

# Predicting carbapenem resistance among gram-negative pathogens in complicated urinary tract infections

Glenn Tillotson, PhD, FIDSA

June 9, 2018

ASM Microbe, Atlanta, GA

# Disclosures

- Study funded by The Medicines Company, Parsippany, NJ, USA and Melinta Therapeutics, New Haven, CT, USA

## Consulting & Advisory Boards

- Melinta Therapeutics
- Spero Therapeutics
- Summit plc
- KBP Biosciences
- Novobiotics
- Shionogi

# Background

- In the US, UTI hospitalizations rose by 50% over the 2000s
  - over 3 million UTI admissions in 2009<sup>1</sup>
- Pathogens<sup>2</sup>
  - Enterobacteriaceae -- common
  - *P. aeruginosa* -- common
  - *A. baumannii* – rare, but often resistant
- Carbapenem resistance (CR) has grown rapidly
  - over 3% of Enterobacteriaceae carbapenem non-susceptible<sup>2-4</sup>
  - CR among PA and AB substantially higher<sup>1</sup>
- Resistance associated with inappropriate empiric therapy (IET)<sup>5-6</sup>
- IET associated with worsened outcomes

# Study aim

- To develop and validate a predictive score to be used at the bedside to identify hospitalized patients with complicated UTI (cUTI) who are at risk for a CR pathogen

# Methods

- Design: multi-center retrospective cohort
- Population: adult patients admitted to a US hospital with cUTI
- Data source: Premier Research database, years 2009-2016
- Modeling: Split cohort method
  - 60% training
  - 40% validation
  - Limited to  $\leq 10$  predictors
  - Score weighted to each predictor's regression coefficient

# Definitions

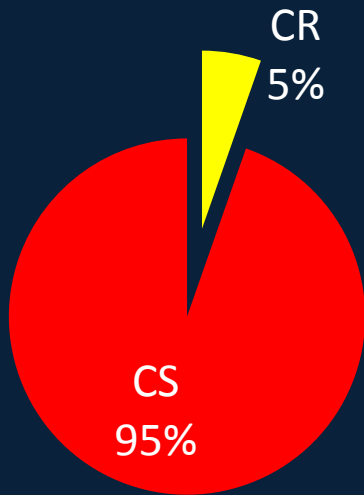
- cUTI defined through an algorithm using ICD-9-CM codes
  - CAUTI analyzed as a subgroup of cUTI
- Appropriate empiric treatment: patient received coverage that
  - Included corresponding organism
  - Within two days of the culture being obtained
- IET: All other regimens
- Predictors: baseline factors, hospital characteristics, processes prior to infection onset

# Organisms of interest

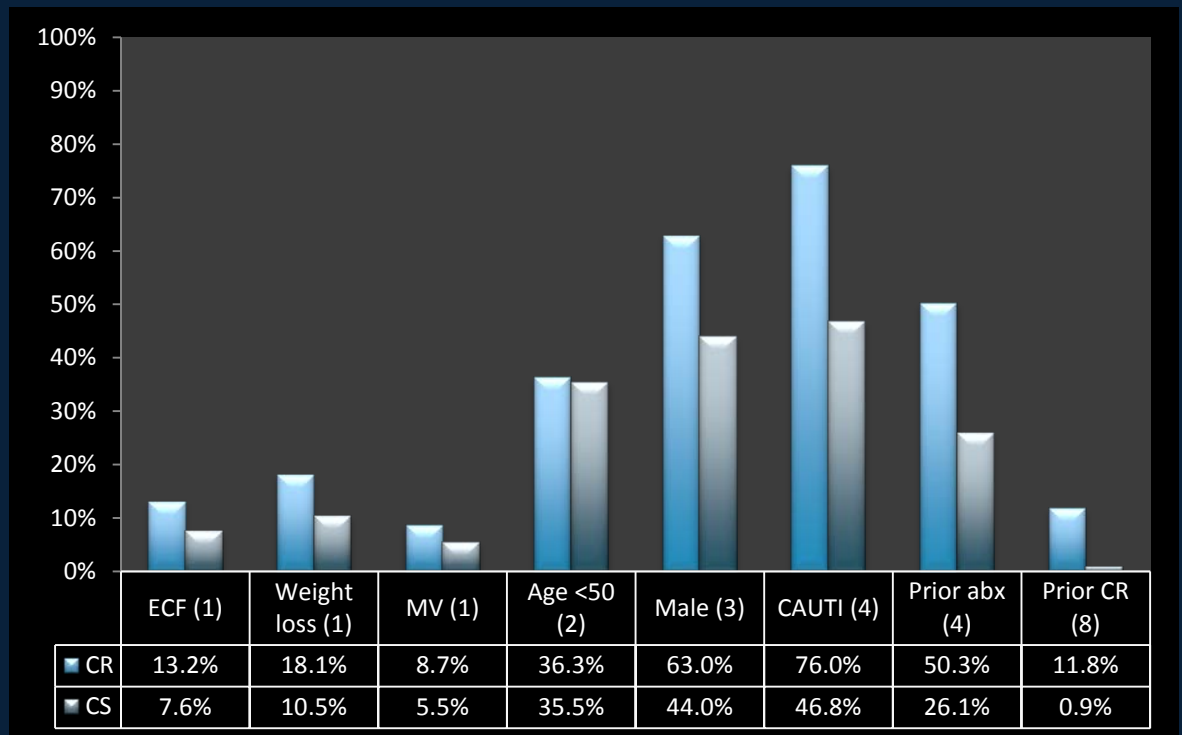
- *Pseudomonas aeruginosa*
- *Acinetobacter baumannii*
- *Stenotrophomonas maltophilia*
- *Escherichia coli*
- *Klebsiella pneumoniae*
- *Klebsiella oxytoca*
- *Enterobacter cloacae*
- *Enterobacter aerogenes*
- *Proteus mirabilis*
- *Proteus spp.*
- *Serratia marcescens*
- *Citrobacter freundii*
- *Morganella morganii*
- *Providencia spp.*

