterial isolates and collects culture and antimicrobial susceptibility data from its 22 sentinel sites in 14 regions of the country.

All sentinel sites implement standard methods for culture and susceptibility testing based on the WHO Manual for the Laboratory Identification and Antimicrobial Susceptibility Testing of Bacterial Pathogens of Public Health Importance in the Developing World[4] and updated Clinical Laboratory Standards Institute (CLSI)[5, 6] references for antibiotic susceptibility testing and quality control.

Table 1.1 ARSP Sentinel sites by region, 2013

Region	ARSP Sentinel Site
NCR	Lung Center of the Philippines (LCP)
	National Kidney Institute (NKI)
	Rizal Medical Center (RMC)
	San Lazaro Hospital (SLH)
	Philippine General Hospital (PGH)
	Research Institute for Tropical Medicine (RTM)
	University of Sto. Tomas Hospital (UST)
	Far Eastern University Hospital (FEU)
LUZON	
Region I	Mariano Marcos Memorial Medical Center(MAR)
CAR	Baguio General Hospital (BGH)
Region II	Cagayan Valley Medical Center (CVM)
Region III	Jose B. Lingad Memorial General Hospital (JLM)
Region IV-A	Batangas Regional Hospital (BRH)
Region V	Bicol Regional Training and Teaching Hospital (BRH)
VISAYAS	
Region VI	Corazon Locsin Montelibano Memorial Hospital (MMH)
Region VII	Gov Celestino Gallares Regional Hospital (GMH)
Region VIII	Vicente Sotto Memorial Medical Center (VSM)
	Eastern Visayas Regional Medical Center (EVR)
MINDANAO	
Region IX	Zamboanga Medical Center (ZMC)
Region X	Northern Mindanao Medical Center (NMC)
Region XI	Southern Philippines Medical Center (DMC)
Region XII	Cotabato Medical Center (CMC)

Table 1.2 Isolates for referral to ARSRL 2013

Isolates	Sampling of Referrals to ARSRL
Isolates with uncommonly seen susceptibility patterns (vancomycin-resistant *S. aureus*- VRSA, vancomycin-resistant *S. epidermidis*- VRSE, vancomycin-resistant Enterococci- VRE, carbapenem-resistant *Enterobacteriaceae*- CRE, XDR *Peudomonas aeruginosa* and *Acinetobacter baumannii*)	All isolates are referred to ARSRL
Isolates with uncommonly seen susceptibility patterns (extended-spectrum beta-lactamase or ESBL producing *Enterobacteriaceae*, methicillin-resistant *S. aureus*- MRSA)	All isolates from days 1-15 of the month are referred to ARSRL
Difficult to identify organisms	All isolates are referred to ARSRL
Isolates for Serotyping (*Haemophilus influenzae, Streptococcus pneumoniae, Shigellae, Salmonellae, Vibrio cholerae*)	All isolates are referred to ARSRL

Sentinel sites likewise send isolates with unusual antimicrobial susceptibility patterns to ARSRL for phenotypic and genotypic confirmatory testing as well as select bacteria for serotyping (Table 1.2) (Annex 2).

Data Management

The culture and antimicrobial susceptibility test results are submitted on a monthly basis by the sentinel sites to the coordinating laboratory of the program – the Antimicrobial Resistance Surveillance Reference Laboratory (ARSRL) (Annex 1). Data are encoded using a database software called WHONET. WHONET is Windows-based database software developed by the WHO Collaborating Centre for Surveillance of Antimicrobial Resistance based at the Brigham and Women's Hospital in Boston for the management and analysis of microbiology laboratory data with a special focus on the analysis of antimicrobial susceptibility test results.[7] The Data Management Unit (DMU) of the ARSRL performs regular data cleaning and validation.

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In the analysis of antimicrobial susceptibility test results, an isolate is considered resistant to an antimicrobial agent when tested and interpreted as resistant (R) in accordance with the clinical breakpoint criteria based on the most recent Clinical Laboratory Standards Institute (CLSI) references for antibiotic susceptibility testing[5, 6]. Data generated by the program are annually summarized, analyzed and reported to stakeholders.

The annual summary report focuses on aerobic bacterial pathogens of public health importance causing significant morbidity and mortality locally (Table 1.3). Analysis of culture results is restricted to the first isolate received (per genus under surveillance) per patient in the calendar year.

The program's annual data are expressed as a cumulative percentage resistance, i.e. the percentage of resistant isolates out of all isolates with antimicrobial susceptibility testing (AST) information on that specific organism–antimicrobial agent combination.

Additionally, for selected analyses, a 95% confidence interval is determined for the resistance percentage using the Paulson-Camp-Pratt approximation method. Cumulative percentages of resistance are also compared as proportions using the Fischer test, using a p value of < 0.05 as statistically significant. Generally, only species with testing data for 30 or more isolates are included in the analysis.

Interpretation of the Annual Report Data

Interpretation of data in this annual report should be undertaken with caution taking into consideration that there may be several factors that could influence and introduce bias to the data resulting in over- or underestimation of resistance percentages. Potential sources of bias include population coverage, sampling, and laboratory routines and capacity.

Most of the resistance data in the program come from regional hospitals which typically caters to patients from towns and cities within the vicinity of the hospital. Resistance variations in local areas not covered by regional hospitals are not represented in the program data. Secondly, data for the National Capital Region come from 8 sentinel sites while data for other regions come from 1 or 2 sentinel sites. Another important sampling factor that should be considered when interpreting changes in trends of resistance over time would be the renewed participation of one of the 2013 annual report's major contributor sentinel site, Philippine General Hospital, after a 6-year hiatus from the program.

Performance of culture and susceptibility tests in the sentinel sites are likewise dependent on the diagnostic habits of the clinicians as well as the financial capability of patients for such test. Given that the program data are from routine clinical samples, differences in these factors may introduce variations in the resistance data.

Lastly, microbiology laboratory routines as well as capacity of the sentinel sites may differ. As a form of quality assurance for the program, an annual external quality assessment (EQAS) as well as periodic monitoring visits to sentinel sites are conducted by the reference laboratory.

Table 1.3 Target organisms for the ARSP, 2013	
Classification	**Pathogens**
Enteric Pathogens	*Salmonella species, Shigellae, Vibrio cholerae*
Respiratory Pathogens	*Haemophilus influenzae, Streptococcus pneumoniae*
Bacterial Organisms causing Sexually-transmitted infections	*Neisseria gonorrheae*
Bacterial Pathogens causing Healthcare-associated Infections	*Staphylococcus aureus, Enterococcus* species, *Escherichia coli, Klebsiella species, Pseudomonas aeruginosa, Acinetobacter baumannii*

References

1 WPR/RC62/5 Antimicrobial Resistance Provisional Agenda item 10 62nd session Regional Committee Meeting Regional Office for the Western Pacific.

2 http://www.who.int/mediacentre/factsheets/fs194/en/

3 Antimicrobial resistance surveillance in Europe 2012. Annual report of the European Antimicrobial Resistance Surveillance Network (EARS-Net) 2012

4 World Health Organization and Center for Disease Control National Center for Infectious Diseases, Manual for the Laboratory Identification and Antimicrobial Susceptibility Testing of Bacterial Pathogens of Public Health Importance in the Developing World, Geneva: World Health Organization, 2003.

5 Clinical Laboratory Standards Institute, Performance Standards for Antimicrobial Susceptibility Testing; 23rd Information Supplement CLSI Document M100-S23, Pennsylvania: Clinical Laboratory Standards Institute, 2013

6 Clinical Laboratory Standards Institute, Methods for Antimicrobial Dilution and Disk Susceptibility Testing of Infrequently Isolated or Fastidious Bacteria; Approved Guideline-Second Edition, M45A2, Pennsylvania: Clinical Laboratory Standards Institute, 2010

7 http://www.who.int/drugresistance/whonetsoftware/en/

2. ARSP 2013 DATA EXECUTIVE SUMMARY

2. ARSP 2013 Data Executive Summary

- Resistance data for 37,629 bacterial isolates coming from 21 hospital bacteriology laboratories located in 14 regions of the Philippines were analyzed for 2013. Luzon sentinel sites contributed 63

- % of the 2013 data, while the remaining 18% and 19% of the data came from the Visayas and Mindanao sentinel sites, respectively.

Streptococcus pneumoniae

- Cumulative resistance rates of *S. pneumoniae* isolates for 2013 against penicillin, using meningitis breakpoints, was at 5%; while there were no reported penicillin-resistant *S. pneumoniae* (PRSP) using non-meningitis breakpoints (n= 255).
- Recently, we see the possible emergence of levofloxacin-resistant pneumococci with resistance rate at 2% for 2013 (n=160). In contrast, there were no reported levofloxacin-resistant *S. pneumoniae* isolates in 2012.
- There remains no reported ceftriaxone-resistant S. *pneumoniae* for 2013.
- The most common invasive *S. pneumoniae* serotype identified for 2013 was serotype 1.

Haemophilus influenzae

- For 2013, 17% of *H. influenzae* isolates were resistant to ampicillin (n= 186) and 7% were resistant to ampicillin-sulbactam (n= 195). These rates did not differ significantly when compared to data from 2012 (*p* value > 0.05).
- All ampicillin-resistant *H. influenzae* isolates tested were positive for beta-lactamase production.
- Resistance rates for 2013 isolates of *H. influenzae* are at 34% for co-trimoxazole (n= 175) and 7% for chloramphenicol (n=151). These rates did not differ significantly when compared to data from 2012 (*p* value > 0.05).

Salmonellae Typhi

- *S.* Typhi isolates have remained susceptible to first line antibiotics ampicillin, co-trimoxazole, and chloramphenicol remaining at less than 5% for 2013 as they have been for the past 10 years.
- One *S.* Typhi isolate from a sentinel site in Mindanao was confirmed ceftriaxone resistant by MIC. Phenotypic and genotypic analysis confirmed the production of the CTX-M gene for ESBL in this isolate.

Nontyphoid Salmonellae

- For 2013, we continue to see high rates of resistance against nontyphoid *Salmonella* species against previous first line agents: ampicillin at 56% (n= 119); chloramphenicol at 16% (n= 87); and co-trimoxazole at 34% (n= 103).
- Increasing resistance of nontyphoid *Salmonella* species to ciprofloxacin (n= 103) is noted with rates at 18% for 2013. Comparatively, 2012 resistance rate against ciprofloxacin was at 14% (n= 97).
- The most common nontyphoid *Salmonella* species serotype identified for 2013 is *Salmonella* Enteritidis.

Shigella species

- Combined 2011-2013 data reveals high rates of resistance for previous 1st line agents against Shigellae with resistance rates at 67% against ampicillin (n=43); 49% against chloramphenicol (n= 35) and 67% against co-trimoxazole (n= 43).
- Emerging resistance of *Shigella* species against the quinolones are seen with cumulative rates of resistance for 2011-2013 data at 13% against nalidixic acid (n=31) and 15% against ciprofloxacin (n=41).

Vibrio cholerae

- *Vibrio cholerae* isolates remain susceptible to first line agents: chloramphenicol, co-trimoxazole and tetracycline with no reported resistant isolate to any of these antimicrobials for the combined 2011 to 2013 data.

Neisseria gonorrhoeae

- Combined 2012 to 2013 *Neisseria gonorrhoeae* isolates have cumulative high rates of resistance against penicillin at 80% (n= 46); tetracycline at 55% (n=47); and ciprofloxacin at 74% (n=46).

- There were no reported spectinomycin, ceftriaxone and cefixime resistant isolates for the 2011 to 2013 data.

Staphylococcus aureus

- MRSA rate for 2013 is at 53% (n= 2,317).
- MRSA rates for 2013 did not differ when comparing invasive MRSA rate (blood specimen isolates) at 55%; against cutaneous specimens isolates' MRSA rate at 55%.
- For 2013, we see the possible emergence of *S. aureus* resistance against vancomycin with 2013 reported rates at 1% (n=1,176). Comparatively, there were no reported vancomycin-resistant *S. aureus* isolates for 2012.

Staphylococcus epidermidis

- High rates of resistance *for Staphylococcus epidermidis* against penicillin at 95% (n= 1,509) oxacillin at 75% (n= 1,375); co-trimoxazole at 50% (n= 1,196) and ciprofloxacin at 33% (n= 1,456) were reported for 2013.
- For 2013 we see the possible emergence of linezolid (n= 741) and vancomycin (n= 566) resistance for *Staphylococcus epidermidis* isolates with reported rates at 1% for each antimicrobial.

Enterococcus species

- For 2013, we continue to report higher rates of ampicillin resistance amongst *Enterococcus* species with rates at 8% for *Enterococcus faecalis* (n=397) and 69% for *Enterococcus faecium* (n= 140).
- High rates of high-level aminoglycoside resistance is noted amongst 2013 *Enterococcus* species. Paucity of isolates with relevant AST data for 2013 against these agents can be addressed by consistent inclusion of high level aminoglycosides in the panel of antibiotics for testing for all *Enterococcus* species isolated which can then provide a better estimate of this resistance phenotype.
- For 2013, we report isolated cases of vancomycin-resistant Enterococci.

Escherichia coli

- High rates of resistance is seen for most agents used to treat *E. coli* infections with 2013 resistance rate at 82% against ampicillin (n=4,333); 32% against ampicillin-sulbactam (n=4,056); 29% against cefuroxime (n= 2,210); 31% against ceftriaxone (n= 4,364); 66% against co-trimoxazole (n= 3,893); 4% against amikacin (n= 4,478) and 43% against ciprofloxacin (n= 4,332).
- Rates of resistance to the reserved drug, imipenem is at 2% for 2013 (n=4,858).
- Urinary *E. coli* isolates from outpatients remain susceptible to nitrofurantoin with rate of resistance at 7% (n= 969). Comparatively urinary *E. coli* isolates from hospitalized patients show variable susceptibility to parenteral agents with rates of resistance ranging from 2% against ertapenem (n= 1,059) to 36% against ceftriaxone (n= 1,683) .

Klebsiella species

- High rates of resistance is seen against most agents used to treat infections caused by *Klebsiella* species with resistance rates at 28% against amoxicillin-clavulanic acid (n= 6,254); 46% against cefuroxime (n= 2,455); 40% against ceftriaxone (n= 5,675); 7% against amikacin (n= 5,755) and 28% against ciprofloxacin (n= 5,674).
- For 2013, we continue to see alarmingly increasing rates of resistance of *Klebsiella* species against the the carbapenems. For the 2013 data, resistance rate of *Klebsiella* species is reported at 6% for imipenem (n= 6,189) and 7% for meropenem (n= 5,833).
- Significantly higher resistance rates were reported for invasive *Klebsiella* sp. isolates compared to rates from all reported 2013 Klebsiella species for the following antimicrobials: cefuroxime, ceftriaxone, imipenem, amikacin & ciprofloxacin (p value < 0.05).

Carbapenem-resistant *Enterobacteriaceae*

- Over-all rates of imipenem-resistance for 2013 *E. coli* and *Klebsiella* sp. isolates were 2% (n= 4,858) and 6% (n= 6,189), respectively.

- Comparatively, 2012 *E. coli* and *Klebsiella* species rates of resistance against imipenem were at 3% and 5%, respectively.
- Most of the carbapenem-resistant *E. coli* and *Klebsiella* species isolates were confirmed for production of the New Delhi Metallo-beta-lactamase (NDM-1) gene at the reference laboratory.
- Antimicrobial susceptibility testing of these carbapenem-resistant isolates reveals that most were resistant to all tested beta-lactams, fluoroquinolones, co-trimoxazole, tetracycline and chloramphenicol. In contrast, isolates tested remained susceptible to colistin and polymyxin B; and had variable susceptibility to the aminoglycosides.

Pseudomonas aeruginosa

- Resistance rate of 2013 *P. aeruginosa* isolates were 17% for ciprofloxacin (n=3,105), 16% for ceftazidime (n= 3,397) and 10% against amikacin (n= 3,313).
- Carbapenem rates of resistance for *P. aeruginosa* were at 20% against imipenem (n=3,417) and 17% against meropenem (n=3283).

Acinetobacter baumannii

- Rates of resistance of 2013 *A. baumannii* is reported at 42% for ampicillin-sulbactam (n= 1,651).
- Rates of resistance of 2013 *A. baumannii* isolates are at 39% each for both amikacin (n= 2,037) and gentamicin (n=1,846).
- Resistance of *A. baumannii* against imipenem have been increasing in the past 10 years with rates of resistance for 2013 reported as high as 40% (n=2,121).

Multidrug-resistant *Pseudomonas aeruginosa* & *Acinetobacter baumannii*

- *P. aeruginosa* MDR and possible XDR rates were at 22% and 13%, respectively. The 2013 reported *P. aeruginosa* MDR rate has increased when compared to data from 2012 which was at 21% while *P. aeruginosa* possible XDR rate decreased from 2012 rate which was at 17%.
- *Acinetobacter baumannii* MDR and possible XDR rates were at 56% and 34%, respectively. Comparatively, reported *A. baumannii* MDR and possible XDR rates for 2012 were 58% and 35%, respectively.

Recommendations

Based on the reported antimicrobial resistance surveillance data for 2013:

Respiratory Bacterial Pathogens

- Infections secondary to *Streptococcus pneumoniae* can still be covered with penicillin or one of the anti-pneumococcal macrolides, although there is a need to closely monitor the changing trends of resistance among pneumococci. Improved local data on serotype distribution will allow for better surveillance information especially to guide vaccination recommendations.

- Due to high resistance rate of *Haemophilus influenzae* to ampicillin, this is no longer recommended for empiric therapy for infections secondary to the pathogen. Recommended empiric treatment for suspected *H. influenzae* infections may consist of beta-lactam-beta-lactamase inhibitor combinations, extended spectrum oral cephalosporins and the newer macrolides.

Bacterial Enteric Pathogens

- Empiric treatment for suspected uncomplicated typhoid fever could still consist of either chloramphenicol or co-trimoxazole or amoxicillin/ampicillin. There are increasing reports of nalidixic acid resistance and ciprofloxacin non-susceptibility which may result to clinical treatment failures. Microbiological data is recommended to aid in pathogen directed therapy.

- Increasing rates of ciprofloxacin resistance should remind clinicians to use antibiotics judiciously in Salmonella gastroenteritis, as this is usually a self-limited disease.

- In view of the emerging resistance of *Shigellae* to the quinolones and limited data available, more vigilant surveillance of the resistance pattern of this organism should be pursued by encouraging clinicians to send specimens for culture.

- Tetracycline, chloramphenicol and co-trimoxazole remain good treatment options for cholera cases.

Sexually-transmitted Bacterial Pathogens

- Limited data is available on *Neisseria gonorrhoeae* in recent years, although based on reported isolates, ceftriaxone remains as empiric antibiotic of choice for gonococcal infections. More vigilant surveillance of the resistance patterns of this organism should be pursued by encouraging clinicians to send specimens for culture.

Gram-positive Cocci

- In view of the continued high rates of methicillin/oxacillin resistance among staphylococci there may be an indication to shift empiric treatment of suspected staphylococcal infections from oxacillin to alternative agents such as co-trimoxazole, doxycycline, clindamycin, linezolid or vancomycin.

Gram-negative Bacilli

- Hospitals should base their treatment recommendations for the *Enterobacteriaceae* on their institution's prevailing resistance patterns as these patterns have been found to be variable from hospital to hospital. High percentage of possible ESBL-producing isolates complicate treatment of serious infections caused by these organisms and may lead to increase use of carbapenems that may favor the further spread of the carbapenemase-producing *Enterobacteriaceae*. Prudent use of antimicrobials and comprehensive infection control measures serve as cornerstones of interventions aimed at preventing selection and transmission of resistant bacteria.

- Increasing resistance among the bacterial organisms *Pseudomonas aeruginosa* and *Acinetobacter baumannii* continues to be a concern as both organisms carry intrinsic resistance to a number of antimicrobial classes and acquisition of additional resistance severely limits the available treatment options. Prudent antimicrobial use, monitoring of resistance patterns & antimicrobial use along with improved standards of infection control are essential in addressing this clinical and public health concern.

3. HIGHLIGHTS OF THE 2013 ARSP DATA

3.1 ARSP 2013 Isolates

Resistance data for 37,629 isolates were reported and analyzed for the year 2013. This was a 39% increase when compared to the reported number of isolates for 2012.

Sentinel Site Data Contribution

The 2013 ARSP data came from the 21 sentinel site hospital laboratories of the program which represents 14 regions of the Philippines (Annex 1). Of the total number of isolates for 2013, 63% were from Luzon, 18% were from Visayas and 19% were from Mindanao.

The 8 Metro Manila sentinel sites contributed 46% of the total annual data (Figure 3.1). This is reflective of the 13% increase in the percentage contribution for the National Capital Region (NCR) when compared to the 2012 data. This 13% increase in percentage contribution of NCR is mostly secondary to the renewed participation of the Philippine General Hospital (PGH) after a six-year hiatus from the program. For the 2013 data alone, the site PGH was the largest contributor responsible for 19% of the the annual data (n= 7,093). Consequently, the percentage contribution of isolates from Luzon (excluding NCR), Visayas and Mindanao decreased by 6%, 3%, and 5%, respectively. These changes in regional contribution of the sites may affect the trends of resistance when comparing resistance rates throughout the years (Table 3.1).

Table 3.1 Percent contribution of data by geographical sites, ARSP 2013

Geographic Area	Percentage Data Contribution		Change in Percentage Data Contribution
	2012	2013	
NCR	33	46	13
Luzon (excluding NCR)	23	17	-6
Visayas	21	18	-3
Mindanao	24	19	-5

Specimen Types

The most common specimen types comprising the 2013 ARSP data were respiratory, blood, urine and cutaneous specimens. Other specimen types contributing to the 2013 data were: tissues, cerebrospinal fluid, other fluids, genital specimens and stool (Table 3.2).

Isolates (Table 3.3)

For 2013, *Klebsiella* species, followed by *Escherichia coli* and *Pseudomonas aeruginosa* were the most commonly isolated bacterial organisms from all specimen types reported.

Looking at isolates by specimen type, coagulase-negative staphylococci was the commonest invasive isolate (blood and cerebrospinal fluid). For blood isolates, after coagulase-negative staphylococci, *Klebsiella* species and *S. aureus* and the next most frequent isolates. For cerebrospinal fluid isolates, after coagulase-negative staphylococci, the gram-negative non-fermenters: *A. baumannii* and *P. aeruginosa* were the next most frequent isolates.

Among respiratory specimen isolates, *Klebsiella* species were the commonest, followed by the gram-negative non-fermenters: *A. baumannii* and *P. aeruginosa.* *E. coli* was the most common urine isolate followed by the other *Enterobacteriaceae-Klebsiella* species and *Enterobacter* species. *S. aureus* was the most commonly reported bacterial organisms for cutaneous and wound specimens. Other common bacterial organisms isolated from cutaneous specimens were *E. coli* and *Klebsiella* species. In contrast, *Vibrio cholerae* comprised the most commonly reported enteric pathogen from stool specimens. Other common stool isolates were *Salmonella* species and *Aeromonas* species.

Figure 3.1. Percent isolate contribution of each sentinel site, ARSP, Jan-Dec 2013

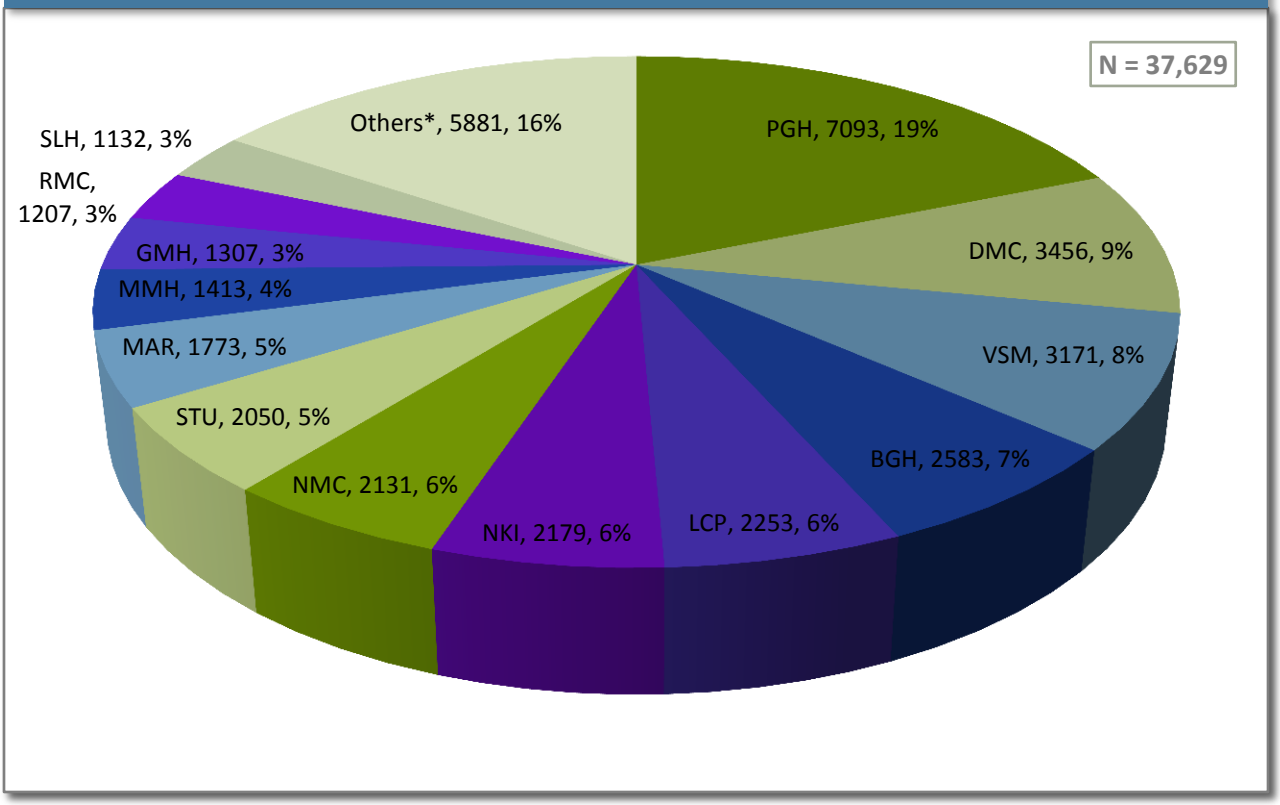


Table 3.2 Number of isolates by specimen type, ARSP, 2013

Specimen Type	Number of 2013 Isolates
1. Respiratory	11,759
2. Blood	8,139
3. Urine	7,044
4. Cutaneous/wound	6,281
5. Tissue	1,448
6. Fluid	1,224
7. Cerebrospinal fluid	570
8. Genital	401
9. Stool	155
10. Others	508

Table 3.3 Most common isolates by specimen type, all ARSP sentinel sites, Jan-Dec 2013

Respiratory Specimens	Blood
1. *Klebsiella* species 2. *P. aeruginosa* 3. *A. baumannii*	1. Coagulase-negative staphylococcus 2. *Klebsiella* species 3. *S. aureus*
Cutaneous / Wound	**Stool**
1. *S. aureus* 2. *E. coli* 3. *Klebsiella* species	1. *Vibrio cholerae* 2. *Salmonella* species 3. *Aeromonas* species
Cerebrospinal Fluid	**Urine**
1. Coagulase-negative staphylococci 2. *A. baumannii* 3. *P. aeruginosa*	1. *E. coli* 2. *Klebsiella* species 3. *Enterobacter* species

Figure 3.2 Distribution of isolates by source, ARSP, Jan-Dec 2013

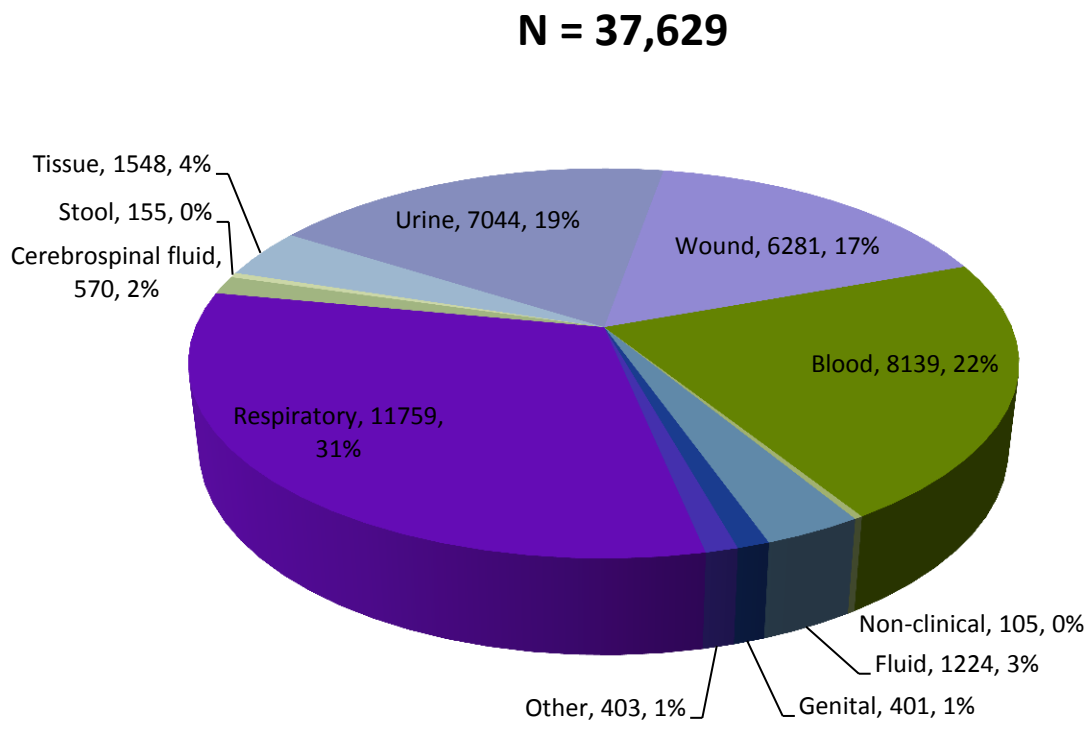
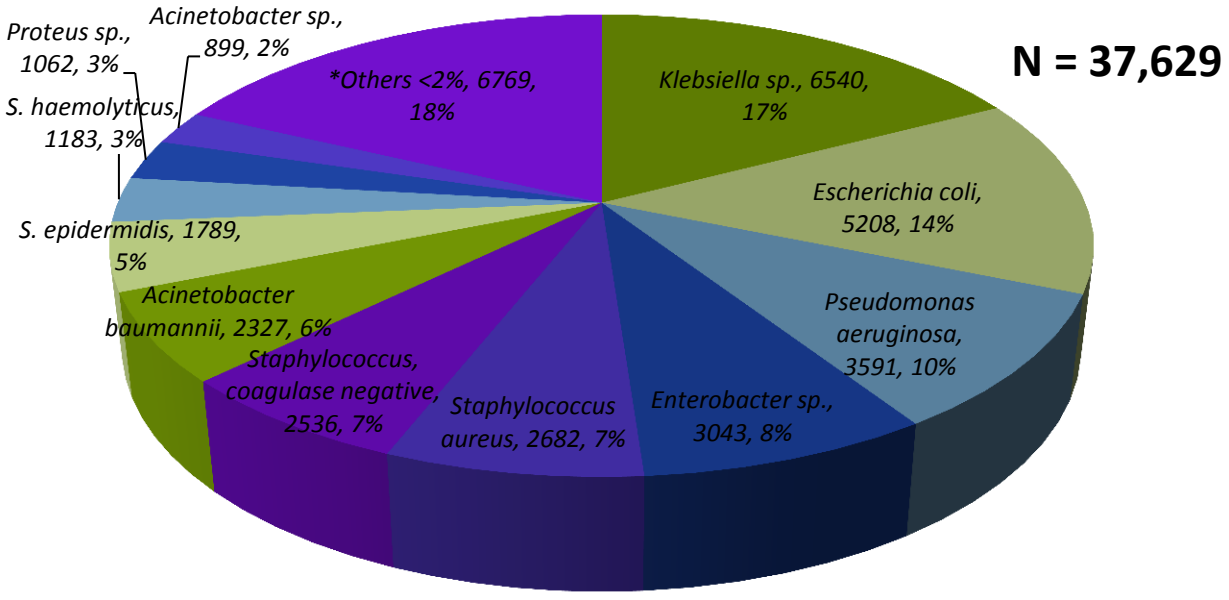


Figure 3.3 Distribution of isolates by organism, ARSP, Jan-Dec 2013



***Other isolates:** Burkholderia cepacia, Enterococcus sp., Pseudomonas sp., S. viridans, alpha -hem., E. faecalis, Citrobacter sp., S. pneumoniae, S. saprophyticus, S. maltophilia, Streptococcus, beta-haemolytic, Serratia sp., H. influenzae, Achromobacter sp., Salmonella sp., E. faecium, Bacillus sp., others <4%*

3.2 *Streptococcus pneumoniae*

Streptococcus pneumoniae is a gram-positive encapsulated diplococci with a polysaccharide capsule that commonly causes serious infections such as pneumonia and meningitis; and less serious but more common infections such as sinusitis and otitis media. About 90 distinct pneumococcal serotypes have been identified worldwide with a small number accounting for most diseases in infants. [1]

Isolates (Figure 3.4)

There were 274 reported *Streptococcus pneumoniae* isolates for 2013. This was 36% more than the 202 isolates reported for 2012. Major contributors of the 2013 *S. pneumoniae* data were PGH (69 isolates), VSM (27 isolates) and LCP, MAR and DMC (25 isolates each). Majority of the *S. pneumoniae* reported were respiratory isolates (56%) and invasive isolates (34%) from blood and CSF specimens.

