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ANTIMICROBIAL RESISTANCE SURVEILLANCE PROGRAM

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FIGHTING ANTIMICROBIAL RESISTANCE THROUGH SURVEILLANCE

2012 DATA SUMMARY REPORT

Executive Summary
2012 ARSP Annual Report

Summary of ARSP 2012 Data

2012 Isolates

- Resistance data for 27,069 bacterial isolates coming from 21 hospital bacteriology laboratories located in 14 regions of the Philippines were analyzed for 2012. Luzon sentinel sites contributed 55.6% of the 2012 data, while the remaining 20.8% and 23.6% of the data came from Visayas and Mindanao sites, respectively.

Antimicrobial Resistance Patterns

Enteric Pathogens

- *Salmonella* Typhi isolates have remained susceptible to first line agents ampicillin, chloramphenicol and co-trimoxazole with resistance rates at <1% for each agent for 2012. There were 6 reported nalidixic acid resistant *S*. Typhi for 2012, of which 5 had zone diameters or minimum inhibitory concentrations (MICS) to ciprofloxacin in the intermediate zone.

- Nontyphoidal *Salmonellae* (NTS) showed higher resistance rates when compared to *S.* Typhi to chloramphenicol 13%, ampicillin 39.6% and co-trimoxazole 34.5%. For 2012, we note marked increase in ciprofloxacin resistance rates of NTS from 1.8% in 2011 to 14.4% in 2012 (*p* value 0.007). The most common serotype of nontyphoidal *Salmonella* identified for 2012 were *S*. Enteritidis (10 isolates) and *S*. Typhimurium (6 isolates).

- Combined 2010 and 2012 data shows high rates of resistance for *Shigella* to previous first line agents: co-trimoxazole was 71.8%, chloramphenicol at 54.3% and ampicillin at 68.3%; and ciprofloxacin at 14.4%.

- *Vibrio cholerae* isolates remain susceptible to first line agents: chloramphenicol, co-trimoxazole and tetracycline with resistance rates <4% for each agent for 2012.

Respiratory Pathogens

- Among the respiratory and invasive isolates of *Streptococcus pneumoniae,* there was a nonsignificant increase in resistance to penicillin (MIC ⩾ 0.12 mcg/ml)) from 4% in 2011 to 8% in 2012. While 2012 resistance rates to other commonly used antibiotics for treatment of pneumococcal infections are 8.7% to chloramphenicol, 22.4% to co-trimoxazole and 4.3% to erythromycin. There was no reported ceftriaxone-resistant isolate for 2012. The most common serotypes identified for 2012 are serotypes 5, 1 and 14.

- Among the 2012 isolates of *Haemophilus influenzae* – 16.7%, 8.2%, 34.1% and 6.7% were resistant to ampicillin, chloramphenicol, co-trimoxazole and ampicillin-sulbactam, respectively. There remains to be no reported azithromycin resistant *H. influenzae* for 2012.

- *Moraxella catarrhalis* isolates reported for 2012 showed relatively high rates of resistance against co-trimoxazole (51.2%) and amoxicillin-clavulanic acid (30.1%). There were no reported erythromycin resistant isolates since 2010.

Gonococci

- Combined 2011 and 2012 Neisseria gonorrheae isolates exhibited high levels of resistance to ciprofloxacin at 78.8% while there remains to be no reported cefixime and ceftriaxone resistant isolate for 2011 to 2012.

Healthcare-associated Pathogens

- There has been increasing oxacillin-resistant *Staphylococcus aureus* (MRSA) rates for the past 10 years with a nonsignificant increase in oxacillin resistance from 52.6% in 2011 to 54.9% in 2012 (p value >0.05). The 2012 *S. aureus* isolates have remained relatively susceptible, as in the previous years, to the antimicrobials tetracycline at 6.8%, clindamycin at 8.4%, co-trimoxazole at 9.3%, erythromycin at 10.9%, and linezolid at 1.6%. There was no vancomycin resistant isolate reported for 2012.

- Ampicillin resistance among *E. faecalis* and *E. faecium* was at 8.5% and 59.2%, respectively. There were no reported vancomycin resistant *E. faecalis* and E. faecium for 2012.

- Many of the Enterobacteriaceae showed high resistance rates to several antibiotics tested and varied from sentinel site to sentinel site. The presence of extended spectrum beta lactamases (ESBLs) has continued to be documented among *E. coli* and *Klebsiella* from almost all sentinel sites in 2012. The estimated rates of ESBL for *E. coli* and *Klebsiella* were 20.9% and 31.7%, respectively. Likewise, resistance to carbapenems is increasingly reported with imipenem resistance rates at 2.6% and 3.4% against *E. coli* and *Klebsiella sp.,* respectively. Carbapenemase production has also been documented amongst the isolates, with majority harboring the NDM gene.

- Multidrug-resistance has been increasingly documented among gram-negative organisms. These are organisms that are resistant to at least 1 agent in 3 or more classes of antimicrobial categories. Among isolates of *Pseudomonas aeruginosa*, 21% (552 out of 2580) were multidrug resistant while 58% (766 out of 1344) of *Acinetobacter baumannii* isolates were multidrug resistant.

- The percentage of bacterial isolates cultured after 48 hours from hospital admission (presumptive nosocomial infections without clinical confirmation) was 38%. The most common presumptively nosocomial pathogens for 2012 are *Klebsiella* sp., *Escherichia coli* and *Pseudomonas aeruginosa*, in decreasing order.

Recommendations

- Empiric treatment for suspected uncomplicated typhoid fever could still consist of either chloramphenicol, cotrimoxazole or amoxicillin/ampicillin. There are increasing reports of nalidixic acid resistance and ciprofloxacin nonsusceptibility which may result to clinical treatment failures. Microbiological testing 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 the subset of patients requiring antibiotics for treatment such as in bacteremia due to nontyphoidal *Salmonellae*, ceftriaxone maybe a better treatment option.

- Ciprofloxacin may still be considered as the drug of choice for treatment of suspected shigellosis among adult patients while nalidixic acid may be considered as empiric treatment for the pediatric age group. In view of the emerging resistance of *Shigellae* to the quinolones, continued surveillance of the resistance pattern of this organism should be pursued with the possibility of considering alternative antimicrobial treatment such as ceftriaxone or azithromycin if the rates continue to rise.

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

- 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.

- Due to high resistance rate of *Haemophilus influenzae* to ampicillin, this is no longer recommended for empiric therapy. 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.

- Ceftriaxone remains as empiric antibiotic of choice for gonococcal infections.

- In view of the continued high rates of methicillin/oxacillin resistance among staphylococci in 2012, 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. The rising MRSA rates necessitate clear local treatment guidelines for managing suspected cases.

- 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. There is need to closely monitor the presence of ESBLs and carbapenemase resistance among the Enterobacteriaceae considering the very limited treatment options available.

- There is a need to closely monitor the emergence of MDR an XDR gram-negative bacteria such as *Pseudomonas aeruginosa* and *Acinetobacter baumannii* as there is little available in terms of antibiotics for treatment.

- Increasing rates of MRSA, ESBL-producing Enterobacteriaceae, carbapenem resistant Enterobacteriaceae and the MDR and possible XDR organisms in the hospital should signal for a review of infection control procedures and its implementation.

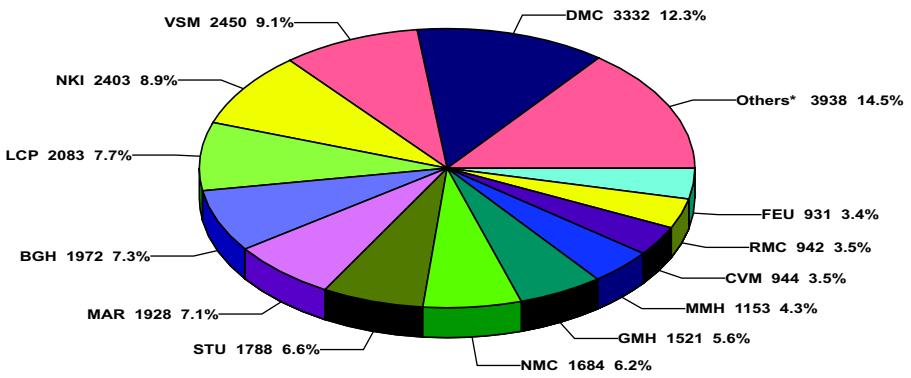
Highlights of the 2012 Data

Highlights of the 2012 Data

Resistance data for 27,069 isolates, at one isolate per patient, were reported and analyzed for 2012. This was a 12% increase in number when compared to that reported in 2011. This was mainly due to an increase in the number of bacterial isolates reported from 15 out of the 21 active sentinel sites, namely STU, LCP, DMC, MMH, GMH, BRT, CVM, RTM, VSM, RMC, CMC, ZMC, MAR, BGH and JLM. On the other hand, 6 sentinel sites had decreased number of reported isolates for 2012, namely: BRH, EVR, SLH, FEU, NKI, and NMC. The Philippine General Hospital (PGH) had no data submission since 2007.

Of the total number of isolates for 2012, 55.6% were from Luzon,20.8% were from Visayas and 23.6% were from the Mindanao hospital sentinel sites. The 7 active Metro Manila sites were able to contribute 32.7% of the total data (Figure 1a and Table 1).

Figure 1a. Percent isolate contribution of each sentinel site, DOH ARSP, 2012
(N =27,069)
1 ISOLATE PER PATIENT



* isolates contribution from the following hospitals are less than 3% of the total:
ZMC=721; BRT=677; JLM=655; CMC=639; EVR=507; RTM=383; SLH=318; BRH=38

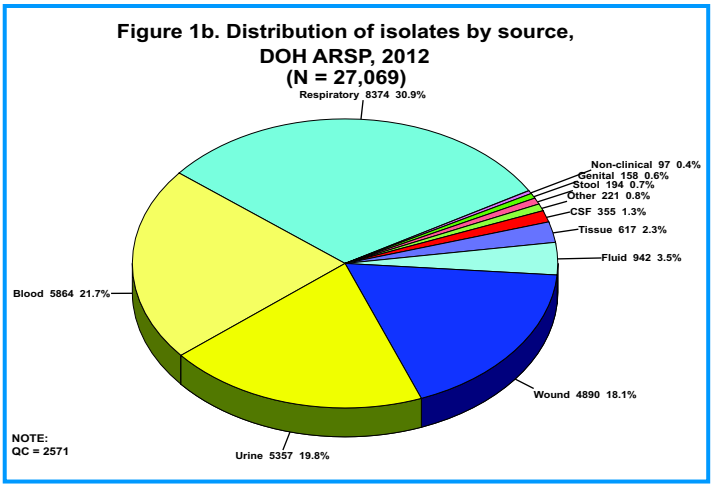
Table 1. Total number of bacterial isolates by sentinel site, DOH ARSP, 2003-2012

SENTINEL SITES	2003	2004	2005	2006	2007	2008	2009	2010	2011		2012
Philippine General Hospital	PGH	5,191	6,383	9,824	4,511	-	-	-	-	-	-
Rizal Medical Center	RMC	1,075	1,007	497	506	757	757	878	962	845	942
National Kidney Institute	NKI	4,412	4,468	5,331	4,009	2,996	3,112	3,345	3,681	2,726	2,403
Lung Center of the Philippines	LCP	739	899	1,949	5,160	2,548	2,701	2,694	2	1,233	2,083
Research Institute for Tropical Medicine	RTM	359	192	515	414	361	335	280	348	328	383
San Lazaro Hospital	SLH	1,213	333	698	881	461	662	468	615	409	318
Gov. Cellestino Gallares Memorial Regional Hospital	GMH	803	799	359	522	886	826	1,151	936	1,119	1,521
Zamboanga Medical Center	ZMC	698	627	788	550	434	440	599	1,060	686	721
Far Eastern University	FEU	948	1,286	1,067	740	684	690	699	864	1064	931
Sto. Tomas University	STU	2,019	2,011	1,381	1,24	1,329	1,180	1,722	1,470	752	1,788
Eastern Visayas Regional Medical Center	EVR	469	145	694	799	491	466	340	530	744	507
Corazon Locsin Montelibano Memorial Hospital	MMH	522	517	451	567	380	525	562	590	855	1,153
Southern Philippines Medical Center	DMC	2,549	2,103	2,369	2,487	2,161	2,374	2,523	2,870	2,439	3,332
Vicente Sotto Memorial Medical Center	VSM	875	967	1,224	991	1,063	1,241	1,447	1,931	2,142	2,450
Baguio General Hospital and Medical Center	BGH	996	1,009	1,344	1,213	1,041	1,329	2,129	2,199	1,916	1,972
Cotabato Medical Center	CMC	690	475	742	796	686	541	459	600	595	639
Bicol Regional Training and Teaching Hospital	BRT	388	344	485	399	388	401	618	486	537	677
Dr. Rafael S. Tumbokon Memorial Hospital	RTH				40	32	19	-	-	-	-
Zamboanga del Norte Medical Center	ZPH				56	67	53	38	11	-	-
Mariano Marcos Memorial Hospital and Medical Center	MAR							2,275	1,898	1,851	1,928
Batangas Regional Hospital	BRH							1,008	791	304	38
Cagayan Valley Medical Center	CVM							248	907	790	944
Jose B. Lingad Memorial Regional Hospital	JLM							387	1024	643	655
Northern Mindanao Medical Center	NMC							814	1,817	1,776	1,684
	TOTAL	**23,946**	**23,749**	**29,782**	**25,768**	**16,765**	**17,652**	**24,684**	**25,592**	**23,754**	**27,069**

SPECIMEN TYPE

The Most Common Specimen Sources (Figure 1b):

1) Respiratory
2) Blood
3) Urine
4) Wound
5) Less common specimens : CSF, tissue, stool and specimens from the genital tract.



SENTINEL SITE QUALITY CONTROL TESTS

Of the 21 sentinel sites that submitted data for 2012, BGH, BRT, CMC, CVM, DMC, EVR, FEU, GMH, MAR, MMH and VSM performed sufficient number of Quality Control(QC) tests (at least 2 QC testing per month for each of the minimum ATCC QC strains required). These tests were for the minimum QC strains:*Escherichia coli* 25922, *Pseudomonas aeruginosa* 27853 and *Staphylococcus aureus* 25923. DMC, EVR, FEU, GMH, MAR and VSM were also able to perform sufficient number of QC tests for the other ATCC QC strains *H. influenzae* 49247 and *Streptococcus pneumoniae* 49619. Only FEU was able to perform sufficient QC tests for *Neisseria gonorrhoeae* 49226.

THE ISOLATES

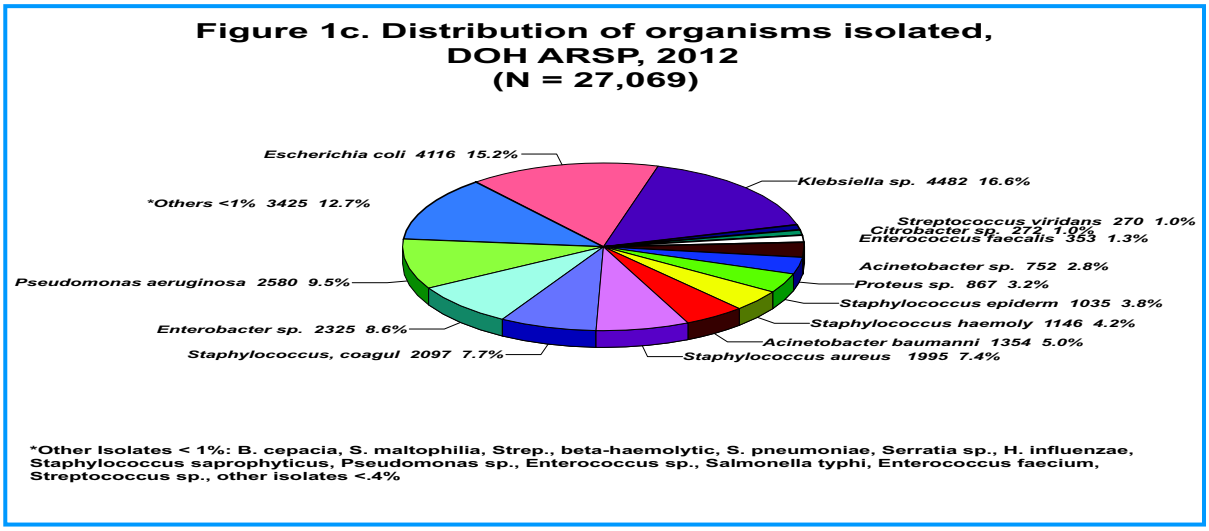


Table 2: The most commonly isolated bacterial organisms by specimen DOH ARSP, 2012

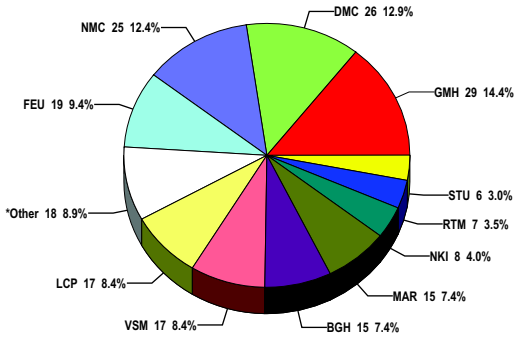
Specimen	Total Number of Isolates	Top 5 Most Commonly Isolated Bacteria
All Specimens	27,069	1) *Klebsiella* sp. 2) *Escherichia coli* 3) *Pseudomonas aeruginosa* 4) *Enterobacter* sp. 5) Coagulase-negative Staphylococci
Blood	5,864	1) Coagulase-negative Staphylococci 2) Klebsiella sp. 3) *Staphylococcus aureus* 4) *Acinetobacter baumannii* 5) *Escherichia coli*
Respiratory	8,374	1) *Klebsiella* sp. 2) *Pseudomonas aeruginosa* 3) *Acinetobacter* sp. 4) *Enterobacter* sp. 5) *Escherichia coli*
Urine	5,353	1) *Escherichia coli* 2) *Klebsiella* sp. 3) *Enterobacter* sp. 4) *Pseudomonas aeruginosa* 5) *Proteus sp.*
Wound	4,890	1) *Staphylococcus aureus* 2) *Escherichia coli* 3) *Klebsiella* sp. 4) *Enterobacter* sp. 5) *Pseudomonas aeruginosa*
Stool	194	1) *Vibrio cholerae* 2) *Salmonella* sp. 3) *Aeromonas* sp. 4) *Salmonella* Typhi 5) *Shigella* sp.
Cerebrospinal Fluid	355	1) Coagulase-negative *Staphyloccus* 2) *Acinetobacter* sp. 3) Klebsiella sp. 4) *Escherichia coli* 5) *Staphylococcus aureus*

I. RESPIRATORY PATHOGENS

a) *Streptococcus pneumoniae*

There were 202 reported *Streptococcus pneumoniae* isolates for 2012. This was 10% more than the 176 isolates reported for 2011. The main contributors of the data on *S.pneumoniae* were GMH (29 isolates); DMC (26 isolates); NMC (25 isolates); FEU (19 isolates); LCP and VSM (17 isolates each); and BGH and MAR (15 isolates each) (Figure 2a).

