Poster #: 642

Facility reported vs. CLSI MIC breakpoint comparison of Carbapenem non-susceptible (Carb-NS) Enterobacteriaceae (ENT) from 2016-2020: A multicenter evaluation

Vikas Gupta, Pharm.D., BCPS[1], Kalvin Yu, MD, FIDSA[1]; Jason Pogue, Pharm.D.[2]; Janet Watts, PhD[1]; Cornelius J Clancy, MD[3]

[1]Becton, Dickinson & Company, Franklin Lakes, NJ, USA; [2]2University of Michigan, Department of Clinical Pharmacy, College of Pharmacy, Ann Arbor, MI USA; [3]University of Pittsburgh, Department of Medicine, Pittsburgh, Pennsylvania.

Background

- Carbapenem (Carb) minimum inhibitory concentration (MIC) breakpoints were lowered by the CLSI in 2010 and recognized by the FDA in 2012.
- Adoption of revised breakpoints is often slow, which may lead to under-reporting of Carb not-susceptible (NS) by facilities.
- We used the BD Insights Research Database, which includes ~13% of annual hospital admissions in the US[1], to compare facility-reported rates of Carb-NS ENT to those assigned by applying the CLSI MIC breakpoints for a large nationwide collection of isolates from 2016-2020[2,3].

Methods

- All adults with a positive non-contaminant ENT culture (first isolate per 30-day period from blood, respiratory, urine, skin/wound, intra-abdominal, or other) in ambulatory and inpatient settings from 298 US hospitals from Q1 2016 to Q4 2020 were evaluated (BD Insights Research Database, Becton, Dickinson & Company).
- Facility-reported antimicrobial susceptibility results were based on laboratory information system feed designations of susceptible (S) or NS (intermediate [I] or resistant [R]) for the following ENT pathogens: *E. coli, K. pneumoniae, K. oxytoca, K. aerogenes, P. mirabilis, E. cloacae, S. marcescens, C. freundii, P. stuartii, and M. morganii*
  - S/NS to ertapenem (ETP), imipenem (IPM), meropenem (MEM), and/or doripenem (DOR) was determined per commercial panels or MIC strips.
  - Where available, MICs were interpreted using CLSI 2010 MIC breakpoints (µg/ml): ≤ 0.5 (S), 1 (I), ≥ 2 (R) for ETP and ≤1 (S), 2 (I), and ≥ 4 (R) for IPM/MEM/DOR. These breakpoints are identical to those in the current CLSI M100 Ed. 31 (2021) standard[2,3].
- For evaluable ENT isolates we compared susceptibility results as reported by the facility to CLSI MIC breakpoints overall and by hospital demographics (teaching/non-teaching, urban/rural, bed size) and location (US Census Region).
- Two proportion Z tests were used to assess the difference between facility-reported and revised susceptibility results overall and by hospital demographics. P-values <0.05 indicate a significant difference between facility-reported and revised CLSI MIC breakpoints in NS determinations.

Results

- Overall, 77.4% (937,926/1,211,845) and 90.6% (2,157,785/2,381,824) of non-duplicate ENT isolates with facility-reported susceptibility results also had interpretable MIC results for ETP and IPM/MEM/DOR, respectively (Figure 1). These were termed the evaluable populations.
- ETP S rates were 99.3% and 99.1% as reported by facilities and using CLSI criteria, respectively.
- Susceptibility rates of other Carbs were 98.9% and 98.4% by facility reporting and CLSI criteria, respectively.
- Systematic application of CLSI breakpoints showed that facilities under-reported EPT-I and –R isolates by 24.2% and 16.4%, respectively, and IPM/MEM/DOR-I and –R isolates by 31.3% and 22.7%, respectively (Table 1).
- Underreporting of Carb-NS isolates was significant across all hospital demographics and regions except for New England for all Carbs and West North Central for ETP and West South Central for IPM/MEM/DOR (Figure 2).

Results

Figure 1. NS evaluations in ENT for (A) ETP and (B) IPM/MEM/DOR.

