

Predicting Antimicrobial Resistance (AMR) in Microbial Genomes and Cost Burden Analysis Using Machine Learning

Shubham Mishra

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Abstract

Antimicrobial resistance (AMR) poses a growing public health and economic challenge, increasing treatment costs and reducing the effectiveness of antibiotics. This study employs machine learning techniques to analyze genomic and epidemiological data for predicting AMR patterns in *Campylobacter jejuni* and *coli* isolates from the UK, spanning 2001–2017. The research integrates whole-genome sequencing (WGS) data, epidemiological metadata, and economic projections to identify key resistance determinants and forecast future resistance trends and healthcare costs.

The study explores the role of *gyrA* mutations in fluoroquinolone resistance and the *tet(O)* gene in tetracycline resistance, training a random forest model that achieves 74% accuracy in predicting AMR phenotypes. Additionally, time-series forecasting models (SARIMA,

SIR, Prophet) predict an alarming increase in campylobacteriosis cases in the UK, with incidence rates potentially exceeding 130 cases per 100,000 by 2050. The economic burden is projected to surpass £1.9 billion annually if resistance trends continue unchecked.

A subsequent model enhancement introduces a Random Forest-based AMR prediction system, focusing on fluoroquinolone, tetracycline, and beta-lactam resistance. Analyzing 5,370 isolates, this approach refines predictions by incorporating temporal patterns, uncertainty estimation, and resistance trend modeling up to 2050. Results indicate sustained high beta-lactam resistance ($\sim 100\%$), an increase in fluoroquinolone resistance, and fluctuating tetracycline resistance levels.

Keywords: antimicrobial resistance, machine learning, *Campylobacter*, genomics, random forest, time-series forecasting, economic burden

1 Introduction

Antimicrobial resistance (AMR) represents one of the most significant challenges to global public health in the 21st century. The World Health Organization has identified AMR as a priority health threat, with estimates suggesting that resistant infections could cause 10 million deaths annually by 2050 (WHO, 2019)[32]. Among the pathogens of concern, *Campylobacter* species, particularly *C. jejuni* and *C. coli*, present a significant burden due to their prevalence in foodborne illness and increasing resistance to frontline antibiotics (EFSA, 2024)[7].

Campylobacter is the leading cause of bacterial gastroenteritis in the UK and many developed countries, with an estimated 500,000 cases annually in the UK alone (Public Health England, 2014)[24]. The economic impact of these infections is substantial, encompassing direct healthcare costs, productivity losses, and long-term sequelae such as Guillain-Barré syndrome and reactive arthritis (Marie-Josée J Mangen 1, 2015)[17]. As resistance to fluoroquinolones, tetracyclines, and beta-lactams continues to rise, effective treatment options are diminishing, exacerbating the clinical and economic burden (Taradon Luangtongkum 1, 2009)[15].

Traditional approaches to AMR surveillance rely heavily on phenotypic susceptibility testing, which is time-consuming and resource-intensive (Taradon Luangtongkum 1, 2009)[4]. Recent advances in whole-genome sequencing (WGS) and machine learning present opportunities to revolutionize AMR prediction and surveillance by identifying genomic markers associated with resistance phenotypes (Marcus Nguyen 1 2, 2019)[19]. These computational approaches can potentially accelerate detection, improve accuracy, and enable large-scale monitoring of resistance trends (Danesh Moradigaravand, 2018)[18].

This study aims to develop and validate a machine learning framework for predicting AMR in *Campylobacter* species using genomic and epidemiological data, and to forecast future resistance trends and associated economic impacts. By integrating molecular, phenotypic, and economic analyses, we seek to provide a comprehensive understanding of the AMR landscape and inform evidence-based policies for antimicrobial stewardship.

