DEPARTMENT OF HEALTH
RESEARCH INSTITUTE FOR TROPICAL MEDICINE
ANTIMICROBIAL RESISTANCE SURVEILLANCE REFERENCE LABORATORY

ANTIMICROBIAL RESISTANCE SURVEILLANCE PROGRAM

ANNUAL REPORT SUMMARY

2021

Antimicrobial Resistance Surveillance Program Annual Report - 2021.

Manila: ARSP; 2022

Suggested citation. Antimicrobial Resistance Surveillance Program Annual Report - 2021. Manila: Antimicrobial Resistance Surveillance Program; 2022.

Printed in the Philippines

Table of Contents

List of Figures

List of Tables

Foreword

The lowering of the number of COVID-19 cases in the second year of the pandemic allowed for a partial return of operations of health care facilities including the bacteriology laboratories to that of pre-pandemic period. Although this allowed for an increase in the data reported to the Antimicrobial Resistance Surveillance Program (ARSP) for 2021 compared with that of 2020, the number of data reports remain less compared to the numbers during the pre-pandemic period. This observation has to be considered in the interpretation of the 2021 ARSP Annual Report.

The 2021 ARSP annual report documents the continued increase in the resistance to carbapenems among the enterobacterales, specifically *Escherichia coli* and *Klebsiella pneumoniae*, as well as among *Acinetobacter baumannii*. Further, the emergence of colistin resistance among the enterobacterales as well as among the non-fermenters was also noted in this report. These observations signify the need to intensify the measures for the judicious use of these last resort antibiotics.

As an initial venture in incorporating data on whole genome sequencing in the ARSP annual report, the base-line genomic survey of methicillin-resistant *S. aureus* (MRSA) collected in 2013-2014 is included in the 2021 ARSP Annual Report. This genomic survey was implemented in 2017-2019 as part of a collaborative project with the Wellcome Trust Sanger Institute to develop the competency for whole genome sequencing and bioinformatics in the Antimicrobial Resistance Surveillance Reference Laboratory (ARSRL). The survey revealed the limited number of clones among the MRSA population in the country. It also provided genomic characterization of the MRSA isolates in the country including elucidation of the genes conferring resistance among these isolates.

The ARSP continually endeavours to adopt towards provision of requisite information for the control and prevention of AMR in the country. In view of the key strategy 2 of the Philippine Action Plan to Combat Antimicrobial Resistance 2019-2023 to "Strengthen surveillance and laboratory capacity", we advocate for the sustained national government support for the program to include resources for genomics as well as strategies to enable generation of quantifiable burden of disease through a case-based AMR surveillance.

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Executive Summary

Resistance data for 70,951 bacterial isolates coming from 24 hospital based bacteriology laboratories as sentinel sites and 1 gonorrhoeae surveillance sites were analyzed for 2021.

Streptococcus pneumoniae

Cumulative resistance rate of *S. pneumoniae* isolates against penicillin using non-meningitis breakpoint at 1.4% (n=144) remained low making this antibiotic a viable option for treatment for non-meningitis infection. Continued increase in resistance to erythromycin was noted until its rate of 11.3% in 2021 and may limit utility of extended spectrum macrolides. *S. pneumoniae* isolates remained susceptible to ceftriaxone (meningitis and non-meningitis breakpoints) at 5% (n=100).

Haemophilus influenzae

Resistance rate of *H. influenzae* for 2021 to ampicillin was at 13.9% - remaining within the range of 7.8% (2016) and 17.2% (2013) in the past 10 years. These isolates remained mostly susceptible to ceftriaxone with nonsusceptibility rate for 2021 being at 3.8%. No resistance to levofloxacin and azithromycin was reported for 2021.

Salmonella enterica serotype Typhi

Salmonella Typhi isolates remained susceptible to ampicillin, chloramphenicol, and azithromycin with no resistance detected against these antibiotics for 2021. Resistance to ciprofloxacin remained below 5% for the past 10 years with 2021 resistance at 2.6%.

Nontyphoidal *Salmonella*

As in the past years, resistance of nontyphoidal *Salmonella* to ampicillin, cotrimoxazole and chloramphenicol are higher compared to *Salmonella* Typhi with noted increase in resistance rates to these antibiotics for 2021 compared to the rates in 2020. Resistance to ciprofloxacin remained within 10-12% range in the past 7 years with 2021 resistance at 11.2%.

Shigella species

Resistance to ceftriaxone and ciprofloxacin for 2021 among *Shigella* are above 10%. Ciprofloxacin resistance had been noted to increase in the past 3 years while resistance to ceftriaxone has been in the 10-12% range in the past 4 years. No azithromycin resistance was reported for 2021.

Vibrio cholerae

Vibrio cholerae isolates remain susceptible to antibiotics with resistance to cotrimoxazole and to tetracycline at less than 4% and no resistance reported to azithromycin and chloramphenicol for 2021 and have been observed to be so in the past several years.

Neisseria gonorrhoeae

There is no confirmed resistance to ceftriaxone, cefixime, azithromycin and spectinomycin for 2021 as it had been for the past 10 years. Resistance to tetracycline and ciprofloxacin continues to be very high for 2021 at 71.4% (n=35) and 83.6% (n=55), respectively.

Staphylococcus aureus

There is a noted continued decrease of oxacillin resistance among ***Staphylococcus aureus*** to its present rate of 46.9% (n=4,126) in 2021. Erythromycin resistance was at 12.3% (4,050) and clindamycin at 10.5% (n=3,937) – both rates appear to be stable for the past years. Vancomycin resistance was noted to be at 2.1% (n=3,664) for 2021 and the increase in the resistance to vancomycin in the past decade was noted to be statistically significant. There is a report of a confirmed daptomycin non-susceptible isolate from NCR.

Enterococcus species

Resistance of *Enterococcus faecalis* to penicillin and ampicillin for 2021 were at 9.1% and 17.5%, respectively, with resistance to penicillin continuously increasing over the past 10 years. Vancomycin resistance continuously increased in the past 10 years to its current level of 4.0% in 2021.

Enterococcus faecium continue to show higher antibiotic resistance with rates for vancomycin and nitrofurantoin being 30.3% and 33.1%, respectively for 2021. There was a continued increase in linezolid resistance to its current rate of 5.2% for 2021.

Escherichia coli

Carbapenem resistance among *E. coli* has remained above 8% imipenem and meropenem and above 6% for ertapenem for year 2021 with the increase in rates over the past decade noted to be statistically significant. Reports of confirmed colistin resistant *E. coli* isolates were noted for 2021 with these isolates noted to be susceptible to the carbapenems, piperacillin/tazobactam, gentamicin and amikacin. Overall ESBL positivity rate among *E. coli* remains over 25%.

Klebsiella pneumoniae

Carbapenem resistance among *K. pneumoniae* isolates continue to rise in 2021 with resistance rates for meropenem at 15.2% (n=10,392), imipenem at 14.5% (n=10,643) and ertapenem at 10.5% (n=9,434). When the subset of invasive blood culture *K. pneumoniae* isolates were analyzed, even higher carbapenem resistance rates were noted with meropenem resistance rate at 20.3% (n=1,056). *K. pneumoniae* extended-spectrum β-lactamase suspect rates for 2021 was at 29.53%.

Pseudomonas aeruginosa

For 2021, resistance of *Pseudomonas aeruginosa* isolates to ceftazidime and piperacillin/tazobactam remains above 10% while resistance to gentamicin decreased at 8.1%. For 2021, carbapenem resistance was reported at 16.6% for imipenem (n=6,026) and 14.3% (n=5,895) for meropenem. Colistin resistance was at 5.1% (n=2,016). MDR and possible XDR rates for *Pseudomonas aeruginosa* were at 20% and 14% respectively for 2021.

Acinetobacter baumannii

For 2021, resistance to most antibiotics remained above 50% with increases in rates for ceftazidime, meropenem, and imipenem noted to be statistically significant. There were 3 confirmed colistin resistant *A. baumannii* isolates reported in 2021. The increase in colistin resistance noted to begin in 2020 was found to be not statistically significant. MDR and possible XDR rates for *A. baumannii* isolates for 2021 were at 64% and 52% respectively.

Introduction

Antimicrobial Resistance (AMR) is the change that occurs over time among bacteria, viruses, fungi and parasites where these organisms no longer respond to medicines making infections harder to treat and increasing the risk of disease spread, severe illness and death[1]. *AMR is a serious public health threat* because of its far reaching and serious implications in health care as well as economies. AMR hampers the control of infectious diseases because patients remain infectious for a longer time increasing the risk of spreading resistant microorganisms to others. AMR 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 increases economic burden to families and societies as it often results in longer duration of illness and treatment.

With the loss of 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.

The Philippine Committee on Antimicrobial Resistance Surveillance Program was created in 1988 through the Department of Health's Department Order 339-J. The program aims to provide critical inputs to the Department of Health's effort to promote rational drug use by determining the status and developing trends of antimicrobial resistance of selected bacteria to specific antimicrobials.

AMR surveillance remains an essential component in the control of AMR in the country. Surveillance data enable correct decisions to be made about treatment options and guide policy recommendations. The Philippine National Action Plan on Antimicrobial Resistance 2019 -2023 [2] reiterates the importance of surveillance as it identifies the strengthening of surveillance and laboratory capacity as among its key strategy.

Even as the COVID-19 pandemic continued on for 2021, the bacteriology sections of the sentinel sites as well as the reference laboratory have slowly shifted back to their regular operations. The culture and susceptibility reports submitted into the program was noted to have increased by more than 13% compared with the reports submitted in 2020. However, the number of data received by ARSP for 2021 still is a lot less compared with the numbers reported prior to the pandemic. This difference must be kept in mind in the interpretation of the surveillance data in the past two years.

As we contend with the impact of the pandemic on AMR, continued surveillance is crucial to understand the changes in AMR trends and patterns among the bacterial isolates of public health importance in the country. Further, efforts to gather data on the burden of disease due to resistant infections may allow for stronger policy support to combat AMR in the country.

SURVEILLANCE, TESTING METHODS, DATA ANALYSIS & LIMITATIONS

The Surveillance

The DOH-ARSP is a sentinel laboratory-based antimicrobial resistance surveillance on aerobic bacteria from clinical specimens.

Currently participating in the program are 24 sentinel sites, and 2 gonococcal surveillance sites, representing 16 out of the 17 regions of the country (**Figure 1 & Table 1**).

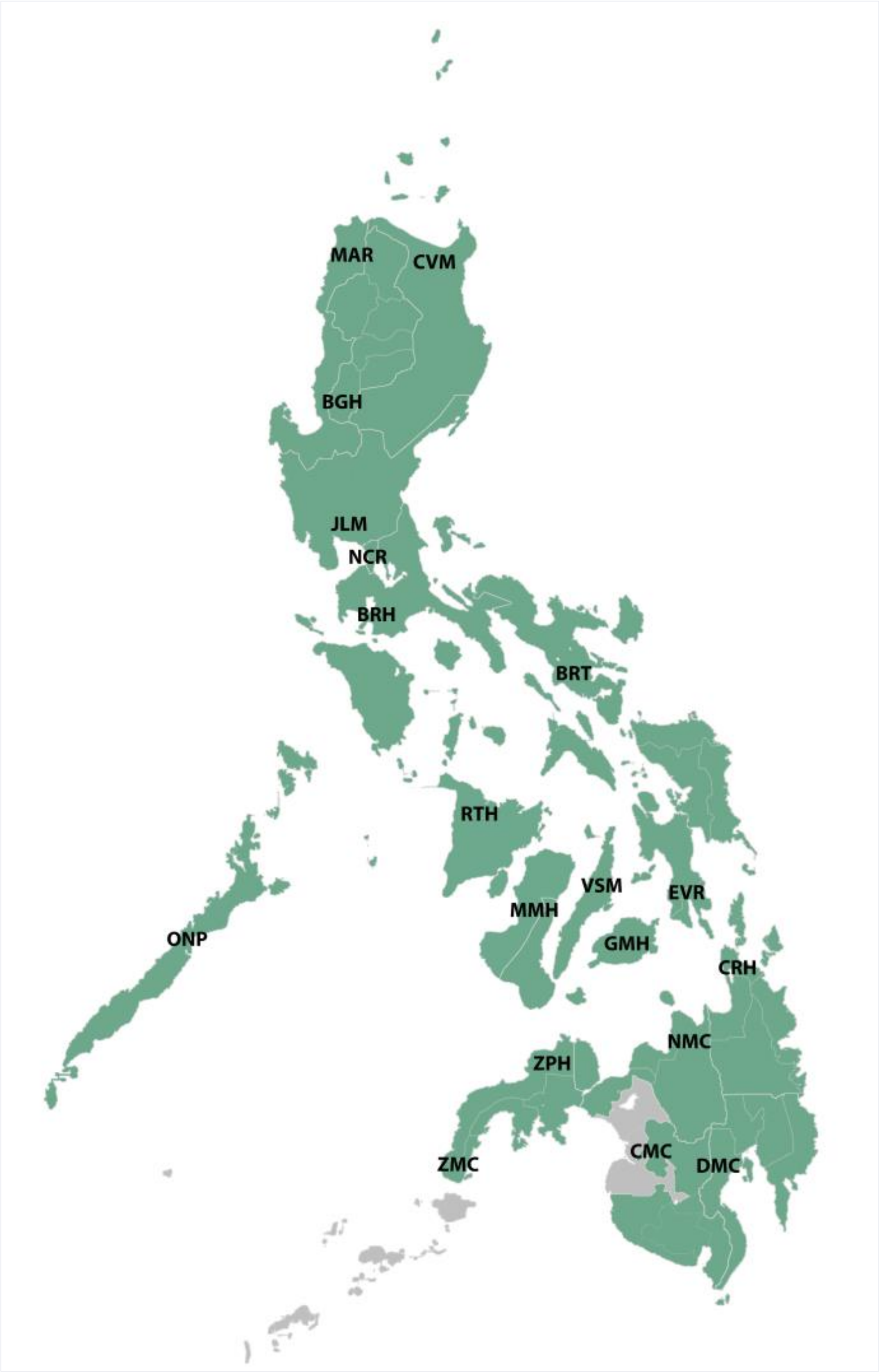


Figure 1. Regional representation in the ARSP 2021

Table 1. ARSP 2021 sentinel sites by region

Region	Sentinel Site
National Capital Region (NCR)	Lung Center of the Philippines National Kidney and Transplant Institute Rizal Medical Center San Lazaro Hospital Philippine General Hospital Research Institute for Tropical Medicine University of Santo Tomas Hospital Far Eastern University Nicanor Reyes Medical Foundation Medical Center
Cordillera Administrative Region (CAR)	Baguio General Hospital and Medical Center
Region 1—Ilocos Region	Mariano Marcos Memorial Hospital and Medical Center
Region 2—Cagayan Valley	Cagayan Valley Medical Center
Region 3—Central Luzon	Jose B. Lingad Memorial Regional Hospital
Region 4-A—CALABARZON	Batangas Medical Center
Region 4-B—MIMAROPA	Ospital ng Palawan
Region 5—Bicol Region	Bicol Regional Training and Teaching Hospital
Region 6—Western Visayas	Corazon Locsin Montelibano Memorial Regional Hospital Dr. Rafael S. Tumbokon Memorial Hospital
Region 7—Central Visayas	Celestino Gallares Memorial Hospital Vicente Sotto Memorial Medical Center
Region 8—Eastern Visayas	Eastern Visayas Regional Medical Center
Region 9—Zamboanga Peninsula	Zamboanga City Medical Center Zamboanga del Norte Medical Center
Region 10—Northern Mindanao	Northern Mindanao Medical Center
Region 11—Davao Region	Southern Philippines Medical Center
Region 12—SOCCSKSARGEN	Cotabato Regional Hospital and Medical Center
Region 13—CARAGA Region	Caraga Regional Hospital
Legend: CALABARZON: Cavite, Laguna, Batangas, Rizal, Quezon; MIMAROPA: Mindoro, Marinduque, Romblon, Palawan; SOCCSKSARGEN: South Cotabato, Cotabato, Sultan Kudarat, Sarangani, General Santos City.	

The surveillance collects data on culture and antimicrobial susceptibility from its *24 sentinel sites and 2* gonococcal surveillance sites. Case finding is based on priority specimens sent routinely to sentinel sites laboratories for clinical purposes.

TESTING METHODS

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[3] and the updated Clinical Laboratory Standards Institute (CLSI) references for antibiotic susceptibility testing and quality control [4].

Panel of antibiotics for testing are based on the latest CLSI recommendations. In the analysis of antimicrobial susceptibility testing, 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.

The culture and antimicrobial susceptibility test results 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.

Using a standard format, routine culture and antimicrobial susceptibility test results are sent by the sentinel sites to the coordinating laboratory of the program – the ***Antimicrobial Resistance Surveillance Reference Laboratory (ARSRL) at the Research Institute for Tropical Medicine***. Beginning January 2018, sentinel sites transmit data daily to the reference laboratory. The automated data transfer facilitates prompt identification of resistant isolates of public health importance as well the identification of clustering of cases and potential outbreaks among sentinel sites. The ARSRL's Data Management Unit manages the cleaning, analysis, storage and security of the program's surveillance data.

Sentinel sites likewise send isolates with unusual antimicrobial susceptibility patterns to ARSRL for phenotypic and genotypic confirmatory testing.

At the reference laboratory, all isolates with unusual susceptibility patterns received for confirmatory testing are re-identified using both automated (Vitek) and conventional methods. Both minimum inhibitor concentration (MIC) - via automated method (Vitek) and gradient E-test, and disk diffusion are employed in antimicrobial susceptibility testing. As indicated, additional testing are done for specific antibiotics which are not included in AST card in use in the reference laboratory and for susceptibility testing for specific bacteria such as *N. gonorrhoeae* which requires manual AST methods. Serotyping for *S. pneumoniae*, *H. influenzae*, Salmonellae and *Vibrio cholera* were done for 2021.

The program sentinel sites participate in an external quality assessment scheme (EQAS) conducted by the reference laboratory to ensure quality of laboratory results. Conditions permitting, periodic monitoring visits to sentinel sites are likewise done.

DATA ANALYSIS

Analysis is restricted to the first isolate received (per genus under surveillance) per patient in the calendar year. Data are expressed as a cumulative resistance percentage, i.e. the percentage of resistant isolates out of all isolates with antimicrobial susceptibility testing (AST) information on that specific organism–antimicrobial agent combination. A 95% confidence interval is determined for the resistance percentage. Cumulative percentages of resistance are compared as proportions using Chi square trend test (Epi Info version 7.2), using a p value of <0.05 as statistically significant. Only species with testing data for 30 or more isolates are included in the analysis.

An annual report with a summary of the surveillance data focusing on aerobic bacterial pathogens of public health importance causing common infectious diseases with significant morbidity and mortality locally are disseminated to the program's stakeholders.

LIMITATIONS

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 capacity.

1) Most of the resistance data in the program come from regional hospitals which typically cater 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.
2) Data for the National Capital Region come from 8 sentinel sites while data for other regions come from 1 or 2 sentinel sites.
3) Given that the program data are from routine clinical samples, differences in factors indicating need for microbiological cultures may introduce variations in the resistance data.
4) Performance of culture and susceptibility tests in the sentinel sites is dependent on the diagnostic habits of the clinicians as well as the financial capability of patients for such test. Differential sampling can occur if cultures are typically only performed after empirical treatment shows no adequate therapeutic response. Predictably, this will lead to a serious overestimation of the percentage resistance by not including susceptible isolates in the denominator.
5) Lastly, the ability of the laboratory to identify the microorganism and its associated antimicrobial susceptibility pattern may differ.

The 2021 ARSP Data

Resistance data for 70,951 were reported and analyzed for 2021. This was 15.32% increase when compared with the reported 61,527 isolates in 2020 (Figure 2). Table 2 shows that 16 of 24 sentinel sites had an increase in data submission for 2021 while 8 sites had decrease in submission.

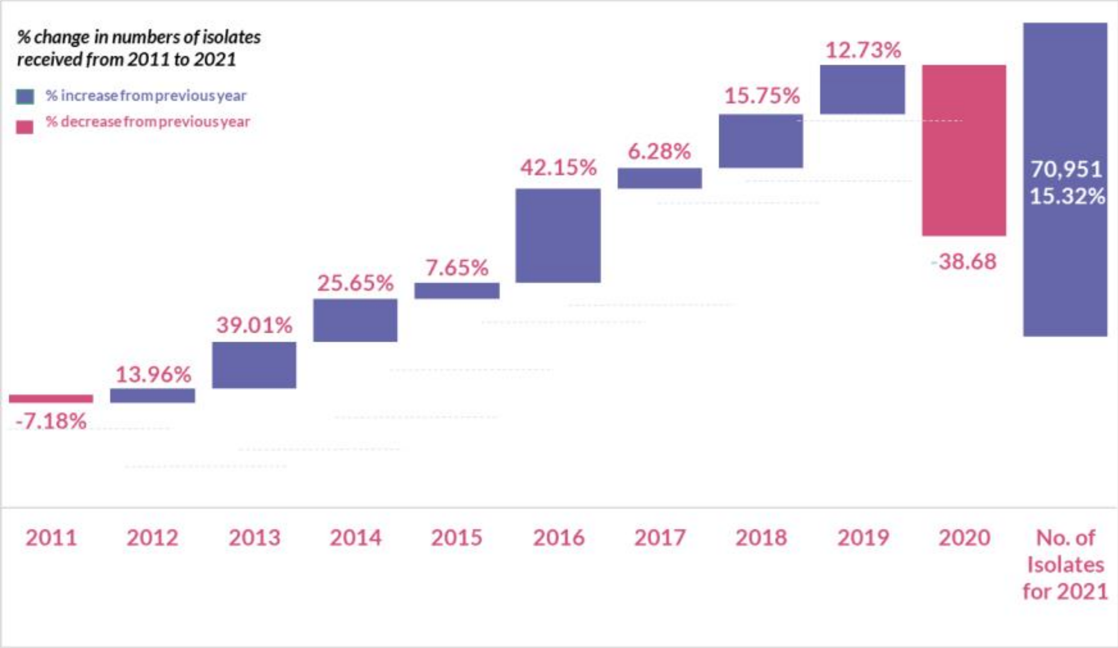


Figure 2. Number and the percentage difference of isolates received from 2012 to 2021

Table 2. Sentinel sites isolate contribution, DOH-ARSP, 2012 to 2021

SENTINEL SITES	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	Change %
PGH	-	7093	12471	11710	12860	14572	12808	13895	6818	9557	28.66
RMC	942	1207	320	1054	3252	3160	3241	2375	2027	1968	-3.00
NKI	2403	2179	2918	1455	5894	627	2959	4358		5571	100.00
LCP	2083	2253	2921	2905	3115	1367	3098	4433	2713	3205	15.35
RTM	383	303	303	336	410	513	598	507	255	423	39.72
SLH	318	1132	575	824	1410	2460	2044	2371	1019	1157	11.93
GMH	1521	1307	1351	1807	1669	3153	3258	3957	2624	2818	6.88
ZMC	721	822	819	841	1142	1222	1346	1644	1192	1341	11.11
FEU	931	1050	956	712	810	1201	1173	548		322	100.00
STU	1788	2050	2002	1923	2275	2088	2184	2722	1419	1250	-13.52
EVR	507	697	823	1514	1731	3303	3879	3874	4056	4584	11.52
MMH	1153	1413	2289	2940	2886	3133	3026	2539	1425	1140	-25.00
DMC	3332	3456	4062	5109	8058	8680	10762	12177	7412	8189	9.49
VSM	2450	3171	3951	3834	4803	6838	8714	10286	6886	6971	1.22
BGH	1972	2583	2625	3214	4628	4842	5775	5234	2968	3191	6.99
CMC	639	796	833	1300	1599	1704	2642	3181	2076	2021	-2.72
BRT	677	611	1047	1251	1584	1640	1842	2521	1176	1903	38.20
RTH	-	-	-	-	25	69	159	352	289	0	0.00
ZPH	-	-	9	8	4	7	3	69	129	1	-12800.00
MAR	1928	1773	1706	1849	2759	3565	4293	4462	3581	3302	-8.45
BRH	38	-	1022	1294	2075	2472	3133	3633	1569	1472	-6.59
CVM	944	1100	1223	1512	3473	4141	4276	5668	3782	2687	-40.75
JLM	655	502	638	1266	2768	3261	3880	4824	3248	3753	13.46
NMC	1684	2131	2416	2237	3105	2245	2961	3409	3735	2780	-34.35
ONP	-	-	-	-	2	5	68	90	13	31	58.06
CRH	-	-	-	-	10	624	879	1205	1115	1314	15.14
TOTAL	27069	37629	47280	50895	72347	76892	89001	100334	61527	70951	

The 2021 ARSP data were collected from 24 sentinel sites and 1 *N. gonorrhoeae* surveillance sites of the program which represents 16 out of 17 regions in the Philippines. Of the total number of isolates for 2021, 56.08% were from Luzon, 21.86% from Visayas and 22.05% were from Mindanao (Figure 3). The eight sentinel sites from NCR contributed to 33.05% of the total 2021 data. Majority of the isolates were from male patients (52.70%) and from 20-64 years of age (60.03%). The most common specimen types were respiratory (30.81%), blood (26.93%) and wound (14.72%) (Figure 4). Table 3 shows the most common isolates by specimen type

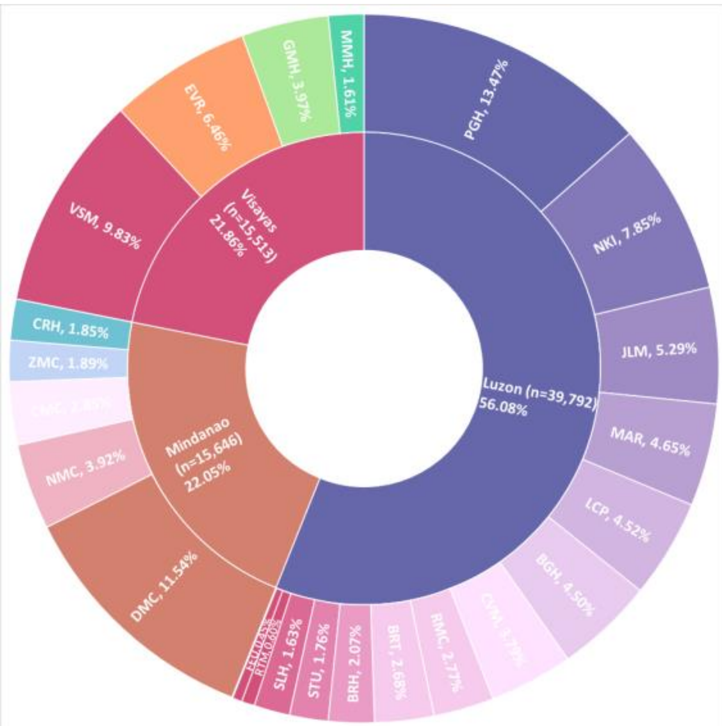


Figure 3. Sentinel sites isolate contribution, DOH-ARSP, 2021 (n=70,951)

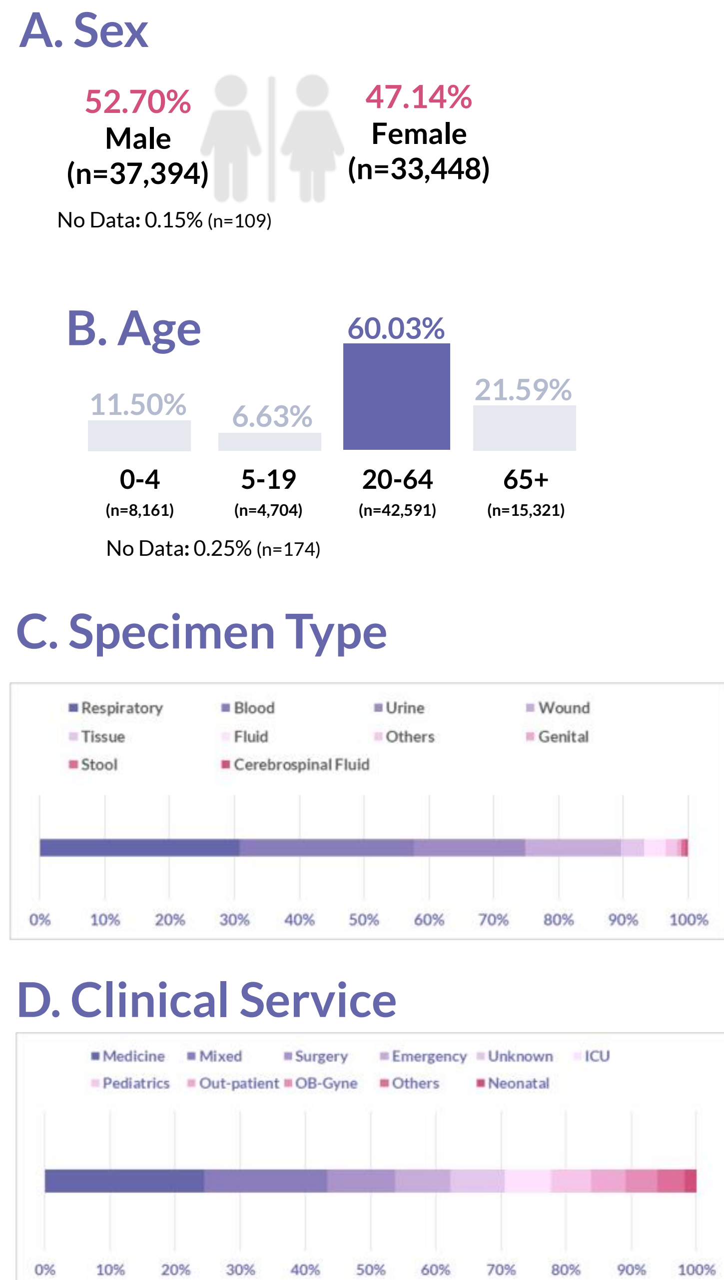


Figure 4. Patient characteristics of the 2021 ARSP isolates, DOH-ARSP, 2021 (n=70,951)

Table 3. Most common isolates by specimen type, DOH-ARSP, 2021

Respiratory Specimens		Blood	
1	*Klebsiella pneumoniae ss. pneumoniae*	1	*Staphylococcus, coagulase negative*
2	*Pseudomonas aeruginosa*	2	*Staphylococcus aureus*
3	*Acinetobacter baumannii*	3	*Klebsiella pneumoniae ss. pneumoniae*
Cutaneous or Wound		**Stool**	
1	*Escherichia coli*	1	*Vibrio cholerae*
2	*Klebsiella pneumoniae ss. pneumoniae*	2	*Escherichia coli*
3	*Staphylococcus aureus*	3	*Non typhoidal salmonella*
Cerebrospinal Fluid		**Urine**	
1	*Staphylococcus,coagulase negative*	1	*Escherichia coli*
2	*Acinetobacter baumannii*	2	*Klebsiella pneumoniae ss. pneumoniae*
3	*Klebsiella pneumoniae ss. pneumoniae*	3	*Enterococcus sp.*

Streptococcus pneumoniae

There were 193 reported *S. pneumoniae* isolates for 2021. Sentinel sites located in Luzon contributed most of the *S. pneumoniae* isolates (53.37%) with 26.42% coming from NCR; 30.57% came from Mindanao and 16.06% were from Visayas (Figure 5).

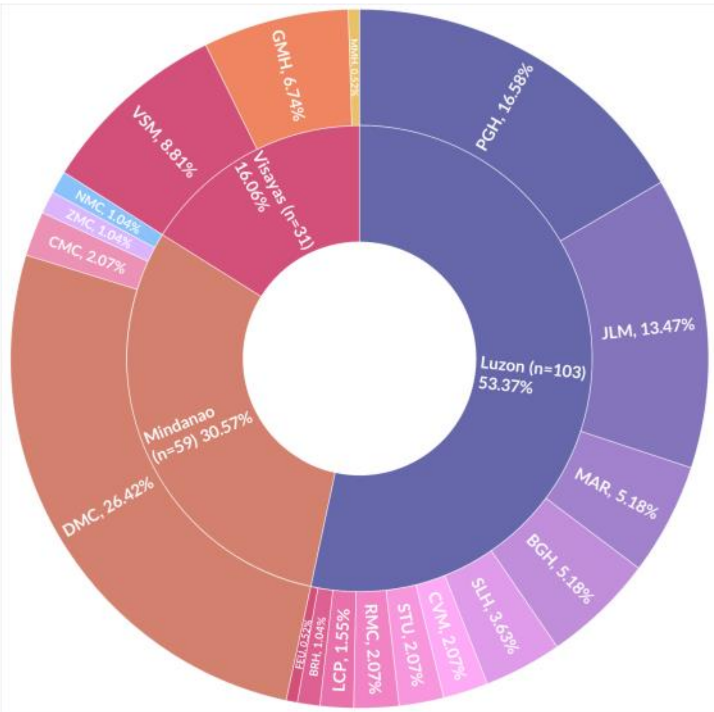


Figure 5. Isolate distribution of *S. pneumoniae* 2021, DOH-ARSP, 2021 (n= 193)

Most (54.40%) isolates came from patients aged 20-64 years old and most (56.48%) (Figure 6) were from male patients. Most (68.39%) of the isolates were from respiratory specimens and 23.8% from blood.

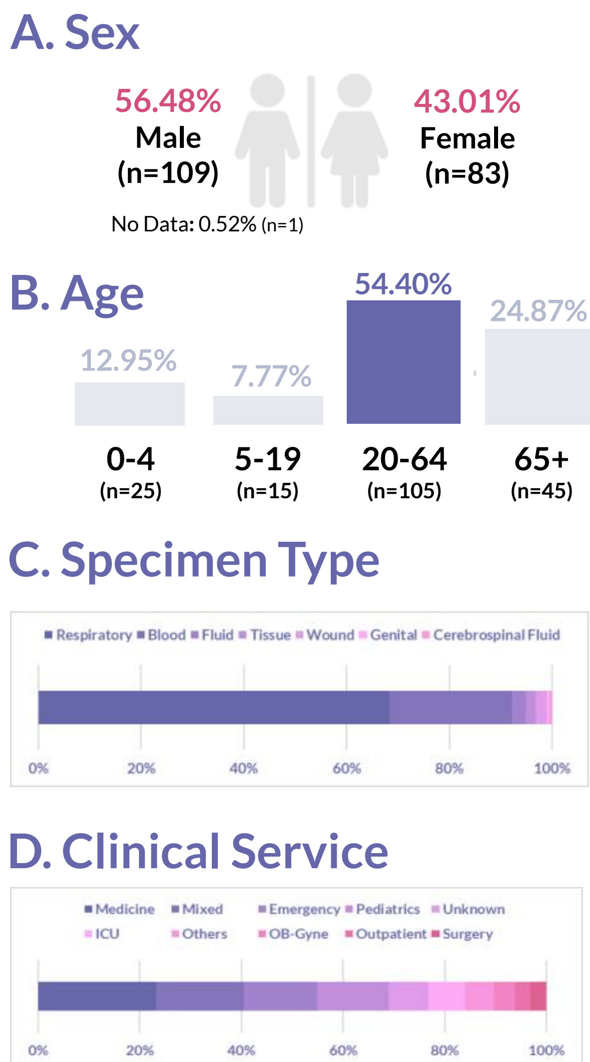


Figure 6. Patient characteristics of *S. pneumoniae* isolates, DOH-ARSP, 2021 (n= 193)

For 2021, penicillin resistance in *S. pneumoniae* isolates is at 16.0% (n=144) using meningitis (M) breakpoint and 1.4% using non-meningitis (NM) (n=144) and oral breakpoints (n=144) (Figure 7). Overall resistance rates for S. *pneumoniae* increased in 2021 for almost all antibiotics except for penicillin (M), however the noted changes in percent resistance were not significant.

There were 15 confirmed penicillin (M) resistant isolates in 2021. Many were from Luzon (40%, n=6) and Mindanao (40%, n=6), and most (60%, n=9) were from male patients. Most (80%, n=12) of the isolates were from respiratory specimens. Among the three (3) penicillin-resistant isolates from blood, two (2) were from age group 20-64 and one from 65+ and all were susceptible to erythromycin, clindamycin and linezolid. Two were tested for ceftriaxone and were found to be susceptible.

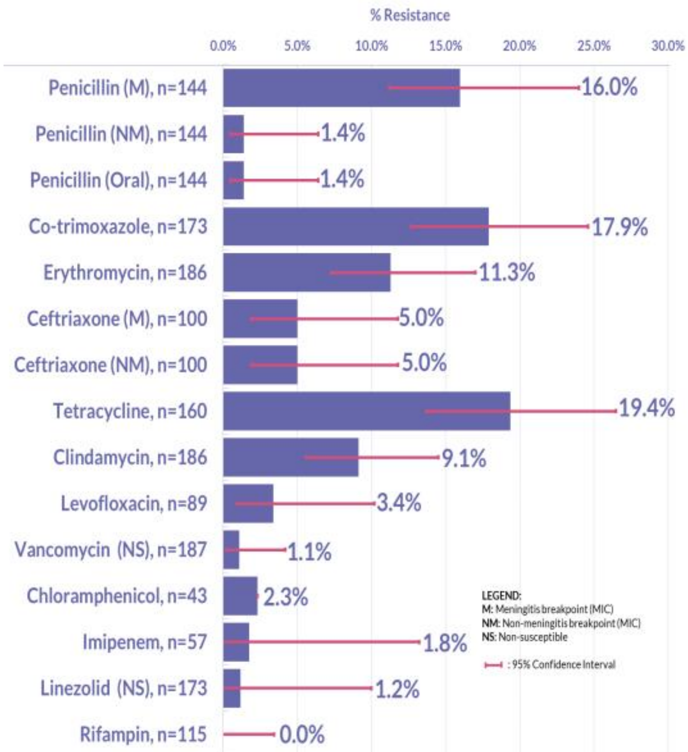


Figure 7. Percent resistance of *S. pneumoniae*, DOH-ARSP, 2021

Figure 9 shows the percent resistance of *S. pneumoniae* isolates from respiratory specimens. Resistance to penicillin (M) was at 17.8% and penicillin (NM) and penicillin oral at 1.0%. Resistance to co-trimoxazole was at 17.6%, to erythromycin at 13.4%, ceftriaxone (M and NM) at 5.6%. No *S. pneumoniae* isolate from respiratory specimens was found resistant against rifampin.