# Results

cUTI N=25,285, 92% CO



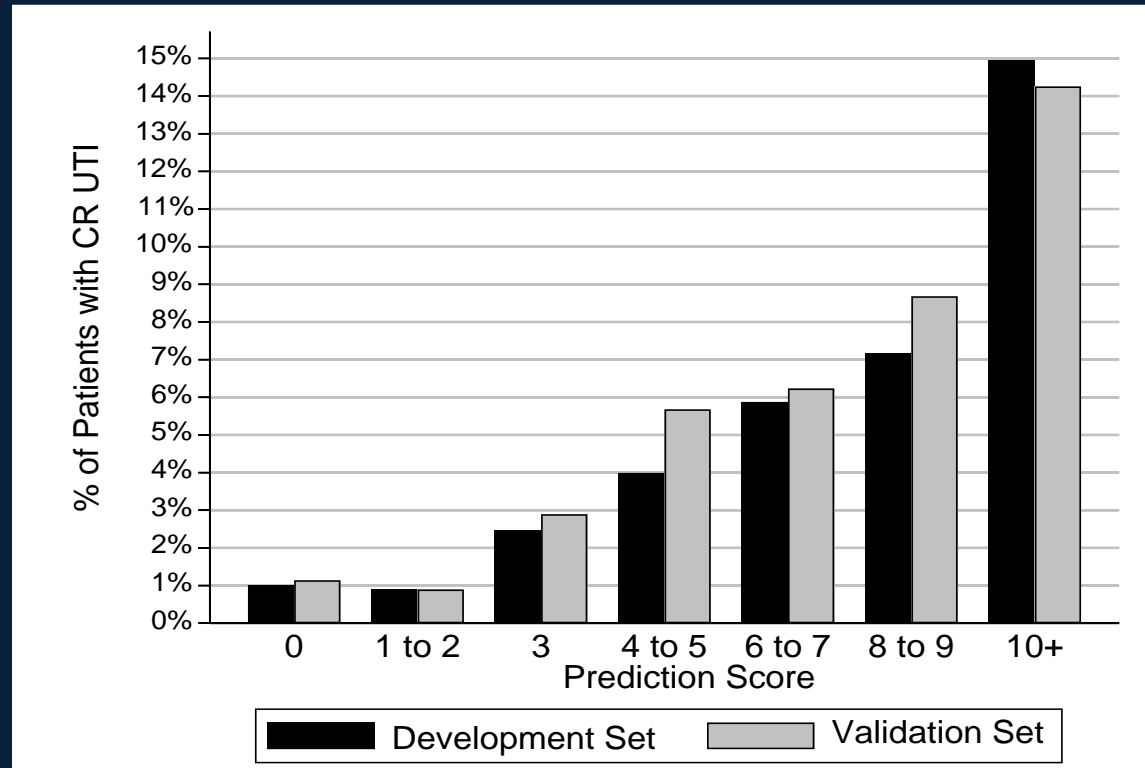
	CR	CS	P-value
Mean age	64.1 (17.9)	64.0 (18.7)	0.86
Mean Charlson	2.9 (2.2)	2.3 (2.2)	<0.001





# Model and prediction score

- C-statistic
  - Training 0.746
  - Validation 0.721
- Performed better among hospitals with lower prevalence of CR
  - tertile 1 – 0.752 [CR prevalence 2.1%]
  - tertile 2 – 0.725 [CR prevalence 4.7%]
  - tertile 3 – 0.703 [CR prevalence 9.2%]



NPV is high (99%) for score  $\leq 3$

# Conclusions

- CR is prevalent in 5% of hospitalized patients with cUTI
- Our simple bedside score was able to identify cUTI patients at low risk for CR
- Using our score may help reduce overuse of broad-spectrum antibiotics in patients with cUTI

# Research Team

- Marya Zilberberg, MD, MPH
  - EviMed, Goshen MA
- Andrew Shorr, MD, MPH
  - Washington Hospital Center
- Kate Sulham, MPH
  - The Medicines Company
- Weihong Fan, MS
  - The Medicines Company
- Brian Nathanson, PhD
  - OptiStatim, LLC

# References

1. Zilberberg MD, Shorr AF. Infect Control Hosp Epidemiol 2013;34:940-6
2. Sievert DM et al. Infect Control Hosp Epidemiol 2013;34:1-14
3. Centers for Disease Control and Prevention (CDC). MMWR Morb Mortal Wkly Rep 2013;62:165-70
4. Braykov NP et al. Infect Control Hosp Epidemiol 2013;34:259-68
5. Zilberberg MD et al. Crit Care 2014;18(6):596
6. Zilberberg MD et al. Crit Care 2016 Jul 11;20:221