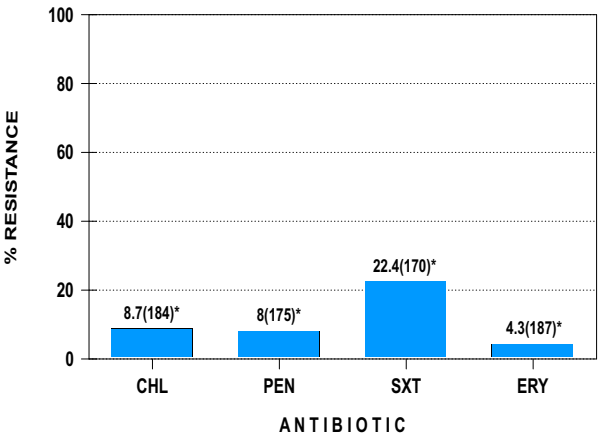
Fig. 2a. Percent sentinel site contribution for *Streptococcus pneumoniae*, DOH ARSP, 2012 (N=202)



* Other isolates contributed by the following hospitals: CVM=5, SLH=4, EVR=3, JLM=3, BRT=1, CMC=1, RMC=1

Among the 2012 respiratory and invasive isolates of *Streptococcus pneumoniae,* the rates of resistance to commonly used antibiotics for treatment of pneumococcal infections are: chloramphenicol at 8.7% (95% CI: 5.2-14); penicillin at 8% (95% CI: 4.6-13.3); co-trimoxazole at 22.4% (95% CI: 16.5-29.6); and erythromycin at 4.3% (95% CI: 2-8.6)(Figure 2b). In recent years, we note rising rates of resistance to these first line agents with significant increase in rates against chloramphenicol at 1.8% in 2011 to 8.7% for 2012 (*p* value 0.0063); and non-significant increase in rates from the previous year for the other first line agents (*p* value >0.05)(Figure 2c). There were no reports of levofloxacin and ceftriaxone-resistant pneumococci for 2012.

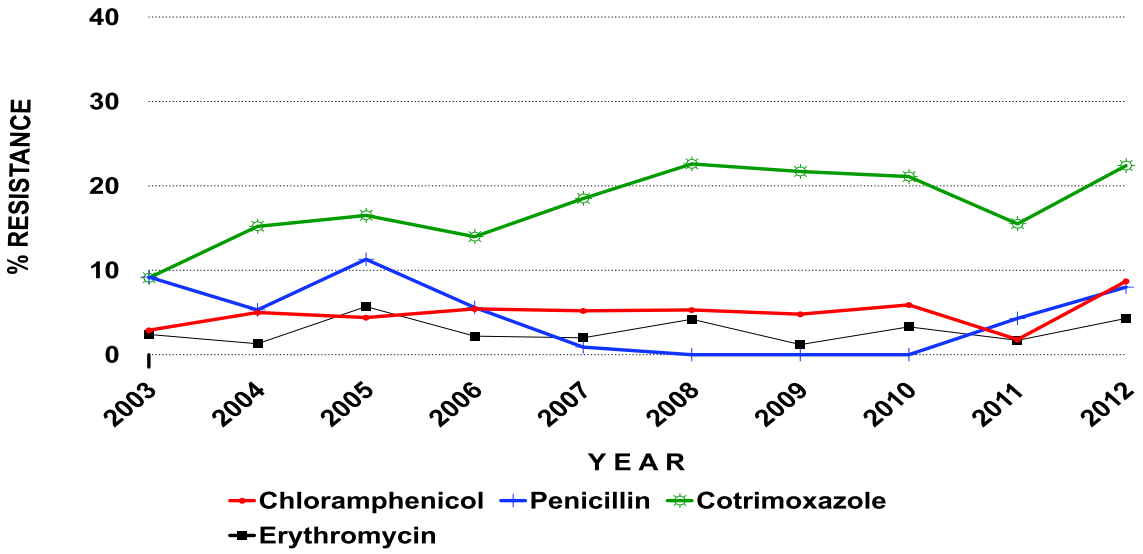
Figure 2b. Percent Resistance of *Streptococcus pneumoniae* DOH ARSP, 2012



CHL=Chloramphenicol PEN=Penicillin
SXT=Cotrimoxazole ERY=Erythromycin

*%R(N)

Figure 2c. Yearly resistance rates of *Streptococcus pneumoniae*
DOH ARSP, 2003 - 2012



Penicillin-Resistant *S. Pneumoniae* (PRSP)

In 2008, CLSI published new susceptibility breakpoints for *S. pneumoniae* (Table 3) (Clinical and Laboratory Standards Institute 2012). The former penicillin breakpoints were based on attainable concentrations of penicillin in CSF and the MIC at which meningitis treatment was thought to fail. However, studies evaluating penicillin therapy for nonmeningitis pneumococcal infections have not shown increased case-fatality rates associated with penicillin MICs <2 µg/ml. These provided evidence that the former CLSI breakpoints underestimated the clinical utility of penicillin intravenous therapy for nonmeningitis pneumococcal infections (Weinstein MP 2009). Since 2008, the CLSI recommends use of different breakpoints for meningitis and nonmeningitis pneumococcal infections. They recommended that CSF isolates have results reported using meningitis breakpoints only since the more stringent breakpoints are warranted due to the poor penetration of penicillin thru the blood brain barrier. While non-CSF isolates should have results reported using both meningitis and nonmeningitis breakpoints on the premise that some patients with meningitis may have negative CSF cultures but present with pneumococcemia. These changes allow clinicians to use parenteral penicillin with confidence (based on the disease appropriate breakpoints) in treating penicillin-susceptible nonmeningitis pneumococcal infections.

Table 3: CLSI Penicillin Breakpoints for *Streptococcus pneumoniae* (Clinical and Laboratory Standards Institute 2012)

	Susceptibility Category MIC(ug/ml)		
Standard	**Susceptible**	**Intermediate**	**Resistant**
Former CLSI Breakpoints	≤0.06	0.12-1	≥2
New CLSI Breakpoints			
Meningitis, intravenous penicillin	≤0.06	-	≥0.12
Nonmeningitis, intravenous penicillin	≤2	4	≥8
Nonmeningitis, oral penicillin	≤0.06	0.12-1	≥2

There were 14 penicillin resistant *S. pneumoniae* (PRSP) isolates reported for 2012 when using parenteral penicillin meningitis breakpoints (MIC >0.12ug/ml). Most of the isolates came from respiratory specimens (9 isolates); there was only 1 CSF isolate; 3 blood culture isolates; and 1 isolate from an unspecified fluid source. Of these, all 13 non-CSF isolates had MICs within the susceptible range when parenteral penicillin non-meningitis breakpoints were used (MIC ≤ 2ug/ml). Among the 6 invasive PRSP (1 CSF isolate and 5 blood culture isolates), all 3 tested (including the CSF isolate) against ceftriaxone had MICs within the susceptible range.

Of these 14 PRSP isolates, 5 were from Metro Manila sites (3 from FEU and 2 from NKI), 4 were from Northern Luzon (4 from MAR), 4 were from the Visayas (3 from GMH and 1 from EVR) and 1 was from NMC in Mindanao.

Streptococcus pneumoniae Serotyping

There were 31 invasive *S. pneumoniae* isolates (isolates from normally sterile specimens) referred to the reference laboratory for serotyping for 2012 (Mudany MA, 2003). These were isolated from 21 blood culture specimens, 7 pleural fluid specimens and 3 cerebrospinal fluid specimens. The most common serotypes causing invasive pneumococcal infections for 2012 were serotypes 6 and 14 for the pediatric age group ≤ 5 years old; serotype 5 for the 19-54 age group; and serotypes 1 and 4 for the >54 years age group (Table 4).

Among the invasive isolates serotyped, 13% or 4 were reported as penicillin-resistant using meningitis breakpoints (MIC $\geqslant$ 0.12 ug/ml). Of these penicillin-resistant pneumococci, 3 were identified as serotype 14 while the 4th isolate was nontypable. These penicillin-resistant *S. pneumoniae* were also nonsusceptible to co-trimoxazole but remained sensitive to chloramphenicol, erythromycin, levofloxacin and ceftriaxone.

Table 4. *Streptococcus pneumoniae* Serotype Distribution by Age Group DOH ARSP, 2012

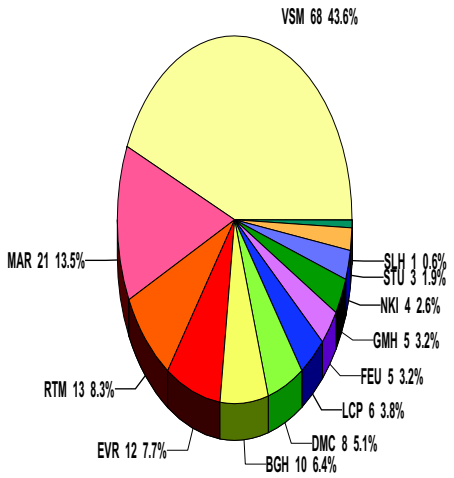
Serotypes	Age Group			Total
	$\leqslant$ 5 years old	6-54 years old	>54 years old	
5	2	4		6
1	1	1	2	4
14	3			3
6	3			3
4			2	2
2			1	1
23	1	1		2
3			1	1
7			1	1
9		1		1
19	1			1
20	1			1
25			1	1
35		1		1
Nontypable		3		3
Total	12	11	8	31

a) *Haemophilus influenzae*

There was an increase in the number of *H. influenzae* isolates submitted for 2012 at 156 compared to 139 reports for 2011. Twelve out of the 21 tertiary care sentinel sites were able to isolate *H. influenzae* with the following hospitals being the main contributors: VSM (68 isolates), MAR (21 isolates), RTM (13 isolates), EVR (12 isolates) and BGH (10 isolates) (Figure 3a).

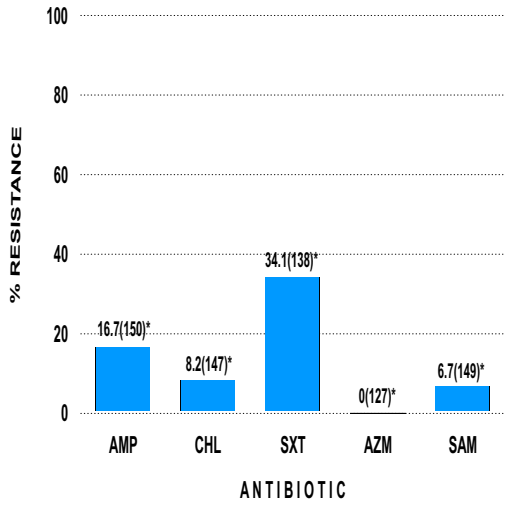
Resistance rates among the isolates of *Haemophilus influenzae* are relatively higher when compared to those of *S. pneumoniae* with 2012 rates against previous first line agents: ampicillin at 16.7% (95% CI: 11.3-23.9); chloramphenicol at 8.2% (95% CI: 4.5-14.2); and co-trimoxazole at 34.1% (95% CI: 26.4-42.7). Although increasing rates are noticeable for the past 10 years to these agents, there was no significant difference in rates when compared to those of the year prior (*p* value >0.05) (Figures 3b and 3c).

Fig. 3a. Percent sentinel site contribution for *Haemophilus influenzae*, DOH ARSP, 2012 (N = 156)



Relatively, *H. influenzae* isolates have remained susceptible to beta-lactam-beta-lactamase inhibitor combinations such as ampicillin-sulbactam with resistance rate at 6.7% (95% CI: 3.4-12.3). There remains to be no reported azithromycin-resistant isolate as of 2012 (Figures3b and 3c).

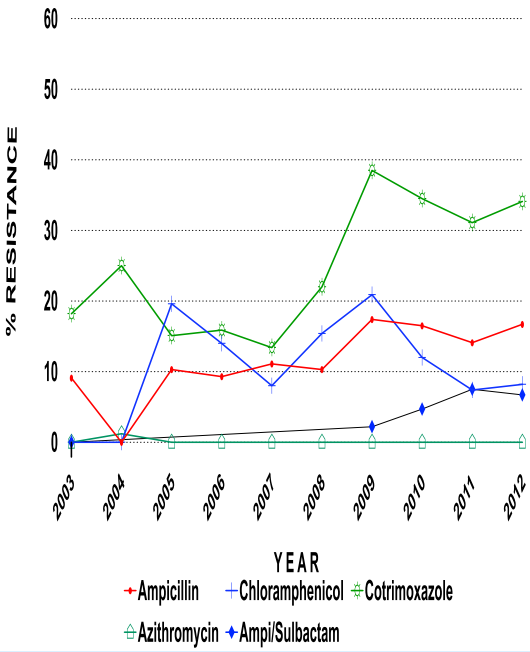
Figure 3b. Percent resistance of *Haemophilus influenzae* DOH ARSP, 2012



AMP=Ampicillin CHL=Chloramphenicol SXT=Cotrimoxazole
AZM=Azithromycin SAM=Ampicillin/Sulbactam

*%R(N)

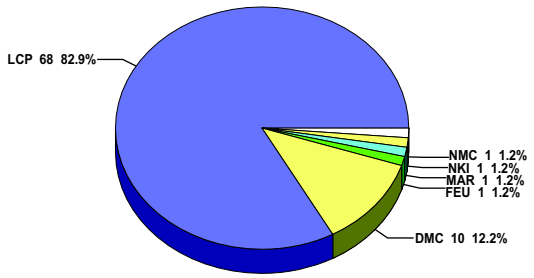
Figure 3c. Yearly resistance of rates of *Haemophilus influenzae* DOH ARSP, 2003 - 2012



b) *Moraxella catarrhalis*

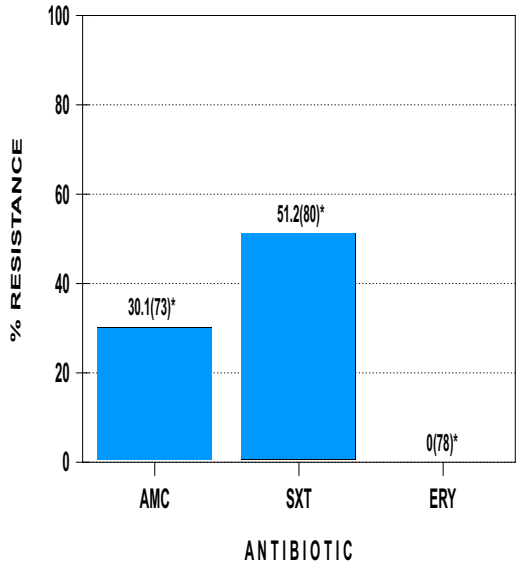
There were 82 isolates of *Moraxella catarrhalis* for 2012, compared to only 39 isolates reported in 2011. LCP in Metro Manila (68 isolates) was the biggest isolate contributor followed by DMC in Mindanao (10 isolates) (Figure 4a).

Fig. 4a. % Percent sentinel site contribution for *Moraxella catarrhalis*, DOH ARSP, 2012 (N =82)



Isolates of *Moraxella catarrhalis* reported for 2012 exhibited relatively high rates of resistance against amoxicillin-clavulanic acid (30.1%) and co-trimoxazole (51.2%).Fortunately, there were no reported erythromycin resistant isolates for 2012 (Figures 4b and 4c).

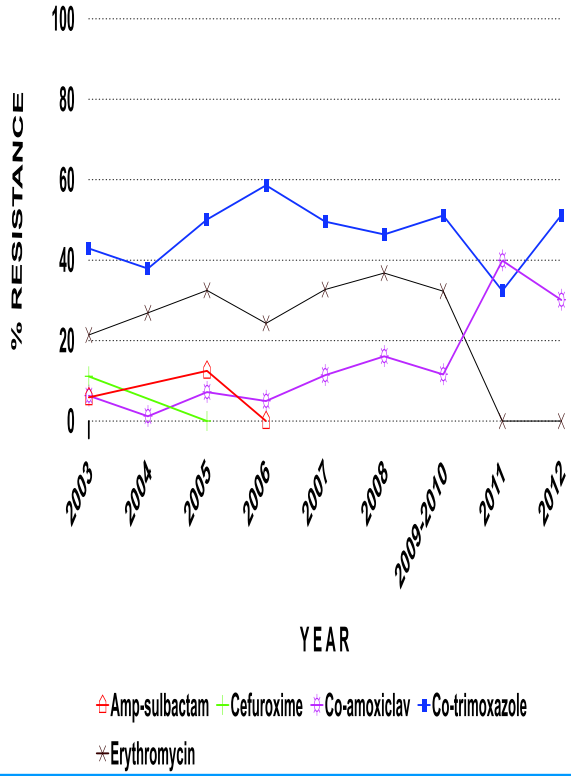
Figure 4b. Percent resistance of *Moraxella catarrhalis* DOH ARSP, 2012



AMC=Amoxi-clav SXT=Co-trimoxazole ERY=Erythromycin

*%R(N)

Figure 4c: Yearly resistance rates of *Moraxella catarrhalis* DOH ARSP, 2003 - 2012

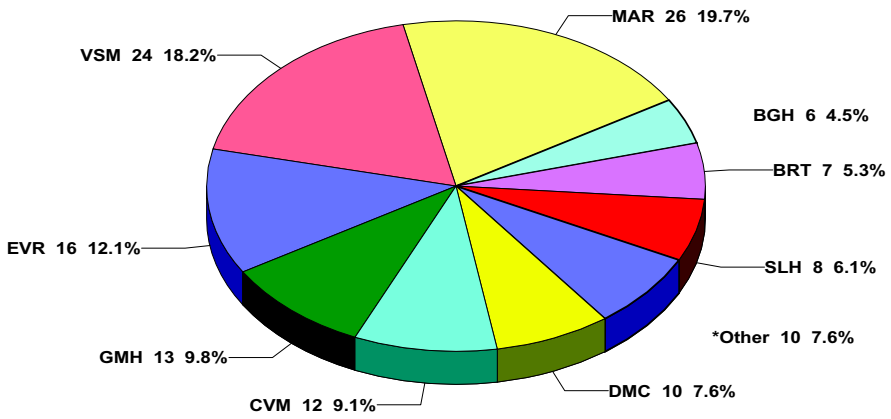


ENTERIC PATHOGENS

a) Salmonella Typhi

For 2012, there were 132 *S*. Typhi, 8 *S*. Paratyphi isolates and 126 Nontyphoidal Salmonella isolates reported. The number of reported *Salmonella* Typhi continues to increase since 2010, with a total of 132 reported for 2012. Major contributors for the *S*. Typhi data are MAR (26 isolates) in Northern Luzon, and Visayas sites VSM (24 isolates) and EVR (16 isolates) (Figure 5a).

