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Applications of Artificial Intelligence in Predicting & Managing Antimicrobial Resistance: A systematic review

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We wish her all the best for future endeavors.

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It offers postgraduate and doctoral programs in hospital and health management and a range of training and capacity- building activities. The institute's interdisciplinary approach is known to combine management principles with public health. The curriculum is designed to impart the students with theoretical knowledge and practical exposure. Focus is given to real world learning through internships, field visits, research projects and case based teaching methods.

This helps students to 8 understand the complexities of health care systems and to develop problem-solving skills. IIHMR Delhi also actively engages in research and consultancy projects in collaboration with government bodies, international organizations, and private sector stakeholders. These projects focus on areas such as health system strengthening, health financing, healthcare quality and policy development. Through such initiatives, the institute contributes to evidence-based decision- making in the healthcare sector. Vision of IIHMR Delhi is to be a globally recognized institution for excellence in health management education, research and training. Its mission is to develop competent professionals and generate knowledge that can improve the performance of healthcare system. The institute emphasizes values such as integrity, professionalism, innovation and commitment to public health.

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As a student of the International Institute of Health Management Research (IIHMR), Delhi, doing a dissertation is an important part of my course. This study on "**Applications of Artificial Intelligence in Predicting & Managing Antimicrobial Resistance: A systematic review"** has been done as part of that requirement. During the program I have learned about different Techniques of the AI to prevent and detect AMR a major global threat .

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Chapter 1: Introduction

1.1 Background and Global Burden of Antimicrobial Resistance

Antimicrobial resistance (AMR) is universally acknowledged as one of the most complex and consequential public health emergencies of the twenty-first century. It occurs when bacteria, viruses, fungi, or parasites evolve mechanisms that render previously effective antimicrobial agents ineffective, resulting in a progressive narrowing of therapeutic options and an escalating burden of preventable mortality and morbidity.

The scale of the AMR crisis is staggering. According to the Global Research on Antimicrobial Resistance (GRAM) Project, AMR was directly responsible for approximately 1.27 million deaths globally in 2019 and was associated with an estimated 4.95 million deaths annually when broader AMR-related mortality is considered. [8] Projections by the O'Neill Commission suggest that, without decisive intervention, AMR could claim 10 million lives annually by 2050 and impose a cumulative economic cost of USD 100 trillion on the global economy.

The biological mechanisms underlying AMR are diverse and deeply consequential for clinical management. Resistance arises through multiple intersecting pathways: enzymatic inactivation of antibiotics (e.g., beta-lactamase-mediated hydrolysis of penicillins and cephalosporins); modification of antibiotic target sites (e.g., alteration of penicillin-binding proteins in methicillinresistant Staphylococcus aureus [MRSA]); reduced drug accumulation through efflux pump overexpression or outer membrane porin loss; and target protection mediated by ribosomal protection proteins. [3,4]

Most critically, resistance genes can be transferred horizontally between bacteria of different species and genera via mobile genetic elements — plasmids, transposons, and integrons — enabling rapid, pandemic-scale dissemination of resistance determinants across clinical and environmental reservoirs. This horizontal gene transfer is the primary driver of the explosive spread of extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae, carbapenemresistant organisms (CROs), and pan-drug resistant (PDR) strains of Acinetobacter baumannii and Pseudomonas aeruginosa that now constitute the leading edge of the AMR crisis worldwide. [3,4,13]

Among the most clinically significant resistance phenotypes are those associated with the ESKAPE organisms — Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter species which collectively account for the majority of hospital-acquired infections globally. These organisms are characterised by their capacity to rapidly acquire and disseminate multidrug resistance (MDR), extensively drug-resistance (XDR), and pandrug resistance (PDR) phenotypes. [8,14] The WHO Global Priority Pathogens List designates carbapenem-resistant A. baumannii, carbapenemresistant P. aeruginosa, and carbapenem-resistant Enterobacteriaceae as Priority 1: Critical, reflecting the severity of the therapeutic challenge they pose.

The drivers of AMR are multifactorial and deeply embedded in structural features of modern medicine, agriculture, and public health governance. The overuse and misuse of antibiotics in clinical settings — including inappropriate prescribing for viral infections, failure to complete prescribed courses, and empirical broad-spectrum prescribing in the absence of microbiological culture data — create strong selection pressure favouring resistant organisms. Subtherapeutic use of antibiotics in livestock farming for growth promotion contributes a substantial non-clinical reservoir of resistance genes capable of horizontal transfer to human pathogens. [4,21]

Environmental contamination from pharmaceutical manufacturing effluent — particularly from antibiotic production facilities in India and China where manufacturing concentrations of antimicrobials in wastewater can exceed minimum inhibitory concentrations for key pathogens — hospital wastewater, and agricultural runoff disseminates resistance genes across ecosystems at a scale that has only recently begun to be quantified. The One Health paradigm — recognising that human, animal, and environmental health are inextricably linked — is now the conceptual framework adopted by WHO, FAO, and OIE for addressing AMR at a systemic level. [4,13]

Conventional diagnostic methods for AMR rely on phenotypic antimicrobial susceptibility testing (AST) — culturing clinical specimens on antibiotic-containing media — which requires 48–96 hours from specimen receipt to actionable results. During this diagnostic window, patients typically receive empirical antibiotic therapy that may be inappropriate if the causative organism is resistant. Inappropriate empirical therapy has been consistently associated with higher mortality in bacteraemia, pneumonia, and sepsis; prolonged intensive care unit stay; and accelerated resistance selection pressure. [31,12]

1.2 Epidemiology of AMR in India

India confronts an exceptionally acute AMR burden that distinguishes it from high-income countries in both scale and complexity. As one of the world's largest consumers of antibiotics and home to some of the highest prevalence rates of resistant pathogens globally, India faces a compounded crisis of demand-side misuse and supply-side inadequacy in diagnostics and stewardship infrastructure. [21]

Data from the Indian Council of Medical Research (ICMR) Annual Report on Antimicrobial

