Predicting Microculture Results for Optimized Antibiotic Treatment

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MOTIVATION

- Antibiotic resistance is a growing public health concern - 700,000 annual deaths globally due to antibiotic resistant bacteria.

- The CDC estimates that up to 50% of antibiotic use in hospital settings are either inappropriate or suboptimal.

- Machine learning has the potential to help physicians reduce the amount of times antibiotics are prescribed when they are not needed, and improve the likelihood that a given patient with an infection will respond to treatment.

Inpatient Antibiotic Prescription Workflow

Day 1: Encounter with patient showing signs of infection. Empiric antibiotics administered & microculture ordered.
Day 3+: Microculture results returned indicating infecting agent if one exist.
Day 5+: Susceptibility results returned indicating drugs effective against infecting agent. Patient de-escalated to directed therapy.

Day 1 **Day 3+** **Day 5+**

Empiric Treatment

Directed Therapy
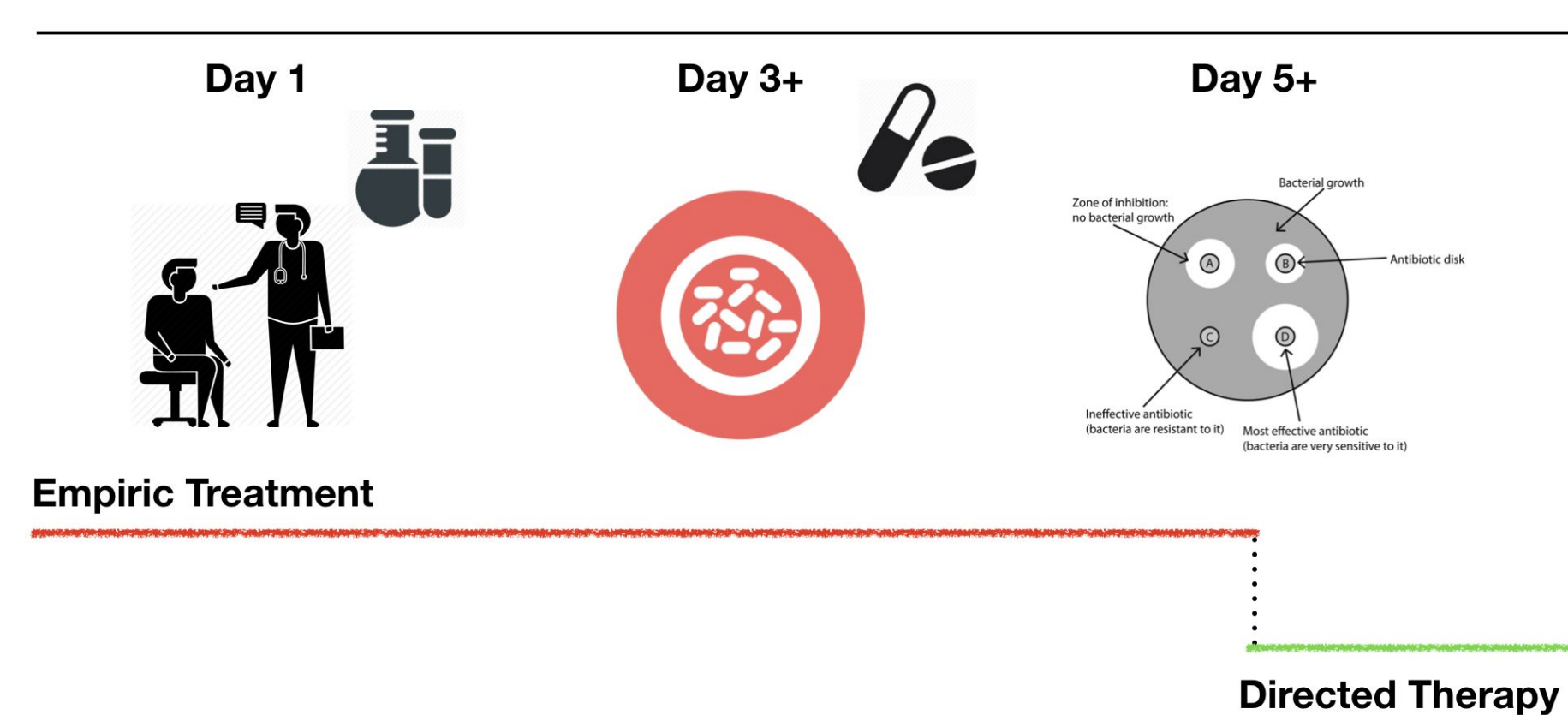
Antibiogram

Proportion of bugs susceptible to given drugs - data is local to a given institution.

Microbe	Isolates Tested	ALL DRUGS	Meropenem	Piperacillin-Tazobactam	Ceftriaxone	Cefazolin
ALL BUGS	1772	91	90	82	75	0
Klebsiella pneumoniae	741	100	100	95	92	92
Proteus mirabilis	262	100	100	100	97	93
Pseudomonas aeruginosa	545	91	90	91	?	?
Enterobacter cloacae	224	99	99	82	75	0

