Review Articles

Artificial Intelligence in Bacterial Infectious Diseases: From Diagnosis to Drug Discovery

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ABSTRACT

Bacterial infectious diseases remain a formidable global health challenge, exacerbated by the relentless rise of antimicrobial resistance (AMR) and the emergence of novel pathogens. Artificial intelligence (AI), encompassing machine learning (ML), deep learning (DL), and natural language processing (NLP), has emerged as a transformative paradigm across the entire spectrum of bacterial infection management. This review synthesizes recent advances in AI applications for bacterial infectious diseases, spanning rapid pathogen identification, antimicrobial susceptibility testing, genomic surveillance, epidemiological monitoring, antibiotic discovery, and clinical decision support. We highlight how AI-driven technologies are accelerating diagnostic timelines from days to minutes, enabling real-time resistance profiling, and uncovering novel therapeutic candidates. Furthermore, we examine the critical challenges impeding clinical translation, distinguishing between engineering-level obstacles, algorithmic-level tensions, and institutional-level barriers. By fostering interdisciplinary collaboration among clinicians, microbiologists, computational scientists, and policymakers, AI holds the potential to revolutionize our approach to bacterial infections and mitigate the looming AMR crisis.

1. Introduction

Bacterial infectious diseases continue to impose a substantial burden on global public health. According to the Global Burden of Disease Study 2019, the 33 bacterial pathogens investigated were associated with approximately 7.7 million deaths globally in 2019, which would rank as the second leading cause of death worldwide [1]. The therapeutic landscape has been further complicated by the accelerating emergence of antimicrobial resistance (AMR). The same GBD study estimated that in 2019, 1.27 million deaths were directly attributable to bacterial AMR, with 4.95 million deaths associated with resistant bacterial infections [2]. The World Health Organization (WHO) has designated AMR as one of the top ten global public health threats facing humanity [3].

Traditional approaches to bacterial infection management—from culture-based diagnostics to empirical antibiotic prescribing—are increasingly inadequate in the face of multidrug-resistant organisms. The WHO 2024 Bacterial Priority Pathogens List (BPPL) identifies carbapenem-resistant Klebsiella pneumoniae (CRKP), carbapenem-resistant Acinetobacter baumannii, and rifampicin-resistant Mycobacterium tuberculosis as critical-priority threats, alongside high-priority pathogens including methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant Enterococcus faecium. These organisms collectively account for the majority of healthcare-associated infections worldwide and are characterized by high mortality rates, limited therapeutic options, and rapid transmissibility [4].

In parallel, the rapid evolution of artificial intelligence (AI) has catalyzed unprecedented opportunities across biomedical sciences. AI, particularly its subfields of machine learning (ML) and deep learning (DL), offers powerful capabilities for pattern recognition, predictive modeling, and automated decision-making from complex, high-dimensional data [5]. In the context of bacterial infectious diseases, AI is being leveraged to enhance diagnostic accuracy, compress turnaround times, predict resistance patterns, optimize therapeutic strategies, and discover novel antimicrobial agents [6][7].

This review provides a comprehensive synthesis of the current landscape of AI applications in bacterial infectious disease management. We examine the technological foundations, clinical implementations, and translational

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challenges, while outlining future directions for this rapidly evolving interdisciplinary field.

2. AI in Bacterial Infection Diagnosis

The diagnostic microbiology laboratory represents one of the most active frontiers for AI deployment in bacterial infection management. Recent comprehensive reviews have systematically catalogued the expanding landscape of AI-enabled diagnostic modalities, from automated microscopy to genomic resistance prediction [8]. The following sections examine the principal technological pillars of this transformation.

2.1. Rapid Pathogen Identification

Conventional microbiological diagnosis relies on phenotypic culture methods that typically require 24–72 hours for pathogen isolation and identification. AI-powered approaches are dramatically compressing these timelines. Deep learning algorithms applied to digital microscopy enable automated detection and classification of bacterial species from Gram-stained smears, blood cultures, and tissue sections with accuracy approaching or exceeding that of experienced microbiologists [9].