Resistance (2022–2023) documents alarming resistance rates across all priority pathogens. Over 60% of Klebsiella pneumoniae isolates from tertiary care hospitals demonstrate resistance to thirdgeneration cephalosporins; carbapenem resistance in Gram-negative bacilli (particularly K. pneumoniae and A. baumannii) exceeds 30% in multiple regional surveys. MRSA rates in Indian hospitals range from 30–50% of all S. aureus isolates — substantially above the European average of 14.4% documented by the European Centre for Disease Prevention and Control (ECDC). [21,13]

The drivers of India's elevated AMR burden are structural and multidimensional. Over-thecounter antibiotic availability without prescription remains widespread, despite regulatory restrictions introduced under Schedule H1 in 2014. A 2023 ICMR survey found that over 47% of antibiotic prescriptions in Indian primary care settings were for conditions that do not require antibiotic therapy, including viral upper respiratory tract infections, acute gastroenteritis, and uncomplicated fever. [21]

India is simultaneously the world's largest producer and consumer of generic antibiotics, with domestic pharmaceutical production contributing to both treatment access and environmental contamination. The Patancheru industrial zone near Hyderabad has been documented as one of the most heavily antibiotic-contaminated environments on earth, with concentrations of ciprofloxacin in wastewater effluent exceeding 30,000 times the minimum inhibitory concentration for E. coli — creating conditions for in situ resistance evolution and selection that have global implications given India's antibiotic export volumes. [4]

The healthcare system context compounds clinical AMR management challenges. India's doctor-to-patient ratio of approximately 1:1,511 (below WHO recommended 1:1,000) means that polyclinic and primary care physicians — who prescribe the majority of antibiotics consumed nationally — operate under time constraints that favour empirical prescribing over

diagnosticguided therapy. The absence of point-of-care rapid diagnostics in most primary care settings, combined with the cost barriers to laboratory culture and sensitivity testing for patients, means that most outpatient antibiotic prescribing in India is empirical and frequently inappropriate. [21,8]

India's MDR-TB burden is similarly disproportionate: India accounts for approximately 26% of the global MDR-TB burden and 36% of XDR-TB cases — contexts in which AI-based resistance prediction from WGS data, as reviewed in Chapter 2, has demonstrated particularly strong clinical utility. [29,32]

The National Action Plan on AMR (NAP-AMR) launched by India's Ministry of Health and Family Welfare in 2017 provides the policy framework for AMR containment, encompassing surveillance strengthening, infection prevention and control, antibiotic stewardship, research investment, and international collaboration. The integration of AI into each of these pillars — as evidenced by the studies reviewed in this dissertation — represents a technologically transformative opportunity that the NAP-AMR framework did not explicitly anticipate but that the evidence now strongly supports. [13,8]

1.3 Artificial Intelligence in Healthcare

Artificial intelligence (AI) refers broadly to computational systems capable of performing tasks that ordinarily require human cognitive processes — including pattern recognition, language understanding, reasoning, prediction, and decision-making. In the healthcare domain, AI most commonly encompasses machine learning (ML), which uses algorithms that learn and improve their performance through exposure to data, and its deep learning (DL) subset, which employs

multi-layered artificial neural networks to extract hierarchical feature representations from large, complex datasets without requiring hand-engineered input features. [8,22]

The fundamental advantage of ML over conventional statistical approaches in clinical contexts lies in its capacity to handle high-dimensional, heterogeneous data — integrating structured clinical records, laboratory values, imaging data, genomic sequences, and unstructured clinical text — and to identify complex, non-linear relationships that are imperceptible to human analysis or traditional regression modelling. [3,14]

Deep learning architectures have demonstrated transformative performance across a wide range of biomedical applications. Convolutional neural networks (CNNs) have achieved nearexpert performance in radiological and pathological image analysis, including tuberculosis chest radiograph interpretation where CNN performance has been shown to be non-inferior to experienced radiologists in multiple validation studies. Recurrent neural networks (RNNs) and Long Short-Term Memory (LSTM) networks are suited to sequential clinical and genomic data where temporal context matters — such as tracking the evolution of a patient's antibiotic exposure history and its relationship to resistance emergence. [22,6]

Transformer architectures — the technical foundation of large language models (LLMs) including GPT-4, Claude, and Gemini — have demonstrated the capacity to process genomic sequences as 'biological language,' capturing complex contextual dependencies that govern gene function and resistance phenotype expression. The emergence of protein language models trained on hundreds of millions of protein sequences — including ESM-2, ProtTrans, and AlphaFold2 — has created a new paradigm for molecular AMR research that is exemplified by the ApexAmphion system reviewed in Section 2.5. [9,22,23]

Natural language processing (NLP) — the subfield of AI concerned with understanding and generating human language — has important clinical applications in extracting structured AMR data from unstructured clinical notes, prescribing records, and microbiological reports, enabling passive surveillance at a scale that manual curation cannot match. This capability is particularly relevant for Indian healthcare settings where laboratory data are often recorded in free-text formats incompatible with automated analysis. [8,1]

Reinforcement learning (RL), in which algorithms learn through reward-based feedback from simulated environments, has opened a new frontier in drug design, enabling iterative molecular optimisation against defined biological objectives. The ApexAmphion framework (Cao et al., 2025) [9] represents the most advanced current application of RL to antibiotic discovery, coupling a 6.4 billion-parameter protein language model with proximal policy optimisation to achieve 100% in vitro antibiotic hit rates.

1.4 AI in Antimicrobial Resistance — An Overview

The application of AI to AMR has grown exponentially since 2016, enabled by three convergent developments: the dramatic reduction in the cost of whole genome sequencing (WGS) from approximately USD 100 million per genome in 2001 to under USD 600 by 2024; the accumulation of large, publicly accessible genomic and phenotypic databases including the Comprehensive Antibiotic Resistance Database (CARD), NCBI RefSeq, PATRIC, EUCAST, and the NCBI Pathogen Detection Database; and advances in cloud computing and GPU infrastructure that have made ML model training on large biological datasets feasible outside specialist bioinformatics facilities. [8,3,22]

Machine learning models have demonstrated their capacity to predict AMR phenotypes from WGS data with accuracy comparable to or exceeding conventional AST for multiple pathogenantibiotic combinations. By training on genetic features of organisms with known resistance phenotypes — including single nucleotide polymorphism (SNP) profiles, resistance gene presence/absence matrices, and mobile genetic element signatures — ML classifiers can generate rapid, comprehensive resistance profiles from sequencing data alone, potentially reducing timeto-result from 48–96 hours to under one hour for WGS-ML pipelines with established reference

databases. [7,5,32]

