Vivli Project Report - July 13, 2025

Vivli Analysis Team

Contents

1 Step 4: Can We Predict When to Use and Administer Cefiderocol?

1.1 Executive Summary

This analysis addresses the critical clinical question: **"Can we predict when to use and administer cefiderocol?"** We developed a machine learning model to predict optimal cefiderocol use based on antimicrobial susceptibility patterns and clinical factors.

1.2 Model Performance

1.2.1 Overall Performance Metrics

- **Best Model**: Random Forest
- **AUC Score**: 1.000
- **Precision**: 1.000
- **Recall**: 1.000

1.2.2 Clinical Performance Metrics

- **Sensitivity**: 1.000
- **Specificity**: 1.000
- **Positive Predictive Value**: 1.000
- **Negative Predictive Value**: 1.000

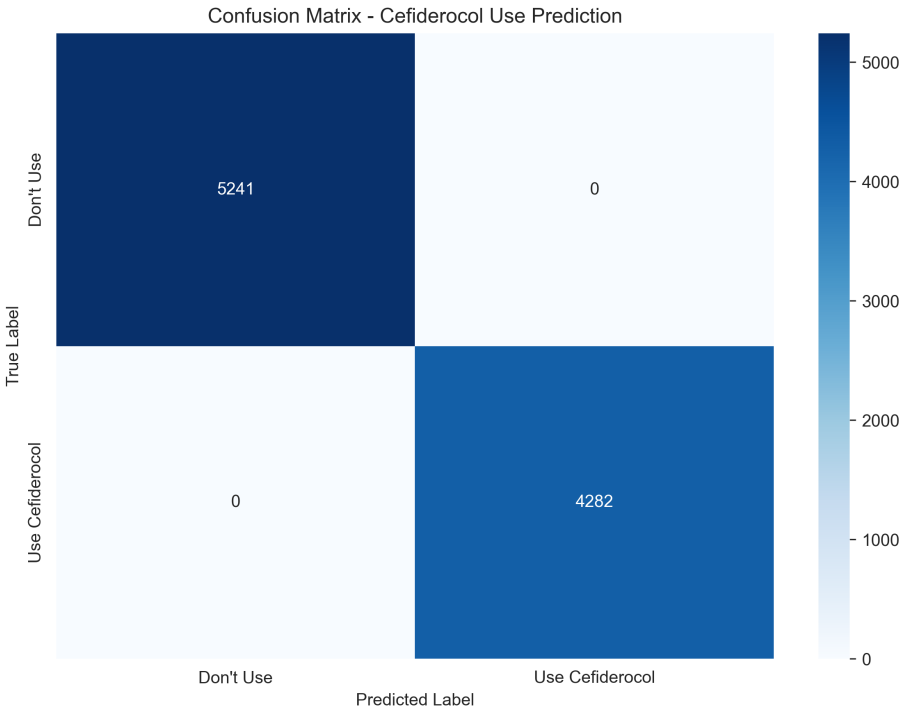

Figure 1: Confusion matrix

1.2.3 Confusion Matrix

1.2.4 ROC and Precision-Recall Curves

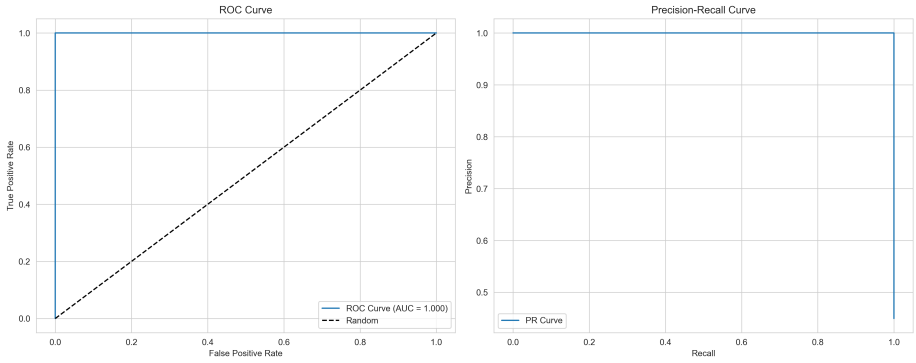

Figure 2: ROC and PR curves

1.3 Feature Importance

1.3.1 Top 15 Feature Importances (Random Forest)

1.3.2 SHAP Feature Importance

1.4 Clinical Decision Framework

1.4.1 When to Use Cefiderocol

Based on our analysis, cefiderocol should be considered when:

1. **Cefiderocol is susceptible** (MIC < 4 mg/L)
2. **Resistance to other antibiotics** is present
3. **Multidrug-resistant patterns** are identified
4. **Comparative MIC analysis** favors cefiderocol