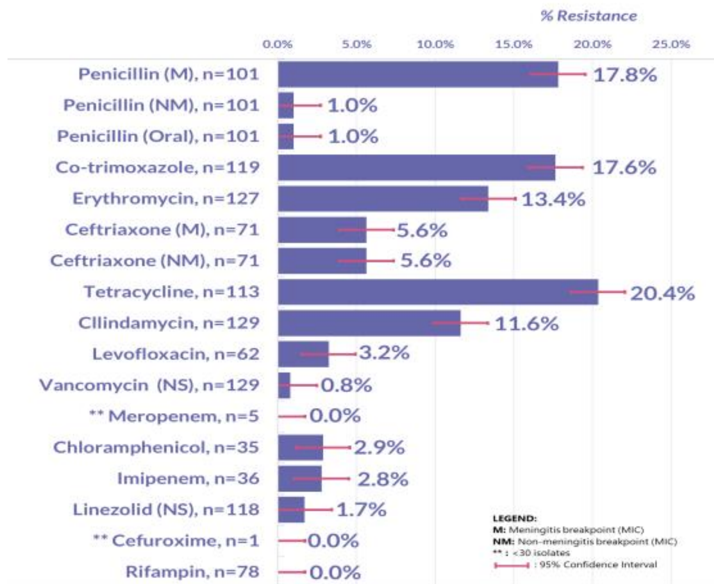


Figure 9. Percent resistance of *S. pneumoniae* respiratory isolates, DOH-ARSP, 2021

Resistance rates of ceftriaxone and tetracycline are fluctuating over the years (Figure 8). Multiple year analysis revealed that changes in the resistance rates over the years were significant for penicillin (p=0.0000) and ceftriaxone (p=0.00703). However, changes in resistance rates for meropenem was not significant (p=0.25102).

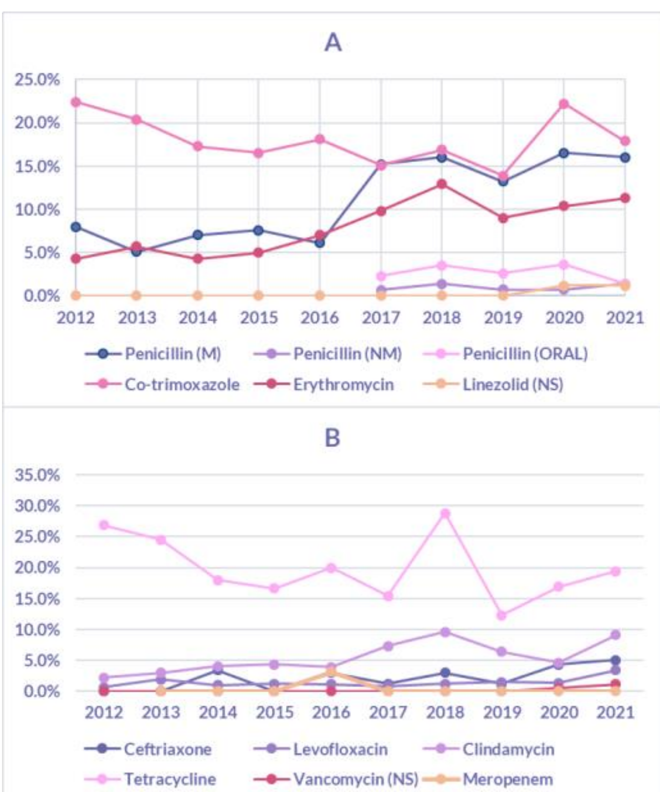


Figure 8. Yearly resistance rates of *S. pneumoniae*, DOH-ARSP, 2012-2021

Among *S. pneumoniae* blood isolates, resistance to co-trimoxazole was highest at 19.5% followed by penicillin (M) at 15.2% and tetracycline at 14.7%. Percent non-susceptible to vancomycin was at 2.3% and resistance to erythromycin was noted to be 4.4%.

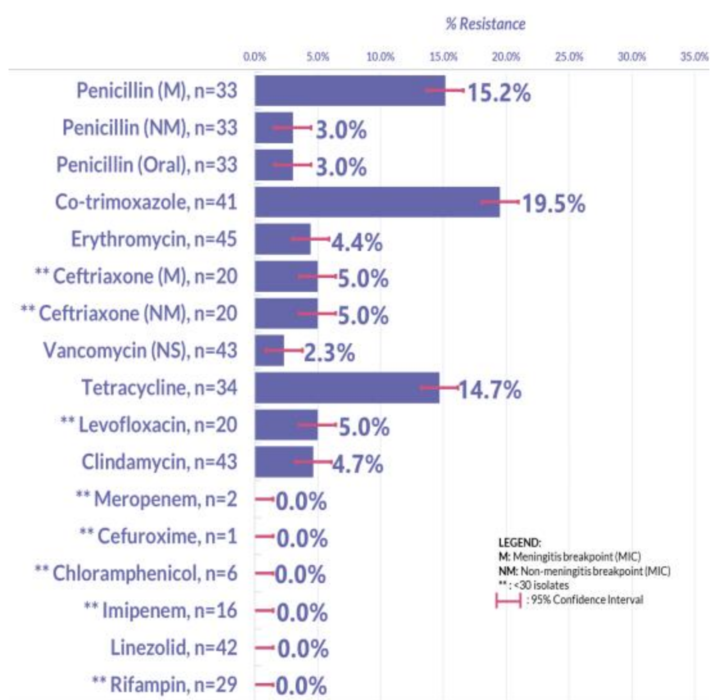


Figure 10. Percent resistance of *S. pneumoniae* blood isolates, DOH-ARSP, 2021

Overall penicillin resistance of *S. pneumoniae* isolates from BGH and CVM were at 33%. *S. pneumoniae* isolates from MAR, JLM, NCR and DMC on the other hand were in the 11-20% range. GMH and VSM were in the 6-10% range and BRH, ZMC, MMH and CMC were in the < 1% penicillin resistance range. (**Figure 11**)

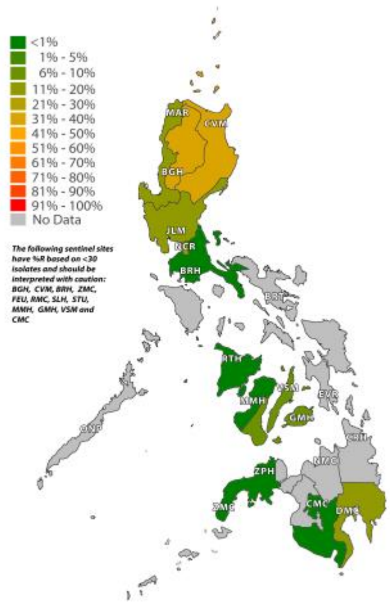


Figure 11. Geographic distribution of penicillin-resistant *S. pneumoniae* in the Philippines, DOH-ARSP, 2021

To identify locally prevailing invasive serotypes, 23 *S. pneumoniae* isolates from blood samples received at the reference laboratory were serotyped. The number of invasive *S. pneumoniae* isolates received by the reference laboratory for 2021 was higher than the number of isolates in 2021 (n=22). For 2021, there were 14 *S. pneumoniae* serotypes/ serogroups identified with the most common being serotypes 3, 4,23, 6, 19A, 10, 11 and 34 (**Figure 12**). Penicillin resistant serotypes include serotype 6, 19 and 23.

Percent pneumococcal vaccine conjugate (PCV) coverage of invasive *S. pneumoniae* isolates was determined by dividing the number of isolates with serotypes included in PCVs over the total number of isolates with identified serotypes. The overall PCV 7 and PCV 10 coverage of 2021 invasive *S. pneumoniae* isolates were both at 30.43% and 56.52% for PCV 13. Based on the limited number of invasive *S. pneumoniae* isolates for 2021, PCV coverages of 2021 invasive *S. pneumoniae* isolates were lower compared to that of 2020 invasive *S. pneumoniae* isolates.

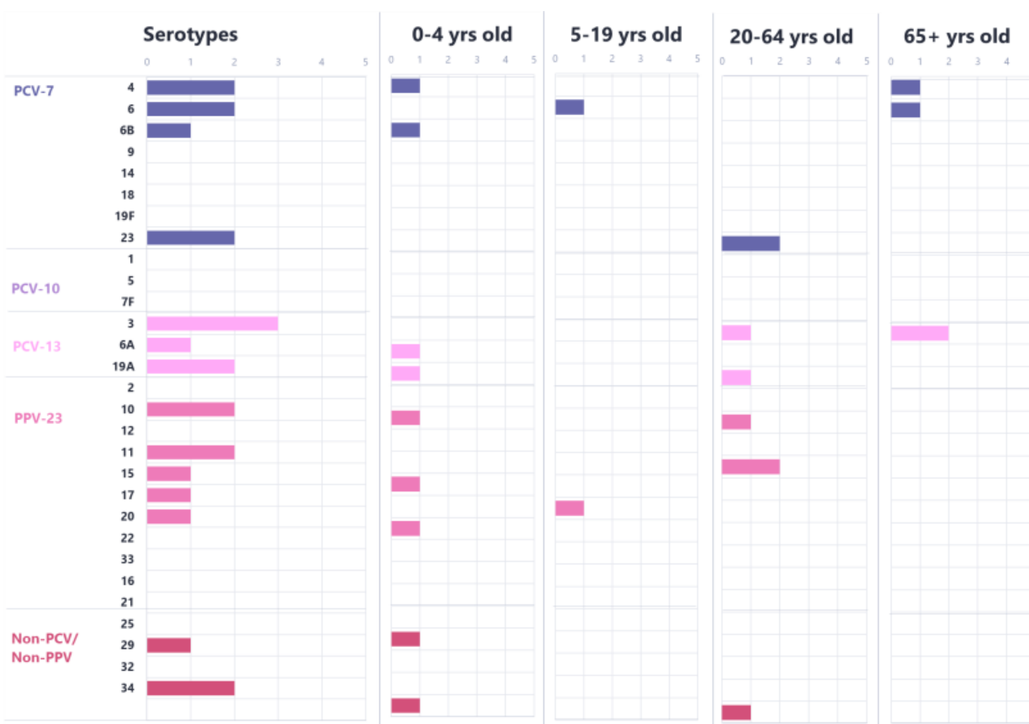


Figure 12. Invasive *S. pneumoniae* serotypes and PCV serotypes, DOH-ARSP, 2021

Haemophilus influenzae

There were 165 reported *H. influenzae* for 2021. This was 7.8% lower than the 179 isolates reported in 2020. The biggest contributors for 2021 *H. influenzae* data were VSM (31.52%), DMC (29.70%) and PGH (15.15%)(Figure 13). Based on island group distribution, 34.55% came from Luzon, with 29.1% coming from NCR, 35.15% from Visayas and 30.30% from Mindanao.

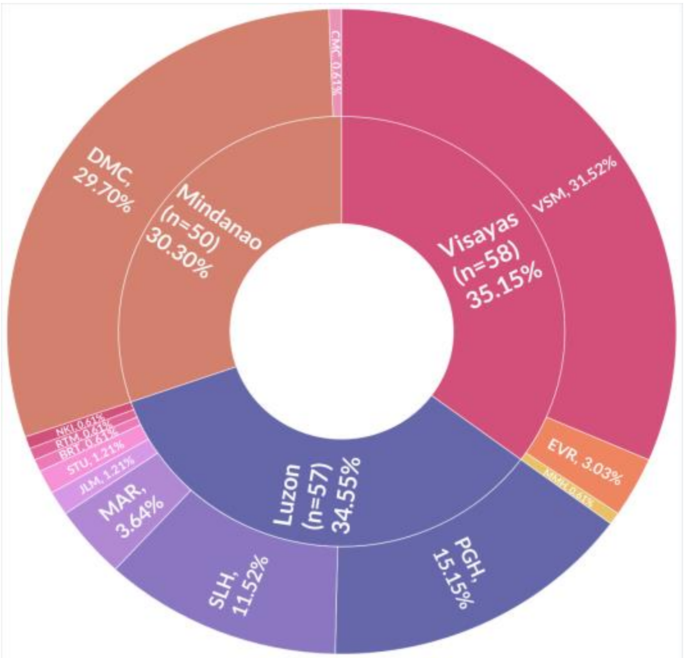


Figure 13. Isolate distribution of *H. influenzae*, DOH-ARSP, 2021 (n=165)

Most (56.36%) of the isolates were from patients 20-64 years old and were from male patient (56.36%)(Figure 14). Majority (89.70%) of the isolates were from respiratory specimens.

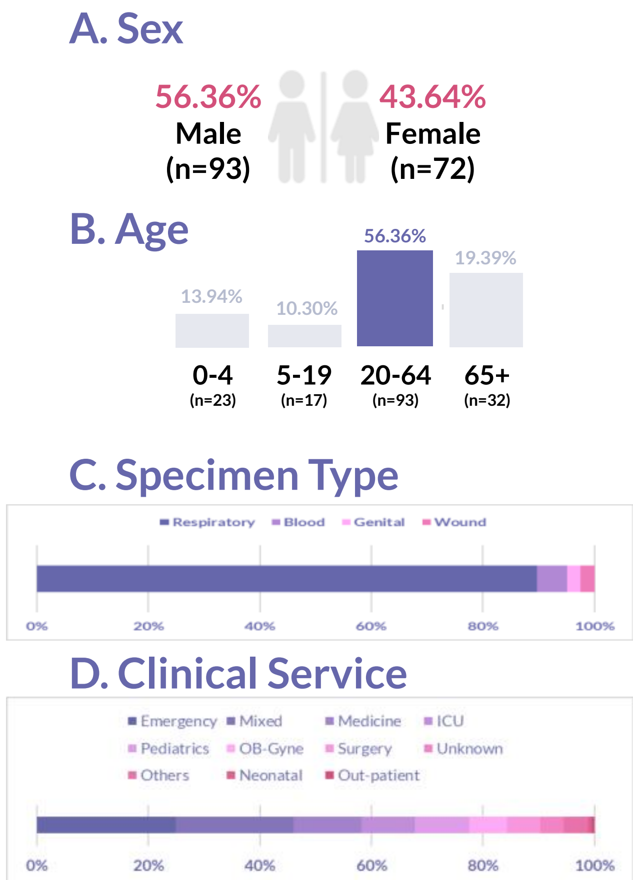


Figure 14. Patients characteristics of *H. influenzae* isolates, DOH-ARSP, 2021 (n=165)

Cumulative resistance rates of *H. influenzae* for 2021 is shown in Figure 15. Resistance to ampicillin was at 13.9% (n=151), 7.9% (n=151) to ampi-sulbactam, and 3.8% (n=156) for ceftriaxone. No *H. influenzae* isolate tested resistant to levofloxacin (n=145). Highest resistance rate was for co-trimoxazole at 38.2% (n=157) followed by tetracycline 19.8% (n=131) which was a significantly lower rate than in 2020 (p= 0.0076). Percent non- susceptible to ceftriaxone (3.8%) and resistance rates to meropenem and amoxiciilin/clavulanic acid increased from 2020 to the current analysis period, however, the differences were not statistically significant (Figure 16). There was 1 confirmed beta lactamase negative ampicillin resistant (BLNAR) *H. influenzae* isolate for 2021. This isolate was susceptible to ceftriaxone, ciprofloxacin, levofloxacin and meropenem. There were two confirmed amoxicillin-clavulanate resistant *H. influenzae* isolates for 2021. Both were from respiratory specimens and were from age group 20-62 years. These isolates were susceptible to ceftriaxone, ciprofloxacin, levofloxacin and meropenem. One confirmed ciprofloxacin non-susceptible isolate was reported and was noted to be susceptible to ampicillin, ceftriaxone, ampicilin-sulbactam, amoxicillin-clavulanic, and meropenem.

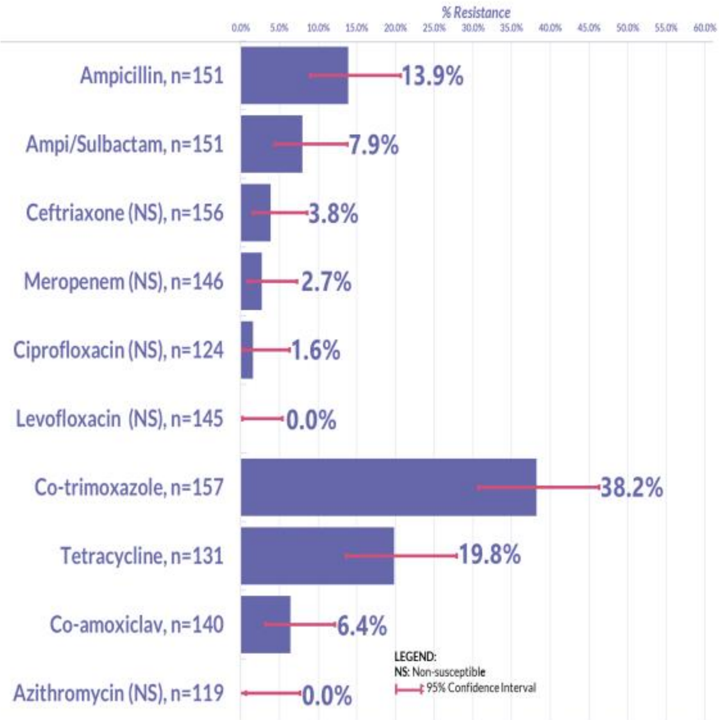


Figure 15. Percent resistance of *H. influenzae* , DOH-ARSP, 2021

Most of the resistance rates increased in 2021 (**Figure 16**). Multiple year analysis showed that the changes in resistance rates from 2012 to 2021 for ampicillin (p=0.07622), amoxicillin/ clavulanic acid (p= 0.22493) and ceftriaxone (p=0.13653) were not statistically significant but the changes in resistance rates for meropenem over the years was noted to be statistically significant at p= 0.0003.

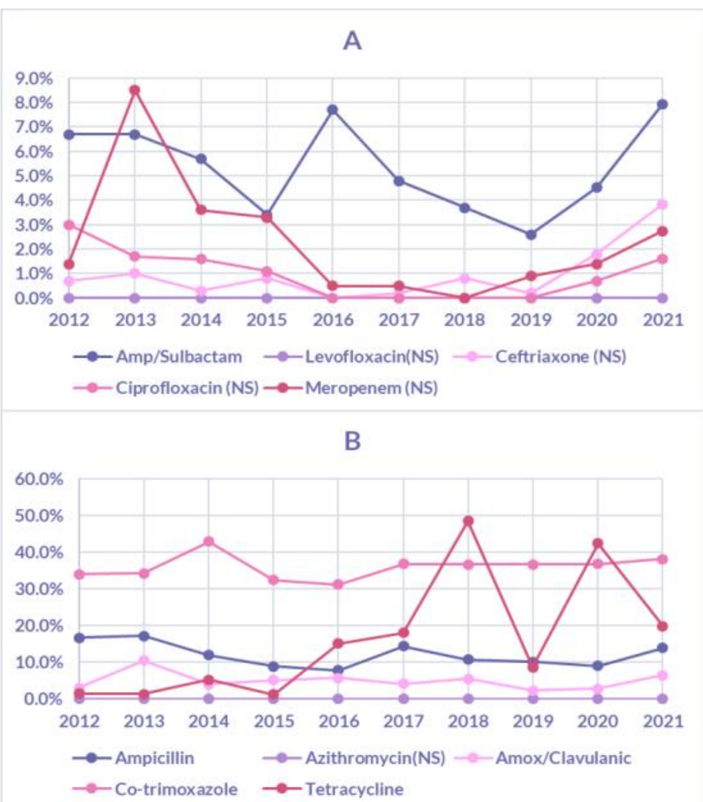


Figure 16. Yearly resistance rates of *H. influenzae*, DOH-ARSP, 2012-2021

Resistance rates among respiratory isolates of *H. influenzae* are shown in Figure 17. Highest resistance rate was noted for co-trimoxazole at 38.9% followed by tetracycline (20.7%) and ampicillin (14.6%). Percent non-susceptible to ceftriaxone, meropenem and ciprofloxacin were all less than 5%.

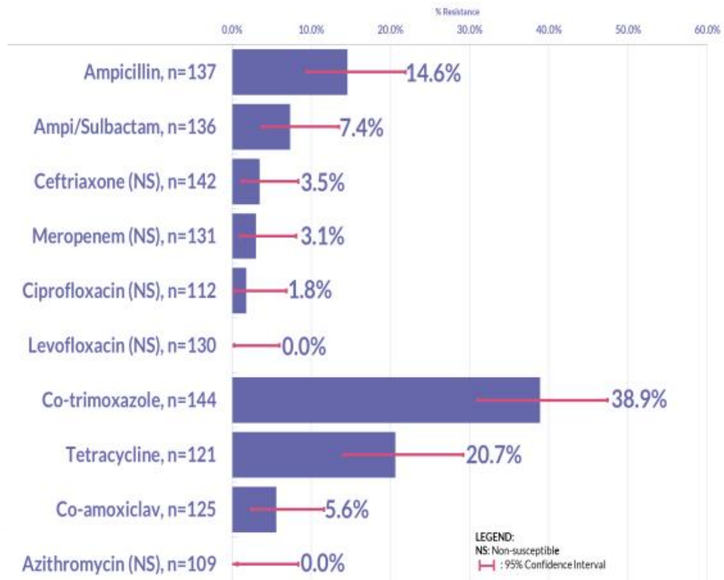


Figure 17. Percent resistance of *H. influenzae* respiratory isolates, DOH-ARSP,2021

To obtain reasonable statistical estimate of the cumulative percentage resistance for *H. influenzae* from blood, data from 2019-2021 were combined. Ampicillin resistance was at 14.6%, ampicillin/ sulbactam at 7.0% and 25% for tetracycline. Percent non-susceptible for ceftriaxone was at 2.6%. No. *H. influenzae* blood and CSF isolate was resistant to ciprofloxacin, levofloxacin, amoxicillin/ clavulanic acid and azithromycin.

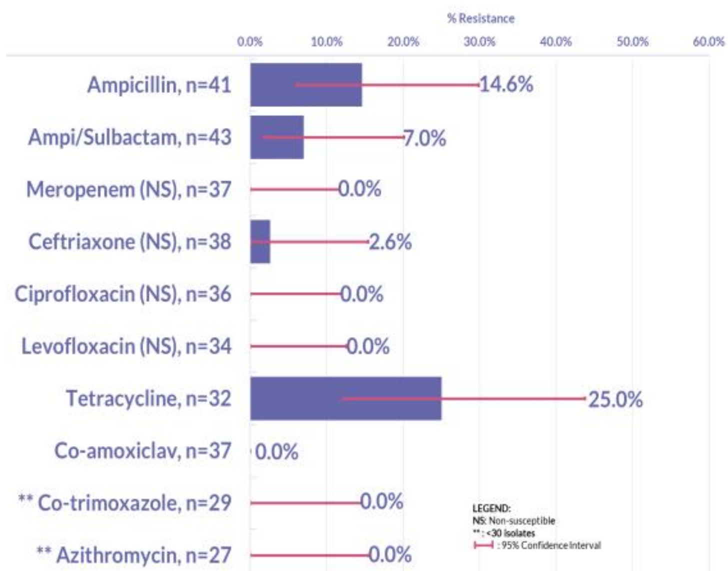


Figure 18. Percent resistance of blood *H. influenzae* isolates, DOH-ARSP, 2019-2021

Salmonella enterica serovar Typhi

There were 42 *S.* Typhi reported and analyzed for 2021. ZMC contributed most to the number of *S.* Typhi isolates (21.43%) (Figure 19). Based on island group distribution, 40.48% came for Mindanao, 35.71% from Luzon and 23.81% from Visayas.

Figure 19. Isolate distribution of *S.* Typhi , DOH-ARSP, 2021 (n=42)

Half of the isolates came from 5-19 age group and mostly (59.52%) were from male patients (Figure 20). Most (80.95%) of the isolates were from blood specimens.

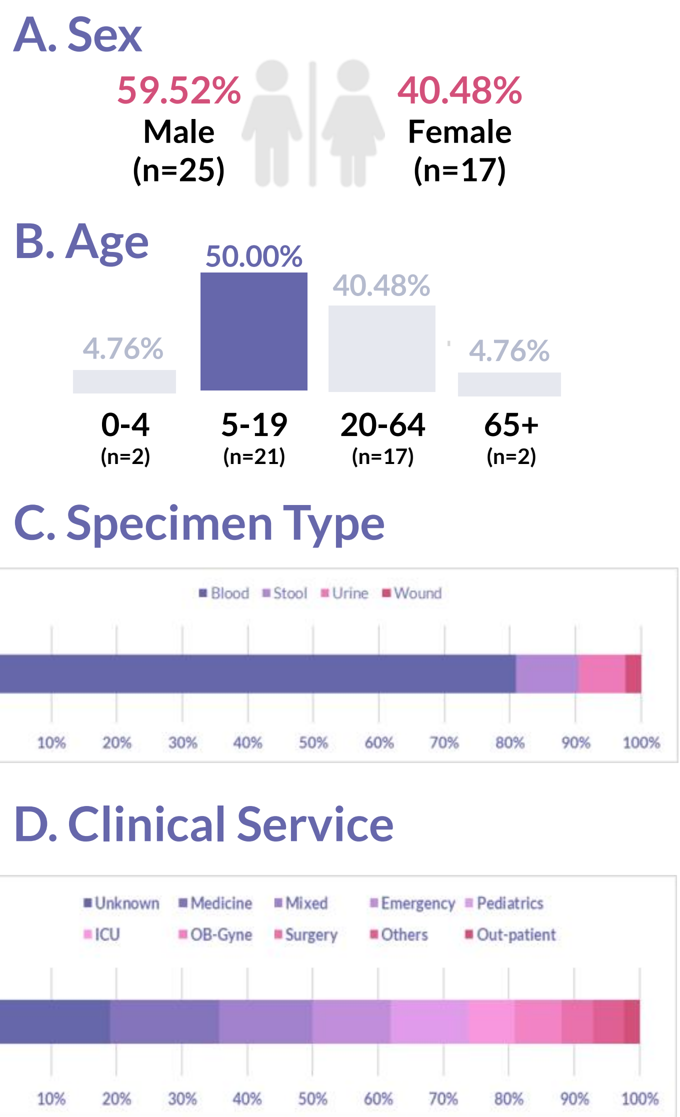


Figure 20. Patients characteristics of *S.* Typhi isolates, DOH-ARSP, 2021 (n=42)

For 2021 *S.* Typhi isolates, resistance to ciprofloxacin was at 2.6%, while no resistance was observed against ampicillin, co-trimoxazole, ceftriaxone, cefotaxime, azithromycin and chloramphenicol (Figure 21). As there were few *S.* Typhi isolates reported for 2021, continued efforts to improve the surveillance of antibiotic resistance among these pathogens has to be done.

One ciprofloxacin-resistant *S.* Typhi isolate was reported from the urine specimen of a 73-year old female from MAR. The isolate was susceptible to cefotaxime, ceftriaxone, aztreonam, ampicillin, chloramphenicol and co-trimoxazole.

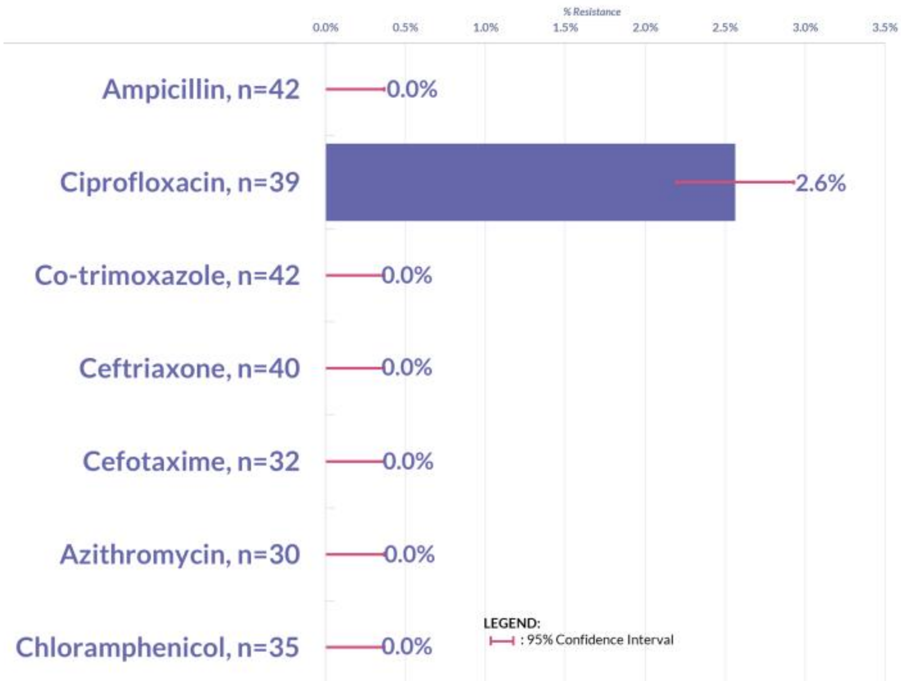


Figure 21. Percent resistance of *S.* Typhi, DOH-ARSP, 2021

Yearly resistance rates of *S.* Typhi remained low in the past ten years and isolates remained susceptible to antibiotics used against them including ampicillin, co-trimoxazole, ceftriaxone, chloramphenicol, azithromycin and cefotaxime (**Figure 22**). Multiple year analysis showed that changes in the resistance rates over the past ten years for ciprofloxacin was statistically significant at p=0.0492.

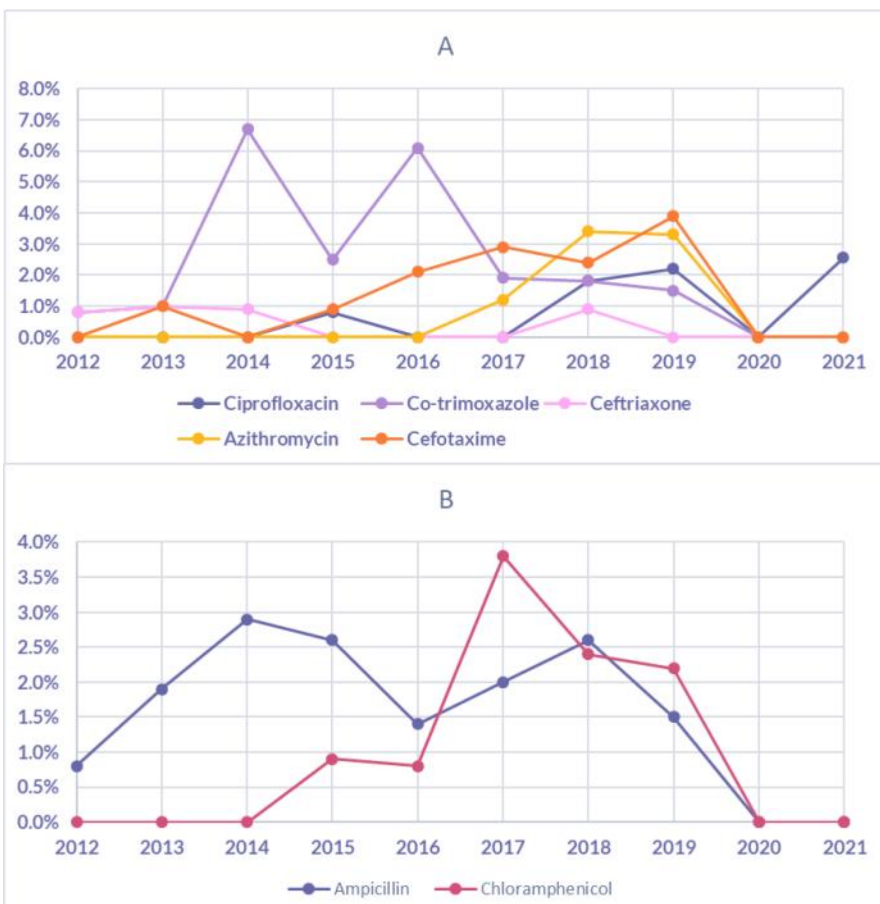


Figure 22. Yearly resistance rates of *S.* Typhi DOH-ARSP, 2012-2021

Non-typhoidal *Salmonella*

A total of 185 non-typhoidal *Salmonella* (NTS) isolates were reported for 2021. This was 11% higher than the reported 167 isolates in 2020. PGH (21.62%) contributed most to the number of NTS isolates. Most (76.76%) of the isolates came from Luzon with 43.78% from NCR, while 16.22% were reported from Mindanao and 7.03% from the Visayas (Figure 23).

Figure 23. Isolate distribution of Non-typhoidal *Salmonella*, DOH-ARSP, 2021 (n=185)

Most (58.92%) of the isolates were from 20-64 age group and mostly (56.22%) were from male patients. Many (47.03%) of the isolates were from blood specimens (Figure 24).

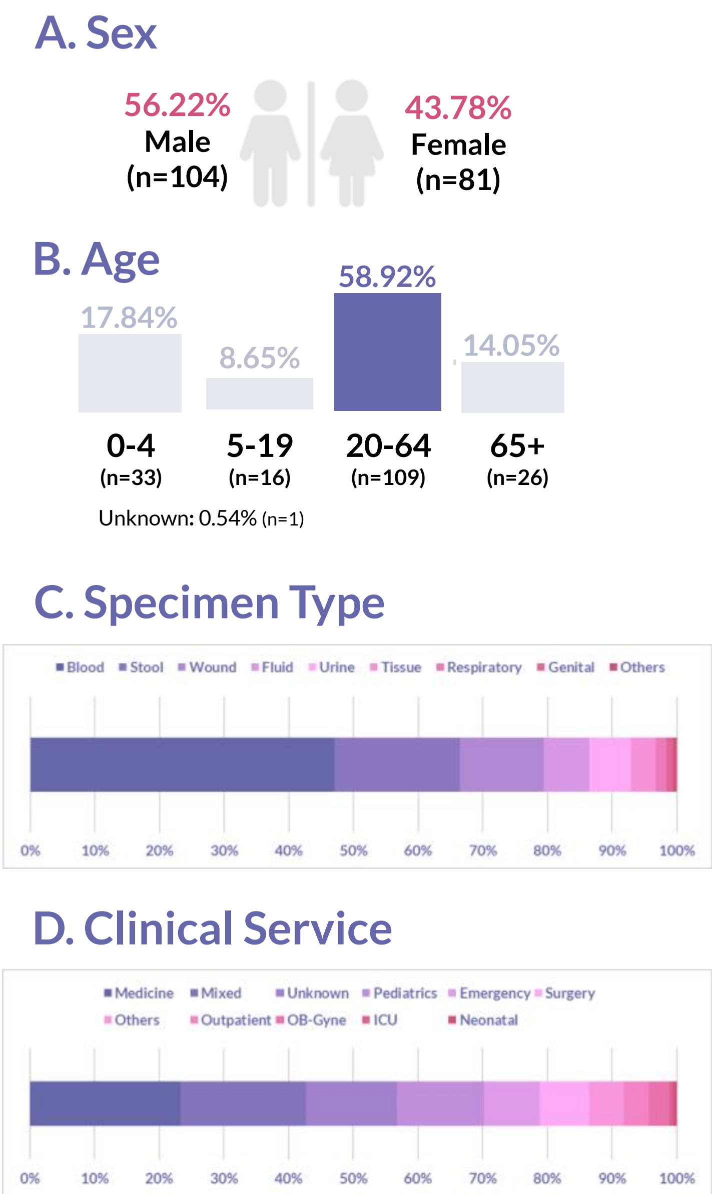


Figure 24. Patients characteristics of Non-typhoidal *Salmonella* isolates, DOH-ARSP, 2021 (n= 185)

Resistance to ampicillin was at 32.9% and 17.5% for cefotaxime (Figure 25). Chloramphenicol resistance was at 16.0% and co-trimoxazole was at 15.9%. Lowest percent resistance was recorded for ciprofloxacin at 11.2%.

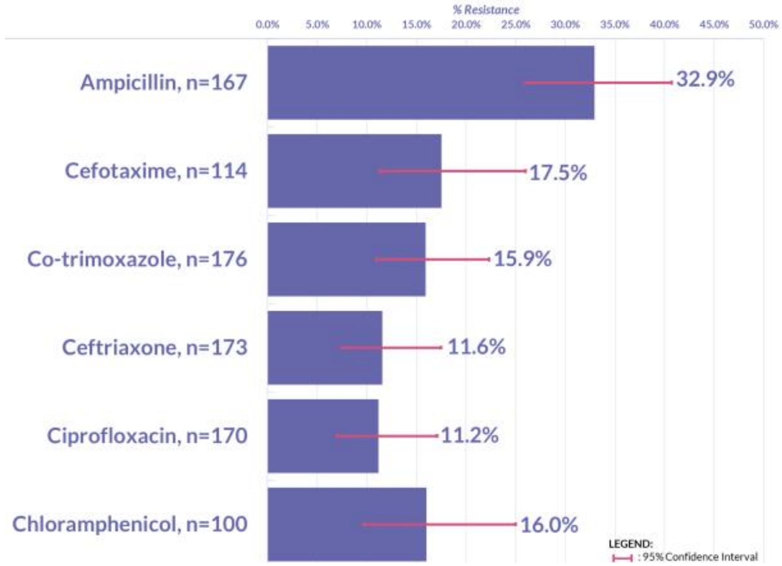


Figure 25. Percent resistance of Non-typhoidal *Salmonella*, DOH-ARSP, 2021

Yearly resistance rates among NTS isolates are shown in **Figure 26**. All of the tested antibiotics increased in 2021, however, the noted differences were not statistically significant.

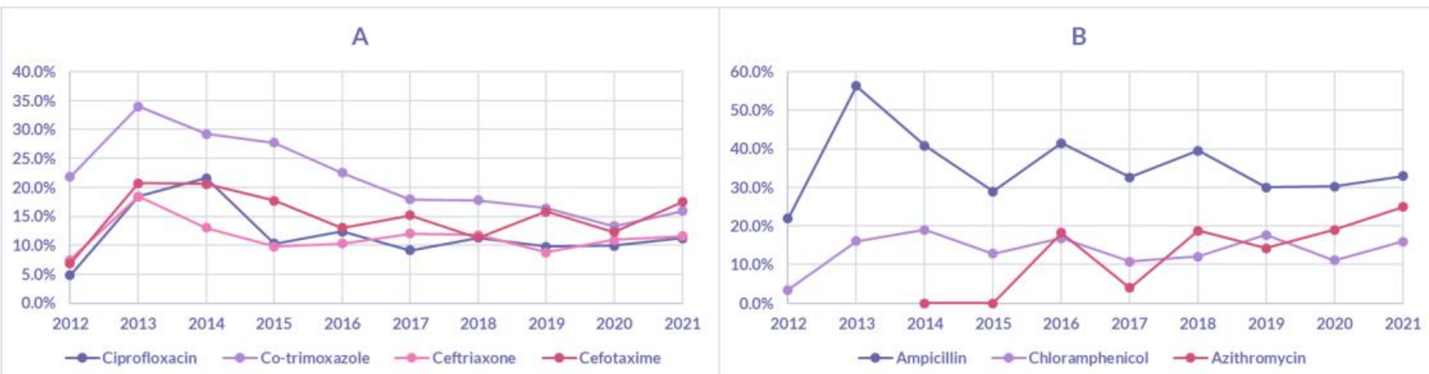


Figure 26. Yearly resistance rates among Non-typhoidal *Salmonella*, DOH-ARSP, 2012-2021

Ampicillin resistance was at 13.4% among NTS blood isolates. Chloramphenicol, ciprofloxacin and co-trimoxazole resistance rates were at 7.5%, 6.2% and 5.9% respectively. Cefotaxime was at 5.8% and ceftriaxone at 2.4%.

