M. Estabrook<sup>1</sup>, M. Wise<sup>1</sup>, F. Arhin<sup>2</sup>, D. Sahm<sup>1</sup>

<sup>1</sup>IHMA, Schaumburg IL, USA <sup>2</sup>Pfizer Inc., Kirkland, Canada

### Introduction

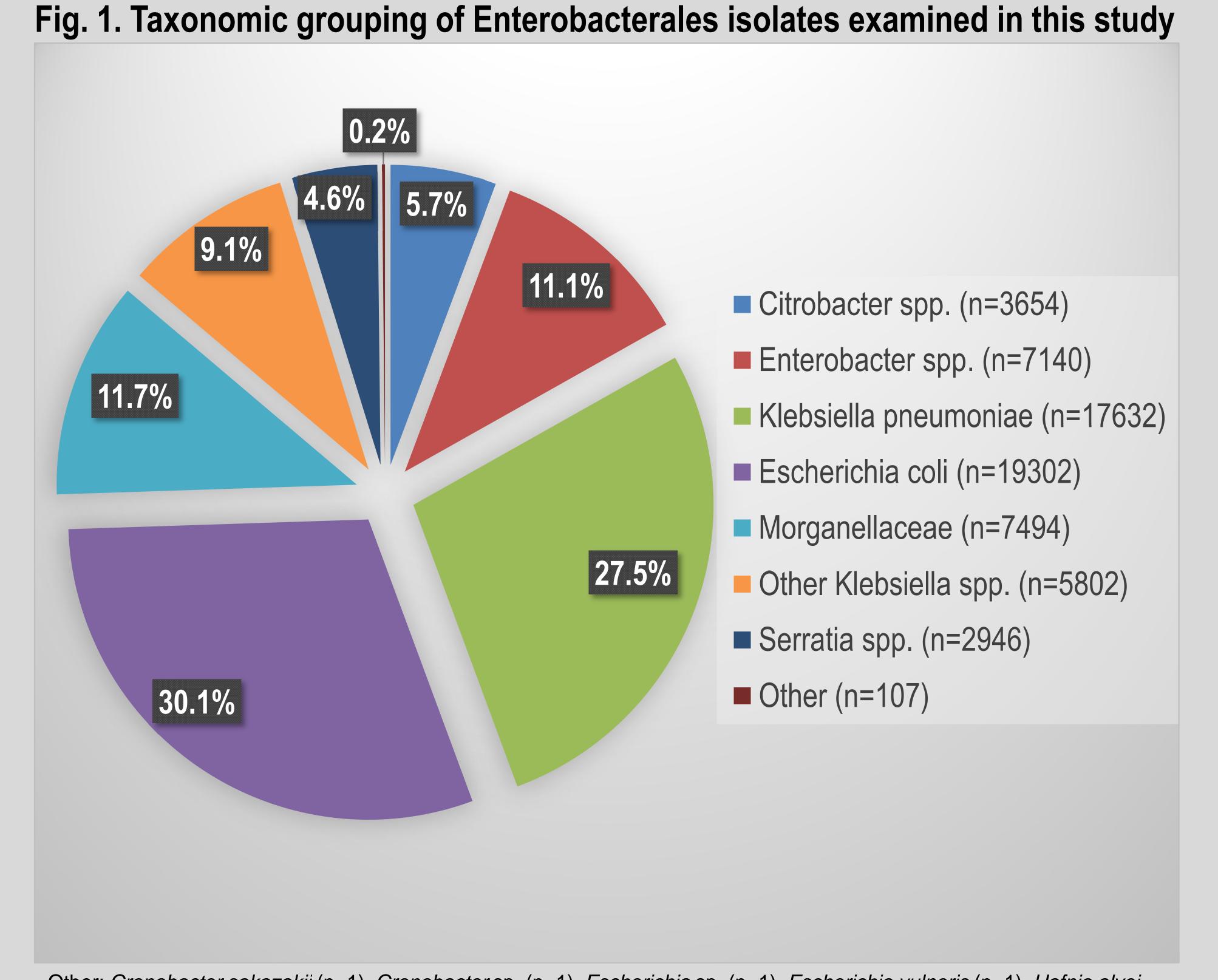
The rapid spread of antimicrobial among clinically Enterobacterales continues to threaten public health. Aztreonam (ATM) is a monobactam stable to hydrolysis by metallo-β-lactamases (MBLs) and avibactam (AVI) inhibits class A, class C, and some class D serine β-lactamases. ATM-AVI is being developed for use against drug-resistant isolates of the Enterobacterales, especially those co-producing MBLs and other β-lactamases. This study evaluated the in vitro activity of ATM-AVI and comparator agents Enterobacterales collected in 2017-2020 from pediatric and adult patients as part of the ATLAS global

