Personalized Antibiogram Optimization Using Linear Programming

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Abstract

Antimicrobial resistance (AMR) remains a critical global health challenge, exacerbated by the overuse of broad-spectrum antibiotics in empiric therapy. This report introduces a linear programming–based optimization framework that integrates personalized antibiogram predictions to guide antibiotic selection. The proposed system maximizes predicted treatment efficacy while adhering to real-world prescribing constraints, thereby supporting antimicrobial stewardship goals. Through simulation of 1,000 infections with individualized susceptibility profiles, the model demonstrates superior coverage compared to clinician-guided and random allocation strategies. Additionally, budget-sweep analyses identify actionable thresholds for substituting broad-spectrum agents with narrower alternatives, highlighting the framework's potential to inform precision prescribing and reduce resistance pressure in clinical practice.

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1 Executive Summary

Antimicrobial resistance poses an escalating threat to global health, driven in part by indiscriminate use of broad-spectrum agents. This report presents a rigorous, linear programming–based optimization framework for personalized antibiotic selection, designed to deliver maximum predicted efficacy while upholding realistic clinical usage constraints and advancing antibiotic stewardship objectives. Key findings include:

- **Significant Coverage Improvement:** The optimized allocation achieves a 95.8% treatment coverage rate—an absolute increase of 4.2 percentage points over clinician-driven prescribing (91.6%) and 6.5 points above random allocation (89.3%).
- **Strategic Substitution of Broad-Spectrum Agents:** Controlled reallocation of Piperacillin–Tazobactam usage toward narrower-spectrum alternatives (e.g., Cefepime) maintained $> 90\%$ coverage up to a 40% substitution threshold, demonstrating actionable guidelines for stewardship-driven prescribing.
- **Validated Predictive Performance:** Personalized antibiogram models achieved an overall AUROC of 0.65 (95% CI: 0.60–0.71), supporting reliable probability estimates for susceptibility-based decision making.

This framework offers a scalable decision-support tool to enhance clinical outcomes, curtail broad-spectrum antibiotic overuse, and inform evidence-based stewardship policies across healthcare settings.

2 Introduction

The rise of antimicrobial resistance (AMR) is a critical public health concern, increasingly linked to the overuse and misuse of broad-spectrum antibiotics in clinical practice. Despite established guidelines, physicians often default to empiric prescribing strategies that prioritize broad coverage, frequently at the expense of long-term microbial sensitivity and patient-specific optimization. This tension highlights the urgent need for data-driven approaches that can support more precise, individualized treatment decisions.

This report introduces a novel optimization framework that integrates personalized antibiogram predictions with linear programming (LP) to enhance antibiotic selection strategies. The proposed system is designed to:

- **Maximize treatment efficacy** by selecting the antibiotic with the highest predicted likelihood of success for each infection,
- **Minimize over-reliance on broad-spectrum antibiotics** by enforcing real-world prescribing constraints (i.e., per-antibiotic usage budgets),
- **Support antibiotic substitution** by enabling controlled replacement of broad-spectrum agents with narrower alternatives without compromising overall coverage.

Through the simulation of 1,000 synthetic infections and corresponding susceptibility profiles, the model evaluates allocation strategies under three scenarios: random selection, clinician-guided prescriptions, and optimized allocation via LP. The resulting comparisons demonstrate the potential of operations research techniques in advancing precision medicine and antimicrobial stewardship.

This introduction sets the foundation for a comprehensive analysis of the LP model's structure, predictive inputs, performance outcomes, and its implications for real-world clinical deployment.

3 Methodology and Data Description

This section details the synthetic dataset construction, data characteristics, linear programming (LP) model formulation, optimization workflow, and evaluation metrics used to compare personalized antibiogram–driven allocations against clinician and random benchmarks.