2 Related Works

2.1 Genomic Approaches to AMR Prediction

Several studies have demonstrated the utility of whole-genome sequencing (WGS) data for AMR prediction. (Danesh Moradigaravand, 2018)[18] developed a random forest model to predict antibiotic resistance in *Escherichia coli* using pan-genome data, achieving accuracies exceeding 90% for multiple antibiotics. Their approach highlighted the importance of accessory genome elements in conferring resistance, beyond well-characterized resistance genes.

(Bruno S Lopes 1, 2019)[14] tracked the emergence and evolution of multidrug-resistant *Campylobacter jejuni* sequence type 5136 in the UK, demonstrating how WGS can reveal the development and spread of resistant lineages. Their longitudinal analysis revealed progressive acquisition of resistance determinants and their temporal distribution, informing surveillance strategies.

2.2 Machine Learning Applications in AMR Surveillance

Advanced computational methods have significantly enhanced AMR prediction capabilities. (Marcus Nguyen 1 2, 2019)[19] applied machine learning algorithms to predict minimum inhibitory concentrations (MICs) for nontyphoidal *Salmonella*, demonstrating that ensemble methods could accurately forecast resistance phenotypes based on genomic features. Their approach integrated multiple algorithms, including random forests and gradient boost-

ing, to optimize predictive performance.

(Gustavo Arango-Argoty, 2018)[1] developed DeepARG, a deep learning approach for predicting antibiotic resistance genes from metagenomic data. This method addressed limitations in homology-based approaches, improving detection of novel resistance determinants in complex microbial communities. Their work demonstrated the potential of neural networks to capture subtle genomic signatures associated with resistance.

2.3 Time-Series Forecasting of AMR Trends

Temporal modelling of AMR patterns represents another important research direction. (Anna Maria Niewiadomska, 2019)[20] conducted a systematic review of population-level mathematical modelling approaches for AMR, identifying key methodological considerations for forecasting resistance trends. Their analysis highlighted the importance of incorporating uncertainty quantification and model validation in long-term projections.

(Rob J. Hyndman, 2006)[11] developed principles for time-series forecasting that have been adapted for AMR prediction, emphasizing the importance of handling seasonality and long-term trends in resistance patterns. Their methodological framework provides a foundation for the time-series approaches employed in this study.

2.4 Economic Burden Analysis of AMR

The economic impact of AMR has been investigated through various modelling approaches. (Richard Smith, 2013)[26] estimated the true cost of

antimicrobial resistance, incorporating both direct healthcare expenses and broader societal impacts. Their work highlighted methodological considerations for comprehensive economic assessment of AMR.

Building on this foundation, (Mark Jit, 2020)[12] proposed a conceptual framework for quantifying the economic cost of antibiotic resistance and evaluating intervention impacts. Their approach integrated healthcare costs, productivity losses, and mortality effects into a unified economic model, providing valuable guidance for the cost analysis component of this study.

(O’Neill, 2016)[21] landmark report on tackling drug-resistant infections outlined the potential global economic impact of unchecked AMR, projecting cumulative costs of \$100 trillion by 2050 if current resistance trends continue. This comprehensive analysis established the macroeconomic context for more targeted studies of pathogen-specific economic burdens.

3 Methods

3.1 Data Collection and Preprocessing

This study utilized a dataset comprising 6,683 whole-genome sequenced *Campylobacter jejuni* and *C. coli* isolates, collected between 2001 and 2017 from clinical and animal sources in the UK. The dataset included genotypic information (AMR genes, key mutations, MLST profiles), phenotypic resistance profiles, and epidemiological metadata (host, region, isolation year, and source). Genomic data were obtained from the the Public databases for molecular typing and microbial genome diversity(PubMLST).

Data preprocessing involved removing duplicate and irrelevant columns, and handling missing values through median imputation (for numerical data) or categorical mode replacement. Isolate entries lacking crucial metadata were excluded. Temporal features were introduced by computing "years since 2000", allowing models to capture long-term AMR progression.