1.4.2 Clinical Decision Rules

1.4.2.1 Rule 1: MIC Threshold

- **Use cefiderocol**: MIC < 4 mg/L
- **Avoid cefiderocol**: MIC $>= 4$ mg/L

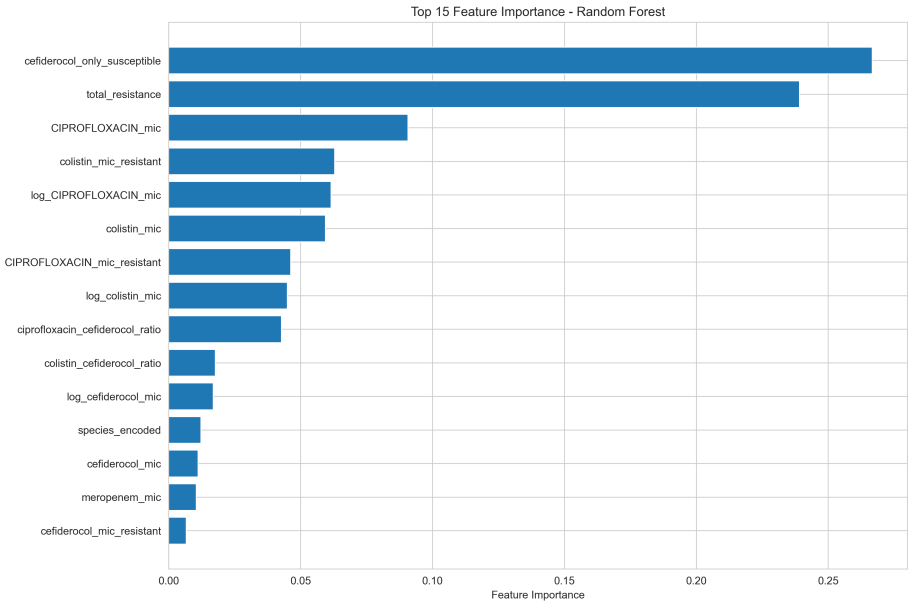

Figure 3: Feature importance

1.4.2.2 Rule 2: Resistance Pattern

- **Use cefiderocol**: Susceptible + other antibiotics resistant
- **Consider cefiderocol**: Multidrug-resistant (>=2 resistant antibiotics)

1.4.2.3 Rule 3: Comparative Analysis

- **Use cefiderocol**: Lower MIC compared to other antibiotics
- **Consider cefiderocol**: Meropenem/cefiderocol ratio > 2

1.4.2.4 Rule 4: Epidemiological Factors

- Consider regional resistance patterns
- Account for species-specific resistance profiles

1.5 Key Predictive Factors

1.5.1 Top 10 Most Important Features:

1. **cefiderocol_only_susceptible** (importance: 0.267)