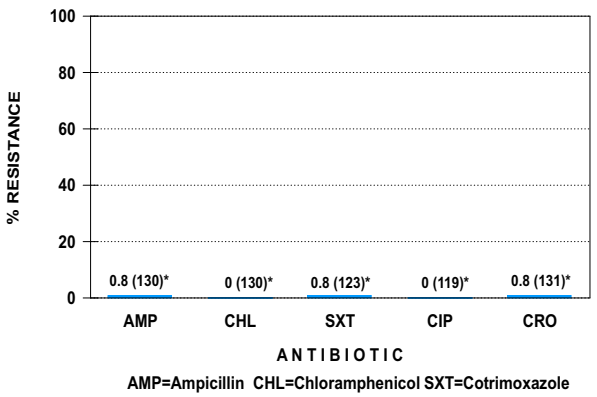
Fig. 5a. Percent sentinel site contribution for *Salmonella Typhi,* DOH ARSP, 2012 (N = 132)



*** Other isolates contributed by the following hospitals: CMC=3, MMH=2, FEU=1, NKI=1, RMC=1, RTM=1, ZMC=1**

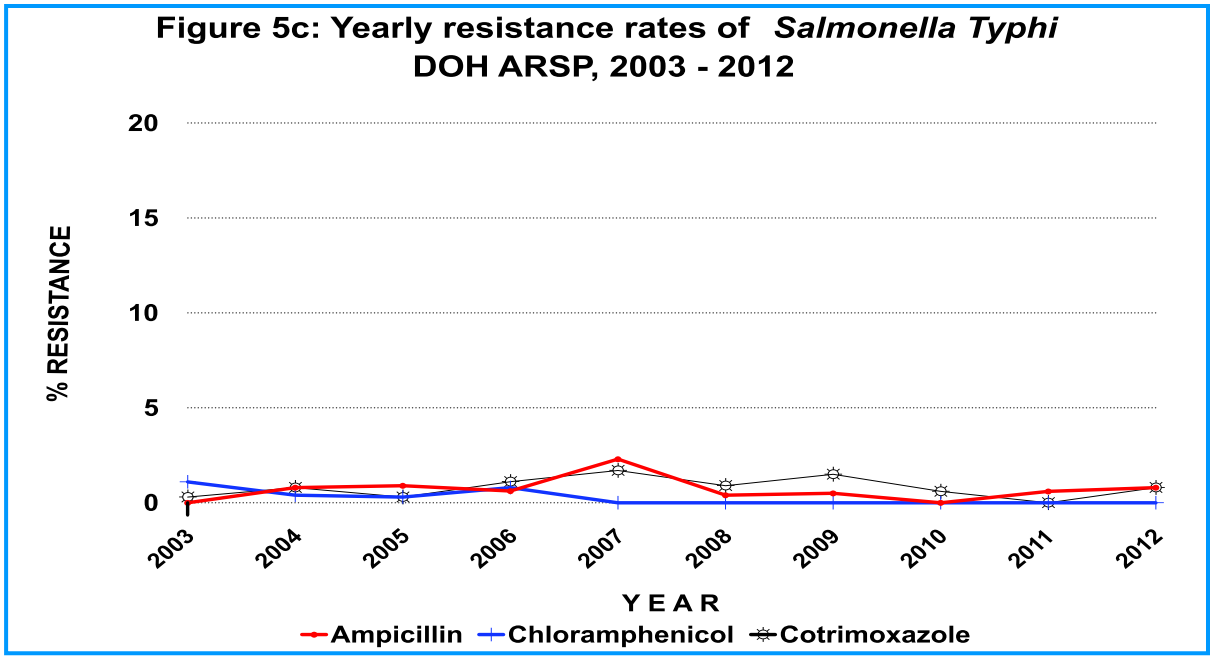
Salmonella Typhi isolates have remained susceptible to first line agents ampicillin, chloramphenicol and co-trimoxazole; with resistance rate at 0.8% for both ampicillin and co-trimoxazole; and no reported chloramphenicol resistance since 2007 (Figures 5b and 5c). These rates do not significantly differ from that of the previous year, 2011 (*p* value > 0.05).

Figure 5b: Percent resistance of *Salmonella Typhi* DOH ARSP, 2012



AMP=Ampicillin CHL=Chloramphenicol SXT=Cotrimoxazole CIP=Ciprofloxacin CRO=Ceftriaxone

*%R(N)



There were 6 reported nalidixic acid-resistant *S*. Typhi isolates for 2012. These isolates were reported from Northern Luzon (2 isolates from MAR and 1 isolate each from BGH and CVM) and Northern Mindanao (2 isolate from DMC). Five of these isolates also tested as nonsusceptible to ciprofloxacin (MICs or zone diameters in the intermediate range). Nalidixic acid resistance among extraintestinal Salmonella isolates may portend poor fluoroquinolone treatment outcomes. All of the 7 isolates remained susceptible to ampicillin and chloramphenicol; while all 5 tested against co-trimoxazole were reported as susceptible.

There was 1 *S*. Typhi isolate reported as ceftriaxone-resistant from a pediatric patient from DMC in Mindanao which was not sent to the reference laboratory for confirmatory testing. This isolate was also resistant to ampicillin and co-trimoxazole, tested as intermediate against ciprofloxacin but remained susceptible to chloramphenicol.

a) Salmonella Paratyphi

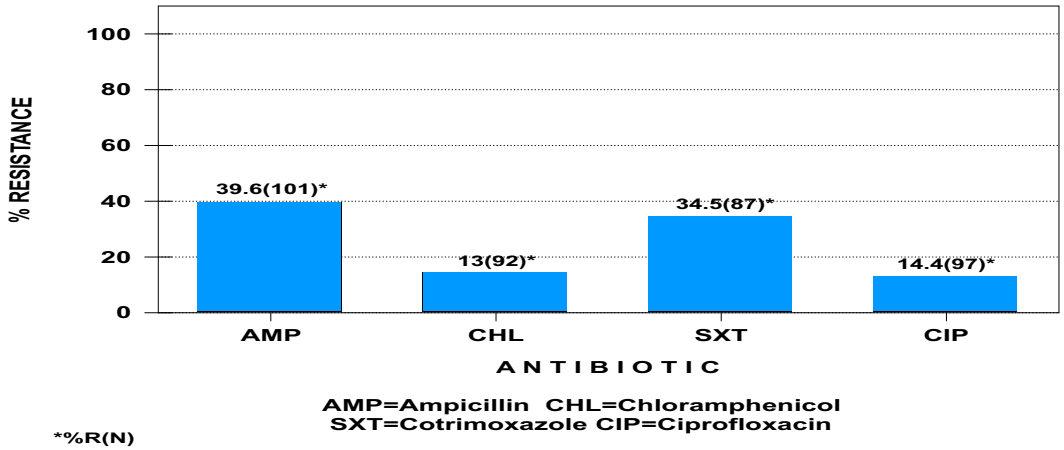
There were 8 *S*. Paratyphi isolates reported for 2012, 5 were S. Paratyphi A, 1 was identified as *S*. Paratyphi B and 2 were reported as *S*. Paratyphi. All of the isolates remained susceptible to chloramphenicol, ciprofloxacin and ceftriaxone.

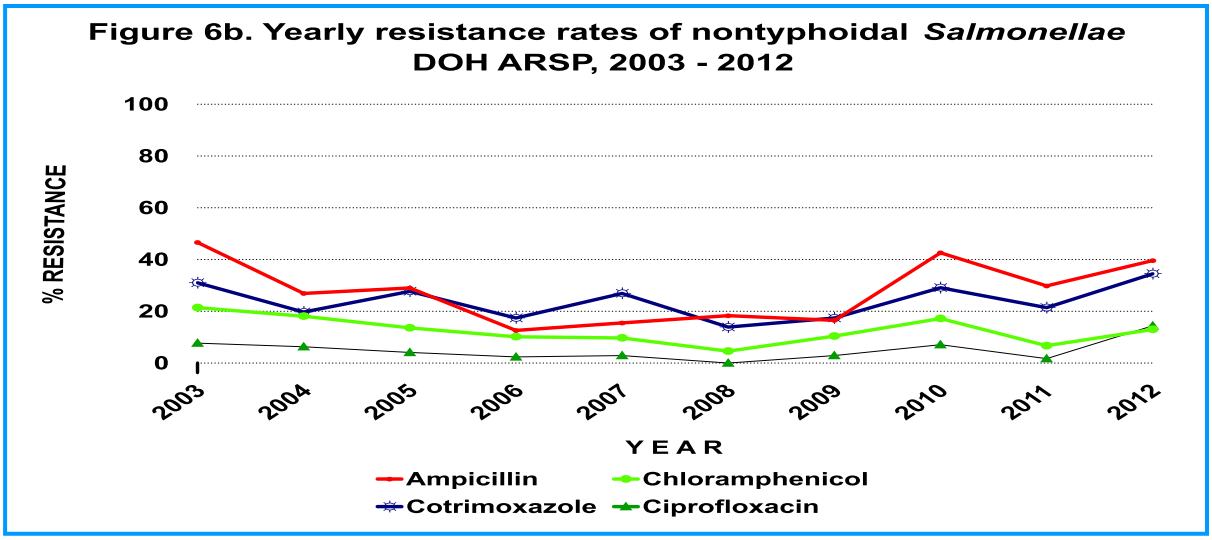
a) Nontyphoidal *Salmonella*

There were 126 reported nontyphoidal *Salmonella* for 2012. As has been previously observed, nontyphoidal *Salmonella* (NTS) showed relatively higher resistance rates when compared to that of *S.* Typhi against the antimicrobial agents: ampicillin at 39.6% (95% CI: 30.2-49.8); chloramphenicol at 13% (95% CI: 7.2-22); co-trimoxazole at 34.5% (95% CI: 24.8-45.5); and ciprofloxacin at 14.4% (95% CI: 8.4-23.3)(Figure 6a). There is a trend towards increasing rates of resistance against these 3 agents for the past few years although rates for 2012 do not significantly differ from those of 2011 (p value >0.05) (Figure 6b).

The past decade showed the emergence of ciprofloxacin resistance among NTS with rates significantly increased from 1.8% in 2011 to 14.4% in 2012 (*p* value 0.0071) (Figure 6b). These ciprofloxacin-resistant NTS were all unconfirmed reports from Mindanao (3 isolates from DMC and 4 isolates from NMC); Metro Manila (2 isolates each from NKI and RMC; and 1 isolate each from LCP and RTM) and Northern Luzon (1 Isolate from CVM). Some of these ciprofloxacin-resistant isolates were also nonsusceptible to ampicillin (12 out of 12 isolates tested as resistant), chloramphenicol (4 isolates tested as resistant while 2 had zone diameters in the intermediate range), co-trimoxazole (8 out of 8 tested as resistant) and ceftriaxone (6 were reported as resistant and 2 had zones in the intermediate range).

Figure 6a. Percent resistance of nontyphoidal *Salmonellae*
DOH ARSP, 2012





Salmonella Serotyping

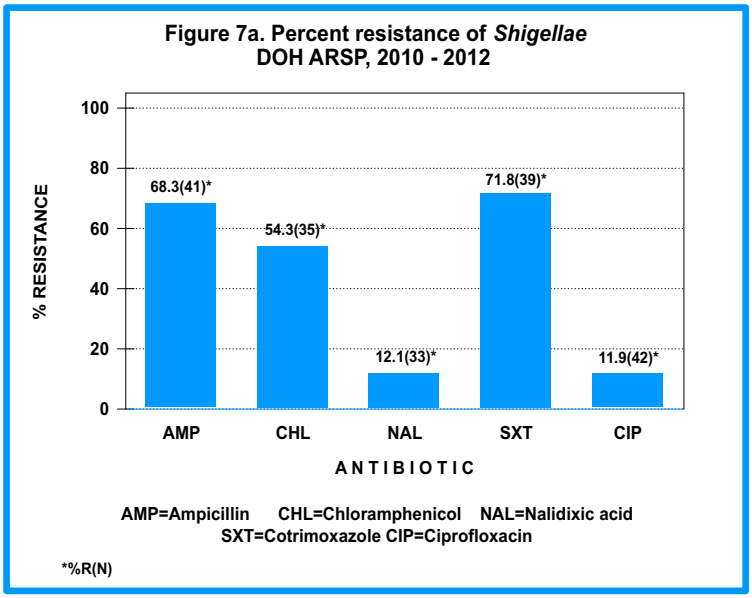
Out of 147 referrals for *Salmonella* serotyping(WHO Global Salm-Surv on Foodborne Disease Surveillance 2009), 138 were confirmed as members of the genus *Salmonella* and 107 were further identified as *S*. Typhi. The most common nontyphoidal *Salmonella* identified for 2012 were *S*. Enteritidis (10 isolates) and *S*. Typhimurium (6 isolates) (Table 5).

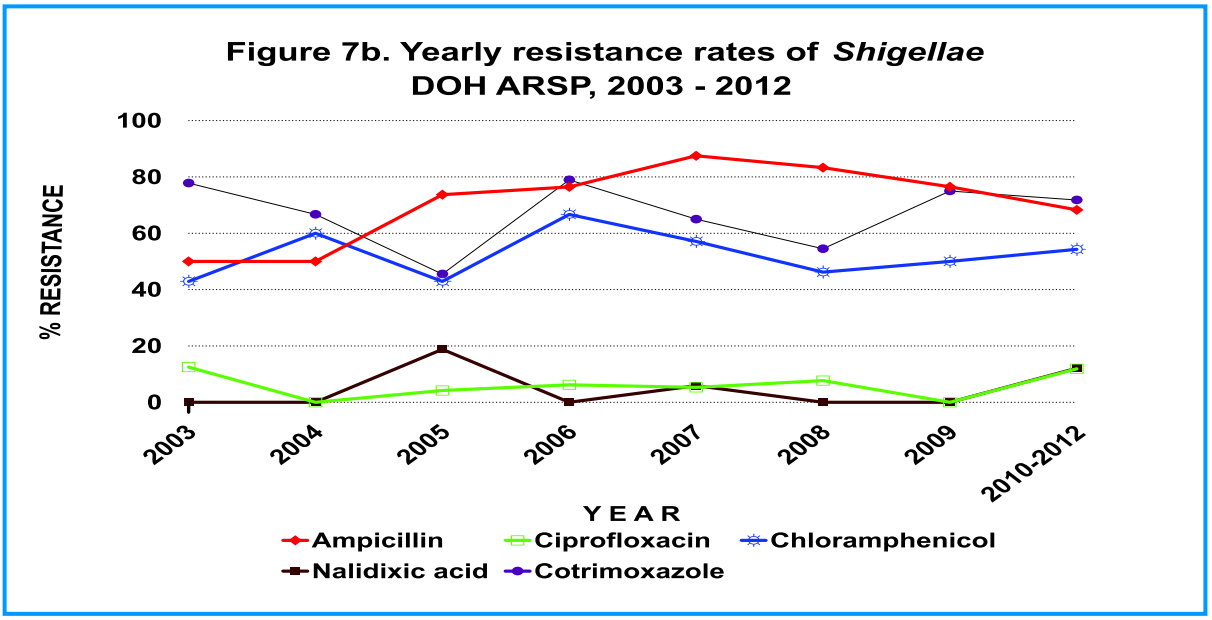
Table 5: *Salmonella* serotypes DOH ARSP, 2012

Salmonella Serotyping	# of Isolates
Salmonella Typhi	107
Salmonella Enteritidis	10
Salmonella Typhimurium	6
Salmonella Paratyphi A	3
Salmonella Stanley	3
Salmonella Weltevreden	3
Salmonella Choleraesuis	2
Salmonella Bournemouth	1
Salmonella Regent	1
Salmonella Rissen	1

d) *Shigella*

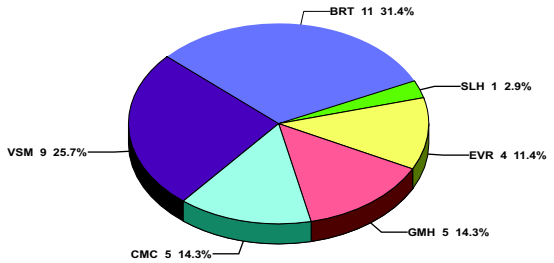
Out of the 12 *Shigella* isolates reported for 2012, 4 were reported as ciprofloxacin resistant. Only 1 was referred to the ARSRL and was identified as *S. flexneri* serotype 2. In order to obtain a reasonable statistical estimate of cumulative percentage resistance for *Shigella,* we combined the results of isolates from 2010 to 2012. The resistance rates of *Shigella* for the combined 2010 to 2012 isolates are as follows: resistance to ampicillin is at 68.3% (95% CI: 51.8-81.4); chloramphenicol at 54.3% (95% CI: 36.9-70-8); co-trimoxazole at 71.8% (95% CI: 54.9-84.5); nalidixic acid at 12.1% (95% CI: 3.9-29.1); and ciprofloxacin at 11.9% (95% CI: 4.5-26.4)(Figure 7a).Although rates of resistance to the previous first line agents: ampicillin, chloramphenicol and co-trimoxazole have been more that 40% for the past 10 years; ciprofloxacin resistance has more recently been emerging with 2010-2012 rates highest for the past decade at 11.9% (95% CI:4.5-26.4) (Figure 7b).





e) *Vibrio cholerae*

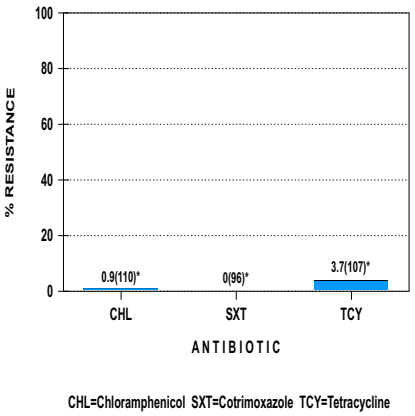
Fig. 8a. Percent sentinel site contribution for *Vibrio cholerae,* DOH ARSP, 2012 (N = 35)



There were only 35 isolates of *Vibrio cholerae* reported for 2012 compared to 82 in 2011. BRT in Southern Luzon remains to be the biggest contributor of *Vibrio cholerae* data at 11 isolates, followed by VSM in Visayas with 9 isolates (Figures 8a).