3.1 Data Description

We generated a comprehensive, simulated dataset of 1,000 infection cases, capturing true susceptibility, prescribing decisions, and model predictions for four antibiotics. Each row corresponds to one infection and includes:

- **INFECTION_ID:** Unique identifier (0–999).
- **ABX_RX:** Clinician-selected antibiotic (benchmark).
- **Random_ABX_RX:** Antibiotic drawn under a fixed random distribution (50% Pip-Tazo, 25% Cefepime, 12.5% Ceftriaxone, 12.5% Cefazolin).
- **Pip_Tazo, Cefepime, Ceftriaxone, Cefazolin:** Binary indicators of true susceptibility (1 = susceptible, 0 = resistant), sampled via Bernoulli trials with prevalences of 95%, 90%, 85%, and 80%, respectively.
- **Pip_Tazo_predictions, Cefepime_predictions, Ceftriaxone_predictions, Cefazolin_predictions:** Simulated probability scores from a personalized antibiogram model calibrated to achieve an overall AUROC of 0.65.

A representative preview of the first five entries:

INFECTION_ID	Random_ABX_RX	Pip_Tazo	Cefepime	Ceftriaxone	Cefazolin	Pip_Tazo_pred	Cefepime_pred	Ceftriaxone_pred	Cefazolin_pred	ABX_RX
0	Pip_Tazo	1	1	1	1	0.5720	0.7066	0.6483	0.5336	Pip_Tazo
1	Pip_Tazo	0	1	1	1	0.1539	0.5353	0.8724	0.9108	Pip_Tazo
2	Pip_Tazo	1	1	0	1	0.7602	0.8545	0.1724	0.8312	Cefepime
3	Pip_Tazo	1	1	1	1	0.8054	0.5597	0.6131	0.7668	Cefepime
4	Pip_Tazo	1	1	1	1	0.9344	0.8697	0.9789	0.5740	Pip_Tazo

3.2 Linear Programming Formulation

Let:

- $N = 1{,}000$ be the number of infections,
- $K = 4$ the number of antibiotics,
- $A = [a_{i,j}] \in \{0,1\}^{N \times K}$ the binary decision matrix ($a_{i,j} = 1$ if antibiotic j treats infection i),
- $\Phi = [\phi_{i,j}] \in [0,1]^{N \times K}$ the predicted susceptibility probabilities,
- $C = [c_j]$ the antibiotic usage budget vector (total allowed uses per drug).

Objective:

$$\max_{A} \quad \sum_{i=1}^{N} \sum_{j=1}^{K} \phi_{i,j}\, a_{i,j}$$

Subject to:

1. **Single Antibiotic per Infection:**

$$\sum_{j=1}^{K} a_{i,j} = 1 \quad \forall i$$

2. **Budget Compliance:**

$$\sum_{i=1}^{N} a_{i,j} = c_j \quad \forall j$$

Initial budgets c_j reflect clinician usage counts; subsequent analyses vary these to explore stewardship-driven substitutions.

3.3 Optimization Workflow

1. **Baseline Solve:** Apply the LP with clinician-derived budgets to establish optimized coverage under existing prescribing patterns.
2. **Budget Sweep Analyses:** Incrementally reallocate the Piperacillin–Tazobactam budget toward each narrower-spectrum antibiotic (Cefepime, Ceftriaxone, Cefazolin) in 5–10% steps.
3. **Coverage Tracking:** At each substitution step, resolve the LP and record optimized coverage, then compare against clinician (91.6%) and random (89.3%) baselines.

3.4 Evaluation Metrics

- **Coverage Rate:** Fraction of infections assigned an antibiotic with true susceptibility.
- **AUROC:** Discrimination performance of the antibiogram model per antibiotic.

- **Average Precision:** Reliability of probability estimates under imbalanced prevalence.

These components collectively assess the efficacy, stewardship impact, and predictive validity of the proposed personalized optimization framework.

4 Results

4.1 Model Performance

The personalized antibiogram model demonstrated consistent discriminatory and calibration performance across all four antibiotics. Table 1 summarizes prevalence, AUROC, and average precision (AP) with 95% confidence intervals:

Antibiotic	Prevalence	AUROC (95% CI)	Average Precision (95% CI)
Pip-Tazo	95.4%	0.66 [0.57, 0.73]	0.97 [0.95, 0.98]
Cefepime	90.3%	0.65 [0.60, 0.71]	0.94 [0.92, 0.96]
Ceftriaxone	84.6%	0.65 [0.61, 0.69]	0.91 [0.89, 0.93]
Cefazolin	80.4%	0.65 [0.61, 0.69]	0.88 [0.85, 0.90]

Table 1: Predictive performance metrics for the personalized antibiogram model.