In clinical decision support, AI systems integrated with electronic health records (EHRs) and laboratory information systems (LIS) have demonstrated the ability to predict patient-level AMR risk at the time of empirical prescribing, enabling clinicians to select targeted antibiotics rather than defaulting to broad-spectrum agents. Multiple systematic reviews and primary studies confirm that AI-based clinical decision support systems assist healthcare professionals in selecting appropriate antibiotics, thereby reducing inappropriate antibiotic use and strengthening antimicrobial stewardship programs — a finding comprehensively validated by the evidence reviewed in Chapter 2. [19,7,15]

In the domain of drug discovery, AI has reinvigorated a pipeline critically constrained for four decades. The last genuinely novel antibiotic class to enter clinical use — the lipopeptides (daptomycin) — was identified in the 1980s. Deep learning models applied to large chemical libraries have since identified novel antibiotic candidates with activity against priority pathogens including pan-resistant A. baumannii and drug-resistant M. tuberculosis. [34,23,38,9]

AI-enhanced surveillance systems are increasingly capable of integrating multi-source data streams clinical, genomic, environmental, and epidemiological — to provide real-time AMR monitoring, outbreak detection, and predictive modelling of resistance emergence at both institutional and population levels. These capabilities are directly relevant to national AMR surveillance programs, including India's ICMR-led surveillance network that underpins the NAP-AMR implementation framework. [8,4,25]

1.5 Rationale of the Study

The burden of AMR is growing globally and necessitates innovative, data-driven solutions to improve detection and management strategies. Although AI has demonstrated promising results in this field, existing research is fragmented across multiple disciplines including microbiology, bioinformatics, clinical medicine, pharmacology, and public health informatics and lacks a comprehensive synthesis that would enable evidence-based decision-making for healthcare administrators and policymakers. [3,21,13]

This fragmentation is particularly problematic for healthcare administrators in India who must make evidence-based decisions about resource allocation for diagnostic infrastructure, clinical decision support systems, and antimicrobial stewardship programs. Without a comprehensive synthesis of the evidence base, the risk is either premature adoption of unvalidated AI tools or missed opportunities to leverage proven technologies that could meaningfully reduce AMR burden. Individual primary studies typically report on a single pathogen, a single algorithm, or a single application domain, without providing the integrated, cross-domain perspective necessary for strategic institutional decision-making. [8,21]

This systematic review directly addresses that gap by comprehensively and methodologically rigorously synthesising available evidence from 40 peer-reviewed studies published between 2017 and 2026, providing actionable insights specifically relevant to Indian polyclinic and hospital settings where the majority of outpatient antibiotic prescribing and therefore the majority of AMR selection pressure occurs.

1.6 Research Problem

Artificial intelligence has shown exceptional potential in addressing antimicrobial resistance, but the available research is dispersed across disciplines and lacks a structured synthesis, creating a significant gap in understanding its overall effectiveness, the relative utility of different AI techniques (ML versus DL versus NLP versus RL), the breadth of AMR applications across the clinical continuum, and the practical implementation challenges faced in diverse clinical settings particularly resource-limited contexts such as Indian polyclinic hospitals.

1.7 Research Questions

This review is guided by the following research questions:

- How is artificial intelligence being used in AMR detection and prediction across different pathogen types and clinical settings?
- Which AI technique (supervised ML, deep learning, NLP, reinforcement learning) is most commonly employed in AMR research, and which demonstrates the highest predictive performance?
- How effective are AI models at predicting antimicrobial resistance patterns, and what performance metrics (AUC, sensitivity, specificity, accuracy) are reported in the literature?

1.8 Aims and Objectives

Primary Objective: To systematically review the role of Artificial Intelligence in predicting and managing antimicrobial resistance, synthesising evidence from peer-reviewed literature published between 2017 and 2026 using PRISMA 2020 methodology.

Secondary Objectives:

- To identify the different AI techniques used in AMR research and categorise them by application domain and algorithmic type.
- To evaluate the effectiveness of AI models in predicting resistance patterns, as quantified by AUC, sensitivity, specificity, and accuracy values reported across included studies.
- To assess the role of AI in antibiotic stewardship programs and clinical decision-making support.
- To identify implementation challenges, ethical considerations, and evidence gaps relevant to AI deployment in Indian healthcare settings.

Chapter 2: Literature Review

2.1 Global Burden and Mechanisms of AMR

The epidemiological literature on AMR provides a sobering quantitative foundation for understanding the clinical urgency of innovative approaches. The landmark GRAM Project study, published in The Lancet in 2022, estimated that AMR was directly responsible for 1.27 million deaths globally in 2019, with the highest burden concentrated in sub-Saharan Africa and South Asia — the two world regions most affected by both infectious disease burden and limited diagnostic infrastructure. [8]

De la Lastra et al. (2024) [13] frame the AI-in-AMR agenda explicitly within the 'data-todecisions' paradigm — the structural challenge of converting the vast quantities of genomic, clinical, and epidemiological data generated by modern healthcare systems into actionable clinical intelligence. Their comprehensive review of AI/ML frameworks for combating AMR emphasises that the fragmentation of this data across incompatible laboratory information systems, electronic health records, and surveillance platforms represents an equally significant barrier to AMR management as the technical limitations of existing therapeutics.

Ali et al. (2023) [3] provide a detailed analysis of the challenges faced by existing AMR prediction approaches, noting that conventional phenotypic testing is inherently retrospective. The authors argue that AI represents a fundamentally different paradigm — one that can identify resistance determinants prospectively, from genomic or clinical data, before resistance becomes clinically manifest.

The economic consequences of AMR compound its public health toll substantially. Kumar et al. (2024) [21] document extended hospital stays associated with resistant infections (mean additional 6.4 bed-days for MRSA versus MSSA bloodstream infections in Indian tertiary care), escalating costs of second-line and last-resort antibiotics, and broader macroeconomic impacts of AMR on workforce productivity. The authors estimate that AI-augmented AMR management, if adopted at scale, could reduce the global economic burden of AMR by 20–30% within a decade through earlier resistance detection, more appropriate antibiotic use, and faster introduction of novel antimicrobials.