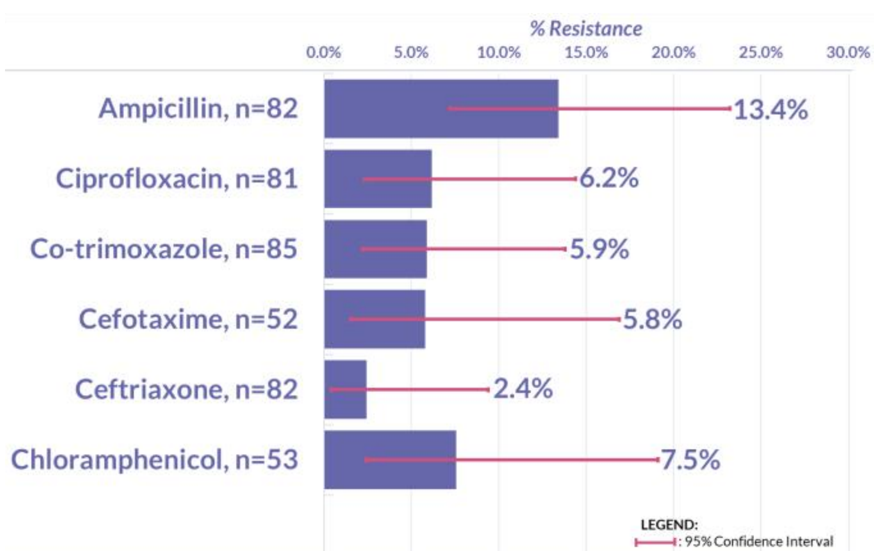


Figure 27. Percent resistance of Non-typhoidal *Salmonella* blood isolates, DOH-ARSP 2021

There were 89 *Salmonellae* referred to the reference laboratory for serotyping. Most of these isolates were *Salmonella enterica* serovar Enteritidis (35.96%) and *Salmonella enterica* serovar Typhi (33.7%) (**Figure 28**). Among the 59 confirmed non-typhoidal *Salmonella*, most common serotypes were *Salmonella enterica* serovar Enteritidis (n= 32) and *Salmonella enterica* serovar Typhimurium (n=6). Antimicrobial resistance among NTS reflects variations in serotypes, its distribution or both.

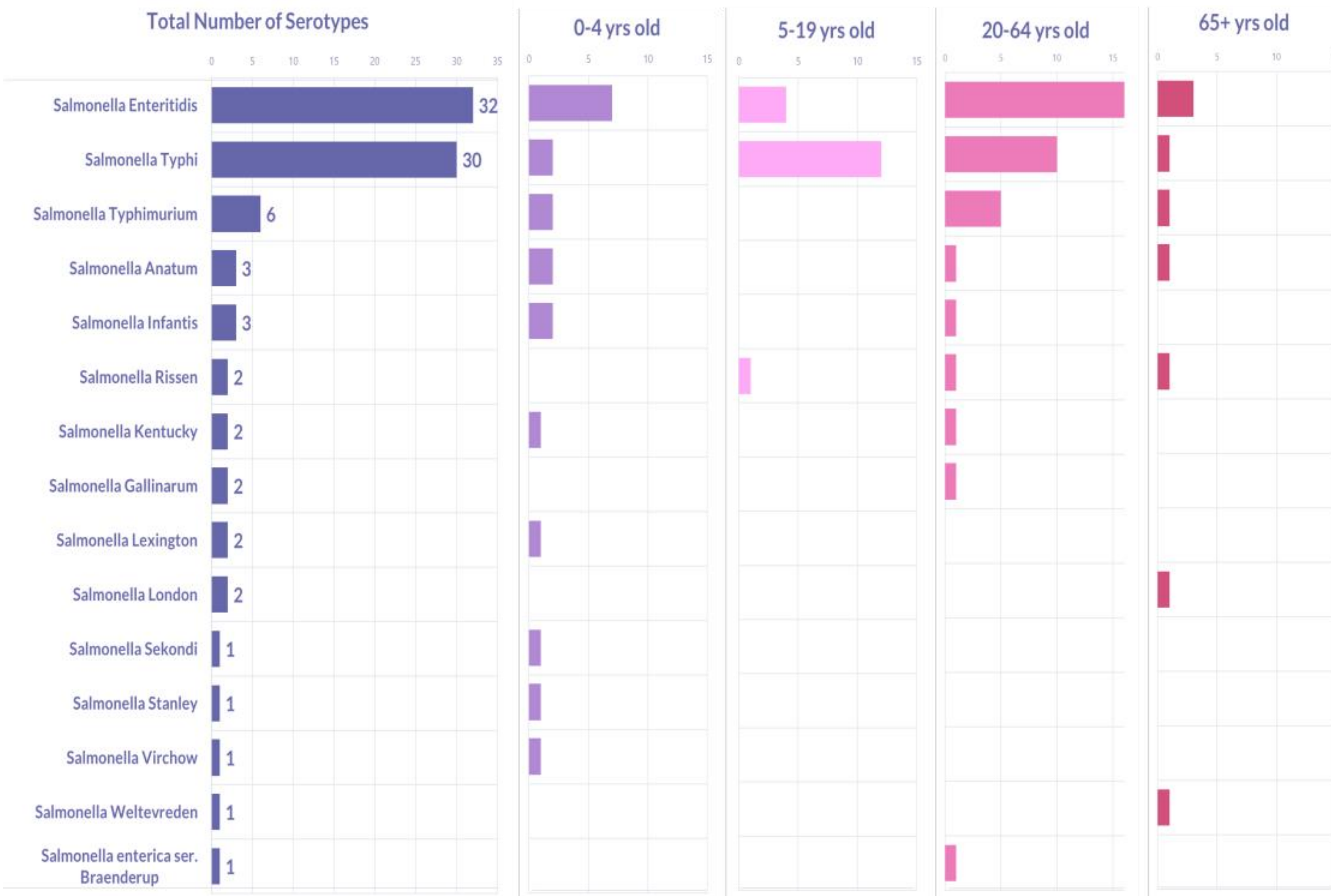


Figure 28. *Salmonella* serotypes per age group, DOH-ARSP, 2021

Shigella species

There were 13 *Shigella* species reported for 2021. VSM and DMC each contributed 46.16% to the total number of isolates. Based on island group distribution, 53.85% were from Mindanao, 30.77% from Visayas and 15.38% from Luzon (Figure 29).

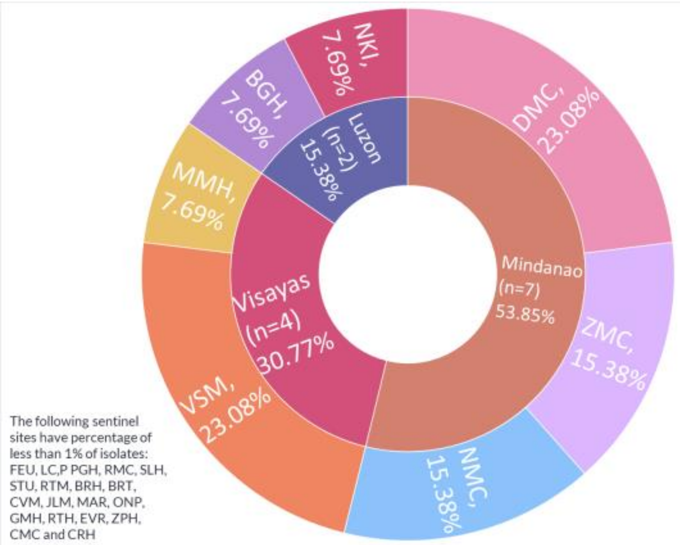


Figure 29. Isolate distribution of *Shigella* species, DOH-ARSP, 2021 (n=13)

Most (61.54%) of the isolates were from female patients and from 20-64 age group (61.54%)(Figure 30). Many (38.46%) of the isolates were collected from stool samples.

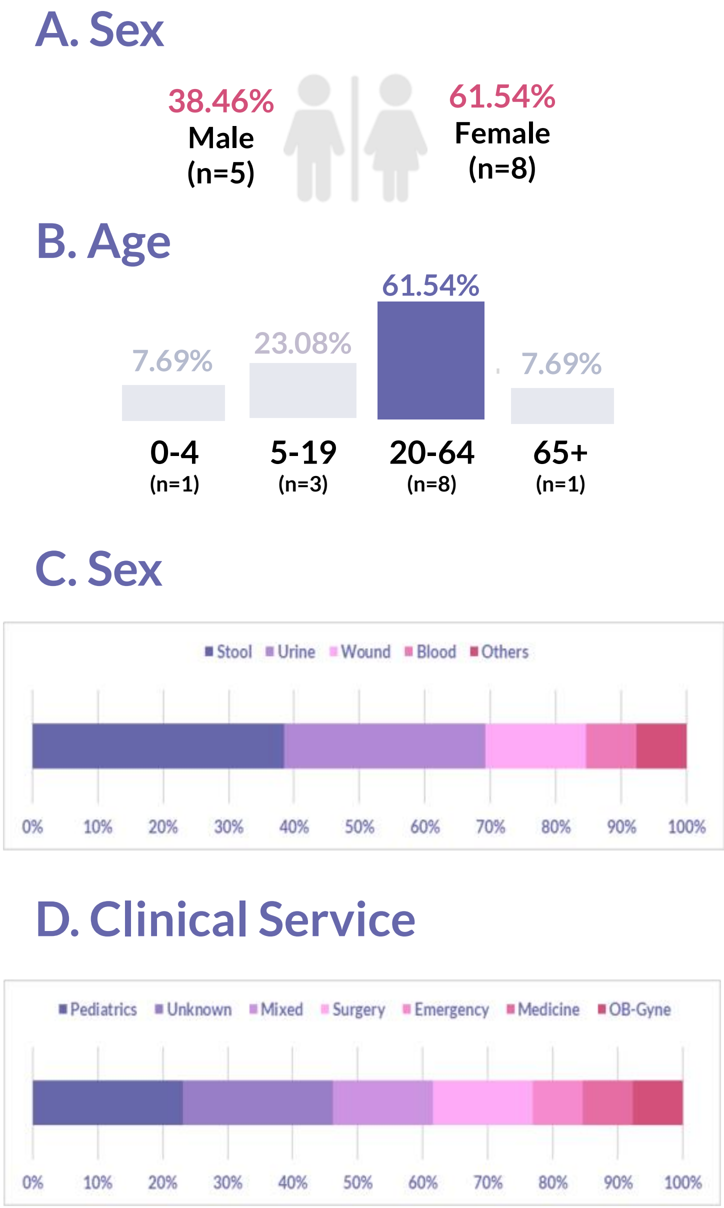


Figure 30. Patients characteristics of *Shigella* species isolates, DOH-ARSP, (n=13)

Figure 31 shows the cumulative resistance rates of *Shigella* species for 2019-2021. Ampicillin resistance was at 57.1%, co-trimoxazole at 60%, and chloramphenicol at 38.6%. Resistance rates for cefotaxime, ceftriaxone and ciprofloxacin were less than 15%. Ciprofloxacin (p=0.02869) and chloramphenicol (p=0.9621) resistance rates increased from 2020 to 2021 (Figure 32); however, the increases were not statistically significant.

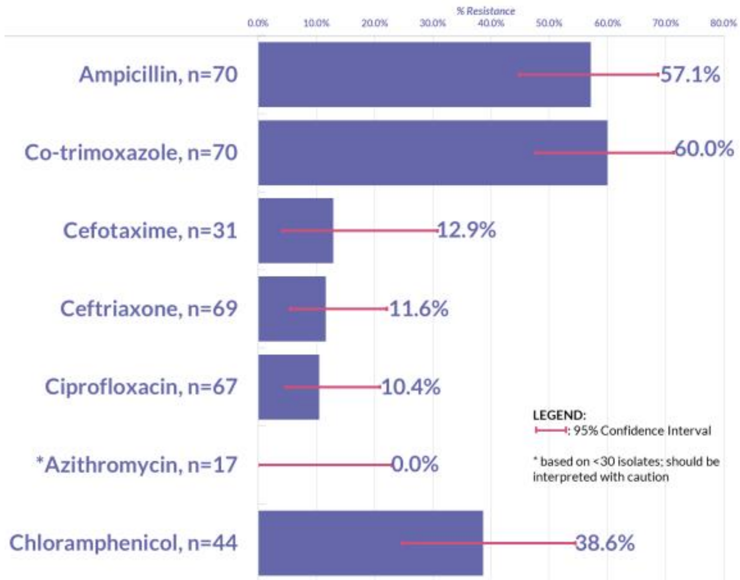


Figure 31. Percent resistance of *Shigella* species, DOH-ASRP, 2019-2021

Multiple year analysis showed that changes in the resistance rates for ciprofloxacin in the past 10 years was not statistically significant (p=0.6369) while the change in resistance rates against ceftriaxone over the past 10 years was noted to be statistically significant (p=0.0286).

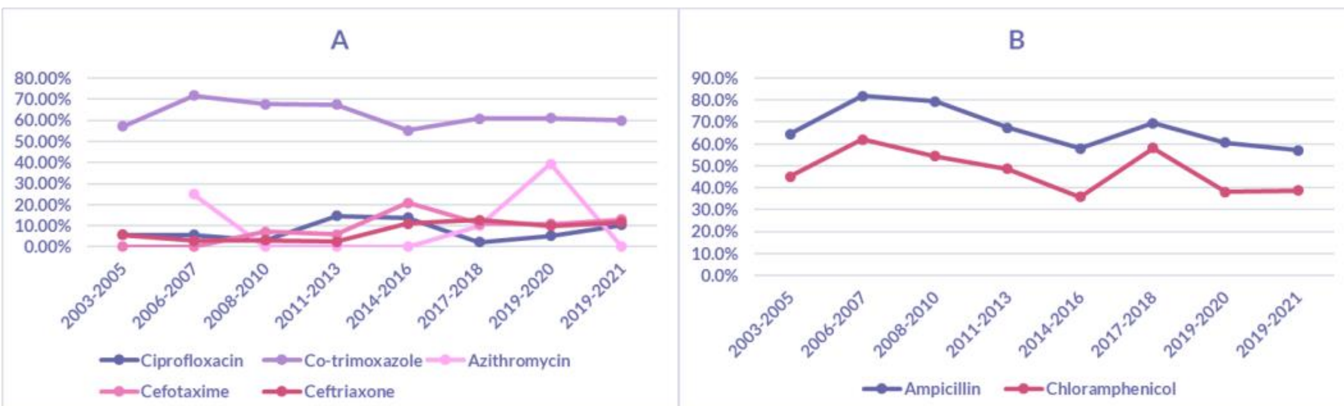


Figure 32. Yearly resistance rates of *Shigella* species, DOH-ARSP, 2003-2021

Figure 33 shows the resistance rates of *Shigella* stool isolates from 2019-2021. Co-trimoxazole resistance was highest at 68.9% followed by ampicillin (66.7%) and chloramphenicol (42.9%). Resistance to cefotaxime, ceftriaxone and ciprofloxacin were less than 15%.

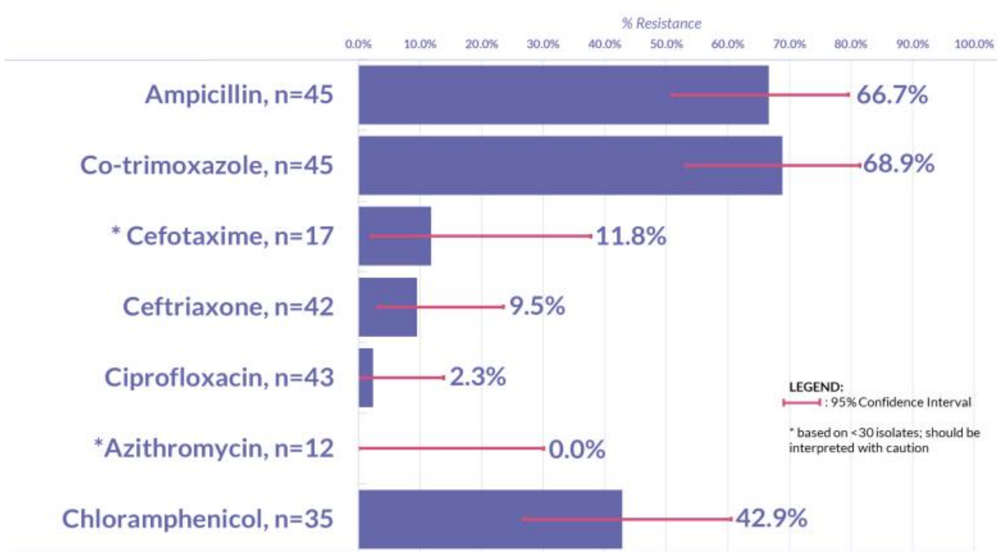


Figure 33. Percent resistance of *Shigella* species stool isolates, DOH-ARSP, 2019-2021

Vibrio cholerae

There were **97** isolates of *Vibrio cholerae* reported for 2021. This is 79.39% higher than the reported isolates in 2020 (n=20). Most isolates were from VSM (46.39%, n=45), DMC (38.14%, n=37) and JLM (8.25%, n=8) (**Figure 34**).

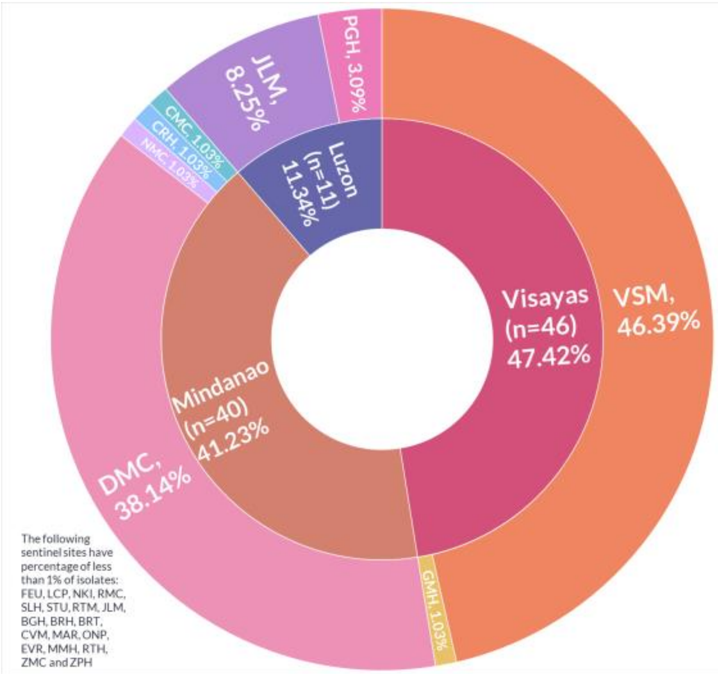


Figure 34. Isolate distribution of *V. cholerae*, DOH-ARSP, 2021 (n=97)

Most (40.21%) of the isolates were from 5-19 years old and many (62.89%) were isolated from male patients. Majority (96.91%) of the isolates were collected from stool samples (**Figure 35**).

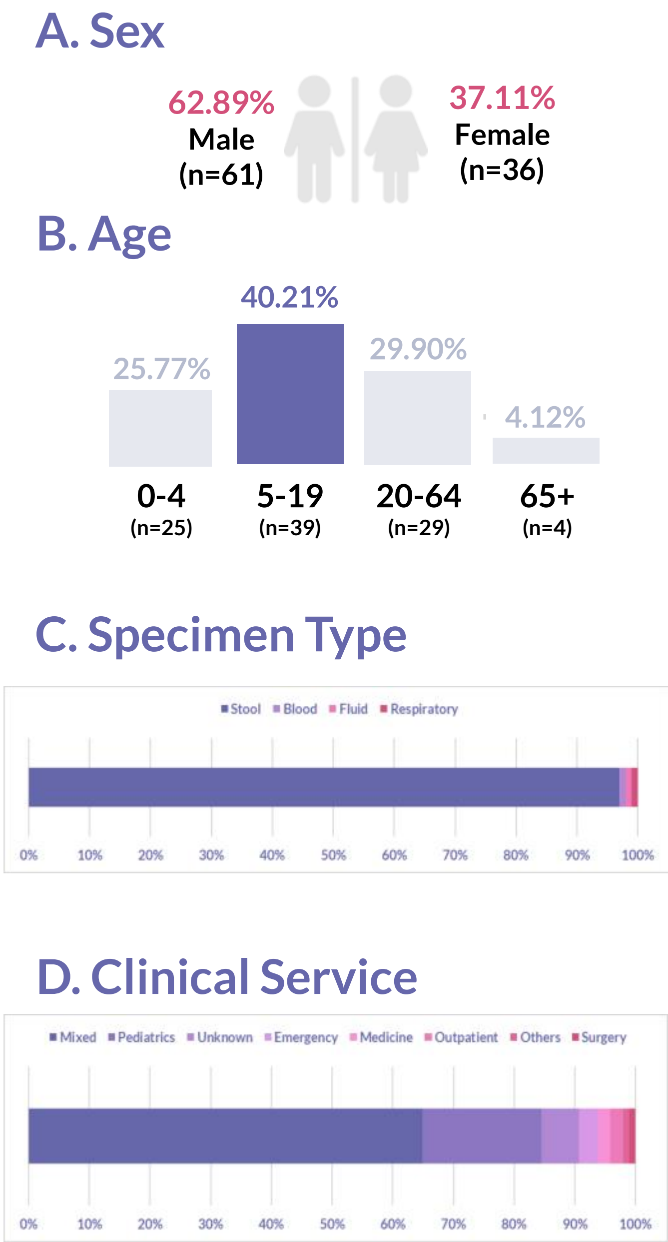


Figure 35. Patients characteristics of *V. cholerae* isolates, DOH-ARSP, 2021 (n=97)

Figure 36 shows the antibiotic resistance rates of *V. cholerae* in 2021. Resistance to ampicillin was highest at 9.6% followed by co-trimoxazole (3.2%) and tetracycline (1.1%). No resistance was noted for chloramphenicol and azithromycin. Ampicillin resistance decreased from 28.9% in 2020 to 9.6% in 2021 and the noted decrease was statistically significant (p=0.0042) (**Figure 37**).

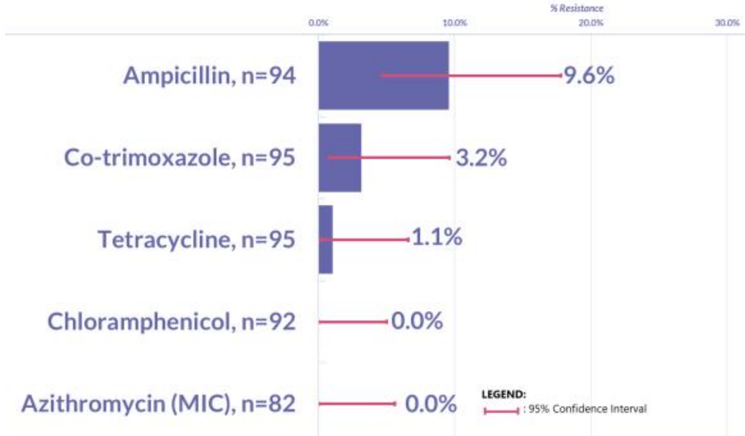


Figure 36. Percent resistance of *V. cholerae*, DOH-ARSP, 2021

Most of the resistance rates decreased in 2021. Chloramphenicol, tetracycline and ampicillin resistance showed fluctuating values over the past 10 years. *V. cholerae* isolates remained susceptible to azithromycin in the last ten years. Multiple year analysis showed that the changes in resistance rates of *V. cholerae* isolates to chloramphenicol, co-trimoxazole, tetracycline and ampicillin from 2004 to 2021 were statistically significant (p = 0.0000).

There were seven ampicillin resistant isolates collected in 2021, most (57.14%) were from 0-4 years old in patients. A resistant isolate was detected from the stool sample of a 1-day old male patient from CMC. The isolate was susceptible to azithromycin, co-trimoxazole and tetracycline.

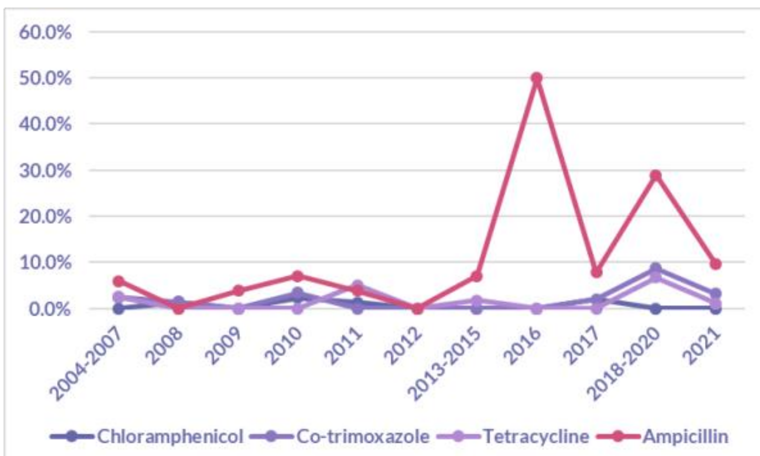


Figure 37. Yearly resistance of *V. cholerae*, DOH-ARSP, 2004-2021

Resistance rates of *V. cholerae* isolates from stool are shown in Figure 38. Ampicillin resistance was at 8.8% and co-trimoxazole resistance at 1.1%. No resistance was noted for tetracycline, chloramphenicol and azithromycin.

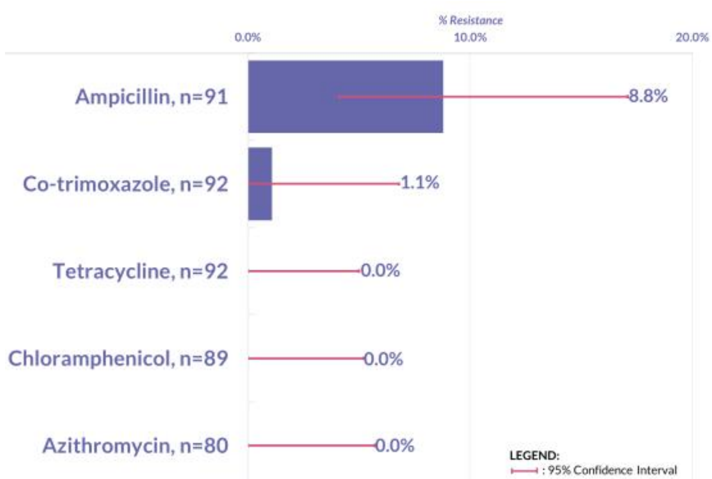


Figure 38. Percent resistance of *V. cholerae* from stool, DOH-ARSP, 2021

Neisseria gonorrhoeae

A total of only 14 *Neisseria gonorrhoeae* isolates were reported for 2021. This was 69.56% lower than the reported number of isolates in 2020. The largest contributors of data were JLM (42.86%) and VSM (21.43%). Based on island group distribution, the number of isolates reported from Luzon was at 71.43% (n=10), 21.43% from the Visayas and 7.14% from Mindanao (Figure 39).

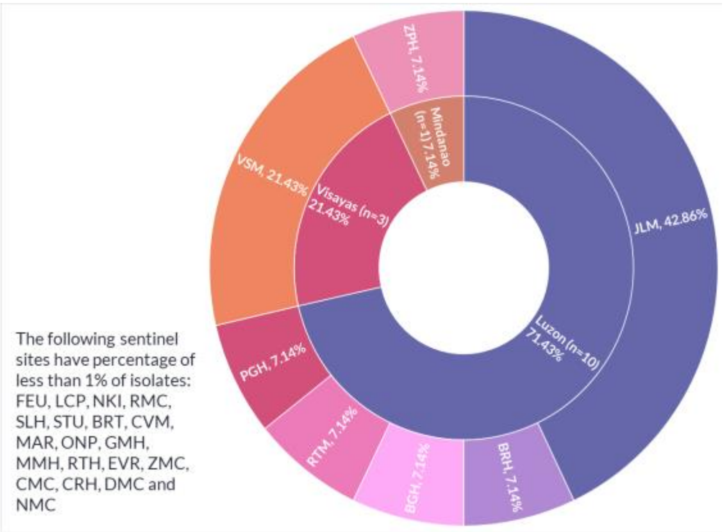


Figure 39. Isolate distribution of *N. gonorrhoeae*, DOH-ARSP, 2021 (n=14)

The 2021 *N. gonorrhoeae* isolates were mostly from 20-64 years old (64.29%) and were from male patients (71.43%). All isolates came from genital samples (Figure 40).

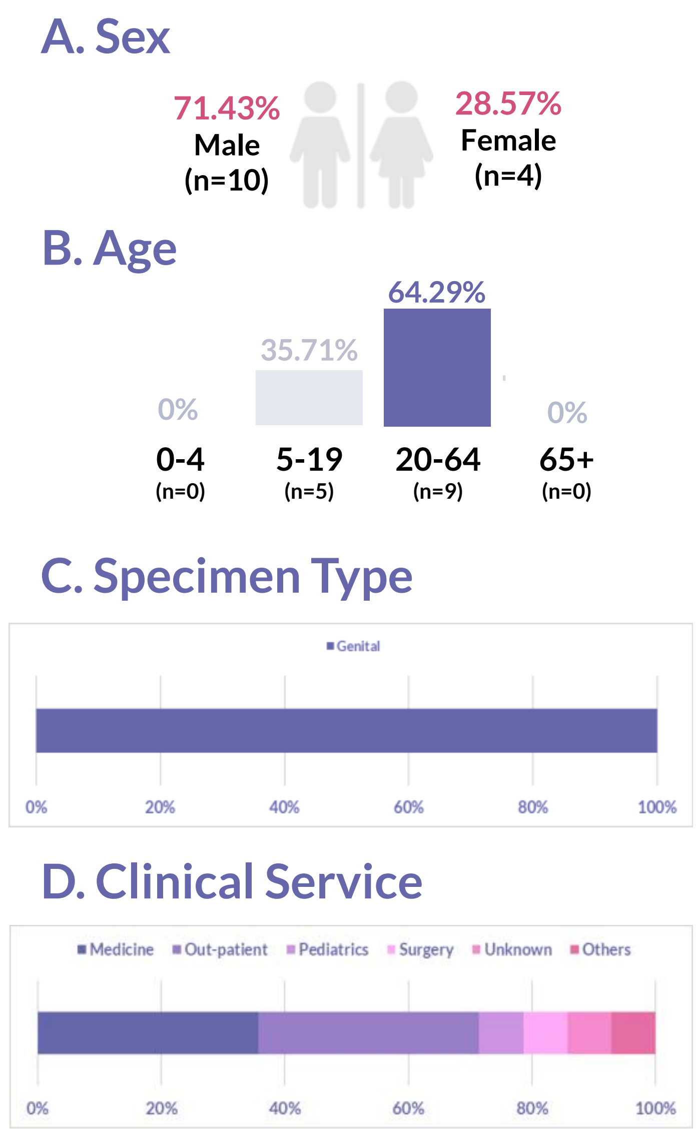


Figure 40. Patients characteristics of *N. gonorrhoeae*, DOH-ARSP, 2021 (n=14)

Figure 41 shows the resistance rates of *N. gonorrhoeae* isolates from 2020-2021. There was a reported non-susceptibility to ceftriaxone but this was not confirmed. There was no reported resistance to cefixime, azithromycin, and spectinomycin. Ciprofloxacin resistance was highest at 83.6%, followed and tetracycline (71.4%).

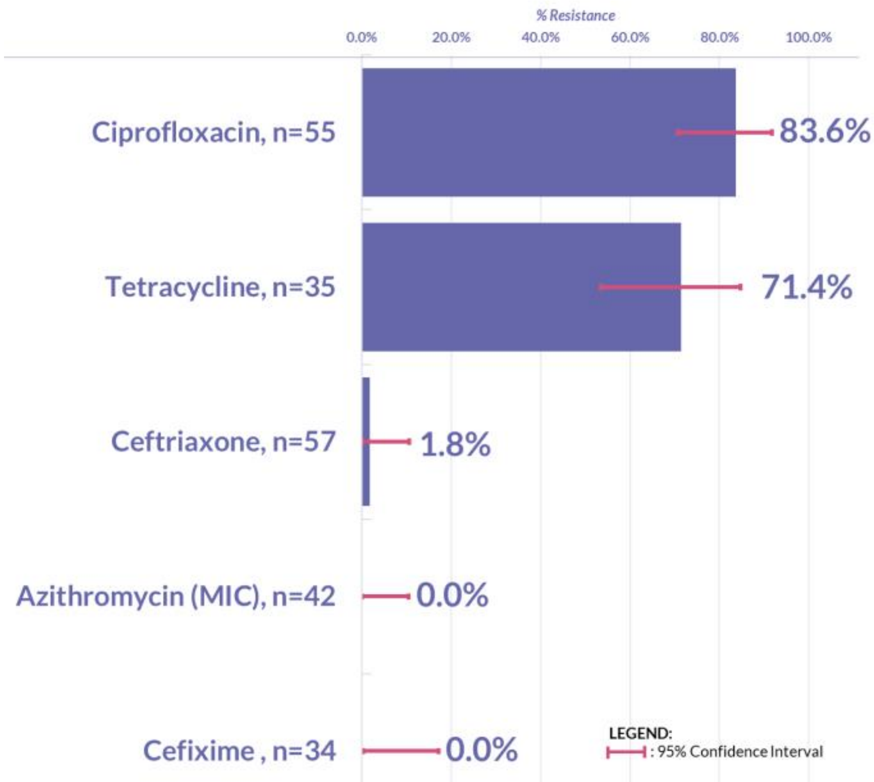


Figure 41. Percent resistance of *N. gonorrhoeae*, DOH-ARSP, 2020—2021

Figure 42 shows the yearly resistance rates of *N. gonorrhoeae*. Resistance rates to tetracycline shows continued increase since 2017. Multiple year analysis revealed that the changes in resistance rates over the years for tetracycline was statistically significant (p=0.0153).

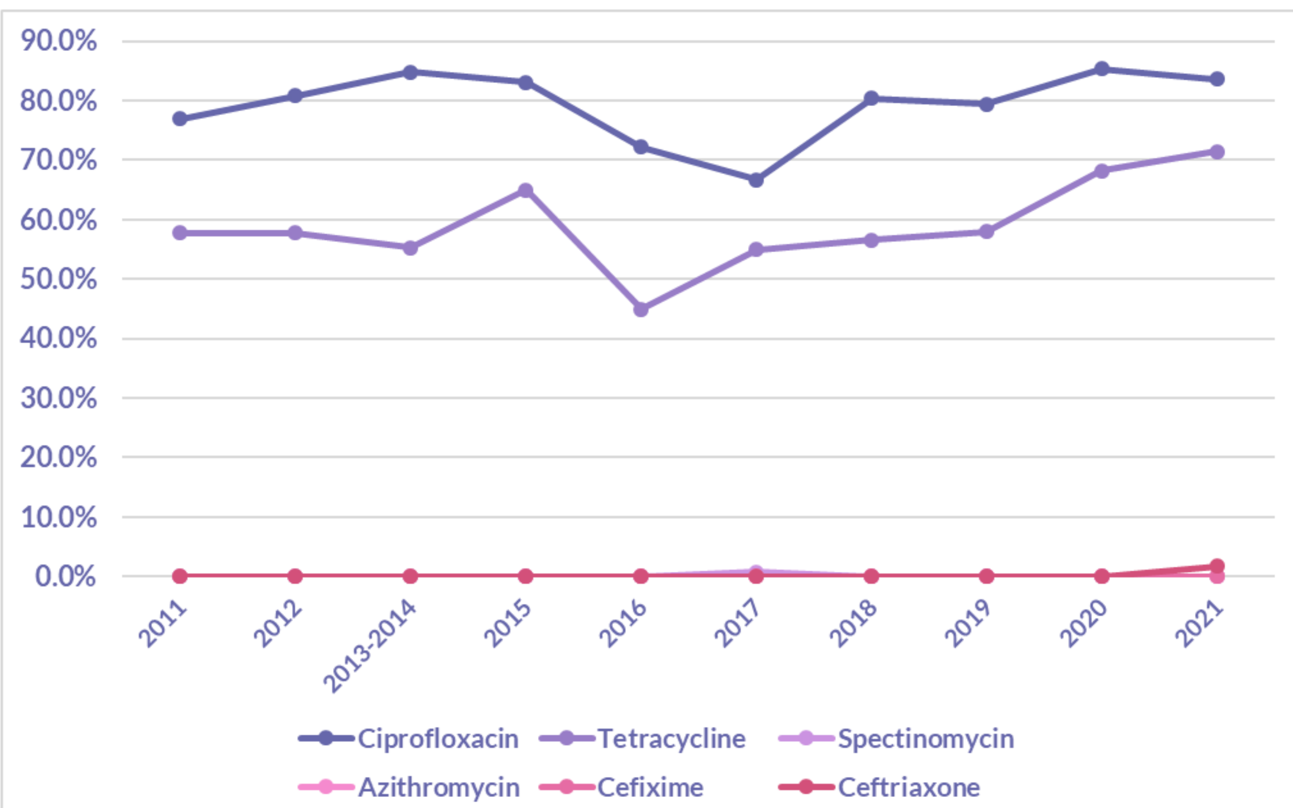


Figure 42. Yearly resistance rates of *N. gonorrhoeae*, DOH-ARSP, 2021

Staphylococcus aureus

A total of 4,198 *Staphylococcus aureus* isolates were reported for 2021. This was a 5% increase in the collected number of isolates compared to 2020 number of isolates. The largest contributors of *S. aureus* isolates were DMC (12.48%), PGH (10.67%) and VSM (9.81%) (Figure 43). Luzon showed the highest number of isolates at 58.81% with 30.66% coming from NCR, Mindanao at 22.70% and Visayas at 18.48%.