Antimicrobial Resistance (Figures 3.5-3.6)

Beta-lactams

Since 2008, CLSI recommends use of distinct breakpoints for meningitis and for nonmeningitis pneumococcal infections for the antibiotics penicillins and certain cephalosporins (Table 3.4).

For CSF isolates, the recommendation is to report only the results for meningitis breakpoint since the more stringent breakpoint is warranted in recognition of the poor penetration of penicillin thru the blood brain barrier.

For non-CSF isolates, results for both meningitis and nonmeningitis breakpoints are reported since some patients with meningitis may have negative CSF cultures but present with pneumococcemia.[2]

Figure 3.4 Sentinel site contribution for *Streptococcus pneumoniae* data, ARSP, Jan-Dec 2013

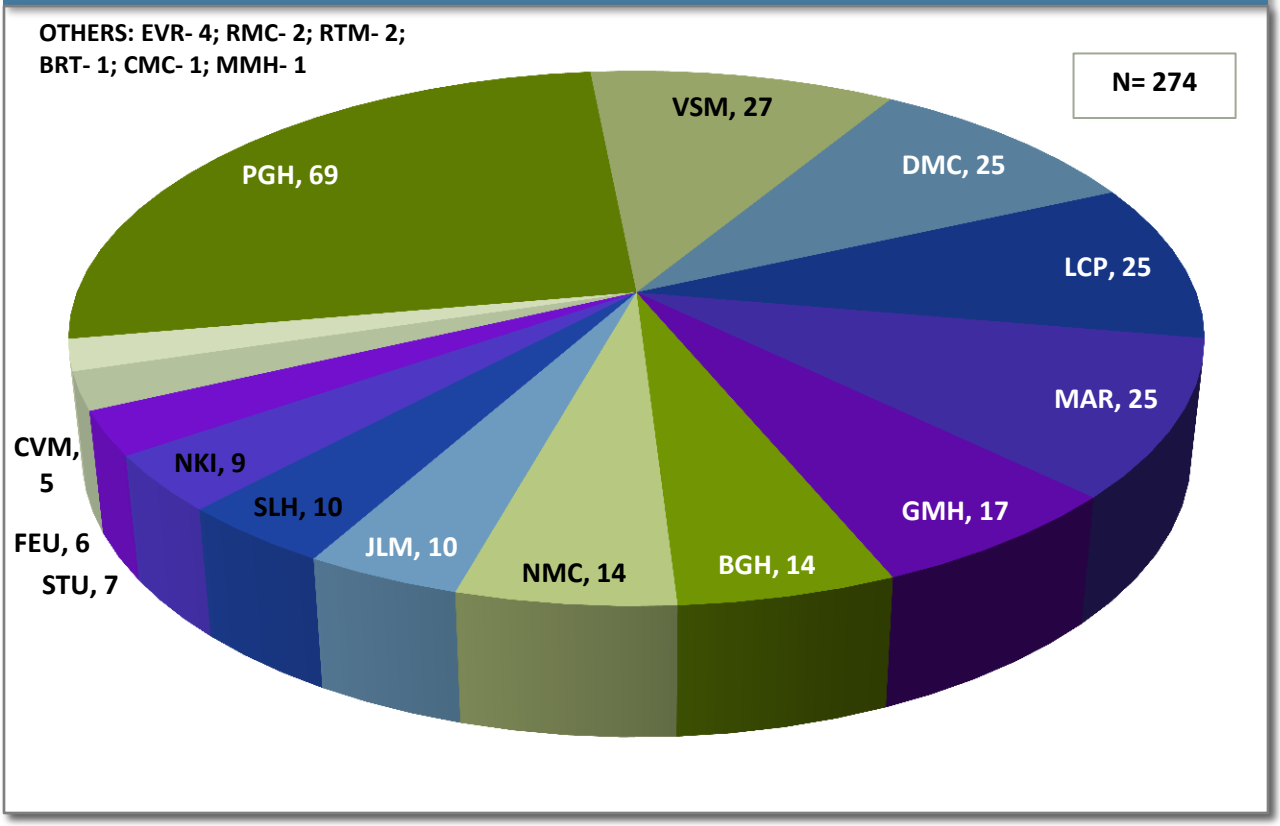


Table 3.4 CLSI penicillin, ceftriaxone and cefotaxime breakpoints *for S. pneumoniae*, 2013[2]

Parenteral Antibiotic	MIC (ug/ml)		
	S	I	R
Penicillin (nonmeningitis)	≤2	4	≥8
Penicillin (meningitis)	≤0.06	-	≥0.12
Ceftriaxone (nonmeningitis)	≤1	1	≥4
Ceftriaxone (meningitis)	≤0.5	1	≥2
Cefotaxime (nonmeningitis)	≤1	1	≥4
Cefotaxime (meningitis)	≤0.5	1	≥2

Legend: S= susceptible; I- intermediate; R- resistant

For 2013, penicillin resistance rate of *S. pneumoniae* isolates was at 5% (95% CI: 3.2-9.3) using meningeal and 0% (no reports) using nonmeningeal breakpoints.

Of the 14 penicillin-resistant *S. pneumoniae* (PRSP) isolates reported using the meningeal breakpoint, only 4 were invasive isolates (from blood specimens) with no cerebrospinal fluid PRSP isolate reported. All invasive isolates tested ceftriaxone and cefotaxime susceptible using meningitis and nonmeningitis breakpoints at the reference laboratory.

When testing nonmeningitis isolates, penicillin susceptibility can already predict susceptibility to most beta-lactams including ceftriaxone.[2] For 2013, only a small subset of isolates were tested against ceftriaxone (n=27) by MIC and, as in previous years, there were no reported ceftriaxone-resistant pneumococci.

Macrolides

Although increasing trends of resistance of *S. pneumoniae* against erythromycin has been reported for the past decade, 2013 reported resistance rate at 6% (95% CI: 3.3-9.4) do not significantly differ from the 2012 reported resistance rate of 4% (*p* value > 0.05).

Fluoroquinolones

For 2013, only a subset of 160 *S. pneumoniae* isolates had relevant AST results against levofloxacin. For 2013 we see the emergence of *S. pneumoniae* resistance against levofloxacin with rates reported at 2% (95% CI: 0.5-5.8). Unfortunately, none of these levofloxacin-resistant isolates were referred to the reference laboratory for confirmatory testing. In contrast, for 2012, there were no reports of levofloxacin-resistant *S. pneumoniae*.

Trimethoprim-sulfamethoxazole

For 2013, 20% (95% CI: 15.3-26.6) rates of resistance were reported against co-trimoxazole for *S. pneumoniae*. Increasing rates of resistance have been reported in the past 10 years against this agent although rates against that of 2012 did not significantly differ from 2013 rates (*p* value >0.05).

Chloramphenicol

For 2013, *S. pneumoniae* resistance rates against chloramphenicol were at 3% (95% CI: 1.6-6.8). When compared to 2012 rates, we note a significant decrease from the reported chloramphenicol resistance rate of 9% in the previous year (*p* value 0.032).

Figure 3.5 Percent resistance of *Streptococcus pneumoniae*, all ARSP sites, Jan-Dec 2013

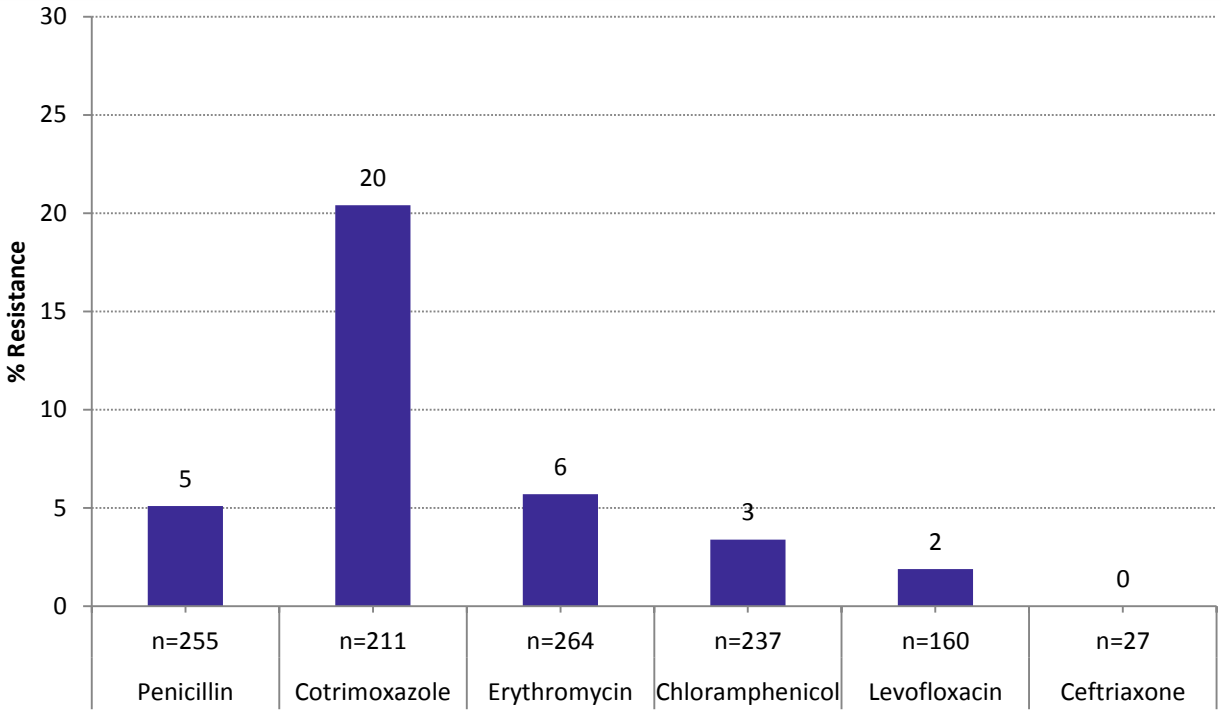


Figure 3.6 Yearly resistance rates of *Streptococcus pneumoniae*, all ARSP sites, 2004-2013

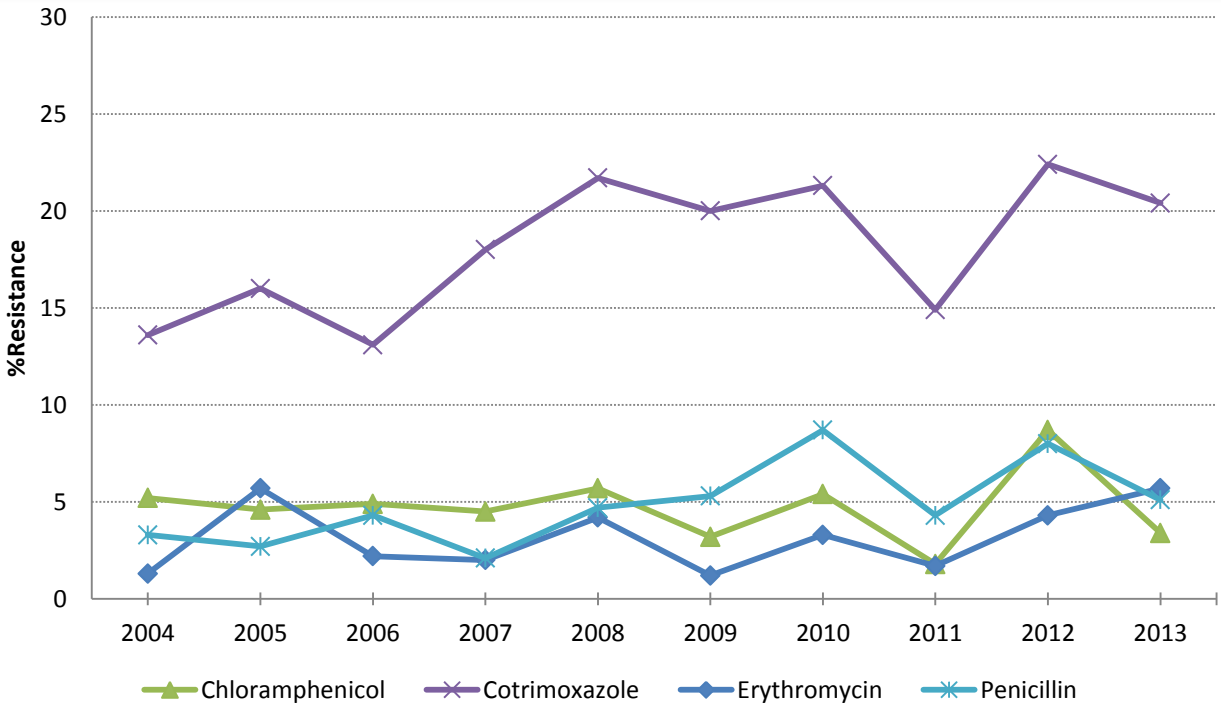


Table 3.5 Invasive *Streptococcus pneumoniae* serotypes, ARSP, 2013

S. pneumoniae Serotypes	0-4 years old	5-19 years old	20-64 years old	≥ 65 years old	All Isolates
Serotype 1	1	1	5		7
Serotype 5	1	1	1		3
Serotype 2	2				2
Serotype 14	2				2
Serotype 23	2				2
Serotype 18		1			1
Serotype 3			1		1
Serotype 4	1				1
Serotype 6	1				1
Serotype 19		1			1
Serotype 20			1		1
Serotype 32				1	1
Serotype 33	1				1
Serotype 34			1		1

Invasive *S. pneumoniae* Serotypes (Table 3.5)

For 2013, there were 25 invasive pneumococci isolated from normally sterile sites sent to the national reference laboratory for confirmatory testing and serotyping. Of these 25 isolates, 18 were from blood specimens while the rest were from normally sterile fluids (pleural and synovial fluid).

The most common serotype from these invasive isolates was serotype 1 (7 isolates). This is in contrast to the 2012 data that reported serotype 5 as the most frequently identified serotype. By age group, serotype 1 was the most common invasive *S. pneumoniae* serotype for adults (20-64 years old).

In contrast, serotypes for the 0-4 years old age group had a variety of reports which included serotypes 2, 14 and 23 at 2 isolates each; and serotypes 1, 4 5 and 33 at 1 isolate each.

Looking at the susceptibility patterns of the referred invasive *Streptococcus pneumoniae* serotypes, there were 4 isolates that tested as penicillin-resistant using meningitis breakpoints. These were serotypes 1, 14 and 32. There were also 3 isolates of serotypes 6, 14 and 19 that tested resistant against co-trimoxazole. None of the invasive pneumococci isolates serotyped tested resistant against erythromycin, chloramphenicol and ceftriaxone.

3.3 *Haemophilus influenzae*

Haemophilus influenzae are small gram-negative coccobacilli found mainly in the respiratory tract and are common causes of otitis media, sinusitis and community-acquired pneumonia.[1]

Isolates

There were 198 reported *H. influenzae* isolates for 2013 (Figure 3.7). This was 27% more than the number reported for 2012. Majority of the 2013 *H. influenzae* isolates were from respiratory specimens (91%) while there were 9 invasive isolates (7 from blood and 2 from cerebrospinal fluid specimens).

Antimicrobial Resistance

(Figures 3.8-3.9)

Beta-lactams

For 2013, 17% (95% CI: 12.2-23.6) of the *H. influenzae* isolates tested resistant against ampicillin (n= 186). Although increasing trends in rates of resistance is noted in the past 10 years, rates for 2013 do not significantly differ from that of 2012 (*p* value > 0.05). In contrast, resistance rates against ampicillin-sulbactam is at 7% (95% CI: 3.8-11.4; n= 195). Resistance to this antimicrobial has been increasing in recent years but the 2013 rates do not significantly differ from the reported resistance rate in 2012 (*p* value > 0.05). All 10 ampicillin-resistant *H. influenzae* isolates referred to the reference laboratory tested positive for beta-lactamase production.

Chloramphenicol

Rates of resistance for 2013 against chloramphenicol is at 7% (95% CI: 3.4-12.1; n= 151). A decreasing trend of resistance is noticeable for the past 10 years although when compared to 2012 data, resistance rates do not differ significantly (*p* value > 0.05).

Co-trimoxazole

Co-trimoxazole resistance rate for 2013 is relatively higher than the other antimicrobials reported at 34% (95% CI: 27.4-41.9; n= 175). Increasing resistance rate against this antibiotic is seen in the past decade although 2013 rates do not differ significantly from that reported for 2012 (*p* value > 0.05).

Figure 3.7 Isolate contribution for *H. influenzae* data, ARSP, Jan-Dec 2013

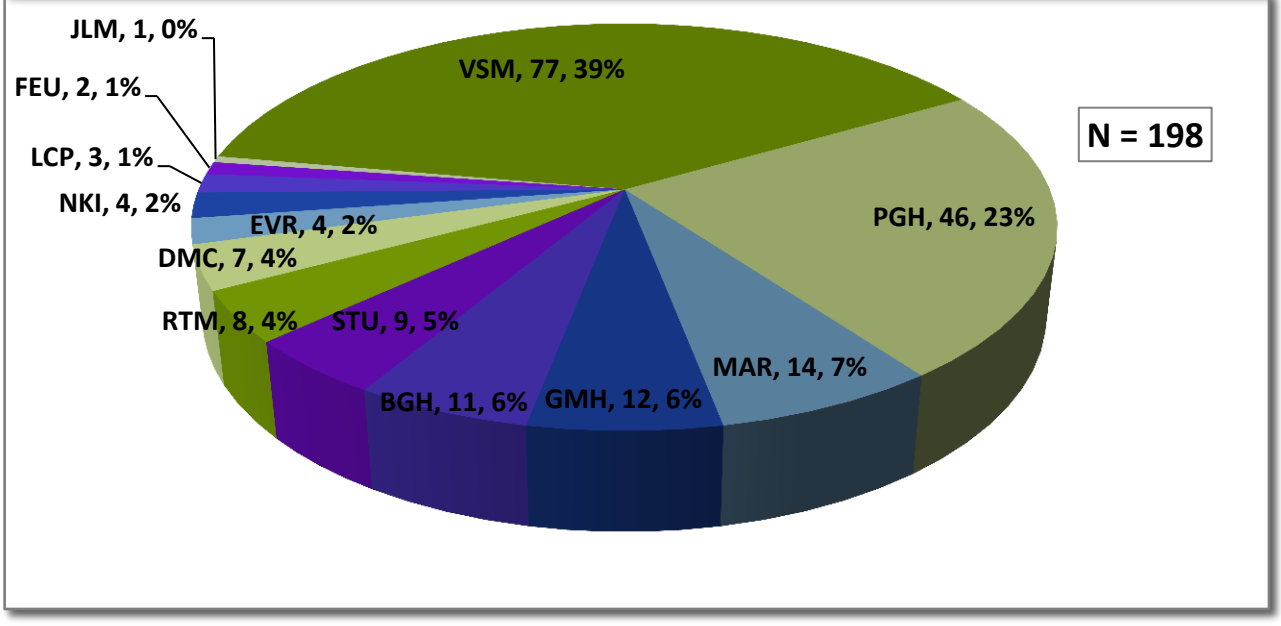


Figure 3.8 Percent resistance of *H. influenzae*, all ARSP sites, Jan-Dec 2013

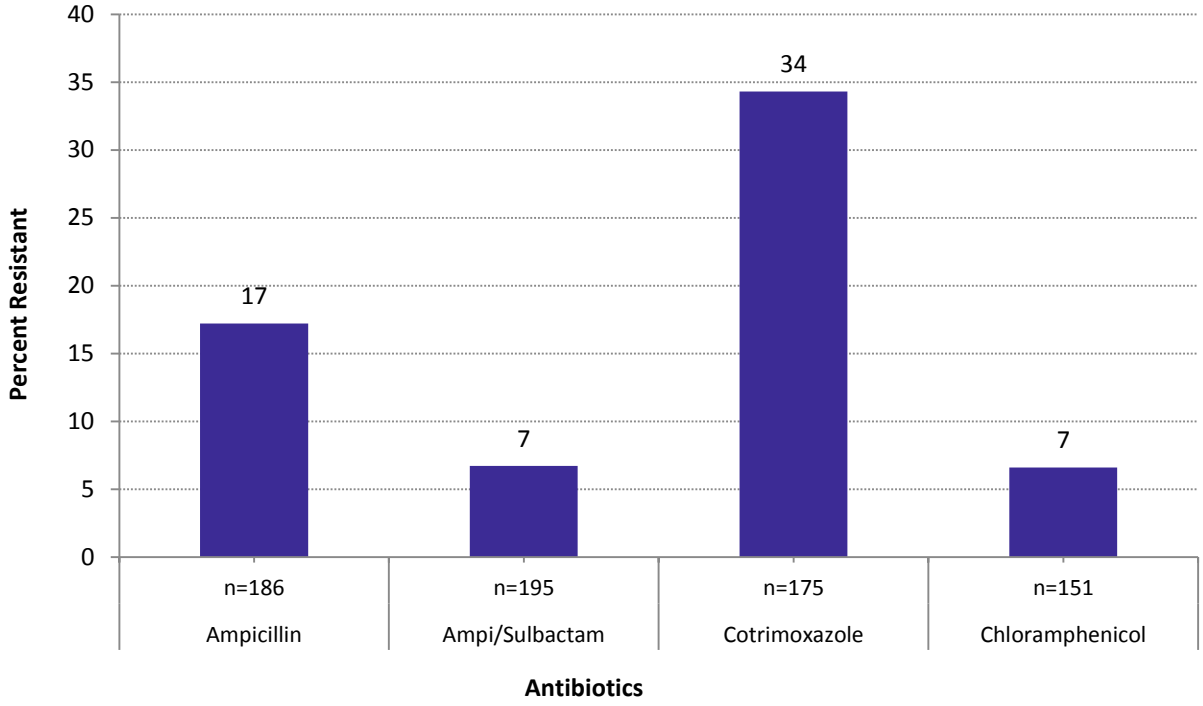
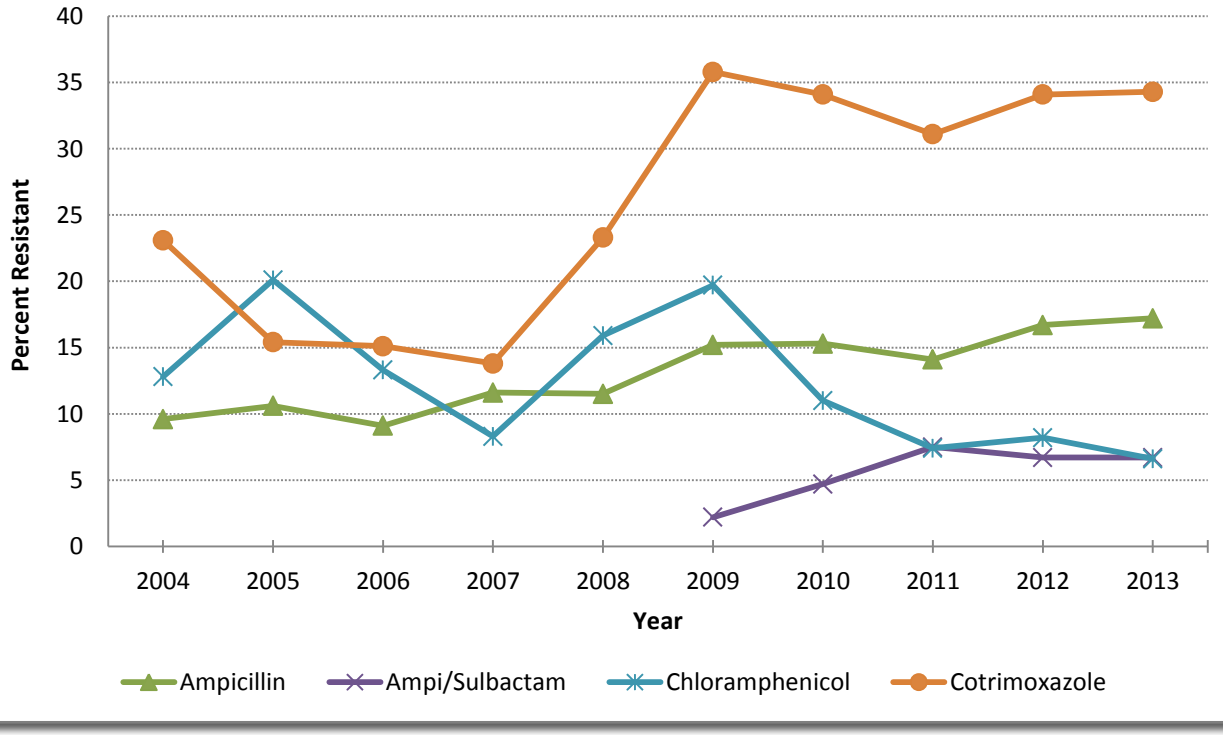


Figure 3.9 Yearly resistance rates of *Haemophilus influenzae*, all ARSP sites, 2004-2013



3.4 *Salmonella* Typhi

Salmonella Typhi are gram-negative rods acquired only from human sources shedding to water, food or waste. This organism causes the systemic infection enteric or typhoid fever.[1]

Isolates (Figure 3.10)

There were 106 *Salmonella* Typhi isolates reported and analyzed for 2013. This is only 80% of the total number of reported *Salmonella* Typhi isolates for the 2012 report. The largest sentinel site contributors for the 2013 *Salmonella* Typhi data were: VSM (19 isolates), CMC (18 isolates) and EVR (13 isolates).

Most of the *Salmonella* Typhi isolates were from blood specimens (98%). Others were isolated from stool, urine, cutaneous and other fluids. For 2013, there were 84 *Salmonella* Typhi isolates sent for confirmatory testing at the reference laboratory (Table 3.5). Of these, 68% were isolated from the pediatric age group.

Antimicrobial Resistance

(Figures 3.11-2.13)

Ampicillin

Salmonella Typhi isolates have remained susceptible to 1st line agent ampicillin with rate of resistance for 2013 at 2% (95% CI: 0.3-7.5; n= 103). *Salmonella* Typhi ampicillin resistance rate has remained at 2% or less for the past 10 years, with no significant difference between the reported 2012 and 2013 rates (*p* value > 0.05).

Co-trimoxazole

Salmonella Typhi isolates have remained susceptible to 1st line agent co-trimoxazole with rates of resistance for 2013 at 1% (95% CI: 0.1-6.1; n= 104). *Salmonella* Typhi ampicillin resistance rate has remained less than 1% for the past 10 years, with no significant difference between the reported 2012 and 2013 rates (*p* value > 0.05).

Chloramphenicol

Salmonella Typhi isolates have remained susceptible to 1st line agent chloramphenicol with no reported resistant isolate for 2013. *Salmonella* Typhi Resistance rates against this antimicrobial has remained below 1% for for the past 10 years, with no significant difference between reported 2012 and 2013 rates (*p* value > 0.05).

Quinolones

For 2012 and 2013, there were no reports of ciprofloxacin-resistant *Salmonella* Typhi.

The 2013 *Salmonella* Typhi rates of resistance against nalidixic acid is reported to be at 4% (95% CI: 1.3-10.7; n= 98). These rates of resistance against nalidixic acid have slowly been increasing for the past decade when compared to the baseline rate of 2.5% as reported 10 years ago.