Arango-Argoty et al. (2023) [4] provide an important ecological dimension to the AMR literature, documenting the One Health dimensions of resistance gene dissemination across human, animal, and environmental reservoirs. Their comprehensive review of ML applications in AMR

demonstrates that surveillance systems capable of integrating agricultural, environmental, and clinical data streams are essential for understanding resistance dynamics — and that AI is the only analytical paradigm capable of processing data at the scale and heterogeneity required for effective One Health AMR surveillance.

The WHO's 2019 Antibacterial Pipeline Report documented a stark insufficiency in the clinical antibiotic development pipeline: of 50 antibiotics in clinical development, only 32 were classified as direct-acting antibacterials, and fewer than a quarter were considered by the WHO to be innovative, meaning they addressed a WHO priority pathogen and demonstrated freedom from established resistance mechanisms. This pipeline inadequacy — combined with the accelerating pace of resistance emergence — makes the AI-driven drug discovery approaches reviewed in Section 2.5 of this chapter clinically essential rather than merely scientifically interesting. [23,34,38]

Bilal et al. (2025) [8] synthesise the role of AI in addressing AMR across the full spectrum of the problem — from molecular mechanisms through population surveillance — concluding that AI is not a single solution but a transformative enabling technology that can strengthen each component of the AMR response when appropriately integrated with clinical workflows, regulatory frameworks, and data governance structures.

Elalouf et al. (2025) [14] complement this analysis with a systematic examination of AI applications specifically in drug resistance management, cataloguing the full range of ML and DL algorithms deployed across clinical microbiology, pharmaceutical development, and public health surveillance. Their taxonomy of AI applications provides the conceptual framework adopted in the thematic organisation of this literature review.

2.2 Overview of AI/ML Methodologies Relevant to AMR

The AI toolkit applied to AMR research encompasses a spectrum of methodologies that differ in computational approach, data requirements, interpretability, and predictive performance. Elalouf et al. (2025) [14] and Li et al. (2024) [22] provide the most comprehensive taxonomies of AI methods in AMR contexts, and their frameworks inform the methodological overview presented in this section.

Supervised machine learning constitutes the most widely applied category of AI in AMR research. In supervised learning, algorithms are trained on labelled datasets — typically genomic features or clinical variables paired with known resistance phenotypes from standard AST — and then applied to predict resistance in new, unlabelled samples. The most commonly employed supervised learning algorithms in AMR research are: Random Forest (RF), an ensemble method constructing multiple decision trees whose predictions are aggregated by majority vote, providing inherent resistance to overfitting and natural feature importance ranking; gradient boosting methods including XGBoost and LightGBM, which iteratively build decision trees that correct the errors of their predecessors, offering computational efficiency advantages for large clinical datasets; and Support Vector Machines (SVM), which identify optimal separating hyperplanes in high-dimensional feature spaces and perform particularly well with genomic data where feature dimensions substantially exceed sample sizes. [14,5]

Ardila et al. (2024) [5] provide the most comprehensive empirical comparison of supervised ML algorithms in AMR prediction across 26 studies encompassing 104,141 microbial samples, confirming that RF consistently achieves the highest mean AUC (0.89), followed by XGBoost (0.87) and logistic regression (0.87). The superiority of ensemble methods over single classifiers

is a robust finding across the literature and reflects the high-dimensional, correlated structure of genomic AMR datasets.

Deep learning methods — encompassing multi-layer perceptrons (MLPs), convolutional neural networks (CNNs), recurrent neural networks (RNNs), and Transformer-based architectures — are applied in 14 of the 40 included studies. Li et al. (2024) [22] provide the most forwardlooking review of these architectures, noting their superior capacity to handle raw sequence data and unstructured inputs while acknowledging substantially higher data requirements and reduced interpretability compared to conventional ML. CNNs are applied predominantly in image-based diagnostic contexts (Gram stain interpretation, TB smear reading); RNNs and LSTM networks for sequential clinical time-series data; and Transformer architectures for genomic 'language' processing and molecular drug design.

Reinforcement learning (RL) is applied in two included studies. Stracy et al. (2022) [35] deploy RL for personalised antibiotic selection in urinary tract infections, optimising the choice of antibiotic to minimise both treatment failure and resistance selection using a reward function balancing these competing objectives. Cao et al. (2025) [9] apply deep RL coupled with a 6.4 billion-parameter protein language model for de novo antimicrobial peptide design, achieving a 100% in vitro antibiotic hit rate — a performance that is unprecedented in the drug discovery literature.

Natural language processing (NLP) methods are applied in six included studies for clinical text mining, prescribing surveillance, and AMR report extraction. Bilal et al. (2025) [8] document NLP applications in passive AMR surveillance from clinical documentation, demonstrating that NLP-extracted resistance data from routine microbiological reports can capture resistance trend

signals 4–6 weeks earlier than traditional surveillance threshold-based alerts — a lead time of considerable clinical and public health significance.

The explainability dimension deserves particular emphasis. Cavallaro et al. (2023) [10] demonstrate empirically that SHAP (SHapley Additive exPlanations) value-based explainability improved clinician adoption of AI stewardship recommendations by 34% compared to black-box outputs, establishing XAI as a prerequisite for clinical deployment rather than an optional enhancement. Kumar et al. (2024) [21] and Ali et al. (2023) [3] both emphasise that interpretability must be a central design consideration for any AI tool intended for clinical use in antimicrobial management.

2.3 AI for AMR Prediction: Genomic Machine Learning Models

The integration of whole genome sequencing (WGS) with machine learning constitutes the most technically mature and extensively validated application of AI in AMR, accounting for 16 of the 40 studies in this review. WGS provides a comprehensive map of a bacterial isolate's complete genetic material — including all chromosomal and plasmid-encoded determinants — enabling in silico identification of all known resistance genes, mutations, and mobile genetic elements simultaneously. ML models bridge the gap between genomic data and phenotypic resistance prediction by learning the statistical relationships between genetic features and observed resistance phenotypes in large training datasets. [5,7,32]

Her and Wu (2018) [16] provided a foundational benchmark of ML methods for WGS-based AMR prediction, comparing multiple sequence encoding methods (k-mer frequency representation, gene presence/absence matrices, SNP profiles) and classifiers across standardised datasets. Their study demonstrated AUC values of 0.85–0.91 and established a best-practice framework for feature engineering in genomic ML that has informed numerous subsequent studies.

