Association of prior resistance results with subsequent susceptibility over time

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Background

- Previous data has shown that identification of a recent, prior Gram-negative organism resistant to a particular antibiotic within the last 12 months is highly specific for resistance and should preclude use of that antibiotic[1]
- There is also an association with increased treatment failure when patients are treated with an antimicrobial to which a previous isolate was resistant[2]
- Institutional antibiograms can assist with the selection of empiric therapy, however, antibiograms may not be helpful for characterizing the likelihood of resistance for individual patients over time

Objective

- Evaluate the association of prior isolate resistance with subsequent susceptibility over time for Gram-negative organism-antibiotic combinations

Methods

- Setting: University of Pennsylvania Health System
- Timeframe: May 2008 to September 2016
- Electronic health record data was used to identify *E. coli* and *P. aeruginosa* clinical isolates that had at least one prior resistant result for our selected antibiotics and their respective antibiotic sensitivities
- Isolates were obtained during routine medical care
- We analyzed the isolates' susceptibility or resistance to levofloxacin, cefepime, piperacillin/tazobactam, and meropenem
- Each isolate was paired with every prior resistant isolate up to two years apart for the same patient, organism, and antibiotic
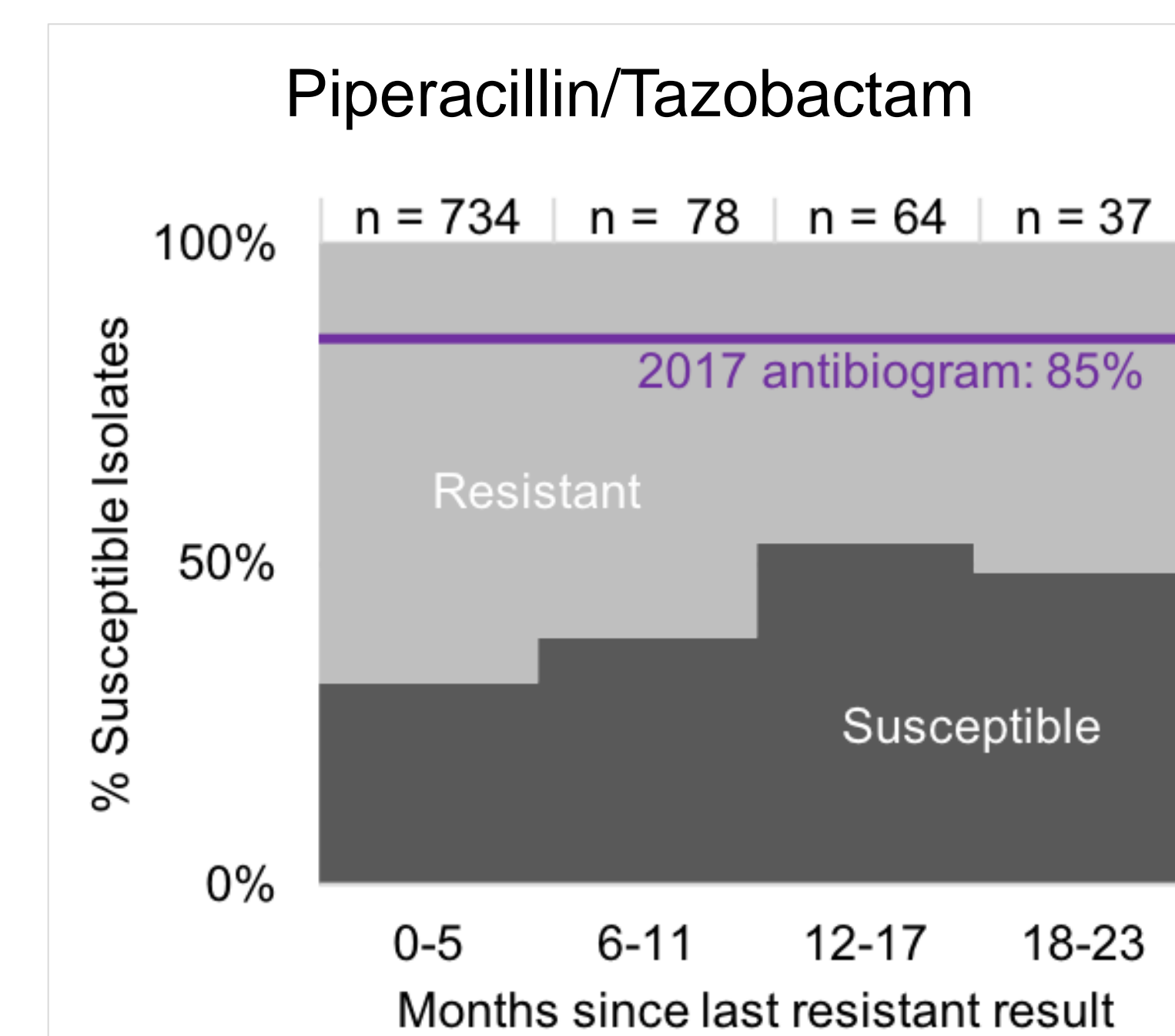- One isolate pair per organism per patient was randomly selected for inclusion in the analysis
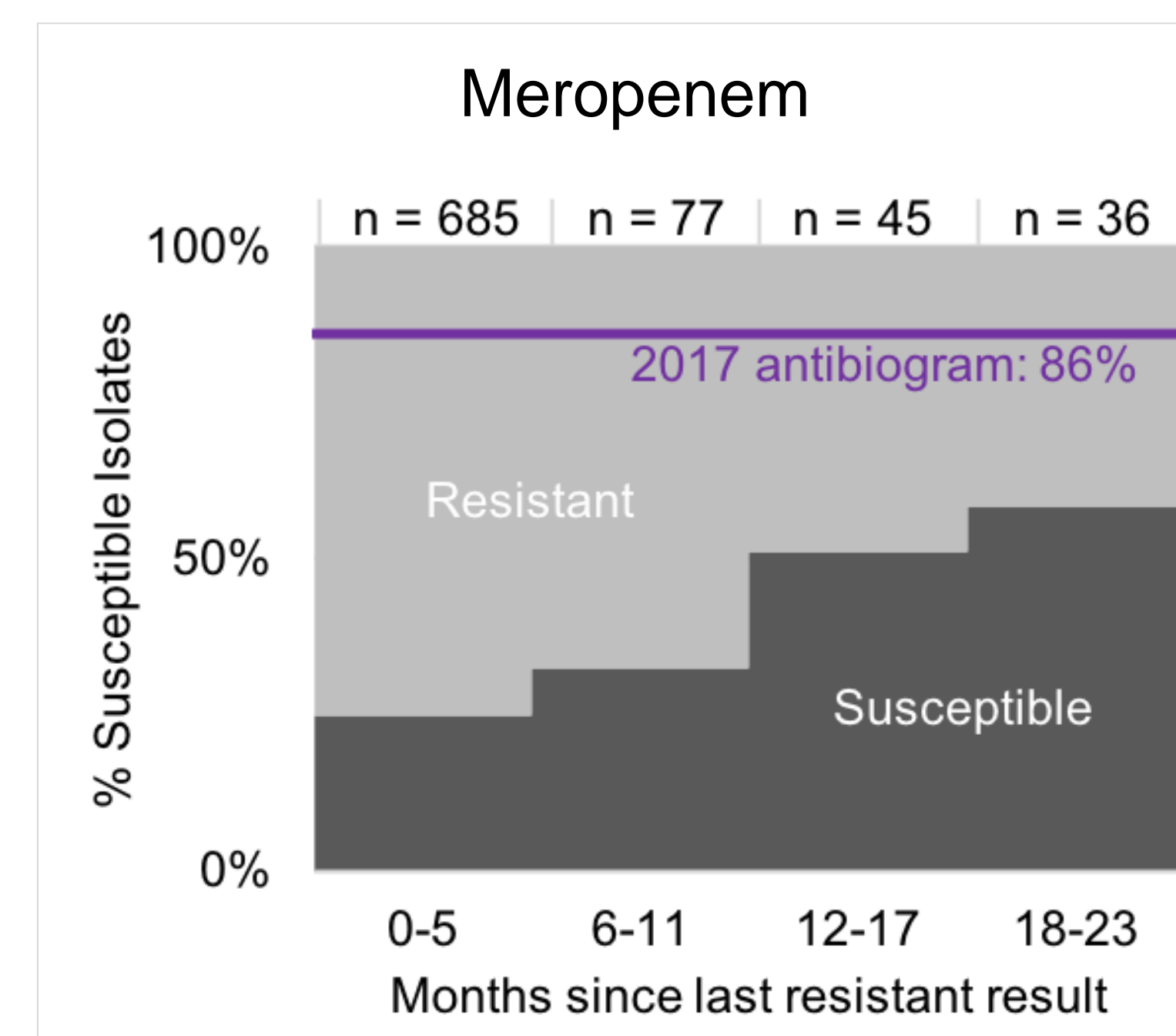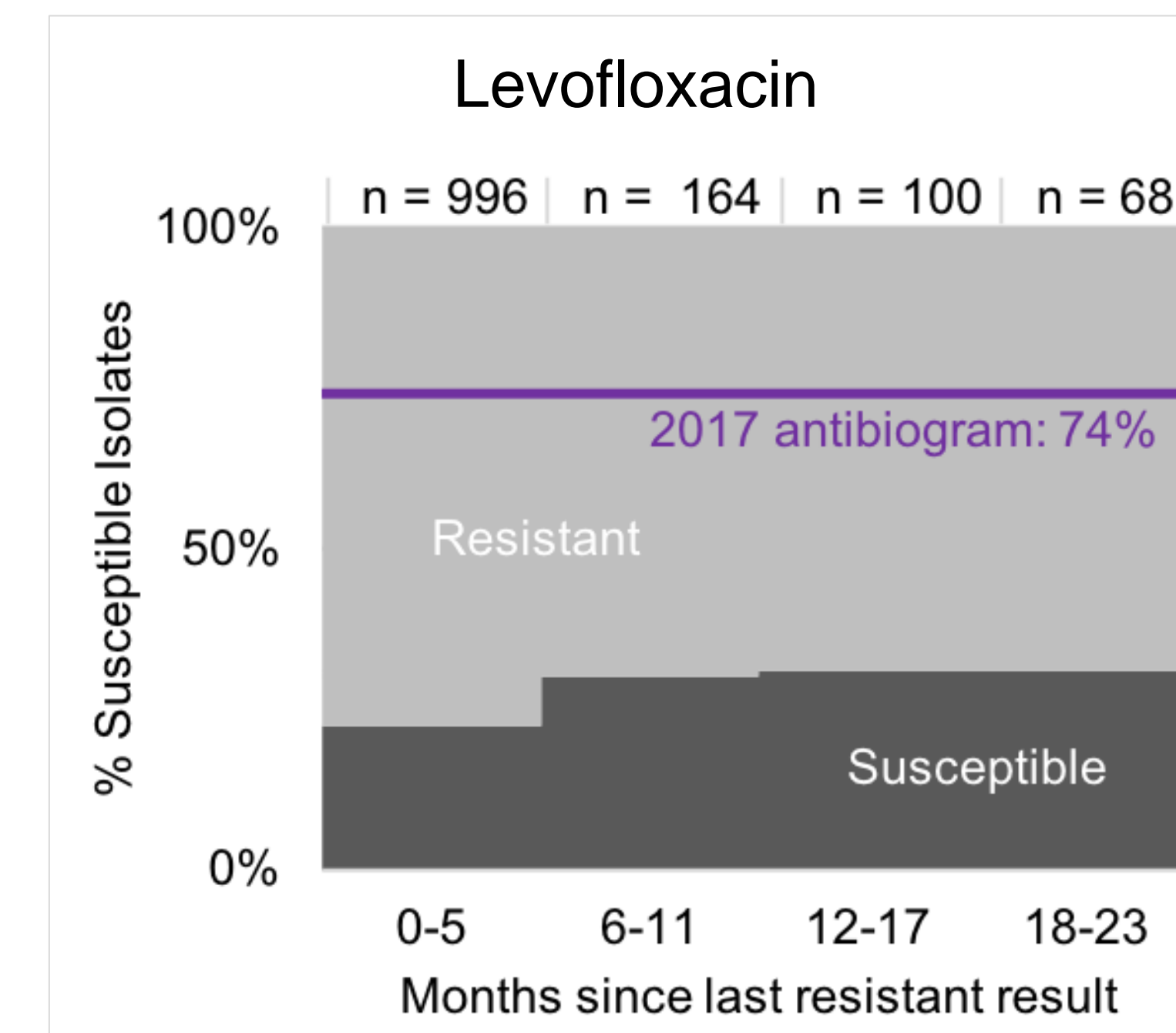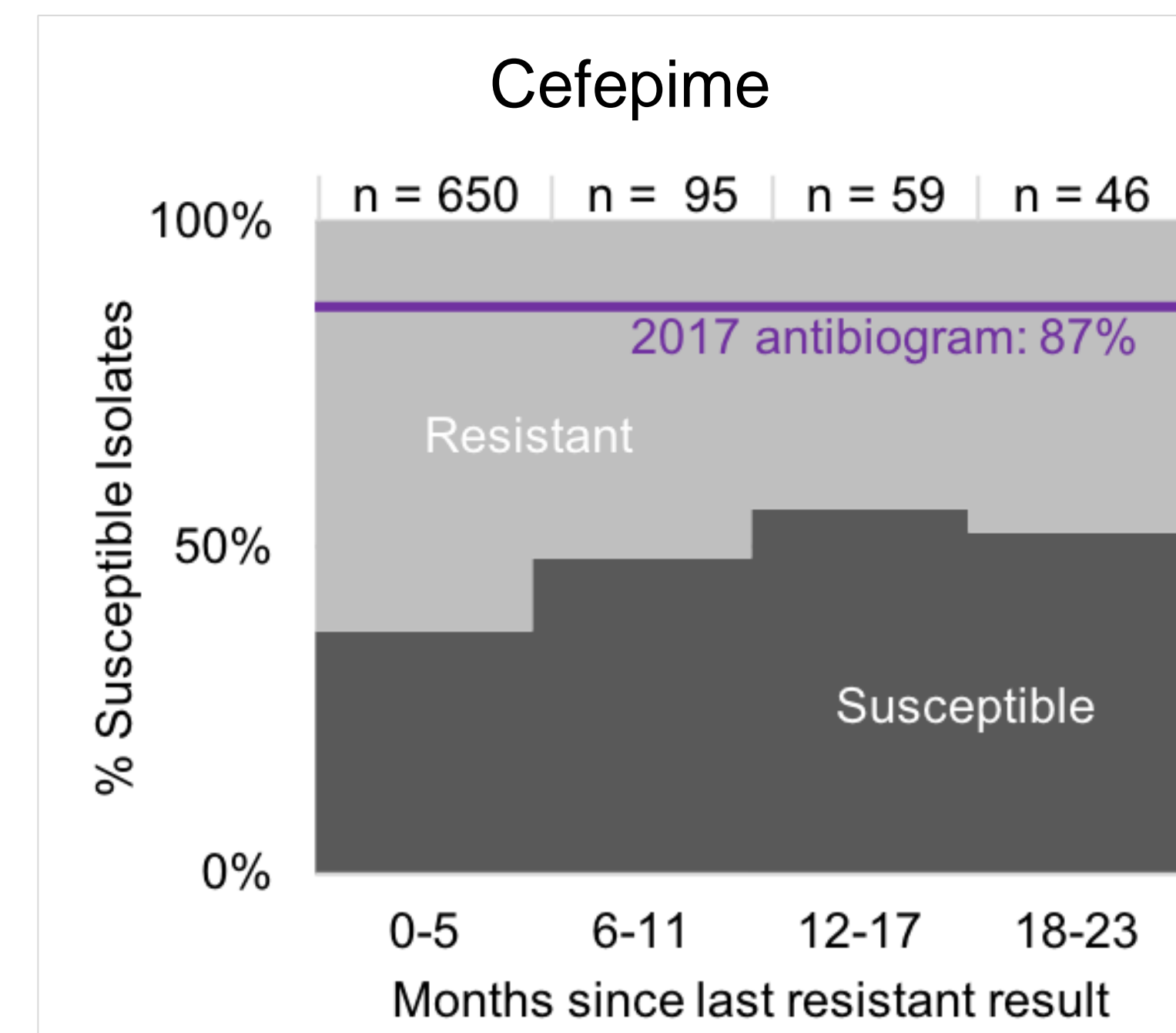
References