For 2013, there were a total of 4 reported nalidixic acid-resistant *Salmonella* Typhi isolates. All of these were isolated from pediatric patients. Only 3 of these nalidixic-acid resistant *Salmonella* Typhi isolates were referred to the reference laboratory and were confirmed, by MIC testing, as nalidixic acid-resistant and ciprofloxacin-intermediate. Nalidixic acid resistance amongst *Salmonella* Typhi isolates may portend poor clinical response with treatment using fluoroquinolones.

Ceftriaxone

For 2013, rates of resistance for *Salmonella* Typhi against ceftriaxone was at 1% (n=106). This single reported ceftriaxone-resistant isolate was confirmed at the reference laboratory by MIC testing as ceftriaxone-resistant *Salmonella* Typhi. This drug-resistant organism was isolated from a stool specimen from a pediatric patient in a sentinel site in Mindanao.

This isolate likewise tested resistant against ampicillin and cefotaxime but remained susceptible to chloramphenicol, co-trimoxazole, nalidixic acid and ciprofloxacin. Phenotypic and genotypic analysis confirmed the production of the CTX-M gene for ESBL in this isolate.[3,4]

Figure 3.10 Percent sentinel site contribution for *Salmonella* Typhi, ARSP, Jan-Dec 2013

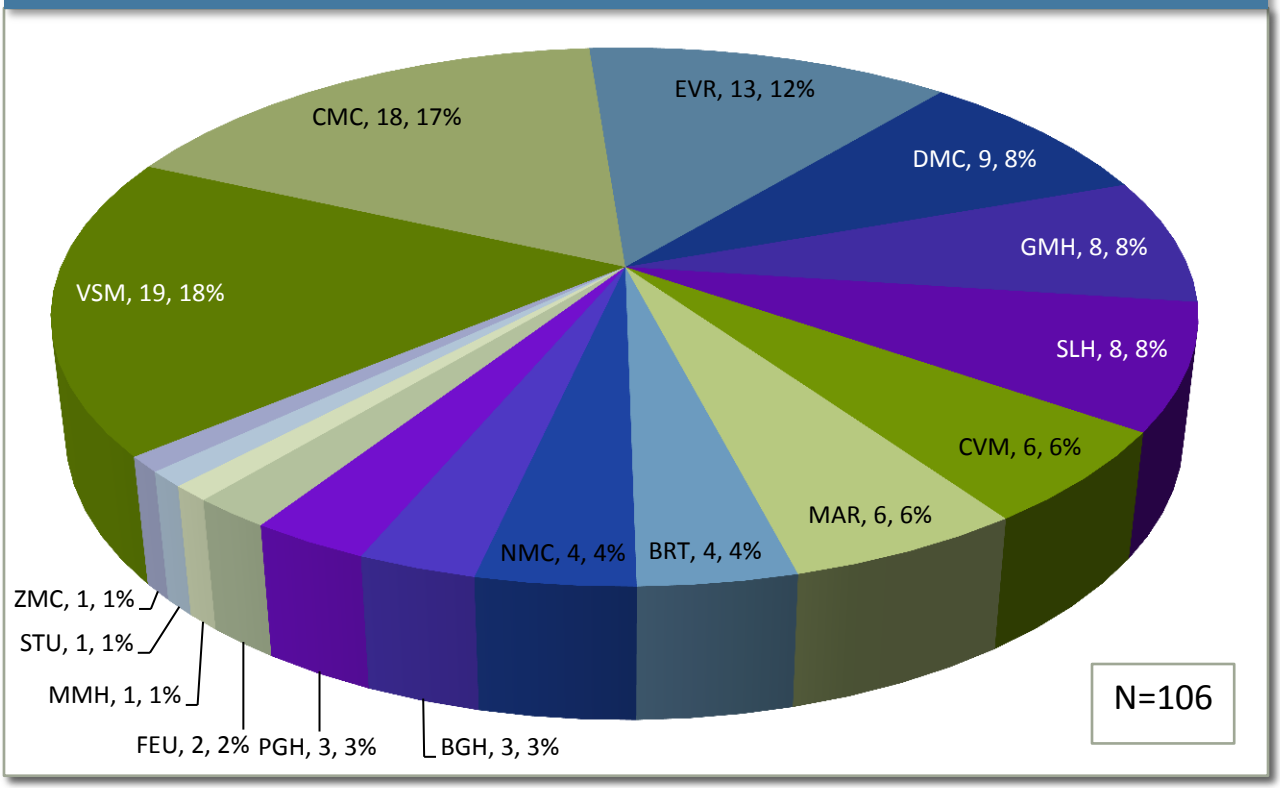


Figure 3.11 Percent resistance of *Salmonella* Typhi, all ARSP sites, Jan-Dec 2013

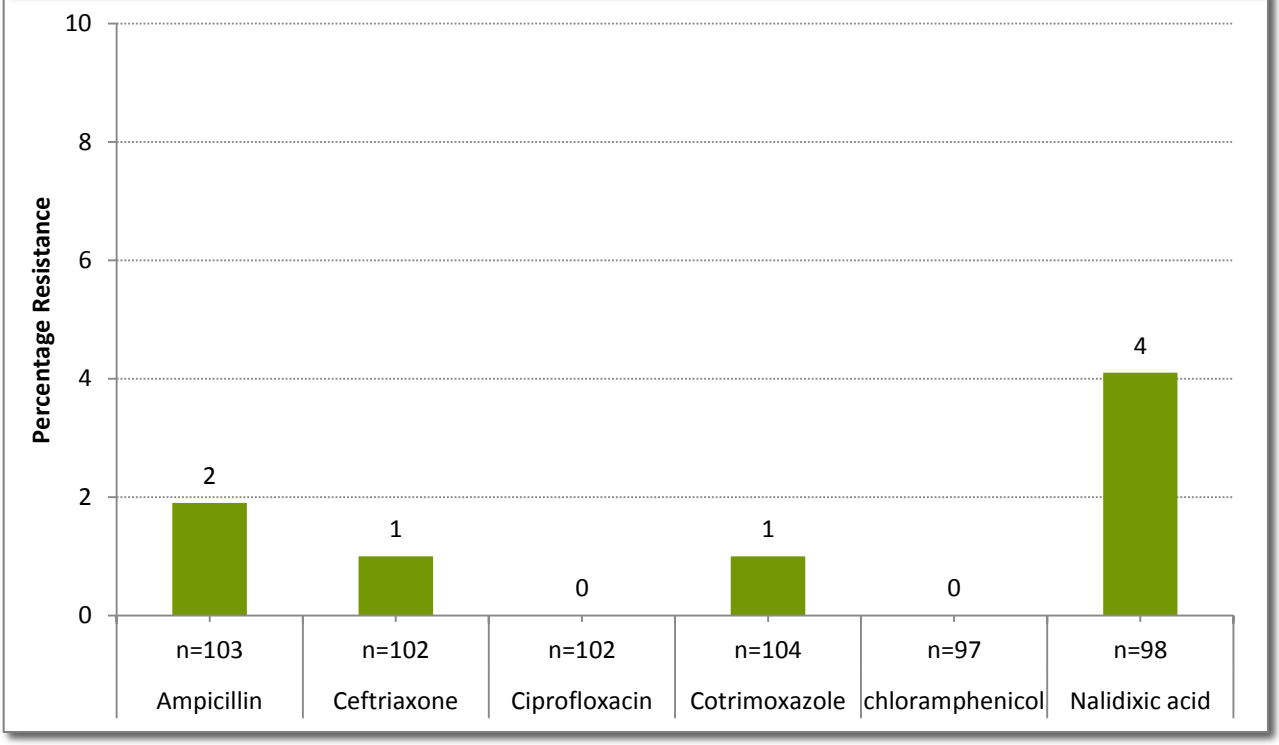


Figure 3.12 Yearly ampicillin, chloramphenicol & co-trimoxazole resistance rates of *Salmonella* Typhi, all ARSP sites, 2004-2013

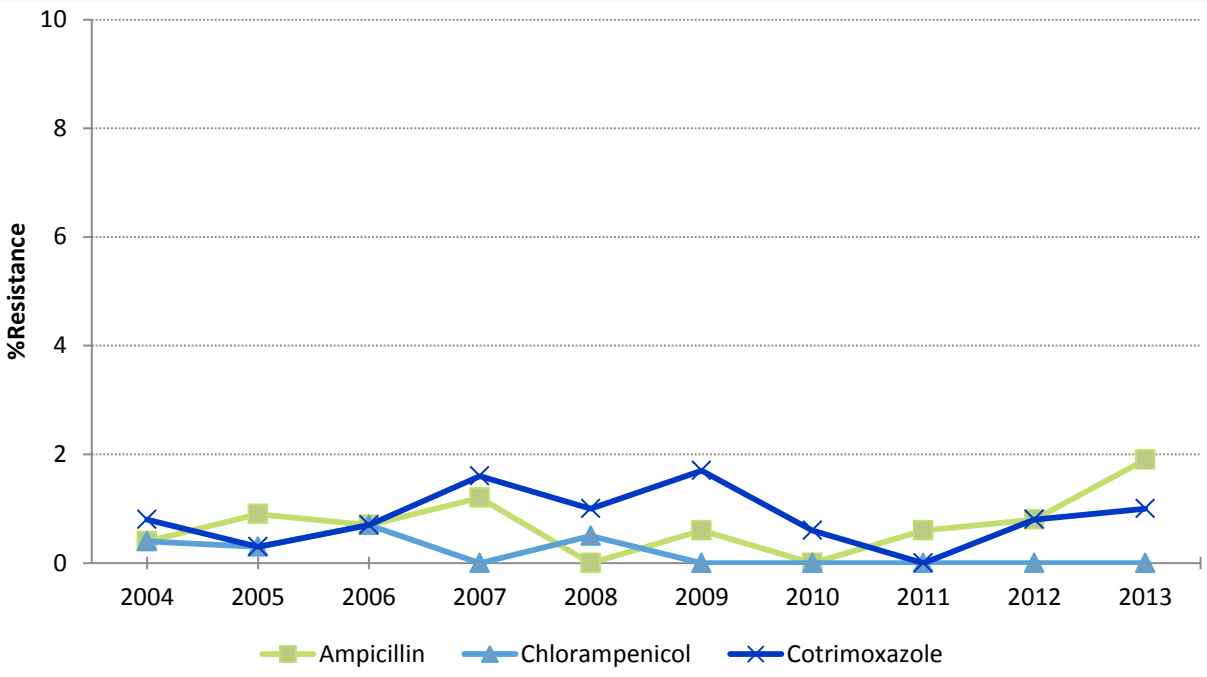
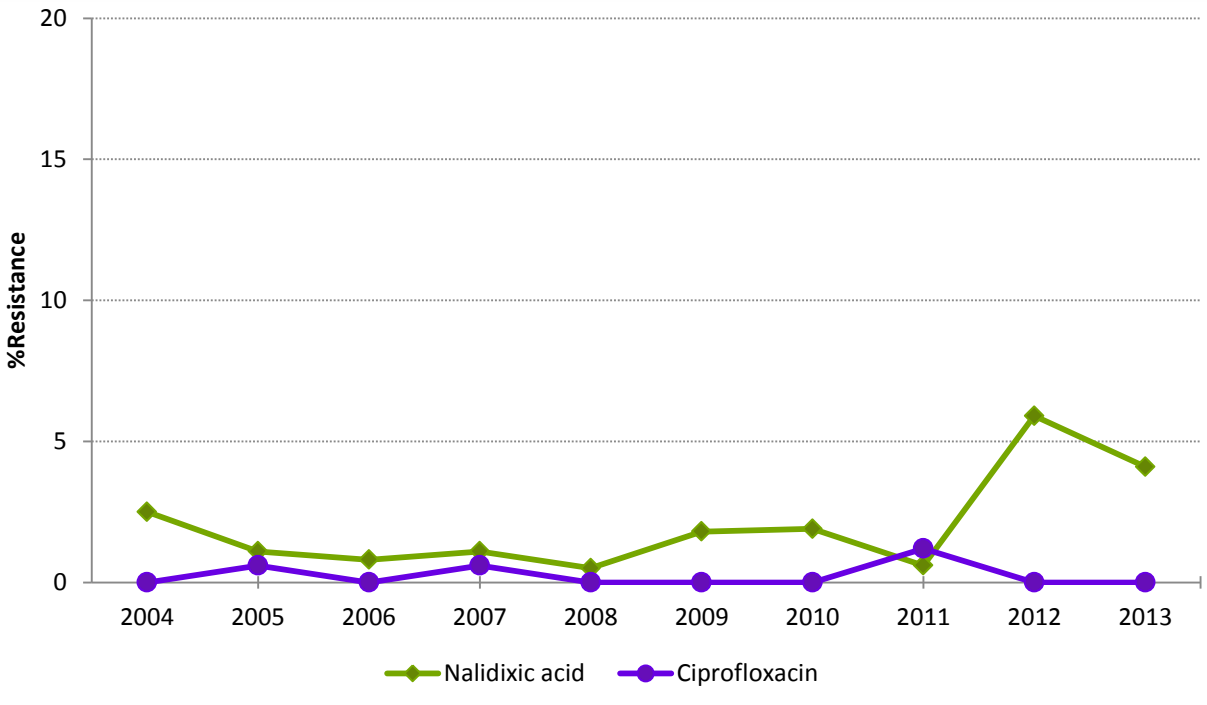


Figure 3.13 Yearly nalidixic acid and ciprofloxacin resistance rates of *Salmonella* Typhi, all ARSP sites, 2004-2013



3.5 Nontyphoid *Salmonella* species

Nontyphoid *Salmonella* (NTS) species are gram-negative rods that are a major bacterial cause of foodborne infections from diverse sources.[1]

Isolates

There were 158 reported nontyphoid *Salmonella* spp. for 2013. This is 25% more than the 126 reported nontyphoid *Salmonella* isolates for 2012. Most of the isolates were from blood specimens (35%). Other specimens from which nontyphoid *Salmonella* species were isolated from were: cutaneous, stool, respiratory, urine, tissues and other fluid specimens.

Antimicrobial Resistance (Figures 3.14-3.16)

Ampicillin, Co-trimoxazole & Chloramphenicol

Nontyphoid Salmonella isolates have higher resistance rates to ampicillin, co-trimoxazole and chloramphenicol than against *S*. Typhi, with rates of resistance for 2013 at 56% (95% CI: 46.9-65.3; n= 119), 34% (95% CI: 25.1-44.1; n= 103) and 16% (95% CI: 0.4-25.9; n=87), respectively. These 2013 resistance rates have increased when compared to 2012 data, with significant increases for ampicillin and chloramphenicol (p value< 0.05); and a non-significant increase for co-trimoxazole (p value 0.144).

Quinolones

For 2013 we continue to see increasing rates of resistance for nontyphoid *Salmonella* species against ciprofloxacin with 2013 rates at 18% (95% CI: 11.7-27.5; n= 103) from a baseline rate of 10% as reported 10 years ago. Unfortunately, none of these ciprofloxacin-resistant nontyphoid *Salmonella* species isolates were sent for confirmatory testing at the reference laboratory.

Ceftriaxone

For 2013, 18% of reported nontyphoid *Salmonella* species isolates were resistant to ceftriaxone (95% CI: 12-27; n= 114). Of these 21 reported ceftriaxone-resistant isolates, only 1 was sent for confirmatory testing at the national reference laboratory. This ceftriaxone-resistant isolate was a blood isolate from a pediatric patient from one of the sentinel sites in Mindanao. This isolate was confirmed by MIC testing at the reference laboratory as ampicillin and ceftriaxone-resistant but susceptible to chloramphenicol, co-trimoxazole and ciprofloxacin. Further phenotypic analysis using disc approximation and E-test showed that this isolate was positive for production of the extended-beta-lactamase (ESBL) enzyme. Further characterization by serotyping showed the isolate to be of the serovar *Salmonella* Stanley.

Figure 3.14 Percent resistance for nontyphoid *Salmonella*, all ARSP sites, Jan-Dec 2013

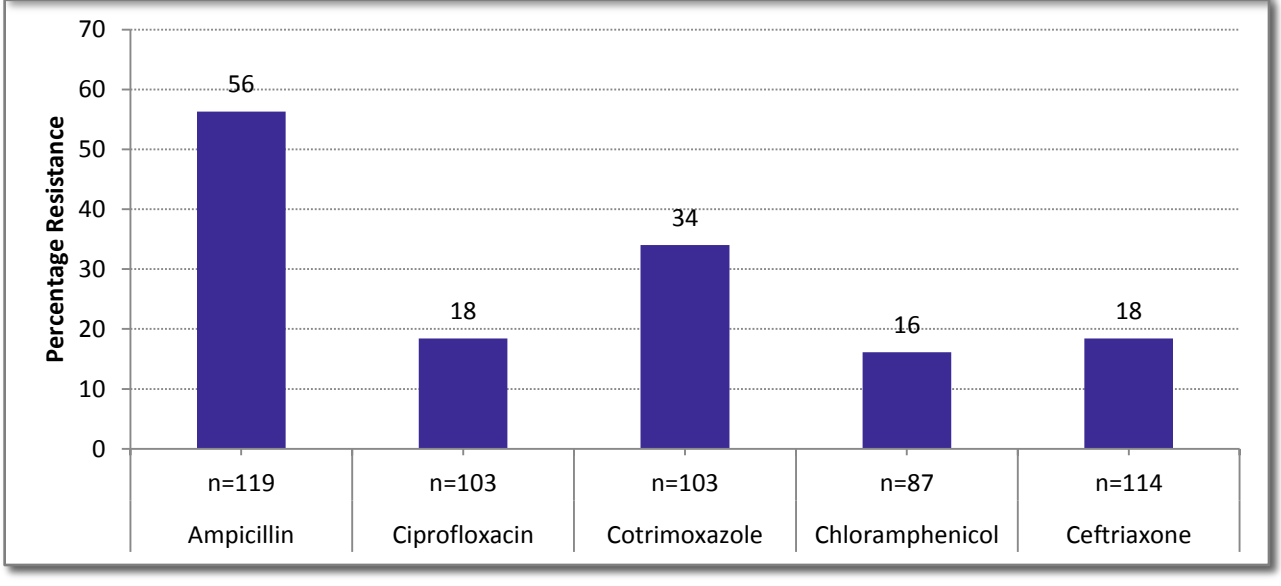


Figure 3.15 Yearly ampicillin, chloramphenicol & co-trimoxazole resistance rates of Nontyphoid Salmonella spp., all ARSP sites, 2004-2013

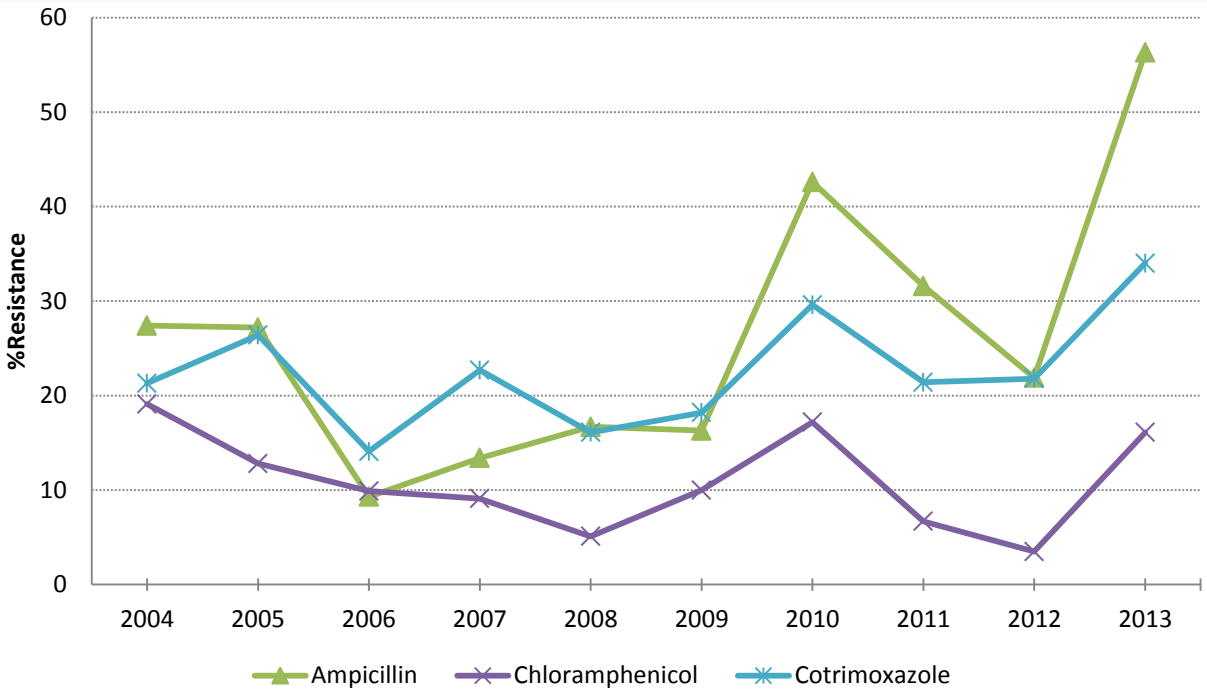


Figure 3.16 Yearly ciprofloxacin & ceftriaxone resistance rates of Nontyphoid Salmonella spp., all ARSP sites, 2004-2013

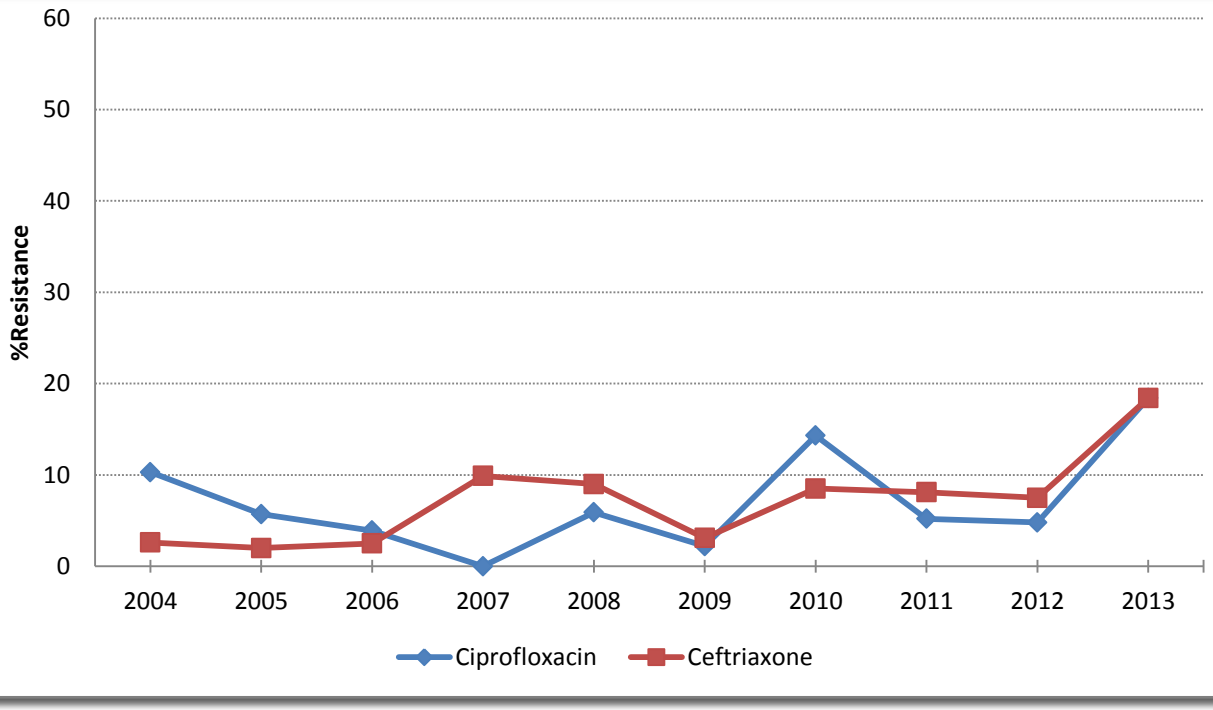


Table 3.6 Salmonellae serotypes, all ARSP sites, Jan-Dec 2013	
Salmonella Serotype	**Number of Isolates**
Salmonella Typhi	84 isolates
Salmonella Enteritidis	12 isolates
Salmonella Typhimurium	5 isolates
Salmonella Heidelberg	3 isolates
Salmonella Anatum	2 isolates
Salmonella Stanley	2 isolates
Salmonella Weltevreden	2 isolates
Salmonella 0:4,12:i:-	2 isolates
Salmonella Choleraesuis var Kurzendorf	1 isolate
Salmonella Derby	1 isolate
Salmonella Mgulani	1 isolate

Nontyphoid Salmonella species Serotypes

There were 31 isolates confirmed as nontyphoid Salmonella spp. at the reference laboratory for 2013 (Table 3.6). The most common serovar identified were *Salmonella* Enteritidis, *Salmonella* Typhimurium and *Salmonella* Heidelberg. Similarly, for 2012, both *Salmonella* Enteritidis and *Salmonella* Typhimurium were the most commonly isolated nontyphoid *Salmonella* species.

Susceptibility patterns of these isolates were analyzed by serovars. Ampicillin resistance was noted in *Salmonella* 0:4:12:i:- (2 out of 2 isolates); *Salmonella* Anatum (2 out of 2 isolates,); *Salmonella* Choleraesuis (1 out 1 isolate); *Salmonella* Derby (1 out of 1 isolate); *Salmonella* Stanley (1 out of 2 isolates) and *Salmonella* Typhimurium (4 out of 5 isolates).

Chloramphenicol resistance was identified in *Salmonella* Derby (1 out of 1 isolate) and *Salmonella* Typhimurium (2 out of 5 isolates).

Co-trimoxazole resistance was identified in the following serovars: *Salmonella* Anatum (2 out of the 2 isolates); *Salmonella* Choleraesuis (1 out of 1 isolate); *Salmonella* Derby (1 out of 1 isolate) and *Salmonella* Heidelberg (3 out of 3 isolates). Serovars identified as ciprofloxacin-resistant were: *Salmonella* Anatum (2 out of 2 isolates) and *Salmonella* Choleraesuis var Kurzendorf (1 out of 1 isolate).

For 2013, we report the *Salmonella* Stanley isolate that tested as ampicillin and ceftriaxone resistant and was positive for production the extended-spectrum beta-lactamase (ESBL) enzyme.

3.6 *Shigella* species

Figure 3.17 Percent resistance of *Shigella* species, all ARSP sites, Jan-Dec 2011- 2013

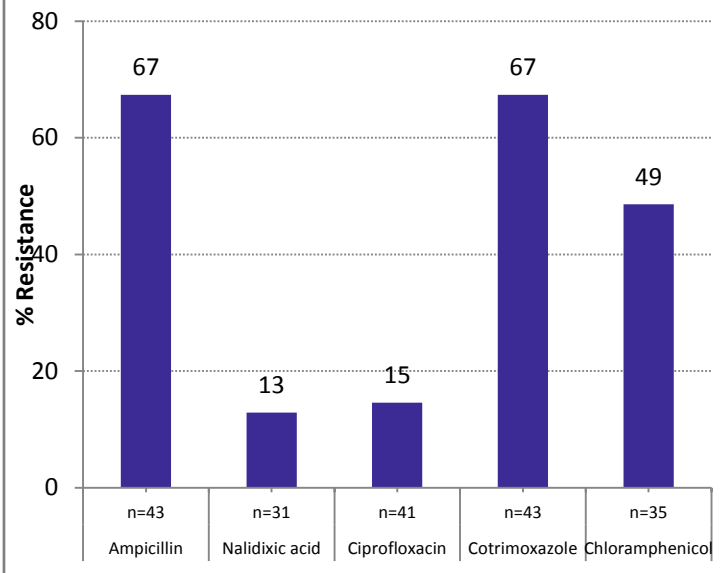
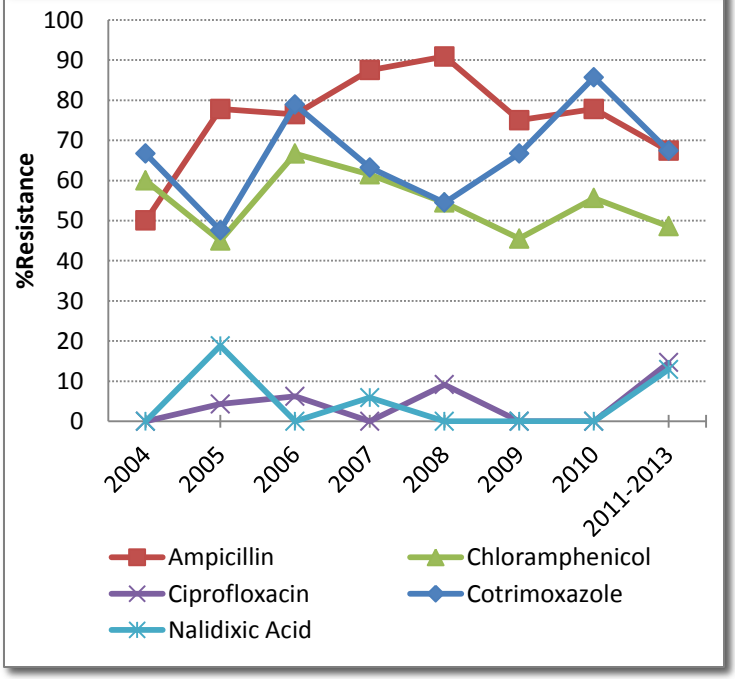


Figure 3.18 Trends of resistance of *Shigella* species, all ARSP sites, 2004-2013



Shigella species are gram-negative bacilli that cause a spectrum of illness from water diarrhea to dysentery or blood diarrhea.[1]

Isolates

For 2013, there were only 12 Shigella species isolates reported. Most were stool isolates (67%). Half of the isolates came from the pediatric age group. Only 2 isolates were referred to the reference laboratory and these were subsequently confirmed as *Shigella flexneri*.

Antimicrobial Resistance (Figures 3.17-3.18)

As there were very few *Shigella* isolates reported for 2013, we combined the results of isolates from 2011 to 2013 in order to obtain a reasonable statistical estimate of the cumulative percentage resistance for *Shigella* species.

Ampicillin, Chloramphenicol and Co-trimoxazole

Rates of resistance to the previous first line agents against Shigellosis: ampicillin, chloramphenicol and co-trimoxazole have been more than 40% for the past 10 years with cumulative 2011-2013 rates at 67% (96% CI: 51.3-80.4; n= 43), 49% (95% CI: 31.7-65.8; n= 35), and 67% (95% CI: 51.3-80.4; n= 43), respectively.