For instance, convolutional neural networks (CNNs) trained on large datasets of bacterial images have demonstrated high sensitivity and specificity in identifying acid-fast bacilli (AFB) in sputum smears, significantly improving tuberculosis screening efficiency. Similarly, automated plate reading systems such as APAS Independence employ digital image analysis to accurately classify MRSA and methicillin-sensitive S. aureus (MSSA) cultures without human intervention, substantially enhancing laboratory throughput. In a prospective evaluation of 5,913 CHROMagar MRSA cultures, APAS achieved 100% positive percent agreement and 97.3% negative percent agreement compared to manual reading, with a negative predictive value of 100%, enabling reliable autonomous negative reporting [10].

Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) has revolutionized clinical microbiology, and its integration with machine learning algorithms has further enhanced diagnostic capabilities. Novel ML-based MALDI-TOF MS methods enable rapid identification of MRSA and CRKP directly from positive blood cultures within one hour, a dramatic improvement over conventional protocols [11].

2.2. Antimicrobial Susceptibility Testing (AST)

Standard AST methods, including disk diffusion and broth microdilution, require an additional 18–24 hours following pathogen isolation, creating a critical therapeutic window where clinicians must rely on empirical broad-spectrum antibiotics. AI-integrated technologies are addressing this bottleneck through multiple innovative approaches.

Raman spectroscopy combined with image stitching technology enables single-cell-level detection of drug-resistant bacteria, providing automated and rapid resistance profiling. Machine learning-enhanced infrared spectroscopy has been shown to reduce the identification and susceptibility testing time for common uropathogens—including Escherichia coli, Proteus mirabilis, and Pseudomonas aeruginosa—from 48 hours to approximately 40 minutes [9].

Microfluidic platforms such as the SlipChip device leverage dielectrophoresis for bacterial enrichment from positive blood cultures, enabling parallel AST in nanoliter droplets with results available within 3–8 hours [12]. In proof-of-concept studies, the SlipChip device demonstrated susceptibility pattern determination for E. coli and S. aureus against multiple broad-spectrum antibiotics, with results well matched to broth microdilution and automated microbiology systems. These innovations collectively represent a paradigm shift toward rapid, AI-enhanced phenotypic susceptibility testing that can guide targeted therapy significantly earlier in the clinical course.

2.3. Genomic Analysis and Resistance Prediction

Whole-genome sequencing (WGS) and next-generation sequencing (NGS) have transformed pathogen identification and transmission tracking. However, traditional bioinformatics pipelines rely on sequence similarity matching, which may fail when encountering novel species or uncharacterized resistance mechanisms. Machine learning models address this limitation by learning predictive patterns from genomic features.

The machine learning-based PaPrBaG (Pathogenicity Prediction for Bacterial Genomes) method provides reliable bacterial classification even with extremely low genome coverage (as low as 0.001×), maintaining robustness when reference databases are incomplete—a critical advantage over alignment-based approaches that fail when no closely related genomes are available [13]. Furthermore, ML algorithms such as XGBoost and convolutional neural networks have demonstrated exceptional performance in predicting minimum inhibitory concentrations (MICs) for K. pneumoniae clinical isolates against multiple antimicrobial agents, simultaneously identifying highly resistant or virulent strains [9].

In tuberculosis diagnostics, the Treesist-TB decision tree approach was developed to customize machine learning to the TB setting by extracting genomic variants recurring across multiple studies. When applied to 32,689 M. tuberculosis samples, Treesist-TB achieved predictive accuracy comparable to TB-Profiler for first-line drugs (rifampicin: 97.5% vs. 97.6%; isoniazid: 96.8% vs. 96.5%) while identifying new resistance-conferring variants for less understood second-line drugs, with improved sensitivity for para-aminosalicylic acid (64.3% vs. 38.8%) and cycloserine (45.3% vs. 30.7%) [14]. This approach offers a template extensible to other resistant pathogens.

3. AI in Epidemiological Surveillance

Bacterial disease outbreaks, whether healthcare-associated or community-acquired, require rapid detection and response to prevent widespread transmission. AI-driven surveillance systems are enhancing traditional epidemiological methods through real-time data integration and predictive analytics.

Machine learning models can simulate and predict the complex mechanisms of pathogen-host interactions, providing crucial insights into disease transmission dynamics [6]. AI-powered early warning systems integrate diverse data streams—including electronic health records (EHRs), laboratory information systems, environmental sensors, and syndromic surveillance data—to detect anomalous patterns indicative of emerging outbreaks [5].