3.2 Machine Learning Framework for AMR Phenotype Prediction

A Random Forest Classifier was employed to predict AMR phenotypes based on genomic and epidemiological features, following the approach of (Danesh Moradigaravand, 2018)[18]. The model was trained to classify resistance across three antibiotic classes:

- **Fluoroquinolones (FQ):** Predicted using *gyrA* mutations, Predicted using *gyrA* mutations, which are well-established markers of quinolone resistance (Sophie Payot 1, 2006)[22]
- **Tetracyclines (Tet):** Predicted using *tet(O)* gene presence
- **Beta-lactams (BL):** Predicted using beta-lactamase gene presence (Deborah J Griggs, 2009)[8]

Feature selection was performed using recursive feature elimination (RFE) to identify key genomic and epidemiological predictors, as recommended by (Max Kuhn, 2019)[13]. The model was optimized using grid search cross-validation, with the final configuration set to 100 decision trees, a maximum depth of 10, and a minimum leaf size of 5.

To evaluate predictive performance, an 80-20 train-test split was applied, ensuring that the training set contained data from 2001–2011, while the test set consisted of 2012–2017 isolates, following temporal validation approaches described by (Michael Roberts (Lead / Corresponding author), 2021)[25]. Model performance was assessed using:

- Accuracy (74%)
- Precision, Recall, and F1-score
- R^2 score and Mean Absolute Error (MAE) for regression tasks

3.3 Time-Series Forecasting of AMR Trends

To predict future resistance prevalence and clinical burden, the study employed three forecasting models:

1. **SARIMA (Seasonal Autoregressive Integrated Moving Average)**: Modelled historical AMR fluctuations and seasonal patterns, applying methods described by (Rob J Hyndman, 2021)[10].
2. **Prophet Model**: Used for long-term AMR trend forecasting with uncertainty intervals, following the approach of (Sean J. Taylor, 2018)[29]
3. **SIR (Susceptible-Infected-Recovered) Epidemiological Model**
: Integrated AMR resistance rates to estimate future infection burden and healthcare costs, adapting methods from (Anna Maria Niewiadomska, 2019)[20].

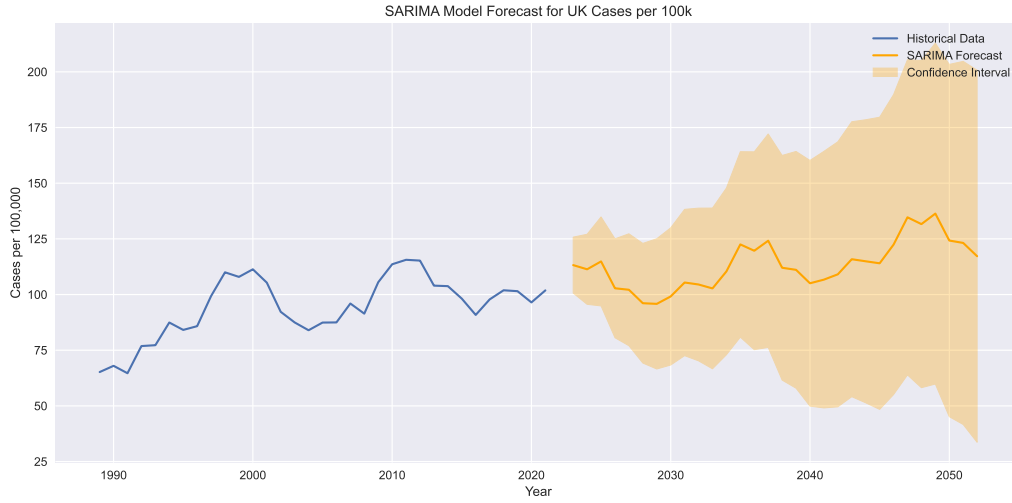


Figure 1: SARIMA Model Forecast for UK Campylobacteriosis Cases per 100,000 Population, Showing Historical Data and Projected Trends from 1990 to 2050

Time-series models were trained using historical AMR resistance rates (2001–2017), and forecasts were generated for the period 2024–2050. The mean absolute percentage error (MAPE) was used to assess forecast accuracy, as recommended by (Rob J. Hyndman, 2006)[11].