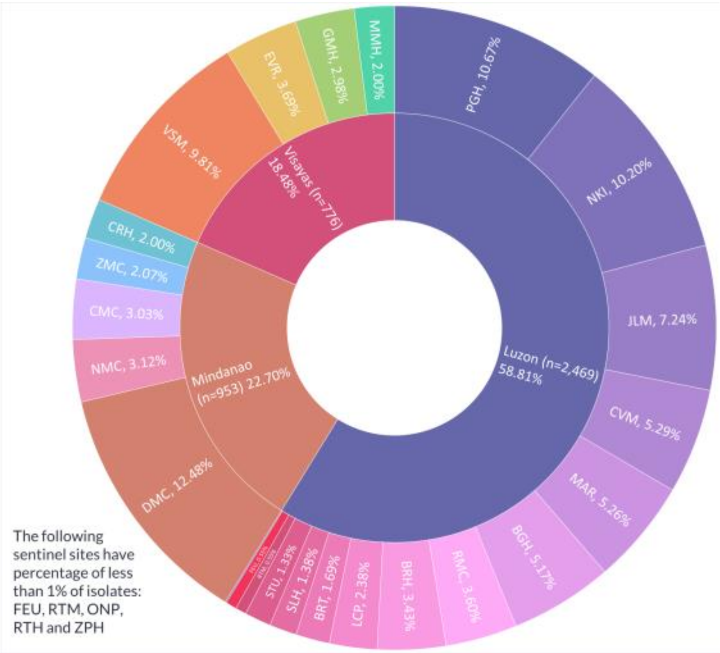


Figure 43. Isolate distribution of *S. aureus*, DOH-ARSP, 2021 (n=4,198)

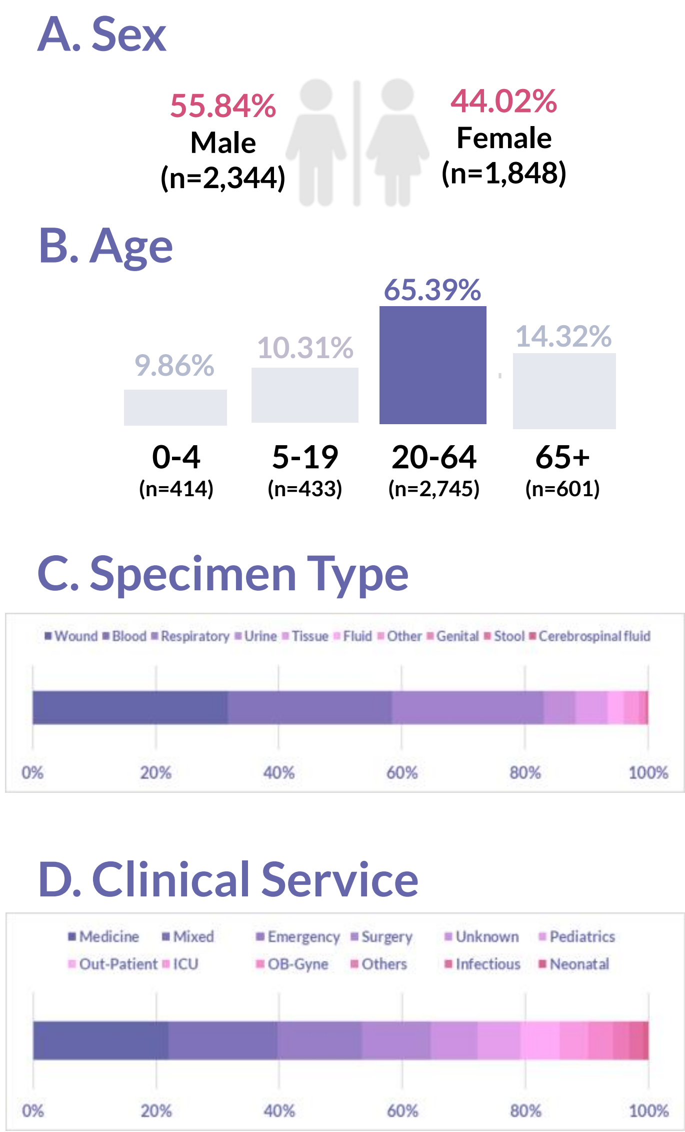


Figure 44. Patients characteristics of *S. aureus*, DOH-ARSP, 2021 (n=4,198)

Most (65.39%) of the isolates were from 20-64 year-old patients and mostly (55.84%) were from male patients (Figure 44). Many (31.71%) of the isolates were collected from wound, blood (26.73%) and respiratory (24.61%) specimens. Most (77.25%) of the isolates were from presumptive community acquired infections.

The overall cumulative resistance rate of *S. aureus* reported for 2021 are shown in **Figure 45**. Penicillin resistance was at 91.1%, oxacillin at 46.9% and co-trimoxazole at 37.9%. Erythromycin resistance was noted to be 12.3% and 10.5% for clindamycin. Percent resistance to tetracycline, rifampin, vancomycin, linezolid, ciprofloxacin and nitrofurantoin were below 10%. Although the computed daptomycin non-susceptibility was zero for 2021, there was a report of an isolate confirmed to be daptomycin non-susceptible. This isolate was from a wound sample of a 55-year old female from one of the sentinel sites in the NCR. The isolate was resistant to oxacillin and co-trimoxazole and susceptible to clindamycin, erythromycin, linezolid, rifampin, tetracycline, ciprofloxacin and vancomycin. Previously reported confirmed daptomycin non-susceptible isolate in 2020 was from a sentinel site in Luzon. There is a need for a continued surveillance for the emergence of daptomycin non-susceptible *S. aureus*.

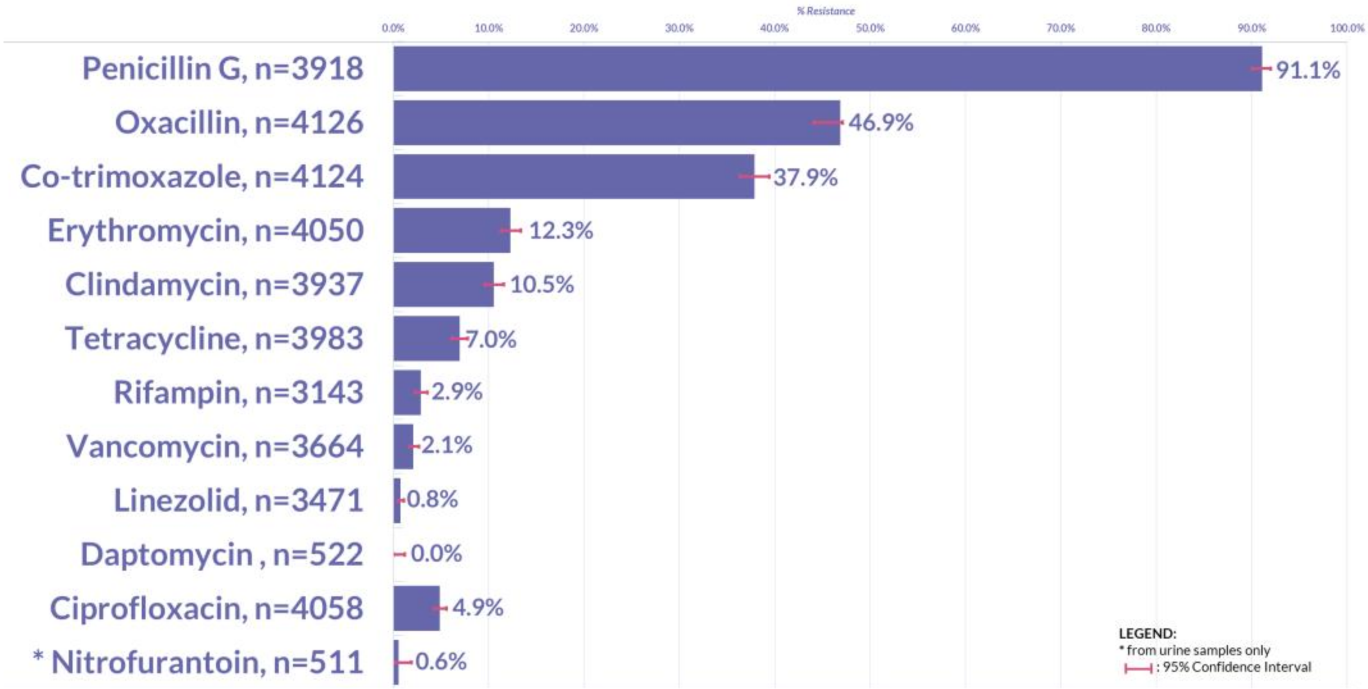


Figure 45. Percent resistance of *S. aureus*, DOH-ARSP, 2021

Yearly resistance rates for *S. aureus* is shown in **Figure 46**. Oxacillin resistance continue to decrease since 2016 and multiple year analysis (2012-2021) showed that the noted changes in resistance rates over the years were statistically significant (p=0.0000). Resistance rates for co-trimoxazole (p=0.0000) and vancomycin (p=0.0001) showed increasing rates over the years and these year by year changes were found to be statistically significant.

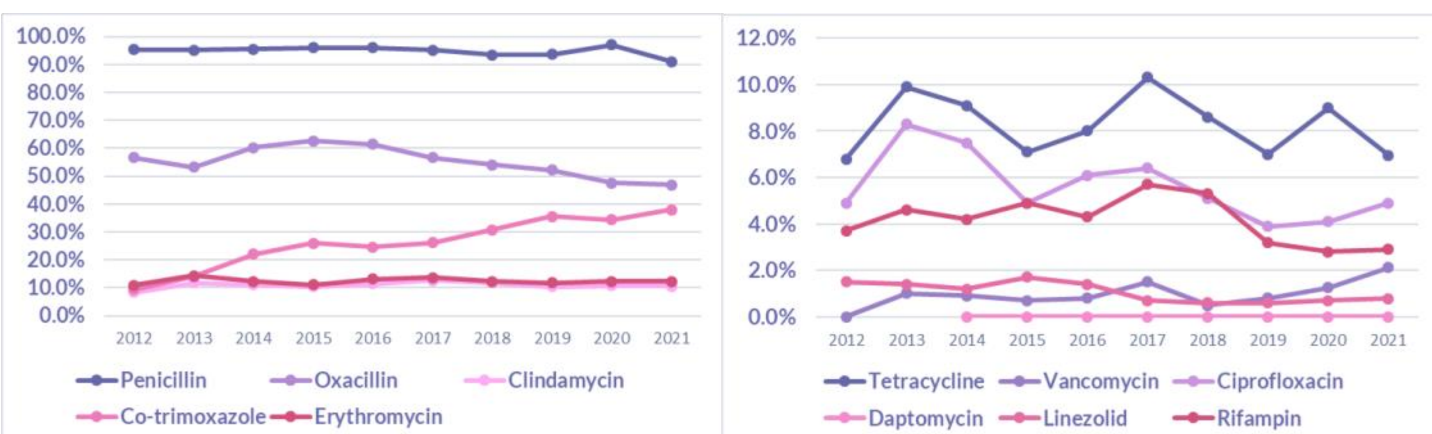


Figure 46. Yearly resistance rate of *S. aureus*, DOH-ARSP, 2012-2021

Figure 47 shows the resistance rates of *S. aureus* isolates from skin and soft tissues. Resistance to penicillin was high at 93.3% followed by oxacillin (46.1%), and co-trimoxazole (45.4%). Resistance rates to erythromycin, clindamycin, tetracycline, vancomycin, rifampin, linezolid, and ciprofloxacin were less than 10%.

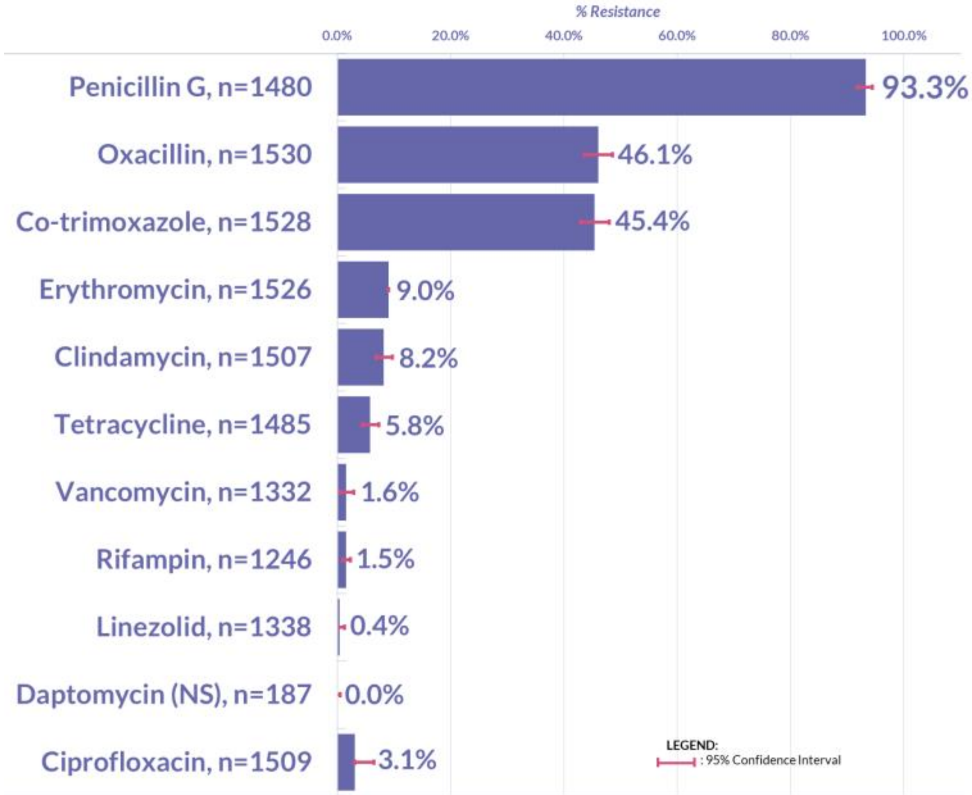


Figure 47. Percent resistance of *S. aureus* skin and soft tissues isolates, DOH-ARSP, 2021

Figure 48 shows the resistance rates of *S. aureus* from blood isolates. Highest resistance rate was detected for penicillin at 90.5% followed by oxacillin (45.2%) and co-trimoxazole (34.6%). Resistance rates to erythromycin, clindamycin, tetracycline, vancomycin, rifampin, linezolid, and ciprofloxacin were less than 15%. No resistance was detected among blood isolates against daptomycin.

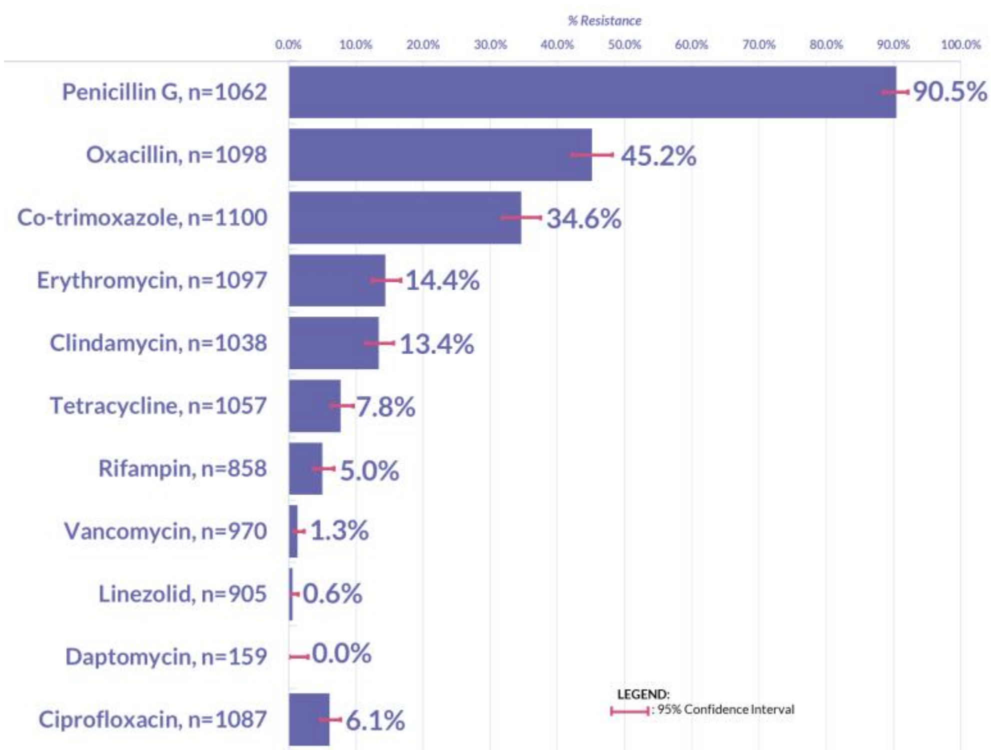


Figure 48. Percent resistance of *S. aureus* blood isolates, DOH-ARSP, 2021

Figure 49 shows the oxacillin resistance rates across the different regions in the country. Sentinel sites from Mindanao have MRSA rates in the range of 50-71% while sentinel sites from the Visayas ranges from 23-57% while in Luzon sentinel sites have MRSA rates ranging from 25 – 100%.

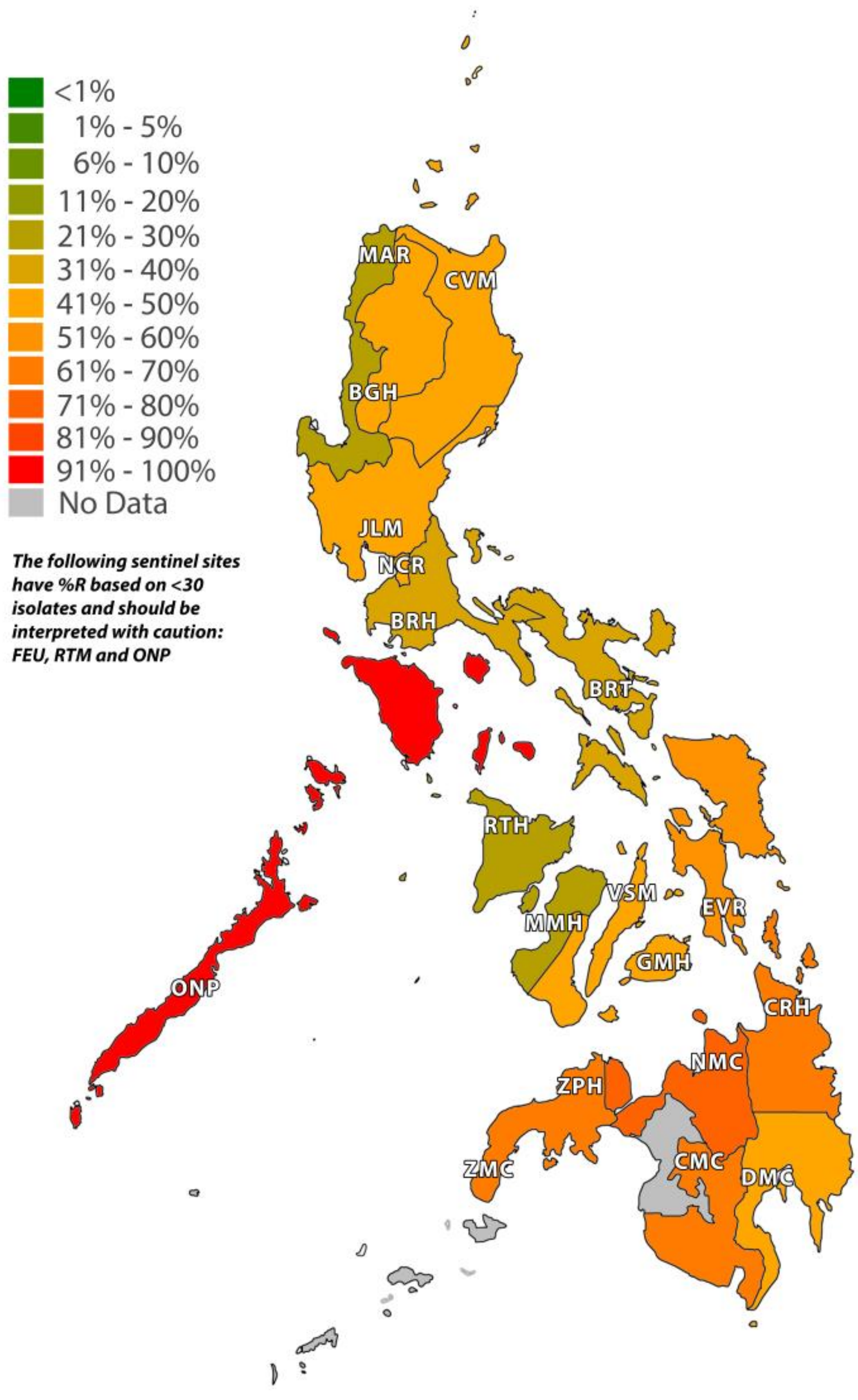


Figure 49. Geographic distribution of oxacillin-resistant *S. aureus* in the Philippines, DOH-ARSP, 2021

Methicillin Resistant *Staphylococcus aureus*

There were **1,644** methicillin resistant *Staphylococcus aureus* (MRSA) isolates reported for 2021. Largest contributors for MRSA include DMC (15.75%), VSM (12.65%) and NKI (11.56%) (**Figure 50**).

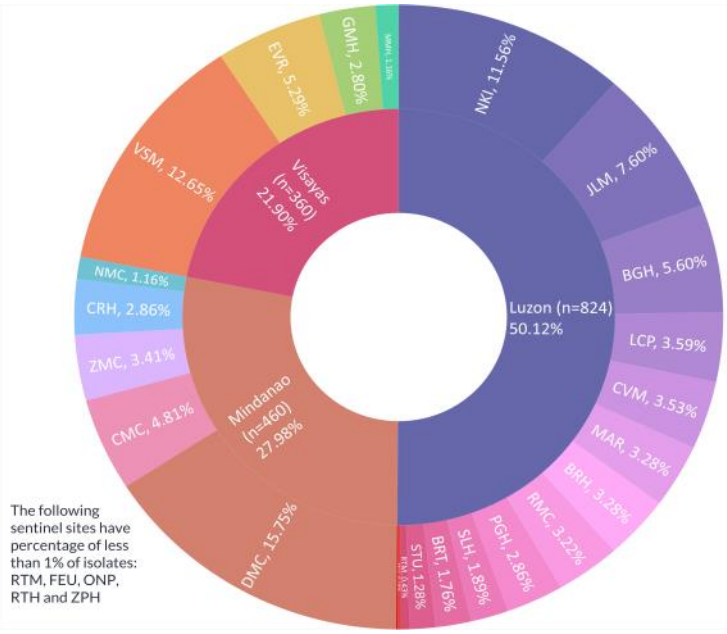


Figure 50. Isolate distribution of methicillin-resistant *S. aureus*, DOH-ARSP, 2021 (n=1, 644)

Most (64.48%) of the isolates were from 20-64 years old group and mostly (57.91%) were from male patients. Many (32%) of the MRSA isolates were from wound specimens and were characterized as presumptive community acquired infections (73.18%) (**Figure 51**).

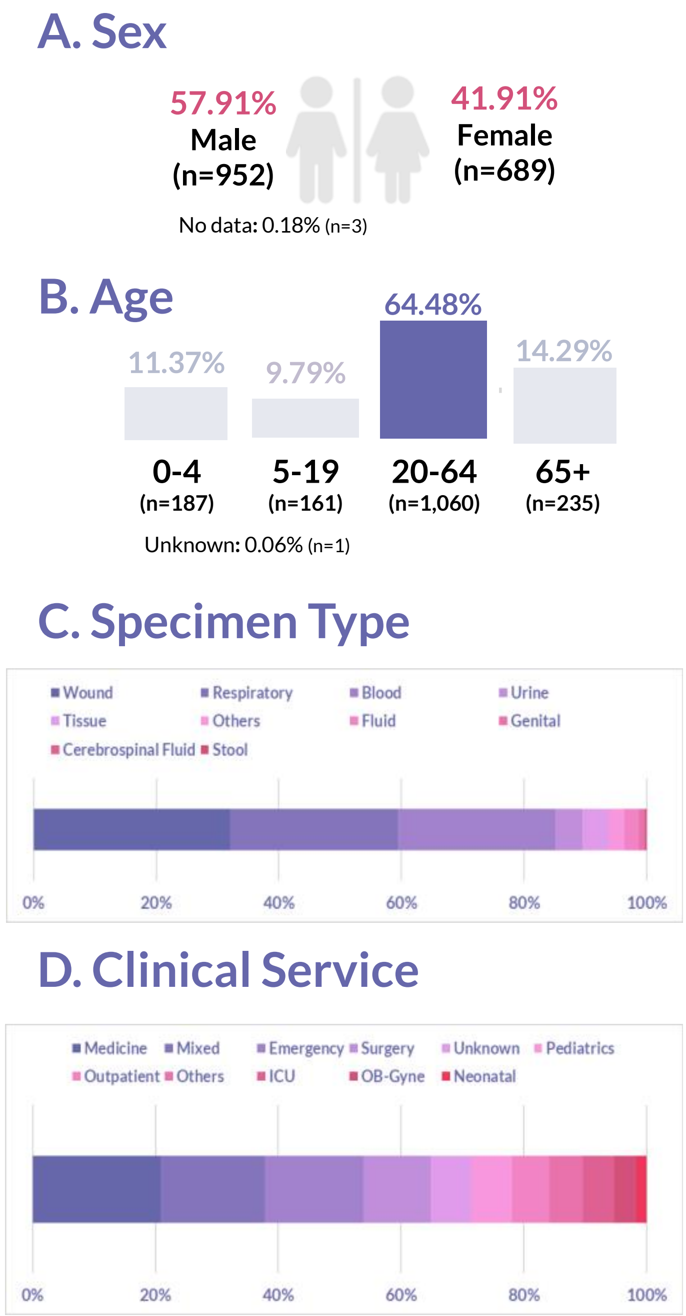


Figure 51. Patients characteristics of methicillin-resistant *S. aureus*, DOH-ARSP, 2021 (n=1,644)

Cumulative resistance rates of MRSA isolates from all specimens are shown in Figure 52. Co-trimoxazole resistance was at 47.8%, 20.5% for erythromycin and 16.7% for clindamycin. Resistance to tetracycline, rifampin, vancomycin, linezolid, and ciprofloxacin were less than 10%. No resistance was detected for daptomycin.

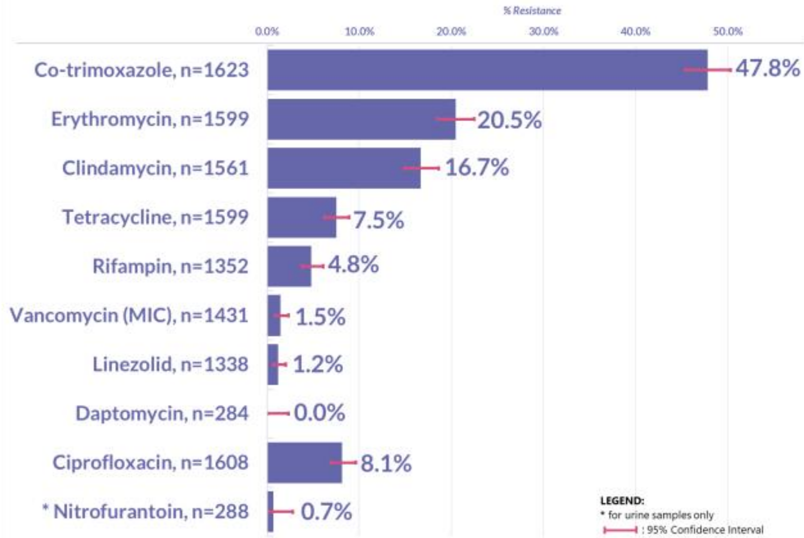


Figure 52. Percent resistance of methicillin-resistant *S. aureus*, DOH-ARSP, 2021

Figure 53 shows the resistance rates of MRSA isolates from skin and soft tissue specimen. Co-trimoxazole resistance was at 46.9%, erythromycin at 16% and clindamycin at 13.7%. Percent resistance to tetracycline, rifampin, vancomycin, linezolid, and ciprofloxacin were less than 10%.

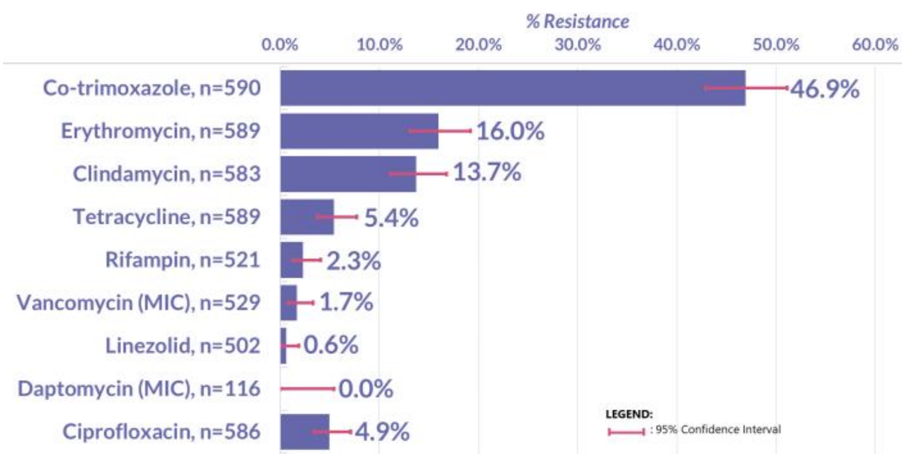


Figure 53. Percent resistance of methicillin-resistant *S. aureus* skin and soft tissues isolates, DOH-ARSP, 2021

Figure 54 shows the resistance rates of MRSA isolates from blood specimens. Co-trimoxazole resistance was at 46.2%, erythromycin at 22.2%, clindamycin at 21.5% and ciprofloxacin at 10.1%. Resistance to tetracycline, rifampin, vancomycin, and linezolid were less than 10%.

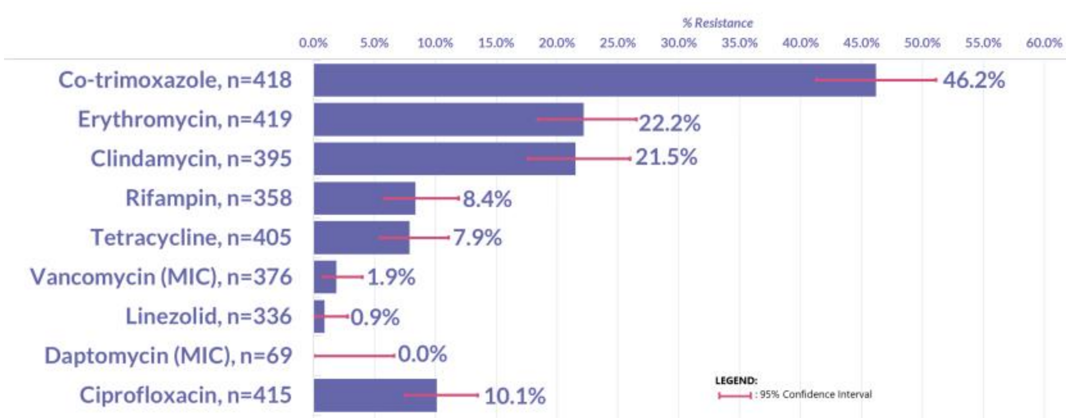


Figure 54. Percent resistance of methicillin-resistant *S. aureus* blood isolates, DOH-ARSP, 2021

Whole Genome Sequencing of Methicillin Resistant *S. aureus* from the ARSP 2013-2014

In 2015, a collaborative project under the Philippine Council for Health Research and Development, Department of Science and Technology was implemented together with the Wellcome Trust Sanger Institute, WHO Collaborating Center for AMR, and the Research Institute for Tropical Medicine. The project was entitled "See and Sequence – Genomic Surveillance of antimicrobial resistance and high-risk clones within the Philippines" and was funded by the UK Medical Research Council. Through the grant, capacity for whole genome sequencing was established at the Antimicrobial Resistance Surveillance Reference Laboratory in order to enhance the understanding of antimicrobial resistance at the genomic level.

In 2017, towards an effort to have a baseline understanding of the genomic epidemiology of MRSA in the country, a total of 116 genomes of MRSA isolates collected through ARSP from 2013-2014 were sequenced [1]. The isolates analyzed were selected based on 1) complete resistance profile; 2) overall prevalence of the resistance profile in the ARSP data (both referred and non-referred), 3) number selected per sentinel site was limited to its relative proportion in the ARSP dataset. The selected isolates were retested against 14 antibiotics in 8 classes. Extracted DNA were sent to Wellcome Trust Sanger Institute for whole genome sequencing. Raw sequences were analyzed using a bioinformatics pipeline from the Sanger Institute. Resistance genes, mutations conferring resistances (also call SNPs – Single Nucleotide Polymorphisim), and sequence types were reported and visualized using an online application called Pathogenwatch (https://pathogen.watch/) and Microreact (https://microreact.org/).

In this summary report, the genomic epidemiology of MRSA as to the distribution of Multi Locus Sequence Types (MLST) and the prevalence of genes (including mutations) conferring resistance will be described.

Distribution of sequence types

The multi-locus sequence typing (MLST) scheme is a bacterial genotyping technique which categorizes bacteria based on 7 housekeeping genes and with the use of a reference database (e.g. pubMLST)., There are 13 distinct sequence types (ST) identified among the MRSA collected through the ARSP in 2013-2014 with the most common being ST 30, 5, and 834 (**Table A**) suggesting that the MRSA population in the Philippines are of limited genetic clones. The geographic distribution of the predominant ST's by sentinel site is shown in **Figure A**.

Table A. ST's, resistance profiles, and genes per sentinel site

Sentinel Site	No. of isolates	No. of Sequence Types	Sequence types detected (No. of isolates)	Resistance Profiles	Resistance Genes
BGH	9	4	30(6), 1(1), 121(1),88 (1)	PEN OXA (9)	blaZ, mecA (6) blaZ, mecA, sdrM (2) blaZ, sdrM (1)
BRH	1	1	30(1)	PEN OXA (1)	blaZ, mecA (1)
CMC	4	1	30(4)	PEN OXA (4)	blaZ, mecA (4)
CVM	10	5	30(4),834(3), 1456 (1), 1457(1),5(1)	PEN OXA (9) PEN OXA SXT (1)	blaZ, mecA (5) blaZ, mecA, sdrM (3) mecA (1) blaZ, mecA, dfrG, sdrM (1)
DMC	7	3	30(5),1649(1), 5(1)	PEN OXA (3) PEN OXA SXT (4)	blaZ, mecA (3) blaZ, mecA, dfrG (3) blaZ, mecA, dfrG, sdrM (1)
EVR	5	3	30(3), 1(1), 508(1)	PEN OXA (5)	blaZ, mecA (4) blaZ, mecA, dfrG, sdrM (1)
FEU	6	1	30(6)	PEN OXA (6)	blaZ, mecA (6)
GMH	5	1	30(5)	PEN OXA (5)	blaZ, mecA (5)
JLM	6	3	5(3),30(2),1(1)	PEN OXA (6)	blaZ, mecA (5) blaZ, mecA, sdrM (1)
MAR	9	2	30(7),239(2)	PEN OXA (7) PEN OXA GEN ERY CLI TCY CIP (2)	blaZ, mecA (7) blaZ, mecA, aacA_aphD, ermC, tetM, tetK, GyrA_S84L, GyrA_G106D, GrlA_S80F, catA1, sdrM, ileS_2 (2)
MMH	3	1	30(3)	PEN OXA (3)	blaZ, mecA (3)
NKI	7	3	30(5),5(1),88(1)	PEN OXA (7)	blaZ, mecA (6) blaZ, sdrM (1)
NMC	6	1	30(6)	PEN OXA (6)	blaZ, mecA (6)
SLH	1	1	30(1)	PEN OXA (1)	blaZ, mecA (1)
STU	10	3	30(8),1456(1), 97(1)	PEN OXA (10)	blaZ, mecA (9) blaZ, mecA, sdrM (1)
VSM	25	6	30(17), 834(4), 1649 (1),5(1), 573(1), 97(1)	PEN OXA (21) PEN OXA SXT (3) PEN OXA ERY (1)	blaZ, mecA (16) mecA, sdrM (1) blaZ, mecA, sdrM (3) blaZ, mecA, sdrM, ileS_2 (1) blaZ, mecA, dfrG (1) blaZ, mecA, dfrG, sdrM (2) blaZ, mecA, msrA, sdrM (1)
ZMC	2	2	30 (1), 5(1)	PEN OXA (1) PEN OXA SXT (1)	blaZ, mecA (1) blaZ, mecA, dfrG, sdrM (1)

Sources: 1) (https://microreact.org/project/ARSP_SAU_2013-2014), 2) Masim, et al. "Genomic Surveillance of MRSA in the Philippines, 2013-2014"

Figure A. Distribution of ST's in the Philippines. (https://microreact.org/project/ARSP_SAU_2013-2014)

Prevalence of resistance genes accounting for phenotypic resistance

Table A shows the genes accounting for the phenotypic resistance of the isolates. The presence of resistance genes among isolates which exhibited phenotypic resistance to each antibiotic classes are presented in Figures B.1.-B.7.