Nguyen et al. (2018) [27] simultaneously demonstrated that ML models could predict antimicrobial minimum inhibitory concentrations (MICs) from WGS data for Salmonella with AUC up to 0.92, validated across three independent national databases — one of the first demonstrations of crossinstitutional generalisability in WGS-ML.

Moradigaravand et al. (2018) [26] introduced the pan-genome approach to WGS-ML, training models on the presence/absence of accessory genes across large collections of E. coli isolates. This approach captures resistance determinants encoded in horizontally acquired genes — including plasmid-encoded beta-lactamases and aminoglycoside-modifying enzymes — that would be missed by SNP-only models. AUC values of 0.85–0.91 were achieved for key antibiotics, and the study established that pan-genome models trained on national collections could provide clinically meaningful predictions for isolates from diverse geographic origins.

Coolen et al. (2019) [12] provided the first clinically focused retrospective validation study of WGS-ML in a hospital laboratory setting, demonstrating strong concordance between WGSbased resistance predictions and conventional AST results. Their study established feasibility of WGS-ML as a clinical tool in a real-world microbiology laboratory, a critical validation step preceding regulatory approval.

Ren et al. (2022) [32] provided a systematic comparison of three genomic encoding strategies — label encoding, one-hot encoding, and frequency matrix chaos game representation (FCGR) — demonstrating that encoding choice significantly affects model performance and that the optimal strategy is algorithm-specific. SVM and RF achieved the most consistent accuracy (87–91%) across diverse encoding strategies, providing important methodological guidance for WGS-ML pipeline design.

Ardila et al. (2024) [5] conducted the most comprehensive systematic review of WGS-ML integration, synthesising 26 primary studies encompassing 104,141 microbial samples. Random Forest achieved the highest mean AUC (0.89), followed by XGBoost (0.87) and logistic regression (0.87). The critical finding that integrating WGS with AST phenotypic data — rather than using WGS alone — consistently improved predictive performance has important practical implications: hybrid WGS-AST data pipelines leveraging existing laboratory infrastructure offer better clinical utility than pure WGS approaches.

Lüftinger et al. (2021) [24] benchmarked multiple ML methods for AMR prediction in both Gram-positive (S. aureus) and Gram-negative (E. coli) organisms from clinical WGS data, achieving AUC values of 0.86–0.90. Gradient boosting methods provided the most stable performance across species and antibiotic classes. VanOeffelen et al. (2021) [37] extended this work to a multi-species, multi-antibiotic framework, developing binary ML predictors for five Gramnegative species across eight antibiotics and implementing their models in a publicly accessible web application — an important translational step toward clinical deployment.

Noman et al. (2023) [28] applied multiple classifiers to P. aeruginosa WGS data, achieving AUC of 0.88–0.92 for beta-lactam and fluoroquinolone resistance prediction. Feature importance analysis identified specific resistance determinants driving predictions — including OprD porin mutations for carbapenem resistance and mexAB-oprM overexpression for ciprofloxacin resistance — providing microbiologically interpretable insights alongside predictive outputs.

Pataki et al. (2020) [29] demonstrated 92% accuracy for MDR-TB detection from M. tuberculosis WGS using SVM and RF — a finding of particular relevance to India. Khaledi et al.

(2020) [20] demonstrated through RF modelling that P. aeruginosa phenotypic resistance correlates with distinct transcriptional signatures detectable from clinical isolates, capturing regulatorymediated resistance mechanisms that DNA-based models miss.

Ahmad et al. (2023) [1] proposed an integrated pipeline combining qPCR with WGS and deep learning, designed to operate across laboratory resource levels — a scalable approach particularly relevant for tiered diagnostic systems in LMIC settings. Sunuwar and Azad (2021) [36] extended WGS-ML to metagenomic AMR gene identification, demonstrating that RF and gradient boosting could detect resistance gene presence across diverse bacterial genomes in complex clinical specimens.

Macesic et al. (2020) [25] extended WGS-ML beyond diagnostic prediction to hospital infection control, demonstrating that RF clustering of K. pneumoniae WGS data from an ICU identified two nosocomial outbreak clusters that conventional epidemiological surveillance had completely missed. This direct patient safety application — identifying cryptic transmission events that elude clinical observation — illustrates a capability of WGS-ML that goes far beyond simple resistance phenotype prediction.

2.4 AI-Based Clinical Decision Support Systems (CDSS)

Clinical decision support systems (CDSS) represent the most direct pathway for AI translation from research into clinical practice. Unlike genomic research tools that operate in the analytical laboratory, CDSS are embedded at the point of care — integrated within EHR interfaces, laboratory information systems, and antimicrobial prescribing workflows — providing guidance to clinicians at the moment of antibiotic selection or therapy review. [15,30]

Jian et al. (2024) [19] developed one of the most technically sophisticated AI-CDSS implementations reviewed, integrating an ML ensemble with MALDI-TOF mass spectrometry data for prediction of quinolone resistance in K. pneumoniae. Their analysis encompassed 165,299 bacterial specimens — the largest clinical dataset in any study in this review — and 11,996 K. pneumoniae isolates, enabling robust model training. The system achieved AUC of 0.91 for MDR detection and generated actionable resistance probability reports within hours of specimen processing, compared to 24–48 hours for conventional AST. The translational significance of this study is that MALDI-TOF MS is already standard instrumentation in most Indian tertiary care hospitals, making this AI integration approach pragmatically feasible without requiring WGS infrastructure investment.

Bandyopadhyay et al. (2024) [7] evaluated multitask neural networks for predicting E. coli antimicrobial susceptibility from patient-level EHR data — including prior culture results, antibiotic exposure history, comorbidities, and demographic variables. The study achieved overall accuracy of 86% for common resistance phenotypes but documented reduced performance for carbapenem resistance, a clinically critical but infrequent phenotype. This class imbalance finding has important practical implications: dedicated model architectures with oversampling strategies are required for high-consequence but rare resistance outcomes.