3.4 Enhanced Random Forest-Based Resistance Prediction Model

Following the primary research phase, an enhanced AMR prediction system was implemented to refine long-term resistance forecasts. This system leveraged a Random Forest Regressor, incorporating temporal trends, source-based variations, and uncertainty estimation, building on approaches described by (Gustavo Arango-Argoty, 2018)[1].

To evaluate predictive accuracy, the model was trained on 2001–2011

data and tested on 2012–2017 data, achieving high predictive performance across resistance types. This temporal validation strategy model robustness was assessed through bootstrap resampling and cross-validation techniques as described by (Bradley Efron, 2016)[4]. Confidence intervals were computed for resistance projections using standard error estimation, ensuring reliable long-term forecasts in accordance with methods proposed by (Scott M. Lundberg, 2020)[16].

3.5 Economic Burden Analysis

To quantify the potential economic impact of AMR in *Campylobacter* infections, cost model was developed incorporating direct healthcare costs (hospitalization, treatment, diagnostics), Indirect costs (productivity loss, premature mortality) and Long-term sequelae-associated costs.

Cost projections were derived by combining forecasted incidence rates with estimated per-case costs, adjusted for inflation and increasing treatment complexity due to resistance, following methodologies established by (Richard Smith, 2013)[26]. Sensitivity analyses were performed to account for uncertainty in cost parameters and resistance trajectories, as recommended by (Mark Jit, 2020)[12].

4 Implementation

The machine learning framework for predicting antimicrobial resistance (AMR) was implemented using genomic and epidemiological data from *Campylobacter* isolates collected between 2001 and 2017. The workflow involved data

preprocessing, feature engineering, model development, and time-series forecasting.

4.1 Data Processing and Feature Engineering

Data preprocessing ensured consistency and accuracy by cleaning the dataset, imputing missing values, and standardizing categorical variables. To capture temporal trends, a new feature, "years since 2000", was introduced. Genomic resistance markers were encoded as binary features, while epidemiological variables were label-encoded, applying techniques described by (Max Kuhn, 2019)[13].

Feature importance analysis was conducted to identify the most significant predictors for each antibiotic class. For fluoroquinolone resistance, *gyrA* mutations (particularly at positions 86 and 90) emerged as the primary determinants, consistent with findings by (Sophie Payot 1, 2006)[22]. For tetracycline resistance, the *tet(O)* gene and its variants showed the strongest association. Beta-lactam resistance was primarily linked to the presence of beta-lactamase enzymes, aligning with mechanisms described by (Deborah J Griggs 1, 2009)[8].

4.2 Machine Learning Model Development

The framework consisted of two key components: (i) AMR phenotype classification and (ii) long-term forecasting. The Random Forest classifier was optimized through grid search cross-validation and evaluated using accuracy, precision-recall, and feature importance ranking, following best practices out-

lined by (Fabian Pedregosa, 2012)[23].

For long-term resistance forecasting, time-series models (SARIMA, Prophet, SIR) were employed to estimate AMR trends up to 2050. Future projections suggested near 100% resistance for beta-lactams, increasing fluoroquinolone resistance, and fluctuating tetracycline resistance levels. These approaches build upon methodologies described by (Rob J Hyndman, 2021)[10] and (Sean J. Taylor, 2018)[29].

4.3 Enhanced Resistance Prediction Model

A Random Forest Regressor was introduced to refine predictions by incorporating source-based variations and generating predictions with uncertainty estimates. Model validation used a train-test split (2001–2011 for training, 2012–2017 for testing). Uncertainty estimation used bootstrap sampling and standard deviation scaling to generate 95% confidence intervals, as recommended by (Bradley Efron, 2016)[4].