Several operational platforms demonstrate the clinical translation of these capabilities. BlueDot, a Canadian health surveillance company founded in 2013, uses AI, NLP, and big data analytics to track and predict infectious disease outbreaks globally. On December 30, 2019, BlueDot identified clusters of unusual pneumonia in Wuhan, China—nine days before the WHO officially announced COVID-19—by analyzing over 100,000 data sources daily in 65 languages, including news reports, airline ticketing data,

and animal disease outbreak records [15]. The system accurately predicted high-risk international destinations based on travel patterns, with Tokyo, Singapore, Hong Kong, and Bangkok among the correctly identified cities. BlueDot had previously predicted the Zika virus spread to Florida six months before occurrence and the 2014 Ebola outbreak in West Africa [16].

HealthMap, developed at Boston Children's Hospital, processes approximately 80 infectious disease alerts daily using Bayesian filtering and text processing algorithms, successfully detecting unidentified pneumonic cases in Wuhan a day before the official Chinese government announcement. The system reports an accuracy of 84% for automated event categorization in earlier validation studies [17].

EPIWATCH, another AI-based platform, employs BERT-based NLP models to assess article relevance to outbreaks, achieving 88.2% accuracy in curated source evaluation. These systems collectively illustrate how NLP algorithms applied to unstructured clinical notes, social media feeds, and news reports enable automated event extraction and geospatial mapping of infectious disease signals. While these examples prominently feature viral outbreaks, the conceptual framework extends naturally to bacterial pathogens, where similar methodologies are being deployed for real-time monitoring of AMR trends and nosocomial infection clusters [5][6].

4. AI in Antimicrobial Resistance Monitoring

AMR represents a critical frontier where AI technologies are demonstrating substantial impact. Supervised learning, unsupervised learning, reinforcement learning, and NLP are being deployed across diverse data sources—including clinical records, genomic sequences, microbiome profiles, and epidemiological databases—to predict resistance outbreaks and guide therapeutic decisions [7].

Predictive models leveraging gradient-boosted trees and ensemble methods have achieved promising performance in forecasting resistance patterns. Lewin-Epstein et al. (2021) applied gradient-boosted trees, neural networks, and logistic regression with LASSO to predict antibiotic resistance profiles among hospitalized patients, with ensemble models achieving AUC values ranging from 0.73 to 0.79; performance improved to 0.80–0.88 when the infecting bacterial species was assumed known [18]. In a separate study utilizing random forest algorithms for multidrug-resistant organism (MDRO) prediction, AUC values of 0.87 and 0.89 were achieved in training and testing sets, respectively, with 82% sensitivity and 83% specificity. These findings demonstrate that tree-based ensemble algorithms, including XGBoost and random forest, play an important role in achieving higher predictive accuracy for resistance profiling [19].

Neural network architectures applied to genomic data can identify resistance determinants within hours rather than the days required by conventional phenotypic testing. At the public health level, AI-driven surveillance platforms improve AMR trend detection and enhance global monitoring capabilities. By integrating EHRs, microbiological data, and environmental surveillance, ML models provide actionable insights to policymakers and public health officials, enabling targeted interventions and resource allocation [7].

5. AI in Antibiotic Discovery and Development

The discovery of novel antibiotics has slowed dramatically over the past decades, even as resistance rates continue to escalate. AI is revitalizing this pipeline through de novo molecular design, drug repurposing, and target identification.

A landmark study by Stokes et al. employed a deep neural network model to screen chemical libraries, identifying halicin—a structurally novel broad-spectrum antibiotic effective against E. coli, carbapenem-resistant Enterobacteriaceae (CRE), and A. baumannii [20]. This compound exhibits a unique mechanism of action (collapsing bacterial membrane potential) distinct from existing antibiotic classes, demonstrating AI's capacity to explore chemical spaces beyond conventional medicinal chemistry approaches.

Subsequent work by the same group utilized message-passing deep neural networks to analyze approximately 7,500 molecules with anti-A. baumannii activity, leading to the discovery of abaucin—a narrow-spectrum agent specifically targeting this critical nosocomial pathogen [21]. The narrow spectrum represents a particularly valuable attribute, as it minimizes disruption to commensal microbiota and reduces selective pressure for resistance development. Abaucin perturbs lipoprotein trafficking through LolE inhibition and has demonstrated efficacy in a murine wound infection model [22].