Quinolones

Comparatively, emerging resistance to quinolones are a more recent event. Reported cumulative rates of resistance of Shigella species for 2011-2013 against nalidixic acid is at 13% (95% CI: 4.2-30.8; n= 31) and ciprofloxacin at 15% (95% CI: 6.1-29.8; n= 41).

3.7 *Vibrio cholerae*

Vibrio cholerae is a gram-negative bacillus that has been known to cause epidemics of the secretory diarrheal syndrome, cholera.[1]

Isolates

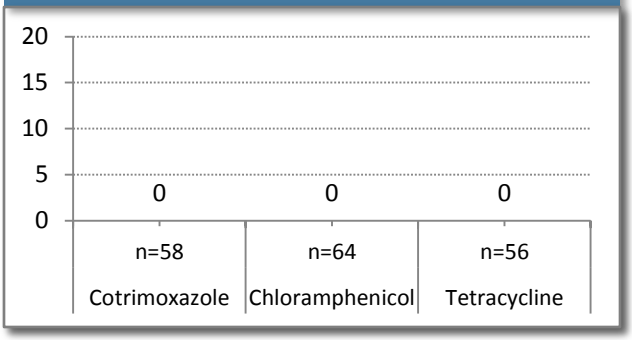
There were only 29 isolates of *Vibrio cholerae* reported for 2013. All were isolated from stool specimens. The sentinel site CMC in Mindanao contributed 83% (24 out of 29 isolates) of the *V. cholerae* 2013 data. Of the 27 isolates referred to the reference laboratory for confirmatory testing, all were identified as *Vibrio cholerae* serogroup 01, serotype Ogawa and biotype El Tor.

Antimicrobial Resistance

(Figure 3.19-3.20)

Since few isolates were reported for 2013, we combined the results of isolates from 2012 and 2013 to arrive at a reasonable statistical estimate of cumulative percentage resistance for *V. cholerae*.

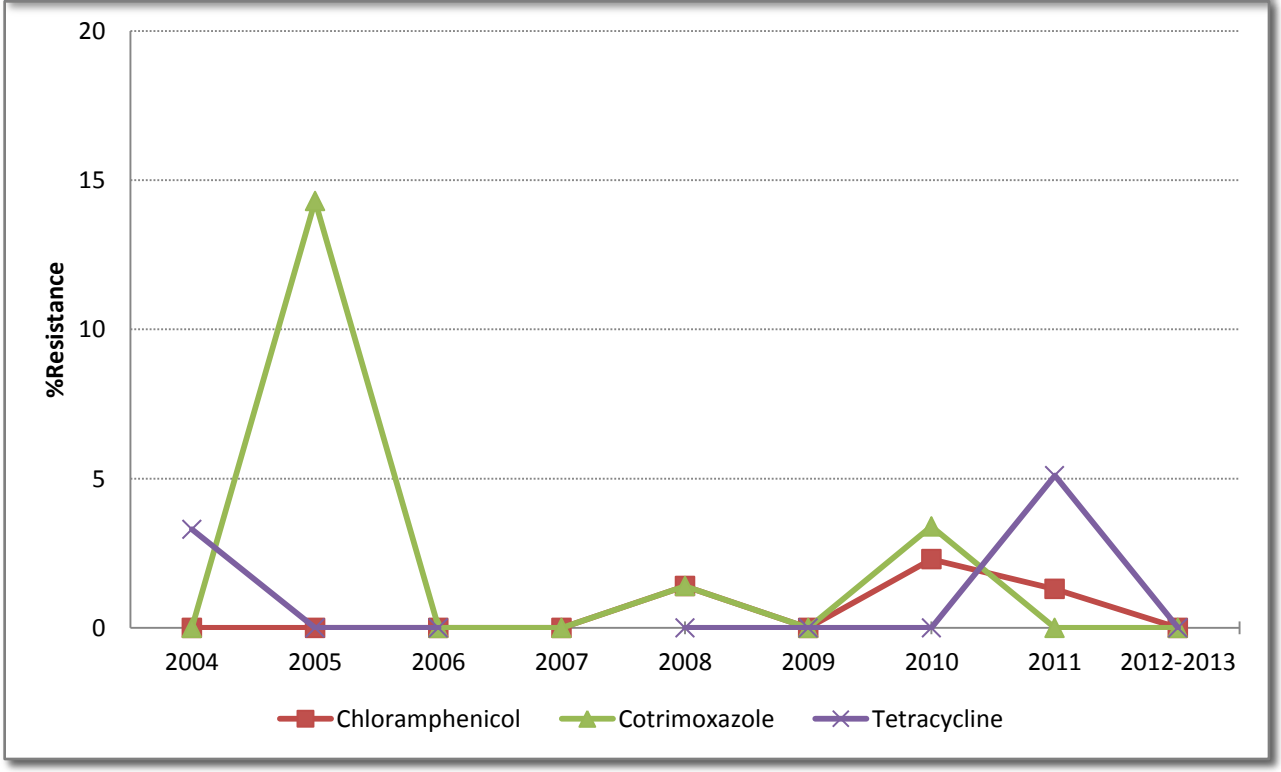
Figure 3.19 Percent resistance *V. cholerae*, all ARSP sites, Jan-Dec 2012-2013



Co-trimoxazole, Chloramphenicol & Tetracycline

For 2012-2013, as in the past years, *V. cholerae* isolates have remained susceptible to the 1st line agents namely co-trimoxazole, chloramphenicol and tetracycline with no reported resistant isolate for the past 2 years. These rates have remained stable for the past 5 years, with reported rates against these antibiotics at 5% or less.

Figure 3.20 Trends of resistance of *V. cholerae*, all ARSP sites, 2004-2013



3.8 *Neisseria gonorrhoeae*

Neisseria gonorrhoeae is a gram-negative diplococci that is one of the commonest sexually transmitted pathogens. It causes a spectrum of illness ranging form asymptomatic urethritis to a disseminated infection with possible complications associated with reproductive health.[1]

Isolates (Figure 3.21)

There were only 24 isolates of *N. gonorrhoeae* reported for 2013. Most of the isolates were from VSM (10 isolates) and RTM (4 isolates). All of the reported isolates for 2013 were from genital area specimens.

Antimicrobial Resistance

(Figures 3.22-3.23)

As there were very few gonococcal isolates reported for 2013, we combined the results of isolates from 2012 to 2013 in order to obtain a reasonable statistical estimate of the cumulative percentage resistance for *N. gonorrhoeae*.

Penicillin & Tetracycline

Rates of resistance of *N. gonorrhoeae* against penicillin has been at least 80% for the past decade with 2012-2013 rates at 80% (95% CI: 65.6-90.1; n= 46). Rates of resistance for gonococci against tetracycline has been at least 44% for the past decade with 2012-2013 rates at 55% (95% CI: 40.2-69.5; n= 47).

Ciprofloxacin

For the past decade, *N. gonorrhoeae* rates of resistance against ciprofloxacin has been at least 50% with 2012-2013 rate at 74% (95% CI: 58.6-85.2; n= 46). These rates do not differ significantly from those reported the previous year at 82% (*p* value > 0.05).

Spectinomycin

There have been no reported spectinomycin resistant gonococci for the past 5 years (2012-2013 n= 32).

3rd Generation Cephalosporins

There remains to be no reported ceftriaxone (2012-2013 n= 46) and cefixime (2012-2013 n= 40) resistant gonococcal isolate for the 2012-2013 data.

Of the 24 *Neisseria gonorrhoeae* isolates identified at the sentinel sites in 2013, 16 were referred and confirmed at the reference laboratory. All isolates tested had susceptible ceftriaxone MICs ranging from <0.002 to 0.094 ug/ml (CLSI M100-S23 *N. gonorrhoeae* breakpoint for ceftriaxone susceptible ≤0.25 ug/ml); and susceptible cefixime MICs ranging from <0.016 to 0.023 ug/ml (CLSI M100-S23 *N. gonorrhoeae* breakpoint for ceftriaxone susceptible ≤0.25 ug/ml).[2]

Figure 3.21 Percent sentinel site contribution for *N. gonorrhoeae* data, all ARSP sites, Jan-Dec 2013

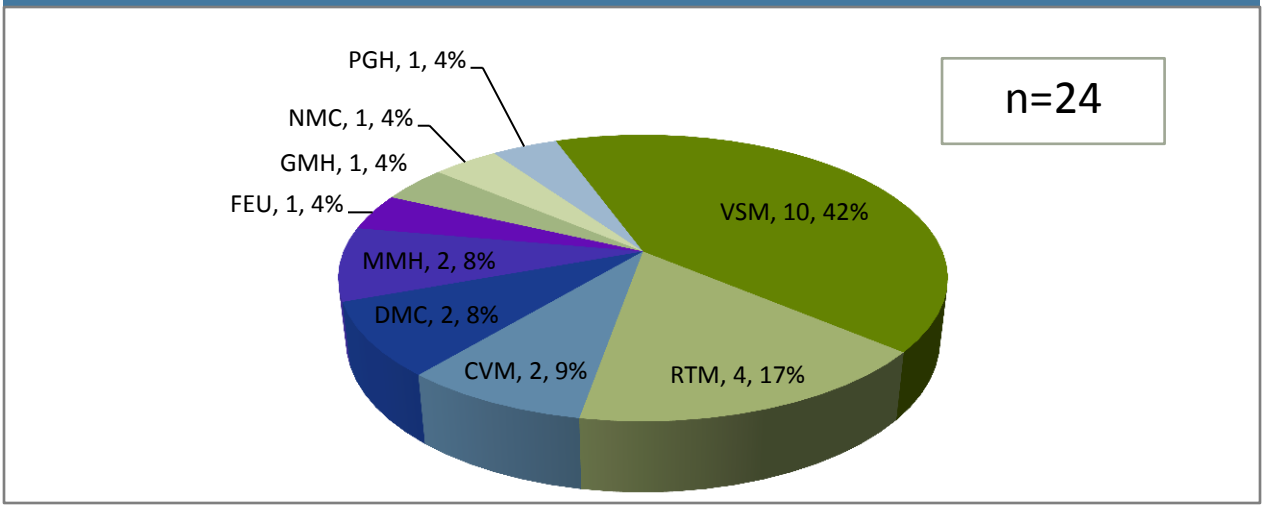


Figure 3.22 Percent resistance of *Neisseria gonorrhoeae*, all ARSP sites, Jan-Dec 2012- 2013

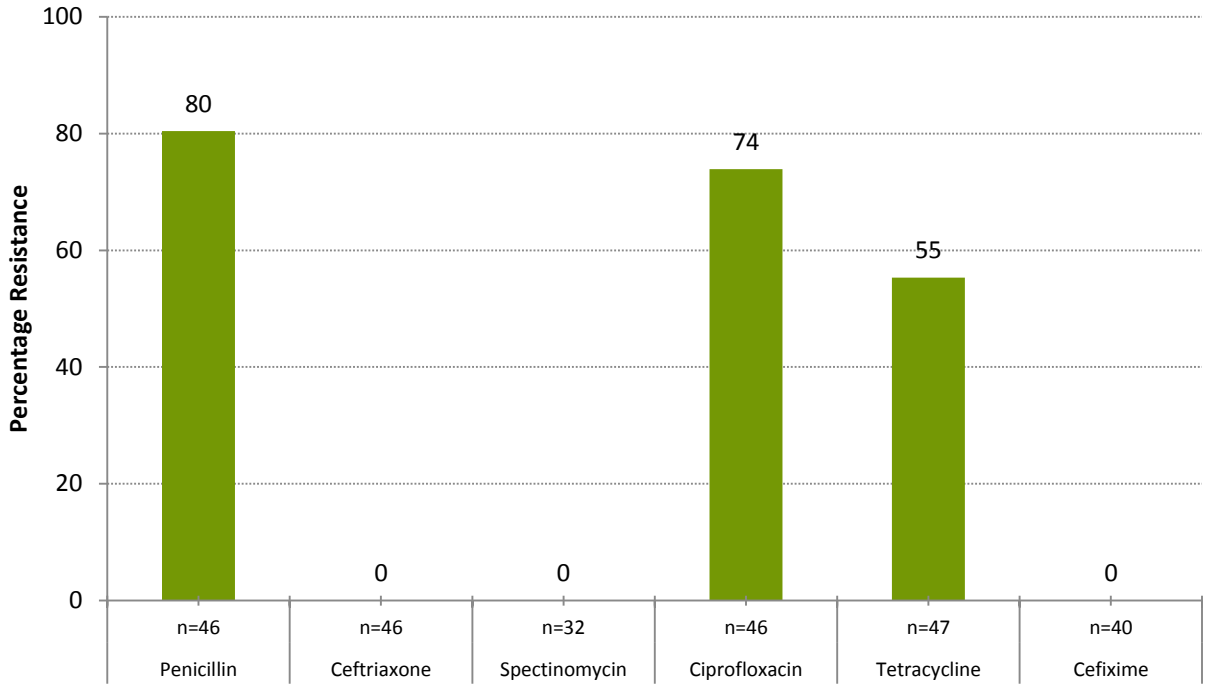
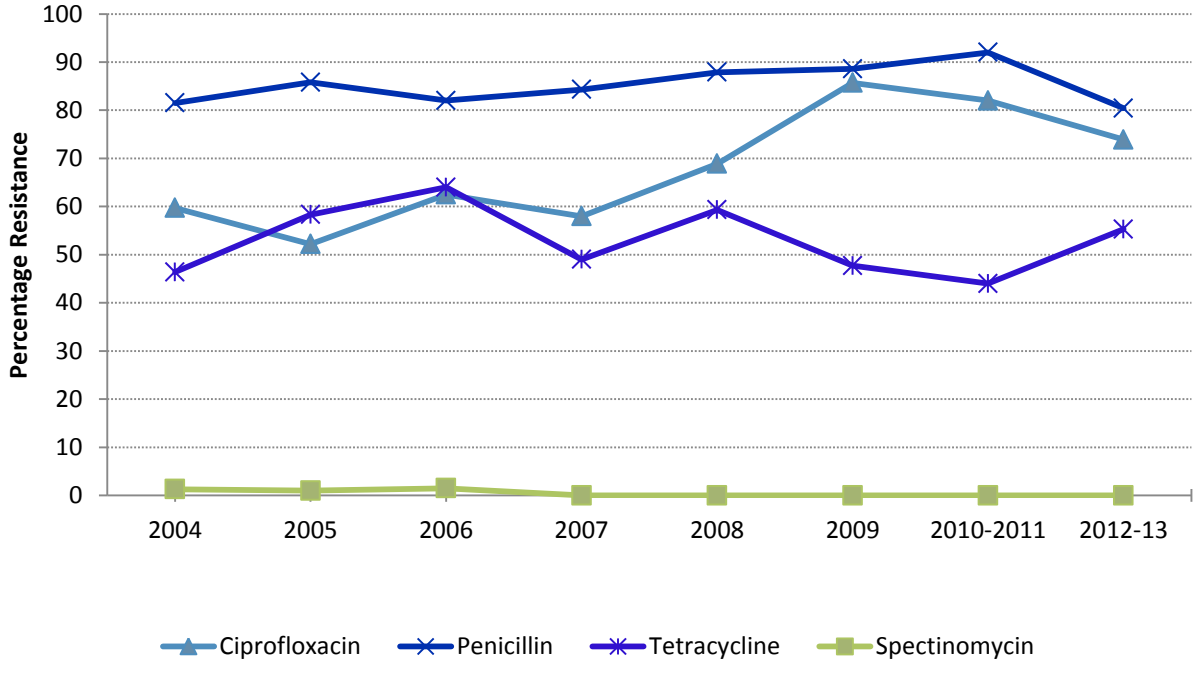


Figure 3.23 Trends of resistance *of Neisseria gonorrhoeae*, all ARSP sites, 2004-2013



3.9 *Staphylococcus aureus*

Staphylococcus aureus are gram-positive bacterial organisms that cause both community and healthcare-associated infections. It also colonizes human skin and mucous membranes. Its methicillin-resistant form (MRSA) has been an important cause of antimicrobial-resistant community and healthcare-associated infections globally.[1]

Isolates

For 2013, there were a total of 2,682 isolates of *S. aureus* reported. This was 34% more than the total number of reported isolates for 2012. These were most commonly isolated from cutaneous, blood and respiratory specimens. For the 2013 data, *S. aureus* was the most common isolate from cutaneous specimens.

Antimicrobial Resistance (Figures 3.24-3.26)

Penicillin

Resistance rates of *S. aureus* isolates against penicillin have been 94% or higher for the past decade with 2013 cumulative resistance rate at 95% (95% CI: 94.1-95.9; n= 2,315).

Methicillin-resistant *S. aureus*

In the past 4 years, more than half of *S. aureus* isolates reported in the program are resistant to oxacillin with 2013 cumulative resistance rate at 53% (95% CI: 51.1-55.2; n= 2,317). Although increasing trends have been observed for the past decade, when compared to the 2012 MRSA data, the 2013 MRSA rate of 53% was significantly lower than the 2012 reported rate of 57% (*p* value 0.0318).

Co-trimoxazole

There were fewer isolates with relevant AST information for co-trimoxazole compared to the other antibiotics tested (N= 966 isolates). Cumulative rates of resistance of *S. aureus* against co-trimoxazole for 2013 is at 14% (95% CI:12.5-15.6). For the past decade, co-trimoxazole resistance have been increasing with rates increasing significantly from 9% in 2012, to 14% in 2013 (*p* value 0002).

Erythromycin & Clindamycin

A smaller proportion of *S. aureus* isolates were tested against erythromycin for 2013 (n= 537 isolates) with 15% reported cumulative resistance rate against the macrolide.

For 2013, 12% (95% CI: 10.5-13; n= 2,513) of *S. aureus* isolates were clindamycin-resistant. These resistance rates have been steadily increasing for the past 4 years with rates significantly higher than the 2012 rates of 8% (*p* value 0.0004). Of the 147 erythromycin-resistant *S. aureus* isolates tested by MIC at the reference laboratory, 6% tested positive for inducible-clindamycin resistance.

Rifampicin

For the 2013 data, there were less number of isolates with relevant AST information for rifampicin compared to the other antibiotics tested (N=1,715 isolates). The percentage of resistance against rifampicin was 5% (95% CI: 3.7-5.7).

Tetracycline

For 2013, there were 10% (95% CI: 8.7-11.2; n= 2,214) of *S. aureus* isolates which tested resistant to tetracycline. This rate is significantly higher than the 7% reported for 2012 (*p* value 0.0005).

Vancomycin

For 2013, we see the possible emergence of vancomycin-resistant *S. aureus* (VRSA) with reported resistance rate at 1% against the comparatively smaller proportion of isolates tested (n= 1,176 isolates). None of these reported VRSA isolates were sent to the national reference laboratory for confirmatory testing.

Linezolid

Of the 1,689 *S. aureus* isolates in 2013 that were tested against linezolid, 2% (95% CI: 1.0-2.2) were reported as resistant. None of these isolates were referred for confirmatory testing at the national reference laboratory. These 2013 linezolid resistance rate do not differ significantly from that reported of the previous year (*p* value > 0.05).

Figure 3.24 Percent resistance of *Staphylococcus aureus*, all ARSP sites, Jan-Dec 2013

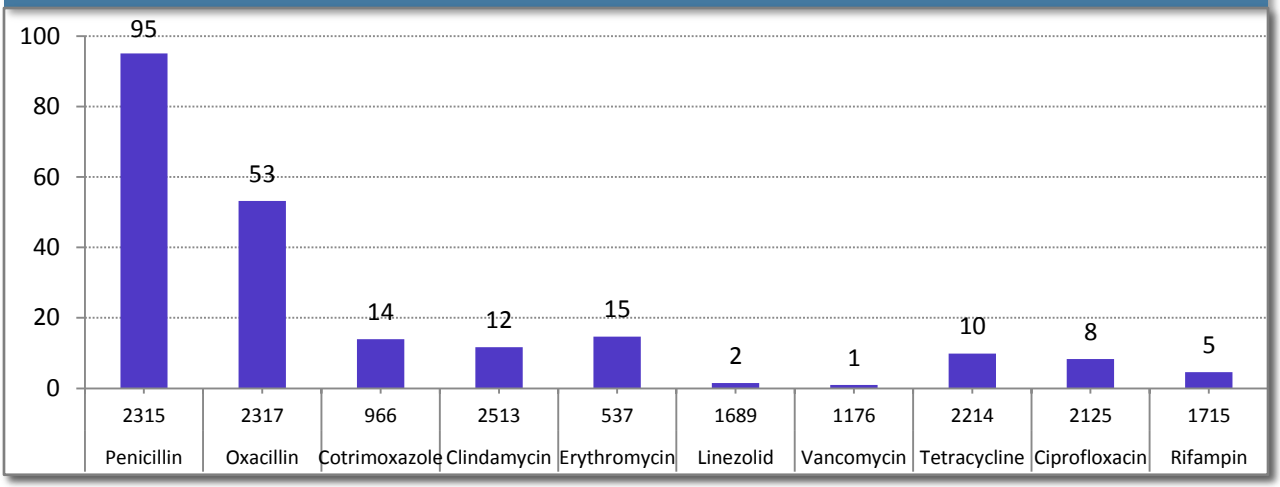


Figure 3.25 Yearly penicillin, oxacillin & vancomycin resistance rates of *S. aureus*, all ARSP sites, 2004-2013

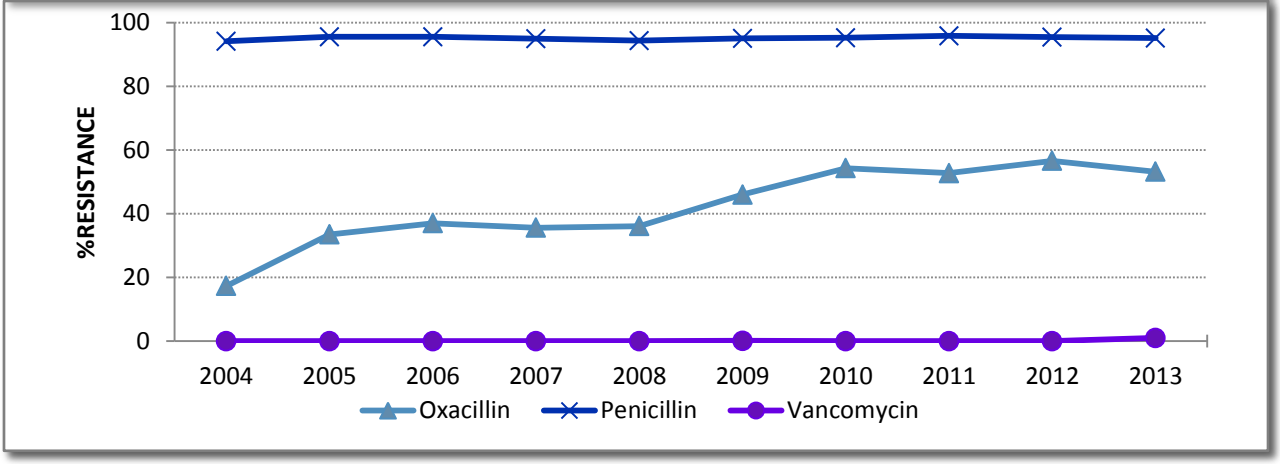


Figure 3.26 Yearly clindamycin, co-trimoxazole & tetracycline resistance rates of *S. aureus*, all ARSP sites, 2004-2013

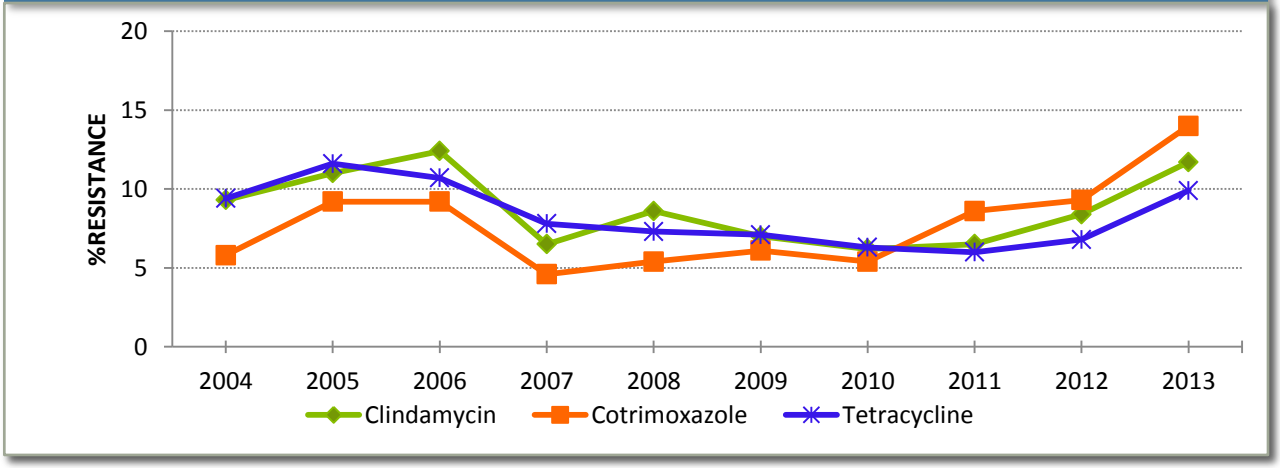


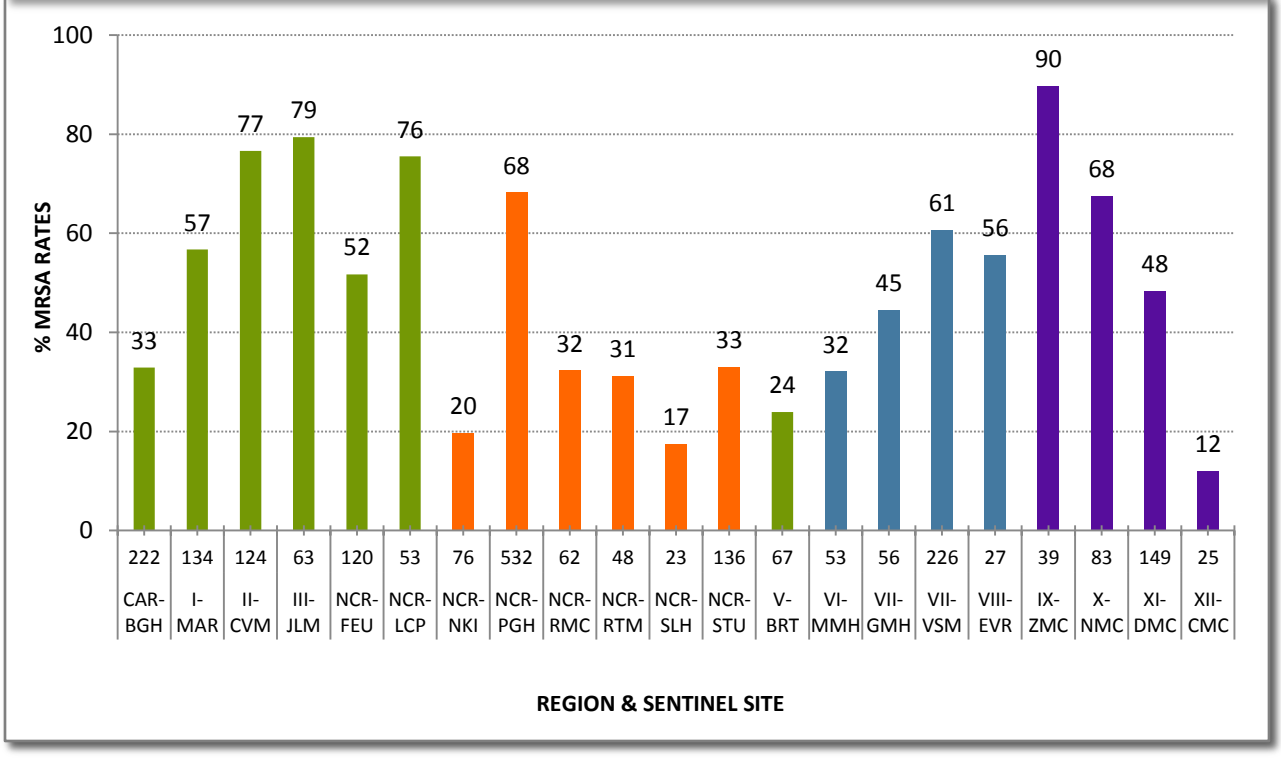
Figure 3.27 Geographic representation of percentage MRSA, ARSP, Jan-Dec 2013

MRSA Rates by Sentinel Site (Figures 3.27-3.28)

Over-all cumulative MRSA rates for 2013 is at 53%. Amongst the sentinel sites with at least 30 isolates of *Staphylococcus aureus* tested for oxacillin-resistance, MRSA rates ranged from 20% (Metro Manila site NKI with N=76) to 90% (Mindanao site ZMC with N=39).

Collectively, when the MRSA rates by sentinel site were analyzed based on geographic location, cumulative MRSA rates from the sites in the National Capital Region was at 54% (n= 1,050). By island group, MRSA rates were highest for Mindanao at 56% (n=296), followed by Visayas at 54% (n= 362) and then Luzon at 53% (n= 1660).