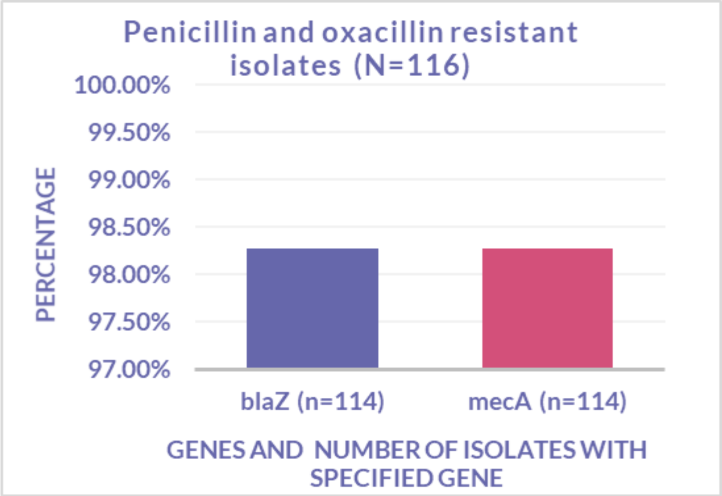


Figure B.1. Isolates with penicillinase resistance genes

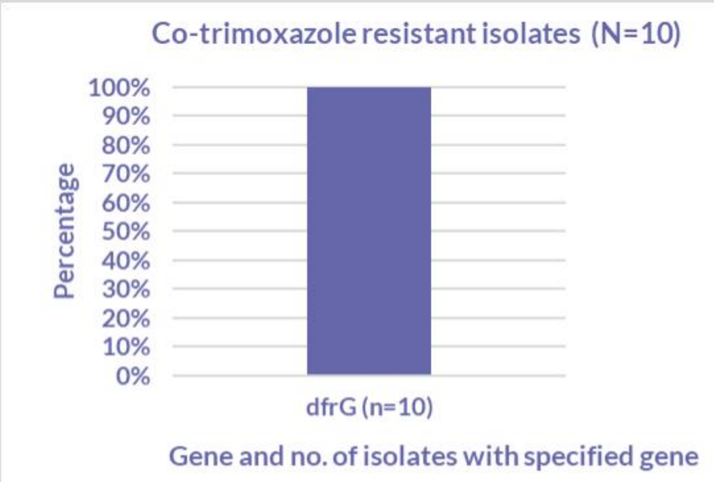


Figure B.2. Isolates with genes conferring resistance to folate pathway antagonists

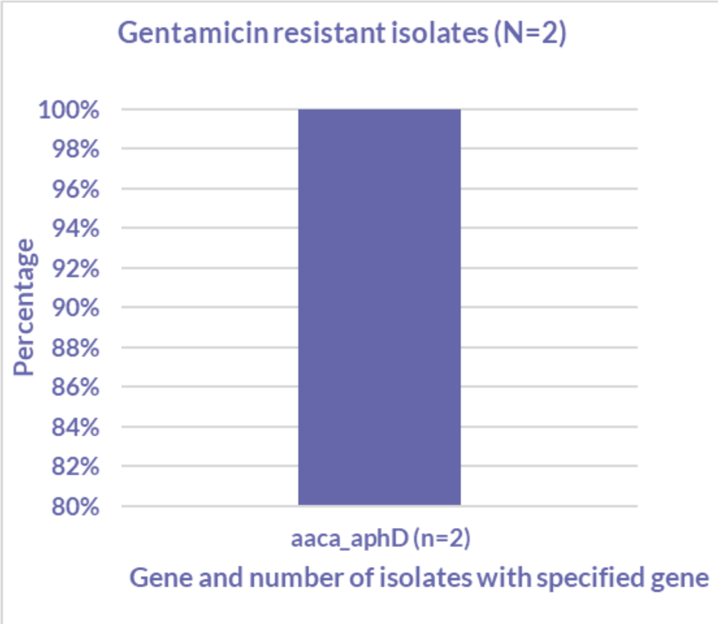


Figure B.3. Isolates with aminoglycoside resistance genes

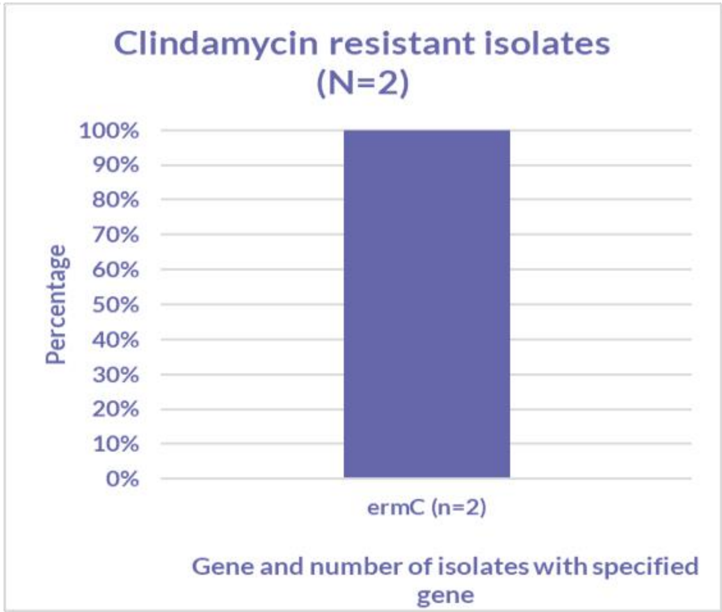


Figure B.4. Isolates with lincosamide resistance genes

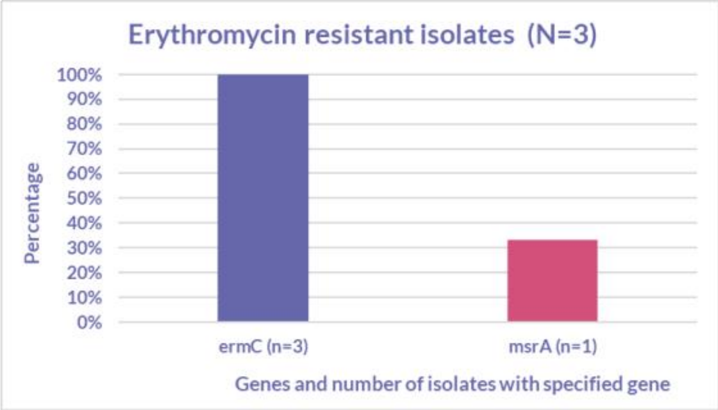


Figure B.5. Isolates with macrolide resistance genes

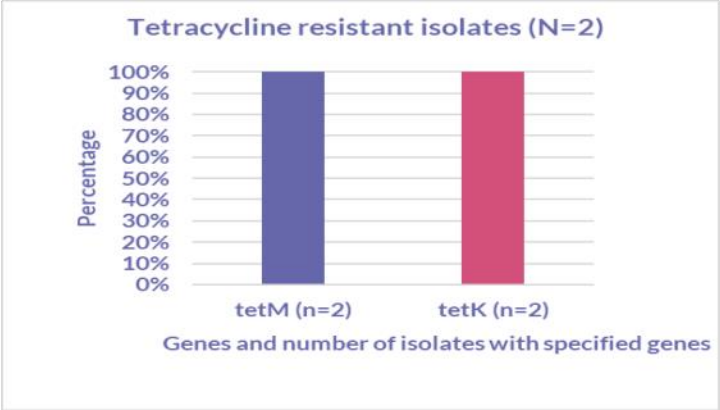


Figure B.6. Isolates with tetracycline resistance genes

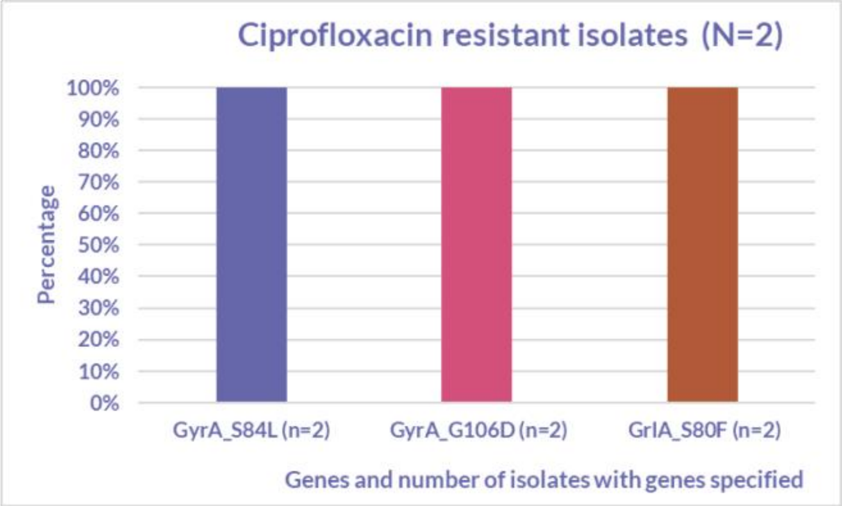


Figure B.7. Isolates with ciprofloxacin resistance genes

Distribution of detected AMR genes in the Philippines

The distribution of AMR genes conferring resistance against oxacillin, erythromycin, and clindamycin by sentinel sites are shown in Figures C-D.

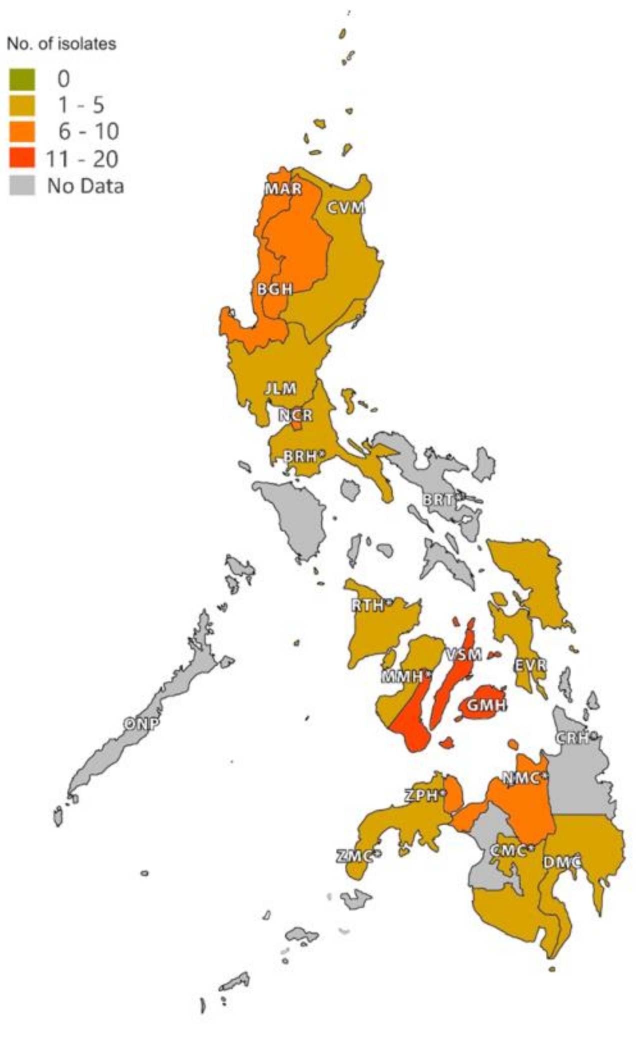


Figure C. Distribution of *mecA* genes among oxacillin resistant *S. aureus* isolates, ARSP, 2013-2014

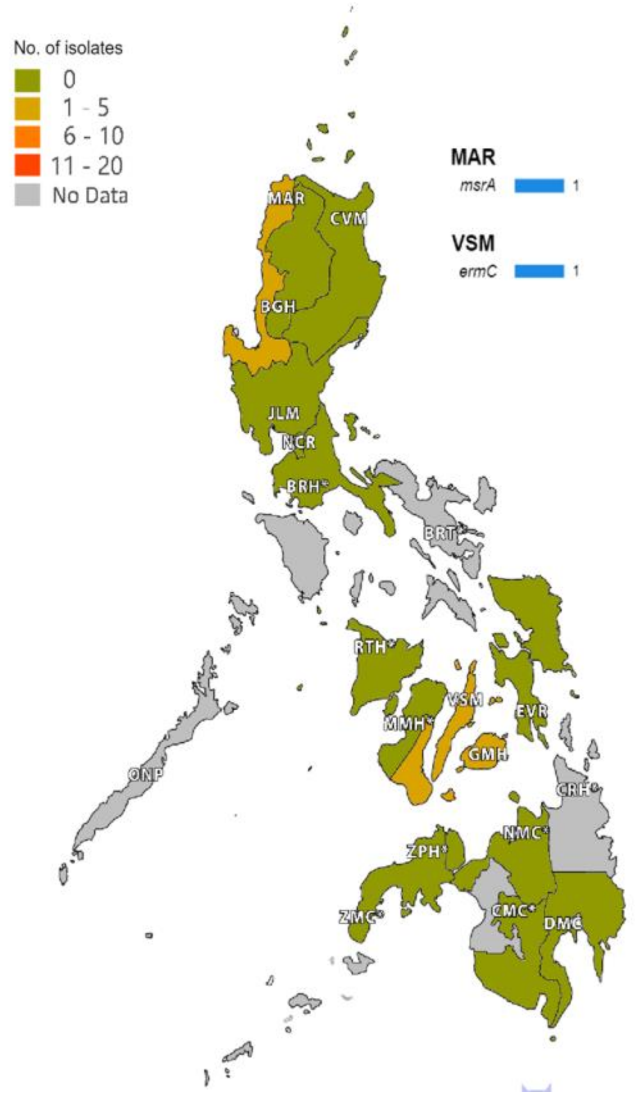


Figure D. Distribution of *msrA* and *ermC* genes among MRSA isolates, ARSP 2013-2014

This summary report provides a baseline genetic background of MRSA in the country. The use of WGS allowed for the identification of prevailing STs and the resistance mechanisms of MRSA in the country.

References:

1. Masim, M., Argimon, S., Espiritu, H., Magbanua, M., Lagrada, M., Olorosa, A., Cohen, V., Gayeta, J., Jeffrey, B. , Abudahab, K., Hufano, M., Sia, S., Holden, M., Stelling, J., Aanensen, D., and Carlos, C. " "Genomic surveillance of methicillin- resistant *Staphylococcus aureus* in the Philippines, 2013-2014. Western Pacific Surveillance and Response Journal. Vol. 12 No.1. Feb. 2021.

Methicillin Susceptible *Staphylococcus aureus*

Cumulative resistance rates of MSSA isolates from all specimens are shown in Figure 55. Penicillin resistance was highest at 85.1% followed by co-trimoxazole 31.8%. Erythromycin resistance was at 6.6% and clindamycin at 5.9%. Resistance rates to tetracycline, rifampin, vancomycin, linezolid, daptomycin, ciprofloxacin and nitrofurantoin were less than 10%.

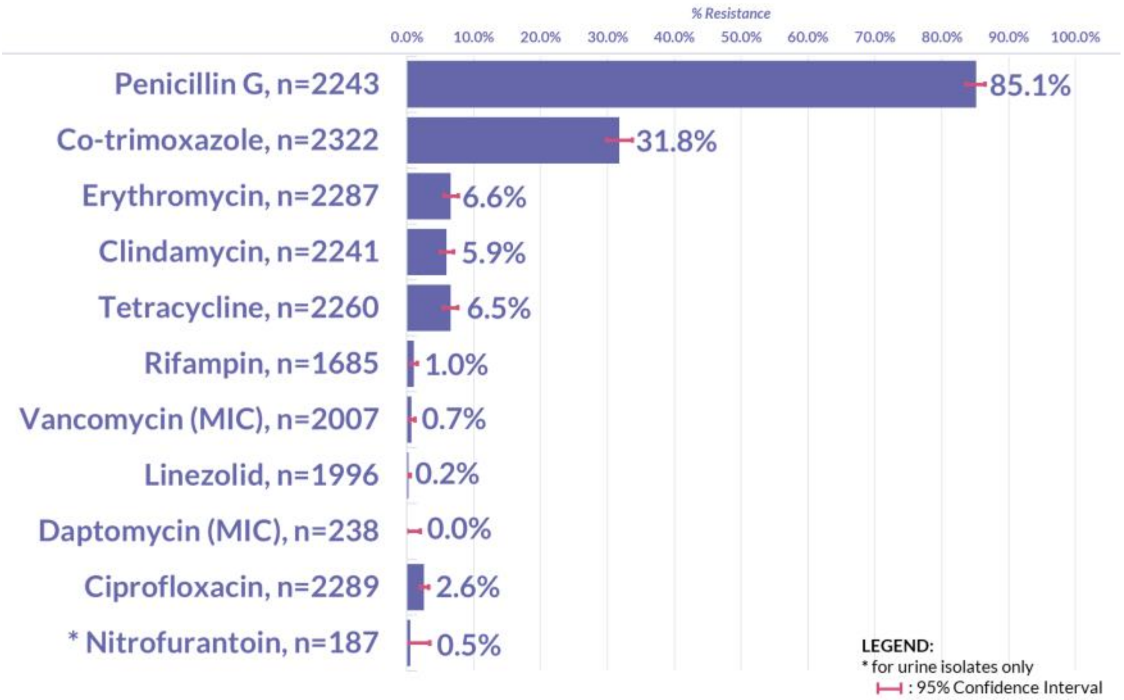


Figure 55. Percent resistance of methicillin-susceptible *S. aureus*, DOH-ARSP, 2021

Figure 56 shows the resistance rates of MSSA from skin and soft tissue isolates. Co-trimoxazole resistance was at 46.9%, erythromycin at 3.5% and clindamycin at 3.8%. Tetracycline resistance was at 6.0% and rifampin at 0.3%. Resistance rates of vancomycin, linezolid and ciprofloxacin were less than 10%.

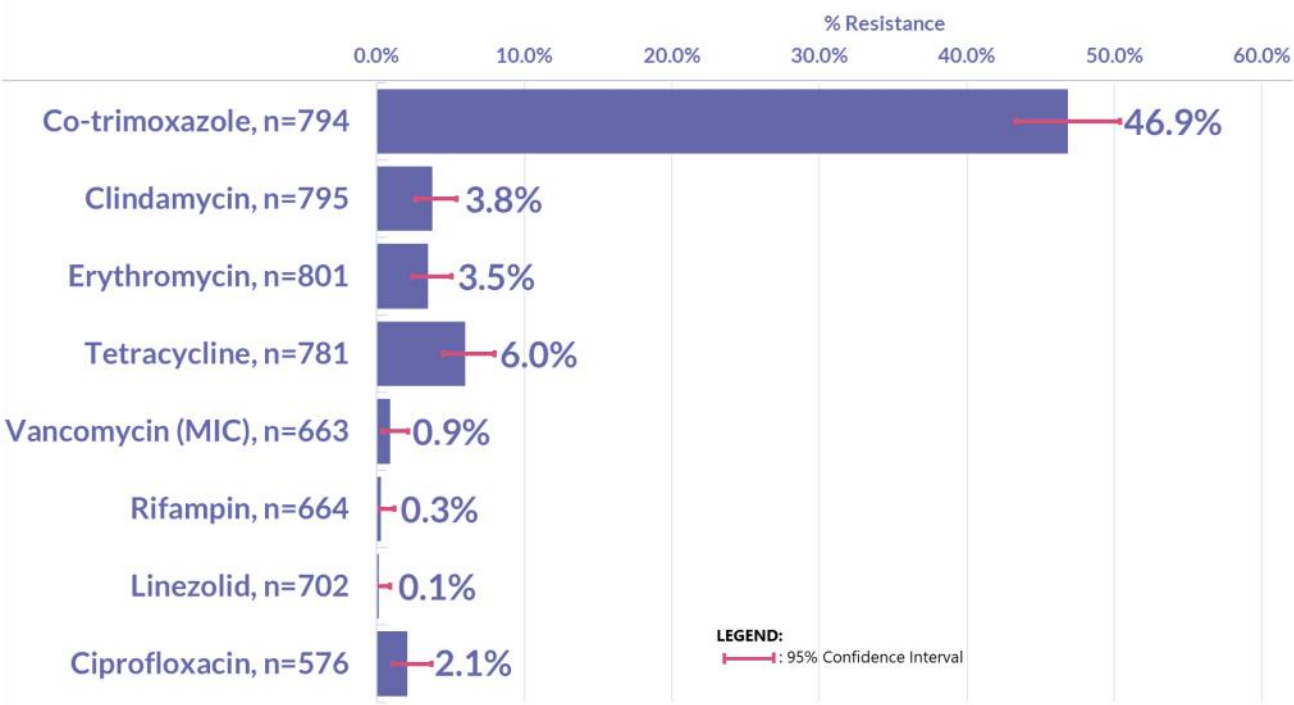


Figure 56. Percent resistance of methicillin-susceptible *S. aureus* skin and soft tissues isolates, DOH-ARSP, 2021

Penicillin and co-trimoxazole resistance rates of MSSA blood isolates were at 84.4% and 27.7% respectively (Figure 57). Erythromycin resistance was at 9.2%, and clindamycin at 7.6%. Resistance rates for tetracycline, rifampin, vancomycin, linezolid, and ciprofloxacin were less than 10%. No resistance was noted for daptomycin.

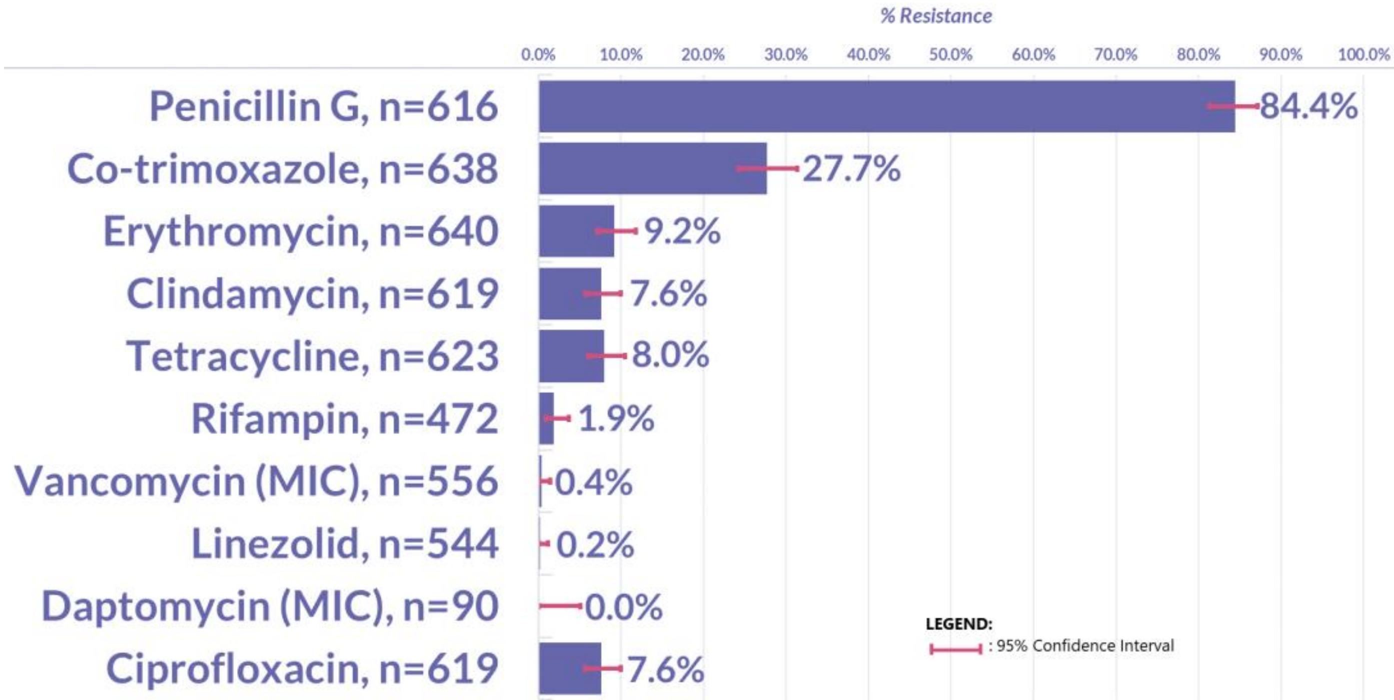


Figure 57. Percent resistance of methicillin-susceptible *S. aureus* blood isolates, DOH-ARSP, 2021

Figure 58 shows the resistance rates of MSSA urine isolates. Penicillin resistance was at 84.0%. Co-trimoxazole resistance was at 29.2%. Resistance rates of tetracycline, rifampin, linezolid and ciprofloxacin were less than 10%. No resistance observed for vancomycin and nitrofurantoin.

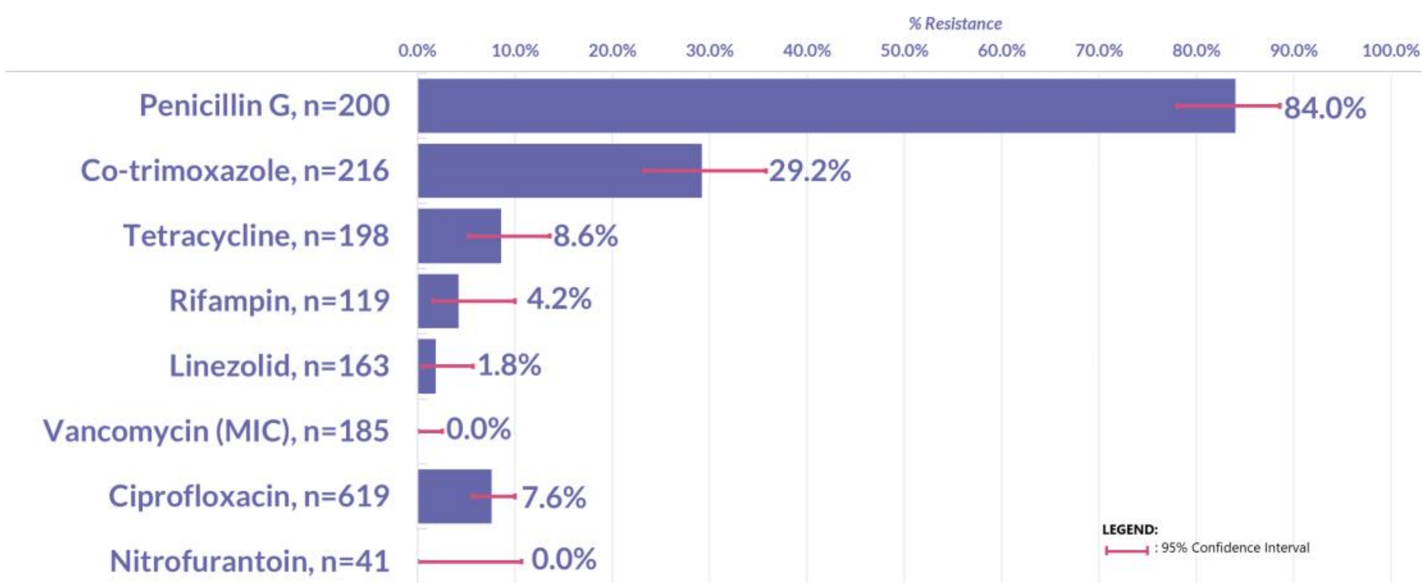


Figure 58. Percent resistance of methicillin-susceptible *S. aureus* urine isolates, DOH-ARSP, 2021

Enterococcus species

For 2021, a total of 3,820 isolates of *Enterococcus* species were reported of which the most common were *Enterococcus faecalis* (53.95%) and *Enterococcus faecium* (35.36%).

Enterococcus faecalis

There were 2,061 isolates of *Enterococcus faecalis* in 2021. DMC (20.82%) contributed most of the data in *E. faecalis* followed by PGH (13.97%) and VSM (6.74%) (Figure 59). The Luzon sentinel sites contributed the most (59.39%) number of isolates.

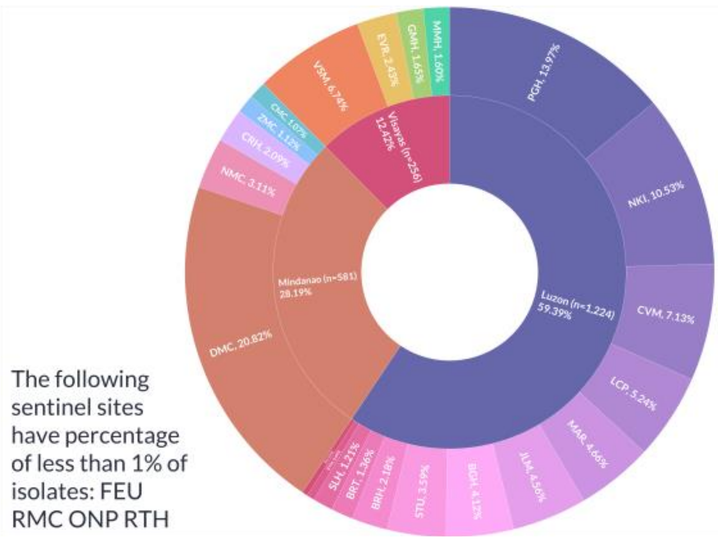


Figure 59. Isolate distribution of *E. faecalis*, DOH-ARSP, 2021 (n= 2,061)

Most (65.79%) of the isolates were from 20-64 age group and were from female patients (51.92%) (Figure 60). *E. faecalis* isolates were mostly (42.89%) collected from urine specimens. Most (70.45%) of the isolates were from presumptive community acquired infections.

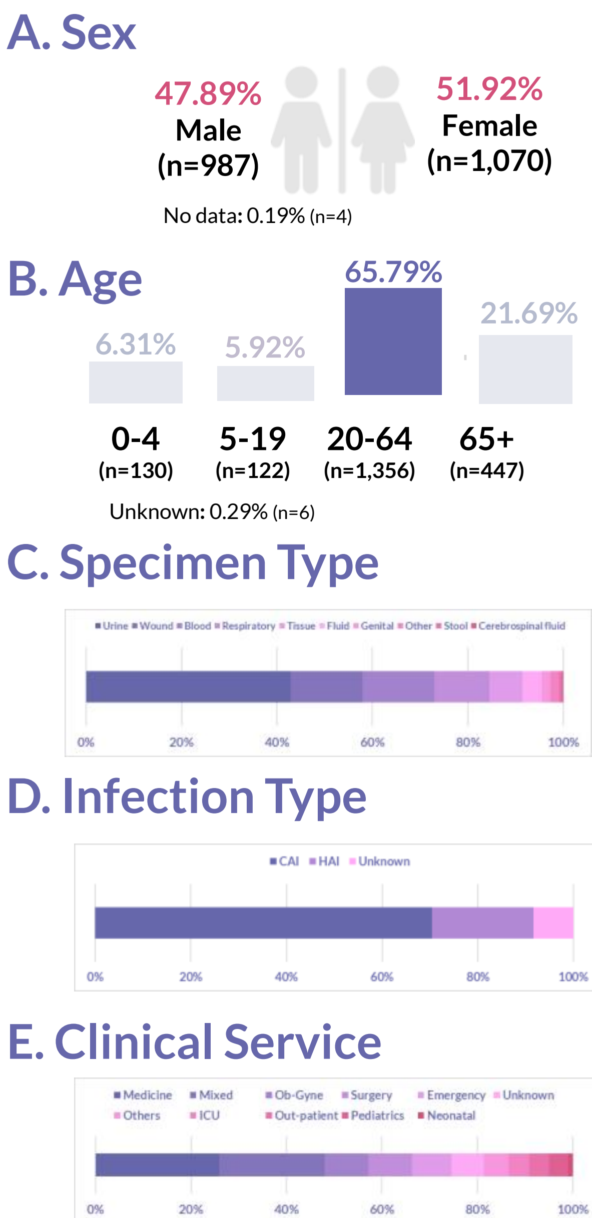


Figure 60. Patients characteristics of *E. faecalis*, DOH-ARSP, 2021 (n=2,061)

Penicillin resistance was at 17.5%, ampicillin at 9.1%, and vancomycin at 4.5% (Figure 61). Percent resistance to linezolid was at 4% while high-level resistance to gentamicin and streptomycin was at 14.1% and 13.8%, respectively.

There was one *E. faecalis* isolate confirmed to be vancomycin resistant. This isolate was from blood specimen of a 38-year old male from a sentinel site in the Visayas. The isolate was susceptible to ampicillin, penicillin, gentamicin high- level and streptomycin high –level.

There were four confirmed linezolid resistant isolates reported in 2021. Isolates were from the Visayas, NCR, north Luzon and Mindanao. Out of the four isolates, two were recovered from urine samples and all patients were from 20-64 years old. All of the isolates were susceptible to ampicillin, penicillin, vancomycin, gentamicin high level and streptomycin high-level.

There were 12 confirmed gentamicin (high level) resistant isolates for 2021. One isolate was detected from the respiratory sample of a 0-day old male patient from a sentinel site in the Visayas. This isolate was noted to be susceptible to vancomycin. Another gentamicin (high level) resistant isolate was from a wound sample of a 77-year old male from a sentinel site in Mindanao. This isolate was susceptible to ampicillin, vancomycin and streptomycin (high-level).

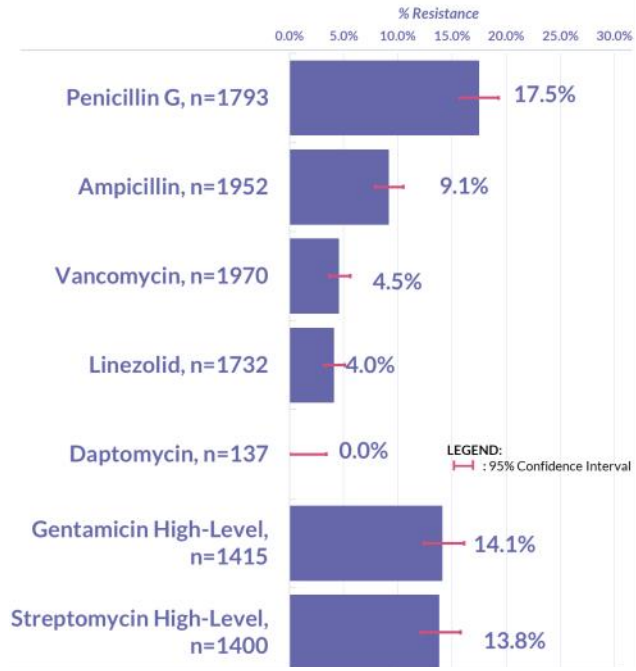


Figure 61. Percent resistance of *E. faecalis*, DOH-ARSP, 2021

High-level resistance to gentamicin and streptomycin was noted to decrease beginning in 2020 (Figure 62) with only the change in high-level resistance to streptomycin over the years found to be statistical significant (p = 0.0043). Multiple year analysis (2012-2021) likewise showed that the changes in resistance rates for vancomycin (p= 0.0000) to be statistically significant.

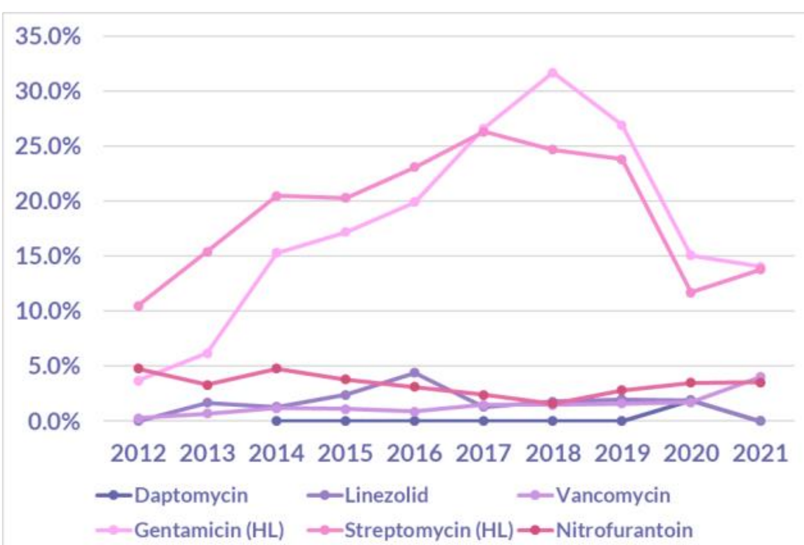


Figure 62. Yearly resistance rates of *E. faecalis*, DOH-ARSP, 2021

Figure 63 shows the resistance rates of *E. faecalis* isolates from blood specimens. Resistance to penicillin was at 20.4%, vancomycin at 5.1% and linezolid at 2.7%. High-level resistance to gentamicin (high level) was noted to be at 21.1% and 16.6% for streptomycin.

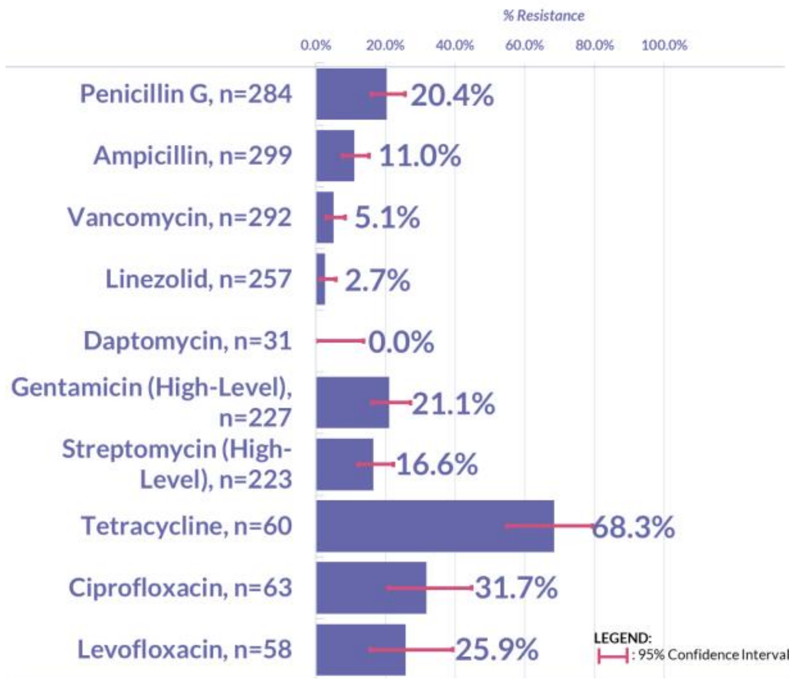


Figure 63. Percent resistance of *E. faecalis* blood isolates, DOH-ARSP, 2021

Figure 64 shows the resistance rates of *E. faecalis* isolates from urine specimens. Resistance to penicillin was at 21.1%, vancomycin at 3.2% and linezolid at 2.8%. High-level resistance to gentamicin was at 14.1% and 13.7% for streptomycin. Percent resistance to tetracycline and ciprofloxacin were at 77.3% and 34.9% respectively. Resistance to levofloxacin was at 29.9% and 3.6% for nitrofurantoin.