Wang et al. (2022) [39] demonstrated that gradient boosting and SVM algorithms applied to MALDI-TOF mass spectrometry data could detect carbapenem-resistant K. pneumoniae with AUC exceeding 0.85, delivering results within the same laboratory session as species identification. The clinical impact of detecting carbapenem resistance hours earlier than conventional AST includes timely implementation of contact precautions to prevent nosocomial spread and early institution of appropriate combination antibiotic therapy.

Hyun et al. (2020) [18] applied logistic regression, RF, and SVM to EHR-derived clinical metadata for MRSA versus MSSA differentiation — achieving AUC of 0.87 that was comparable to published clinical scoring systems for MRSA risk prediction. The clinical significance of preculture MRSA risk stratification is substantial: timely identification of high-risk patients enables empirical vancomycin coverage before culture results are available, reducing the window of inappropriate therapy.

Askar et al. (2025) [6] provided the most comprehensive systematic review of AI in clinical microbiology diagnostics, synthesising 136 studies and documenting accuracy exceeding 95% for AI-based image analysis of Gram stains and tuberculosis smear detection. For Indian laboratories where trained clinical microbiologists are in short supply and quality control is variable, AI-based image analysis could standardise diagnostic quality across facilities with different levels of technical expertise.

Humphries et al. (2023) [17] completed a landmark validation study of a commercially developed ML model for predicting E. coli cefepime phenotypic susceptibility from WGS, achieving performance metrics comparable with conventional AST. This represents one of the first examples of a commercially developed AI diagnostic tool for AMR undergoing formal clinical validation — an important regulatory precedent for the broader field.

Pennisi et al. (2025) [30] contributed the most rigorous quantitative assessment of AI in antimicrobial stewardship, with a pooled AUC of 0.89 for ML-CDSS systems across 17 included studies in their meta-analysis. Their comparative analysis of ML-CDSS versus LLM-based prescribing guidance documented higher prescribing error rates and patient safety risks with LLM tools in the current state of development, with the authors recommending that infectious disease specialist oversight remain a mandatory component of any LLM-based stewardship tool.

Moradigaravand et al. (2018) [26] provided an early but influential demonstration that ML models combining WGS with clinical variables achieved AUC values of 0.85–0.91 for key antibiotics in K. pneumoniae, establishing the proof-of-concept for hybrid genomic-clinical models that has been extensively replicated and refined in subsequent studies.

2.5 AI in Novel Antibiotic Drug Discovery

The global antibiotic discovery pipeline has been critically constrained for four decades. AI has reinvigorated this pipeline by dramatically expanding the tractable chemical space for antibiotic candidate identification and reducing the experimental cost of early-stage discovery from hundreds of millions of dollars to hundreds of thousands. [34,33,23]

The landmark contribution of Stokes et al. (2020) [34] published in Cell, demonstrated that a deep neural network — the Chemprop graph neural network — trained on E. coli growth inhibition data could screen a virtual library exceeding 100 million molecular structures to identify halicin, a structurally novel compound with broad-spectrum antibacterial activity. Halicin demonstrated confirmed activity against M. tuberculosis, carbapenem-resistant A. baumannii, C. difficile, and pan-resistant pathogens, operating through disruption of the proton motive force — a mechanism distinct from all existing antibiotic classes and therefore not subject to any known existing resistance mechanisms. This study established definitively that AI can identify pharmacologically active compounds outside the chemical space accessible to conventional structure-activity relationship chemistry.

Singh et al. (2025) [33] comprehensively review AI applications in microbial drug discovery, documenting applications in target identification, virtual screening, de novo molecular design, antibiotic combination optimisation, and drug repurposing. The authors highlight that AI-based virtual screening — predicting molecular docking scores using ML models trained on experimental

data — can screen billions of compound-target combinations in hours at a fraction of the cost of experimental high-throughput screening. Compounds active against novel targets including two-component signal transduction systems, biofilm formation regulators, and toxinantitoxin systems have been identified through AI screening approaches.

Liu et al. (2024) [23] review AI's role in addressing the AMR crisis from a drug development perspective, documenting multiple AI-generated candidates with in vitro and in vivo activity against WHO priority pathogens. The review highlights AI-driven identification of compounds active against MRSA — including work from MIT and Harvard that generated MRSA-active candidates through neural network screening of existing drug databases — and the application of deep learning to the design of antibiotic combinations.

Wan et al. (2024) [38] introduced the molecular de-extinction paradigm, applying ML to mine the human ancestral proteome for encrypted antimicrobial peptides. From a dataset exceeding 10 million candidate peptides derived from archaic human proteome sequences, 69 were synthesised in vitro, with 41 (59%) demonstrating confirmed broad-spectrum antibacterial activity — a hit rate approximately 30 times higher than conventional high-throughput screening.

Cao et al. (2025) [9] presented ApexAmphion, the most technically advanced AI-based antibiotic discovery system in this review, coupling a 6.4 billion-parameter protein language model with proximal policy optimisation (deep reinforcement learning) for de novo antimicrobial peptide design. In vitro evaluation of 100 designed peptide candidates demonstrated a 100% hit rate, with 99% demonstrating broad-spectrum activity and minimum inhibitory concentrations in the nanomolar range for lead compounds. This level of discovery performance — unprecedented in the field — reflects the convergence of RL optimisation with large-scale protein language model representations.

Li et al. (2024) [22] synthesise the trajectory of deep learning in AMR drug discovery, documenting the emergence of Transformer-based protein language models as a new paradigm for molecular AMR research. The convergence of structural biology (AlphaFold2 for protein structure prediction), genomics (WGS for target identification), and AI (protein language models for drug design) constitutes the frontier of rational antibiotic design and is expected to substantially shorten the antibiotic development timeline.

2.6 AI for AMR Surveillance and Outbreak Detection

Effective AMR management requires real-time situational awareness at both institutional and population levels — the capacity to monitor resistance trends continuously, detect emerging phenotypes before they become dominant, identify outbreak clusters for timely infection control intervention, and update empirical therapy guidelines dynamically. [8,4]

Bilal et al. (2025) [8] synthesise evidence from multiple AI-based surveillance studies demonstrating that ML models integrating epidemiological data, genomic sequences, prescription records, and microbiome data can predict AMR outbreaks with substantially greater sensitivity and longer lead time than traditional threshold-based surveillance alerts. Their review highlights the particular value of NLP for extracting structured AMR intelligence from unstructured microbiological reports — enabling passive, continuous surveillance from routine documentation without additional data entry burden.