# Methods

surveillance program.

- 64,077 non-duplicate clinical Enterobacterales isolates for patient age was specified were collected in 2017-2020 from 240 sites in 55 countries in Europe, Latin Asia/Pacific America, (excluding mainland China and India), and Middle East/Africa.
- Susceptibility performed microdilution and interpreted using CLSI 2022 breakpoints [2].
- PCR and sequencing were used to determine the \betalactamase genes present in all isolates with meropenem MIC >1 µg/mL, and Escherichia coli, Klebsiella pneumoniae, K. variicola and Proteus mirabilis with ATM or ceftazidime MIC  $>1 \mu g/mL [3].$

# Results



Other: Cronobacter sakazakii (n=1), Cronobacter sp. (n=1), Escherichia sp. (n=1), Escherichia vulneris (n=1), Hafnia alvei (n=1), Kosakonia (Enterobacter) cowanii (n=1), Lelliottia amnigena (n=1), Pantoea agglomerans (n=4), Pantoea dispersa (n=2), Pantoea septica (n=1), Pantoea sp. (n=1), Pluralibacter gergoviae (n=11), Raoultella ornithinolytica (n=60), Raoultella planticola (n=12), Raoultella sp. (n=1), Raoultella terrigena (n=1), Salmonella sp. (n=7).

Table 1. In vitro activity of aztreonam-avibactam and comparator antimicrobials

MIC<sub>90</sub> [µg/mL] / % Susceptible

MEM

AMK

FEP

against Enterobacterales isolated from pediatric and adult patients

ATM

Pediatric (1-17 y.o.)

# Figure 2. Distribution of aztreonam-avibactam and aztreonam MIC values against Enterobacterales isolates from pediatric patients (n=5,766) Aztreonam/Avibactam