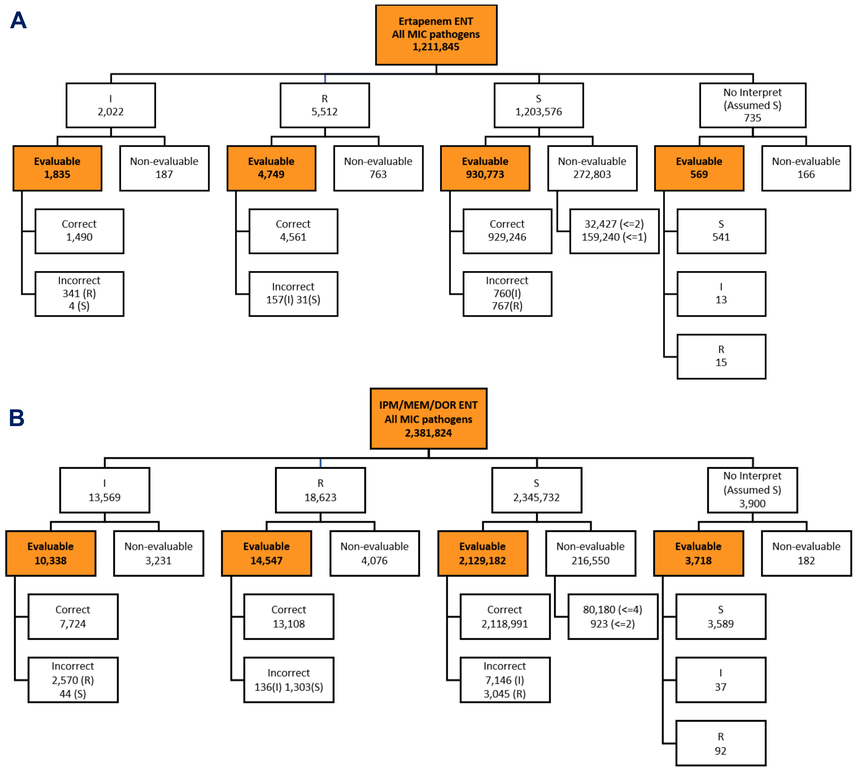
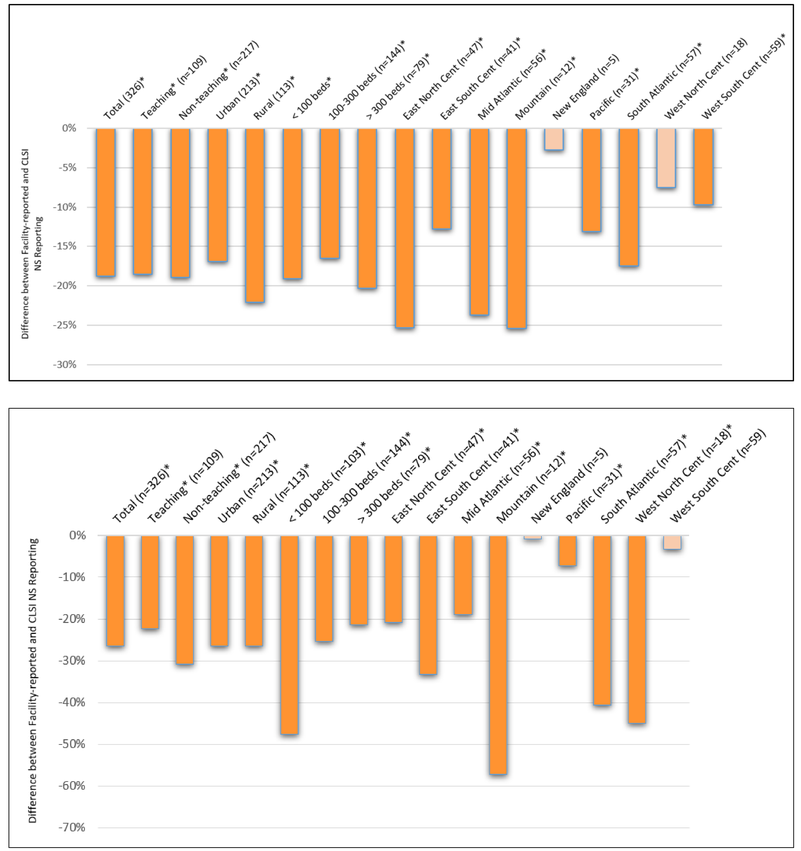


Table 1. Comparison of S/NS (I or R) for facility-reported and CLSI Carb breakpoints in ENT.

ETP ENT MIC breakpoints (Evaluable)			
Interpretation (MIC in µg/mL.)	**Facility Reported: n (%)**	**Revised per CLSI: n (%)**	**Facility vs. Revised per CLSI**
I (1)	1,835 (0.20%)	2,420 (0.26%)	↓ by 24.2%
R (>=2)	4,749 (0.51%)	5,684 (0.61%)	↓ by 16.4%
S (<=0.5)	931,342 (99.30%)	929,822 (99.13%)	
Total	**937,926**	**937,926**	

IPM/MEM/DOR ENT MIC breakpoints (Evaluable)			
Interpretation (MIC in µg/mL.)	**Facility Reported: n (%)**	**Revised per CLSI: n (%)**	**Facility vs. Revised per CLSI**
I (2)	10,338 (0.48%)	15,043 (0.70%)	↓ by 31.3%
R (>=4)	14,547 (0.67%)	18,815 (0.87%)	↓ by 22.7%
S (<=1)	2,132,900 (98.85%)	2,123,927 (98.43%)	
Total	**2,157,785**	**2,157,785**	

Figure 2. Carb NS underreporting by hospital demographics (n=facility count; * p < 0.018 [darker color]) for ETP (A) and IPM/MEM/DOR (B)



Conclusions

- Systematic application of CLSI breakpoints in 2016-20 would have had minimal impact on ENT S rates in the US.
- However, facility reporting failed to identify 18.8% of ETP I or R and 26.5% of IPM/MEM/DOR I or R isolates and this discordance was significant across hospital types and regions.
- Facilities should know their local epidemiology, decide if under-reporting might be an issue, and then assess if there is any impact on their patients.
- Further analyses are required to understand whether the Carb-NS reporting discordances as seen in this analysis also apply more broadly to other hospitals in the US.

Acknowledgements: This work was supported by Venatorx Pharmaceuticals, Inc.

References
1. Centers for Disease Control and Prevention. Antibiotic resistance threats in the United States, 2019. November 2019. Available at: www.cdc.gov/DrugResistance/Biggest-Threats.html. Accessed September 16, 2021.
2. CLSI. Performance Standards for Antimicrobial Susceptibility Testing. 31st ed.
3. CLSI supplement M100. Clinical and Laboratory Standards Institute; 2021