DATA

- **Dataset**: We leveraged STRIDE's (Stanford Translational Research Integrated Database Environment) inpatient clinical data warehouse which contains over 115k unique patient identifiers and over 200k patient encounters. Of particular interest was the STRIDE microculture table - which contained results for over 80k blood cultures and 30k urine cultures.
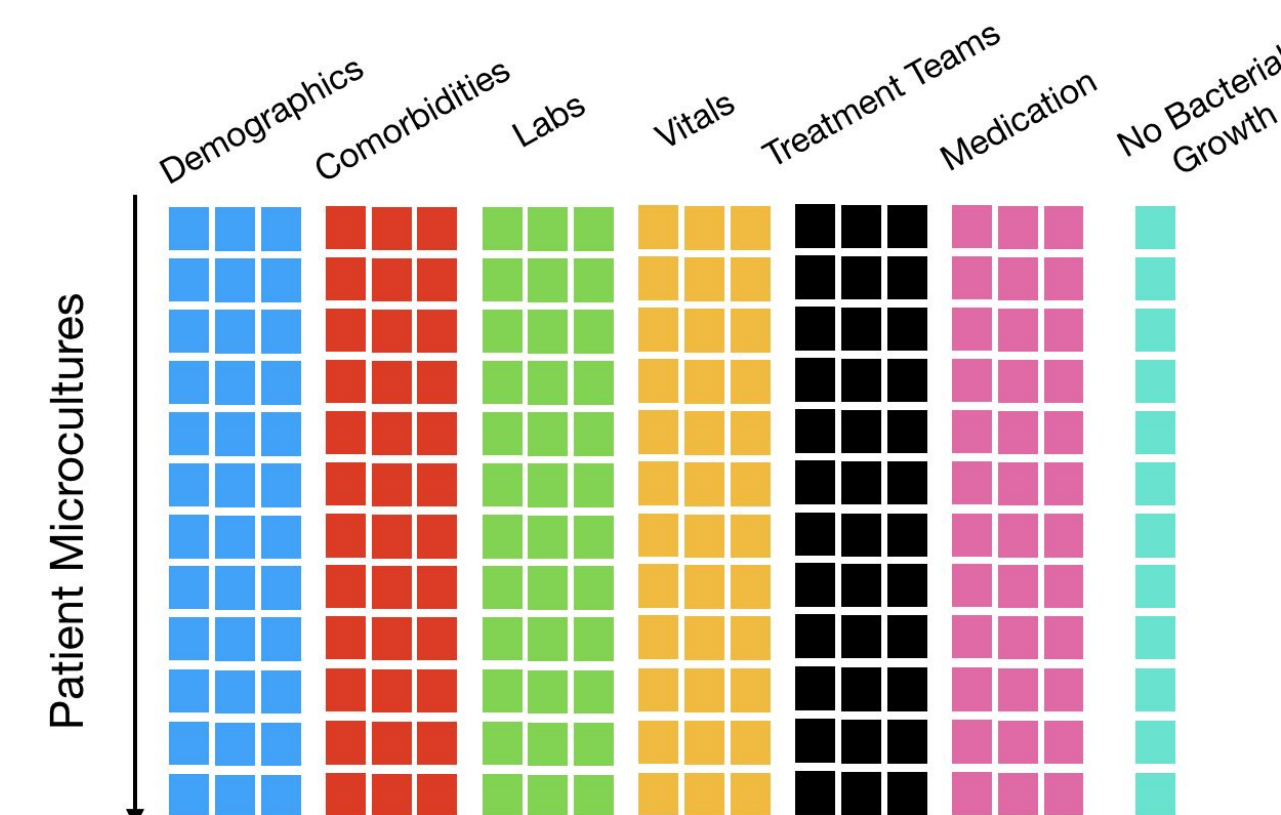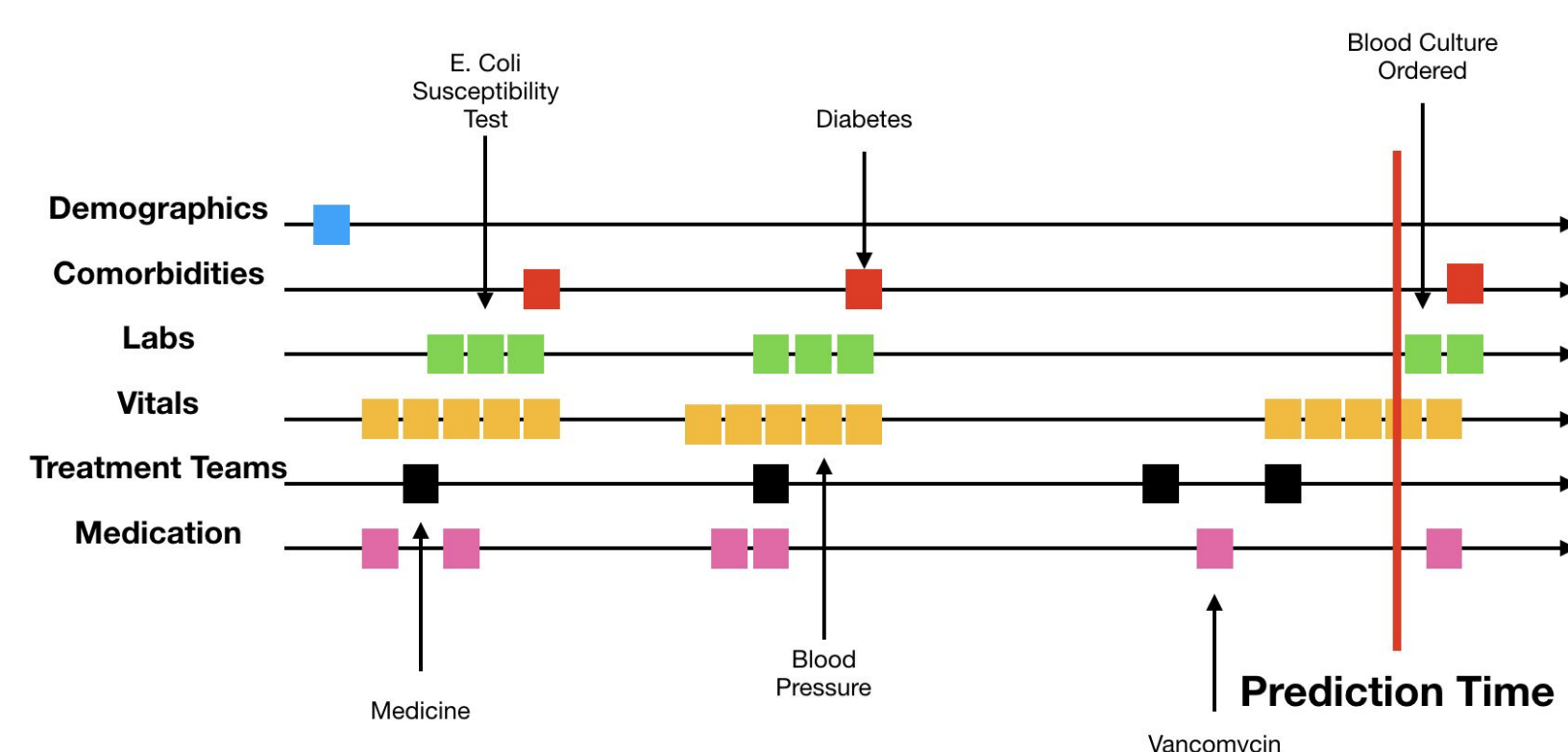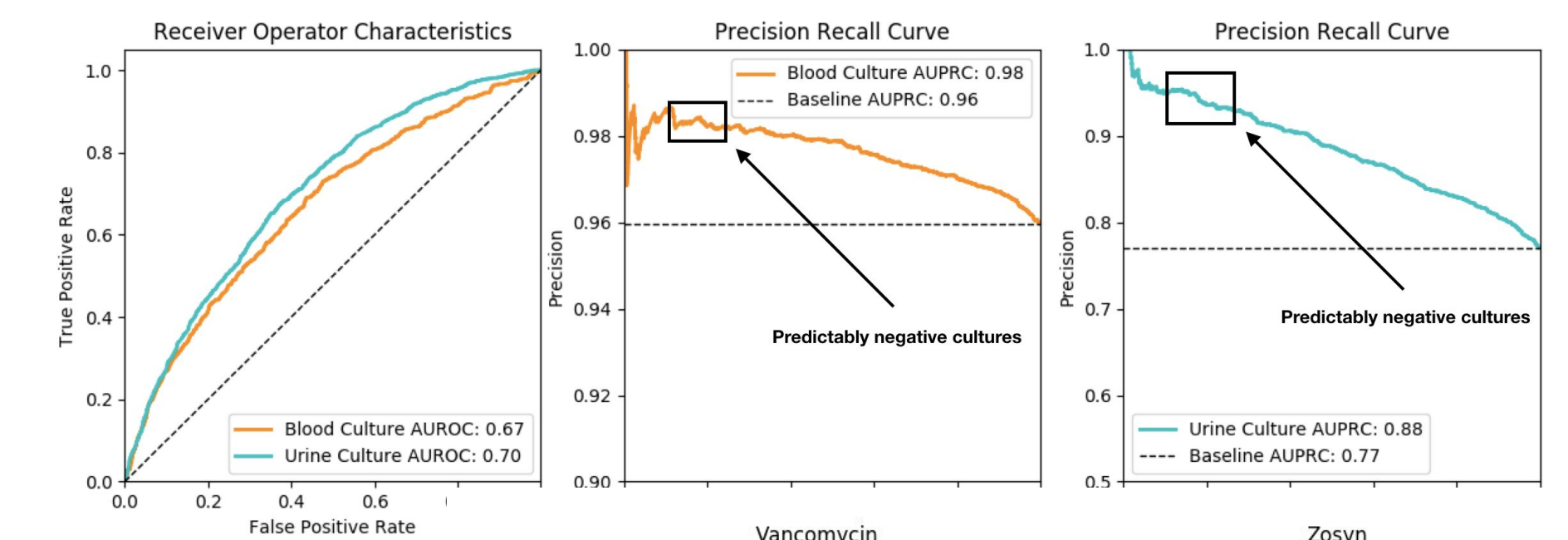
METHODS