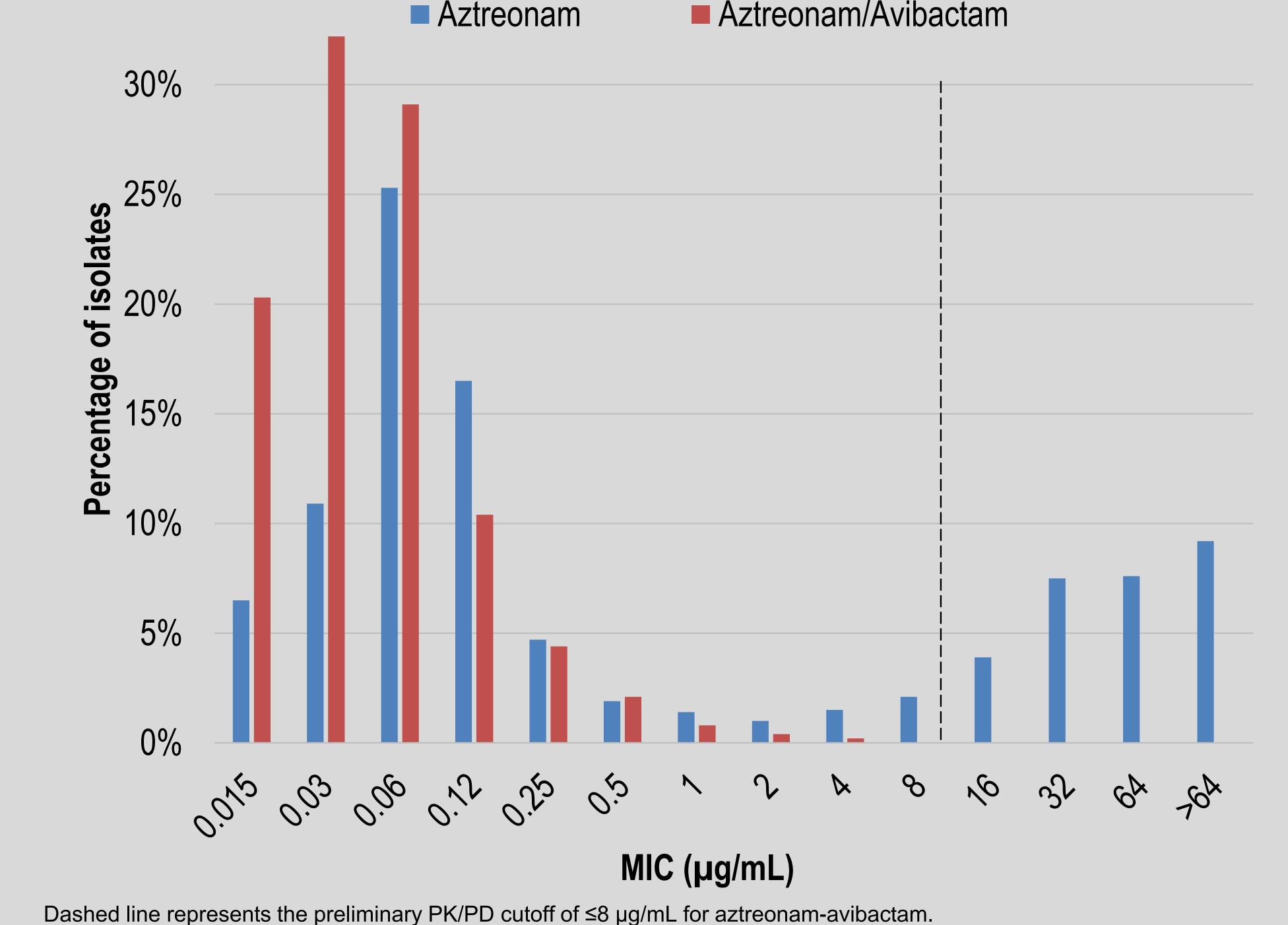
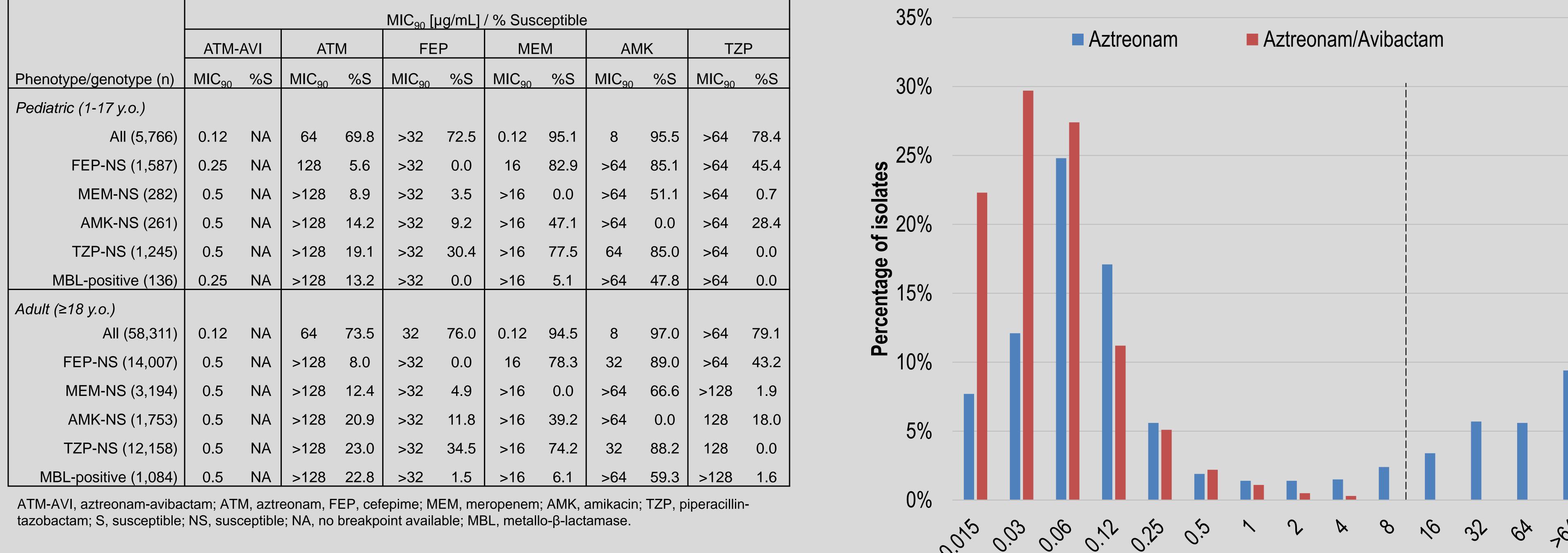