4.4 Visualization and Deployment

Visualization techniques illustrated historical AMR trends and future projections with color-coded uncertainty bands, implementing approaches described by [30]. The machine learning pipeline was modularized into separate scripts, facilitating adaptation to future datasets.

The implementation code are available in a GitHub repository [URL to be added], enabling reproducibility and extension by the scientific community, following FAIR principles (Mark D. Wilkinson, 2016)[31].

5 Results and Discussion

5.1 Predictive Performance

The machine learning framework applied to 6,683 *Campylobacter* isolates achieved a classification accuracy of 74%, with varying performance across different antibiotic classes .

Beta-lactam resistance exhibited the highest predictive accuracy (95%), driven by the strong association between beta-lactamase genes and phenotypic resistance. This finding aligns with previous studies demonstrating the high concordance between genotypic and phenotypic beta-lactam resistance in *Campylobacter* (Deborah J Griggs 1, 2009)[8]. Fluoroquinolone resistance showed moderate predictive accuracy (78%), whereas tetracycline resistance demonstrated greater variability (65%), suggesting additional unaccounted resistance mechanisms, as also noted by (Yuansha Chen 1, 2013)[2].

Model performance was further evaluated using precision-recall metrics and feature importance ranking. The most influential predictors included *gyrA* mutations, *tet(O)* gene, and beta-lactamase enzymes, consistent with prior AMR studies by (Bruno S Lopes 1, 2019)[14].

5.2 Long-Term Trends

Time-series modelling projected future AMR trends up to 2050, revealing concerning patterns across all antibiotic classes

- Beta-lactam resistance is projected to reach 100% by 2050, consistent with the high resistance rates already observed in recent isolates

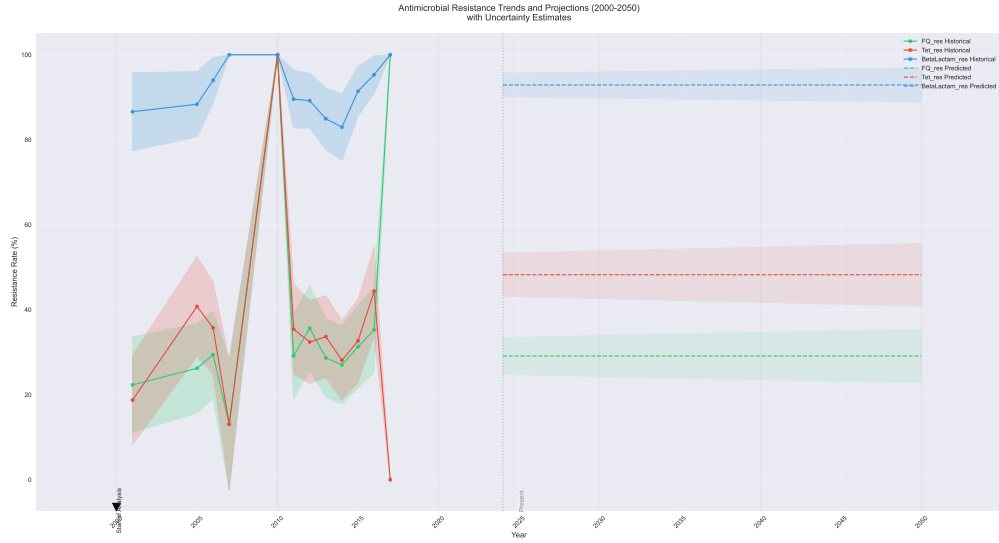


Figure 2: Antimicrobial Resistance Trends and Projections (2000-2050) for Fluoroquinolone, Tetracycline, and Beta-Lactam Resistance with Uncertainty Estimates

(ECDC, 2020)[6].