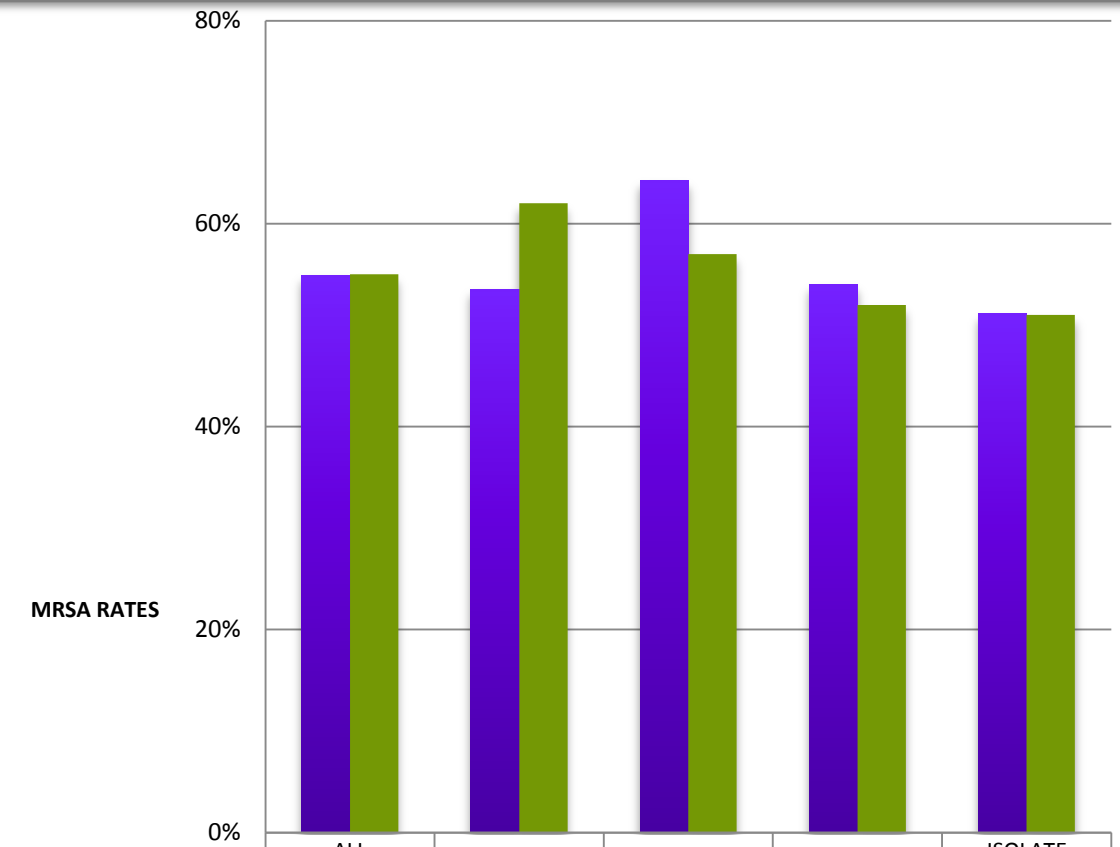
Figure 3.28 MRSA rates by sentinel site, ARSP, Jan-Dec 2013



MRSA Rates by Specimen Type and Age Groups (Figure 3.29)

MRSA rates were analyzed by age groups and by the type of specimen, with blood isolates representing invasive MRSA against cutaneous or cutaneous isolates. MRSA rates did not differ significantly when comparing invasive MRSA rates against that of MRSA rates from cutaneous or wound specimens with both at 55% for 2013 (invasive MRSA= 415 isolates) and cutaneous or wound MRSA= 1105 isolates). Analyzing in subgroups based on age, there is a trend towards higher invasive MRSA rates in the 5-19 years age group (64%) and higher MRSA rates among cutaneous specimens from the 0-4 age group (62%).

Figure 3.29 MRSA rates by specimen type and age, all ARSP sites, Jan-Dec 2013



	ALL BLOOD & WOUND ISOLATES	ISOLATES FROM 0-4 YEARS OLD	ISOLATES FROM 5-19 YEARS OLD	ISOLATES FROM 20-64 YEARS OLD	ISOLATES FROM 65 YEARS OR OLDER
MRSA Rates from Blood Isolates	55%	54%	64%	54%	51%
MRSA Rates from Wound Isolates	55%	62%	57%	52%	51%

# of isolates tested: blood- all 415, 0-4 years 155, 5-19 years 56, 20-64 years 161 and 65 and older 43; Cutaneous (wound) specimens- all 1105, 0-4 years 258, 5-19 years 175, 20-64 years 568 and 65 and older 104;

MRSA Percent Resistance
(Figure 3.30)

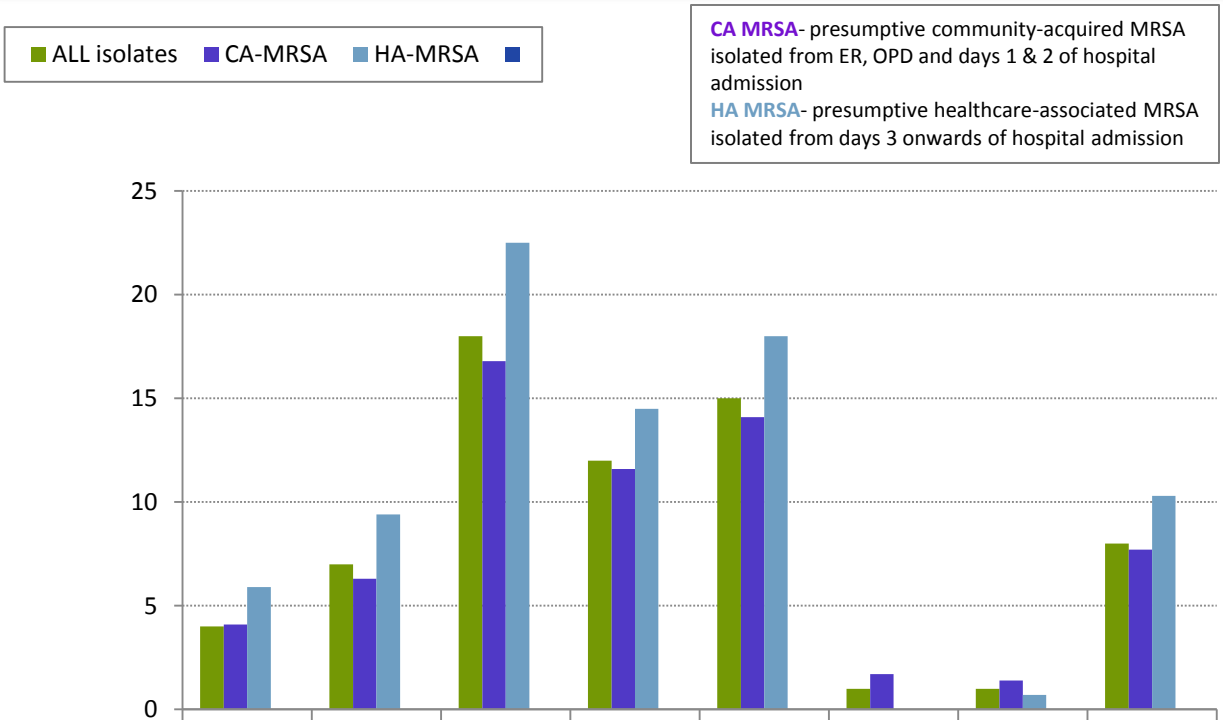
The subset of methicillin-resistant *S. aureus* (MRSA) isolates were analyzed for their susceptibility against commonly used antibiotics.

Resistance rates against agents available in oral formulation for MRSA are at: 4% for rifampicin (n=1,004); 7% for ciprofloxacin (n= 1,071), 8% for tetracycline (n=1,116), 12% for clindamycin (n=1,299), 15% for erythromycin (n=1,306) and 18% for co-trimoxazole (n=1,105). Comparatively, rates for vancomycin (n= 865) and linezolid (n=1,026) were at 1% against each antibiotic tested.

MRSA Percent Resistance by Location
(Figure 3.30)

MRSA isolates were also classified according to the location of specimen collection. Isolates taken from patients at the emergency room (ER), outpatient department (OPD) and on the 1st 2 days of hospital admission were classified as presumptively community-acquired (CA) MRSA isolates. While isolates taken from day 3 onwards of hospital admission were presumptively classified as healthcare-associated (HA) MRSA isolates. Comparing the susceptibility testing results of the 2 groups, rates do not significantly differ (p value>0.05).

Figure 3.30 Percent resistance of MRSA isolates, all ARSP sites, Jan-Dec 2013



	RIF	CIP	SXT	CLI	ERY	LNZ	VAN	TCY
ALL isolates	4	7	18	12	15	1	1	8
CA-MRSA	4	6	17	12	14	2	1	8
HA-MRSA	6	9	23	15	18	0	1	10

# of isolates tested: RIFAMPICIN – ALL 1004, CA 785, HA 219; CIPROFLOXACIN- ALL 1071 CA 879, HA 192; CO-TRIMOXAZOLE- ALL 1105, CA 918, HA 187; CLINDAMYCIN- ALL 1299, CA 1079, HA 220; ERYTHROMYCIN- ALL 1306, CA 1089, HA 217; LINEZOLID- ALL 1026, CA 827, HA 199; VANCOMYCIN- ALL 865, CA 718, HA 147; TETRACYCLINE- ALL 1,116, CA 932 HA 184

3.10 *Staphylococcus epidermidis*

Staphylococcus epidermidis is one of the 40 recognized species of coagulase-negative staphylococci inhabiting human skin and mucous membranes. Although often a contaminant, it is recently becoming a common cause of primary bacteremia and infections of indwelling medical devices.[1]

Isolates

For 2013, there were 8,552 staphylococci isolates reported, of which 67% were identified as coagulase-negative *Staphylococcus* species. Of these coagulase-negative staphylococci, *Staphylococcus epidermidis* was the most common comprising 31% of these group of isolates.

For 2013, there were a total of 1,789 isolates of *Staphylococcus epidermidis* reported. This was 72% more than the 1,035 isolates reported the previous year. Majority of these 2013 *Staphylococcus epidermidis* isolates were from blood specimens.

Antimicrobial Resistance

(Figures 3.31-3.32)

Penicillin

Resistance rates of *Staphylococcus epidermidis* isolates against penicillin is reported at 95% for 2013 (95% CI: 94.2-96.4; n= 1,509). In the past 10 years resistance rates have continue to steadily increase although the 2012 rates did not significantly differ from that of 2013 (p value > 0.05).

Oxacillin

Resistance of *Staphylococcus epidermidis* isolates against oxacillin is reported at 75% (95% CI: 72.7-77.2; n= 1,375) for 2013. These rates are almost double the resistance rates reported 10 years ago at 38% against oxacillin for *Staphylococcus epidermidis*.

Clindamycin

For 2013, 45% of reported *Staphylococcus epidermidis* were resistant to clindamycin (95% CI: 42.1- 46.9; n= 1,713).

Co-trimoxazole

For the 2013 data, cumulative resistance rate of *Staphylococcus epidermidis* against co-trimoxazole was at 50% (95% CI:47.3-53.3; n= 1,196). This rate did not differ significantly from the 54% reported for 2012 (*p* value > 0.05).

Ciprofloxacin

For 2013, S*taphylococcus epidermidis* ciprofloxacin resistance is reported at 33% (95% CI: 30.7-35.6; n= 1,456). This *Staphylococcus epidermidis* rate of resistance against ciprofloxacin has shown an increasing trend for the past decade with 2012 rate of resistance at 21% significantly increased to the reported 33% cumulative resistance rate for 2013 (*p* value 0.0001).

Linezolid

For the 2013 data, there were less number of isolates with relevant AST information for linezolid compared to the other antibiotics tested (n=741 isolates). The reported percentage of resistance of *Staphylococcus epidermidis* against linezolid for 2013 was at 1% (95% CI: 0.4-2.0). None of these 7 reported linezolid-resistant *Staphylococcus epidermidis* isolates for 2013 were referred to the reference laboratory for confirmatory testing.

Vancomycin

For 2013, there were less number of isolates with relevant AST information for vancomycin compared to the other antibiotics tested (n= 566). For the past year, we see the possible emergence of vancomycin-resistant *Staphylococcus epidermidis* (VRSE) with reported rates of resistance at 1% (95% CI: 0.5-2.5) against the smaller subset of isolates with relevant AST results. None of these isolates were sent for confirmatory testing at the reference laboratory. Comparatively, there were no reported vancomycin-resistant *Staphylococcus epidermidis* for the 2012 data.

Figure 3.31 Percent resistance of *S. epidermidis*, all ARSP sites, Jan-Dec 2013

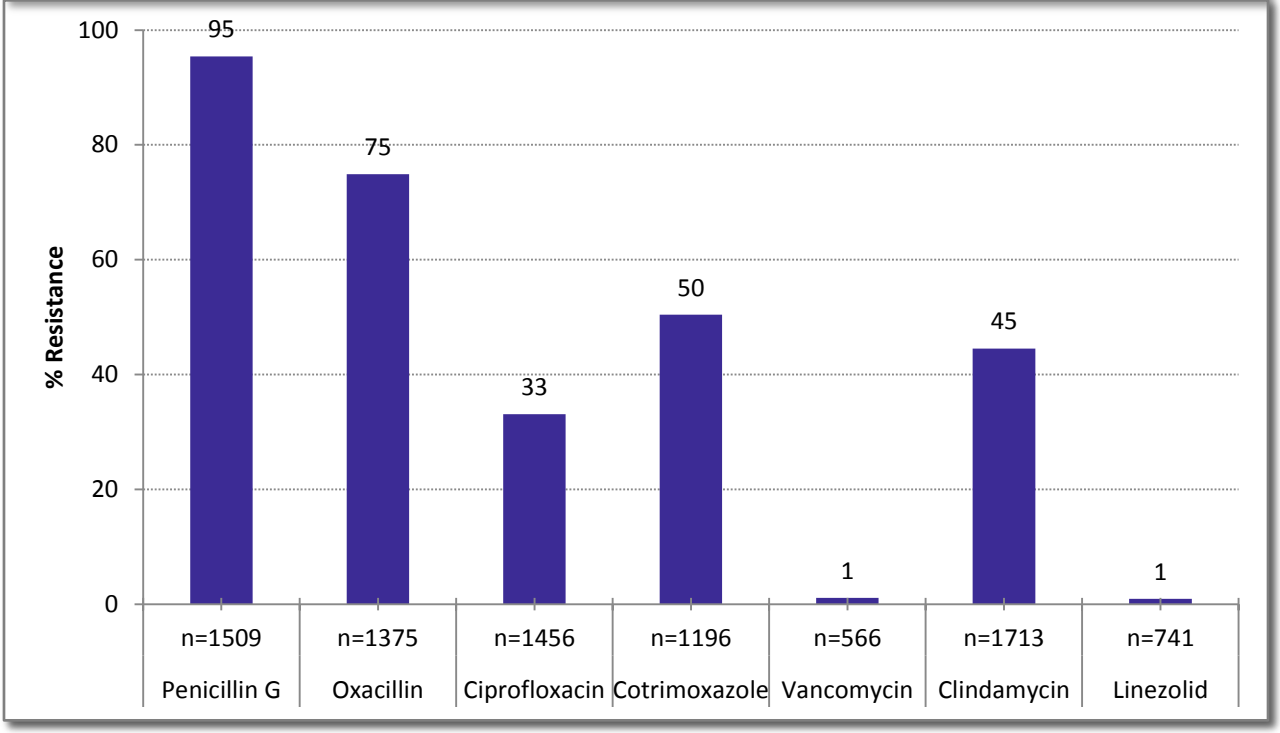
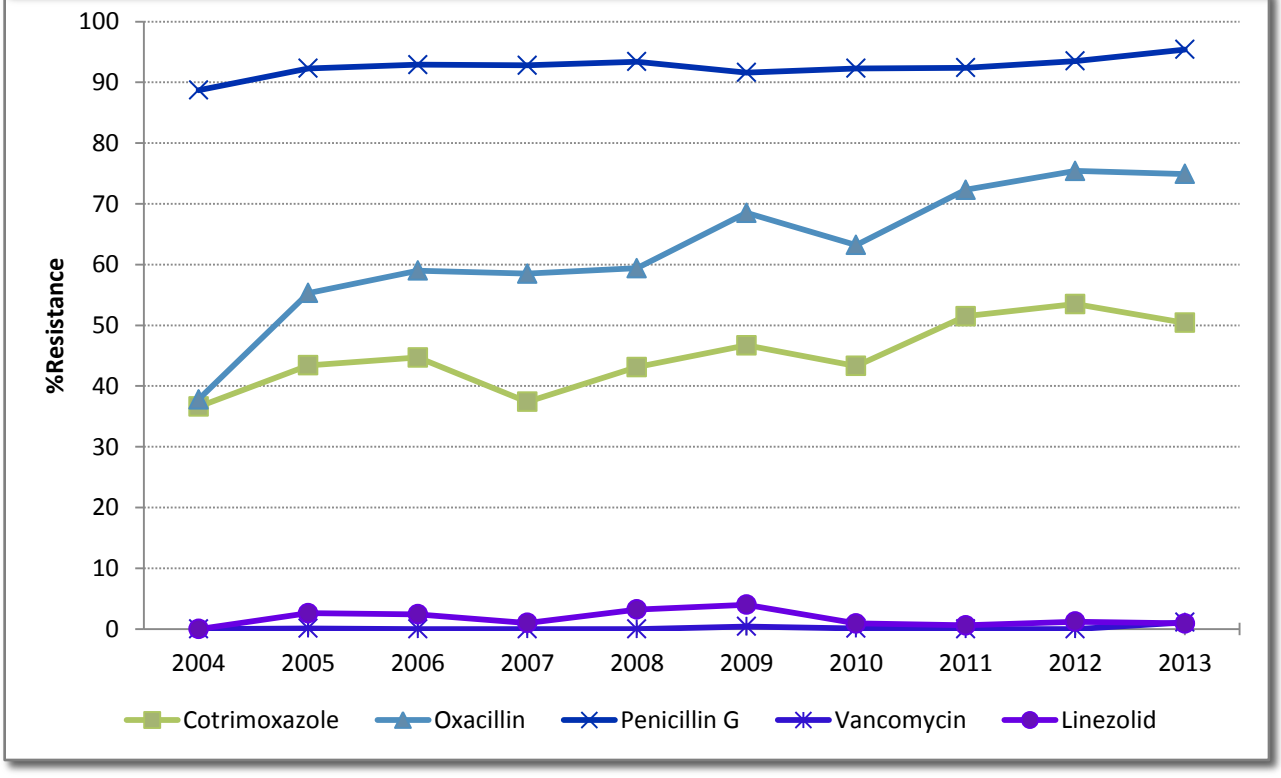


Figure 3.32 Yearly resistance rates of *S. epidermidis*, all ARSP sites, 2004-2013



3.11 *Enterococcus species*

Enterococci are gram-positive cocci that can cause a wide spectrum of infections including UTIs, bacteremia, meningitis, intraabdominal and cutaneous infections. These bacteria are intrinsically resistance to a wide spectrum of antibiotics narrowing the available antimicrobials for treatment.

A globally urgent concern currently amongst these enterococcal organisms is their acquisition of vancomycin-resistance and the increasing prevalence of this resistance phenotype causing healthcare-associated infections.[1]

The Isolates

For 2013, *Enterococcus faecalis* remains to be the most commonly isolated Enterococci with 430 reported isolates, followed by *Enterococcus faecium* with 156 isolates. These are 22% more that the reported *Enterococcus faecalis* and 19% more that the *Enterococcus faecium* reported for 2012.

Most of the 2013 enterococcal isolates were from urine specimens with 190 urine isolates for *Enterococcus faecalis* and 95 urine isolates for *Enterococcus faecium*. For *Enterococcus faecalis*, 45 isolates were from blood and CSF. Comparatively, 17 of the reported *Enterococcus faecium* were isolated from from either blood or CSF specimens.

Antimicrobial Resistance (Figures 3.33-3.34)

Aminopenicillins

Ampicillin resistance among *Enterococcus faecalis* was at 8% (95% CI: 5.9-11.6). Comparatively, ampicillin-resistance against *Enterococcus faecium* was reported at 69% (95% CI: 60.9-76.7). Ampicillin resistance have been increasing in the past years although these rates of resistance did not significantly differ from 2012 rates for both species of *Enterococcus* (p value > 0.05).

High-level Aminoglycosides

For Enterococci, high-level aminoglycoside resistance signifies loss of the synergistic effect of aminoglycosides with beta-lactams and glycopeptides.

For 2013, only a small subset of the *Enterococcus faecalis* and *Enterococcus faecium* were tested for high-level aminoglycoside resistance. For *Enterococcus faecalis*, 15% of the 39 isolates tested were positive for high-level streptomycin resistance (95% CI; 8.1-34.2). Of the 64 *Enterococcus faecalis* isolates tested, 6% were positive for high-level gentamicin resistance (95% CI: 2-16). For *Enterococcus faecium*, of the 12 isolates tested, 50% were positive for high-level streptomycin resistance (95% CI: 22.3-77.7). Of the 25 *Enterococcus faecium* isolates tested, 28% were positive for high-level gentamicin resistance (95% CI: 12.9-49.6).

Linezolid

For 2013, we document the possible emergence of linezolid-resistance amongst *Enterococcus faecalis* isolates, with reported 2% resistance rates (95% CI: 0.5-4.6; n= 237). None of these reported isolates were sent for confirmatory testing at the reference laboratory. Comparatively, there were no reports of linezolid- resistance among *Enterococcus faecium* isolates for 2013 (n= 124).

Vancomycin

For 2013 we see the emergence of vancomycin-resistant Enterococci. For the 403 isolates of *E. faecalis* tested, 1% were reported as resistant (95% CI: 0.2-2.3). Comparatively, for the 142 *E. faecium* isolates tested, 25 were reported as resistant (95% CI: 0.5-6.5). Of these vancomycin-resistant *Enterococci* isolates identified, only 1 isolate, a vancomycin-resistant *E. faecium* from a Metro Manila site, was sent to the national reference laboratory in RITM for confirmatory testing. The isolate was confirmed by MIC as vancomycin-resistant *E. faecium* and was isolated from a urine specimen from a 75-year old female.

Figure 3.33 Percent resistance of *E. faecalis*, all ARSP sites, Jan-Dec 2013

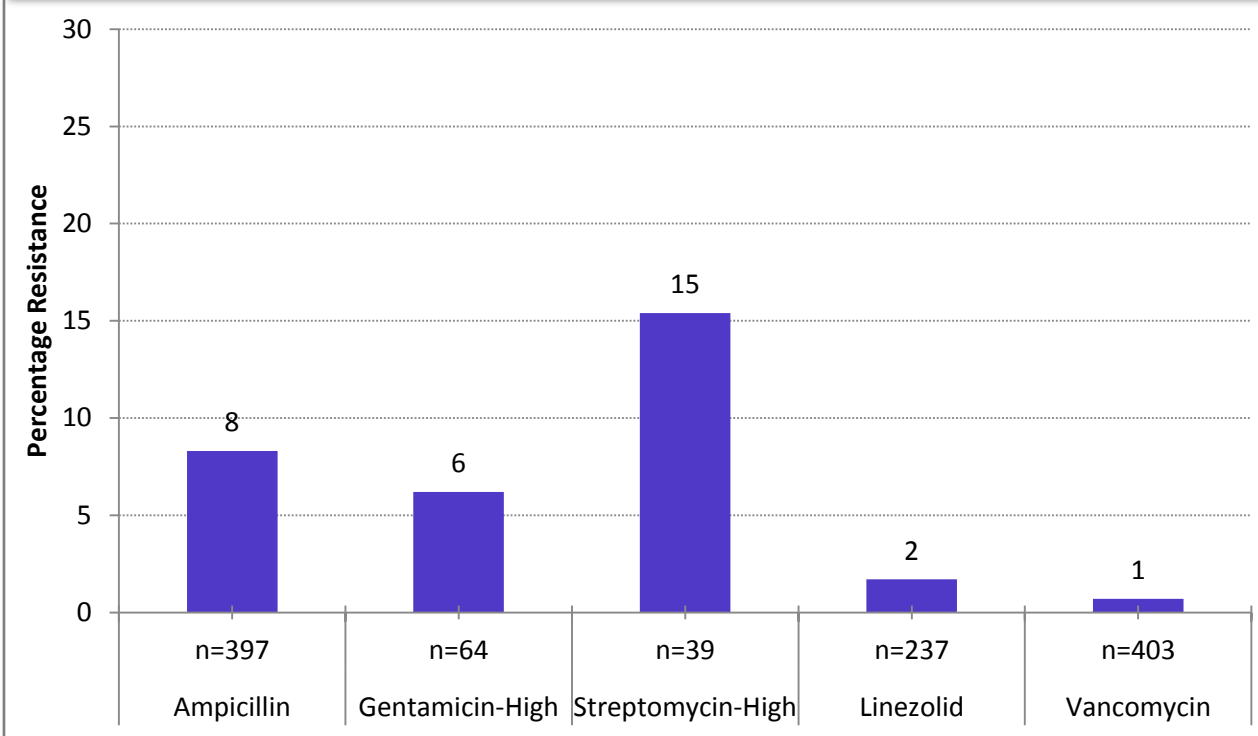
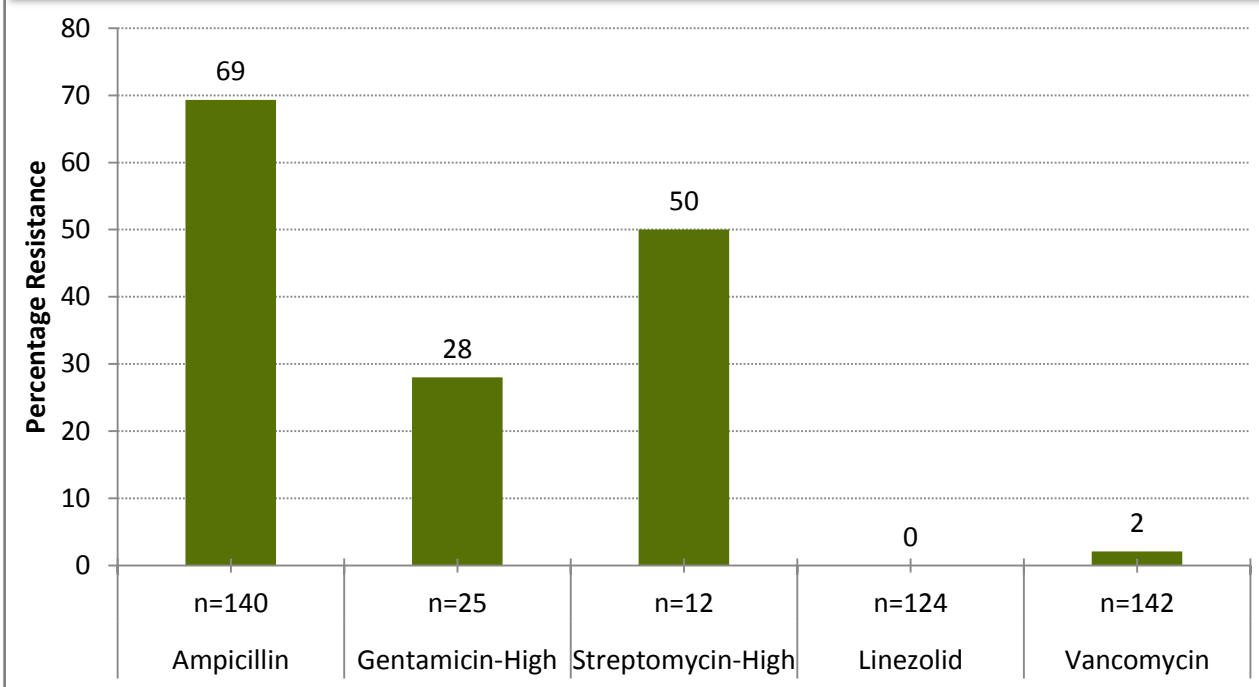


Figure 3.34 Percent resistance of *E. faecium*, all ARSP sites, Jan-Dec 2013



3.12 *Escherichia coli*

Escherichia coli is the commonest cause of urinary tract infection (UTI), and a common pathogen causing neonatal meningitis, traveler's diarrhea, intraabdominal infections, nosocomial pneumonia, post-operative cutaneous infections and central line infections.[1]

Isolates

For 2013, there were a total of 5,208 reported *E. coli* isolates. Majority of the isolates (60%)were from urine specimens. Other *E. coli* 2013 isolates came from respiratory, blood, CSF and cutaneous specimens.

For the 2013 data, *E. coli* was the most frequently reported isolate from urine specimens and was the second most common cutaneous or cutaneous isolate.

Antimicrobial Resistance

(Figures 3.35-3.38)

Penicillins

Cumulative resistance rates of 2013 *Escherichia coli* isolates was 82% for ampicillin ((95% CI: 80.5-82.8; n= 4,333). Annually reported resistance rates of *E. coli* against ampicillin have been at least 70% in the past decade.

In contrast, 2013 *E. coli* resistance rates for ampicillin-sulbactam was reported at 32% (95% CI: 30.4-33.3; n=4,056). Ampicillin-sulbactam resistance amongst *E. coli* isolates have been slowly increasing the past decade, with 2013 cumulative rate significantly higher than that reported the previous year at 28% (p=0.0008).

Cephalosporins

For 2013, a smaller subset of the *Escherichia coli* isolates was tested for cefuroxime resistance (n= 2,210). Cumulative rate of resistance of *E. coli* isolates tested against cefuroxime is reported at 29% (CI: 26.7-30.5). This resistance rate has been increasing in the past years although 2012 cefuroxime resistance rate of 26% did not differ significantly from that of 2013 (p value . 0.05).

For 2013, resistance of *E. coli* isolates to ceftriaxone was at 31% (CI: 29.1-31.9; n= 4,364). Increasing trends of resistance to this 3rd generation cephalosporin has been noted for the past decade with ceftriaxone resistance rate doubling in the last 6 years.

For 2013, resistance of *E. coli* isolates to cefepime was at 11% (95% CI: 10.2-12.1; n= 4,529). Increasing rates have been reported in the past years with *E. coli* cefepime 2013 resistance rates being significantly higher than the 9% rate reported in 2012 (p value 0.014).

Co-trimoxazole

For 2013, *E. coli* resistance rate to trimethoprim-sulfamethoxazole is at 66% (CI: 64.2-67.2) with rates of resistance ranging from 64% to 69% in the past decade. This rate did not differ significantly from that reported in 2012 (p value > 0.05).

Fluoroquinolones

For 2013, 43% of *E. coli* isolates were reported to be resistant to ciprofloxacin (CI: 41.9-44.9; n= 4,332). These resistance rates have been slowly increasing in the past 10 years with 2013 rates significantly higher than the 41% ciprofloxacin resistant *E. coli* rates for 2012 (p value 0.0247).

Aminoglycosides

Resistance of *E. coli* isolates to aminoglycosides are at 23% (CI: 21.6-24.1; n= 4,357) for gentamicin and 4% for amikacin (CI: 3.5-4.7; n= 4,478). These rates did not differ significantly from those reported for 2012 (p value > 0.05).

Carbapenems

For 2013, we continue to see carbapenem-resistant *E. coli* as in the past few years with resistance rates at 2% each for ertapenem (95% CI: 1.5-2.6; n= 2,684), imipenem (95% CI: 1.2-1.9; n= 4,858) and meropenem (95% CI: 1.7-2.6; n= 4,269), for 2013. Although imipenem resistance rates have decreased from the 3% reported in 2012 (p value 0.0003); rates for ertapenem and meropenem did not significantly differ from those of the previous year (p value >0.5).