Figure 3. Distribution of aztreonam-avibactam and aztreonam MIC values



Dashed line represents the preliminary PK/PD cutoff of ≤8 µg/mL for aztreonam-avibactam..

MIC (µg/mL)

against Enterobacterales isolates from adult patients (n=58,311)

from pediatric patients (n=136\*) 100%

Figure 4. Cumulative percent inhibited by increasing concentrations of

aztreonam-avibactam and aztreonam, MBL-producing Enterobacterales isolates

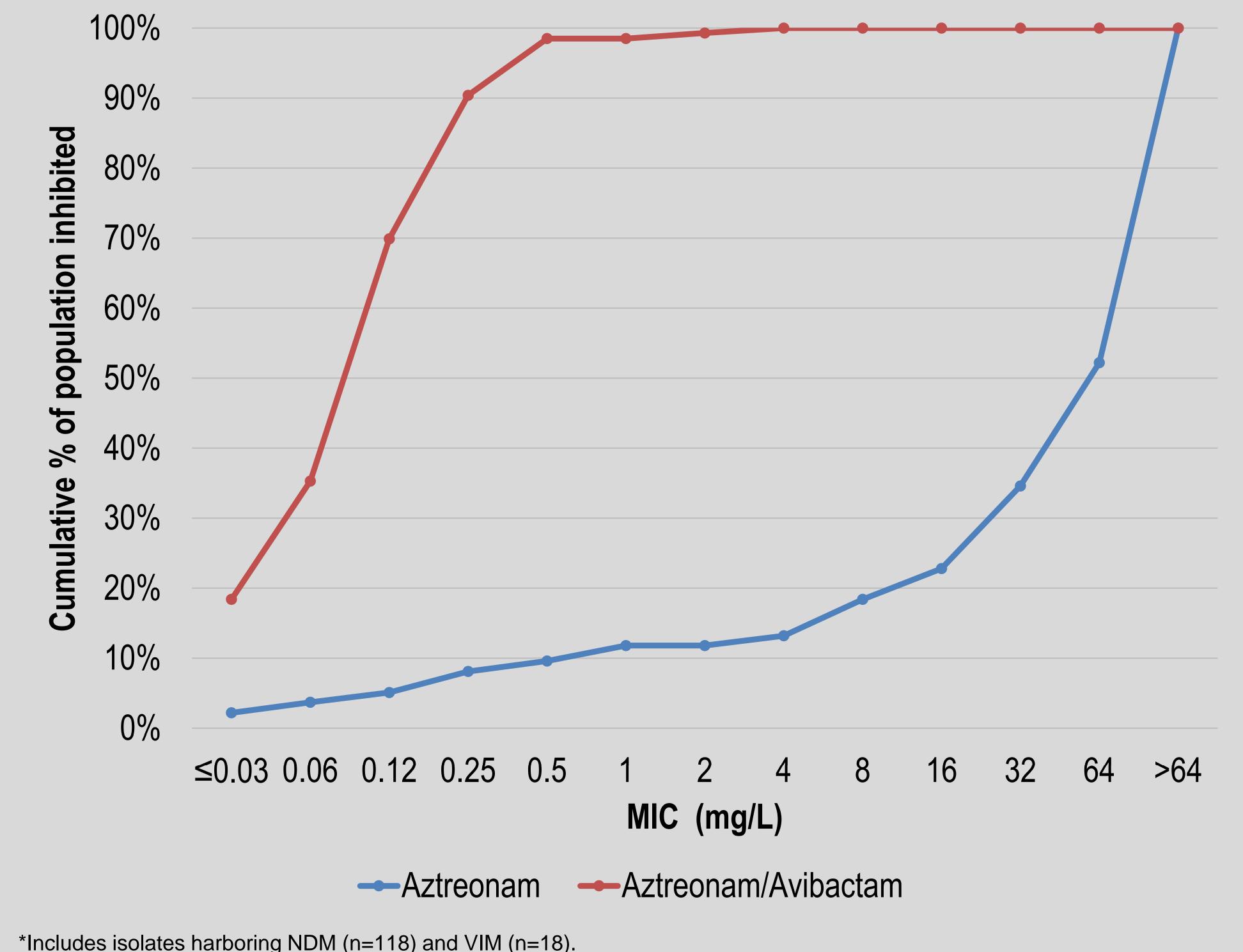
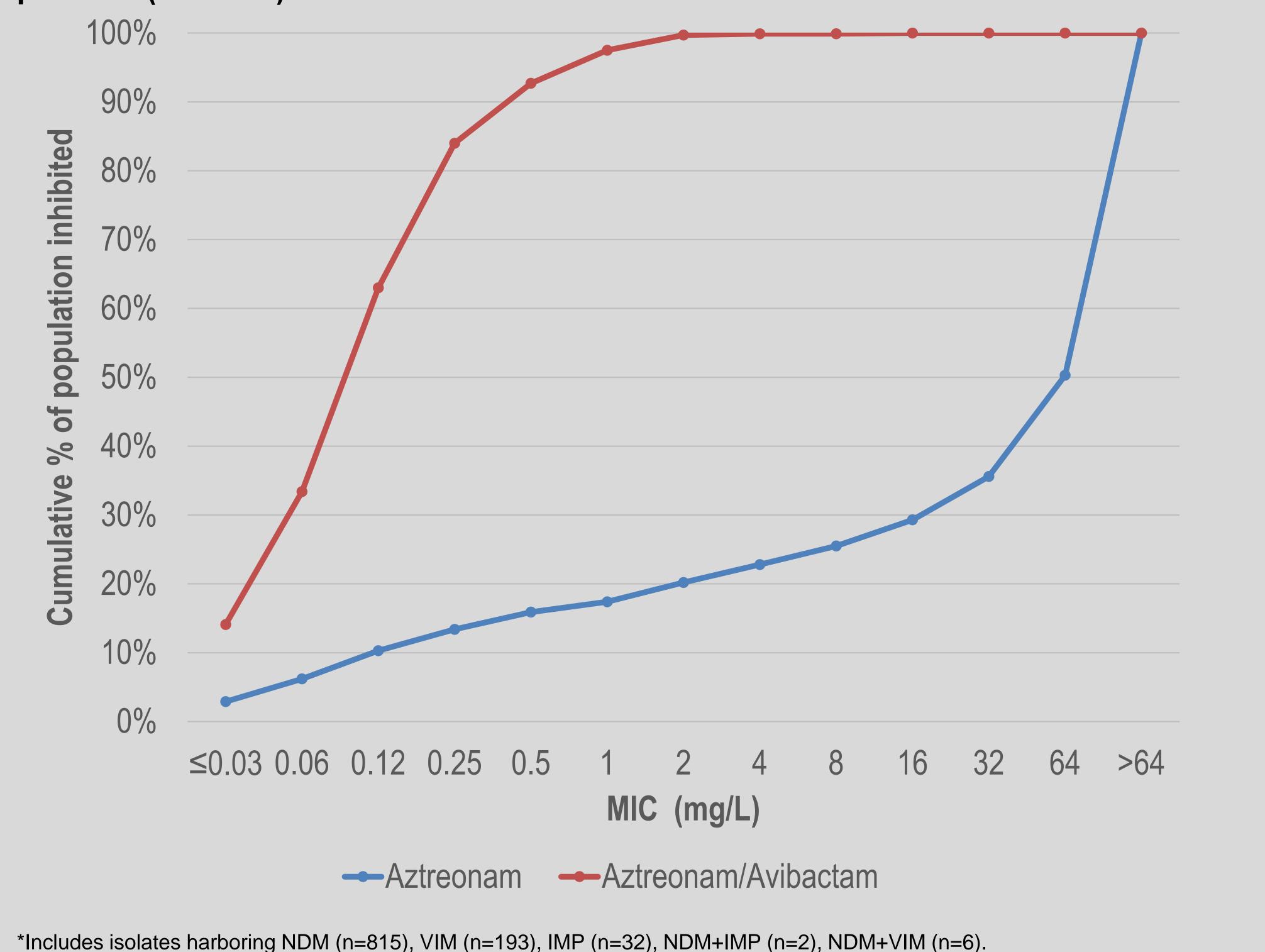