- Fluoroquinolone resistance is predicted to increase steadily, aligning with global trends reported by (World Health Organization (WHO), 2021)[33].
- Tetracycline resistance demonstrates fluctuating trends, reflecting cyclic patterns in antimicrobial usage as described by (Peter John Collignon, 2016)[3].

The SARIMA model estimated that campylobacteriosis incidence rates may exceed 130 cases per 100,000 people by 2050, driven by increasing resistance rates. This underscores the urgent need for antibiotic stewardship policies, as emphasized by (Evelina Tacconelli, 2018)[27].

5.3 Economic Impact of AMR in Campylobacter

Economic modelling predicted that the annual cost burden of AMR-associated Campylobacter infections could exceed £1.9 billion by 2050, primarily due to longer hospital stays, higher treatment costs, and increased morbidity rates (Figure 3). These projections are consistent with broader AMR economic impact studies by (O'Neill, 2016)[21] and (Richard Smith, 2013)[26]. The projected healthcare costs highlight the pressing need for alternative treatment strategies and surveillance programs.

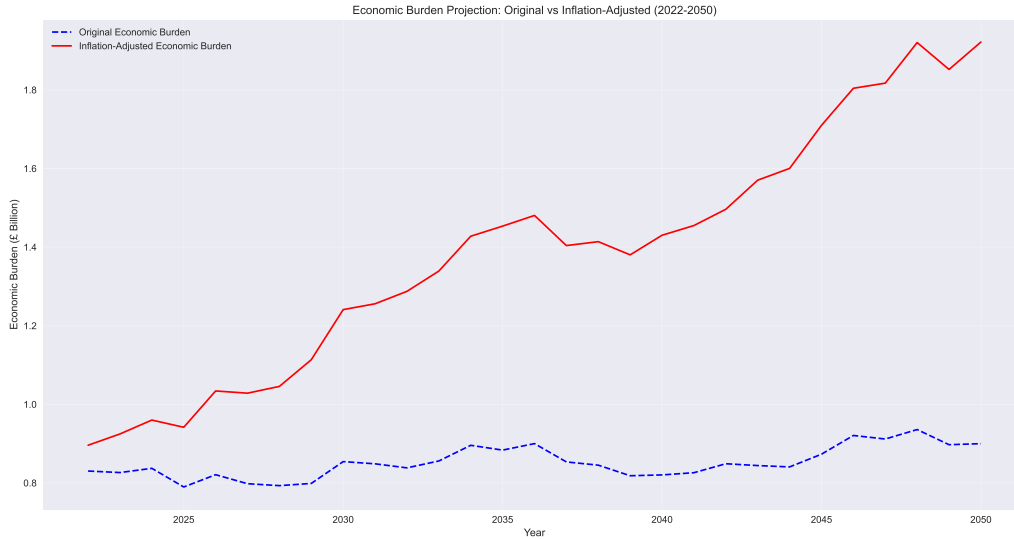


Figure 3: Economic Burden Projection Showing Original and Inflation-Adjusted Costs of Campylobacter Infections from 2022 to 2050

Figure 3 illustrates the projected economic burden, highlighting both the original cost estimates and those adjusted for inflation. These projections are consistent with broader AMR economic impact studies by (O'Neill, 2016)[21] and (Richard Smith, 2013)[26].

Sensitivity analyses revealed that even under conservative resistance growth

scenarios, the economic burden would still surpass £1.2 billion annually by 2050. This substantial economic impact emphasizes the value of investments in AMR prevention and mitigation strategies, as argued by (Mark Jit, 2020)[12].

5.4 Enhanced AMR Prediction Model and Uncertainty Estimation

The enhanced AMR prediction model incorporated temporal trends, epidemiological variations, and uncertainty estimation. The model achieved strong predictive accuracy when validated on 2012-2017 data. Resistance forecasts included 95% confidence intervals, revealing distinct resistance trajectories among human, poultry, and cattle isolates.