1. MacFadden DR, et al. Utility of prior cultures in predicting antibiotic resistance of bloodstream infections due to Gram-negative pathogens: a multicentre observational cohort study. Clin Microbiol Infect. 2018 May;24(5):493-499.
2. Daneman N, et al. Macrolide resistance in bacteremic pneumococcal disease: implications for patient management. Clin Infect Dis. 2006 Aug 15;43(4):432-8.
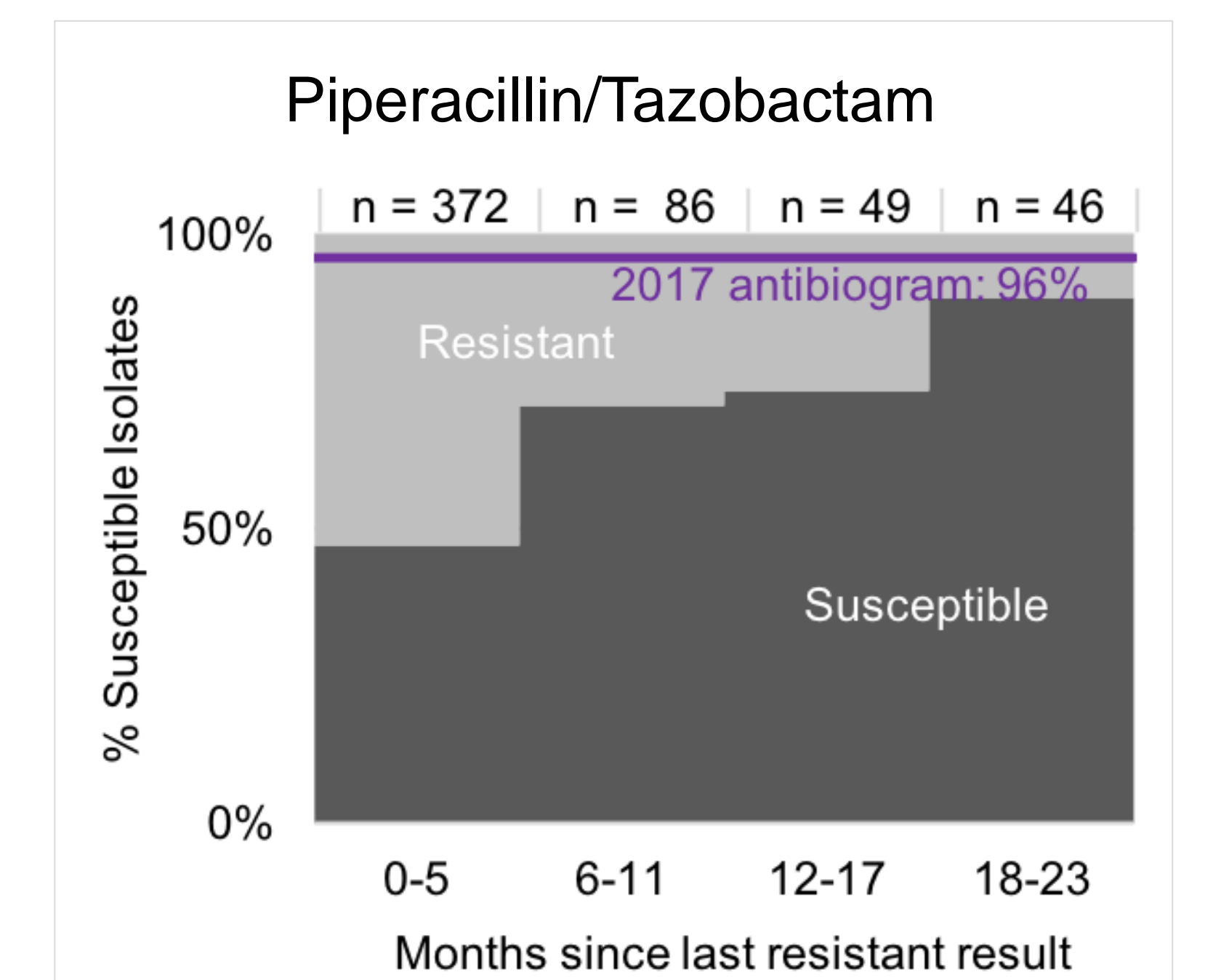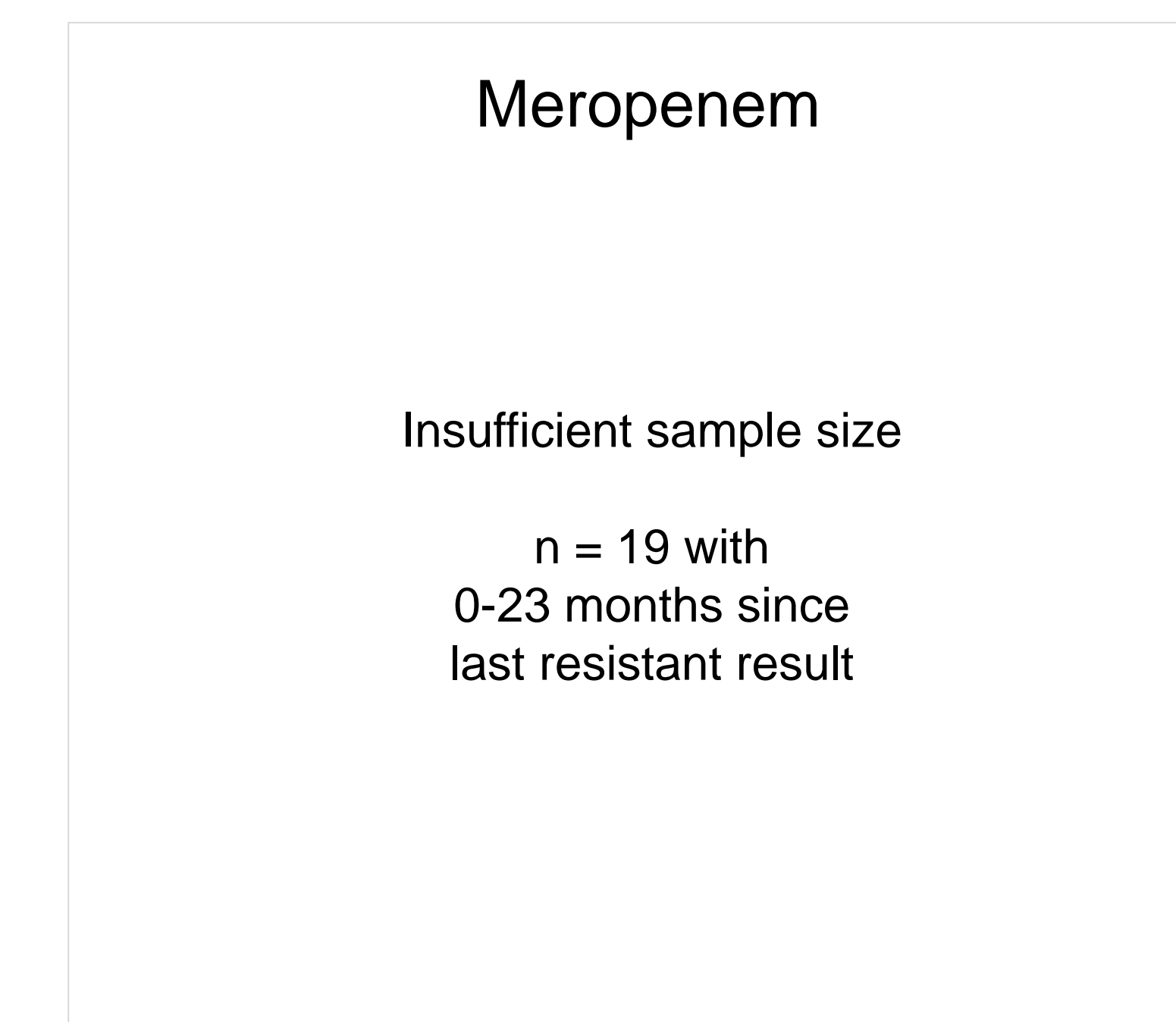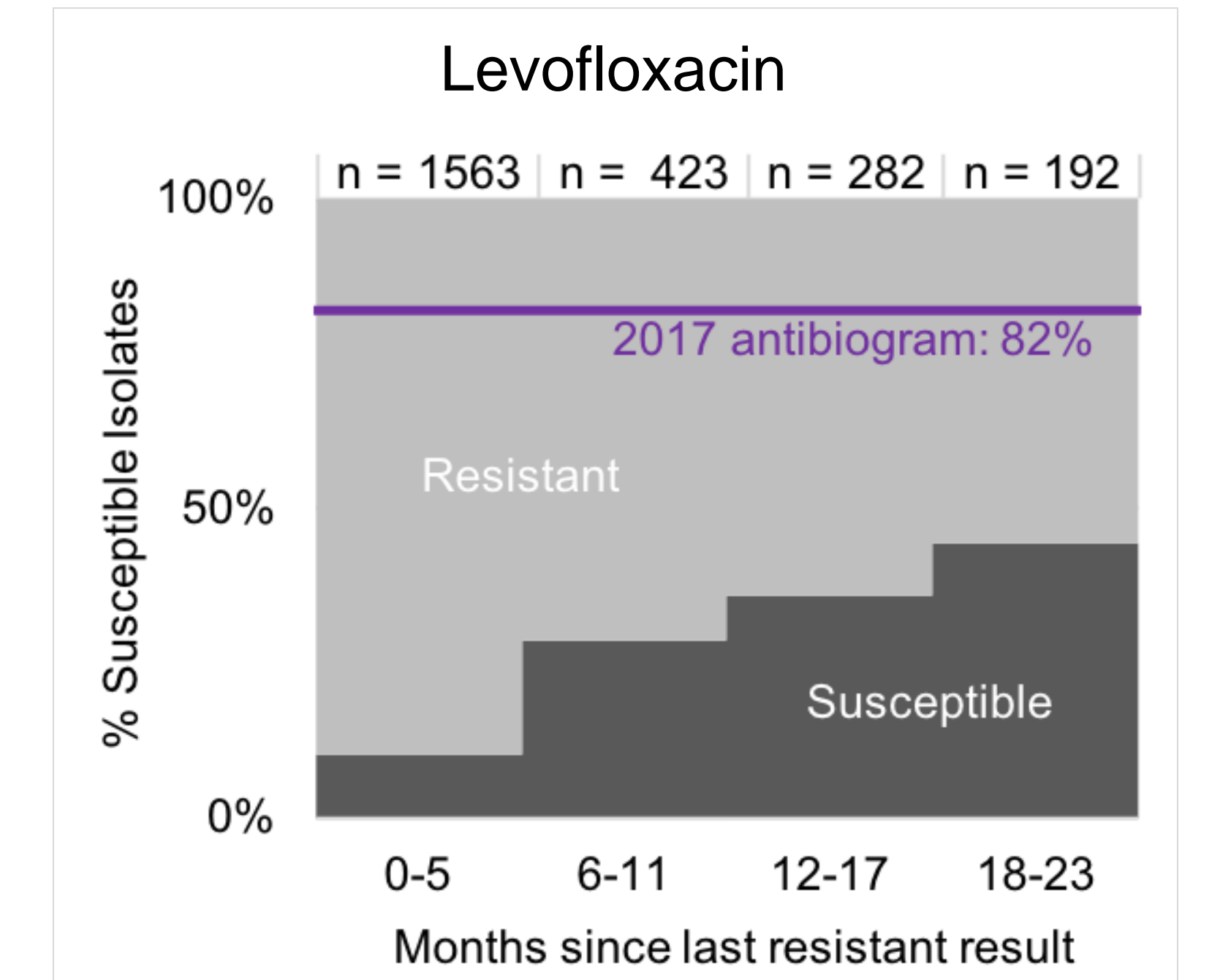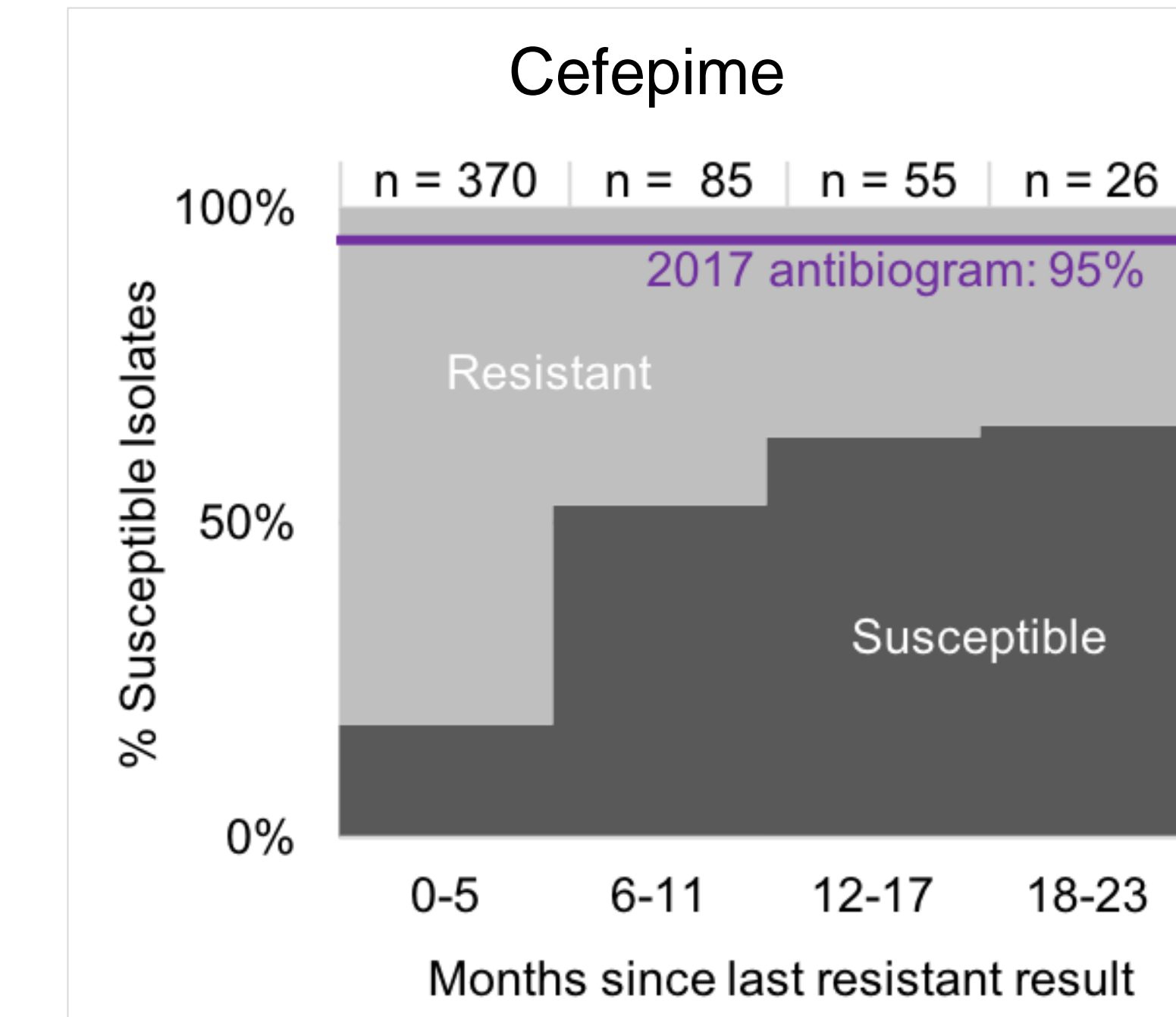
Results