To arrive at a reasonable statistical estimate of cumulative percentage resistance for *V. cholerae*, we combined the results of isolates from 2011 and 2012. The resistance rates of *V. cholerae* for the combined 2011 to 2012 isolates are as follows: chloramphenicol resistance at 0.9% (95% CI: 0-5.7), tetracycline resistance at 3.7% (95% CI: 1.2-9.8); and no co-trimoxazole resistant isolate for both 2011 and 2012(Figure 8b). The isolates have remained susceptible to these first line agents with rates less than 5% for the past 5 years to these 3 antibiotics (Figure 8c).

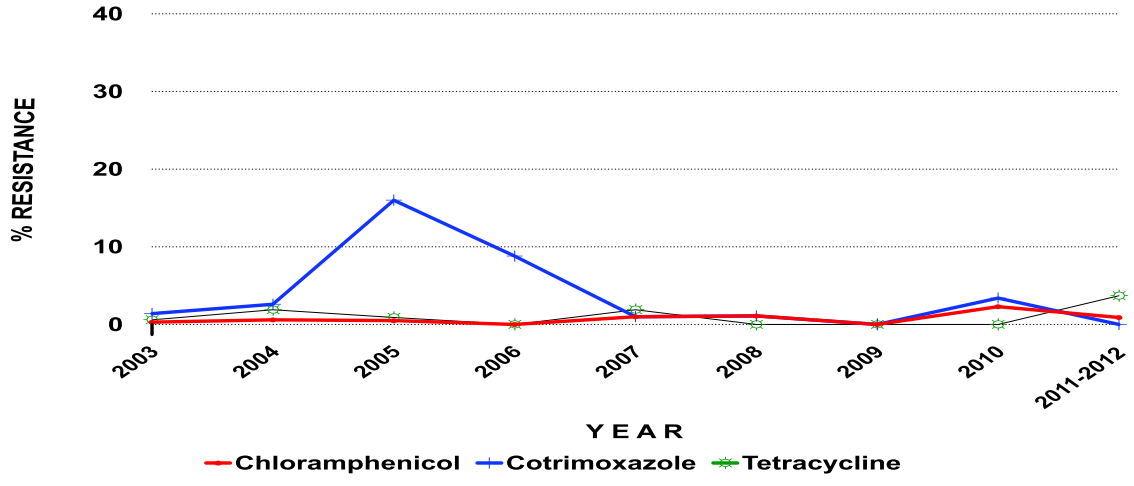
Figure 8b. Percent resistance of *Vibrio cholerae* DOH ARSP, 2011 - 2012



CHL=Chloramphenicol SXT=Cotrimoxazole TCY=Tetracycline

*%R(N)

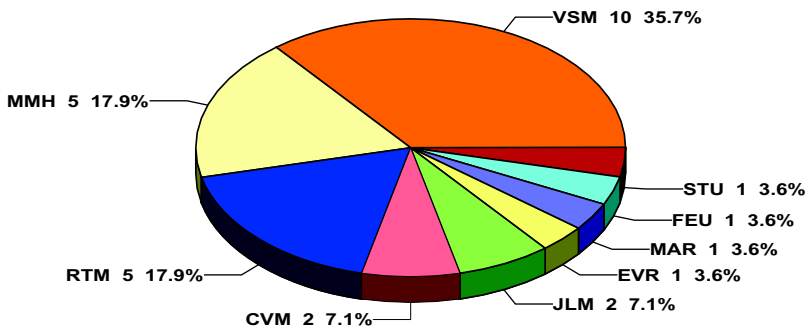
Figure 8c. Yearly resistance rates of *Vibrio cholerae* DOH ARSP, 2003 - 2012



III. *Neisseria gonorrheae*

There is a decrease in isolation and reporting of *Neisseria gonorrheae* isolates from the sites since 2005, with only 28 isolates reported for 2012 (Table 6). Ten of the gonococcal isolates (35.7%) were from patients of VSM. Other contributors for the Gonorrheae data include MMH and RTM with 5 isolates each; CVM and JLM with 2 isolates each; and STU, FEU, MAR and EVR each with 1 isolate (Figure 9a).

Fig. 9a. Percent sentinel site contribution for *Neisseria gonorrhoeae,* DOH ARSP, 2012 (N =28)

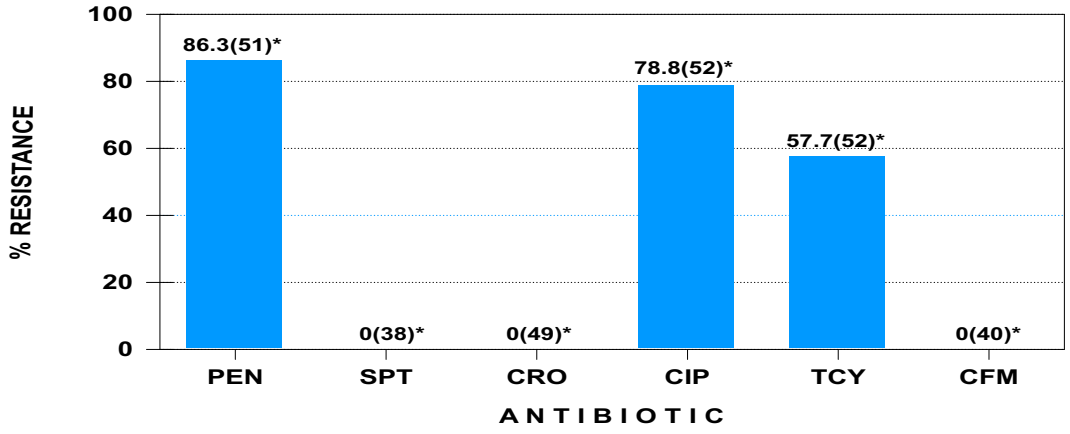


NOTE: ZPH, RTH and SLH-NO *NGO* DATA SUBMITTED

Resistance data for the 28 *Neisseria gonorrheae* isolates reported for 2012 were combined with that of 2011 to arrive at a reasonable statistical estimate of cumulative percentage resistance for the organism. The resistance rate of *N. gonorrheae* for the combined 2011-2012 isolates are as follows: resistance to penicillin at 86.3% (95% CI: 73.2-93.9); ciprofloxacin at 78.8% (95% CI: 64.9-88.4); and tetracycline at 57.7% (95% CI: 43.3-71).There were no reported cefixime, ceftriaxone and spectinomycin resistant isolate for 2012 (Figures 9b and 9c).

Nineteen of the 28 *N. gonorrheae* isolates were sent to ARSRL for confirmatory testing, MIC determination were done to verify susceptibility of the isolates to ceftriaxone and cefixime. All isolates tested susceptible to ceftriaxone with MIC ranging from <0.0016ug/ml to 0.016ug/ml (CLSI 2012 ceftriaxone MIC breakpoint for susceptibility $\leqslant$ 0.25ug/ml). Likewise, all isolates tested as susceptible to cefixime with MIC ranging from $\leqslant$ 0.008ug/ml to <0.016ug/ml (CLSI 2012 cefixime MIC breakpoint for susceptibility $\leqslant$0.25ug/ml).

Figure 9b. Percent resistance of *Neisseria gonorrhea*
DOH ARSP, 2011 - 2012



PEN=Penicillin SPT=Spectinomycin CRO=Ceftriaxone
CIP=Ciprofloxacin TCY=Tetracycline CFM=Cefixime

*%R(N)

Figure 9c. Yearly resistance rates of *Neisseria gonorrhea*
DOH ARSP, 2003 - 2012

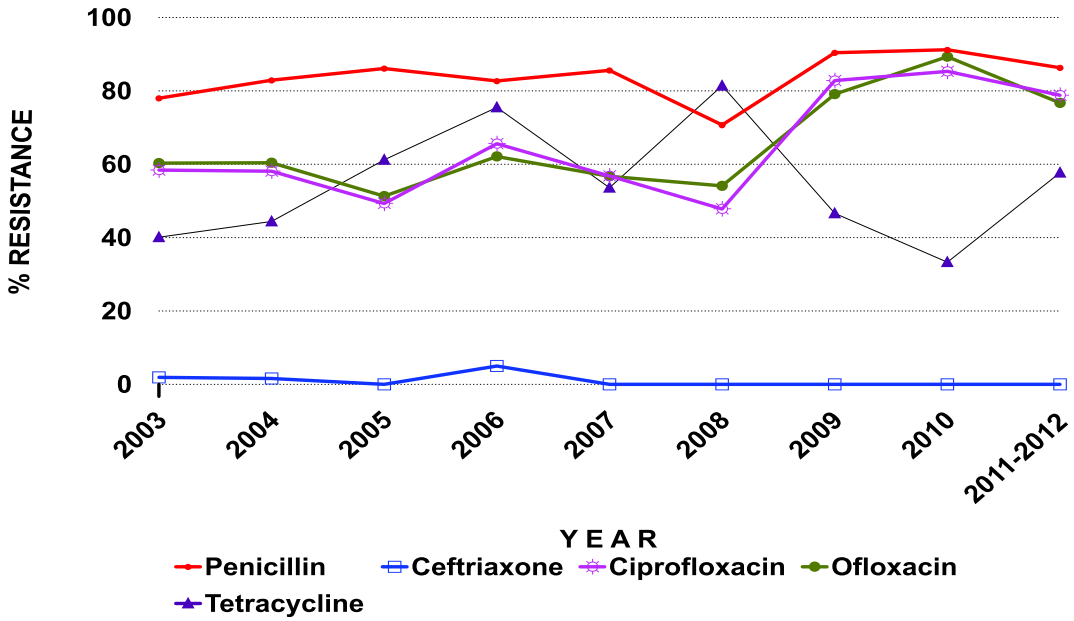


Table 6. Number of *Neisseria gonorrheae*isolates reported DOH ARSP ,2003-2012

SITE	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
ARS		37	5							
BGH				1	2		1		1	
BRL										
BRT	32	64	72						1	
CVM								1	1	2
DMC			1				1			
EVR					1					1
FEU	2	1								1
GMH							3			
JLM									3	2
LCP										
MAR								2		1
MMH						2	8	12	6	5
NKI			1	1	1			1		
NMC								1	2	
PGH	8									
PPH	4									
RMC	2		1	2	1	2	1		1	
RTH	32	69	8	39	32	19				
RTM	65	33	5	1	6	2		5	5	
SLH			52	50						
STU		3		4	1	1	7			1
VSM		5	1	8	3	4	15	3	10	10
ZPH		45	51	56	67	53	37	11		
TOTAL	**145**	**257**	**197**	**162**	**114**	**83**	**73**	**36**	**30**	**28**

IV. Gram-positive Cocci

a) Staphylococcus aureus

The 2012 methicillin-resistant *S. aureus* (MRSA) rates are at 54.9% (95% CI: 54.3-58.9). This has been increasing for the past few years with a non-significant increase inMRSA rates from 52.6% in 2011 to 54.9% in 2012 (*p* value >0.05). *S. aureus* isolates have remained relatively susceptible, as in the previous years, to the antimicrobials co-trimoxazole at 9.3% (95% CI: 8-10.8); erythromycin at 10.9% (95% CI: 9.6-12.4); clindamycin at 8.4% (95% CI: 7.2-9.8), linezolid at 1.6% (95% CI: 1.0-2.4); and tetracycline at 6.8% (95% CI: 5.7-8.1)(Figure 10a). These rates do not significantly differ from 2011 resistance rates for co-trimoxazole, tetracycline and linezolid. Rates for both erythromycin and clindamycin significantly increased from that of the previous year: erythromycin resistance rates increased from 7.4% in 2011 to 10.9% in 2012 (*p* value 0.0002); and clindamycin resistance rates at 6.5% in 2011 to 8.4% in 2012 (*p* value 0.0179).There were no vancomycin resistant isolates reported for 2012 (Figure 10b).

Figure 10a. Percent resistance of *Staphylococcus aureus*
DOH ARSP, 2012

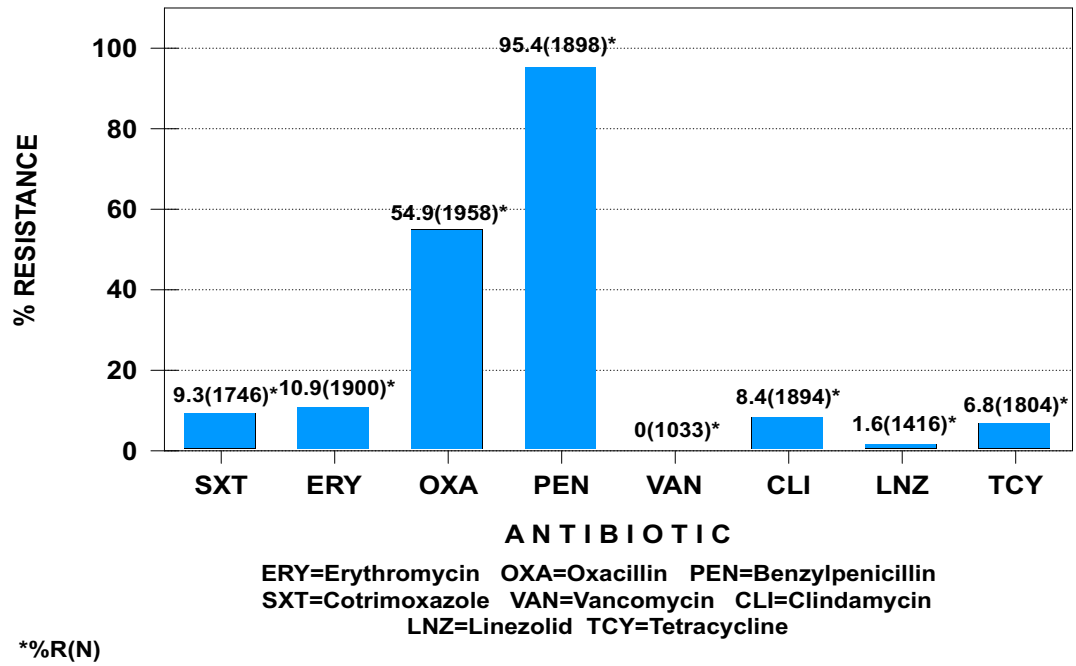
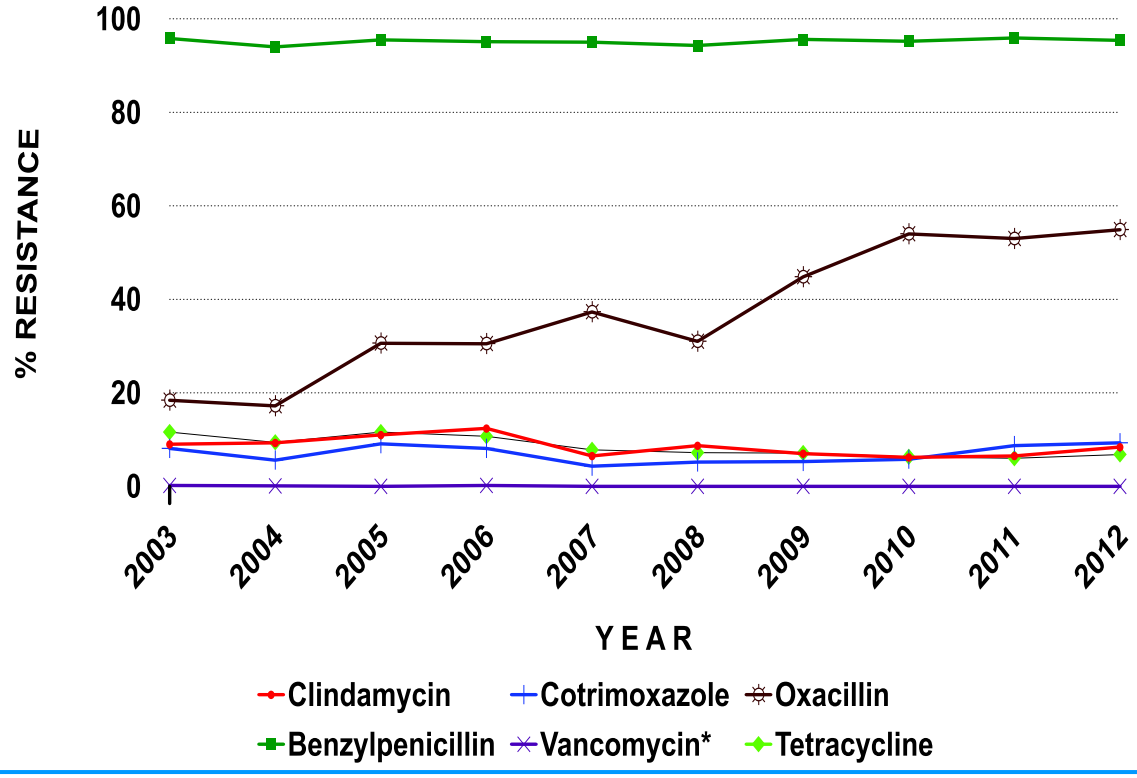


Figure 10b. Yearly resistance rates of *Staphylococcus aureus*
DOH ARSP, 2003 - 2012



Methicillin-resistant *Staphylococcus aureus* (MRSA)

There were 1075 MRSA isolates reported for 2012. All of the active 21 sentinel sites contributed to the MRSA data. Of the total MRSA 2012 isolates, 61% came from sites in Luzon (672 MRSA isolates), 17% from sites in Visayas (187 MRSA isolates) and 22% were from sites in Mindanao (237 MRSA isolates). Metro Manila sites contributed 316 MRSA isolates (29% of the total MRSA isolates for 2012). The sites with the biggest MRSA isolate contribution were: DMC with 116 isolates, VSM with 90 isolates and BGH with 86 isolates (Figure 10d).

MRSA isolates have also been increasingly isolated from the outpatient setting. For 2012, there were 342 *S. aureus* isolates from the outpatient department and 58.5% tested as resistant to oxacillin.