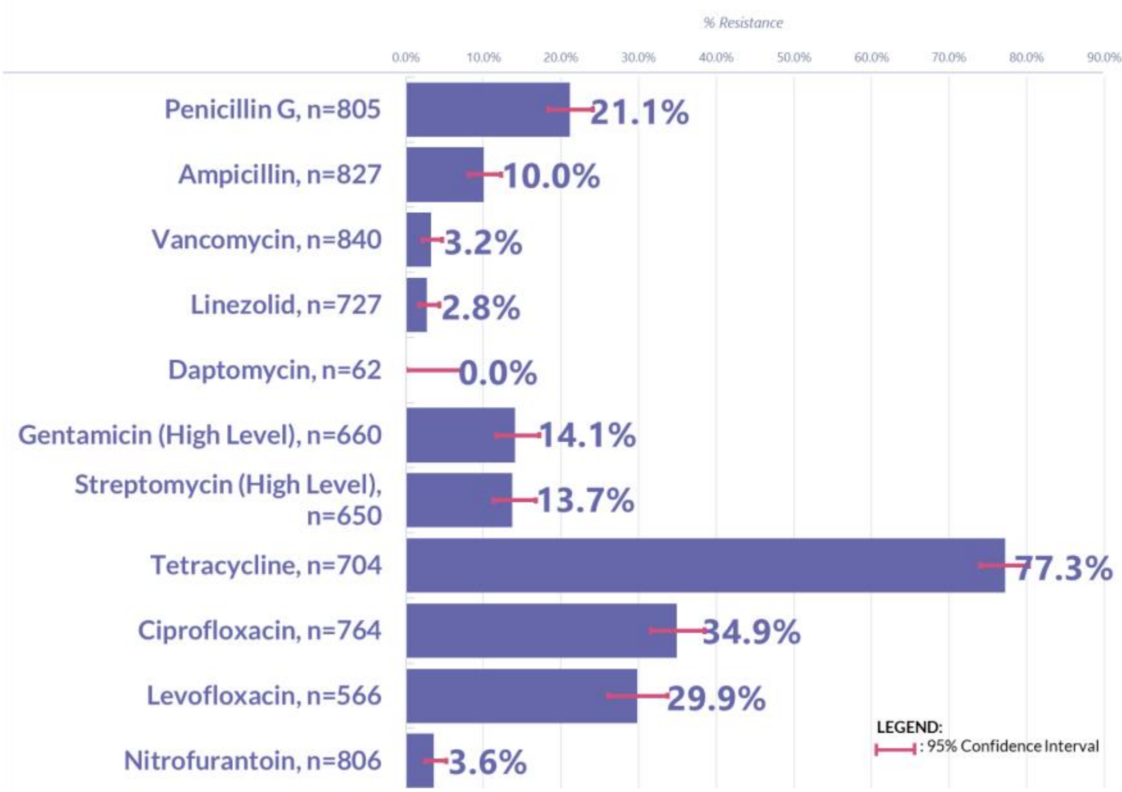


Figure 64. Percent resistance of *E. faecalis* urine isolates, DOH-ARSP, 2021

Figure 65 shows the geographical distribution of vancomycin-resistant *E. faecalis* isolates across the country. Sentinel sites from NCR, BGH, CVM, BRH and NMC have linezolid resistance rates at 6-10% range. While JLM, BRT, MMH and DMC have resistance rates at 1-5% range.

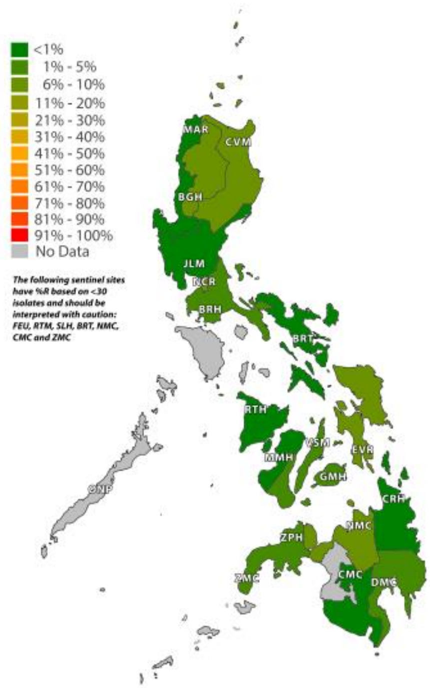


Figure 65. Geographic distribution of vancomycin- resistant *E. faecalis* in the Philippines, DOH-ASRP, 2021

Figure 66 shows the geographical distribution of linezolid-resistant *E. faecalis* isolates across the country. Sentinel sites from NCR, BGH, CVM, BRH and NMC have linezolid resistance rates at 6-10% range. While JLM, BRT, MMH and DMC have resistance rates at 1-5% range.

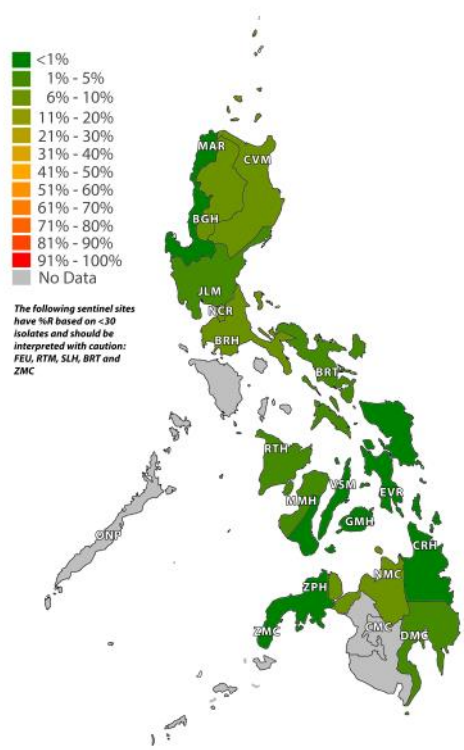


Figure 66. Geographic distribution of linezolid- resistant *E. faecalis* in the Philippines, DOH-ASRP, 2021

Enterococcus faecium

There were **1,351** *Enterococcus faecium* isolates reported for 2021. Highest contribution of data for *Enterococcus faecium* were PGH (24.13%), DMC (19.39%) and VSM (10.58%) (**Figure 67**). The sentinel sites from Luzon contributed most (55.59%) of the data with 38.64% coming from the NCR.

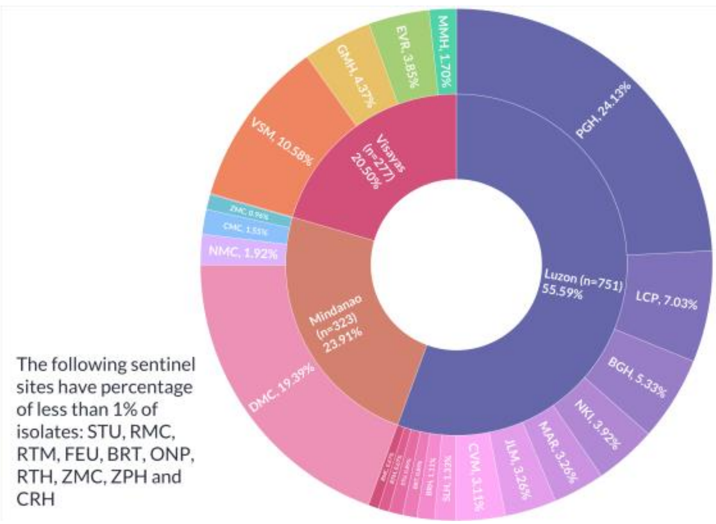


Figure 67. Isolate distribution of *E. faecium*, DOH-ARSP, 2021 (n=1,351)

Most (54.63%) of the isolates were from 20-64 years old and were collected from female patients (55.14%) (**Figure 68**). More than half (52.63%) of the isolates were from presumptive community acquired infections and most (60.47%) were from urine specimens.

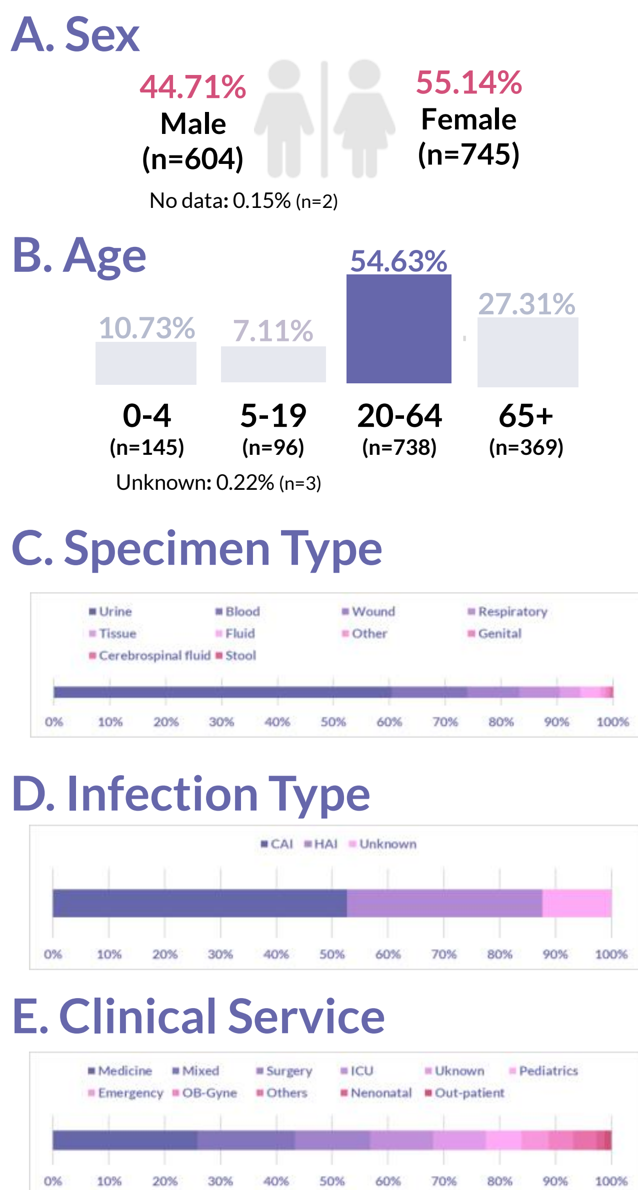


Figure 68. Patients characteristics of *E. faecium* isolates, DOH-ARSP, 2021 (n=1,351)

Cumulative resistance rates of *E. faecium* are shown in **Figure 69**. Ampicillin resistance rate was at 90.9%, penicillin at 89.9%, ciprofloxacin at 87.1% and 83.8% for levofloxacin. Percent resistance to vancomycin, tetracycline, and nitrofurantoin were less than 40% and resistance to linezolid was at 5.2%. Resistance to gentamicin (high-level) was at 26.7% and 18.5% for streptomycin (high-level).

There were 4 confirmed linezolid-resistant *E. faecium* reported for 2021. Three of the isolates were from urine samples and one was from a wound sample. Two of the isolates were isolated from Mindanao, and one each from the Visayas and the NCR. All of the isolates were susceptible to nitrofurantoin and to gentamicin (high-level) and streptomycin (high-level).

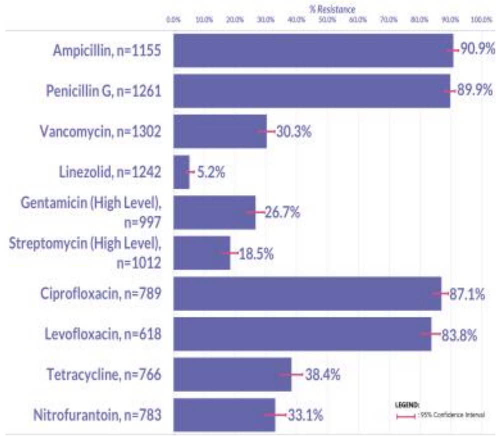


Figure 69. Percent resistance of *E. faecium*, DOH-ARSP, 2021

Penicillin and ampicillin resistance were at high level in the past ten years (**Figure 70**). Resistance to vancomycin and linezolid began to increase in 2017 and 2019, respectively. Multiple year analysis showed that the changes in resistance rates over the years for vancomycin (p =0.0000), gentamicin (high-level) (p=0.0000) and streptomycin (high-level) (p=0.0000) were all statistically significant.

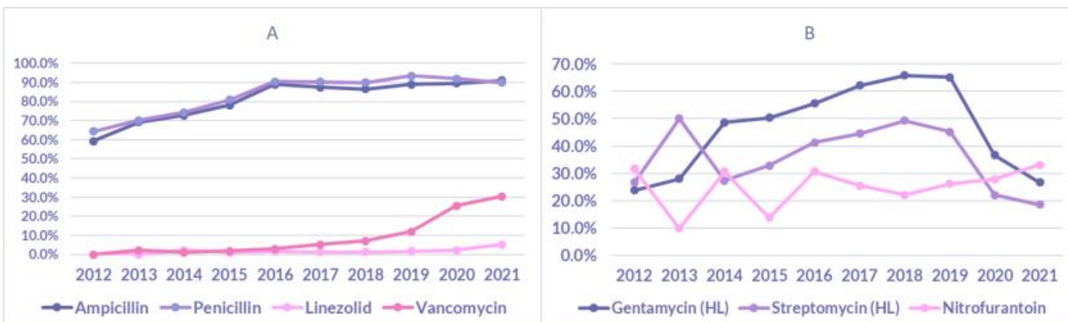


Figure 70. Yearly resistance rates of *E. faecium*, DOH-ARSP, 2012-2021

Figure 71 shows the resistance rates of *E. faecium* isolates from blood specimens. Penicillin was at 91.5% and ampicillin at 90.4%. Percent resistance to gentamicin (high-level) was noted at 36.5% and 20% for streptomycin (high-level).

Figure 72 shows the resistance rates of *E. faecium* isolates from urine specimens. Penicillin was at 95.0%, ampicillin at 93.9%, vancomycin at 30.8% and linezolid at 4.0%. Percent resistance to gentamicin (high-level) was noted at 25.6% and 17.7% for streptomycin (high-level). Among the antibiotics tested for isolates from urine samples, lowest resistance is for linezolid at 4.0%.

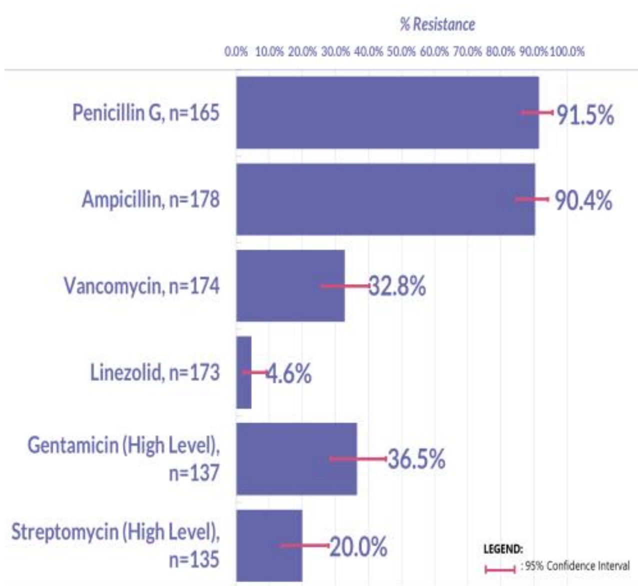


Figure 71. Percent resistance of *E. faecium* blood isolates, DOH-ARSP, 2021

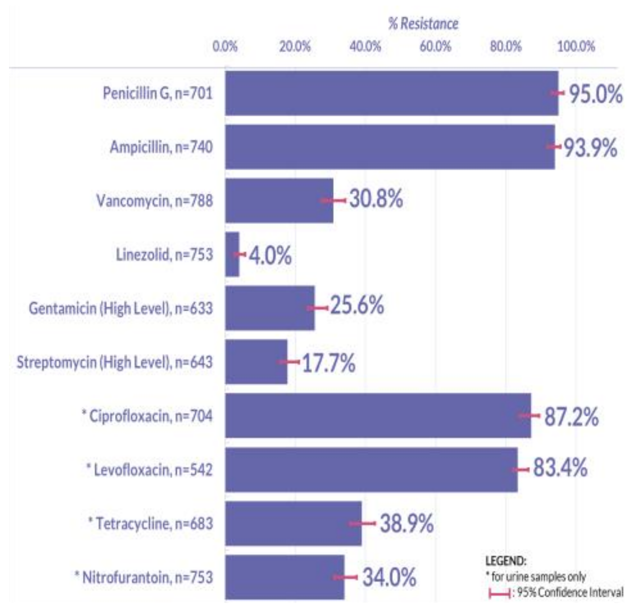


Figure 72. Percent resistance of *E. faecium* urine isolates, DOH-ARSP, 2021

Figure 73 shows the distribution across the country of vancomycin-resistant *E. faecium*. NMC showed vancomycin resistance within 31 -40%. While, sentinel sites from BGH, CVM and BRH have resistance rates ranging from 11-20%.

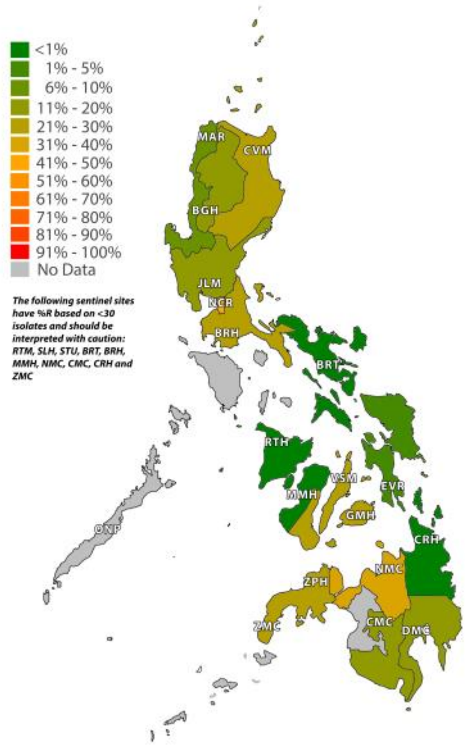


Figure 73. Geographic distribution of vancomycin- resistant *E. faecium* in the Philippines, DOH-ASRP, 2021

Figure 74 shows the distribution across the country of linezolid-resistant *E. faecium*. NMC showed linezolid resistance rate at 15.4%. While, sentinel sites from NCR, BGH, CVM and BRH have resistance rates ranging from 6-10%.

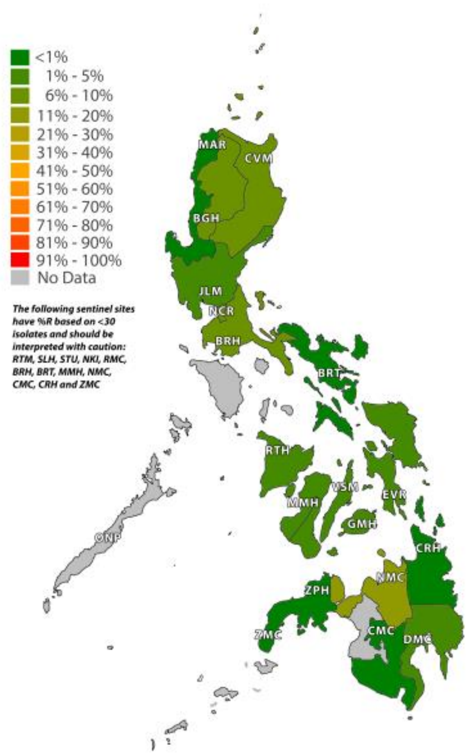


Figure 74 Geographic distribution of linezolid- resistant *E. faecium* in the Philippines, DOH-ASRP, 2021

Escherichia coli

A total of 7,404 isolates of *E. coli* were reported for 2021. PGH (16.18%) contributed most to the number of isolates followed by DMC and NKI (9.74%) and VSM (8.91%)(Figure 75). Based on island group distribution, 60.41% were from Luzon with 36.43% from NCR.

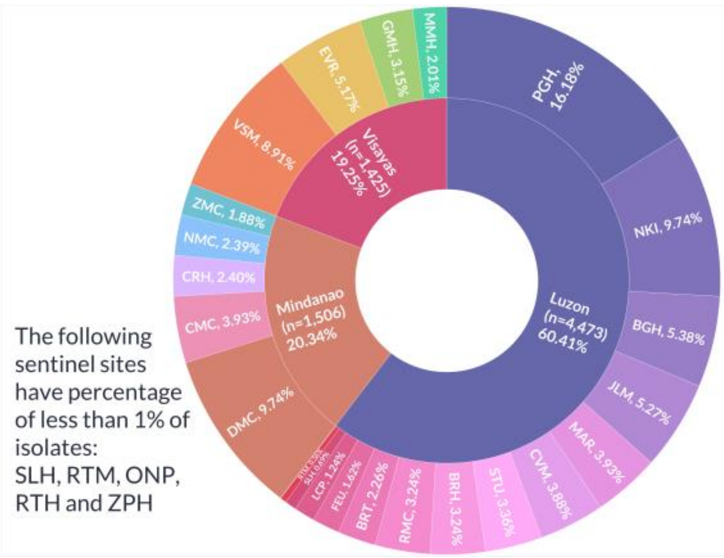


Figure 75. Isolate distribution of *E. coli*, DOH-ARSP, 2021 (n= 7,404)

More than half (62.72%) of the isolates were from patients aged 20-64 years old and most (59.40%) were from female patients (Figure 76). Many (48.34%) of *E. coli* isolates were from urine specimens. Most (75.26%) of the cases were presumptive community acquired infections.

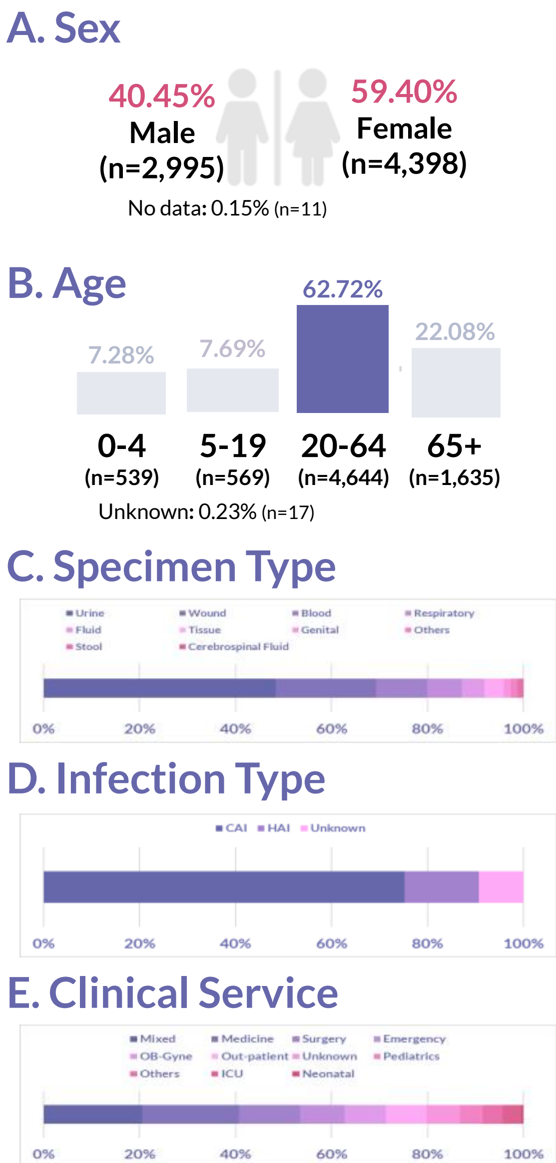


Figure 76. Patient characteristics of *E. coli* isolates, DOH-ARSP, 2021 (n=7,404)

Cumulative resistance rates of *E. coli* for 2021 is shown in Figure 77. Resistance rates of *E. coli* to almost all of the antibiotics were above 20%. There were significant differences in the resistance rate of the following antibiotics from 2020 compared with 2021 rates: ampicillin (p=0.0001), co-trimoxazole (p=0.0000), cefotaxime (p=0.0256), cefepime (p=0.0250), ceftazidime (p=0.0095), aztreonam (p=0.0432) and nitrofurantoin (p=0.0105) (Figure 77). Lowest resistance rates for 2021 were for colistin (1.9%) and amikacin (3.9%).

There were 3 confirmed colistin resistant isolates reported for 2021. These were isolates from urine and wound specimens of patients aged 49-72 years old. These isolates were susceptible to the carbapenems, piperacillin/tazobactam, gentamicin and amikacin.

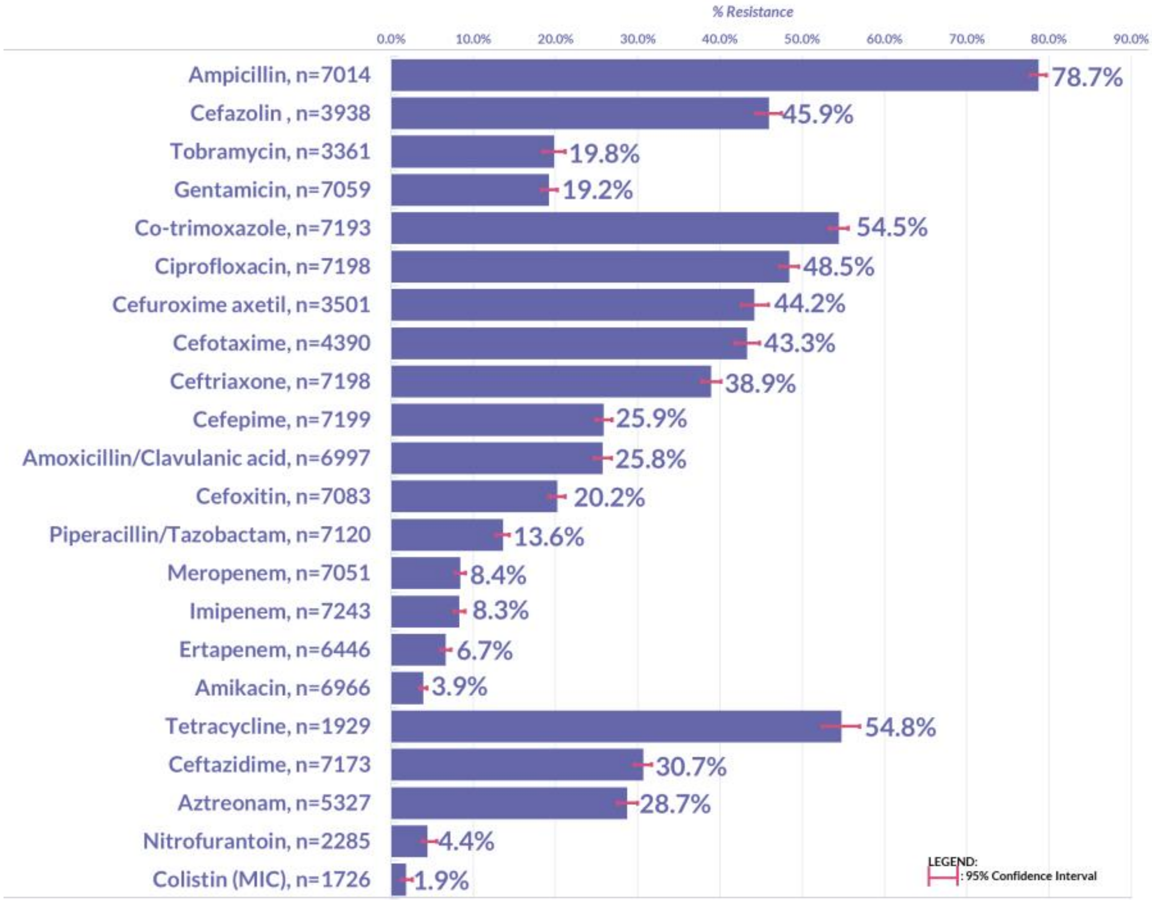


Figure 77. Percent resistance of *E. coli*, DOH-ARSP, 2021

The yearly resistance rate of *E. coli* is shown in **Figure 78**. Multiple year analysis revealed that the annual changes in resistance rates for ertapenem (p=0.0000), meropenem (p=0.0000), imipenem (p=0.0000), ciprofloxacin (p= 0.0003) and colistin (p=0.0000) were all statistically significant.

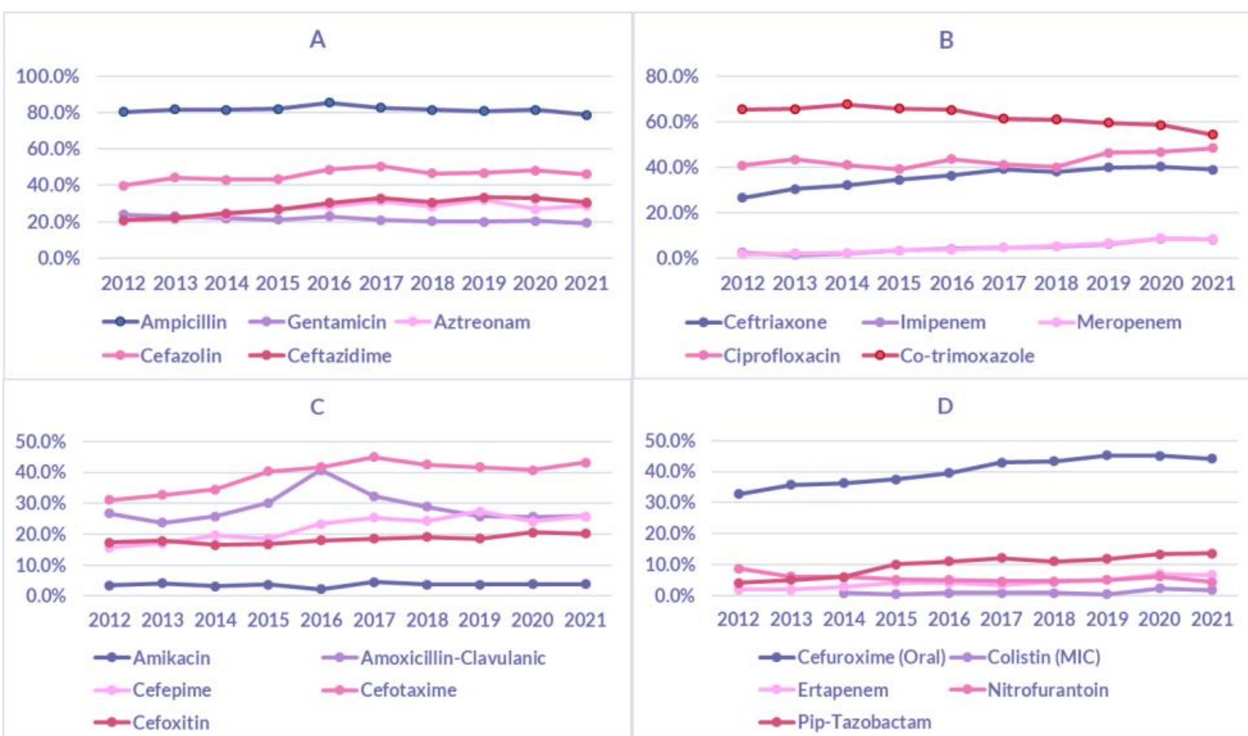


Figure 78. Yearly resistance rates of *E. coli*, DOH-ARSP, 2012-2021

Figure 79 shows the resistance rates of *E. coli* isolates from blood. Resistance rates to most antibiotics were above 20%. Resistance rates to carbapenem antibiotics were less than 10%. Amikacin resistance rate was at 4.4% and 1.0% for colistin.

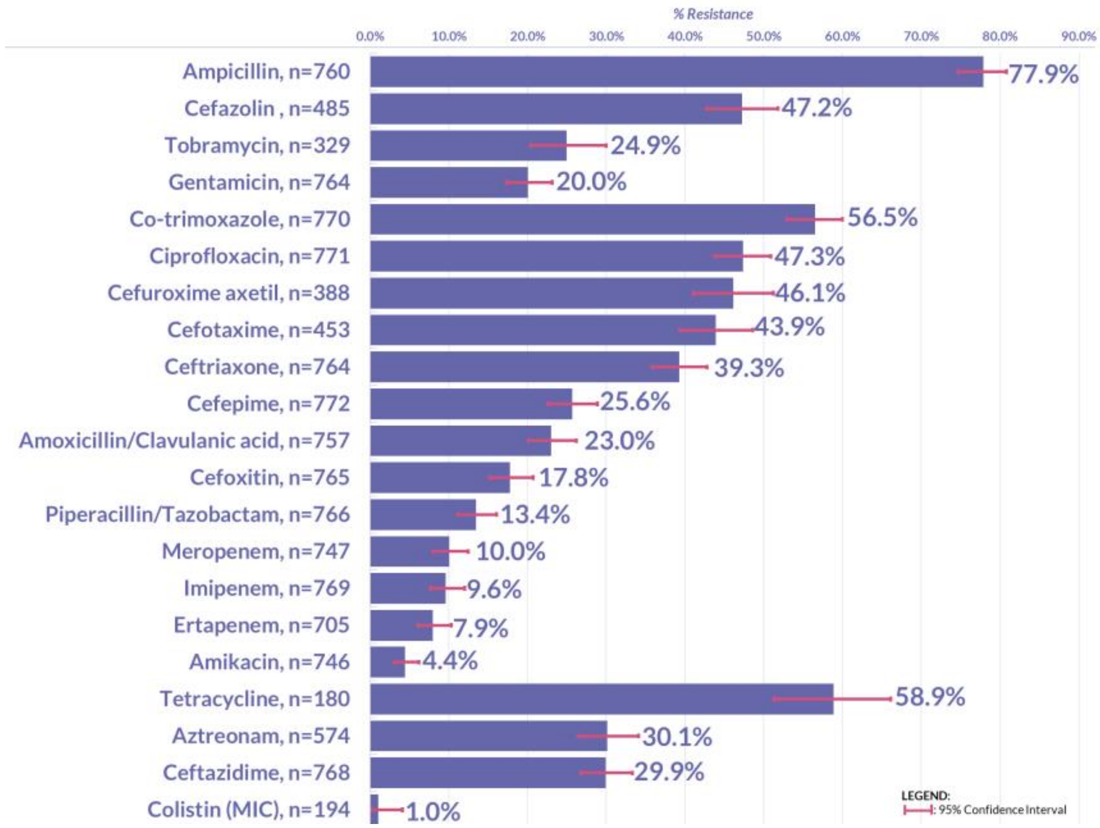


Figure 79. Percent resistance of *E. coli* blood isolates, DOH-ARSP, 2021

Resistance rates of inpatient and outpatient *E. coli* urine isolates against commonly used antibiotics are shown in Figure 80. Among urinary *E. coli* from in-patients, ciprofloxacin resistance was highest at 53.7%, while resistance to cefuroxime, ampi/sulbactam, amox/clavulanic and ceftriaxone ranged from 24-40%. Resistance to pip/tazobactam was 13.2%, ertapenem was at 5.6%, amikacin at 4.2% and 3.8% for nitrofurantoin. Among urinary *E. coli* from out-patients, resistance to co-trimoxazole was at 55.2% and to ciprofloxacin at 48.9%. Resistance to nitrofurantoin was at 5.9% and to cefazolin at 49.2%

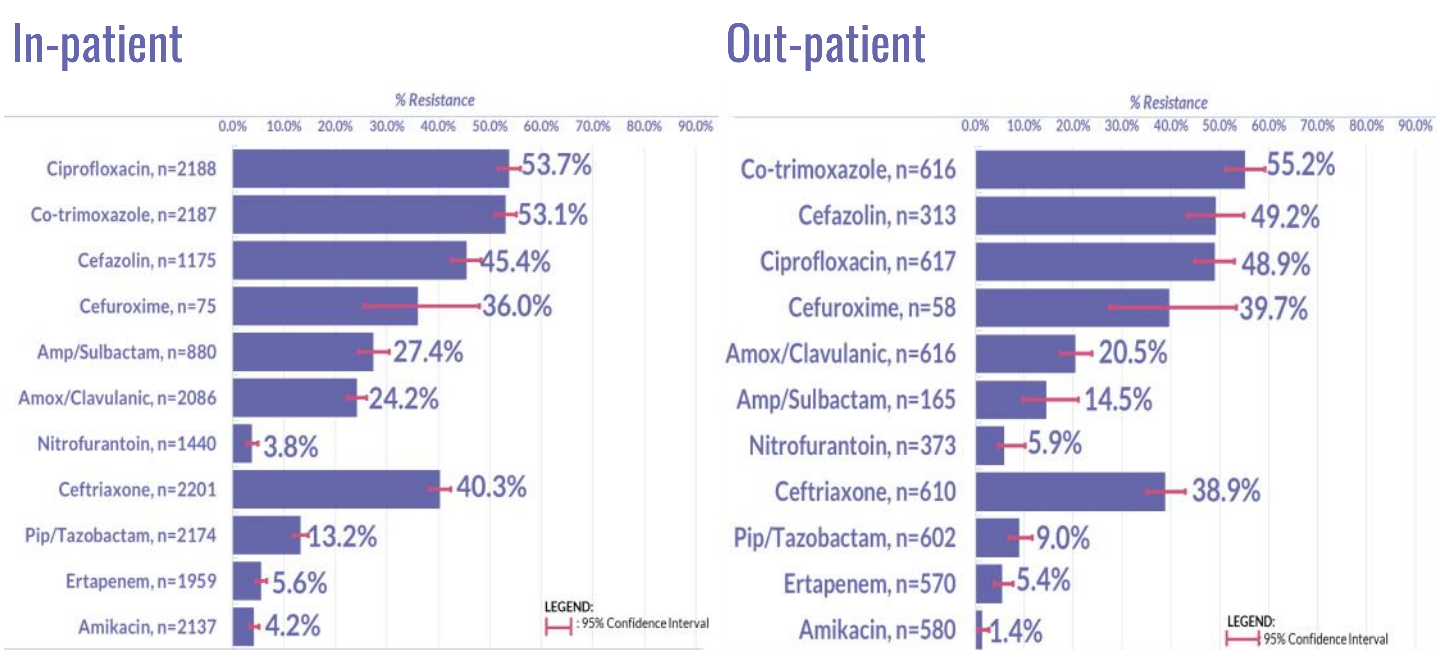


Figure 80. Percent resistance of *E. coli* urine isolates from in-patients and out-patients, DOH-ARSP, 2021

Figure 81 shows the antibiogram of carbapenem-resistant *E. coli isolates*. Resistance rates to most of the antibiotics were high from 70-99%. Ampicillin resistance was at 99.5%, cefazolin at 96.8% and tobramycin at 71.4%. Resistance to amikacin, nitrofurantoin and colistin were relatively lower at 25.1%, 14.8% and 18.8%.