Figure 5. Cumulative percent inhibited by increasing concentrations aztreonamavibactam and aztreonam, MBL-producing Enterobacterales isolates from adult patients (n=1048\*)



#### Results

- MIC<sub>90</sub> values for ATM-AVI of 0.12 μg/ml were observed for Enterobacterales isolates collected from both the pediatric and adult patient populations (Table 1).
- Against all Enterobacterales isolates, ≤8 μg/ml of ATM-AVI was sufficient to inhibit >99.9% of isolates from pediatric and adult patients, whereas only 69.8% of pediatric and 73.5% of adult isolates were susceptible to ATM alone (Figs. 2-3, Table 1).
- Among isolates that screened positive for a metallo-β-lactamase (MBL), ATM-AVI MIC<sub>90</sub> values were 0.25 μg/ml (pediatric) and 0.5 µg/ml (adult).
- ATM-AVI inhibited 100% (pediatric) and 99.9% (adult) of the MBL-producing isolates at concentrations ≤8 µg/ml. In contrast, 13.2% of pediatric and 22.8% of adult isolates carrying MBLs were susceptible to ATM alone (Figs. 4-5, Table 1).
- Aztreonam-avibactam MIC values >8 μg/ml were only observed against 30 isolates (0.045% of the total population) and included Enterobacter cloacae (n=2), Escherichia coli (n=19) Klebsiella oxytoca (n=1), Klebsiella pneumoniae (n=5), Proteus mirabilis (n=1) and *Providencia rettgeri* (n=2).

## Conclusions

Based on MIC<sub>90</sub> values, ATM-AVI demonstrated potent in vitro activity against Enterobacterales isolated both from pediatric and adult patients. The capability of AVI to potentiate ATM against MBLpositive isolates warrants its continued development.

## References

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- 2. The European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters. Version 11.0, 2021. http://www.eucast.org. 3. Lob SH, Kazmierczak KM, Badal RE, Hackel MA, Bouchillon SK, Biedenbach DJ, Sahm, DF. 2015. Trends in susceptibility of Escherichia coli from intra-abdominal infections to ertapenem and comparators in the United States according to data from

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## Disclosures

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TZP-NS (12,158) | 0.5 NA | >128 23.0 | >32 34.5 | >16 74.2 | 32 88.2 | 128 0.0 MBL-positive (1,084) 0.5 NA >128 22.8 >32 1.5 >16 6.1 >64 59.3 >128 1.6

ATM-AVI, aztreonam-avibactam; ATM, aztreonam, FEP, cefepime; MEM, meropenem; AMK, amikacin; TZP, piperacillintazobactam; S, susceptible; NS, susceptible; NA, no breakpoint available; MBL, metallo-β-lactamase.

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