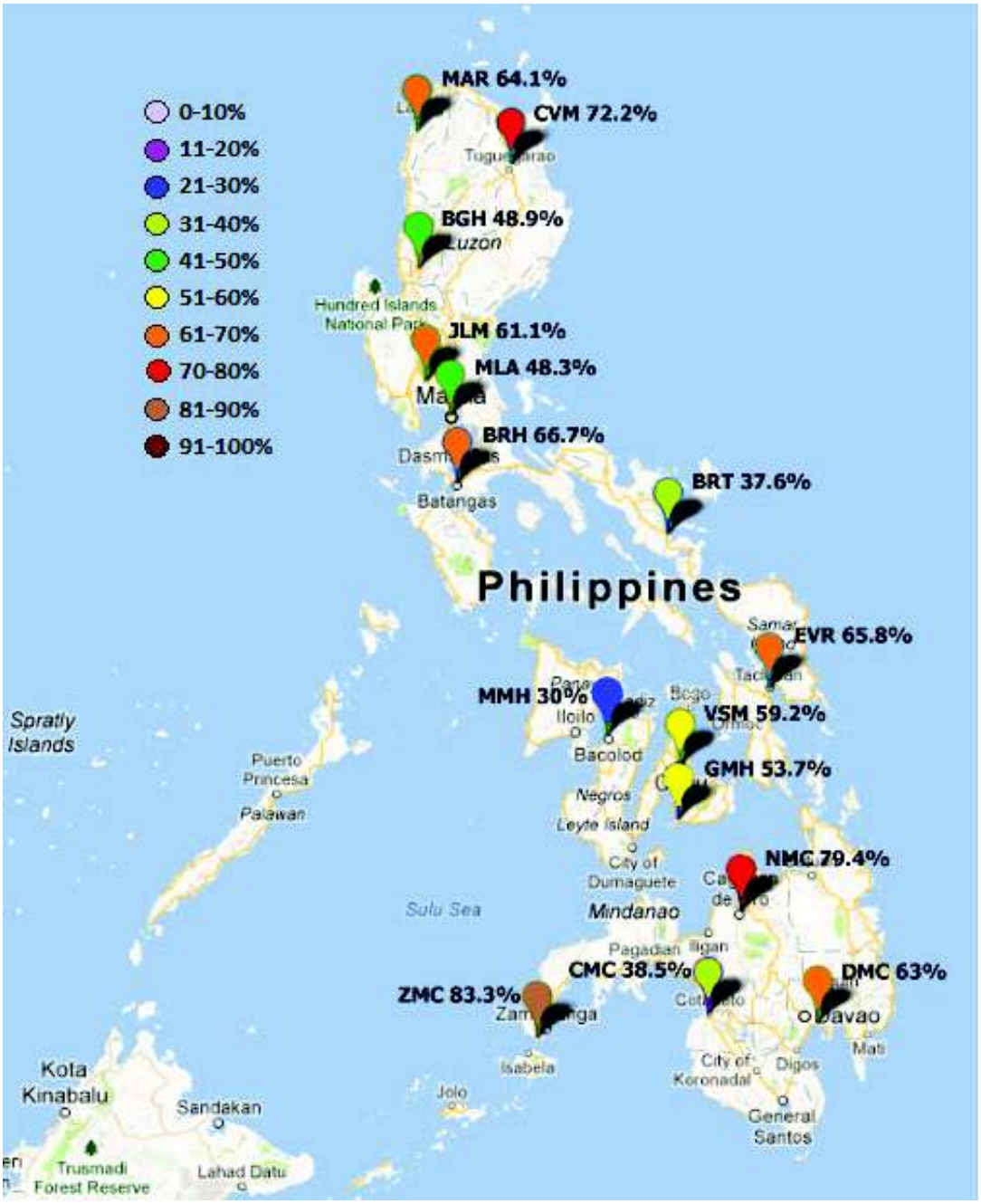
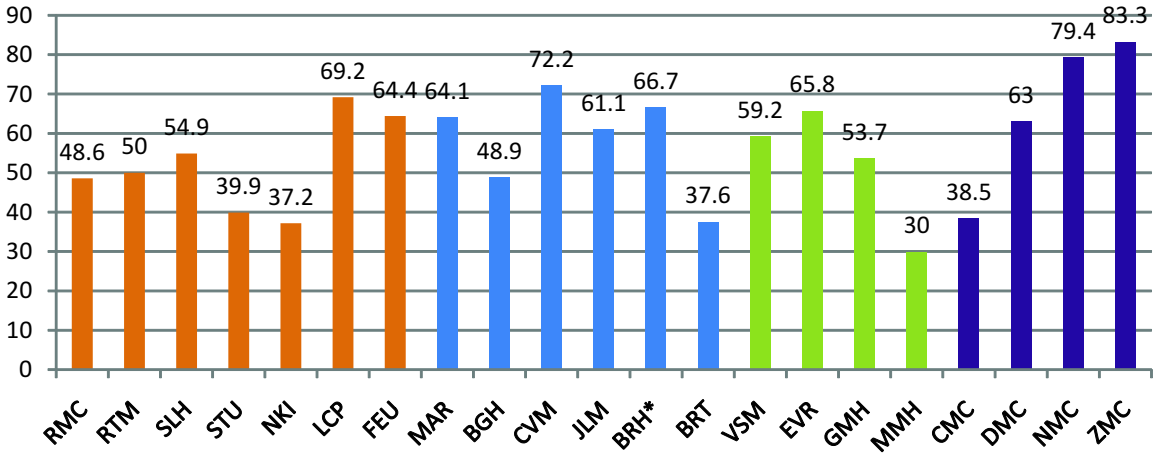


Figure 10c: MRSA rates by sentinel site DOH ARSP, 2012

Looking at the 21 sites with data for 2012, the highest MRSA rate was for a site in Mindanao, ZMC at 83.3% (n=30). While the lowest MRSA rate was for MMH in Visayas at 30% (n=70). Regional rates reveal cumulative MRSA rates were 48% for sites in Metro Manila (n=654), 57% for sites from the rest of Luzon (n=626), 53% for sites in Visayas area (n=355) and 67% for sites in Mindanao (n=355) (Figures 10c and 10d).

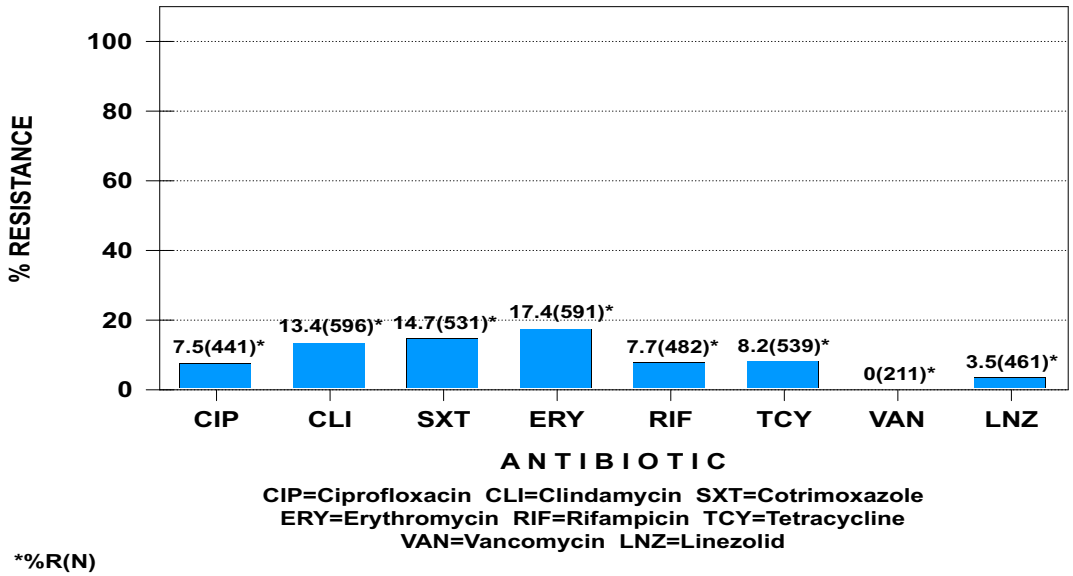
FIgure 10d: Percentage MRSA by Site DOH ARSP, 2012



tested: RMC 74, RTM 52, SLH 71, STU 71, NKI 145, LCP 52, FEU 87, MAR 103, BGH 177, CVM 108, JLM 113, BRH 36, BRT 95, VSM 152, EVR 39, GMH 95, MMH 124, CMC 39, DMC 190, NMC 103, ZMC 30

MRSA isolates remain susceptible to most antimicrobials used for treatment with no vancomycin resistant isolate reported for 2012. Figure 10e illustrates the resistance pattern of MRSA isolates for 2012.

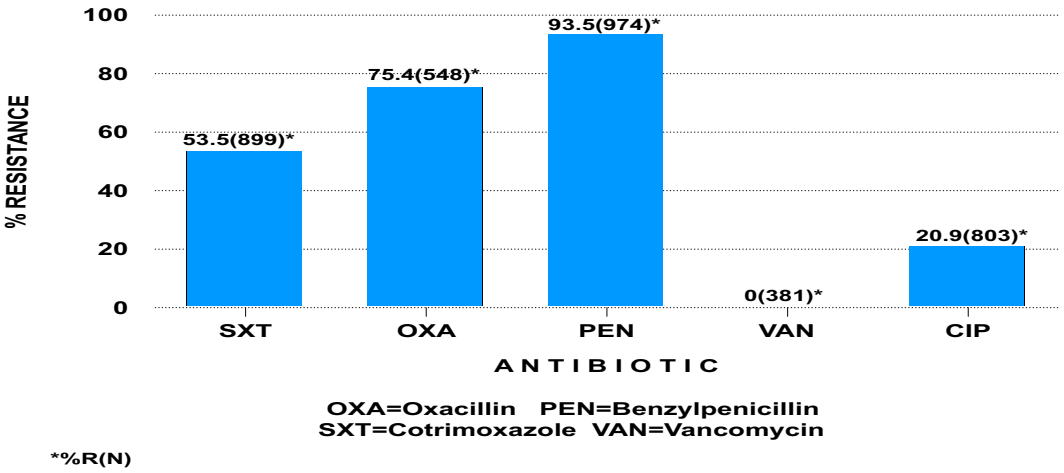
Figure 10e. Percent resistance of methicillin resistant *Staphylococcus aureus,* DOH ARSP, 2012



b) *Staphylococcus epidermidis*

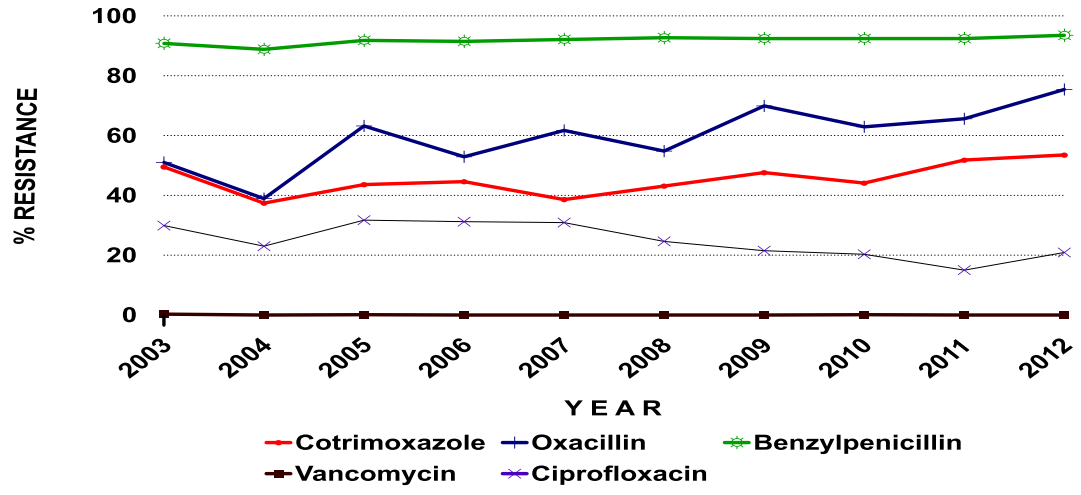
There was a non-significant increase in oxacillin resistance among *Staphylococcus epidermidis* (MRSE) isolates from 66% in 2011 to 75.4% (95% CI: 71.5-79.9) in 2012 (p>0.05). Resistant rates of *S. epidermidis* for 2012 against co-trimoxazole was at 53.5% (95% CI: 50.2-56.8); while rates against ciprofloxacin was at 20.9% (95 CI: 18.2-23.9); these rates did not differ significantly from rates of 2011 (p value >0.05). There remains to be no vancomycin-resistant *S. epidermidis* isolate reported for 2012 (Figures 11a & 11b).

Figure 11a. Percent resistance of *Staphylococcus epidermidis*
DOH ARSP, 2012



*%R(N)

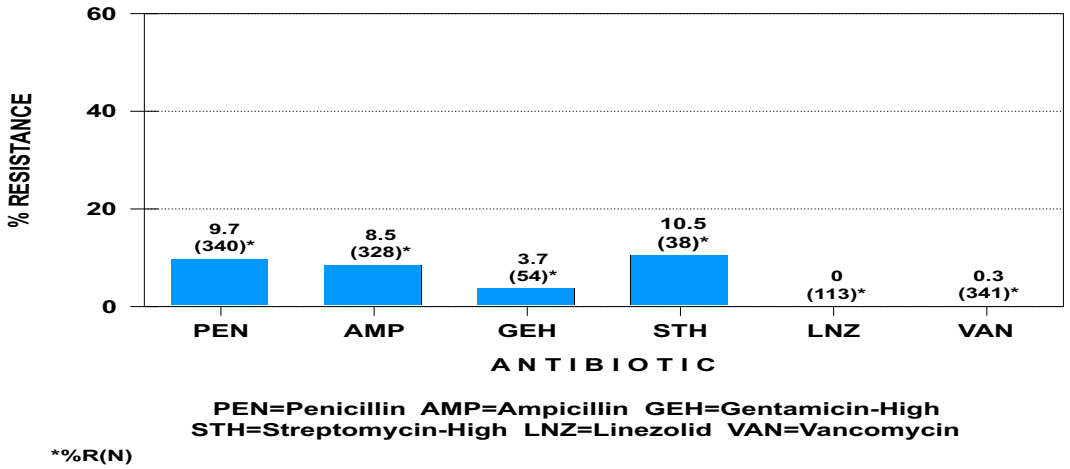
Figure 11b. Yearly resistance rates of *Staphylococcus epidermidis*
DOH ARSP, 2003 - 2012



c) Enterococci

There were 353 *Enterococcus faecalis* and 131 *Enterococcus faecium* isolates reported for 2012. Ampicillin resistance among *E. faecalis* and *E. faecium* was at 8.5% (95% CI: 5.8-12.2) and 59.2% (95% CI: 49.8-68), respectively. There were no reported vancomycin resistant *E. faecalis* and *E. faecium* for 2012 (Figures 12a and 12b).

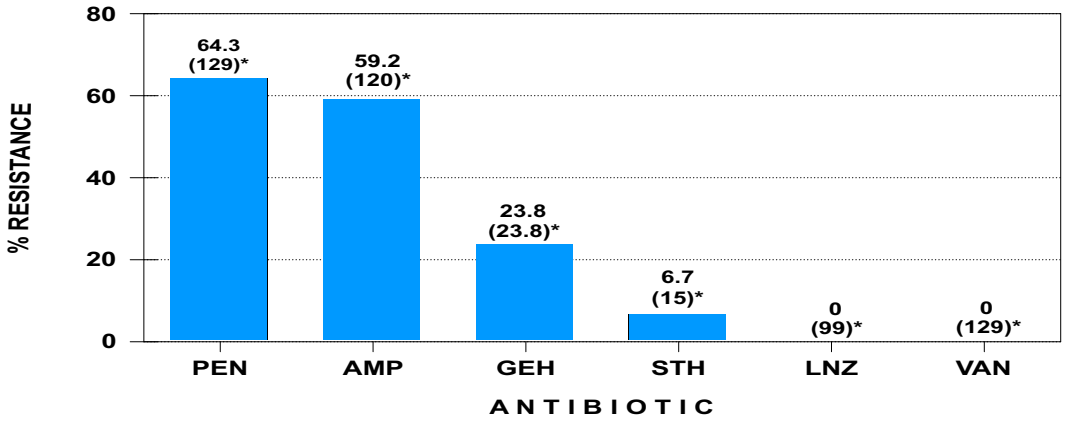
Figure 12a. Percent resistance of *Enterococcus faecalis*
DOH ARSP, 2012



PEN=Penicillin AMP=Ampicillin GEH=Gentamicin-High
STH=Streptomycin-High LNZ=Linezolid VAN=Vancomycin

*%R(N)

Figure 12b. Percent resistance of *Enterococcus faecium*
DOH ARSP, 2012



PEN=Penicillin AMP=Ampicillin GEH=Gentamicin-High
STH=Streptomycin-High LNZ=Linezolid VAN=Vancomycin

*%R(N)

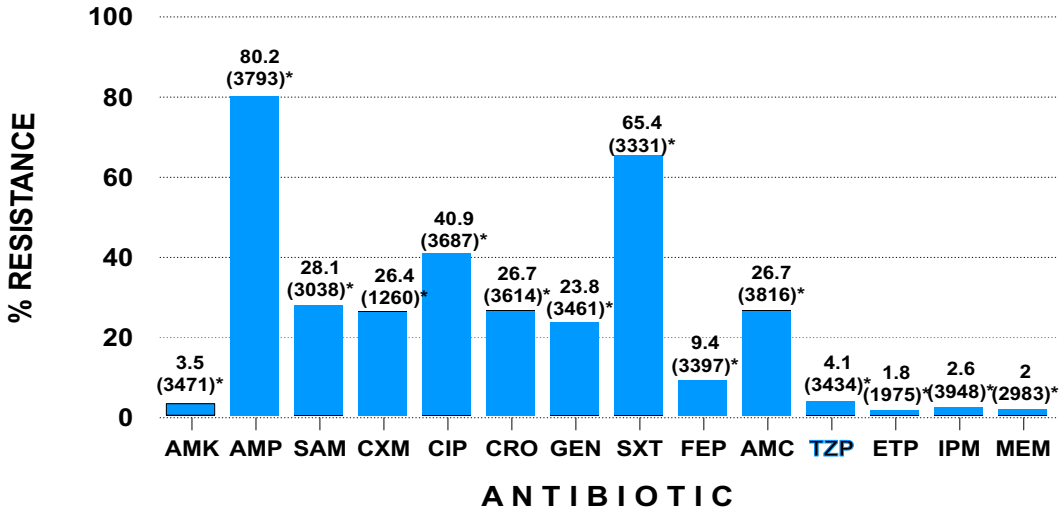
V. Gram-negative Bacilli

a) *Escherichia coli*

Escherichia coli 2012 isolates are noted to be relatively resistant to commonly used oral agents with rates at 80.2% (95% CI: 78.9-81.5) for ampicillin, 65.4% (95% CI: 63.8-67) for co-trimoxazole, 40.9% (95% CI: 39.3-42.5) for ciprofloxacin, 26.4% (95% CI: 24-28.9) for cefuroxime and 26.7% (95% CI: 25.3-28) for amoxicillin-clavulanic acid for 2012 (Figure 13a).