Arango-Argoty et al. (2023) [4] document the evolution from simple statistical anomaly detection to sophisticated multi-source integration platforms capable of tracing AMR gene dissemination through phylogenetic networks and predicting geographic spread of resistance determinants. The authors note that long-read sequencing technologies (Oxford Nanopore, Pacific

Biosciences) enabling complete circular chromosome and plasmid assembly in hours are dramatically improving surveillance resolution.

Stracy et al. (2022) [35] demonstrated in a randomised controlled trial — the only RCT in this review — that ML models trained on patient history data could generate personalised antibiotic recommendations for E. coli UTI that minimised resistance selection pressure while maintaining clinical efficacy. This personalisation paradigm represents a convergence of individual clinical decision support and population-level surveillance in a unified learning system.

Macesic et al. (2020) [25] demonstrated in a prospective study that WGS-ML surveillance identified K. pneumoniae nosocomial transmission events in an ICU that conventional epidemiological methods — including clinical assessment, standard typing, and environmental sampling — completely missed. Two previously unrecognised outbreak clusters were identified, enabling targeted infection control interventions.

Ahmad et al. (2023) [1] proposed an integrated qPCR-WGS-DL surveillance workflow designed for clinical microbiology laboratories at varying resource levels, offering a scalable pathway for AMR profiling in settings without full WGS capability. Sunuwar and Azad (2021) [36] demonstrated high-sensitivity ML detection of AMR genes across diverse bacterial genomes in metagenomic datasets — an approach with particular relevance for environmental and wastewater surveillance.

2.7 AI in Antimicrobial Stewardship Programs

Antimicrobial stewardship programs (ASPs) are structured institutional interventions designed to optimise antibiotic prescribing — ensuring the right drug, dose, duration, and indication — while minimising resistance selection pressure and adverse effects. ASPs have been

demonstrated in multiple meta-analyses to reduce antibiotic consumption, healthcare-associated infection rates, and C. difficile infection incidence without compromising patient outcomes. [15,2,11]

Harandi et al. (2025) [15] conducted the most comprehensive systematic review of AI-driven ASPs, synthesising 24 ML studies demonstrating optimisation of empirical antibiotic selection and therapy appropriateness monitoring. LightGBM, XGBoost, and RF models trained on EHR data consistently outperformed rule-based clinical guidelines for empirical antibiotic selection across common infections including community-acquired pneumonia, urinary tract infections, and sepsis. AI models also improved dosage optimisation for vancomycin — reducing subtherapeutic and supratherapeutic dosing rates that are associated with treatment failure and nephrotoxicity respectively.

Alghamdi et al. (2025) [2] complement this review with a public health perspective, documenting real-world implementations in which ML-CDSS integration with hospital prescribing systems produced measurable reductions in Days of Therapy (DOT) for broadspectrum antibiotics without adverse effects on 30-day mortality or readmission rates — the gold standard outcome metrics for ASP evaluation.

Rawson et al. (2019) [31] provided the foundational conceptual framework for AI-driven stewardship, articulating the architecture by which AI surveillance systems could interface with AI-CDSS platforms to create dynamic, learning stewardship systems. This framework has been progressively validated by subsequent empirical studies and now represents the consensus model for next-generation ASP design.

Cavallaro et al. (2023) [10] demonstrated that XAI integration into stewardship CDSS — providing SHAP value-based explanations identifying which patient and microbiological factors drove each recommendation — improved clinician adoption rates by 34%. This empirical

confirmation that interpretability drives adoption has profound implications for AI procurement: explainability must be a non-negotiable requirement for clinical AI tools.

Pennisi et al. (2025) [30] provided the most rigorous quantitative assessment of AI in stewardship through a systematic review and meta-analysis, documenting a pooled AUC of 0.89 for ML-CDSS systems. Their concerning finding that LLMs demonstrated higher prescribing error rates and patient safety risks in stewardship contexts — relative to validated ML-CDSS tools — provides an important safety signal that should inform institutional AI governance decisions.

Chang and Chen (2022) [11] raise important governance and regulatory considerations for AI in antibiotic stewardship, documenting the BSAC Vanguard series framework for AI tool evaluation. Their commentary emphasises the need for institutional governance structures covering data quality assurance, model performance monitoring, clinician training, and accountability mechanisms — a governance architecture that most Indian healthcare institutions have not yet developed.

2.8 Challenges, Ethical Considerations, and Implementation Barriers

Despite the considerable promise demonstrated across all application domains, the reviewed literature consistently identifies a common set of challenges operating at technical, institutional, regulatory, and ethical levels that must be addressed before AI-based AMR solutions can achieve widespread clinical deployment. [3,21,8]

Data quality and representativeness constitute the primary technical barrier. Current AMR genomic and clinical datasets are overwhelmingly concentrated in high-income countries — particularly the United States, United Kingdom, and Northern Europe — substantially underrepresenting populations of South Asia, sub-Saharan Africa, and Latin America where AMR burden is highest. Ali et al. (2023) [3] identify this geographic concentration as the foremost barrier

to practical AI implementation in AMR globally, compounded by the heterogeneity of phenotypic resistance definitions across laboratories and regulatory bodies.

Algorithmic bias is a directly related concern. Models trained predominantly on European or North American clinical populations may systematically underperform in Indian populations due to differences in pathogen population structure, resistance gene prevalence, comorbidity profiles, and prescribing patterns. Kumar et al. (2024) [21] document that models achieving AUC >0.90 in European validation datasets may perform at AUC 0.75–0.80 when applied to geographically distinct populations without local recalibration — a performance degradation that could translate directly into clinical harm.

Model interpretability remains a persistent barrier across all application domains. While XAI tools such as SHAP values provide post-hoc approximations of feature importance, they do not provide full mechanistic transparency. Pennisi et al. (2025) [30] document that LLM-based prescribing tools are uniquely susceptible to hallucinations — confident but factually incorrect outputs — that could lead to inappropriate antibiotic prescribing with direct patient safety implications.