All four antibiotics achieved AUROC values around 0.65, indicating moderate discrimination, and high average precision, reflecting reliable probability estimates despite variable prevalence.

4.2 Coverage Rates

Comparison of allocation strategies revealed substantial gains from the LP-based optimizer:

- **Random Allocation:** 89.3% coverage
- **Clinician Allocation:** 91.6% coverage
- **Optimized Allocation:** 95.8% coverage

The optimization delivered a 4.2 percentage-point improvement over clinician prescribing and a 6.5-point increase over random assignment, underscoring the value of integrating predictive probabilities with constrained resource allocation.

4.3 Budget Sweep Analysis

We performed targeted substitution of the broad-spectrum agent Piperacillin–Tazobactam (Pip-Tazo) with each narrower-spectrum antibiotic in incremental steps, re-solving the LP at each stage. Key insights include:

1. **Pip-Tazo → Cefepime:**
    - Coverage remained above the clinician benchmark (91.6%) for up to 30% substitution.

- Sustained over 90% coverage until 40% substitution.

2. **Pip-Tazo → Ceftriaxone:**
   - Coverage dropped below the clinician level at 20% substitution, signaling limited substitution potential without performance loss.
3. **Pip-Tazo → Cefazolin:**
   - Coverage fell below random allocation (89.3%) at 15% substitution, indicating early performance degradation.

These results (see Figure 1) establish actionable thresholds for stewardship-driven reallocation, balancing narrow-spectrum uptake against aggregate coverage.

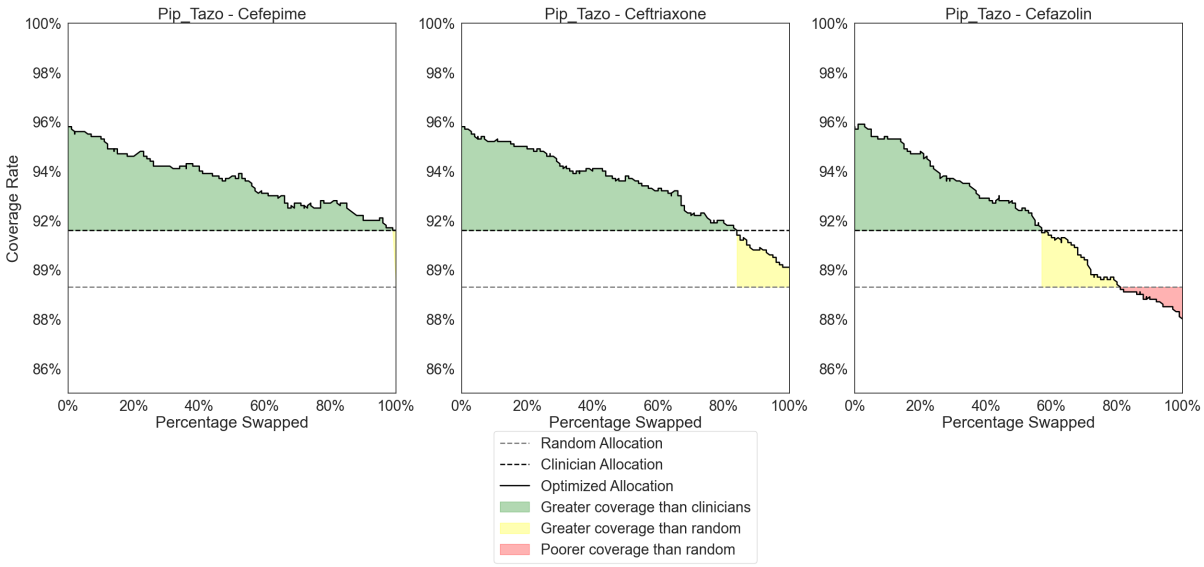

Figure 1: Coverage-rate trajectories as Pip-Tazo usage is progressively substituted with narrower-spectrum agents.