Figure 3.35 Percent penicillins, cephalosporins & co-trimoxazole resistance of *Escherichia coli*, all ARSP sites, Jan-Dec 2013

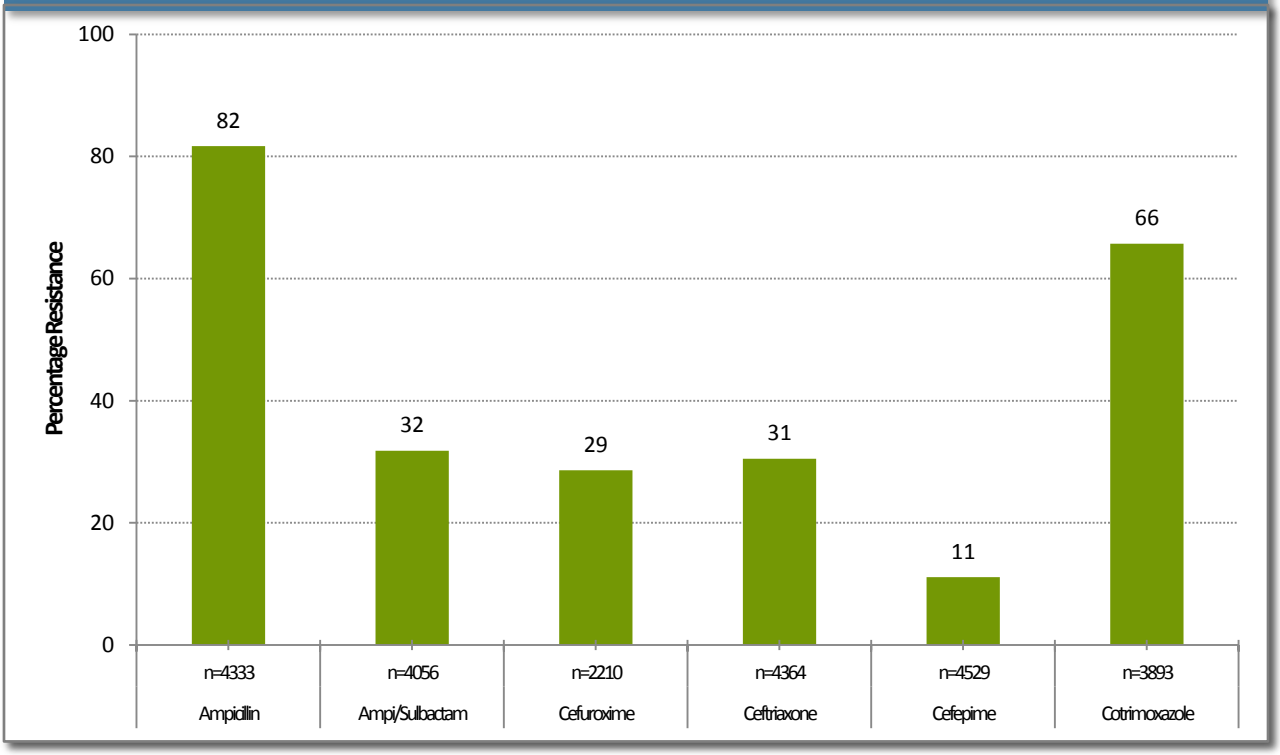


Figure 3.36 Percent carbapenems, aminoglycosides, & ciprofloxacin resistance of *Escherichia coli*, all ARSP sites, Jan-Dec 2013

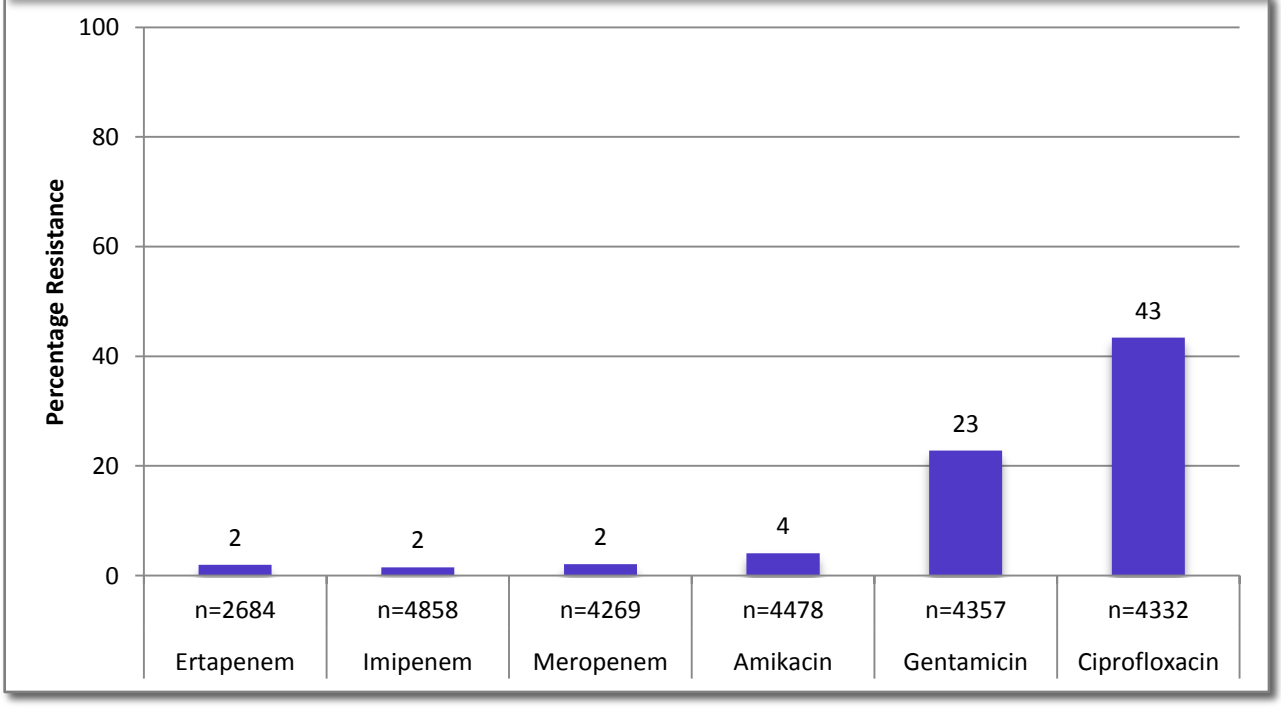


Figure 3.37 Yearly ampicillin, ampicillin-sulbactam, ciprofloxacin and co-trimoxazole percent resistance of *Escherichia coli*, all ARSP sites, 2004-2013

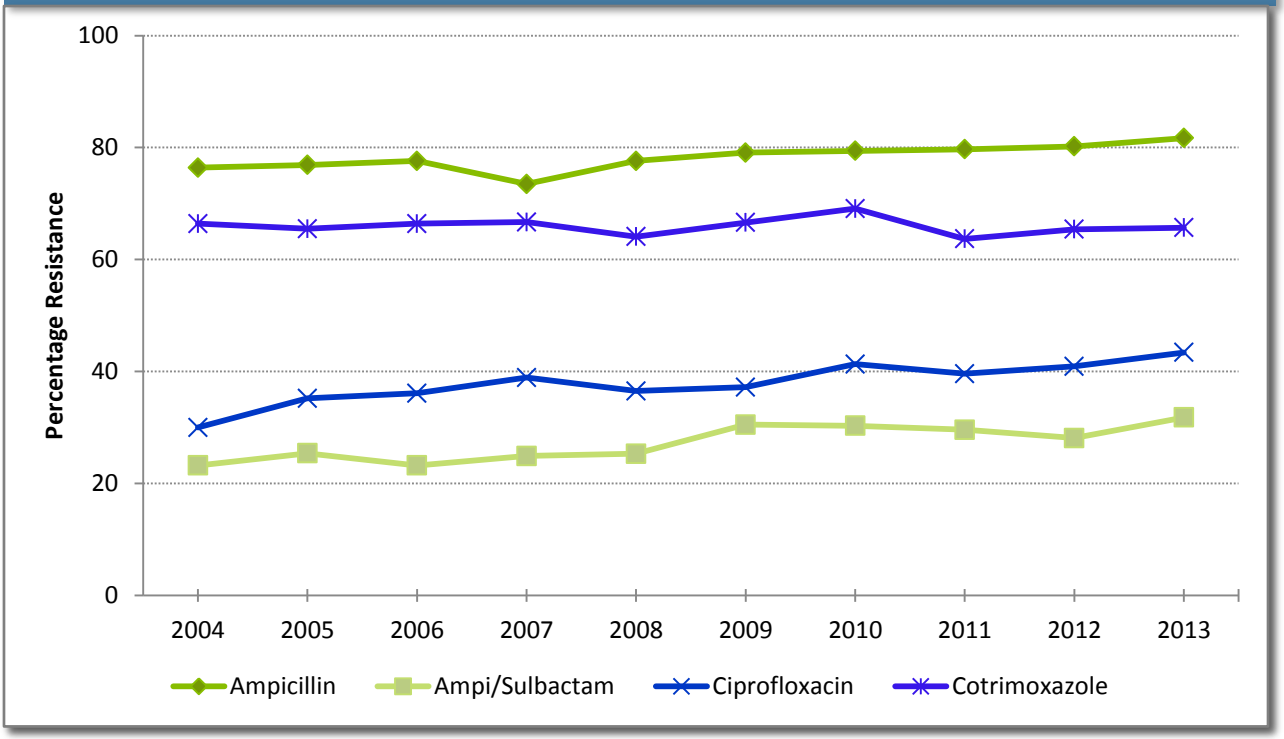
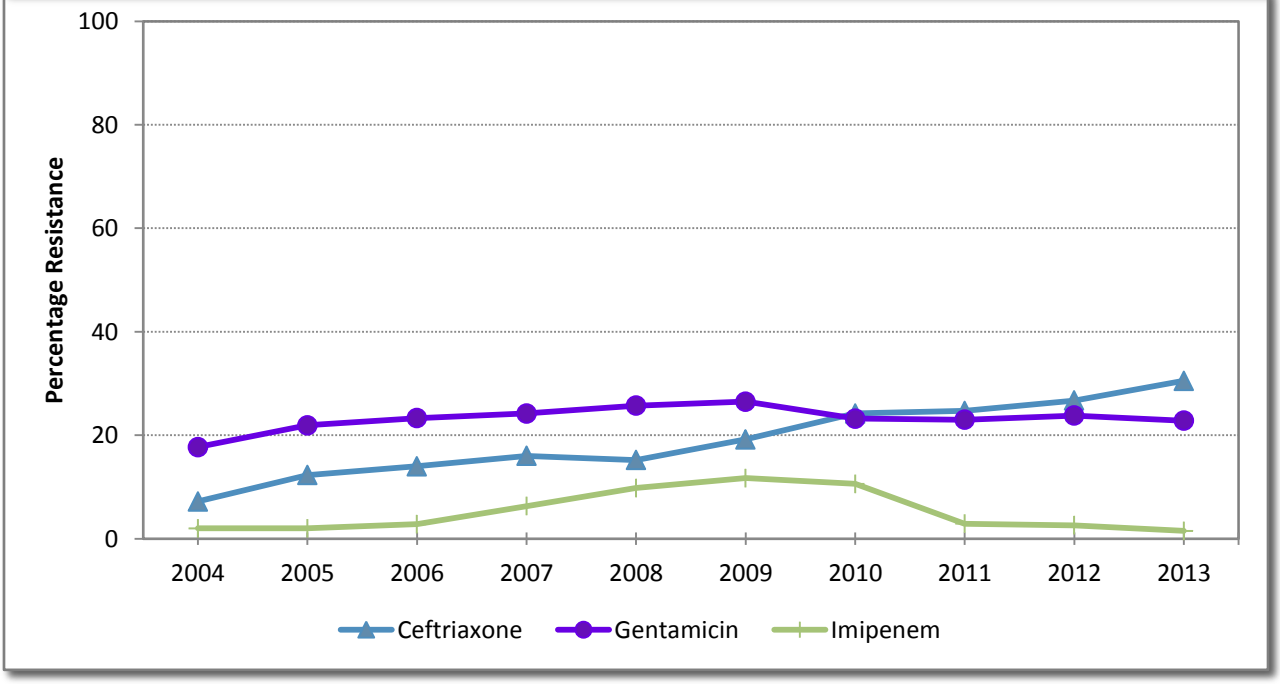


Figure 3.38 Yearly ceftriaxone, gentamicin & imipenem percent resistance of *Escherichia coli*, all ARSP sites, 2004-2013



Outpatient Urinary *E. coli* (Table 3.7)

Amongst urinary isolates taken from the outpatients (i.e. urine isolates from patients at the emergency room and outpatient department), least resistance was noted for nitrofurantoin at 7% (95% CI: 5.5-8.8; n= 969) amongst the oral agents. Comparatively, rates of resistance to the other oral agents used to treat uncomplicated UTI are higher at 65% for co-trimoxazole (95% CI: 62.3-68.4; n= 974); at 52% for ciprofloxacin (95% CI: 48.8-55.2; n= 955), at 32% for cefuroxime (95% CI: 27.5-36; n= 551) and at 20% for co-amoxiclav (95% CI: 17.4-22.3; n= 1,051).

When 2013 outpatient urinary *E. coli* resistance rates were compared to that of 2012, nitrofurantoin rates significantly decreased from 10% in 2012 to 7% in 2013 (*p* value 0.027); co-amoxiclav rates decreased from 25% in 2012 to 20% in 2013 (*p* value 0.011); while the rest of the oral agents' resistance rates did not differ significantly from that reported of the previous year.

Inpatient Urinary *E. coli* (Table 3.7)

For inpatient (i.e. urine isolates from patients admitted in the hospital) urinary *E. coli* 2013 isolates, ertapenem had the lowest resistance rate at 2% (95% CI: 1.5-3.4; n= 1,059) among the other parenteral antibiotics tested. Relatively higher resistance rates are noted for ceftriaxone at 36% (95% CI: 33.3-37.9; n= 1,683); amikacin at 6% (95% CI: 4.8-7.0; n= 1,835); and piperacillin-tazobactam at 6% (n= 1,835).

Comparing 2012 rates against that of 2013 for inpatient urinary *E. coli* isolates, ceftriaxone rates significantly increased from the 31% reported in 2012, to 36% for 2013 (*p* value 0.006); while the rest of the 2013 rates against the other parenteral agents reported did not differ significantly.

Table 3.7 Percentage resistance of urinary *Escherichia coli*, all ARSP sites, Jan-Dec 2013

ANTIMICROBIAL	OUTPATIENT		INPATIENT	
	N	%R	N	%R
ORAL AGENTS				
Ampicillin	955	77%	1,670	85%
Cefuroxime	551	32%	871	40%
Ciprofloxacin	955	52%	1,635	46%
Co-amoxiclav	1,051	20%	1,974	23%
Co-trimoxazole	974	65%	1,465	69%
Nitrofurantoin	969	7%	1,622	6%
INTRAVENOUS AGENTS				
Ceftriaxone	934	24%	1,683	36%
Ertapenem	679	1%	1,059	2%
Amikacin	1,026	2%	1,835	6%
Piperacillin-tazobactam	979	3%	1,835	6%

3.13 *Klebsiella* species

Klebsiella species is a gram negative bacilli that commonly causes pneumonia, urinary tract infections and nosocomial infections. Multidrug-resistant *Klebsiella* species producing extended-spectrum beta-lactamases and/or carbapenemases have been increasingly common pathogens especially in the healthcare setting.[1]

Isolates

For 2013, there were a total of 6,540 reported isolates of *Klebsiella* species. This is 46% more than reported *Klebsiella* species isolates for 2012. This bacteria was the most common isolate from respiratory specimens, and was also the second most common blood and urine isolate for 2013.

Antimicrobial Resistance

(Figure 3.39-3.42)

Beta-lactams

Percentage resistance rates against amoxicillin-clavulanic acid for *Klebsiella* sp. is at 28% (CI: 27-29.2; n= 6,254). Reported amoxicillin-clavulanic acid resistance rates for 2013 do not differ significantly from that of 2012 (*p* value > 0.05).

Percentage resistance rates of 2013 *Klebsiella* sp. Isolates against piperacillin-tazobactam is at 14% (95% CI: 13.2-15.0; n= 5,949). These rates against piperacillin-tazobactam have *Klebsiella* sp. significantly increased from the 2012 reported resistance rate of 9% (*p* value 0.0001).

For 2013, a smaller subset of *Klebsiella* species isolates were tested against cefuroxime (n= 2,455). Cumulative resistance rates of the 2013 Klebsiella species isolates was at at 46% (95% CI: 43.5-47.5).

Comparatively, resistance rate of 2013 *Klebsiella* species isolates against the third generation cephalosporin- ceftriaxone is at 40% (95% CI: 38.9-41.5; n= 5,675). Increasing rates of resistance have been seen against ceftriaxone for the past years with 2012 rates at 36% significantly increasing to 40% for 2013 (*p* value 0.0002)

Fluoroquinolones

For 2013, 28% of *Klebsiella* species isolates were reported to be resistant to ciprofloxacin (95% CI: 27.2-29.6; n= 5,674). These resistance rates have been slowly increasing in the past 10 years with 2013 rates significantly higher than that of the year prior at 26% (*p* value 0.0092).

Aminoglycosides

Resistance rates of of *Klebsiella* species isolates for 2013 to the aminoglycosides are at 7% for amikacin (95% CI: 6.1-7.8; n= 5,755) and 27% for gentamicin (95% CI: 25.4-27.8; n= 5,536). These rates do not significantly differ from those reported for 2012 (*p* value > 0.05).

Carbapenems

We continue to see carbapenem-resistant *Klebsiella* species, as in the past few years. For 2013 *Klebsiella* species isolates, resistance rate is at 6% against imipenem (95% CI: 5.2-6.4; n= 6,189) and 7% against meropenem (95% CI: 6.5-7.8; n= 5,833). In contrast, only a smaller subset of the 2013 *Klebsiella* species isolates were tested against ertapenem (n= 3385), with reported rates of resistance at 9% (95% CI: 1.5-2.6).

These reported 2013 cumulative resistance rates for *Klebsiella* species isolates against the carbapenems are significantly increased from those reported for 2012 for both imipenem and meropenem. *Klebsiella* species imipenem rates of resistance for 2012 at 5% significantly increased to 6% for 2013 (p value 0.0001). Similarly, meropenem rates of resistance for 2012 at 3% significantly increased to 7% for 2013 (*p* value 0.0001). In contrast, *Klebsiella* species 2013 rates of resistance against ertapenem have significantly decreased when compared to the 2012 reported rate of 12% (*p* value 0.0001).

Figure 3.39 Percent beta-lactams resistance of *Klebsiella species,* all ARSP sites, Jan-Dec 2013

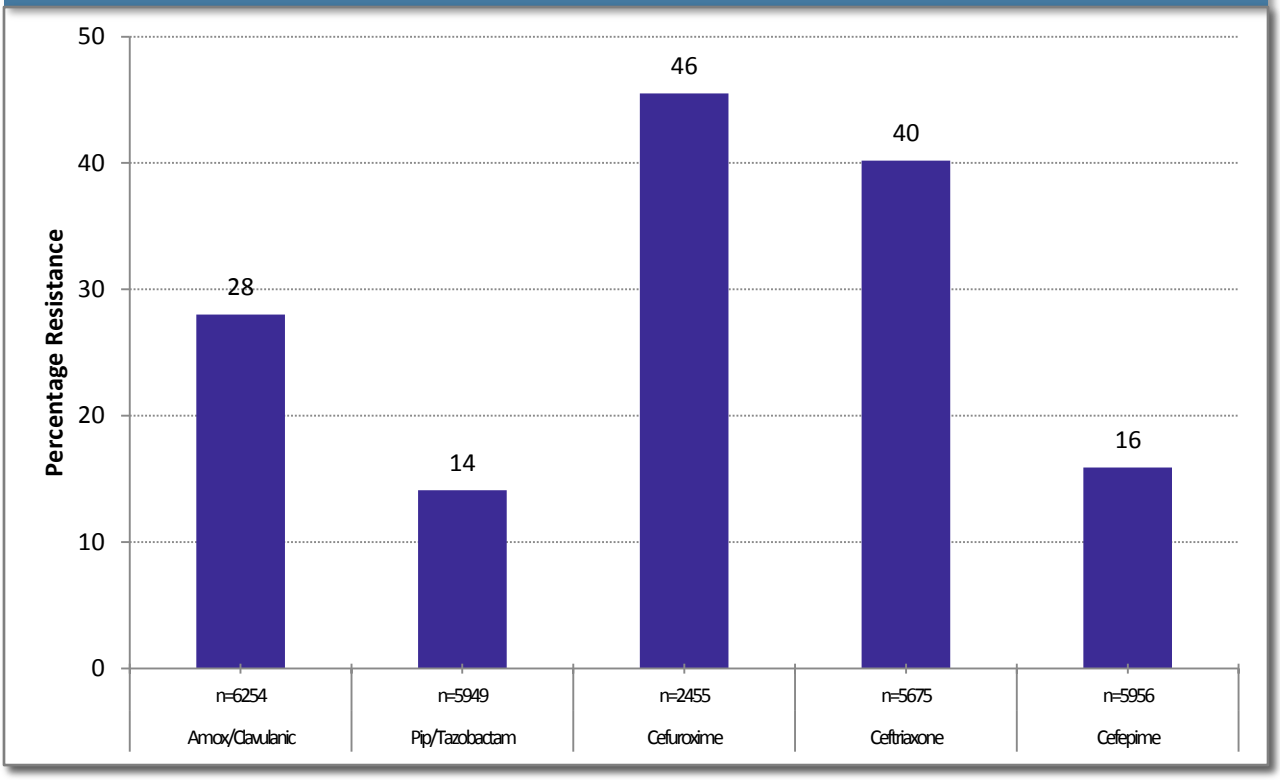


Figure 3.40 Percent carbapenems, aminoglycosides & ciprofloxacin resistance of *Klebsiella species*, all ARSP sites, Jan-Dec 2013

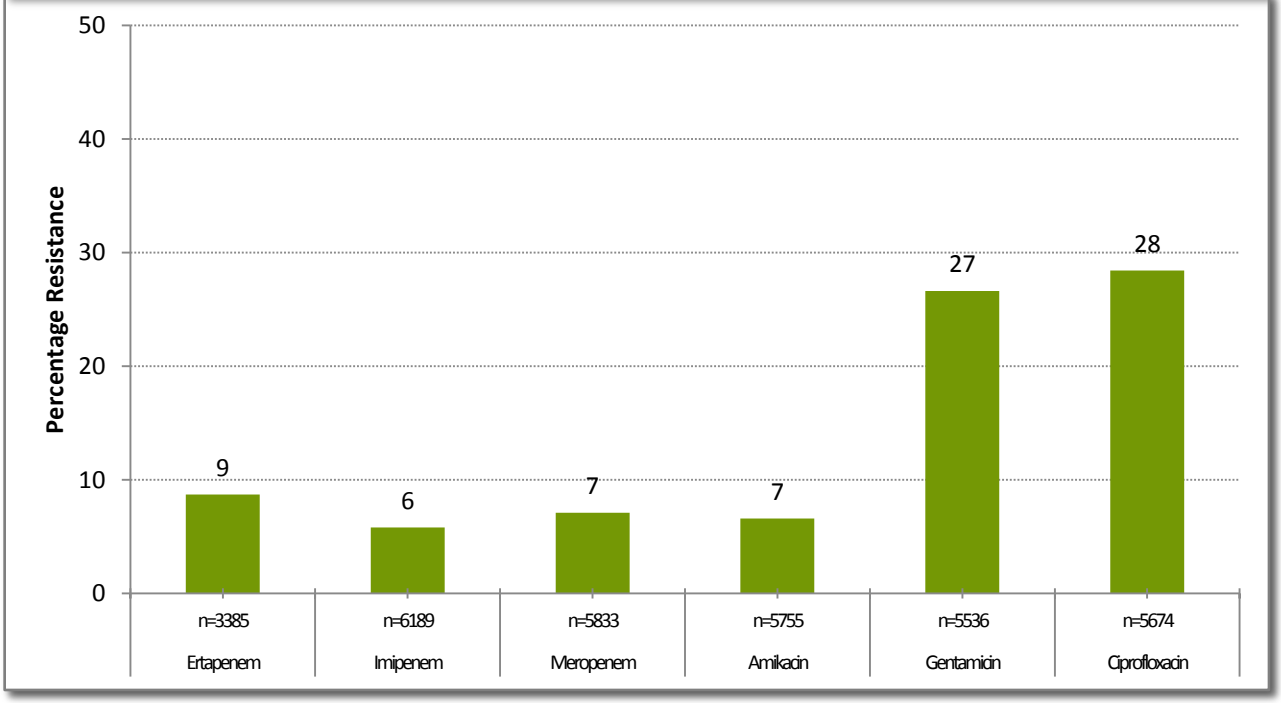


Figure 3.41 Yearly amoxicillin-clavulanic acid, ceftriaxone and ciprofloxacin resistance rates of *Klebsiella* species, all ARSP sites, 2004-2013

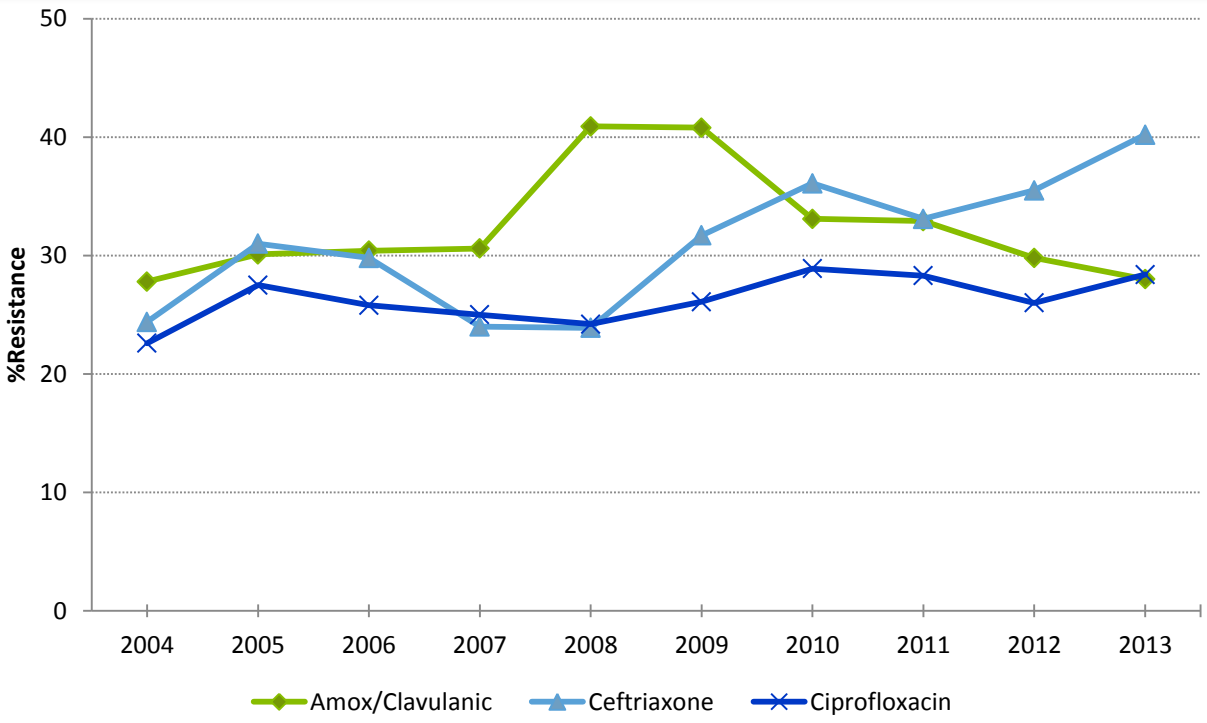
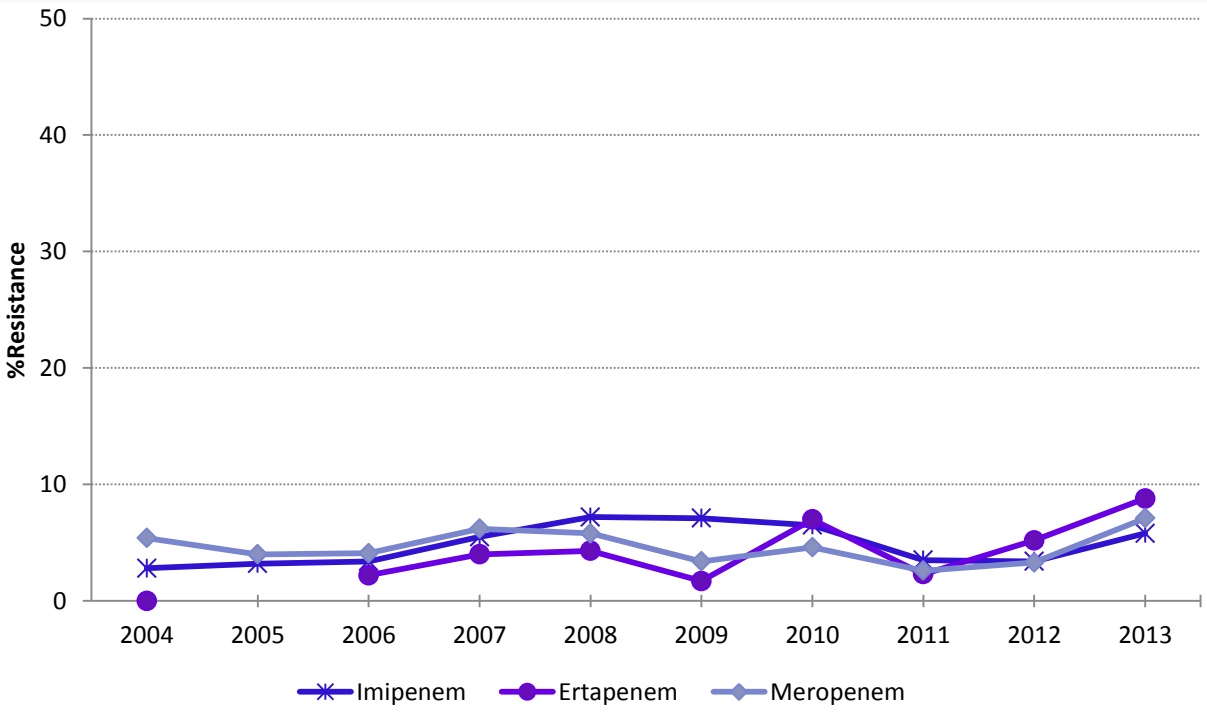