- **Feature Engineering**: Counts of categorical events across varying time windows of patient timeline. Summary stats (mean, min, max, slope, first, last, std) of numerical features over the same time windows.
- **Feature Pruning:** Recursive feature selection to reduce the variance of our models
- **Machine Learning Models:** Logistic Regression with L1 regularization and Random Forest
- **Hyperparameters:** Tuned with k=10 fold cross validation over the training set.

## Experiments & Results

Predicting No Growth Cultures

- 80k Blood Cultures, 96% Negative
- 30k Urine Cultures, 77% Negative
- L1 Logistic Regression AUROC/AUPRC = 0.64/0.97 0.65/0.85 for blood and urine cultures respectively.
- Random Forest results shown on right .

Receiver Operator Characteristics — Blood Culture AUROC: 0.67; Urine Culture AUROC: 0.70

Precision Recall Curve — Blood Culture AUPRC: 0.98; Baseline AUPRC: 0.96; Predictably negative cultures

Precision Recall Curve — Urine Culture AUPRC: 0.88; Baseline AUPRC: 0.77; Predictably negative cultures

Predicting Bug Susceptibility

- 16 antibiotics - 16 binary classifiers
- + Labels: positive cultures and bug susceptible to drug
- - Labels: positive cultures and bug not susceptible to drug

Antibiotic	AUROC	AUPRC	Positive Prevalence
Vancomycin	0.86	0.98	0.92
Zosyn	0.70	0.96	0.93
Daptomycin	0.67	0.97	0.95
•	•	•	•
Amp/Sulbactam	0.55	0.61	0.56
Ceftriaxone	0.50	0.88	0.87
Oxacillin	0.49	0.71	0.71

Vancomycin / *Zosyn* — Susceptible / Not Susceptible
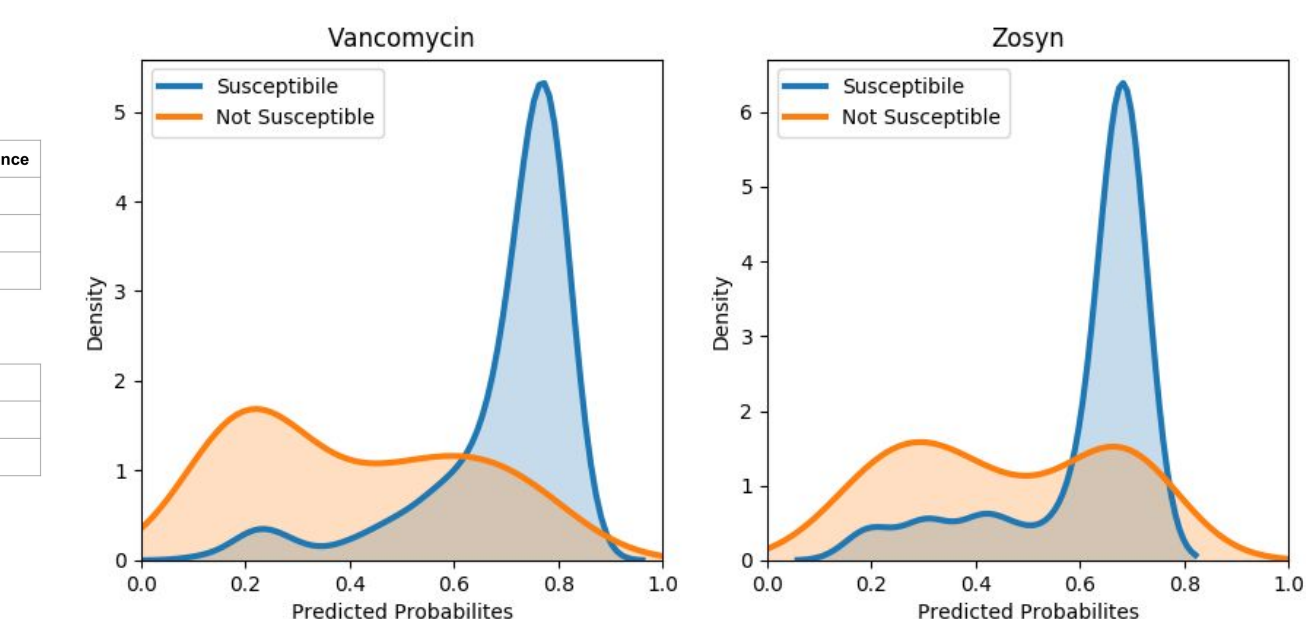
Personalized Antibiograms