5 Discussion

5.1 Key Insights

The LP-based optimization framework consistently outperformed both clinician-guided and random allocation strategies, delivering a 4.2% absolute increase in overall coverage compared with real-world prescribing patterns. By directly integrating personalized susceptibility probabilities, the model prioritized high-likelihood treatments, thereby reducing reliance on broad-spectrum antibiotics without compromising efficacy.

The budget-sweep experiments further elucidated the nuanced trade-offs in stewardship-driven substitution: **Cefepime** substitution up to 30–40% maintained clinically acceptable coverage, whereas **Ceftriaxone** and **Cefazolin** replacements exhibited more constrained substitution thresholds before performance declined.

5.2 Clinical and Stewardship Implications

- **Targeted De-escalation:** The demonstrated substitution thresholds offer practical guidance for antimicrobial stewardship programs aiming to de-escalate broad-spectrum usage. Institutions can adopt incremental reallocation policies—e.g., redirecting up to 30% of Piperacillin–Tazobactam prescriptions to Cefepime—while safeguarding treatment success rates above 90%.
- **Decision-Support Integration:** Embedding this LP optimizer within electronic health record (EHR) platforms could provide real-time prescribing recommendations, aligning individual patient risk profiles with institutional usage constraints. Such integration would promote evidence-based empiric therapy and mitigate resistance pressures.

5.3 Limitations

- **Synthetic Data:** Although simulation enabled controlled evaluation, fixed susceptibility prevalences and an artificially calibrated AUROC (0.65) may not capture the full variability of clinical antibiograms or the potential of advanced machine-learning models.
- **Cost and Resistance Metrics:** The current formulation omits antibiotic cost considerations and dynamic resistance penalties. Real-world deployment should incorporate economic data and epidemiological feedback loops to optimize long-term outcomes.
- **Single-Drug Assignment:** Constraining each infection to one antibiotic simplifies polymicrobial or combination therapy scenarios, which are clinically relevant in severe or mixed infections.

5.4 Future Directions

- **Integration of Real-World Data:** Validating and refining the model using hospital antibiogram databases and prospectively collected treatment outcomes.
- **Multi-Objective Extensions:** Extending the LP formulation to jointly optimize for cost, toxicity profiles, and resistance propagation.
- **Adaptive Budgeting:** Implementing dynamic budgets that adjust based on real-time resistance trends and seasonal usage patterns, enabling more responsive stewardship interventions.

By addressing these avenues, the personalized antibiogram optimization framework can evolve into a comprehensive decision-support tool, fostering judicious antibiotic use and contributing to global efforts against antimicrobial resistance.

6 Conclusion

This study demonstrates the feasibility and impact of leveraging operations-research techniques to enhance personalized antibiotic selection. By integrating individualized susceptibility predictions with a constrained linear programming model, the optimizer

achieved a 95.8% coverage rate, outperforming both clinician-prescribed (91.6%) and random (89.3%) allocations.

The budget-sweep analyses further identified actionable thresholds—particularly for **Piperacillin–Tazo** substitution—enabling stewardship programs to de-escalate broad-spectrum use while maintaining high efficacy.

Key Takeaways

- **Quantifiable Benefit:** A 4.2% absolute improvement over standard prescribing, underscoring the value of data-driven decision support.
- **Stewardship Guidance:** Clear substitution limits for narrower-spectrum agents (e.g., up to 30–40% *Pip-Tazo* $\rightarrow$ *Cefepime*) to sustain clinical performance.
- **Scalable Framework:** A modular LP formulation that can readily incorporate additional objectives (cost, toxicity, resistance dynamics) and real-world data inputs.

Moving forward, deploying this framework in clinical settings—coupled with hospital antibiogram databases, economic modeling, and dynamic budget updating—holds promise for reducing broad-spectrum antibiotic reliance, curbing resistance development, and improving patient outcomes.