Figure 3.42 Yearly carbapenems resistance rates of *Klebsiella* species, all ARSP sites, 2004-2013

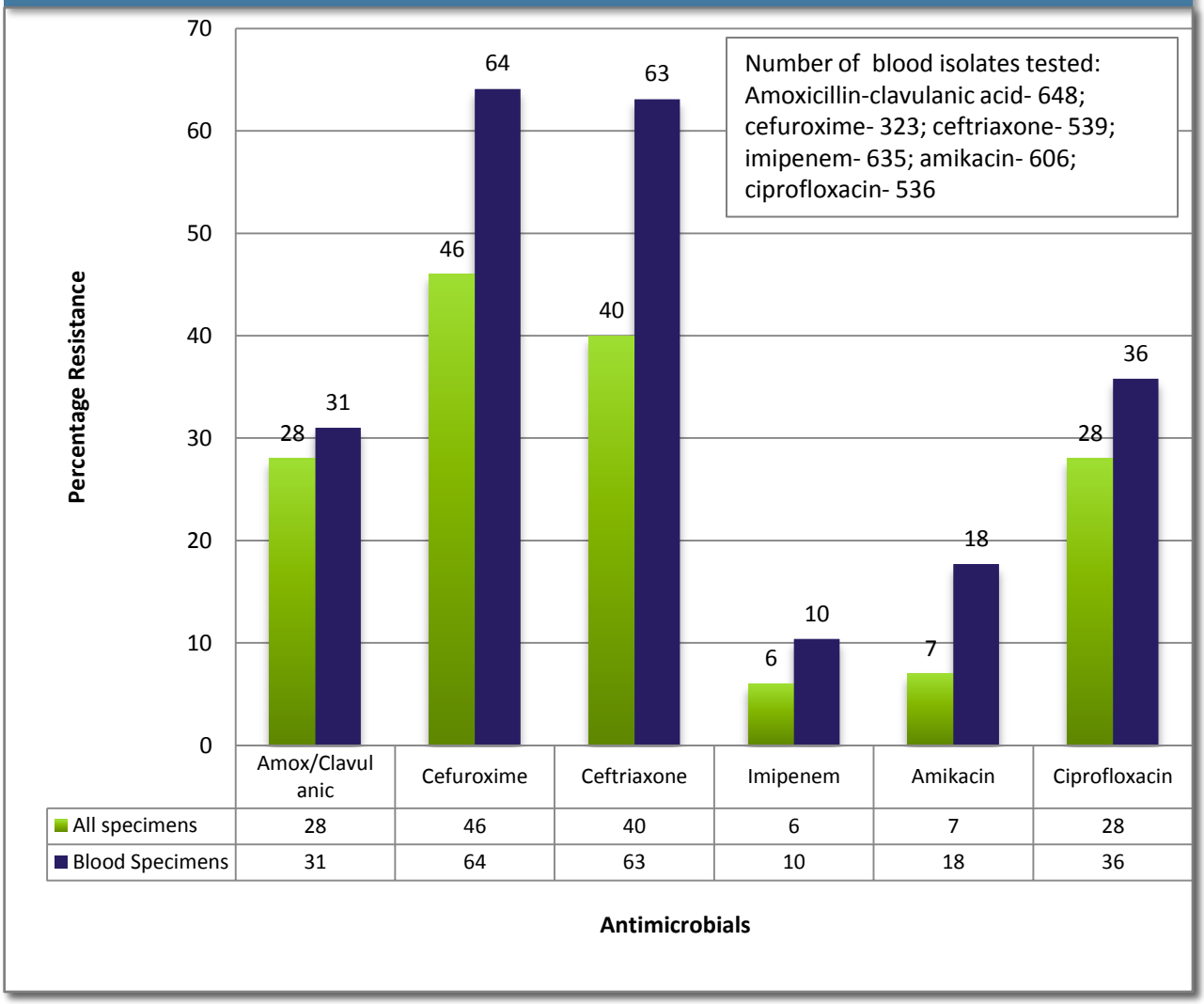


Invasive *Klebsiella* species

Klebsiella species is the second most common isolate from blood specimens for the 2013 data. The subset of invasive *Klebsiella* isolates (blood isolates) were analyzed for their antimicrobial susceptibility to common antimicrobials for treatment. Resistance rates of invasive *Klebsiella* species isolates for amoxicillin-clavulanic acid was at 31% (n= 648); cefuroxime was at 64% (n= 323); ceftriaxone was at 63% (n= 539); imipenem was at 10% (n= 635); amikacin was at 18% (n= 606); and ciprofloxacin was at 36% (n= 536).

Resistance rates of these isolates of invasive *Klebsiella* species were also compared to the cumulative rates of resistance for all *Klebsiella* species reported for the 2013 data (Figure 3.43). Resistance rates of the invasive isolates of *Klebsiella* species were higher for antibiotics used empirically for treatment. Comparatively significantly higher resistance rates were reported for invasive *Klebsiella* sp. isolates versus those for all reported 2013 *Klebsiella* species for the following antimicrobials: cefuroxime, ceftriaxone, imipenem, amikacin and ciprofloxacin (p value < 0.05).

Figure 3.43 Percentage resistance of isolates from all types of specimen against invasive *Klebsiella* sp., all ARSP sites, Jan-Dec 2013



Extended-spectrum Beta-lactamase-producing *Enterobacteriaceae*

Extended-spectrum beta-lactamases (ESBLs) are enzymes that mediate resistance to extended-spectrum cephalosporins and monobactams but do not affect cephamycins or carbapenems.[3]

E. coli ESBL-suspect Rates

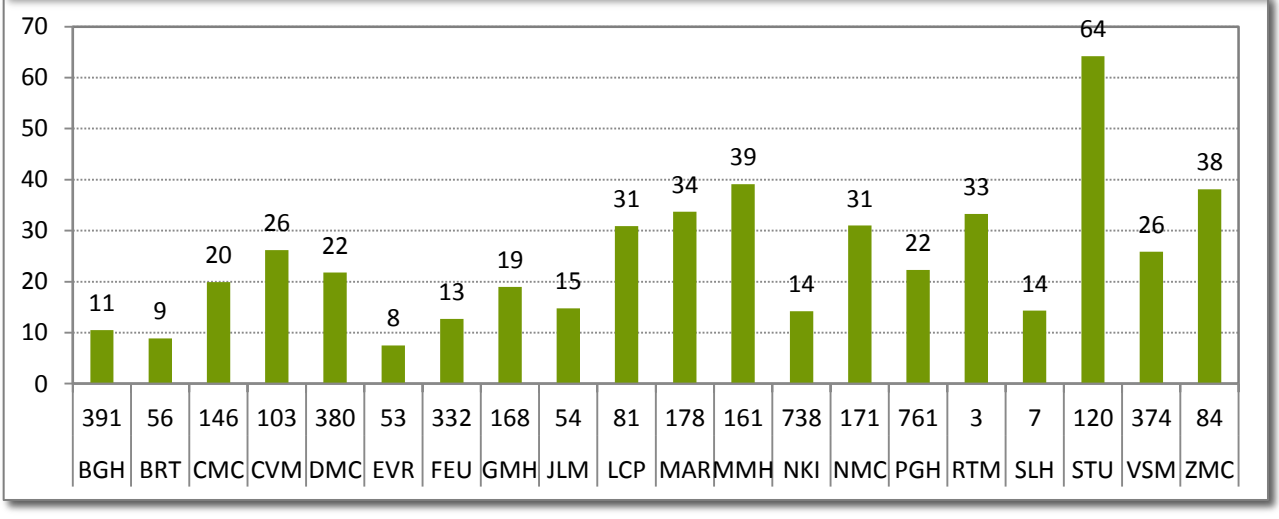
(Figures 3.44-3.45)

The *Enterobacteriaceae* producing ESBLs have been increasingly reported locally. Using ceftazidime to screen for ESBL-production,[2] the percentage of ESBL-suspects for the 2013 *E. coli* isolates are at 22%, with rates not significantly different from the 2012 reported rates (*p* value > 0.05).

Among the sentinel sites with at least 30 isolates of *E. coli* tested for ceftazidime-resistance, ESBL-suspect rates ranged from 8% to 64%. Collectively, when the *E. coli* ESBL-suspect rates by sentinel site were analyzed based on geographic location, cumulative rates from the sites in the National Capital Region was at 21% (n= 2,042). By island group, *E. coli* ESBL-suspect rates were highest for Visayas at 26% (n= 756), followed by Mindanao at 25% (n= 781) and then Luzon at 11% (n=2,824).

Figure 3.44 Geographic representation of percentage ESBL- suspect (ceftazidime-resistant) rates for *E. coli*, all ARSP sites, Jan-Dec 2013

Figure 3.45 Percentage ESBL- suspect (ceftazidime-resistant) *E. coli*, all ARSP sites, Jan-Dec 2013



Klebsiella sp. ESBL-suspect Rates

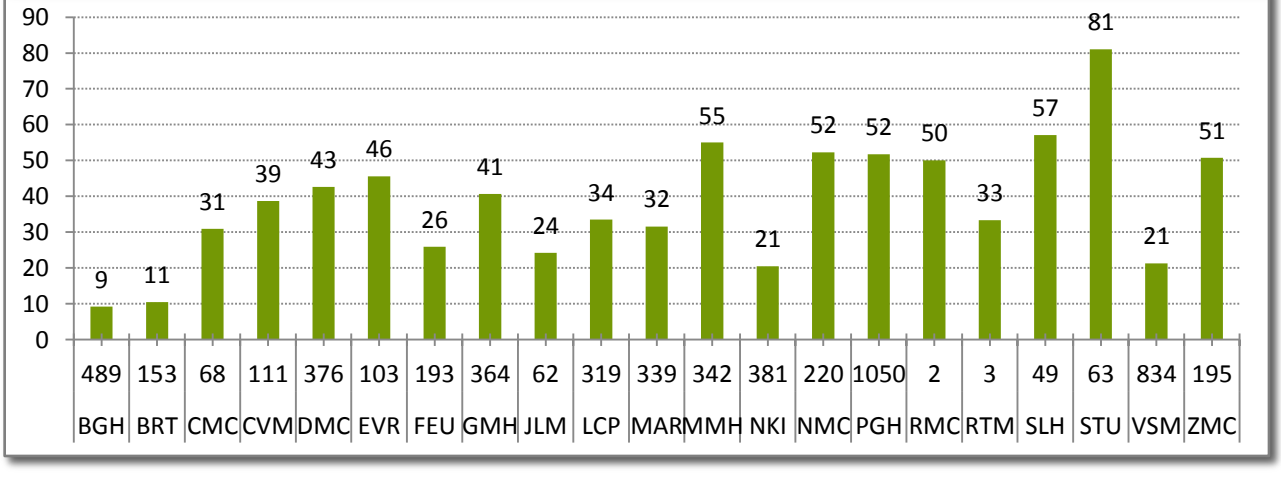
(Figures 3.46-3.47)

Using ceftazidime to screen for ESBL-production,[2] percentage of ESBL-suspects among *Klebsiella* sp. isolates for 2013 are at 36%. This *Klebsiella* species ESBL-suspect rate have significantly increased from 32% in 2012 to 36% in 2013 (*p* value 0.0001).

Over-all cumulative *Klebsiella* sp. ESBL-suspect rate for 2013 is at 36%. Among the sentinel sites with at least 30 isolates of *Klebsiella* sp. tested for ceftazidime-resistance, ESBL-suspect rates ranged from 9% to 81%. Collectively, when the *Klebsiella* sp. ESBL-suspect rates by sentinel site were analyzed based on geographic location, cumulative rates from the sites in the National Capital Region was at 42% (n= 2,060). By island group, *Klebsiella* sp. ESBL-suspect rates were highest for Mindanao at 46% (n= 859), followed by Visayas (n= 1,643) and Luzon (n= 3,214) at 34% each.

Figure 3.46 Geographic representation of percentage ESBL-suspect (ceftazidime-resistant) rates for *Klebsiella* sp., all ARSP sites, Jan-Dec 2013

Figure 3.47 Percentage ESBL- suspect (ceftazidime-resistant) *Klebsiella* sp., all ARSP sites, Jan-Dec 2013



ESBL-suspect *Enterobacteriaceae* Rates by Age Groups (Figure 3.48)

ESBL-suspect rates for *Escherichia coli* and *Klebsiella* species for 2013 were analyzed by age groups.

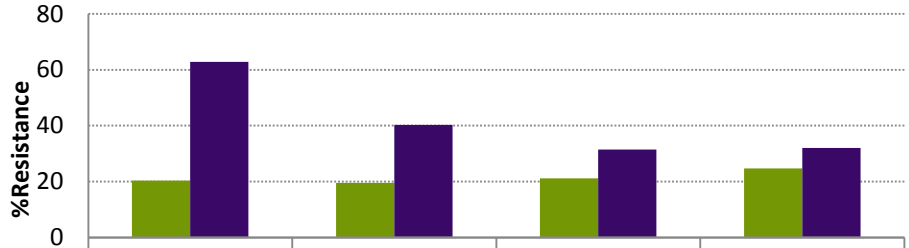
ESBL-suspect rates for *E. coli* were generally lower than those for *Klebsiella* species. ESBL-suspect rates for *E. coli* was highest for the 65 years and older age group at 25% (n= 1,105). In comparison, the 0-4 years age group had the highest ESBL-suspect rates for *Klebsiella* species at 63% (n=730).

ESBL-producing Isolates' Antimicrobial Susceptibility (Figure 3.49)

A subset of these ESBL-suspect isolates were also referred to the national reference laboratory at RITM for confirmatory testing; and a total of 221 and 392 isolates of *E. coli* and *Klebsiella* sp. respectively were subsequently confirmed to be ESBL-producing by phenotypic methodology.[2] Amongst the 221 *E. coli* and 392 *Klebsiella* species that were confirmed as ESBL-producing isolates, susceptibility data were analyzed and only the carbapenems retained predictable activity against these organisms.

Figure 3.48 ESBL-suspect (ceftazidime resistance) rates of *E. coli* % and *Klebsiella* sp., all isolates by age group, all ARSP sites, Jan-Dec 2013

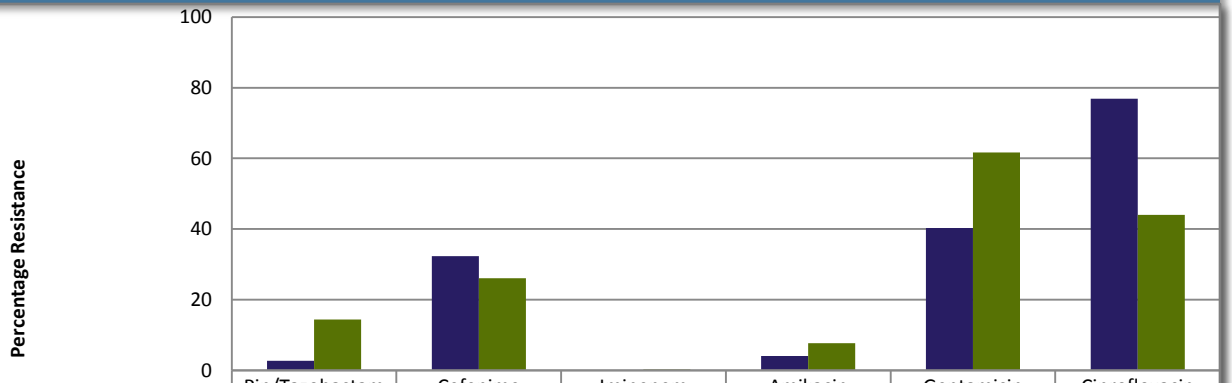
Number of isolates tested: 0-4 years old- E. coli 590, Klebsiella sp. 730; 5-19 years old- E. coli 374, Klebsiella sp. 404; 20-64 years old- E. coli 2416, Klebsiella sp. 3167; 65 years and older- E. coli 1015 Klebsiella 1580



	0-4	5-19	20-64	65+
% ceftazidime-resistant E. coli	20	20	21	25
% ceftazidime-resistant Klebsiella sp.	63	40	32	32

Age groups, in years

Figure 3.49 Percentage resistance of ESBL-producing *E. coli* and *Klebsiella* sp., all ARSP sites, Jan-Dec 2013



	Pip/Tazobactam	Cefepime	Imipenem	Amikacin	Gentamicin	Ciprofloxacin
ESBL(+) E. coli %R	3	32	0	4	40	77
ESBL(+) Klebsiella sp. %R	14.4	26.1	0.3	7.7	61.7	44

Carbapenem-resistant *Enterobacteriaceae*

Carbapenem-resistance amongst *Enterobacteriaceae* (CRE) is often secondary to the organism's production of carbapenemases. These are enzymes that directly hydrolyze beta-lactams, especially carbapenems. These isolates are often not only resistant to carbapenems but to most of available antibiotics.[3] For 2013 we used imipenem (the most widely tested carbapenem) to identify carbapenem-resistance amongst commonly isolated *Enterobacteriaceae* isolates locally. Over-all rates of imipenem-resistance amongst *E. coli* and *Klebsiella* sp. isolates for 2013 were 2% (n= 4,858) and 6% (n= 6,189), respectively.

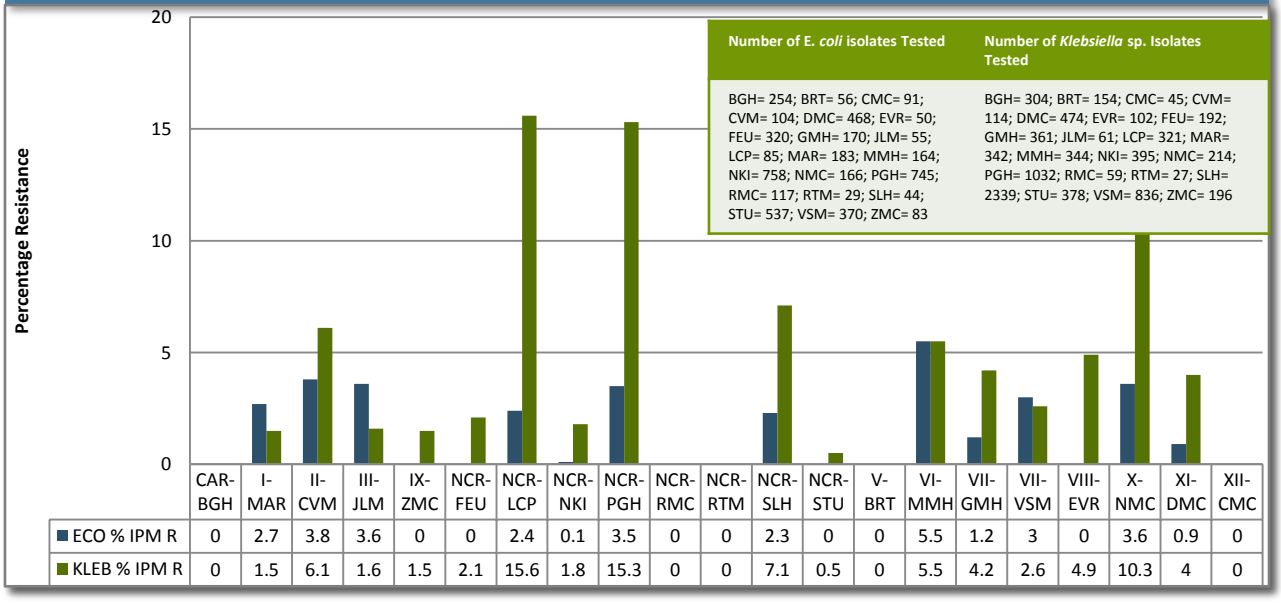
Comparing rates amongst participating sentinel sites with at least 30 *E. coli* isolates tested for susceptibility against imipenem, *E. coli* resistance rates for imipenem ranged from 0% to as high as 6% in one of the Visayas sites (n=164 *E. coli* isolates tested). Comparing rates amongst participating sentinel sites with at least 30 *Klebsiella* species isolates tested for susceptibility against imipenem, *Klebsiella* sp. resistance rates for imipenem ranged from 0% to as high as 16% in one of the Metro Manila sites (n=321 *Klebsiella* sp. isolates tested) (Figure 3.50).

Carbapenem-resistant *E. coli* and *Klebsiella* species isolates that were referred to the reference laboratory underwent phenotypic and genotypic analysis for carbapenemase production.

For 2013, 96% (21 out of the 22) of the carbapenem-nonsusceptible *E. coli* isolates were confirmed for production of the New Dehli Metallo-beta-lactamase (NDM-1) gene at the reference laboratory. Comparatively, 84% (64 out of the 75) of the carbapenem-nonsusceptible *Klebsiella* species isolates tested were similarly confirmed for production of the New Delhi Metallo-beta-lactamase (NDM-1) gene.

Antimicrobial susceptibility testing of these carbapenem-resistant isolates reveals that these isolates were mostly resistant to all tested beta-lactams including carbapenems, penicillins, beta-lactam-beta-lactamase inhibitor combinations, cephalosporins; monobactams; the fluoroquinolones; co-trimoxazole; tetracycline and chloramphenicol. In contrast, for those tested, these 2013 isolates remained susceptible to colistin and had variable susceptibility to the aminoglycosides.

Figure 3.50 Percentage imipenem-resistant *E. coli* and *Klebsiella* sp. by sentinel site, ARSP, Jan-Dec 2013



	CAR-BGH	I-MAR	II-CVM	III-JLM	IX-ZMC	NCR-FEU	NCR-LCP	NCR-NKI	NCR-PGH	NCR-RMC	NCR-RTM	NCR-SLH	NCR-STU	V-BRT	VI-MMH	VII-GMH	VII-VSM	VIII-EVR	X-NMC	XI-DMC	XII-CMC
ECO % IPM R	0	2.7	3.8	3.6	0	0	2.4	0.1	3.5	0	0	2.3	0	0	5.5	1.2	3	0	3.6	0.9	0
KLEB % IPM R	0	1.5	6.1	1.6	1.5	2.1	15.6	1.8	15.3	0	0	7.1	0.5	0	5.5	4.2	2.6	4.9	10.3	4	0

3.14 *Pseudomonas aeruginosa*

Pseudomonas aeruginosa is a gram-negative non-fermentative bacilli that is ubiquitous in nature and a major cause of healthcare-associated infection. It's intrinsic resistance to majority of antimicrobial agents & inherent versatility makes it a difficult to control & treat pathogen.[3]

Isolates

For 2013, there were 3,591 *Pseudomonas aeruginosa* isolates with relevant antimicrobial susceptibility test results analyzed. Most the these isolates were from the respiratory tract (58%) with 8% being comprised of invasive isolates (blood and CSF).

Antimicrobial Resistance

(Figure 3.51-3.52)

Piperacillin-tazobactam

Rates of resistance of *Pseudomonas aeruginosa* isolates for 2013 against piperacillin-tazobactam was at 11% (95% CI: 10.1-12.4; n= 3,087). Compared to rates from the previous year, *Pseudomonas aeruginosa* 2013 isolates showed significant increase in resistance for piperacillin-tazobactam from 9% in 2012 to 11% in 2013 (*p* value 0.0001).

Cephalosporins

Pseudomonas aeruginosa cumulative resistance rate for 2013 against the third generation cephalosporin ceftazidime is at 16% (95% CI; 14.4-16.9; n= 3,397) while rates against the fourth generation cephalosporin cefepime is at 14% (95% CI: 12.9-15.3; n= 3,302).

These *Pseudomonas aeruginosa* resistance rates against the cephalosporins have increased significantly for both antimicrobials when compared to reported 2012 rates. Ceftazidime resistance rates have increased from 13% in 2012 to 16% in 2013; while cefepime rates have also increased from 11% in 2012 to 14% in 2013 (*p* value 0.0001).

Monobactams

Rates of resistance of *Pseudomonas aeruginosa* isolates for 2013 against aztreonam is reported at 14% (95% CI: 12..6-15.1; n= 2,882). Compared to 2012 aztreonam resistance rates, 2013 *Pseudomonas aeruginosa* rates of resistance showed significant increase from the reported rate of 13% in 2012 to the 14% resistance rate for 2013 (*p* value 0.0001).

Aminoglycosides

Rates of resistance of *Pseudomonas aeruginosa* isolates for 2013 10% for amikacin (95% CI: 8.8-10.9; n= 3,313) and 17% for gentamicin (95% CI: 15.9-18.6; n= 3,046). Amikacin resistance rates significantly increased from the reported rate of 9% in 2012 to 10% in 2013 (*p* value 0.0001). Comparatively, gentamicin rates remained at 17% for both 2012 and 2013.

Fluoroquinolones

Rates of resistance for *Pseudomonas aeruginosa* against ciprofloxacin for 2013 is at 17% (95% CI: 15.5-18.2; n= 3,105). Although declining rates of resistance against ciprofloxacin are noted for the past 10 years, rates for 2013 do not differ significantly from that reported for 2012 (*p* value 0.942)

Carbapenems

Cumulative resistance rates of *Pseudomonas aeruginosa* against the carbapenems- imipenem is at 20% (95% CI: 18.3-21; n= 3,417); while resistance rates against meropenem is at 17% (95% CI: 15.8-18.3; n= 3,283) for 2013. Both cumulative rates of resistance have significantly increased when compared to 2012 *Pseudomonas aeruginosa* resistance rates. *Pseudomonas aeruginosa* imipenem resistance rates have increased significantly from the reported rate of 17% in 2012 to the 20% for 2013. Similarly, *Pseudomonas aeruginosa* resistance rate against meropenem have increased from the reported rate of 15% in 2012 to 17% in 2013 (*p* value 0.0001).

Figure 3.51 Percent resistance of *Pseudomonas aeruginosa*, all ARSP sites, Jan-Dec 2013

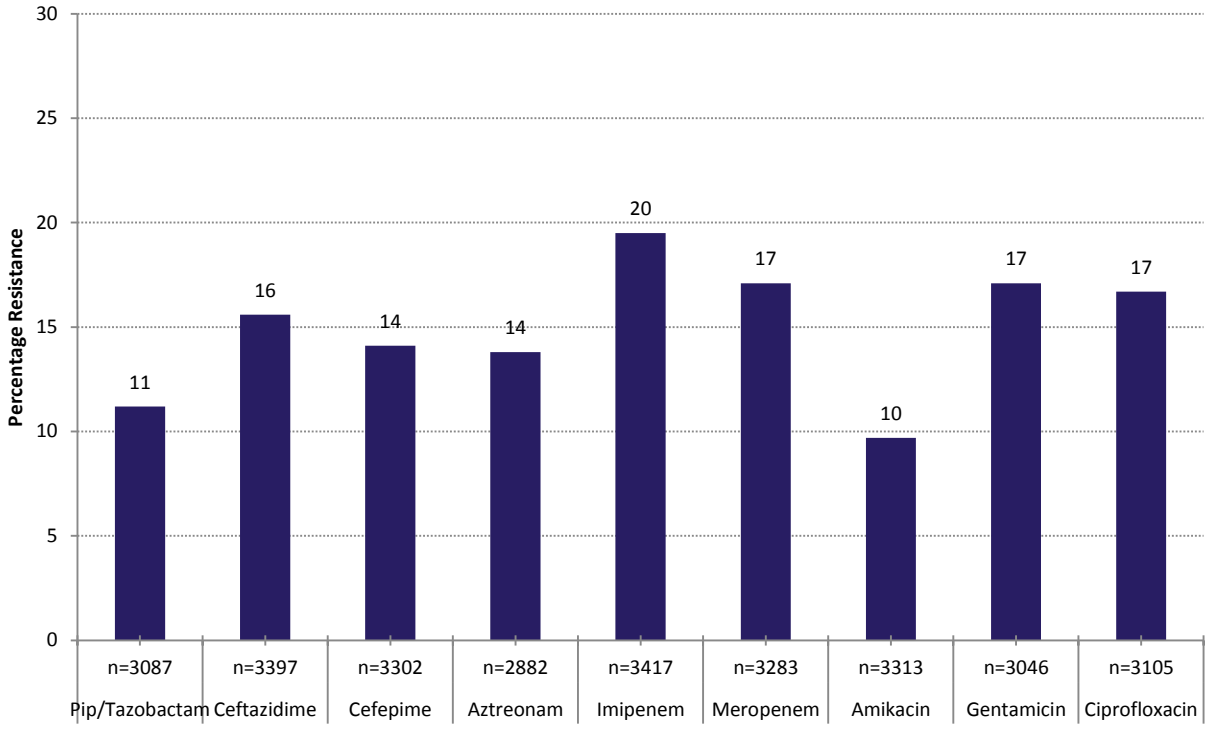
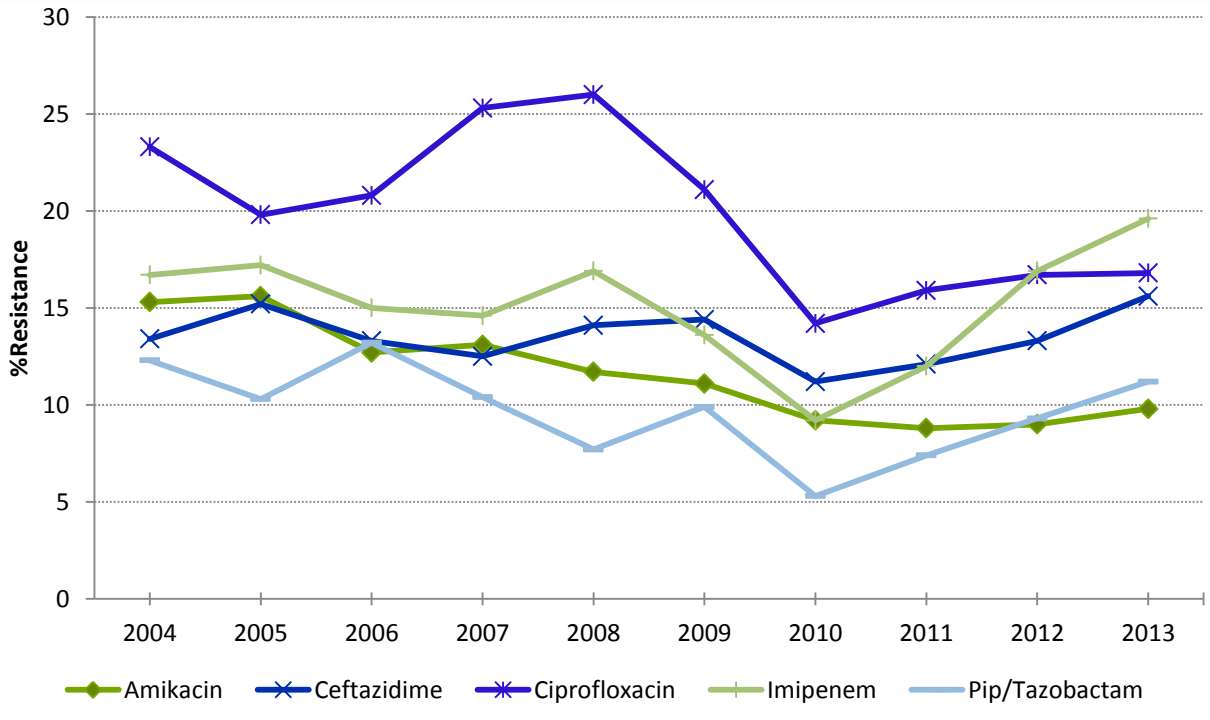


Figure 3.52 Yearly resistance rates of *Pseudomonas aeruginosa*, all ARSP sites, 2004-2013



3.15 *Acinetobacter baumannii*

Acinetobacter baumannii are gram-negative, non-fermentative rods that are common in environment and hospitals and is emerging as an important global, multidrug-resistant gram-negative nosocomial pathogen especially amongst compromised hosts.[3]

Isolates

For 2013, there were 2,327 *Acinetobacter baumannii* isolates with relevant antimicrobial susceptibility test results analyzed. This was 72% more than the number of isolates for 2012. The most common specimens were respiratory isolates (57%). *Acinetobacter baumannii* is also the 2nd most frequent CSF and 3rd most common respiratory specimen isolate for 2013.