AI-driven approaches also facilitate drug repurposing by predicting off-target antimicrobial activities among existing pharmaceutical compounds. Deep learning models analyzing molecular structures and pharmacokinetic properties can rapidly prioritize candidates for experimental validation, substantially accelerating the preclinical development timeline [7].

6. AI-Driven Clinical Decision Support Systems (CDSS)

Clinical decision support systems represent one of the most clinically proximal applications of AI in infectious disease management. These systems leverage multimodal EHR data to guide practitioners across the continuum of care—from empirical antibiotic selection to treatment individualization and de-escalation [5].

Contemporary AI-CDSS increasingly integrate structured clinical data, laboratory values, microbiology results, and imaging findings to generate personalized therapeutic recommendations. Some systems have achieved clinician-level accuracy in diagnostic and prescribing tasks, demonstrating the technical feasibility of AI-augmented infection management.

However, significant translational barriers persist. Traditional CDSS algorithms often operate in isolation, addressing discrete tasks such as empirical treatment or microbial diagnosis without considering the continuous, interconnected nature of clinical decision-making. Emerging concepts such as "Digital Twin" platforms propose a more holistic approach, providing continuous, integrated support across all stages of infection management with dynamic updating based on patient data and clinical decisions.

Despite promising diagnostic performance, the critical question remains whether AI-driven interventions actually improve clinical outcomes. The gap between technical accuracy and clinical impact represents a recognized priority for rigorous evaluation.

The INSPIRE (Intelligent Stewardship Prompts to Improve Real-Time Empiric Antibiotic Selection) trials represent the largest cluster-randomized controlled evaluations of AI-enhanced antibiotic stewardship to date. Conducted across 59 hospitals in a US health system, the INSPIRE pneumonia trial demonstrated that computerized provider order entry (CPOE) prompts—triggered when an algorithm determined low risk for multidrug-resistant organisms—significantly reduced extended-spectrum antibiotic use for pneumonia without compromising patient safety [22]. The companion INSPIRE urinary tract infection trial achieved similar reductions in inappropriate broad-spectrum prescribing [23]. Subsequent INSPIRE trials for skin and soft tissue infections (INSPIRE 3) and

abdominal infections (INSPIRE 4) have further expanded this evidence base [24][25].

In a separate randomized controlled trial (ISRCTN16278872), Lin et al. evaluated an AI-CDSS integrated with MALDI-TOF MS for Stenotrophomonas maltophilia infection management. The AI-CDSS group demonstrated significantly higher confidence in antibiotic prescription and improved decision-making efficiency. Most importantly, mortality was lower in the AI-CDSS group (11.5%) than in the control group (15.1%) (absolute risk difference 3.6%, p = 0.03), with a hazard ratio for mortality of 0.75 (95% CI: 0.57–0.98), indicating a 25% reduction in death risk associated with AI-guided therapy [26].

These RCTs provide crucial evidence that AI-driven stewardship interventions can translate technical accuracy into measurable clinical benefit. Nevertheless, the overall body of RCT evidence remains limited, and future research should prioritize randomized designs evaluating hard clinical endpoints—including mortality, length of stay, and resistance emergence—rather than surrogate measures of diagnostic accuracy alone [27].

7. Challenges and Future Perspectives

Despite remarkable technological advances, several critical challenges impede the widespread clinical adoption of AI in bacterial infectious disease management. These challenges operate at distinct levels and require differentiated solution strategies.

7.1. Engineering-Level Challenges: Implementation and Integration

Data quality and standardization represent the most immediate and tractable obstacles. AI models require large, high-quality, annotated datasets for training and validation. Current limitations include small sample sizes, single-center biases, inconsistent labeling conventions, and limited demographic diversity [5][6]. The development of standardized, multi-institutional datasets with robust metadata—facilitated by initiatives such as the WHO Global Antimicrobial Resistance and Use Surveillance System (GLASS)—remains an urgent but achievable priority [2].

Clinical workflow integration presents another engineering challenge. Successful implementation necessitates seamless embedding into existing clinical workflows, with careful attention to user interface design, alert fatigue mitigation, and interoperability with electronic health record systems [5]. AI tools that fail to account for stakeholder workflow requirements are unlikely to achieve sustained adoption. These challenges have mature technical solutions and require primarily coordinated investment and implementation rather than fundamental breakthroughs.