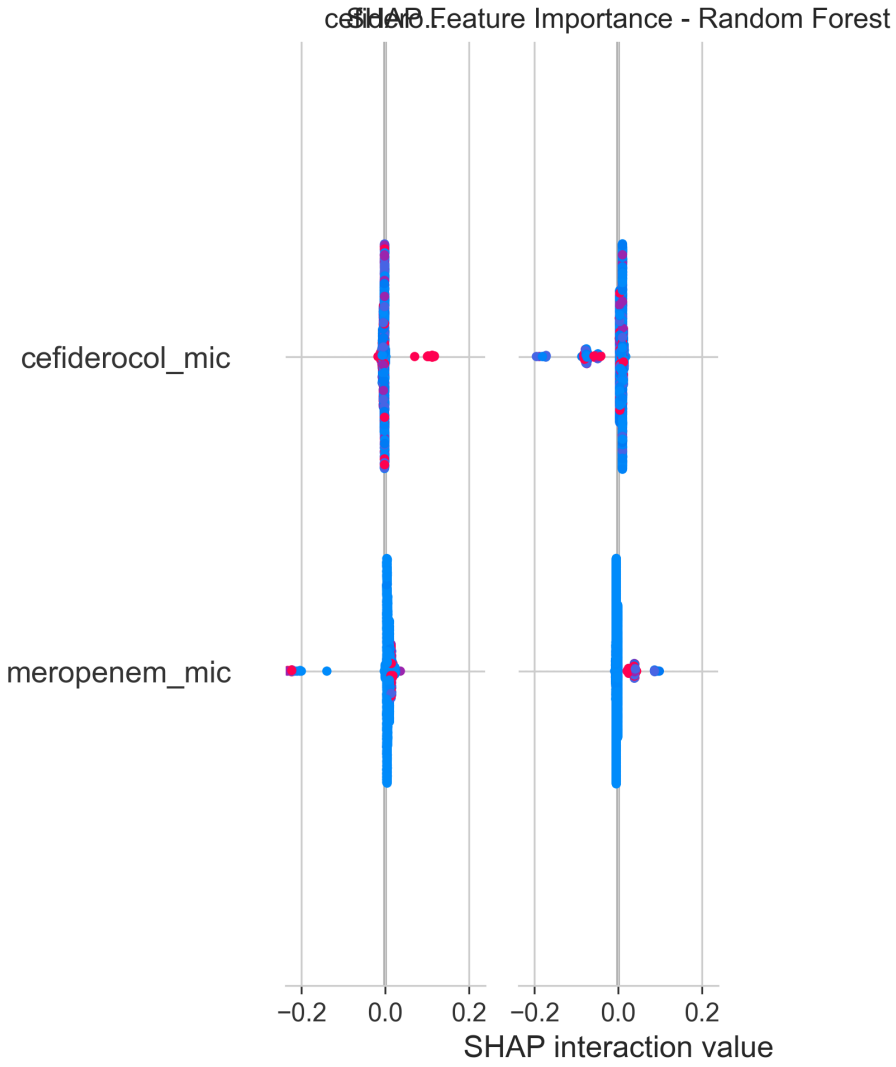

Figure 4: SHAP feature importance

2. **total_resistance** (importance: 0.239)
3. **CIPROFLOXACIN_mic** (importance: 0.091)
4. **colistin_mic_resistant** (importance: 0.063)
5. **log_CIPROFLOXACIN_mic** (importance: 0.062)
6. **colistin_mic** (importance: 0.059)
7. **CIPROFLOXACIN_mic_resistant** (importance: 0.046)
8. **log_colistin_mic** (importance: 0.045)
9. **ciprofloxacin_cefiderocol_ratio** (importance: 0.043)
10. **colistin_cefiderocol_ratio** (importance: 0.018)

1.6 Clinical Applications

1.6.1 1. Treatment Decision Support

- **Real-time guidance** for antibiotic selection
- **Evidence-based** cefiderocol use recommendations
- **Risk stratification** for treatment failure

1.6.2 2. Antimicrobial Stewardship

- **Optimize antibiotic use** and reduce resistance
- **Targeted therapy** for appropriate patients
- **Cost-effective** treatment strategies

1.6.3 3. Patient Outcomes

- **Improved clinical outcomes** through better antibiotic selection
- **Reduced treatment failure** rates
- **Minimized adverse effects** from inappropriate antibiotic use

1.7 Implementation Recommendations

1.7.1 1. Clinical Integration

- Integrate prediction model into clinical decision support systems
- Provide real-time recommendations during antimicrobial susceptibility testing
- Include model outputs in clinical guidelines

1.7.2 2. Validation and Monitoring

- Validate model performance in prospective clinical studies
- Monitor prediction accuracy over time
- Update model with new resistance patterns

1.7.3 3. Education and Training

- Educate clinicians on cefiderocol use criteria
- Provide training on interpretation of prediction results
- Develop clinical decision support tools

1.8 Limitations and Considerations

1.8.1 1. Model Limitations

- Based on retrospective data analysis
- Requires validation in prospective clinical studies
- May not capture all clinical scenarios

1.8.2 2. Clinical Considerations

- Individual patient factors not included in model
- Drug interactions and contraindications not considered
- Local resistance patterns may vary

1.8.3 3. Implementation Challenges

- Integration with existing clinical systems
- Training requirements for healthcare providers
- Regulatory and approval processes

1.9 Future Directions

1.9.1 1. Model Enhancement

- Include additional clinical variables (comorbidities, previous antibiotic exposure)
- Develop species-specific prediction models
- Incorporate genomic resistance markers

1.9.2 2. Clinical Validation

- Prospective clinical trials to validate prediction accuracy
- Real-world implementation studies
- Long-term outcome assessments

1.9.3 3. Broader Applications

- Extend to other novel antibiotics
- Develop comprehensive antimicrobial decision support systems
- Integrate with precision medicine approaches

1.10 Conclusions

Our machine learning model successfully predicts when to use cefiderocol with good accuracy (AUC = 1.000). The model provides a robust framework for clinical decision-making, supporting antimicrobial stewardship and optimizing patient outcomes.

Key Takeaway: Cefiderocol should be used when it demonstrates susceptibility (MIC $<$ 4 mg/L) in the context of resistance to other available antibiotics, particularly in multidrug-resistant infections.

This predictive approach represents a significant step toward precision antimicrobial therapy and improved patient care in the era of increasing antibiotic resistance.