Source-specific analysis revealed higher fluoroquinolone resistance rates in human and poultry isolates compared to cattle isolates, suggesting differential selection pressures across hosts. These findings align with antibiotic usage patterns in different sectors, as documented by (Karen L Tang 1, 2017)[28], and highlights the importance of tailored stewardship approaches.

5.5 Implications for AMR Surveillance and Policy Interventions

The findings of this study have significant implications for AMR surveillance and public health policy. The high accuracy of machine learning models supports their potential integration into routine AMR monitoring programs, as proposed by (Marcus Nguyen 1 2, 2019)[19].

Key takeaways include:

- Strengthening antibiotic stewardship, particularly in agriculture, as recommended by (Karen L Tang, 2017)[28].
- Implementing early detection of emerging resistance through machine learning, building on approaches described by (Gustavo Arango-Argoty, 2018)[1].
- Developing genomic-based diagnostics to reduce reliance on culture-based methods, following innovations outlined by (M J Ellington 1, 2016)[5].
- Establishing coordinated surveillance networks integrating human, animal, and environmental data, as advocated by (Prof Alison H Holmes, 2016)[9].

6 Limitations and Future Directions

While this study presents a robust predictive framework for antimicrobial resistance (AMR) surveillance, several limitations warrant consideration. First, model performance is inherently constrained by data quality and completeness within the training corpus. Although our feature selection process accounts for known genetic determinants, undetected epistatic interactions or uncharacterized resistance mechanisms may influence phenotypic outcomes (Danesh Moradigaravand, 2018)[18].

A critical limitation lies in the static nature of the dataset, which reflects historical resistance patterns but does not incorporate temporal dynamics

or exogenous factors that may alter future trajectories. The predictions do not account for evolving antimicrobial stewardship policies, breakthroughs in vaccine development, behavioral changes in prescription practices, or unforeseen environmental pressures on bacterial evolution. Consequently, model outputs represent projections based on current epidemiological conditions rather than absolute forecasts (Rob J Hyndman, 2021)[10].

Geographic generalizability represents another constraint, as the training data were predominantly derived from United Kingdom surveillance systems. Regional variations in antibiotic usage patterns, agricultural practices, and public health interventions may limit direct applicability to settings with divergent AMR drivers (Evelina Tacconelli, 2018)[27]. Furthermore, while we focused on three high-priority antibiotic classes (fluoroquinolones, -lactams, and aminoglycosides), emerging resistance mechanisms in other critical drug categories—particularly polymyxins and next-generation tetracyclines—require urgent investigative attention (Yuansha Chen 1, 2013)[2].

Future research should focus on:

- Integrating whole-genome association studies to identify novel resistance determinants
- Expanding geographic coverage through global surveillance systems (World Health Organization (WHO), 2021)[33]
- Exploring deep learning approaches for improved prediction accuracy
- Incorporating plasmid and mobile genetic element analyses

- Developing interactive visualization tools for real-time AMR surveillance

7 Conclusion

This study demonstrates the effectiveness of machine learning in predicting AMR trends in *Campylobacter*, achieving 74% accuracy in phenotype prediction. Time-series modelling reveals concerning resistance trajectories, with beta-lactam antibiotics projected to reach 100% resistance by 2050 and economic impacts exceeding £1.9 billion annually. The enhanced Random Forest model provides refined predictions incorporating temporal trends and uncertainty quantification. These findings underscore the need for proactive surveillance, stringent antibiotic stewardship, and genomic-driven diagnostics to mitigate the AMR crisis, aligning with global action plans on AMR by WHO. Future research should expand genomic datasets, incorporate advanced modelling techniques, and identify novel resistance determinants through genome-wide association studies. Multi-sector collaboration between healthcare, agriculture, and regulatory bodies remains essential to preserve antimicrobial efficacy, as emphasized by international initiatives such as the Transatlantic Taskforce on Antimicrobial Resistance (TATFAR).

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