Amongst the parenteral antibiotic preparations used to treat *E. coli* infections, there were relatively higher rates of resistance for ceftriaxone at 26.7% (95% CI:25.3-28.2); ampicillin-sulbactam at 28.1% (95% CI: 26.5-29.7); and gentamicin at 23.8% (95% CI: 22.4-25.3) when compared to amikacin 3.5% (95% CI: 2.9-4.2), the carbapenems: ertapenem at 1.8% (95% CI: 1.3-2.5); meropenem at 2% (95% CI: 1.5-2.6); imipenem at 2.6% (95% CI: 2.1-3.2); and cefepime at 9.4% (95% CI: 8.4-10.4) (Figure 13a).

Figure 13a. Percent resistance of *Escherichia coli*
DOH ARSP, 2012

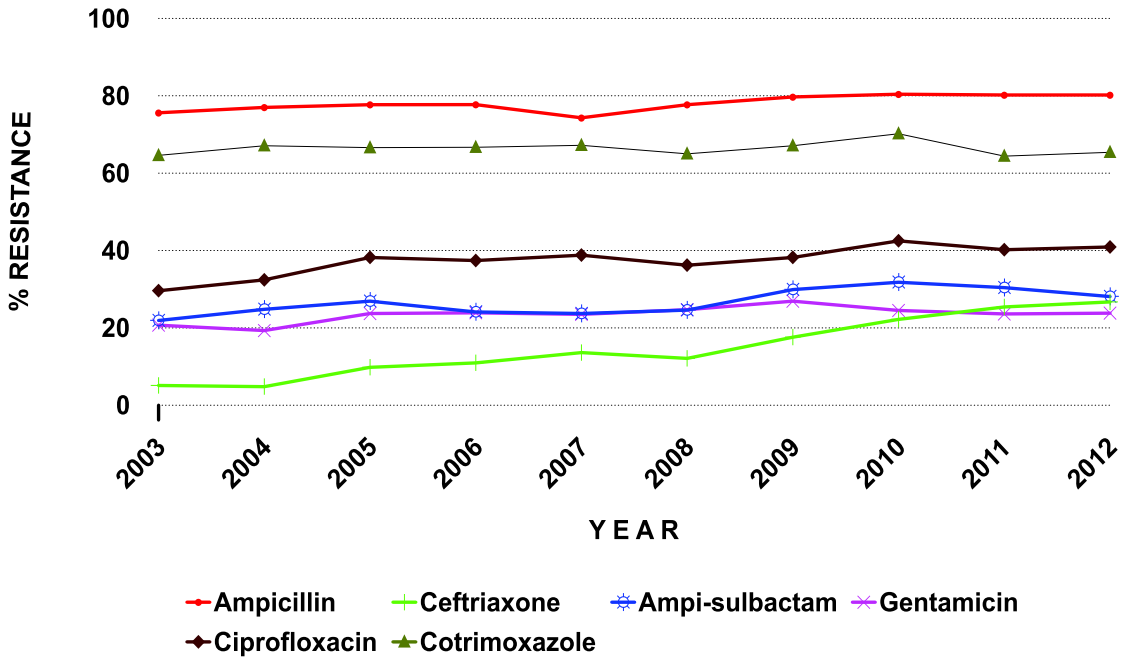


AMK=Amikacin AMP=Ampicillin SAM=Ampi-sulbactam CXM=Cefuroxime
CIP=Ciprofloxacin CRO=Ceftriaxone GEN=Gentamicin SXT=Cotrimoxazole
FEP=Cefepime AMC=Amoxicillin/Clavulanic TZP=Piperacillin/Tazobactam
ETP=Ertapenem IPM=Imipinem MEM=Meropenem

*%R(N)

There has been a rising trend of resistance for *E. coli* against ceftriaxone for the past decade; with a notably significant increase in rates of resistance from 25% in 2011 to 26.7% at 2012 (*p* value 0.0223)(Figure 13b). Likewise,slowly rising rates of resistance to ciprofloxacin, gentamicin and ampicillin-sulbactam is also evident for the past few years although rates for 2012 did not differ significantly from 2011 (*p* value > 0.05). A more recent noticeable trend amongst *E. coli* isolates is the emergence of carbapenem resistance, with meropenem rates at 1% in 2011 to 2% in 2012 (*p* value 0.003) ; and imipenem rates at 1% in 2011 to 2.6% in 2012 (p value 0.001).

Figure 13b. Yearly resistance rates of *Escherichia coli*
DOH ARSP, 2003 - 2012



Urinary *E. coli*

Amongst isolates taken from the outpatients (e.g. specimens from patients at the emergency room and outpatient department), least resistance was noted for nitrofurantoin at 9.8% (95% CI: 7.9-12) amongst the oral agents; and ertapenem at 1% (95% CI: 0.4-1.8) for the parenteral antibiotics. These results were also mirrored among inpatient (specimens from patients admitted in the hospital) urinary *E. coli* with resistance to nitrofurantoin at 8.3% (95% CI: 6.9-10) and

ertapenem at 2.1% (95% CI: 1.8-3.5) (Table 7).

Comparing outpatient and inpatient isolates, inpatient *E. coli* isolates show significantly higher resistance rates for co-trimoxazole at 63.9% versus 68.9% (*p* value 0.0102); ceftriaxone 22.3% versus 30.8% (*p* value 0.0001); and amikacin at 2.1% versus 5.2% (*p* value 0.0002); respectively. While rates of resistance are significantly higher for outpatient urinary *E. coli* against ciprofloxacin at 50.6%, compared to 42.1% for inpatient isolates (*p* value 0.0001) (Table 7).

Table 7. Percent Resistance of Urinary *E. coli* All Sites DOH ARSP, 2012

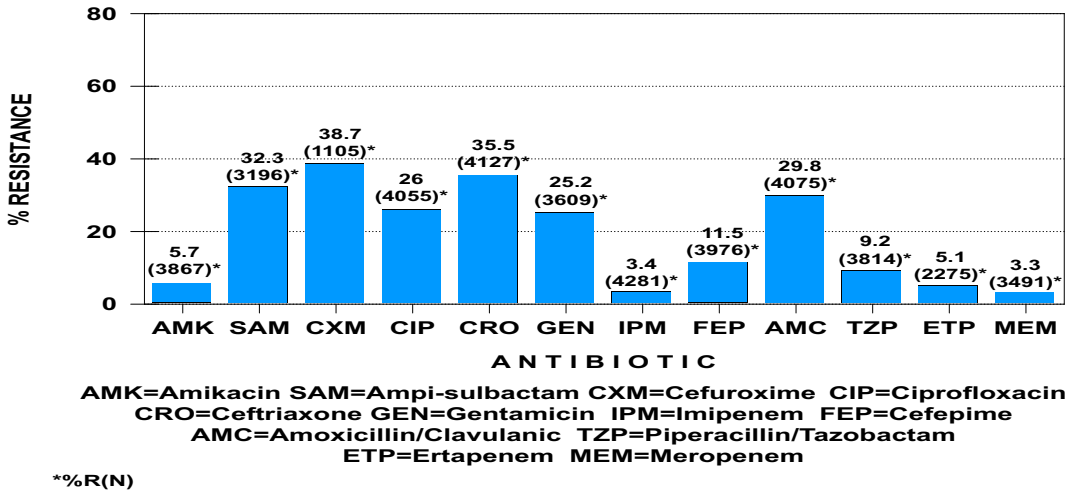
ANTIMICROBIAL AGENT	OUTPATIENT URINE SPECIMENS (n=988)		INPATIENT URINE SPECIMENS (n=1513)		*p* value
	% R	# Tested	% R	# Tested	
Co-trimoxazole	63.9	823	68.9	1239	**0.0102**
Nitrofurantoin	9.8	859	8.3	1264	0.1377
Amoxicillin-clavulanic Acid	24.5	948	27.1	1397	0.0819
Ciprofloxacin	50.6	876	42.1	1362	**0.0001**
Cefuroxime axetil	31.2	443	34.2	443	0.176
Ceftriaxone	22.3	849	30.8	1326	**0.0001**
Amikacin	2.1	823	5.2	1253	**0.0002**
Ertapenem	1	482	2.1	1452	0.0973

Outpatient- isolates taken from patients at the outpatient department and emergency room
Inpatient- isolates taken from patients admitted in the hospital

b) *Klebsiella* species

There were high rates of resistance for the 2012 *Klebsiella* species against the cephalosporins: cefuroxime at 38.7% (95% CI: 35.8-41.7), ceftriaxone at 35.5% (95% CI: 34-37) and cefepime at 11.5% (95% CI: 10.5-12.5; β-lactam-β-lactamase-inhibitor combinations: amoxicillin-clavulanic acid at 29.8% (95% CI: 28.4-31.2) and ampicillin-sulbactam at 32.3% (95% CI: 30.7-34); ciprofloxacin at 26% (95% CI: 24.7-27.4); and gentamicin at 25.2% (95% CI: 23.8-26.7). Comparatively, *Klebsiella* species for 2012 remain susceptible to the following antimicrobials: amikacin with resistance rate at 5.7% (95% CI: 5-6.5), piperacillin-tazobactam with resistant rate at 9.2% (95% CI: 8.3-10.2), ertapenem with resistance rate at 5.1% (95% CI: 4.2-6.1), meropenem with resistance rate at 3.3% (95% CI: 2.7-4) and imipenem with resistance rate at 3.4% (95% CI: 2.9-4) (Figure 14a).

Figure 14a. Percent resistance of *Klebsiella spp*
DOH ARSP, 2012

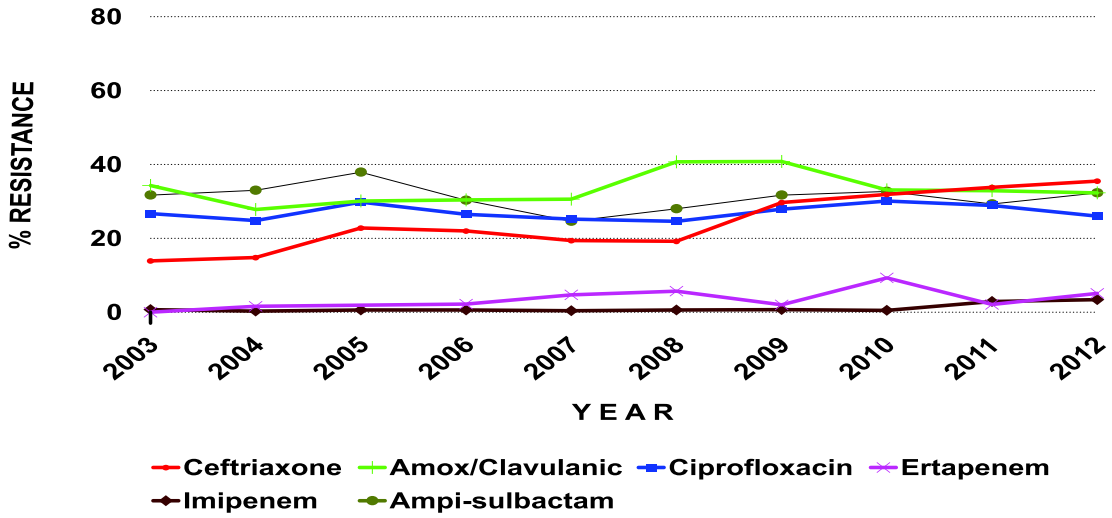


AMK=Amikacin SAM=Ampi-sulbactam CXM=Cefuroxime CIP=Ciprofloxacin
CRO=Ceftriaxone GEN=Gentamicin IPM=Imipenem FEP=Cefepime
AMC=Amoxicillin/Clavulanic TZP=Piperacillin/Tazobactam
ETP=Ertapenem MEM=Meropenem

*%R(N)

Similar to *E. coli*, we note increasing trends in resistance rates of *Klebsiella* sp. against ceftriaxone with a significant rise from 33.1% in 2011 to 35.5% in 2012 (*p* value 0.0152). In contrast, ciprofloxacin rates of resistance showed decreasing rates for the past 2 years, with resistance rates at 28.3% in 2011 to 26% in 2012 (Figure 14b). We also recently note the emerging resistance to carbapenems among *Klebsiella* sp. This is reflected in the significant increase in resistance rates of *Klebsiella* sp. against ertapenem from 2.2% in 2011 to 5.1% in 2012; and meropenem from 2.5% in 2011 to 3.3% in 2012.

Figure 14b. Yearly resistance rates of *Klebsiella spp*
DOH ARSP, 2003 - 2012



Extended-spectrum Beta-lactamase (ESBL)

Extended-spectrum Beta-lactamase ESBL) are enzymes that mediate resistance to extended-spectrum (third generation) cephalosporins (e.g., ceftazidime and ceftriaxone) and monobactams (e.g., aztreonam) but do not affect cephamycins (e.g., cefoxitin and cefotetan) or carbapenems (e.g., meropenem or imipenem) (Centers for Disease Control and Prevention National Center for Emerging and Zoonotic Infectious Diseases (NCEZID) Division of Healthcare Quality Promotion (DHQP) 2010). Enterobacteriaceae producing ESBLs have been increasingly reported locally. Using ceftazidime to screen for ESBL production(Clinical and Laboratory Standards Institute 2012), percentage of ESBL-suspects among *E. coli* and *Klebsiella* sp. isolates for 2012 are 20.9% and 31.7%, respectively. A subset of these ESBL-suspect isolates were referred to the ARS reference laboratory; of these, 66.8% and 70.6% were subsequently confirmed by phenotypic methodology (Clinical and Laboratory Standards Institute, 2012)to be ESBL-producing *E. coli* and *Klebsiella* sp., respectively (Table 8).

Table 8: Extended-spectrum Beta-lactamase-producing Isolates DOH ARSP, 2012

Organism	Total # of Isolates tested against CAZ	Total # of CAZ resistant isolates (ESBL suspect)	% ESBL Suspect	Total # of CAZ resistant isolates referred to ARSU	Total # of referred CAZ resistant isolates confirmed by ARSRL to be ESBL	% of referred CAZ resistant isolates confirmed by ARSRL to be ESBL
E. coli	3505	701	20.9%	202	135	66.8% (135/202)
Klebsiella sp.	4010	1224	31.7%	445	314	70.6% (314/445)

Out of the 19 sentinel sites with at least 30 isolates tested and reported for 2012, the highest ESBL-suspect rates were noted in Metro Manila at STU with rates at 48.4% for *E. coli* (n=64) and 66.7% for *Klebsiella* sp. (n=46).

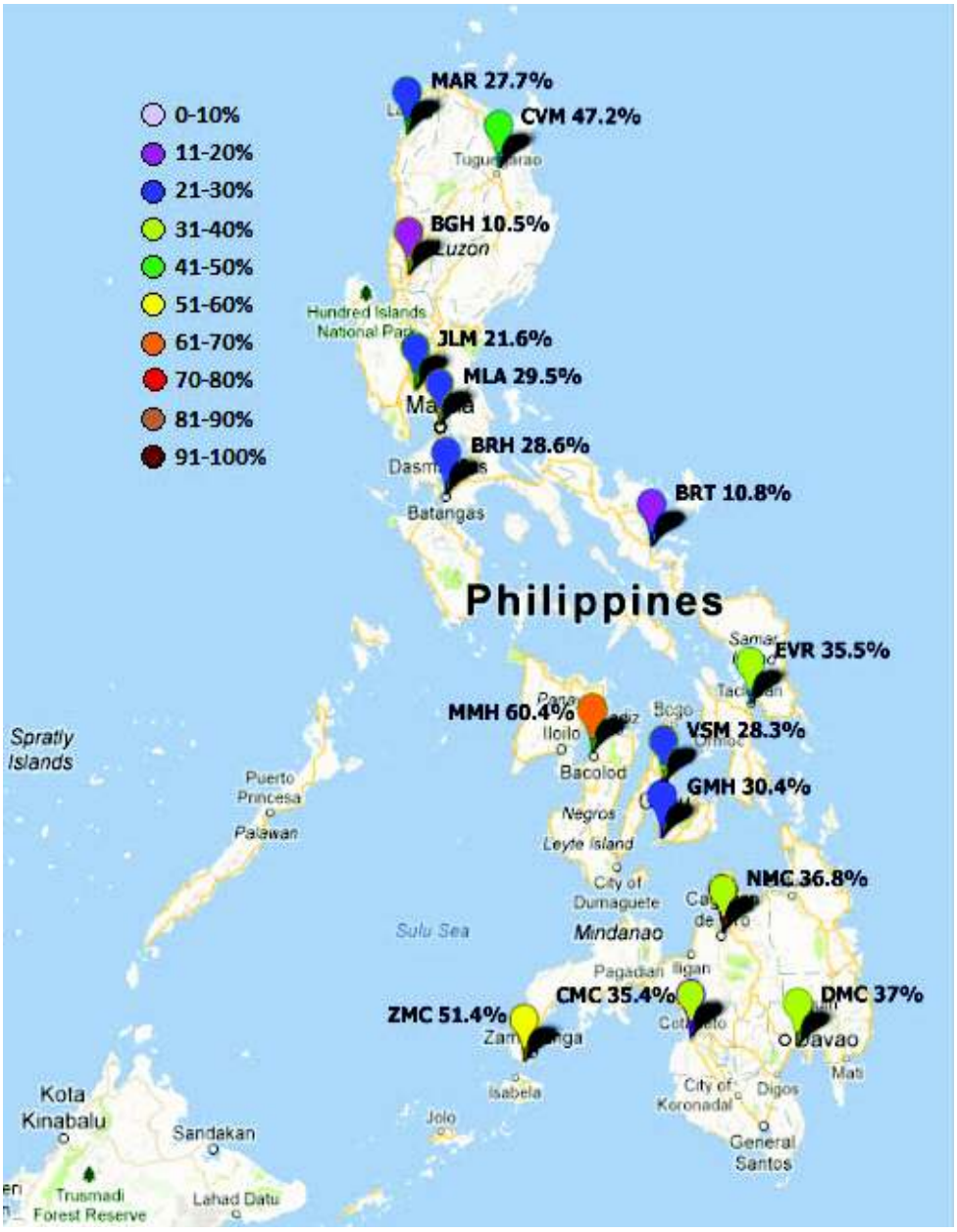


Figure 15a. *E. coli* ESBL-suspect Rates by Site for 2012, DOH ARSP

Comparing rates by regions, Mindanao had the highest cumulative rates for ESBL-suspect *E. coli* at 26% (n=787) and ESBL-suspect *Klebsiella* sp. at 39% (n=860) (Table 9, Figures 15a and 15b).