Antimicrobial Resistance

(Figures 3.53-3.56)

Sulbactam

Rates of resistance of 2013 *Acinetobacter baumannii* isolates against ampicillin-sulbactam is at 42% (95% CI: 39.3-44.1; n= 1,651). These rates have been steadily increasing for the past 10 years, with 2013 rates of 42% more than twice of that reported 10 years ago in 2004 at 17%.

Aminoglycosides

Rates of resistance of 2013 *A. baumannii* isolates was at 39% each for both amikacin (95% CI: 36.4-40.7; n= 2,037) and gentamicin (95% CI: 36.6-41.1; n= 1,846). Amikacin and gentamicin resistance rates have been increasing for the past few years. *A. baumannii* amikacin resistance rates have significantly increased from the reported rate of 31% in 2012 to 39% in 2013 (*p* value 0.0001). *A. baumannii* resistance rate against gentamicin have similarly increased non-significantly from the reported rate of 35% in 2012 to 29% in 2013 (*p* value 0.059).

Fluoroquinolones

Rates of resistance for *Acinetobacter baumannii* against ciprofloxacin for 2013 is at 42% (95% CI: 40.2-44.6; n= 1,970). Increasing rates of resistance for *Acinetobacter baumannii* against ciprofloxacin were noted for the past few years. *Acinetobacter baumannii* ciprofloxacin resistance have significantly increased from the reported rate of 29% in 2012, to the 42% cumulative resistance rate for 2013 (*p* value 0.0001).

Cephalosporins

Rates of resistance of *Acinetobacter* baumannii is at 40% against ceftazidime (95% CI: 38-42.1; n= 2,205) and 42% against cefepime (95% CI: 40.3-44.5; n= 2,205) for 2013. These rates have increased when compared to the *Acinetobacter baumannii* 2012 rate against ceftazidime of 30% and cefepime of 22%.

Carbapenems

Cumulative resistance rates of *Acinetobacter baumannii* against the carbapenem imipenem is at 40% (95% CI: 37.6-41.8; n= 2,121) for 2013. These resistance rates have significantly increased when compared to reported 2012 cumulative resistance rate against imipenem with reported 2012 rate at 32% in 2012 increasing to 40% for 2013 (*p* value 0.0001).

Invasive *A. baumannii* Resistance Rates

In order to characterize the pathogenic subset of the *Acinetobacter baumannii* isolates, the subset of isolates from blood specimens were analyzed for their susceptibility patterns.

Compared to rates for all *Acinetobacter baumannii* isolates reported for 2013, we report similar cumulative resistance rates for the following antibiotics tested: ampicillin-sulbactam at 41% (n= 174); gentamicin at 38% (n=248); and amikacin at 37% (n=288). In contrast, the invasive isolates of *Acinetobacter baumannii* had significantly lower resistance rates against ciprofloxacin at 23% (n= 258) and imipenem at 19% (n= 291) when compared to all *Acinetobacter baumannii* isolates' cumulative resistance rates for 2013 (*p* value < 0.05).

Figure 3.53 Percent resistance of *Acinetobacter baumannii*, all ARSP sites, Jan-Dec 2013

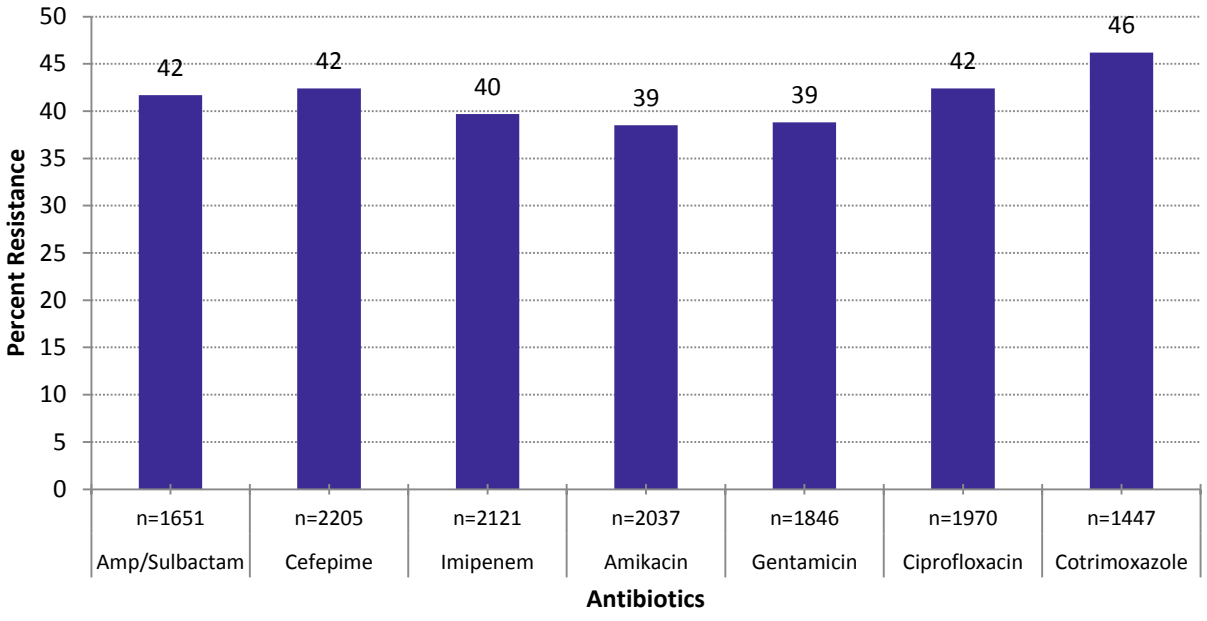


Figure 3.54 Percent resistance of invasive *Acinetobacter baumannii* (blood isolates), all ARSP sites, Jan-Dec 2013

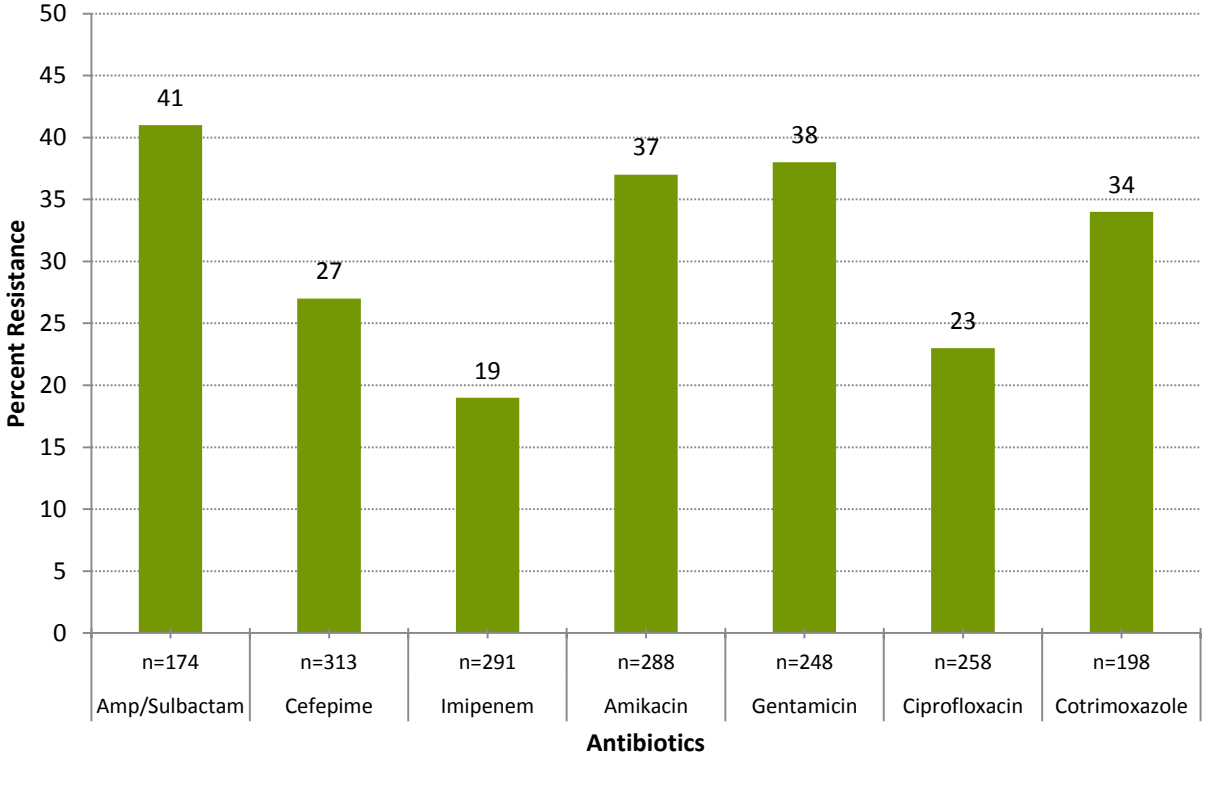


Figure 3.55 Yearly ampicillin-sulbactam, amikacin & gentamicin resistance rates of *A. baumannii*, all ARSP sites, 2004-2013

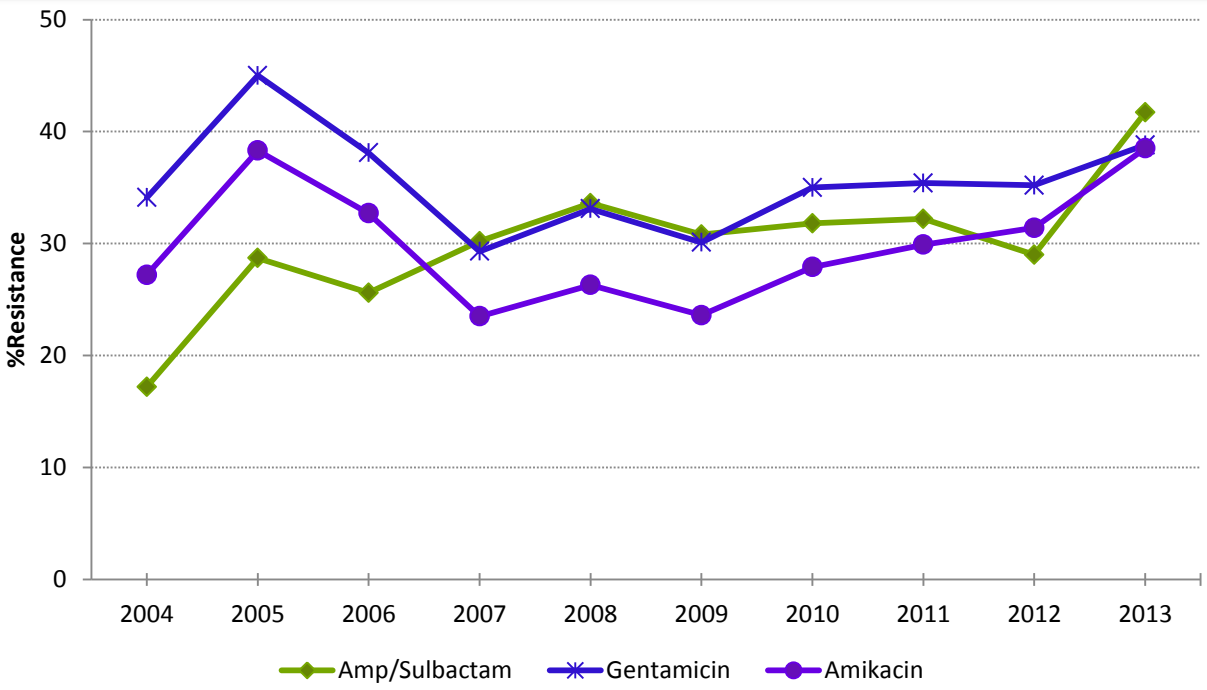
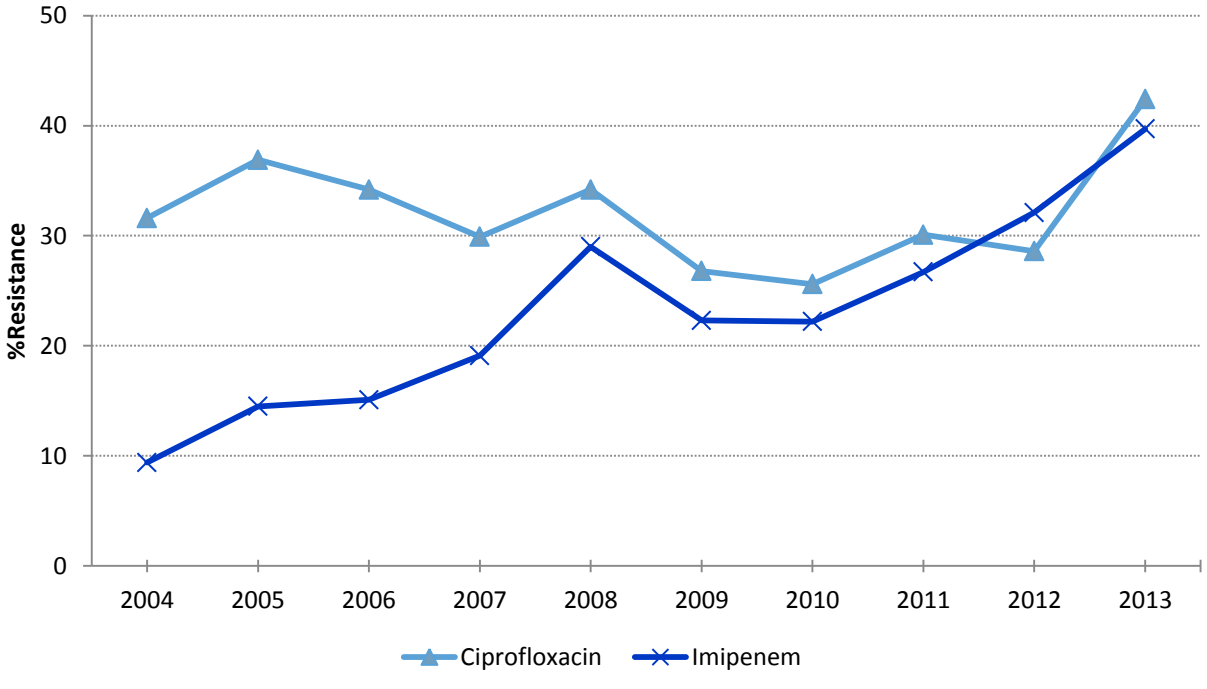


Figure 3.56 Yearly ciprofloxacin & imipenem resistance rates of *A. baumannii*, all ARSP sites, 2004-2013



Multidrug-resistant *Pseudomonas aeruginosa* & *Acinetobacter baumannii*

In the recent years, there had been a growing recognition of the emergence of gram-negative bacteria, most especially *Pseudomonas aeruginosa* and *Acinetobacter baumannii,* with resistance to several classes of antibiotics.

The definitions employed for **multidrug-resistant (MDR), extensively drug resistant (XDR)** and **pandrug-resistant (PDR)** *Pseudomonas aeruginosa* and *Acinetobacter baumannii* in this section would be as described in Tables 3.8 and 3.9 below.

Table 3.8 Antibiotic categories for *Pseudomonas aeruginosa* and *Acinetobacter baumannii* (Magiorakos AP etal, 2012)

Antibiotic Categories for *P. aeruginosa*	Antibiotic Categories for *A. baumannii*
Aminoglycosides	Aminoglycosides
Antipseudomonal carbapenems	Antipseudomonal carbapenems
Antipseudomonal cephalosporins	Extended-spectrum cephalosporins
Antipseudomonal fluoroquinolones	Antipseudomonal fluoroquinolones
Antipseudomonal penicillin+ β-lactamase inhibitors	Antipseudomonal penicillin+β-lactamase inhibitors
Monobactams	Penicillins plus beta-lactamase inhibitors
Phosphonic acid	Folate pathway inhibitors
Polymyxins	Polymyxins
	Tetracyclines

Table 3.9 Definition of MDR, XDR and PDR (Magiorakos AP etal, 2012)

Term	Definition
MDR	Multi-drug resistant: Resistance of the organism to at least 1 or more agents in 3 or more classes of antimicrobial categories
XDR	Extensively-drug resistant: Resistance to at least 1 agent in all but 2 or fewer antimicrobial categories
PDR	Pandrug-resistant: Non-susceptibility to all agents in all antimicrobial categories
Possible XDR/PDR	In cases when incomplete panel of antimicrobials are tested

MDR & Possible-XDR Rates of *Pseudomonas aeruginosa* (Table 3.10)

For 2013, we looked at data for all isolates of *Pseudomonas aeruginosa* from all types of specimens. These were analyzed for rates of multi-drug resistance (MDR) and possible-extensively drug-resistance (XDR) (some of the panel antimicrobials as defined previously were not available for testing and use locally as of this publication).

For 2013, MDR rate for *Pseudomonas aeruginosa* was at 22% while possible-XDR rate was at 13% (n= 3,591 isolates). In comparison, reported rates for 2012 *Pseudomonas aeruginosa* MDR and possible-XDR were at 21% and 17%, respectively.

MDR & Possible XDR Rates of Invasive *Pseudomonas aeruginosa* (Table 3.10)

When the 2013 subgroup of *Pseudomonas aeruginosa* isolates from blood specimens (invasive isolates) were analyzed, MDR rates were reported at 13% while possible-XDR rates were at 6% (n= 249 blood isolates).

MDR & Possible XDR Rates of *Acinetobacter baumannii* (Table 3.10)

For 2013, we looked at data for all isolates of *Acinetobacter baumannii* from all types of specimens. These were analyzed for rates of multi-drug resistance (MDR) and possible-extensively drug-resistance (XDR) (some of the panel antimicrobials as defined previously were not available for testing and use locally as of this publication).

Comparatively, for 2013 MDR rate for *Acinetobacter baumannii* was at 56% while possible-XDR rate was reported at 34% (n= 2,327 isolates). In comparison, reported rates for 2012 were 58% and 35%, respectively.

MDR & Possible XDR Rates of Invasive *Acinetobacter baumannii* (Table 3.10)

When the subgroup of *Acinetobacter baumannii* isolates from blood specimens (invasive isolates) were analyzed, MDR rate was at 21% while possible-XDR rate was at 5% (n= 335 blood isolates).

Table 3.10 Rates of MDR and Possible XDR *Pseudomonas aeruginosa* and *Acinetobacter baumannii*, all ARSP sites, Jan-Dec 2013

Organism	Number of isolates tested	Percentage MDR	Percentage Possible XDR
Pseudomonas aeruginosa			
All Isolates	3,591	22%	13%
Blood Isolates	249	13%	6%
Acinetobacter baumannii			
All Isolates	2,327	56%	34%
Blood Isolates	335	21%	5%

3.16 Recommendations

Based on the reported antimicrobial resistance surveillance data for 2013:

Respiratory Bacterial Pathogens

- Infections secondary to *Streptococcus pneumoniae* can still be covered with penicillin or one of the anti-pneumococcal macrolides, although there is a need to closely monitor the changing trends of resistance among pneumococci. Improved local data on serotype distribution will allow for better surveillance information especially needed for vaccination recommendations.
- Due to high resistance rate of *Haemophilus influenzae* to ampicillin, this is no longer recommended for empiric therapy for infections secondary to the pathogen. Recommended empiric treatment for suspected *H. influenzae* infections may consist of beta-lactam-beta-lactamase inhibitor combinations, extended spectrum oral cephalosporins and the newer macrolides.

Bacterial Enteric Pathogens

- Empiric treatment for suspected uncomplicated typhoid fever could still consist of either chloramphenicol or co-trimoxazole or amoxicillin/ampicillin. There are increasing reports of nalidixic acid resistance and ciprofloxacin non-susceptibility which may result to clinical treatment failures. Microbiological data is recommended to aid in pathogen directed therapy.
- Increasing rates of ciprofloxacin resistance should remind clinicians to use antibiotics judiciously in Salmonella gastroenteritis, as this is usually a self-limited disease.
- In view of the emerging resistance of *Shigellae* to the quinolones and limited data available, more vigilant surveillance of the resistance pattern of this organism should be pursued by encouraging clinicians to send specimens for culture.
- Tetracycline, chloramphenicol and co-trimoxazole remain good treatment options for cholera cases.

Sexually-transmitted Bacterial Pathogens

- Limited data is available on *N. gonorrhoeae* in recent years, although based on reported isolates, ceftriaxone remains as empiric antibiotic of choice for gonococcal infections. More vigilant surveillance of the resistance patterns of this organism should be pursued by encouraging clinicians to send specimens for culture.

Gram-positive Cocci

- In view of the continued high rates of methicillin/oxacillin resistance among staphylococci there may be an indication to shift empiric treatment of suspected staphylococcal infections from oxacillin to alternative agents such as co-trimoxazole, doxycycline, clindamycin, linezolid or vancomycin.

Gram-negative Bacilli

- Hospitals should base their treatment recommendations for the *Enterobacteriaceae* on their institution's prevailing resistance patterns as these patterns have been found to be variable from hospital to hospital. High percentage of possible ESBL-producing isolates complicate treatment of serious infections caused by these organisms and may lead to increase use of carbapenems that may favor the further spread of the carbapenem-resistant *Enterobacteriaceae*. Prudent use of antimicrobials and comprehensive infection control measures serve as cornerstones of interventions aimed at preventing selection and transmission of resistant bacteria.
- Increasing resistance among the bacterial organisms *P. aeruginosa* and *A. baumannii* continues to be a concern as both organisms carry intrinsic resistance to a number of antimicrobial classes and acquisition of additional resistance severely limits the available treatment options. Prudent antimicrobial use, monitoring of resistance patterns and antimicrobial use along with improved standards of infection control are essential in addressing this clinical and public health concern.

3.17 References

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4 Magiorakos AP, Srinivasan A, Carey RB, etal. "Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance." *Clin Microbiol Infect*, 2012: 18: 268-281.

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5. CONTACT DETAILS OF ARSP SENTINEL SITES

5. Contact Details of ARSP Sentinel Sites

Table 5.1 Table of details of ARSP sentinel sites, 2013

HOSPITAL NAME	ADDRESS	CONTACT NUMBER
Baguio General Hospital and Medical Center	Governor Pack Road, Baguio City Benguet 2600	074-442-6230/4216 loc.358 Fax: 074-443-8342
Batangas Regional Hospital	Kumintang Ibaba, Batangas City	043-723-0517/ 043-980-1738 Fax: 043-723-0165
Bicol Regional Training and Teaching Hospital	Rizal St. Legaspi City Albay	052-483-1089 loc. 2648 Fax: 052-483-0016
Cagayan Valley Medical Center	Carig, Tuguegarao City	078-304-0033 loc. 160 Fax: 078-304-3789/ 846-7269
Corazon Locsin Montelibano Memorial Hospital	Bacolod City	034-435-5600 Fax: 034-433-2697
Cotabato Regional Hospital and Medical Center	Cotabato Regional Hospital and Medical Center Cotabato City	064-421-2340 loc. 116 Fax: 064-421-2192
Dr. Rafael S. Tumbokon Memorial Hospital	Kalibo, Aklan	036-268-7062/036-268-6299 Fax: 036-268-8579
Eastern Visayas Regional Medical Center	Tacloban City, Leyte	053-321-3136 Fax: 053-321-8724
Far Eastern University Hospital	Regalado Ave., West Fairview Quezon City 1118	02-427-0213 loc. 1128 Fax: 427-5755
Gov. Celestino Gallares Memorial Regional Hospital	Tagbilaran City, Bohol	038-501-7531 loc. 220 Fax: 038-412-3181
Jose B. Lingad Memorial Regional Hospital	Dolores, City of San Fernando, Pampanga	045-961-2808 Telefax: 045-961-3921
Lung Center of the Philippines	Quezon Avenue, Diliman Barangay Central, Quezon City	02-924-6101 loc 286 Fax: 02-928-8125
Mariano Marcos Memorial Hospital and Medical Center	San Julian, Batac Ilocos Norte 2906	077-792-3144 Fax: 077-792-3133/077-617-1517
National Kidney and Transplant Institute	East Avenue, Quezon City 1100	02-981-0400 loc. 1048 Fax: 926 - 8921
Northern Mindanao Medical Center	Capitol Compound, Cagayan de Oro City 9000	08822-725-735 Fax: 08822-721-794 Trunkline 08822-726-362
Philippine General Hospital	Taft Avenue, Ermita Manila	02-554-8400 loc. 3206 Fax: 02-536-4659
Pangasinan Provincial Hospital	San Carlos, City Pangasinan	Fax: 075-532-2603
Rizal Medical Center	Shaw Boulevard Extension Pasig City, 1600	02-671-9740 to 43 loc 103 Fax: 02-671-9617/ 671-9616
Research Institute for Tropical Medicine	FCC Compound, Alabang Muntinlupa, City 1781	02-807-2628 loc. 604
San Lazaro Hospital	Bldg. 17 Quiricada St. Sta. Cruz, Manila	02-732-3776 loc. 476 Fax: 711-4117
Southern Philippines Medical Center (formerly Davao Medical Center)	J.P.Laurel Avenue, Davao City Davao del Sur 8000	082-227-2731 Fax: 082-221-7029
University of Sto. Tomas Hospital	España St., Manila 1008	02-731-3001 loc. 2426 Fax: 02-731-1985
Vicente Sotto Memorial Medical Center	B. Rodriguez St., Cebu City Cebu 6000	032-253-9891-99 Fax: 032-254-0057
Zamboanga City Medical Center	Veterans Ave., Sta. Catalina, Zamboanga 7000	062-991-2934 loc. 146 Fax: 062-991-0573
Zamboanga del Norte Medical Center	Dipolog City	065-212-5080 to 84 Fax: 065-212-2975 Fax: 065-212-3625 (ZaNorte)

ANNEXES

Annex 1. Total number of bacterial isolates by sentinel site, DOH-ARSP, 2004-2013

SENTINEL SITES	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	Change %
PGH^	6383^	9824	4511^	-	-	-	-	-	-	7093	100
RMC	1007	497	506	757	757	878	962	845	942	1207	22
NKI‡	4468	5331	4009	2996	3112	3345	3681	2726	2403	2179	-10
LCP	899	1949	5160	2548	2701	2694	2	1233	2083	2253	8
RTM^^	192^^	515	414	361	335	280	348	328	383	303	-26
SLH	333	698	881	461	662	468	615	409	318	1132	72
GMH*	799	359	522	886	826	1151	936	1119	1521	1307	-16
ZMC*	627	788	550	434	440	599	1060	686	721	822	12
FEU	1286	1067	740	684	690	699	864	1064	931	1050	11
STU	2011	1381	1124	1329	1180	1722	1470	752	1788	2050	13
EVR§	145	694	799	491	466	340	530	744	507	697	27
MMH§	517	451	567	380	525	562	590	855	1153	1413	18
DMC//	2103	2369	2487	2161	2374	2523	2870	2439	3332	3456	4
VSM//	967	1224	991	1063	1241	1447	1931	2142	2450	3171	23
BGH&	1009	1344	1213	1041	1329	2129	2199	1916	1972	2583	24
CMC¶	475	742	796	686	541	459	600	595	639	796	20
BRT&	344	485	399	388	401	618	486	537	677	611	-11
RTH#			40	32	19	-	-	-	-	-	-
ZPH#			56	67	53	38	11	-	-	-	-
MAR						2275	1898	1851	1928	1773	-9
BRH						1008	791	304	38	-	-
CVM**						248	907	790	944	1100	14
JLM**						387	1024	643	655	502	-30
NMC**						814	1817	1776	1684	2131	21
TOTAL	23749	29782	25768	16765	17652	24684	25592	23754	27069	37629	

* Data from August 1994 only

‡ No data submitted from July - December 1997

§ Data from October 1998 only; No data June 2008

// Data from February 2000

¶ Data from September 2000

&Data from January 2001

^ Data from January - June 2004 only, No data for Apr, Jun-Dec 2006

^^ Data from January to May 2004 only

Neisseria gonorrhoea isolates only

**Data from August 2009 only

Annex 2. Isolate Referrals to ARSRL, DOH ARSP, 2013

Organisms Identification at the Sentinel Site	Number of 2013 Isolate Referrals
Respiratory Pathogens	
Streptococcus pneumoniae	126 isolates
Haemophilus influenzae	106 isolates
Moraxella species	17 isolates
Enteric Pathogens	
Salmonella Typhi	69 isolates
Salmonella species	54 isolates
Salmonella Paratyphi B	2 isolates
Shigella species	4 isolates
Vibrio cholerae	29 isolates
Neisseria gonorrhoeae	24 isolates
Staphylococcus aureus	406 isolates
***Staphylococcus* species**	675 isolates
***Enterococcus* species**	28 isolates
Escherichia coli	383 isolates
***Klebsiella* species**	622 isolates
Pseudomonas aeruginosa	442 isolates
***Acinetobacter* species**	216 isolates
Others	530 isolates