- De-escalation pathway: Meropenem -> Pip/Tazo -> Ceftriaxone -> Cefazolin
- + Labels: E. Coli grew and susceptible to drug
- - Labels: E. Coli grew and not susceptible to drug
- Antibiogram is baseline prevalence
- N ~ 3129 samples

Drug	Susceptibility
Pip/Tazobactam	0.92
Ceftriaxone	0.76

Ceftriaxone — Random Forest AUPRC: 0.86
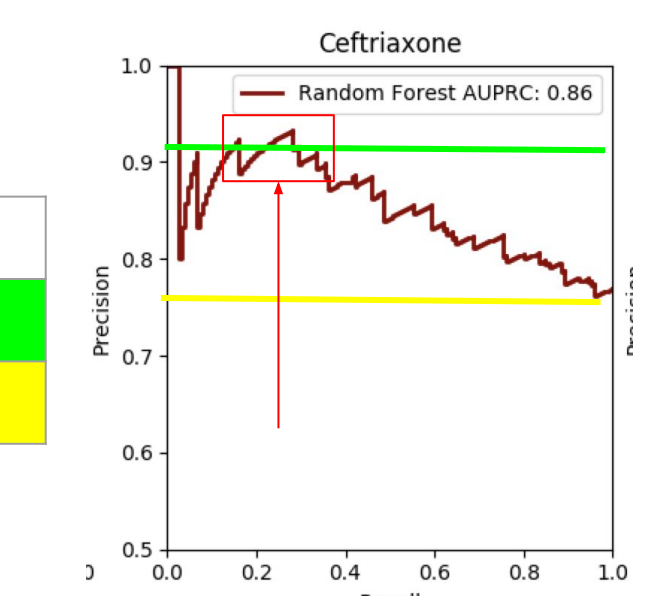
CONCLUSIONS

- Machine learning tools can be leveraged to predict no growth lab cultures, which may help prevent inappropriate antibiotic prescriptions.

- Personalized antibiograms allow de-escalation in cases where antibiograms alone do not.

- **Future Work:**

  ○ Expand personalized antibiograms to multiple bacteria type

  ○ Predict absence of MRSA (Methicillin Resistant Staph Aureus) in patients given Vanc Zosyn.

Refs: [1]Anstey, James E., Sara Murray, and Joanne W. Yim. "PREDICTING BACTEREMIA IN HOSPITALIZED PATIENTS: AN ANALYSIS OF ELECTRONIC HEALTH RECORD DATA." *JOURNAL OF GENERAL INTERNAL MEDICINE*. Vol. 33. 233 SPRING ST, NEW YORK, NY 10013 USA: SPRINGER, 2018. [2]Hernandez, Bernard, et al. "Supervised learning for infection risk inference using pathology data." *BMC medical informatics and decision making* 17.1 (2017): 168. [3]Paul, Mical, et al. "Improving empirical antibiotic treatment using TREAT, a computerized decision support system: cluster randomized trial." *Journal of Antimicrobial Chemotherapy* 58.6 (2006): 1238-1245. [4]Rawson, T. M., et al. "A systematic review of clinical decision support systems for antimicrobial management: are we failing to investigate these interventions appropriately?." *Clinical Microbiology and Infection* 23.8 (2017): 524-532.