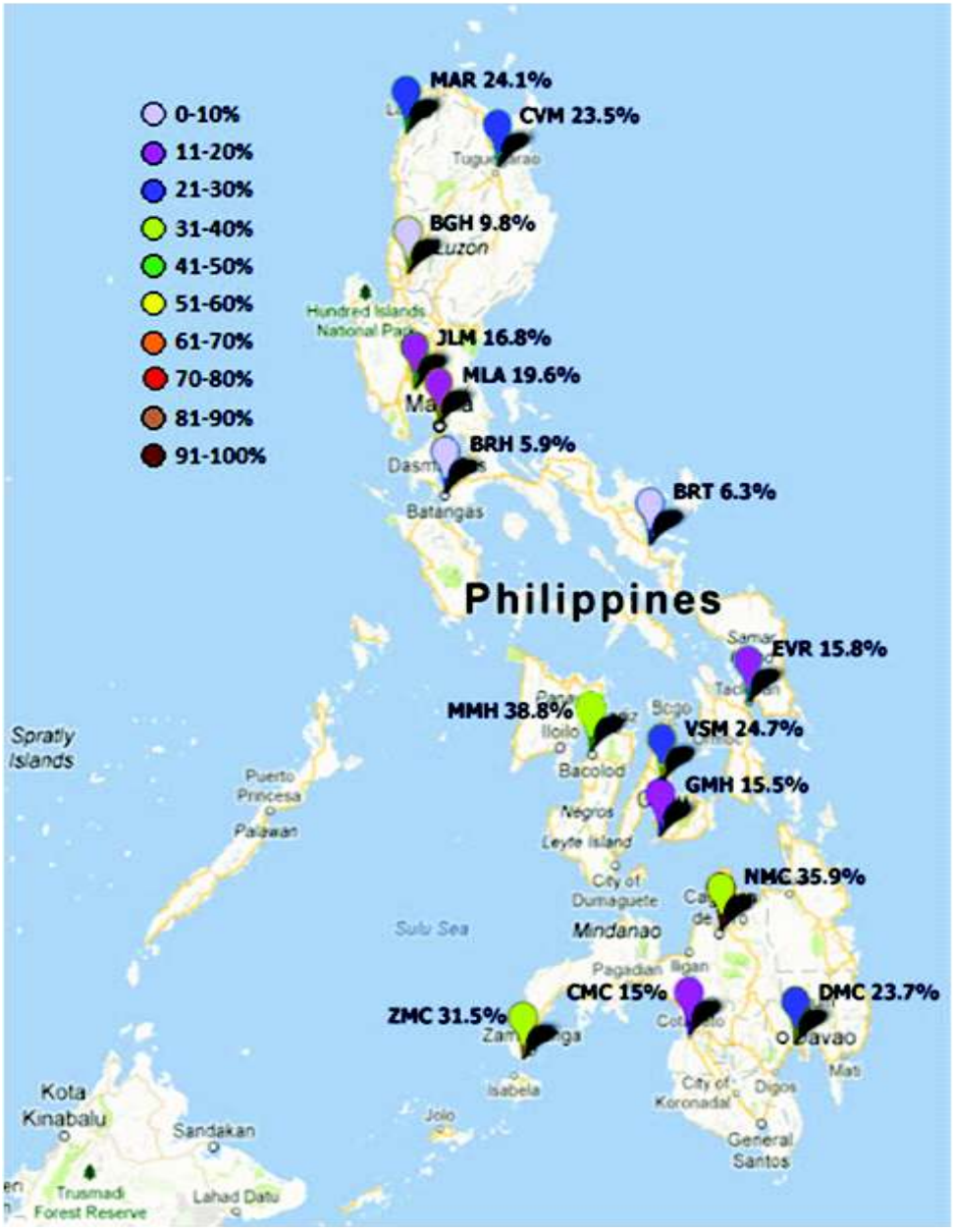


Figure15b. *Klebsiell a*sp. ESBL-suspect Rates for 2012, DOH ARSP

Table 9: ESBL-suspect (Ceftazidime-resistant) Rates by Region DOH ARSP, 2012

Organism	Region	# of Isolates Tested	% ESBL Suspect
E. coli	NCR	1196	20%
	Luzon	840	16%
	Visayas	683	23%
	Mindanao	787	26%
Klebsiella sp.	NCR	265	29%
	Luzon	954	20%
	Visayas	1296	37%
	Mindanao	860	39%

Carbapenem-resistant Enterobacteriaceae (CRE)

Carbapenem resistance amongst Enterobacteriaceae (CRE) is often secondary to the organism's production of carbapenemases. Carbapenemases are enzymes that directly hydrolyze beta-lactams, especially carbapenems. The New Delhi Metallo-ß-lactamase (NDM) is a novel carbapenemase first reported in a patient who had been hospitalized in New Delhi, India back in 2007 (Yong D 2009). These isolates are often not only resistant to carbapenems but to most of available antibiotics, only remaining susceptible to colistin and tigecycline. This enzyme is a particular concern because these usually are encoded on plasmids that harbor multiple resistance determinants and are transmitted easily to other Enterobacteriaceae and other genera of bacteria (Nordmann P 2011). Locally, it has first been confirmed in an *E. coli* isolate from MMH in Visayas last 2011(Antimicrobial Resistance Surveillance Program, 2012).

For 2012 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 2012 were 2.6% and 3.4%, respectively. Comparing rates amongst participating sentinel sites, NMC in Mindanao had the highest imipenem resistance rates for both *E. coli* and Klebsiella sp. at 29.5% (n=146) and 43.2% (n=146), respectively. Consequently, when rates are analyzed by region, Mindanao had the highest cumulative rates of resistance against imipenem for *E. coli*at 6% (n=783) and Klebsiella sp. at 9% (n=782) (Table 10, Figures 16a and 16b).

Table 10: Imipenem Resistance Rates of Enterobacteriaceae by Region DOH ARSP, 2012

Organism	Region	# of Isolates Tested	% Resistance to Imipenem
E. coli	NCR	1684	2%
	Luzon	827	1%
	Visayas	655	3%
	Mindanao	783	6%
Klebsiella sp.	NCR	1224	3%
	Luzon	942	1%
	Visayas	1277	2%
	Mindanao	782	9%

There were 52 Enterobacteriaceae isolates (22 *E. coli*, 25 *K. pneumoniae*, 4 *E. cloacae* and 1 *C. sedlakii*) referred to ARSRL for 2012 that tested as nonsusceptible (intermediate or resistant) to at least 1 carbapenem (ertapenem, imipenem or meropenem). Most of these isolates were from the Visayas region (21 isolates from VSM, 22 isolates from MMH and 1 isolate from GMH) and the rest were from Luzon (3 isolates from NKI and 1 isolate each from BGH and STU) and Mindanao (1 isolate for ZMC and 2 isolates from DMC)).

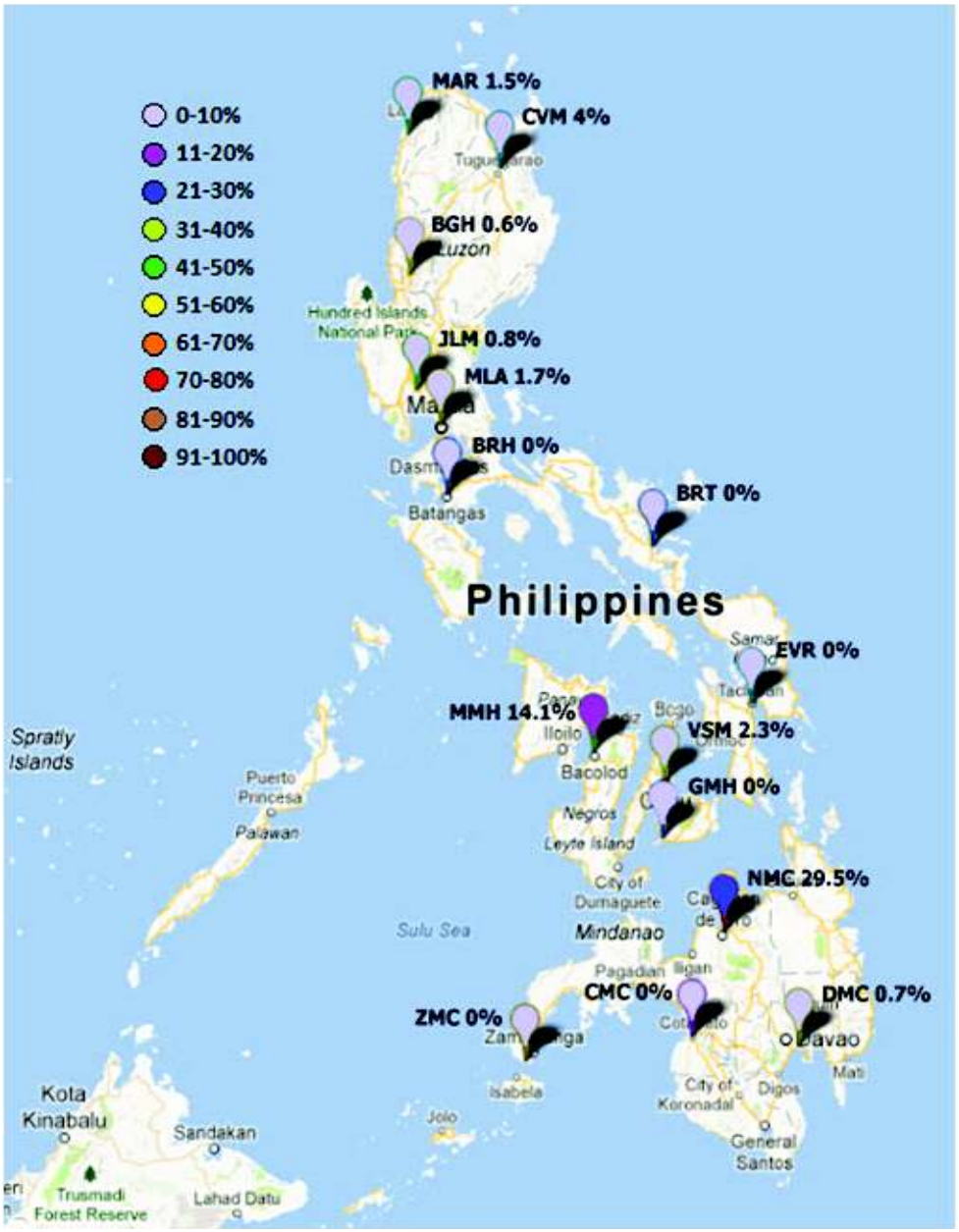


Figure 16a. *E. coli* imipenem resistance rates by sentinel site DOH ARSP, 2012

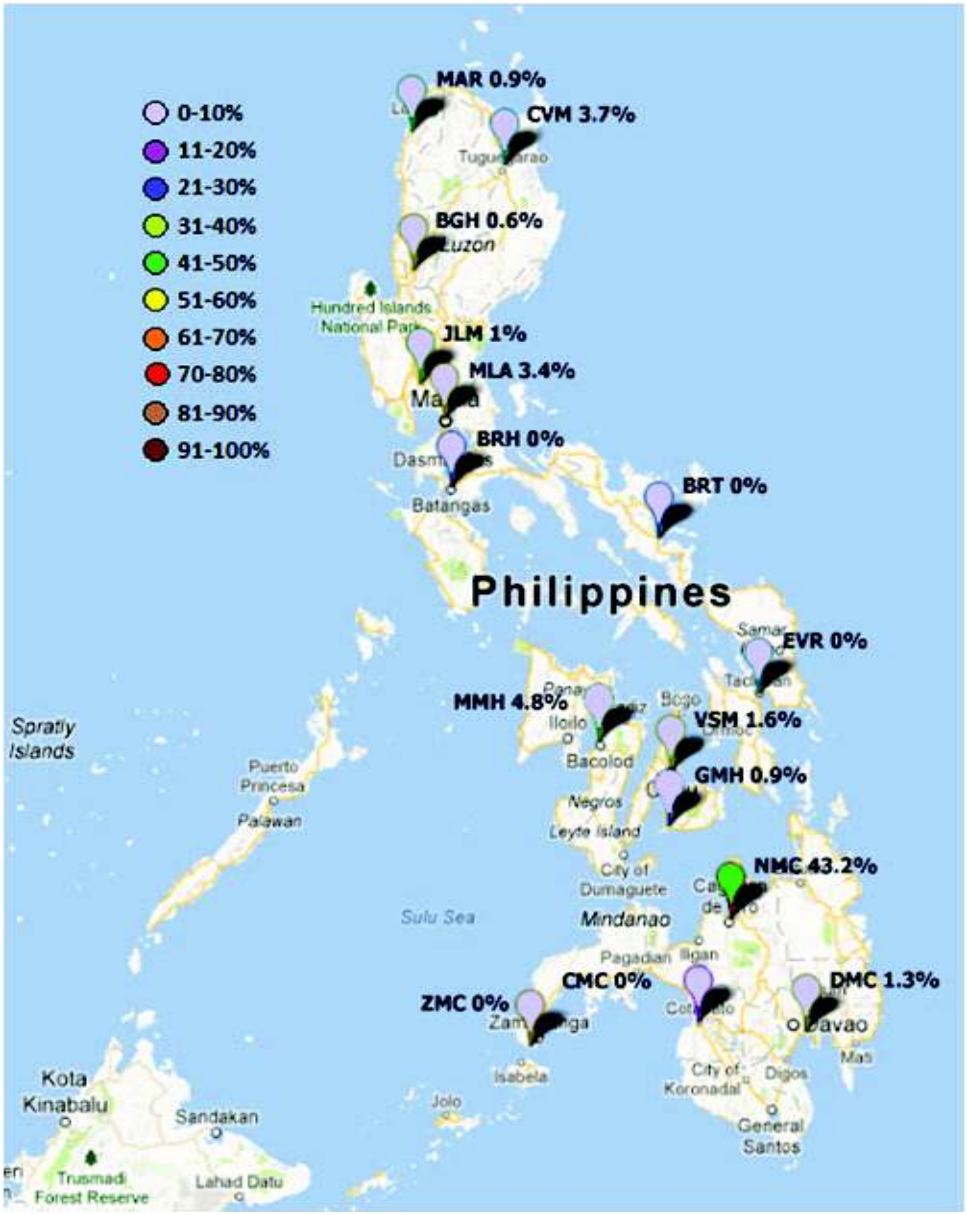


Figure 16b. *Klebsiell a*sp. imipenem resistance rates by sentinel site DOH ARSP, 2012

At the reference laboratory, these referred Enterobacteriaceae isolates with resistance to at least 1 carbapenem were processed for phenotypic confirmatory testing for carbapenemase production using the modified Hodge test (Clinical and Laboratory Standards Institute, 2012). There were 43 out of the 52 isolates or 83% that tested as positive for carbapenemase production. Genotypic confirmatory testing using PCR (Mulvey MR, Jan 2011) revealed that 91% or 39 of the 43 carbapenemase-producing isolates tested (19 *E. coli*, 16 *K. pneumoniae*, 3 *E. cloacae* and 1 *C. sedlakii*) harbored the NDM-1 gene. These carbapenem-resistant Enterobacteriaceae identified as carrying the NDM gene were mostly

from the Visayas region (19 isolates for MMH and 14 isolates from VSM), while the rest were from Metro Manila (1 isolate from STU and 3 isolates from NKI) and Mindanao (2 isolates from DMC) (Figure 16c).

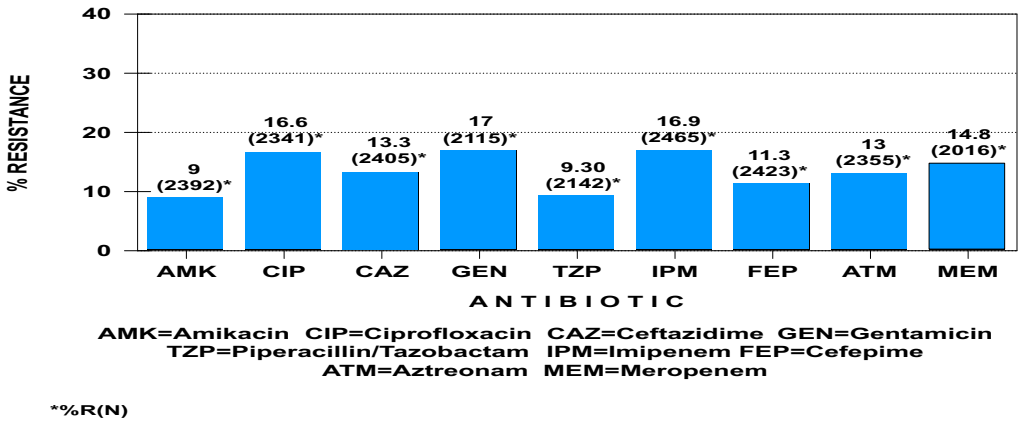
Antimicrobial susceptibility testing reveals that these isolates were also resistant to all tested beta-lactams including carbapenems, penicillins, beta-lactam-beta-lactamase inhibitor combinations, monobactams, cephalosporins, the fluoroquinolones, co-trimoxazole, tetracycline and chloramphenicol. These isolates remained susceptible only to aminoglycosides, tigecycline and colistin.

16c. Distribution of NDM producing Enterobacteriaceae in the Philippines, DOH ARSP, 2012

c) *Pseudomonas aeruginosa*

Rates of resistance of *Pseudomonas aeruginosa* isolates for 2012 against antibiotics used for treatment ranged from 9% against amikacin to as high as 17% against gentamicin (Figure 17a). Compared to rates from the previous year, *P. aeruginosa* 2012 isolates showed significant decrease in resistance rates from 15.2% in 2011 to 13.3% in 2012 against ceftazidime (*p* value 0.0381). Trends of resistance against ciprofloxacin also showed decreasing rates for the past decade, although no significant change was noted when 2012 rates were compared to those of 2011 (*p* value >0.05) (Figure 17b).