7.2. Algorithm-Level Challenges: Methodological Tensions

Model interpretability and trust pose deeper methodological tensions. The "black box" nature of deep learning models creates substantial barriers to clinical acceptance. Clinicians require transparent, interpretable explanations of AI-generated recommendations to ensure accountability and facilitate informed decision-making [6][7]. Explainable AI (XAI) techniques—including SHAP, LIME, and attention mechanisms—are increasingly being integrated to identify clinically relevant features and align model reasoning with established medical knowledge. However, the tension between predictive performance (often maximized by complex, opaque models) and interpretability (often requiring simpler architectures) remains an inherent methodological trade-off without a universal resolution.

Generalizability and external validation constitute related algorithmic concerns. Many AI models demonstrate excellent performance on internal validation cohorts but fail to generalize across different healthcare settings, patient populations, or geographic regions [5]. Rigorous external validation using prospectively collected, geographically diverse data is essential before clinical deployment, yet remains underrepresented in the current literature [6]. Addressing these challenges requires sustained methodologic innovation in domain adaptation, federated learning, and causal inference frameworks.

7.3. Institutional-Level Challenges: Policy and Governance

Regulatory and ethical frameworks represent the most protracted barriers. The regulatory landscape for AI-based medical devices remains fragmented and evolving across jurisdictions. Issues surrounding data privacy, algorithmic bias, liability assignment, and equitable access require comprehensive policy frameworks that balance innovation with patient safety [5][6]. The WHO has issued guiding principles for AI in health, emphasizing transparency, inclusivity, and accountability, but national regulatory pathways for AI-diagnostic devices remain heterogeneous and often lag behind technological development.

Equity and access concerns are particularly acute. AI models trained predominantly on data from high-resource settings may perform poorly when deployed in low- and middle-income countries (LMICs) where AMR burdens are often highest. Ensuring equitable benefit from AI innovations requires deliberate investment in locally representative datasets, infrastructure capacity building, and technology transfer mechanisms.

7.4. Future Directions

Looking ahead, several promising trajectories emerge. Multimodal AI systems that integrate genomics, metabolomics, imaging, and clinical data will likely provide more comprehensive diagnostic and prognostic capabilities. Federated learning approaches may enable collaborative model development while preserving data privacy across institutions [6]. Advances in edge computing and portable diagnostic devices will facilitate AI deployment in resource-limited settings, addressing global health disparities. Finally, the convergence of AI with phage therapy, CRISPR-based diagnostics, and synthetic biology promises novel therapeutic and diagnostic paradigms for bacterial infections [7].

8. Conclusion

Artificial intelligence is fundamentally transforming the landscape of bacterial infectious disease management. From accelerating pathogen identification and antimicrobial susceptibility testing to enabling predictive resistance surveillance and de novo antibiotic discovery, AI technologies address critical unmet needs across the entire care continuum. While substantial challenges remain—particularly regarding data standardization, model interpretability, clinical integration, and regulatory frameworks—the trajectory of innovation is unmistakably promising.

Realizing the full potential of AI in combating bacterial infections and the associated AMR crisis will require sustained interdisciplinary collaboration among clinicians, microbiologists, data scientists, engineers, and policymakers. By embracing adaptive, holistic approaches that prioritize clinical utility, transparency, and equitable access, AI can transition from a promising research tool to an indispensable component of global infectious disease management. The stakes could not be higher: in an era of

diminishing antibiotic efficacy, AI may prove to be our most powerful ally in preserving the therapeutic armamentarium upon which modern medicine depends.

CRediT authorship contribution statement

Sarah Mitchell: Conceptualization, Investigation, Methodology, Formal analysis, Visualization, Writing – original draft. **James Patterson:** Data curation, Formal analysis, Methodology, Writing – review & editing. **Emily Davidson:** Investigation, Methodology, Software, Validation, Writing – review & editing. **Rebecca Thornton:** Investigation, Validation, Data curation, Writing – review & editing. **Andrew K. Williams:** Conceptualization, Funding acquisition, Project administration, Resources, Supervision, Writing – review & editing.

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