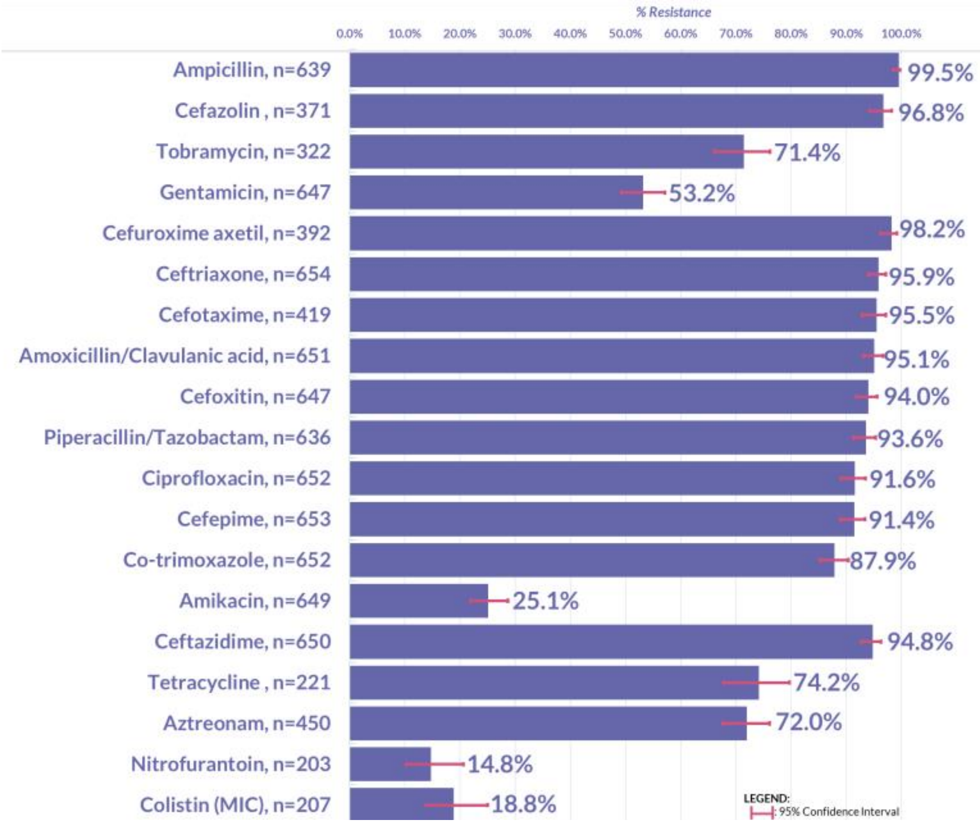


Figure 81. Percent resistance of *E. coli* (carbapenem-resistant) , DOH-ARSP, 2021

From the subset of 2021 *E. coli* isolates screened phenotypically for ESBL production, ESBL positivity rate was at 24.51% (**Figure 82**).

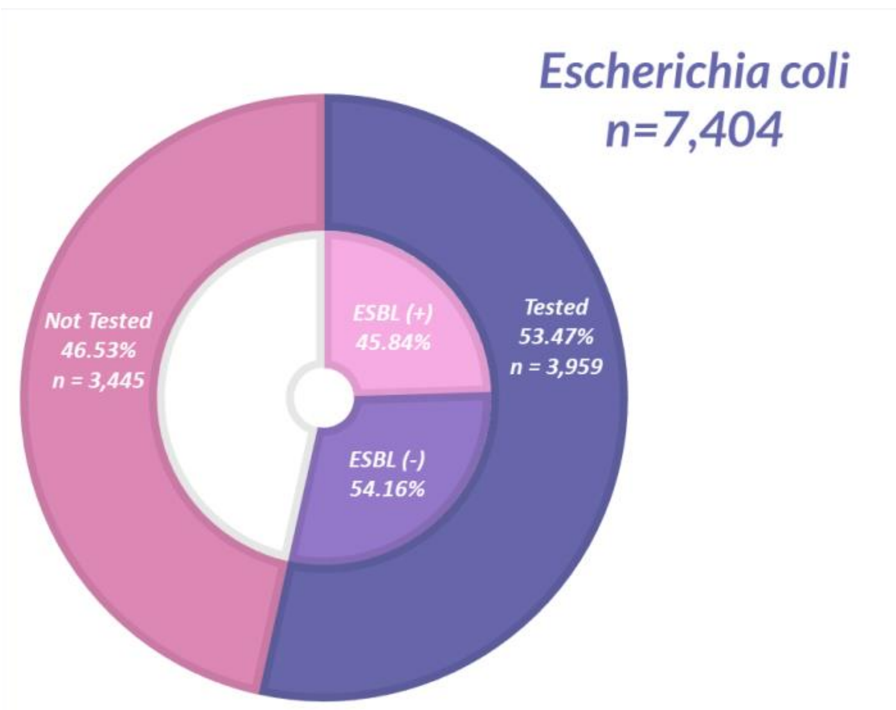


Figure 82. Percentage of ESBL- producing *E. coli* in the Philippines, DOH-ARSP, 2021 (revised)

A. Imipenem

B. Ertapenem

C. Meropenem

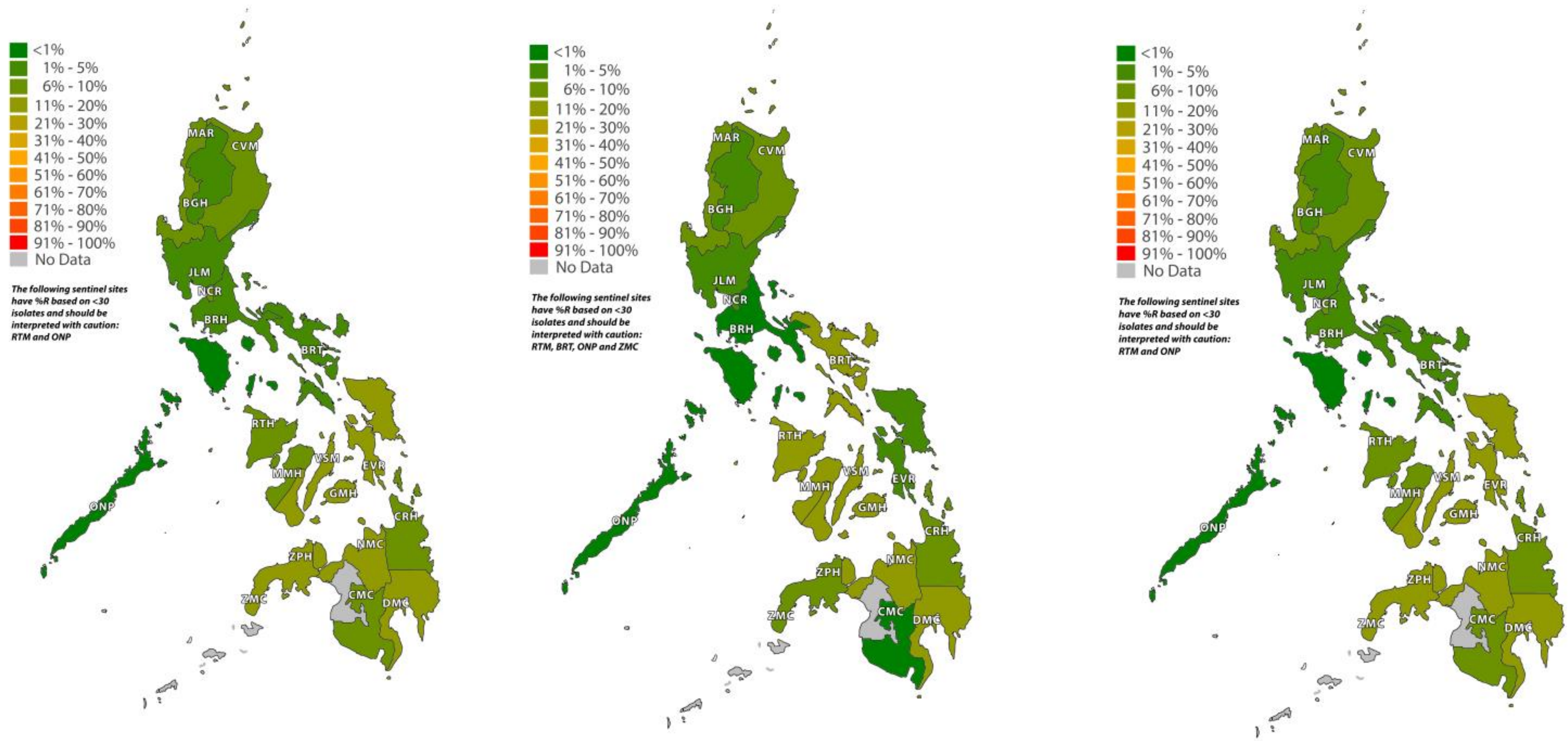


Figure 83. Resistance maps of *E. coli* for (A) imipenem, (B) ertapenem and (C) meropenem, DOH-ARSP, 2021

Figure 83 shows the carbapenem resistance rates of *E.coli* across different regions represented by the sentinel sites. The carbapenem resistance of *E.coli* isolates from Luzon sentinel sites mostly are below 10% while the rates for most of the sentinel sites from the Visayas and Mindanao were in the 10-15% range.

Klebsiella pneumoniae

A total of 10, 876 *K. pneumoniae* isolates were reported in 2021, which is 7% higher than the total isolates reported in 2020. VSM (15.56%) contributed the most number of isolates followed by PGH (14.37%) and DMC (10.45%) (Figure 84). Based on island group distribution, 47.21% were from Luzon, with 27.92% coming from NCR sentinel sites, 33.16% from the Visayas and 19.62% from Mindanao (Figure 84).

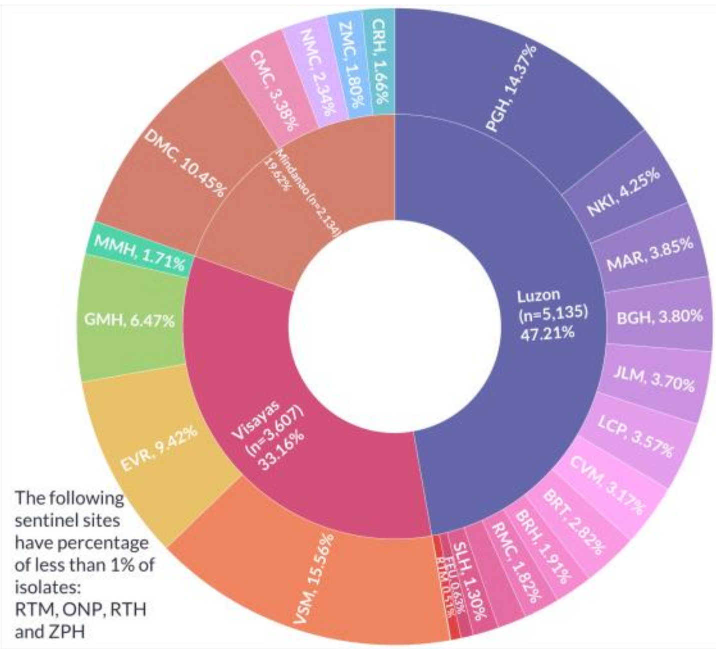


Figure 84. Isolate distribution of *K. pneumoniae*, DOH-ARSP, 2021 (n =10,876)

Most (62.07%) of the isolates were from 20-64 age group, and more than half (54.37%) were from male patients. Most of *K. pneumoniae* isolates were from respiratory (56.57%), urine (14.40%) and wound (12.59%) specimens. Most (59.72%) of the cases were from presumptive community acquired infections (Figure 85).

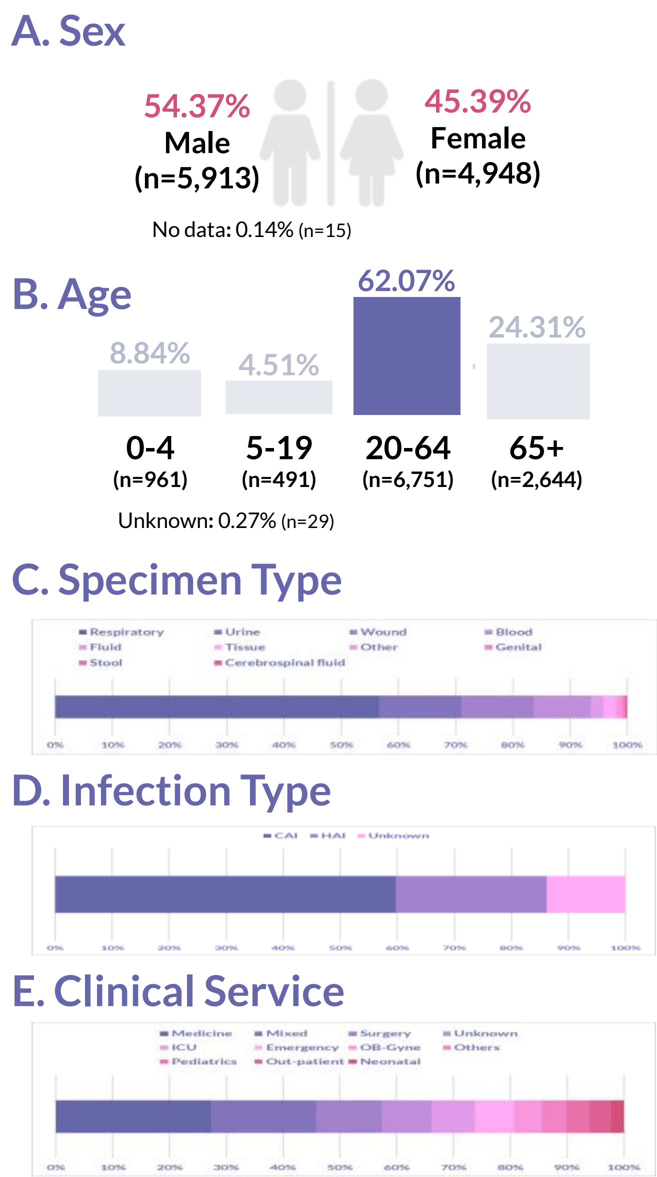


Figure 85. Patients characteristics of *K. pneumoniae* isolates, DOH-ARSP, 2021 (n=10, 876)

Cumulative resistance rates of *K. pneumoniae* from all specimens are shown in Figure 86. As known to be commonly resistant to multiple classes of antibiotics, *K. pneumoniae* antimicrobial rates to most of the antibiotics were above 20%. Resistance to amoxicillin/clavulanic acid was at 36.4% and 26.4% to piperacillin/tazobactam. Resistance to meropenem, imipenem and ertapenem were 15.2%, 14.5% and 10.5%, respectively. The 2021 resistance rates for ciprofloxacin (p=0.0004), cefotaxime (p=0.0357), piperacillin/tazobactam (p=0.0007) and amikacin (p=0.0430) for 2021 were significantly higher than the observed rates for 2020. Resistance rates to the carbapenems were higher for 2021; however, the differences from the rates in 2020 were not statistically significant. Colistin resistance rate decreased to 5.0% in 2021 from 5.4% in 2020 (p=0.4758).

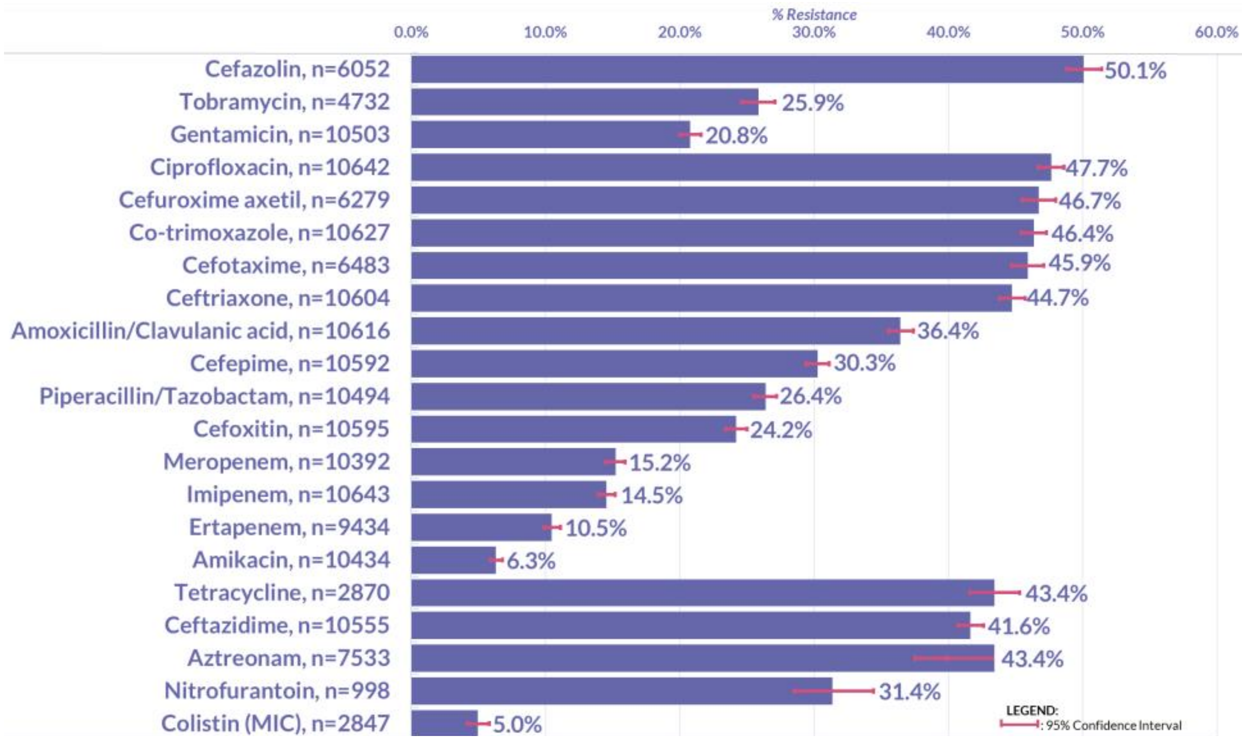


Figure 86. Percent resistance of *K. pneumoniae*, DOH-ARSP, 2021

Figure 87 shows the yearly resistance of *K. pneumoniae*. Cefoxitin, ceftazidime, cefazolin and cefuroxime showed relatively constant rates over the years. The multiple year analysis showed that the increase in the resistant rates for the carbapenem antibiotics - meropenem (p=0.0000), ertapenem (p=0.0000) and imipenem (p=0.0000) were all statistically significant. The increase in resistance rates of ciprofloxacin noted to begin in 2019 was also statistically significant (p=0.0000).

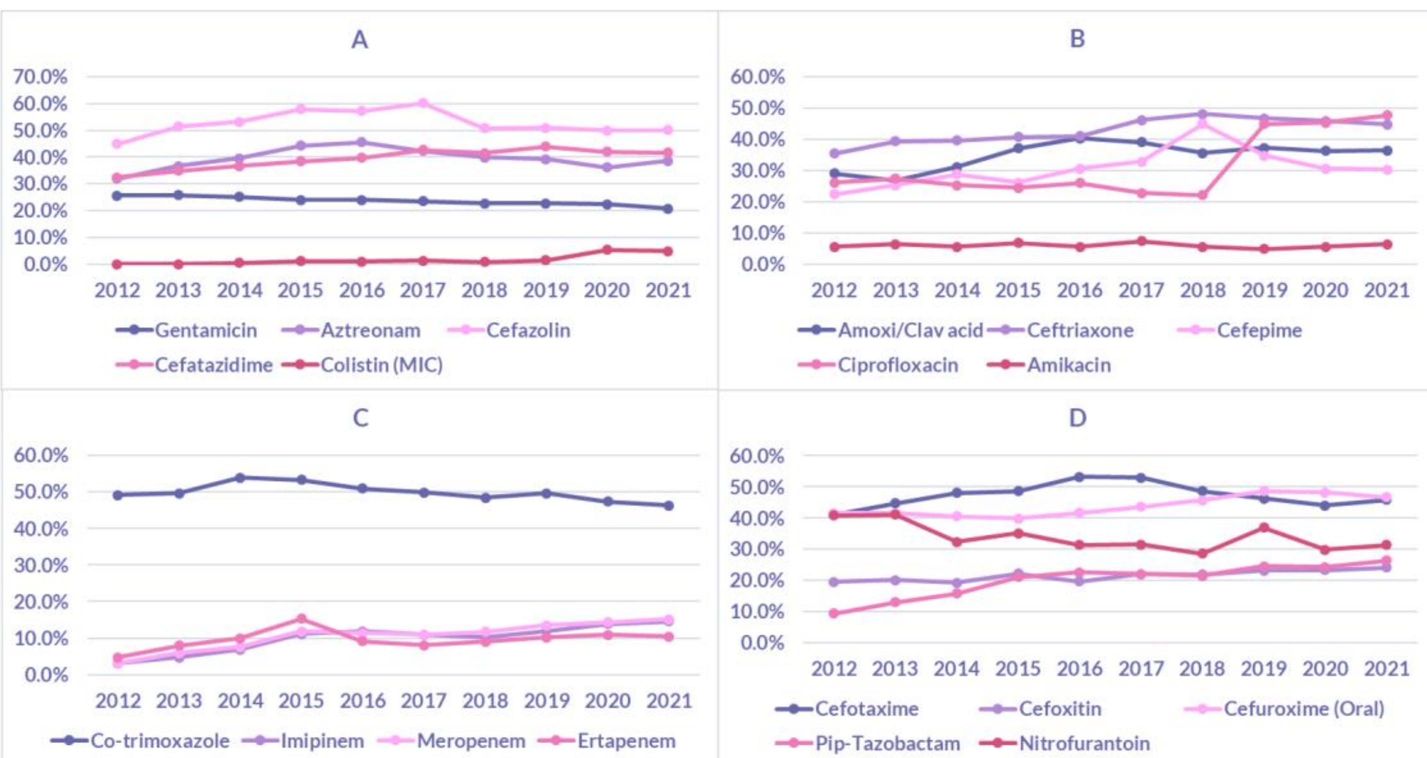


Figure 87. Yearly resistance rates of *K. pneumoniae*, DOH-ARSP, 2012-2021

Figure 88 shows the resistance rates of *K. pneumoniae* isolates from blood specimens. Resistance rates for most of the antibiotics were above 20%. Resistance to amoxicillin/clavulanic acid was at 42% and 31.3% to piperacillin/tazobactam. Resistance to meropenem, imipenem and ertapenem were 20.3%, 19.4% and 13.5%, respectively. Colistin resistance was at 5.2%.

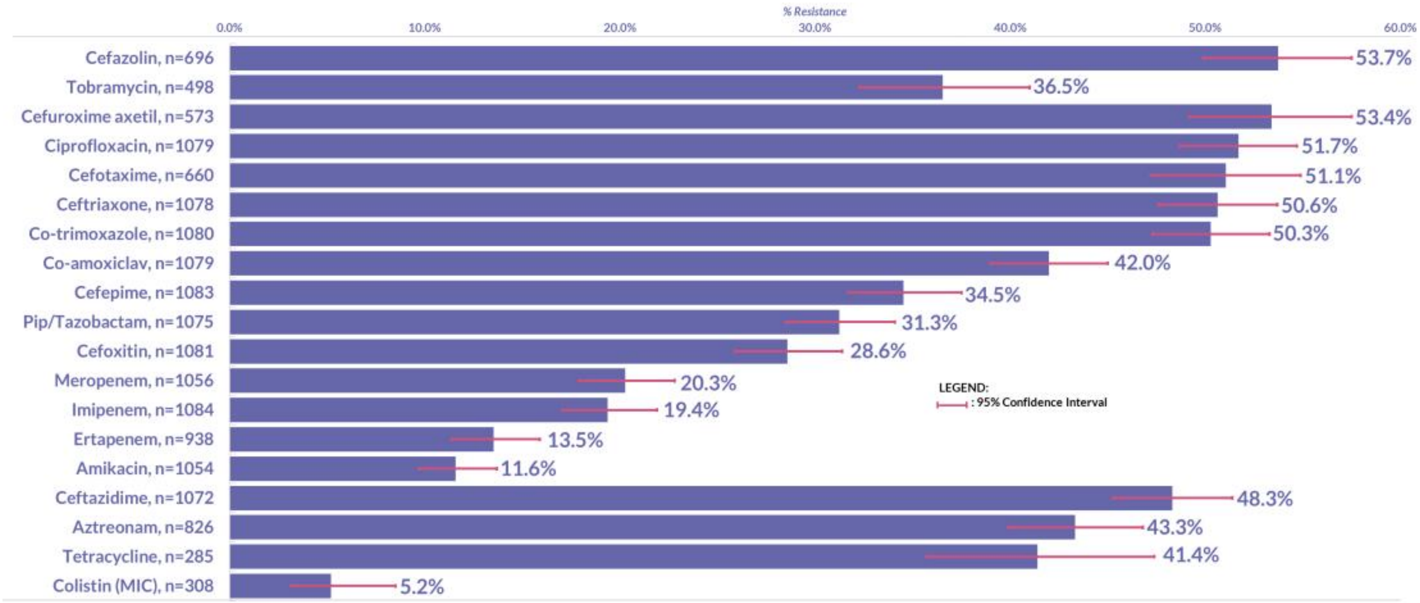


Figure 88. Percent resistance of *K. pneumoniae* blood isolates, DOH-ARSP, 2021

Figure 89 shows the antibiotic resistance rates of *K. pneumoniae* isolates from urine specimens. Resistance to combination antibiotics to amoxicillin/clavulanic acid and piperacillin/tazobactam were at 37.3% and 27.9%, respectively. Resistance to carbapenems ranged from 12 -17%. Colistin resistance was at 6.5%.

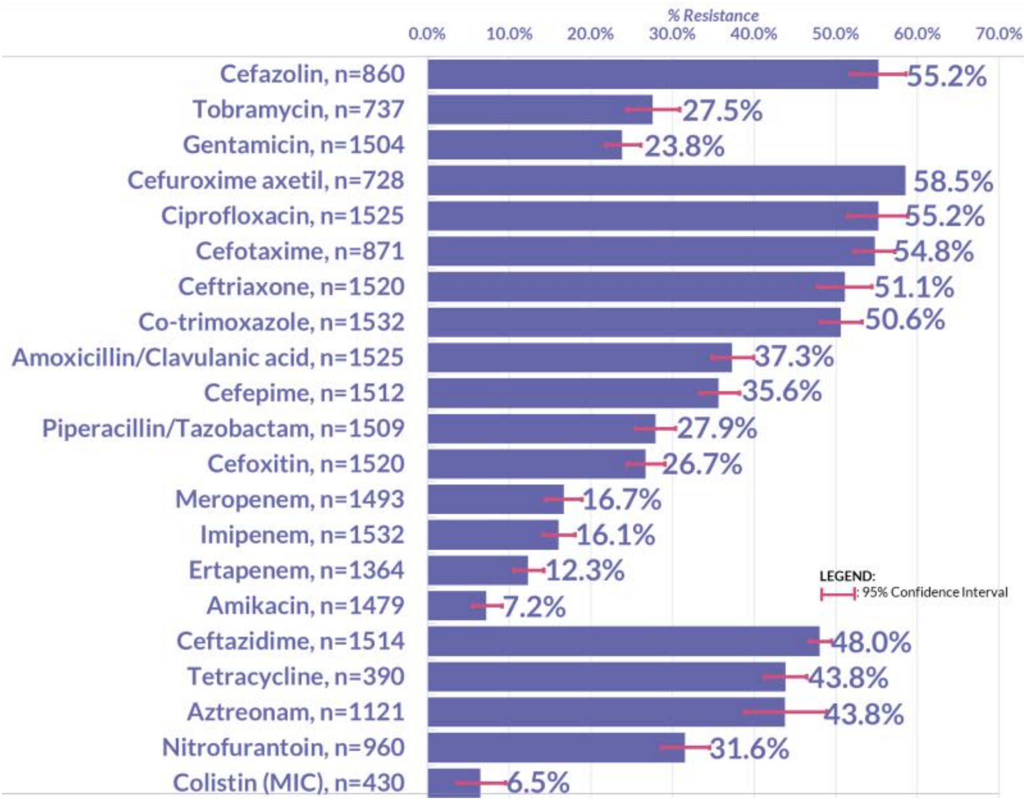


Figure 89. Percent resistance of *K. pneumoniae* urine isolates, DOH-ARSP, 2021

Figure 90 shows the percent resistance of *K. pneumoniae* isolates found to be resistant to at least one of the carbapenems. Among these isolates, resistance rates to most antibiotics were high ranging from 50% to 90%. Cefazolin resistance was at 95.1%, tobramycin at 74.3%, gentamicin at 59.5% and ceftriaxone at 95%. Resistance rates for amikacin and colistin were relatively low at 31.6% and 24.1% respectively.

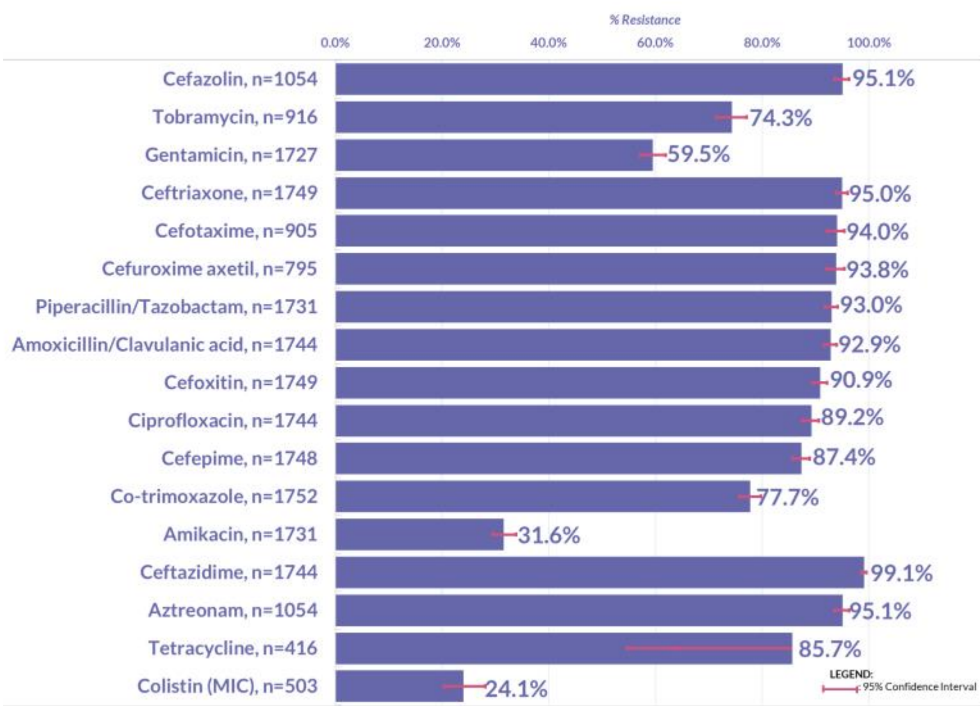


Figure 90. Percent resistance of *K. pneumoniae* (carbapenem-resistant) isolates, DOH-ARSP, 2021

There were 74 confirmed colistin-resistant *K. pneumoniae* isolates in 2021. Percent resistance of these isolates are shown in **Figure 91**. Resistance to most antibiotics were more than 20%. Relatively lower resistance for this group of isolates was for amikacin (5.5%) and the carbapenems: imipenem (10.8%), meropenem (11.0%) and ertapenem (13.7%).

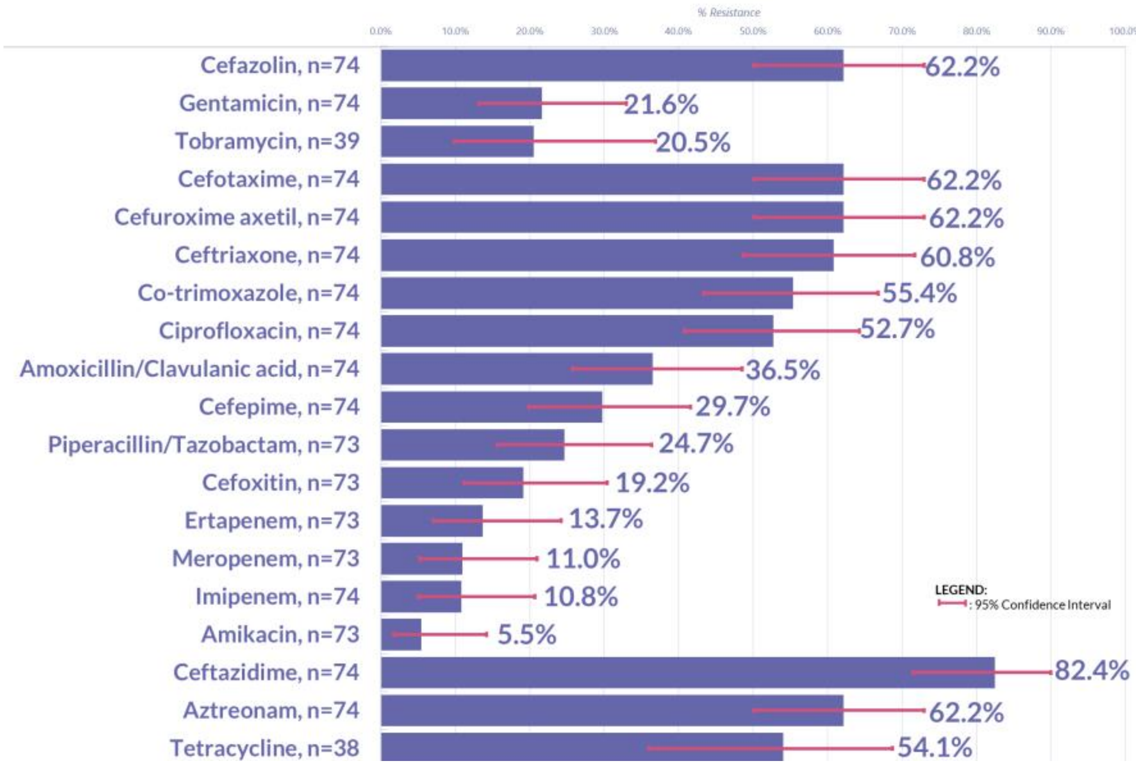


Figure 91. Percent resistance of *K. pneumoniae* (confirmed colistin-resistant) isolates, DOH-ARSP, 2021

From the subset of 2021 *K. pneumoniae* isolates screened phenotypically for ESBL production, ESBL positivity rate was at 29.53% (**Figure 92**).

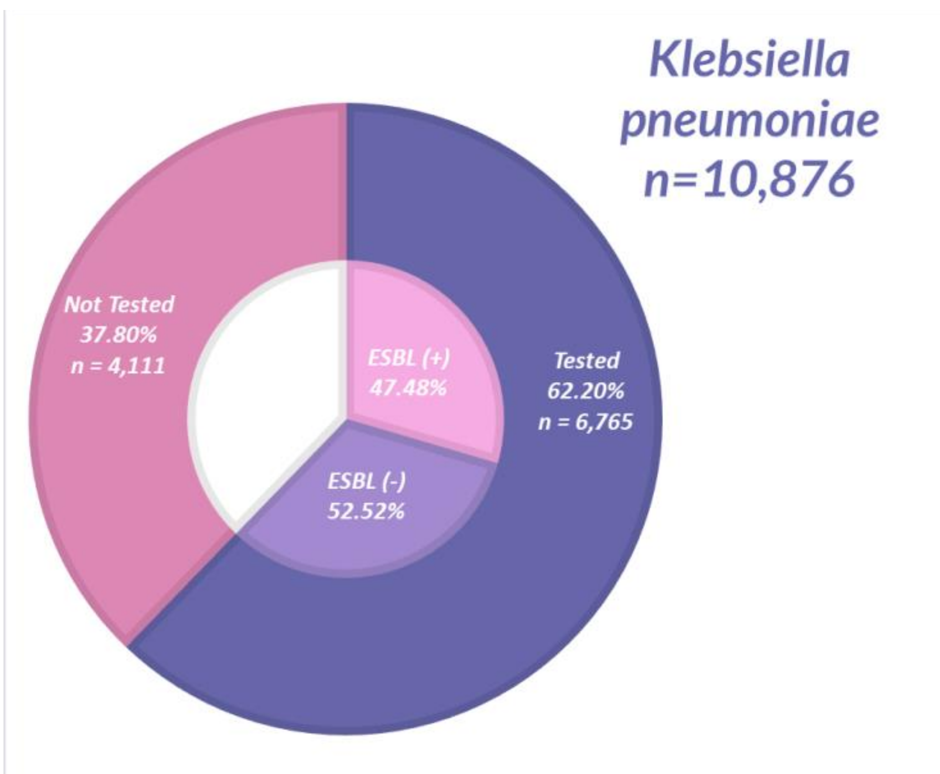
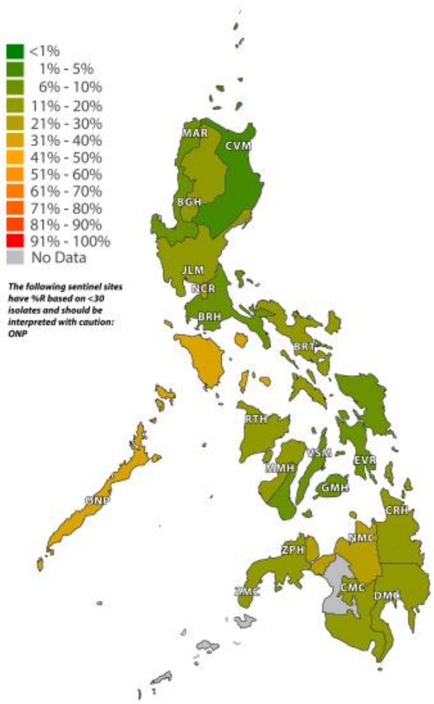


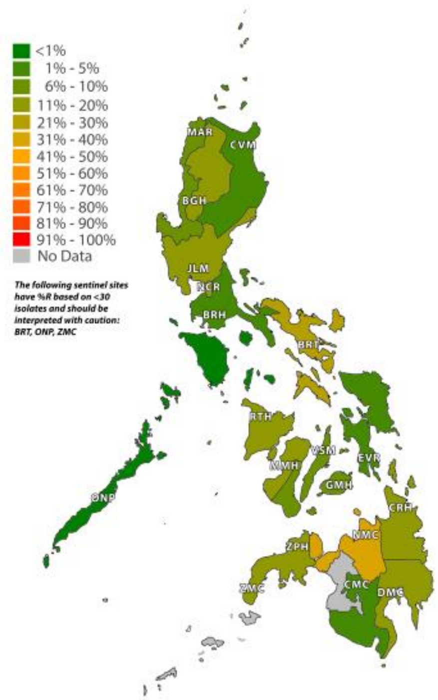
Figure 92. Percentage of ESBL- producing *K. pneumoniae* in the Philippines, DOH-ARSP, 2021 (revised)

Figure 93 shows the carbapenem and colistin resistance rates of *K.pneumoniae* across different regions as represented by the sentinel sites. The carbapenem resistance of *K. pneumoniae* isolates from Luzon sentinel sites ranged from 1% to 35% with most below 20%. The rates for most of the sentinel sites from the Visayas ranged from 7% to 18% while the rates for Mindanao sentinel sites were mostly in the 11% to 30% range but with one site in the 31-40%. Confirmed colistin-resistant isolates have been reported from almost all the sentinel sites except for BGH, ONP and MMH.