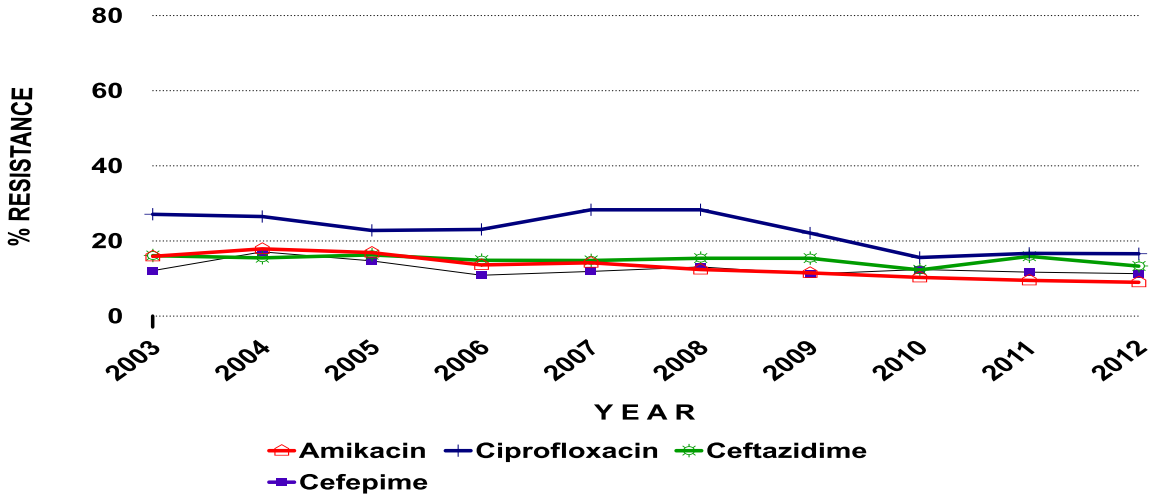
Figure 17a: Percent resistance of *Pseudomonas aeruginosa*
DOH ARSP, 2012



AMK=Amikacin CIP=Ciprofloxacin CAZ=Ceftazidime GEN=Gentamicin
TZP=Piperacillin/Tazobactam IPM=Imipenem FEP=Cefepime
ATM=Aztreonam MEM=Meropenem

*%R(N)

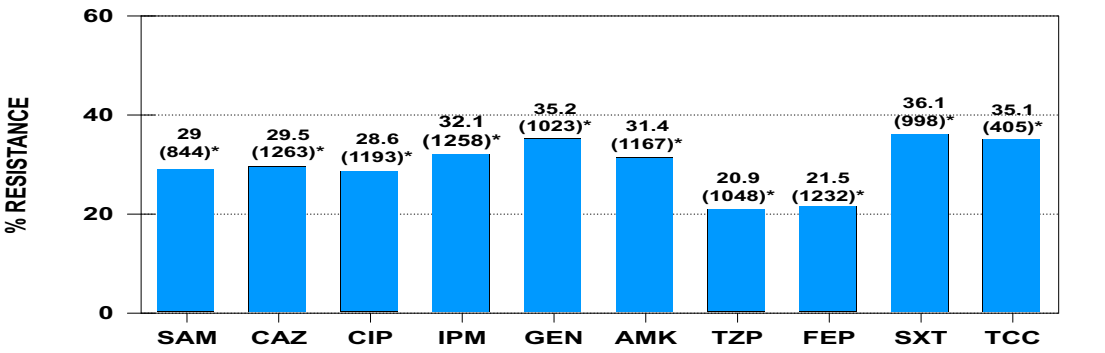
Figure 17b: Yearly resistance rates of *Pseudomonas aeruginosa*
DOH ARSP, 2003 - 2012



d) *Acinetobacter baumannii*

When compared to *P. aeruginosa*, isolates of *Acinetobacter baumannii* for 2012 showed higher rates of resistance against antibiotics used for treatment which ranged from 20.9% against piperacillin-tazobactam to as high as 36.1% against co-trimoxazole (Figure 18a). Rates of resistance against imipenem significantly increased from 26.4% in 2011 to 32.1% in 2012 (*p* value 0.0004). The rest of the antibiotics tested showed similar rates to that of the previous year (*p* value > 0.05) (Figure 18b).

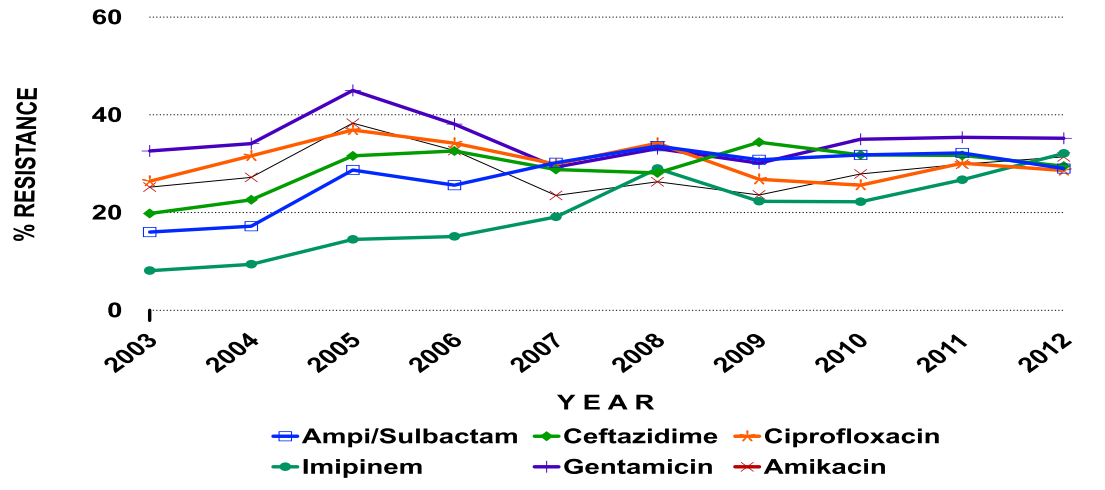
Figure 18a. Percent resistance of *Acinetobacter baumannii*
DOH ARSP, 2012



SAM=Ampicillin/Sulbactam CAZ=Ceftazidime CIP=Ciprofloxacin IPM=Imipinem
GEN=Gentamicin AMK=Amikacin TZP=Piperacillin/Tazobactam FEP=Cefepime
SXT=Trimethoprim/Sulfamethoxazole TCC=Ticarcillin/Clavulanic

*%R(N)

Figure 18b. Yearly resistance rates of *Acinetobacter baumannii*
DOH ARSP, 2003 - 2012



VI. Multidrug Resistant Pathogens

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 definition employed for **multidrug-resistant (MDR)** in this report would be resistance of an organism to at least one agent in three or more classes of antimicrobial categories. **Extensively drug resistant (XDR)** isolates are those that exhibit resistance to at least one agent in all but two or fewer antimicrobial categories (i.e. bacterial isolates remain susceptible to only one or two categories). **Pandrug-resistant (PDR)** is defined as non-susceptibility of an organism to all agents in all antimicrobial categories. In cases of incomplete testing, bacterial isolates can only be characterized as **possible XDR** or **possible PDR**(Table 11 and 12)(Magiorakos AP, 2012).

Table 11: Definition of MDR, XDR and PDR (Magiorakos AP, 2012)

Term	Definition
MDR	Resistance of the organism to at least one agent in three or more classes of antimicrobial categories
XDR	Resistance to at least one agent in all but two or fewer antimicrobial categories (i.e. bacterial isolates remain susceptible to only one or two categories)
PDR	Non-susceptibility to all agents in all antimicrobial categories

Table 12: Antibiotic Categories Used to Define MDR, XDR and PDR *Pseudomonas aeruginosa* and *Acinetobacter baumannii* (Magiorakos AP, 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 Flouroquinolones
Antipseudomonal Penicillinplus beta-lactamase inhibitor	Antipseudomonal Penicillin plus beta-lactamase inhibitor
Monobactams	Folate Pathway Inhibitors
Phosphonic Acid	Penicillins plus beta-lactamase inhibitor
Polymyxins	Polymyxins
	Tetracyclines

MDR and Possible XDR *P. aeruginosa*

ARSP 2012 data shows that 21% (552 out of 2580 isolates) of *Pseudomonas aeruginosa* isolates are MDR and as many as 17% (442 out of 2580 isolates) are possible XDR. MDR and possible XDR *P. aeruginosa* were reported by all 21 active sentinel sites.

Among the sentinel sites with at least 30 isolates of the *P. aeruginosa* reported, NMC in Mindanao had the highest MDR rates at 44% and possible XDR rates at 34% (n= 32). When rates of MDR-*P. aeruginosa* were analyzed by region, NCR rates were the highest at 28%, followed by Mindanao at 23%, Visayas at 19% and the rest of Luzon at 11%. Similarly, possible XDR-*P. aeruginosa* rates were highest at the NCR at 24%, followed by Mindanao at 17%, Visayas at 14% and the rest of Luzon at 8% Table 13).

Table 13. MDR *Pseudomonas aeruginosa* (PAE) Rates DOH ARSP, 2012

Region	# PAE Isolates	# MDR PAE Isolates	% MDR	# Possible XDR	% Possible XDR
Luzon	1473	325	22%	274	19%
• NCR	979	271	28%	235	24%
• excluding NCR	494	54	11%	39	8%
Visayas	611	114	19%	84	14%
Mindanao	496	113	23%	84	17%
Total	**2580**	**552**	**21%**	**442**	**17%**

MDR and Possible XDR *Acinetobacter baumannii*

ARSP 2012 data shows even higher MDR rates for *Acinetobacter baumannii* 2012 isolates with as much as 58% (766 out of 1344 isolates) already MDR and as many as 35% (475 out of 1344 isolates) are possible XDR. MDR- *A. baumannii* was reported by 20 of the 21 active sentinel sites while possible XDR isolates were from 19 sentinel sites.

Among the sites that reported at least 30 *Acinetobacter baumannii* isolates for 2012, NMC of Mindanao had the highest MDR rates 92% (n 136); while LCP of the NCR had the highest possible XDR rates at 61% (n= 204). When rates of MDR *A. baumannii* were analyzed by region, Mindanao rates were the highest at 67%, followed by NCR at 63%, the rest of Luzon at 50%, and Visayas at 38%. Conversely,

possible XDR- *A. baumannii* rates were highest at the NCR at 46%, followed by Mindanao at 41%, the rest of Luzon 25%, and Visayas at 17% (Table 14).

Table 14. MDR *Acinetobacter baumannii* (ABA) Rates DOH ARSP, DOH ARSP

Region	# ABA Isolates	# MDR ABA Isolates	% MDR	# Possible XDR	% Possible XDR
NCR	460	291	63%	210	46%
• Luzon	807	463	57%	296	37%
• w/o NCR	347	172	50%	86	25%
Visayas	166	63	38%	28	17%
Mindanao	371	250	67%	151	41%
Total	**1344**	**776**	**58%**	**475**	**35%**

VII. Presumptive Etiologic Agents of Nosocomial Infections

In 2005, the ARSP processed a department order requiring all clinical laboratories and consequently all ARSP sentinel sites to include the patient's hospital number and date of admission on the laboratory test request. This was for purposes of creating a database of presumptive nosocomial infections without clinical confirmation. An **inpatient** is defined as a patient admitted in the hospital. A **presumptive nosocomial isolate** was defined as an isolate from an inpatient taken from the 3rd hospital day onwards. Starting 2012, all sentinel sites have also been requested to include in their data submissions, information on clinical diagnosis preferably expressed in ICD 10 codes. This was to allow the program to gather data on actual nosocomial infections.

Of the 27,069 total number of isolates reported for 2012, 85% (23,006 specimens) were from inpatients. Of these inpatients, 96% had information on the date of hospital admission on their laboratory test request form (range: 72%-100%) (Table 15).

Of the 23,006 specimens from inpatients, 38% are presumptively nosocomial pathogens. Range of possible hospital nosocomial infection rate are 13% as noted for FEU in Metro Manila to 64% as noted for ZMC in Mindanao (Table 15).

The most common presumptively nosocomial pathogens for 2012 were *Klebsiella* sp., *Escherichia coli* and *Pseudomonas aeruginosa*, in decreasing order (Table 16).

When analyzed by sentinel site, 14 out of the 21 sites (BGH, BRT, CMC, DMC, EVR, FEU, GMH, JLM, MAR, NKI, NMC, STU, VSM and ZMC) had *Klebsiella* sp. as their most frequent nosocomial isolate for 2012; while 2 sites (BRH and SLH) had *Pseudomonas aeruginosa* as the commonest (Tables 17).

Table 15: Percentage of Inpatient Specimens that are Presumptive Nosocomial Pathogens DOH ARSP, 2012

Name of Laboratory	Number of Inpatient Specimens	Number of Inpatient Specimens with Date of Admission on Laboratory Request Form	% of Inpatient Specimens with Date of Admission Laboratory Request Form	Number of Inpatient Specimens Taken from the 3rd Hospital Day Onwards	% of Inpatient Specimens that are Presumptively Nosocomial Pathogens
BGH	1,755	1,731	99%	444	25%
BRH	20	20	100%	11	55%
BRT	659	650	99%	171	26%
CMC	518	512	99%	146	28%
CVM	814	812	100%	192	24%
DMC	3,143	3,098	99%	1,666	53%
EVR	461	457	99%	162	35%
FEU	649	648	100%	83	13%
GMH	1,471	1,471	100%	509	35%
JLM	584	575	98%	154	26%
LCP	1,701	1,698	100%	728	43%
MAR	1,594	1,590	100%	658	41%
MMH	1,096	1,092	100%	666	61%
NKI	1,480	1,344	91%	400	27%
NMC	1,647	1,577	96%	581	35%
RMC	823	673	82%	144	17%
RTM	157	141	90%	25	16%
SLH	307	220	72%	102	33%
STU	1,344	1,050	78%	352	26%
VSM	2,140	2,138	100%	1,157	54%
ZMC	643	643	100%	414	64%
TOTAL	**23,006**	**22,140**	96%	**8765**	**38%**

Table 16. Top 10 Commonest Presumptive Nosocomial Isolates DOH ARSP, 2012

Organism	Number of patients (n=27,069)
Klebsiella sp.	3,934
Escherichia coli	2,992
Pseudomonas aeruginosa	2,281
Enterobacter sp.	2,026
Staphylococcus, coagulase negative	1,875
Staphylococcus aureus	1,662
Acinetobacter baumannii	1,230
Staphylococcus haemolyticus	1,017
Staphylococcus epidermidis	947
Proteus sp.	705

Table 17. Most Common Presumptive Nosocomial Isolate by Site DOH ARSP, 2012

SITE	Most Common Presumptive Nosocomial Isolate
BGH	*Klebsiella* sp.
BRH	*Pseudomonas aeruginosa*
BRT	*Klebsiella* sp.
CMC	*Klebsiella* sp.
CVM	*Staphylococcus epidermidis*
DMC	*Klebsiella* sp.
EVR	*Klebsiella* sp.
FEU	*Klebsiella* sp.
GMH	*Klebsiella* sp.
JLM	*Klebsiella* sp.
MAR	*Klebsiella* sp.
NKI	*Klebsiella* sp.
NMC	*Klebsiella* sp.
RMC	*Enterobacter* sp.
SLH	*Pseudomonas aeruginosa*
STU	*Klebsiella* sp.
VSM	*Klebsiella* sp.
ZMC	*Klebsiella* sp.

VIII.2012 Referrals to the ARS Reference Laboratory

In 2012, a total of 3676 isolate referrals from 19 out of 21 active sentinel sites were processed for confirmatory testing at the Antimicrobial Resistance Surveillance Reference Laboratory (ARSRL). The most number of isolates were received from VSM who had 878 isolate referrals, followed by MAR with 437 isolate referrals. There were 185 referrals presumptively identified as respiratory pathogens at the sentinel sites; 155 referrals presumptively identified as enteric pathogens at the sentinel sites; 18 *N. gonorrheae* isolates; 463 *S. aureus* and 557 coagulase-negative staphylococci referrals; 69 Enterococcus sp. isolate referrals; 399 *E. coli* isolate referrals, 611 Klebsiella sp. isolate referrals, 510 *P. aeruginosa* isolate referrals and 98 Acinetobacter sp. isolate referrals (Table 18).

Table18: Isolate Referrals to ARSRL DOH ARSP, 2012

Organism Identification at the Sentinel Site	Number of 2012 Isolate Referrals
Respiratory Pathogens	
Streptococcus pneumoniae	78 isolates
Haemophilus influenzae	105 isolates
Moraxella sp.	2 isolates
Enteric Pathogens	
Salmonella Paratyphi A	3 isolates
Salmonella sp.	24 isolates
Salmonella Typhi	104 isolates
Shigella sp.	1 isolate
Vibrio cholerae	23 isolates
Neisseria gonorrheae	18 isolates
Staphylococcus aureus	463 isolates
Staphylococci	557 isolates
Enterococci	69 isolates
Escherichia coli	399 isolates
Klebsiella sp.	611 isolates
Pseudomonas aeruginosa	510 isolates
Acinetobacter sp.	98 isolates
Others	611 isolates

IX: Recommendations

Based on the above-mentioned antimicrobial resistance surveillance data for 2012:

- Empiric treatment for suspected uncomplicated typhoid fever could still consist of either chloramphenicol, cotrimoxazole or amoxicillin/ampicillin. There are increasing reports of nalidixic acid resistance and ciprofloxacin nonsusceptibility which may result to clinical treatment failures. Microbiological testing 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 the subset of patients requiring antibiotics for treatment such as in bacteremia due to nontyphoidal *Salmonellae*, ceftriaxone maybe a better treatment option.

- In view of the emerging resistance of *Shigellae* to the quinolones, continued surveillance of the resistance pattern of this organism should be pursued with the possibility of considering alternative antimicrobial treatment such as ceftriaxone or azithromycin if the rates continue to rise.

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

- 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.

- 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.

- Ceftriaxone remains as empiric antibiotic of choice for gonococcal infections.

- In view of the continued high rates of methicillin/oxacillin resistance among staphylococci in 2012, 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. The rising MRSA rates necessitate clear local treatment guidelines for managing suspected cases.

- 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. There is need to closely monitor the presence of ESBLs and carbapenemase resistance among the Enterobacteriaceae considering the very limited treatment options available.

- There is a need to closely monitor the emergence of MDR and XDR gram-negative bacteria such as *Pseudomonas aeruginosa* and *Acinetobacter baumannii*as there is little available in terms of antibiotics for treatment.

- Increasing rates of MRSA, ESBL-producing Enterobacteriaceae, carbapenem resistant Enterobacteriaceae and the MDR and possible XDR organisms in the hospital should signal for a review of infection control procedures and its implementation.

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