- In general, as time from the resistant culture increased, later isolates were more likely to be susceptible
- However, the proportion of susceptible results did not approach that of the institution's antibiogram with the exception of *E.coli* + piperacillin/tazobactam
- The sample size of *E. coli* isolates with prior meropenem resistance was too small to include for analysis
- 2017 antibiogram data is represented for each organism-antibiotic combination

Antibiotic susceptibility over time for *P. aeruginosa*

Cefepime — n = 650 | n = 95 | n = 59 | n = 46 — 2017 antibiogram: 87%

Levofloxacin — n = 996 | n = 164 | n = 100 | n = 68 — 2017 antibiogram: 74%

Meropenem — n = 685 | n = 77 | n = 45 | n = 36 — 2017 antibiogram: 86%

Piperacillin/Tazobactam — n = 734 | n = 78 | n = 64 | n = 37 — 2017 antibiogram: 85%

Results (continued)

Antibiotic susceptibility over time for *E. coli*

Cefepime — n = 370 | n = 85 | n = 55 | n = 26 — 2017 antibiogram: 95%

Levofloxacin — n = 1563 | n = 423 | n = 282 | n = 192 — 2017 antibiogram: 82%

Meropenem — Insufficient sample size — n = 19 with 0-23 months since last resistant result

Piperacillin/Tazobactam — n = 372 | n = 86 | n = 49 | n = 46 — 2017 antibiogram: 96%

Conclusions

- This ecologic analysis of individual patients demonstrates the potential for persistent resistance up to two years between isolates of the same species
- It also suggests that individuals who have previous antimicrobial resistance infrequently regress to the expected level of susceptibility shown by the institutional antibiogram
- The prolonged effect shown here could have implications for both empiric antimicrobial prescribing as well as infection control and prevention
- Future studies are warranted to control for individual patient factors and routine serial sampling at set intervals