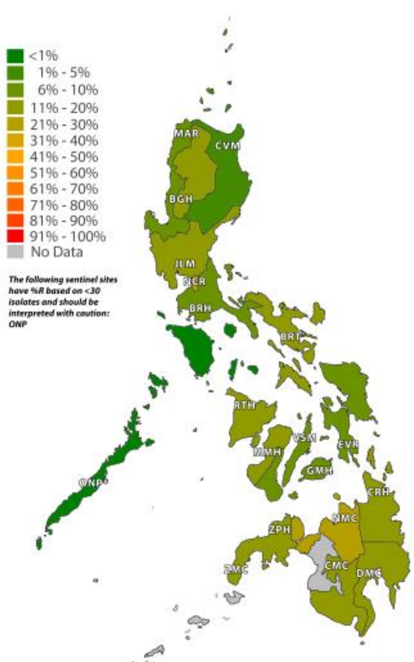
A. Imipenem



B. Ertapenem



C. Meropenem



D. Colistin

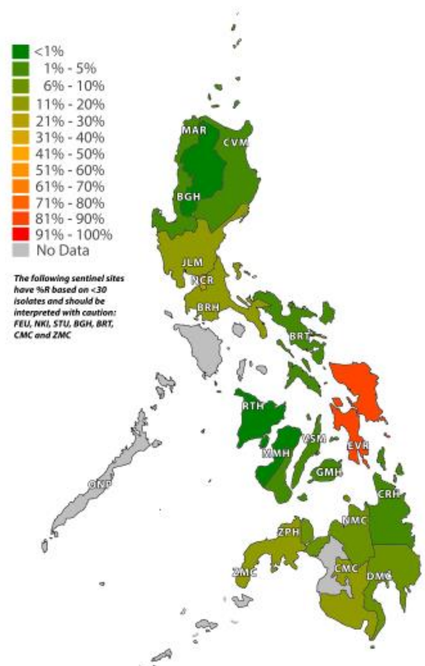


Figure 93. Resistance maps of *K. pneumoniae* for (A) imipenem, (B) ertapenem, (C) meropenem (D) colistin, DOH-ARSP, 2021

Pseudomonas aeruginosa

There were 6, 271 *P. aeruginosa* isolates for 2021. Large contributors of *P. aeruginosa* isolates data were DMC (13.89%), VSM (11.69%) and PGH (12.68%). Sentinel sites from Luzon contributed 53.6% of the isolates, 24.10% from Visayas and 22.23% from Mindanao (Figure 94).

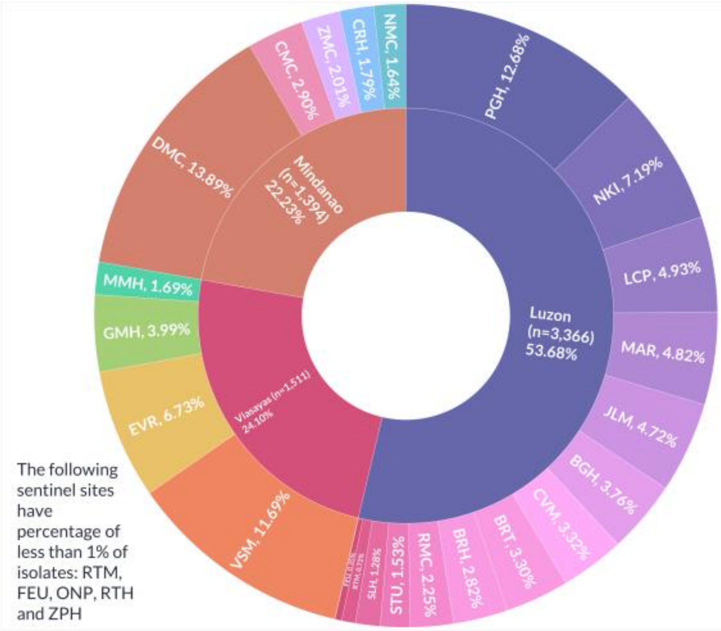


Figure 94. Isolate distribution of *P. aeruginosa*, DOH-ARSP, 2021 (n =6,271)

Most (63.96%) of the isolates were from patients within 20-64 age group, and most were from male patients (57.57%) (Figure 95). Most (51.62%) of the *P. aeruginosa* isolates were from respiratory samples followed by wound (20.59%) and urine (9.68%). Most (61.25%) cases were presumptive community acquired infections.

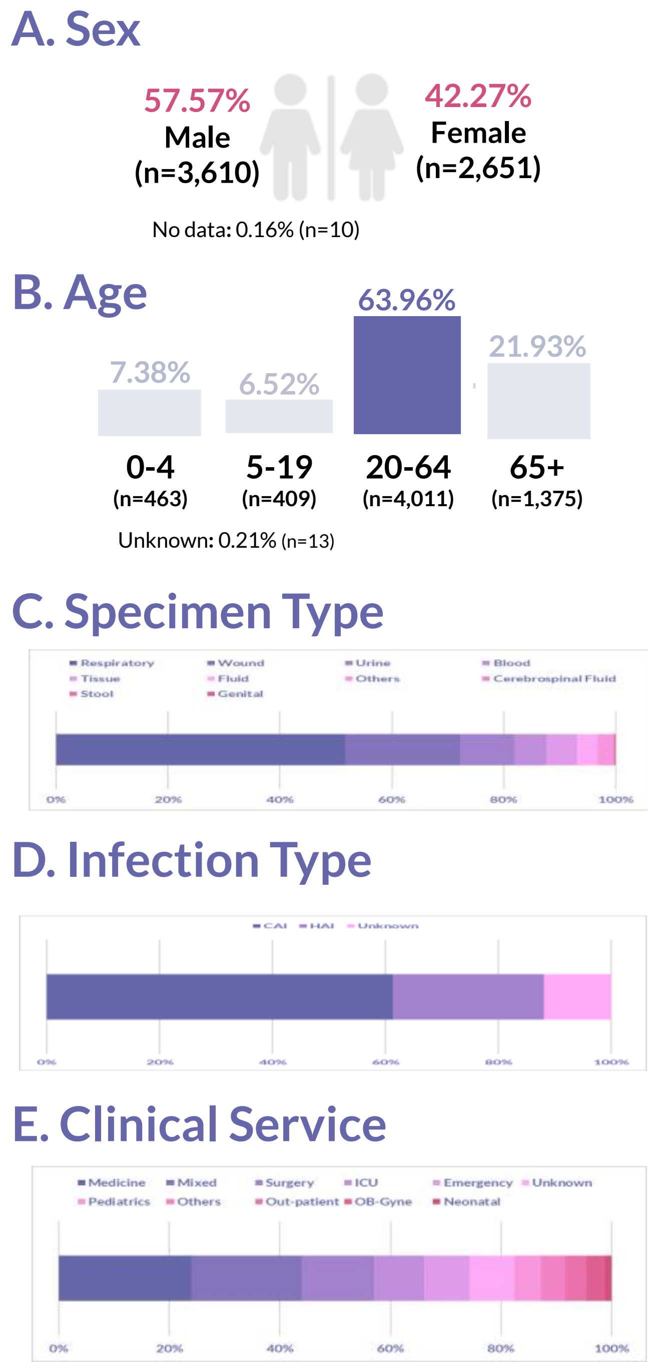


Figure 95. Patients characteristics of *P. aeruginosa* isolates, DOH-ARSP, 2021 (n=6,271)

Figure 96 shows the cumulative resistance rates of *P. aeruginosa* in 2021. Resistance to ceftazidime was at 15.7%, to piperacillin-tazobactam at 12.9%, to ciprofloxacin at 10.3%, aztreonam at 13.3% and to colistin at 5.1%. These rates are higher compared to the resistance rates for 2020; however, the differences were statistically significant only for ciprofloxacin (*p*=0.0006) and aztreonam (p=0.0111). Imipenem resistance was at 16.6%, meropenem at 14.3%, cefepime at 12.9%, and aztreonam at 13.3% (**Figure 96**). These resistance rates were noted to be lower than that for 2020 but the decreases were noted to be not statistically significant.

There were 8 confirmed colistin-resistant *P. aeruginosa* isolates for 2021. Majority (62.5%, n=5) of the isolates were from the Visayas. A colistin-resistant *P. aeruginosa* was isolated from a CSF specimen of a 28-day old male patient from a sentinel site in Luzon. The isolate was also resistant to tobramycin but susceptible to ciprofloxacin, ceftazidime, amikacin and carbapenem antibiotics (meropenem and imipenem). Another colistin-resistant *P. aeruginosa* was isolated from the respiratory specimen of 79-year old female from a sentinel site in Luzon. The isolate was susceptible to amikacin, cefepime, ceftazidime, ciprofloxacin, gentamicin and the carbapenems.

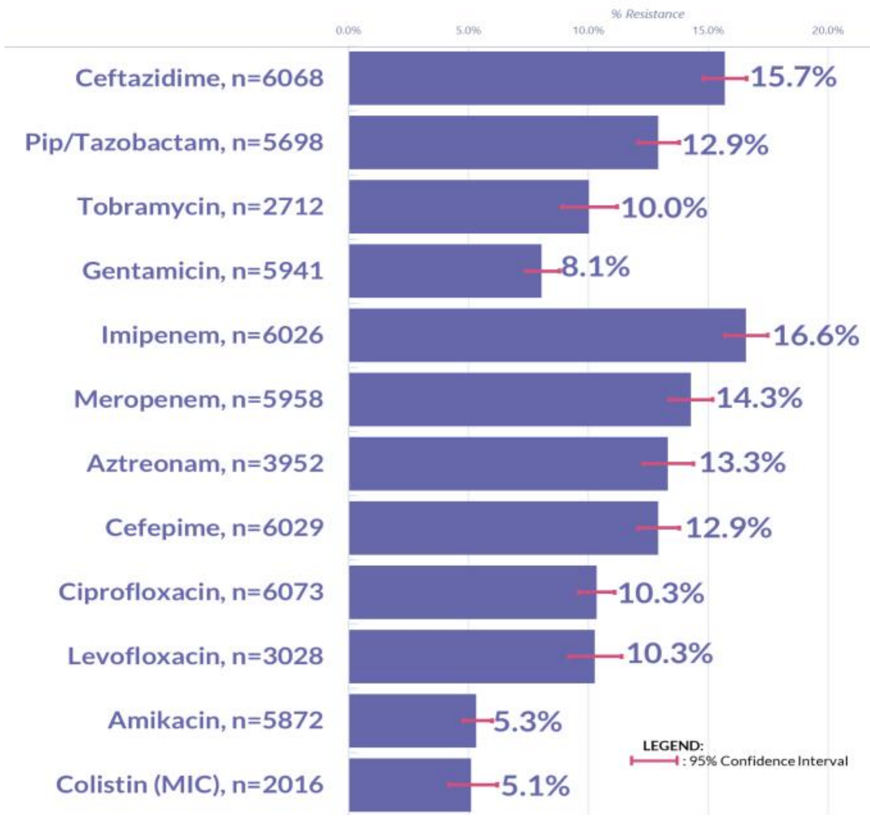


Figure 96. Percent resistance of *P. aeruginosa*, DOH-ARSP, 2021

Figure 97 shows the yearly resistance rates of *P. aeruginosa*. Multiple year analysis revealed that changes in resistance rates for colistin (*p* = 0.0008) and meropenem (p = 0.0217) were statistically significant, However, the changes in resistance rates for imipenem was noted to be not statistically significant.

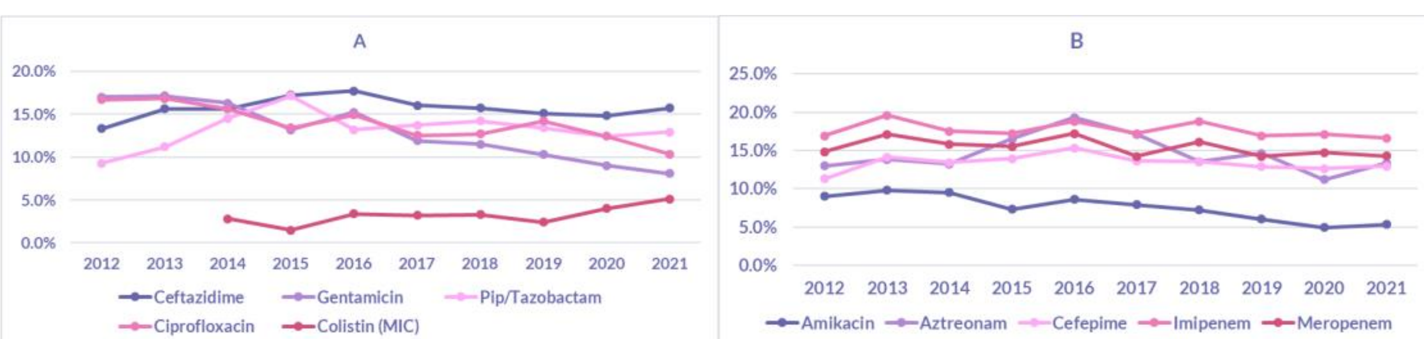


Figure 97. Yearly resistance rates of *P. aeruginosa*, DOH-ARSP, 2012-2021

Figure 98 shows the antibiotic resistance rates of *P. aeruginosa* isolates from blood samples. Highest resistance rates were for ceftazidime and imipenem at 16.8% and 12.8% respectively. Resistance rate for colistin was higher in 2021 than in 2020, however the difference was not statistically significant (p= 0.8098).

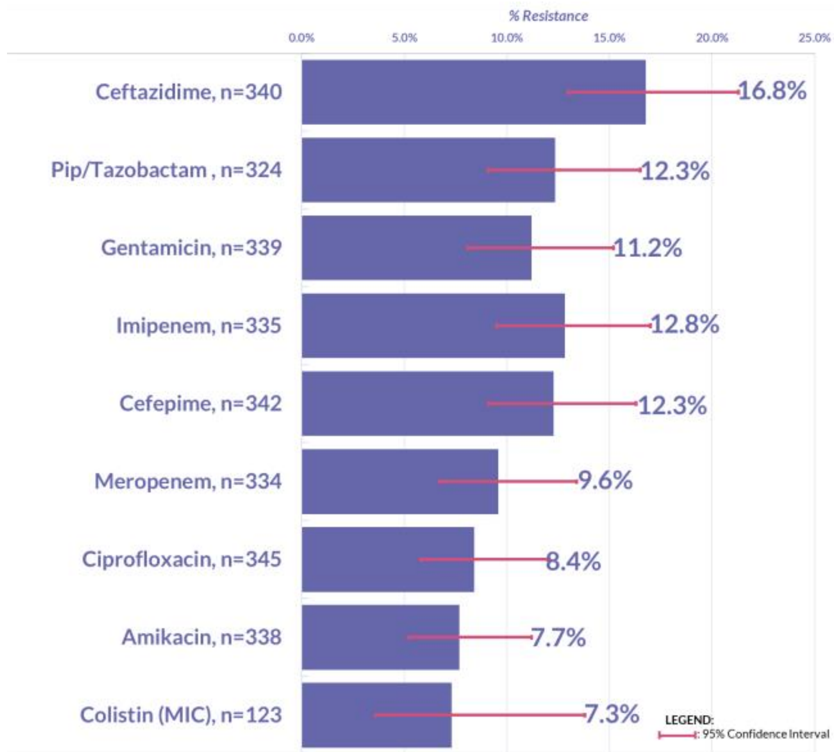


Figure 98. Percent resistance of *P. aeruginosa* blood isolates, DOH-ARSP, 2021

Figure 99 shows the carbapenem resistance rates of *P.aeruginosa* across different regions represented by the sentinel sites. The *P. aeruginosa* isolates from most of the regions have carbapenem resistance rates in the range of 11-20%. NMC has relatively higher resistance to carbapenems with rates higher than 40%.

A. Imipenem

B. Meropenem

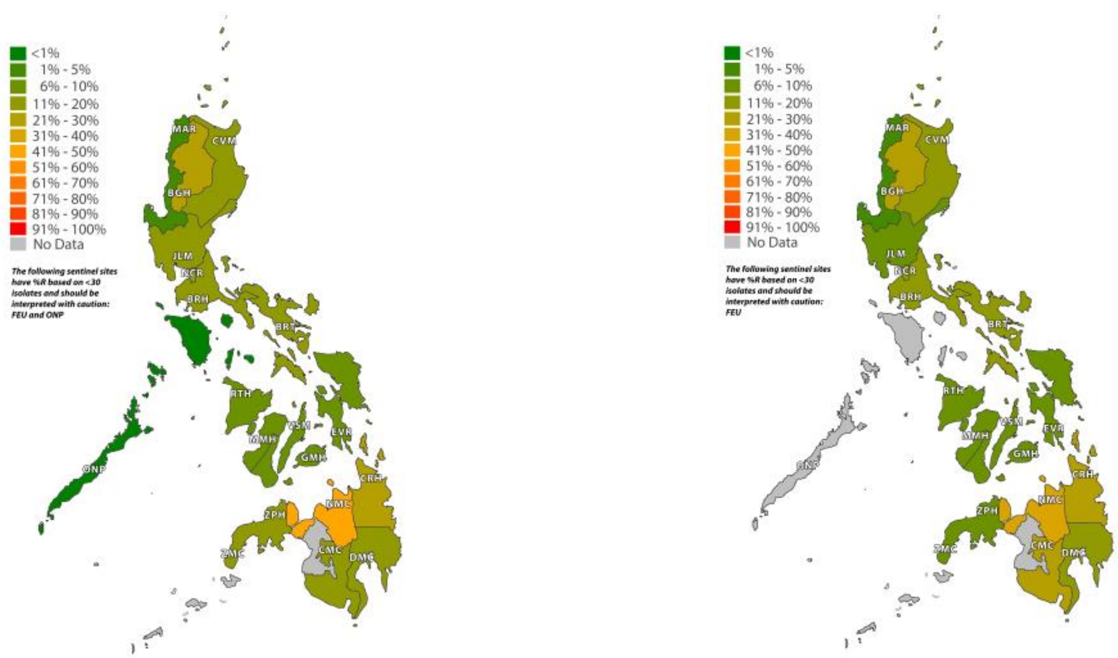


Figure 99. Resistance maps of *P. aeruginosa* for (A) imipenem and (B) meropenem, DOH-ARSP, 2021

Acinetobacter baumannii

There were 4,672 isolates of *Acinetobacter baumannii* reported for 2021, which was higher than the number reported in 2020. Largest contributors of *A. baumannii* isolates were PGH (22.95%), DMC (14.77%) and VSM (8.22%) (Figure 100).

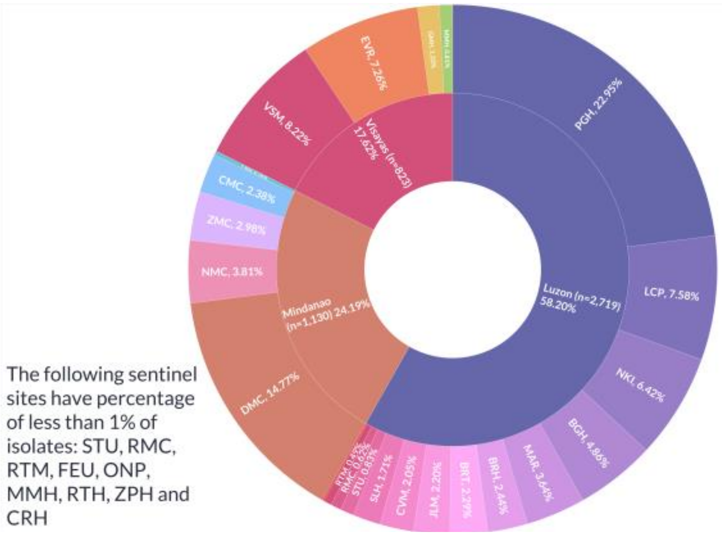


Figure 100. Isolate distribution of *A. baumannii*, DOH-ARSP, 2021 (n =4,672)

Most (58.95%) of the isolates were from 20-64 years old group and mostly were from male patients (56.81%). Most (61.13%) of the isolates were from respiratory specimens and were from presumptively community acquired infections (59.05%)(Figure 101).

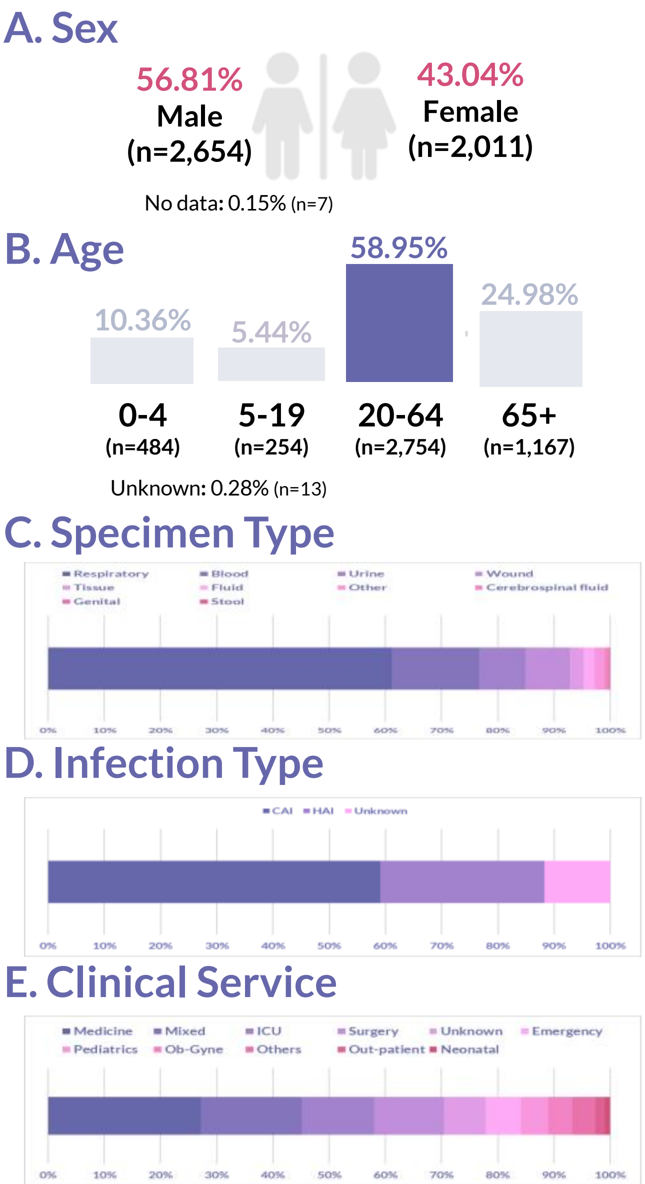


Figure 101. Patients characteristics of *A. baumannii* isolates, DOH-ARSP, 2021 (n=4,672)

Figure 102 shows the cumulative resistance rates of *A. baumannii* in 2021. Most of the resistance rates were more than 50% with the highest for meropenem (62.2%), followed by imipenem (61.4%) and ceftazidime (60.8%). The noted increases in antibiotic resistance rates for *A. baumannii* from 2020 to 2021 were statistically significant.

There were 3 confirmed colistin-resistant *A. baumannii* isolates reported in 2021. Two of the isolates were from a sentinel site in the Visayas and one from northern Luzon. The isolates were from blood specimens - one was susceptible to most antibiotics while the other was only susceptible to gentamicin and tobramycin. The isolate from northern Luzon was resistant to most antibiotics tested except for ampicillin-sulbactam.

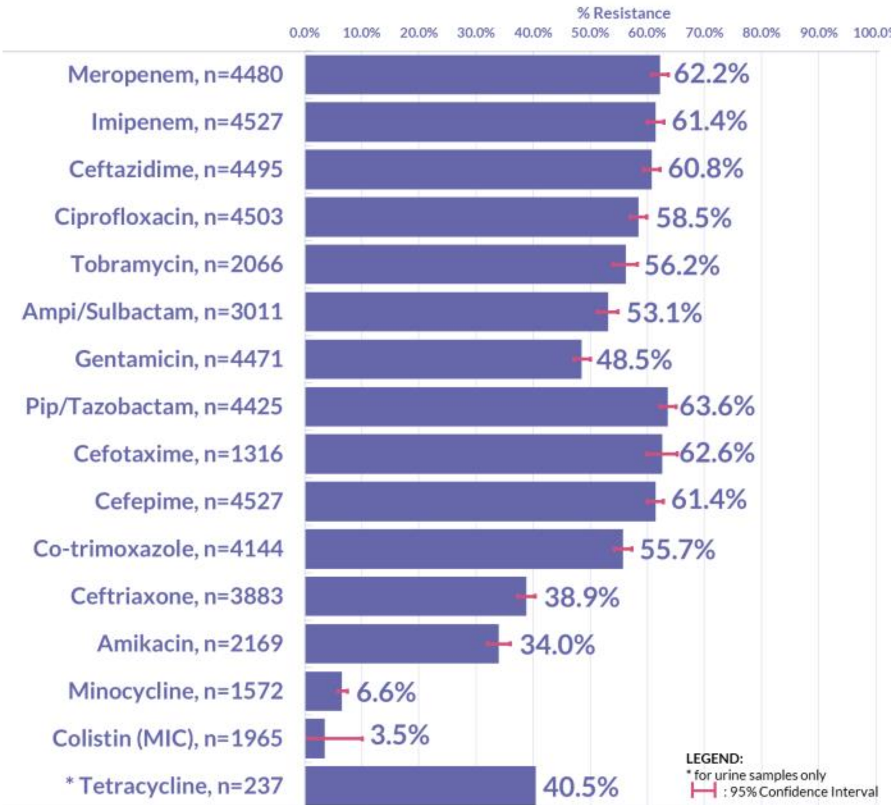


Figure 102. Percent resistance of *A. baumannii*, DOH-ARSP, 2021

Figure 103 shows the yearly resistance rates of *A. baumannii* isolates. Resistance to most antibiotics were noted to increase in 2021 compared to the rates in 2020 except for ampicillin-sulbactam.

Ampicillin- sulbactam, cefepime, ciprofloxacin and co-trimoxazole resistance rates showed relatively constant rates over the last five to six years. Multiple year analysis (2012-2021) revealed that the changes in resistance rate for ceftazidime (p=0.0000) and the two carbapenems, meropenem (p=0.0000) and imipenem (p=0.0000) were statistically significant. Colistin resistance started to increase in 2020, however, multiple year analysis showed that the change is not statistically significant (p=0.13966).

Figure 103. Yearly resistance rates of *A. baumannii*, DOH-ARSP, 2012-2021

Figure 104 shows the resistance rates of *A. baumannii* from blood samples. Most of the resistance rates were above 40%. Resistance rate to amikacin was at 28.7% which is higher (p = 0.0411) than 20.2% in 2020. Moreover, colistin resistance rate (6.6%) for 2021 was also higher compared to the rate in 2020 (p = 0.0010).

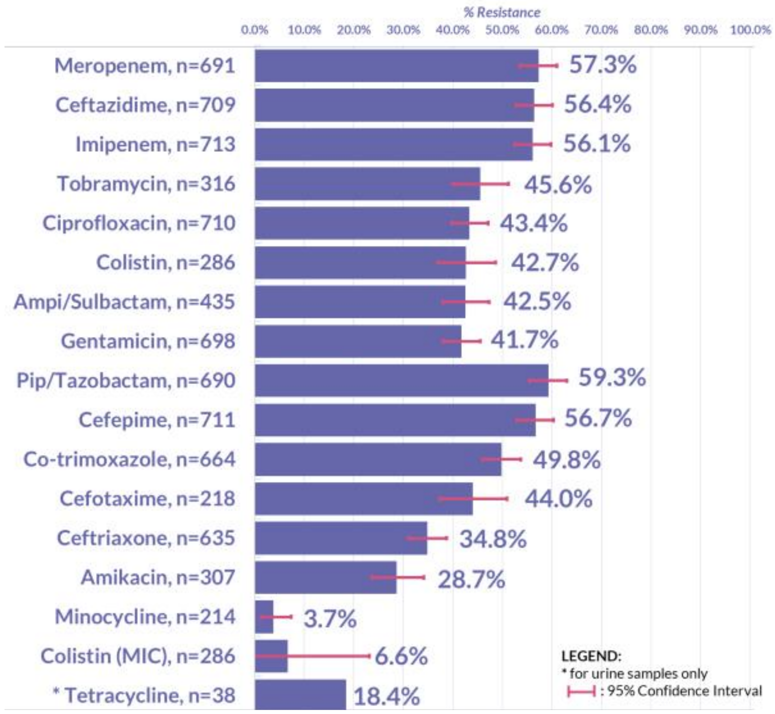


Figure 104. Percent resistance of *A. baumannii* blood isolates, DOH-ARSP, 2021

Figure 105 shows the carbapenem resistance rates of *A. baumannii* across different regions as represented by the sentinel sites. Carbapem resistance among many sentinel sites varies but most rates are very high.

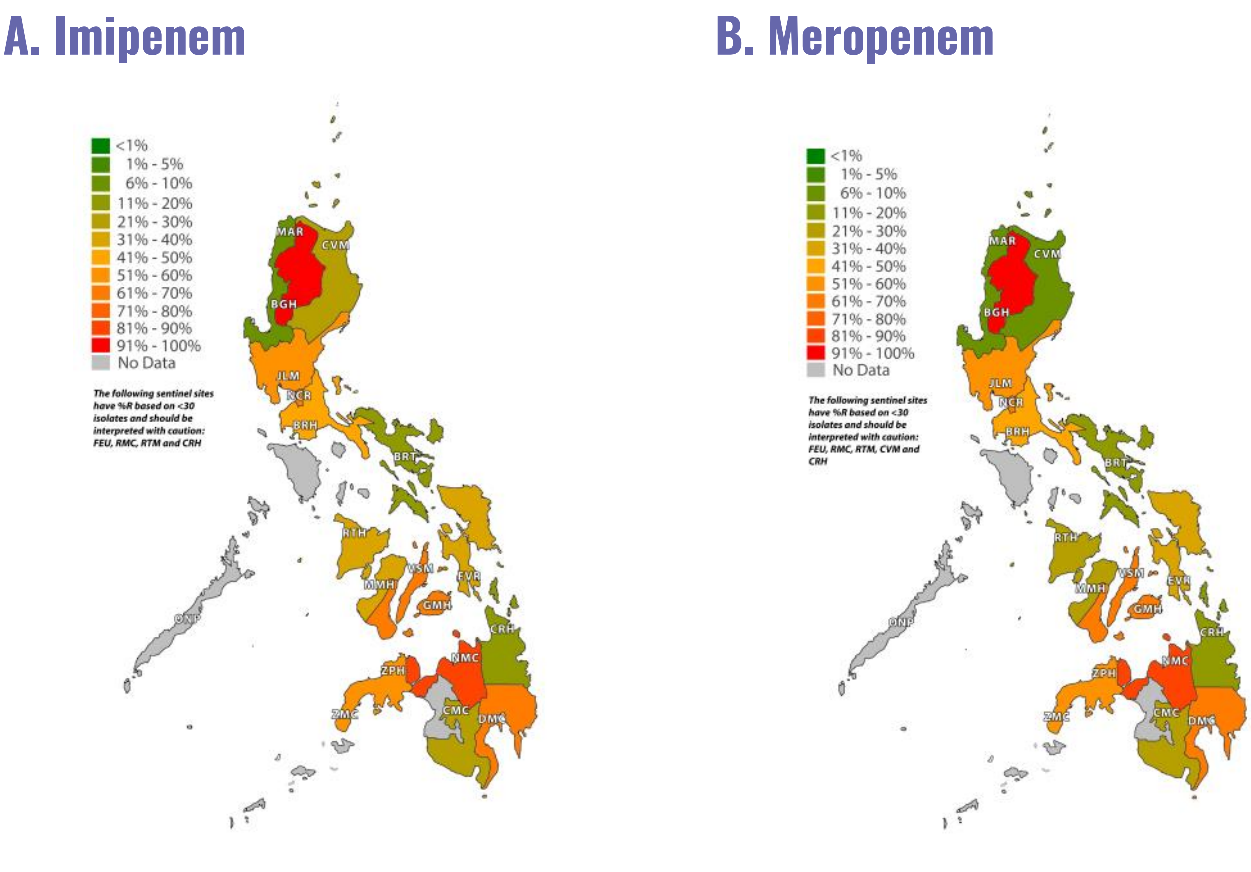


Figure 105. Resistance maps of *A. baumannii* for (A) imipenem and (B) meropenem, DOH-ARSP, 2021

Multidrug Resistant *Pseudomonas aeruginosa* and *Acinetobacter baumannii*

Multidrug-resistant pathogens are increasingly recognized globally. Terminologies are summarized in Table 4.

Among the 2021 *P. aeruginosa* isolates from all types of samples, 20% were MDR and 14% were possible XDR (Table 5). Among *P. aeruginosa* from blood samples, 19% were MDR and 14% were possible XDR.

Among the 2021 *A. baumannii* isolates from all specimens, 67% were MDR and 58% were possible XDR, while among the blood isolates of *A. baumannii*, 64% were MDR and 52% were possible XDR.

Table 4. Multi-drug resistant, extensively drug-resistant and pandrug-resistant bacteria- an international expert proposal interim standard definitions for acquired resistance

Term	Definition
MDR Multidrug-resistant	Acquired non-susceptibility to at least one agent in three or more antimicrobial categories
XDR Extensively drug-resistant	Non-susceptibility to at least one agent in all but two or fewer antimicrobial categories
PDR Pandrug-resistant	Non-susceptibility to all agents in all antimicrobial categories

Table 5. MDR and possible XDR *P. aeruginosa* and *A. baumannii*, DOH-ARSP, 2021

	Number of isolates tested	Percentage MDR	Percentage Possible XDR
Pseudomonas aeruginosa			
All isolates	6,271	20%	14%
Blood isolates	359	19%	14%
Acinetobacter baumannii			
All isolates	4,672	67%	58%
Blood isolates	724	64%	52%

Figure 106 shows the yearly resistance rates of MDR and XDR isolates of *P. aeruginosa*. Both the MDR and XDR rates for *P. aeruginosa* isolates from all samples as well as from blood samples appear to be decreasing in the past 6 years and multiple year analysis showed that the changes were statistically significant (p= 0.0001).

Figure 106. Yearly resistance rates of MDR and XDR isolates of *P. aeruginosa* DOH-ARSP 2016-2021

Figure 107 shows the yearly resistance rates of MDR and XDR isolates of *A. baumannii*. Both the MDR and XDR rates for *A. baumannii* isolates from all samples as well as from blood samples appear to be increasing in the past 6 years and multiple year analysis showed that the changes were statistically significant (p=0.0000).

Figure 107. Yearly resistance rates of MDR and XDR isolates of *A. baumannii* DOH-ARSP 2016-2021

Conclusions, Recommendations and Future Directions

Antimicrobial resistance continues to increase for most of the bacterial pathogens considered of public health importance included in this surveillance.

Recommendations based on the reported 2021 data:

Non-meningitis infections secondary to *Streptococcus pneumoniae* can still be covered with penicillin even as the changing trends of resistance among pneumococci has to be closely monitored. With the continued increase in resistance to erythromycin and penicillin using meningitis breakpoint, utilization of extended spectrum macrolides and penicillin for meningitis secondary to *Streptococcus pneumoniae* may best be guided by susceptibility data. Improving AMR surveillance of *Streptococcus pneumoniae* isolates to include pneumococcal serotyping will allow for better monitoring and evaluation of the government's vaccination strategy for this vaccine preventable pathogen.

Due to high resistance rate of *Haemophilus influenzae* to ampicillin, recommended empiric treatment for suspected *H. influenzae* infections may consist of extended spectrum oral cephalosporins and beta-lactam-beta-lactamase inhibitor combinations.

Empiric treatment for suspected uncomplicated typhoid fever could still consist of either chloramphenicol or co-trimoxazole or amoxicillin/ampicillin. Microbiological data is recommended to aid in pathogen directed therapy in view of increasing reports of ciprofloxacin resistance of *S*. Typhi which may result to clinical treatment failures.

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 *Shigella* to the quinolones and extended spectrum cephalosporins and the continued limited data available, more vigilant surveillance of the resistance pattern of this bacteria should be pursued by encouraging clinicians to send specimens for culture.

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

With the limited available data on *Neisseria gonorrhoeae*, 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 and confirmatory testing at the reference laboratory.

Even as statistically significant decrease in MRSA rates continue to be noted beginning in 2017 until 2021, continued high rates of oxacillin resistance among *S. aureus* limits use of this antibiotic as empiric treatment option. With the noted lower resistance rates to clindamycin and the macrolides, these antibiotics could be considered as alternative options. Judicious use of the reserve antibiotic vancomycin should be observed.

Multidrug resistance among the bacterial organisms *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Acinetobacter baumannii* continues to be a public health concern because of the limited treatment options and infection control challenge in containment. Real time data analysis, genotyping to establish linkages will allow for timely isolation and infection control interventions. Stratified, institute specific antibiograms will allow clinicians to identify the best empiric antibiotic options for suspected infections.

Future Program Directions

Explore and pursue the establishment of a case-based AMR surveillance in line with the objectives of the Philippine Action Plan to Combat Antimicrobial Resistance (2019-2023) to enable the gathering of quantifiable burden of disease due to resistant infections.

Pursue continuous integration of whole genome sequencing into ARSP through cultivation of the technical expertise and skills in molecular diagnostics of the reference laboratory as well as advocacy for requisite fund and resource requirements.

Improve detection of clustering of cases and possible outbreaks among the sentinel sites through implementation of WHONET SaTScan analysis on ARSP data.

Improve data management, security and sharing through personnel capacity building of the reference laboratory data management unit and equipment upgrade.

Continue efforts to improve quality of data by sentinel site and reference laboratory capacity building thru training, efforts to improve facilities, equipment and services.

Strengthen and expand the gonococcal surveillance network and harmonize with available clinical data by working with the Bureau of Epidemiology of the Department of Health (DOH-EB).

Actively contribute and participate in the implementation of the Philippine Action Plan to Combat Antimicrobial Resistance.

Harmonize with the national antibiotic use data and antimicrobial resistance surveillance data on animal specimens with ARSP data by collaborating with the Pharmaceutical Division of the Department of Health and the Department of Agriculture to enhance the relevance and significance of the surveillance information generated and present a more cohesive picture of the local state of AMR.

Incorporate the technology of geographic information system and mapping in the surveillance.

Work with DOH-EB to develop a protocol for notification of reportable drug-resistant pathogens

Pursue ISO 15189 accreditation for the reference laboratory.

Generate more relevant collaborative and investigator initiated research.

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