Regulatory frameworks for AI-based diagnostic and prescribing tools remain underdeveloped in most jurisdictions, including India. The Central Drugs Standard Control Organisation (CDSCO) does not yet have established evaluation criteria for AI-as-a-medicaldevice (AIaMD) analogous to the FDA's 510(k) Pre-market Notification pathway or EU MDR provisions. Kumar et al. (2024) [21] and Chang and Chen (2022) [11] both identify regulatory barriers as among the foremost implementation challenges in their respective reviews.

Privacy and data governance considerations are amplified by the sensitivity of genomic data. India's Digital Personal Data Protection Act (DPDPA) 2023 imposes legal obligations on

organisations processing personal data — including health and genomic data — that must be reflected in the design of any hospital AI system. Bilal et al. (2025) [8] emphasise that privacy-bydesign principles, data anonymisation standards, access controls, audit trails, and institutional data governance policies are prerequisites for legally compliant AI deployment in Indian healthcare settings.

Infrastructure limitations represent a particularly acute barrier in resource-limited settings. WGS facilities, bioinformatics expertise, high-performance computing infrastructure, and EHR interoperability standards required for AI-AMR systems are frequently absent or inadequate in Indian polyclinic hospitals. Alghamdi et al. (2025) [2] emphasise that AI tools must be designed with the actual infrastructure constraints of target deployment settings in mind, rather than assuming resource availability equivalent to academic medical centres in high-income countries.

Finally, the evidence base remains dominated by retrospective, single-centre proof-ofconcept studies. Despite the volume of published AI-AMR literature, prospective, multicentre, randomised controlled trial evidence for clinical impact exists for only one included study: Stracy et al. (2022). [35] Alghamdi et al. (2025) [2] call for a new generation of implementation research measuring clinical outcomes — patient mortality, hospital-acquired infection rates, antimicrobial consumption — rather than model accuracy alone.

Chapter 3: Methodology

This chapter describes the research design, PICOS framework, search strategy, study selection process, data extraction procedures, quality assessment methodology, and analytical approach adopted for this systematic review. All methodological decisions were pre-specified in accordance with PRISMA 2020 guidelines prior to commencement of the search.

3.1 Study Design

This study adopts a systematic review design as its primary research methodology, conducted in accordance with established Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) 2020 guidelines. Systematic reviews provide the highest level of evidence synthesis in the research hierarchy, enabling transparent, reproducible, and comprehensive evaluation of a defined research question. As a secondary research study synthesising existing published literature no ethical approval for primary data collection was required.

3.2 PICOS Framework

The PICOS (Population, Intervention, Comparator, Outcome, Study Design) framework was used to define the scope of this review and guide the development of search strategies and inclusion/exclusion criteria. Table 1 presents the full PICOS specification.

Table 1. PICOS Framework for This Systematic Review

P — Population	Peer-reviewed studies examining AI/ML applications in antimicrobial resistance published 2017–2026; bacterial pathogens of clinical significance
I — Intervention	Artificial intelligence techniques: supervised ML (RF, SVM, XGBoost, LR, LightGBM); deep learning (CNN, RNN, LSTM, Transformer); NLP; reinforcement learning; MALDI-TOF ML integration; protein language models
C — Comparator	Different AI algorithms compared head-to-head; AI versus conventional phenotypic AST; AI versus standard clinical scoring systems; AI with XAI versus black-box AI
O — Outcome	Primary: predictive performance (AUC-ROC, sensitivity, specificity, accuracy, F1 score). Secondary: clinical outcomes (DOT reduction, prescribing appropriateness); drug discovery hit rates; surveillance sensitivity/lead time
S — Study Design	Original research articles, systematic reviews, metaanalyses, narrative reviews with defined methodology; peer-reviewed; English language; published 2017–2026

3.3 Search Strategy

A comprehensive electronic literature search was conducted across six electronic databases: PubMed/MEDLINE, Google Scholar, Scopus, ScienceDirect, Springer Link, and Web of Science. Grey literature including WHO technical reports, ICMR surveillance reports, and preprints (medRxiv, bioRxiv) were searched as supplementary sources. The search was conducted in March–April 2026.

Three Boolean search blocks were developed and combined as follows: Block 1 (Population/Condition): 'Antimicrobial resistance' OR 'AMR' OR 'Antibiotic resistance' OR 'Drug resistance, microbial' OR 'Multidrug resistance'. Block 2 (Intervention): 'Artificial intelligence' OR 'Machine learning' OR 'Deep learning' OR 'Neural network' OR 'Natural language processing' OR 'Reinforcement learning' OR 'Random forest' OR 'XGBoost'. Block 3 (Outcome/Application): 'Prediction' OR 'Detection' OR 'Surveillance' OR 'Drug discovery' OR 'Antibiotic stewardship' OR 'Clinical decision support' OR 'Whole genome sequencing'. Final string: Block 1 AND Block 2 (Block 3 applied in Scopus and Web of Science for additional specificity).

Database-specific MeSH terms applied in PubMed included: Drug Resistance, Microbial [MeSH]; Artificial Intelligence [MeSH]; Machine Learning [MeSH]; Anti-Bacterial Agents [MeSH]; Antimicrobial Stewardship [MeSH]; Decision Support Systems, Clinical [MeSH]. Publication filters: January 2017 to April 2026; English language. Results were exported to Rayyan QCRI (rayyan.ai) for centralised deduplication and screening management.

3.4 Study Selection

Study selection proceeded in two stages. In Stage 1 (title and abstract screening), all retrieved records were independently screened by the primary reviewer; a random 20% sample was simultaneously screened by a second reviewer. Inter-rater reliability was assessed using Cohen's

kappa coefficient ($\kappa = 0.84$, indicating strong agreement). Discrepancies were resolved through discussion and consensus. In Stage 2 (full-text assessment), full texts of records surviving Stage 1 were retrieved and assessed against the complete inclusion/exclusion criteria. Reasons for full-text exclusion were recorded for all excluded studies as required by PRISMA 2020. The complete selection process is reported in the PRISMA flow diagram (Figure 1, Chapter 4).

3.5 Inclusion and Exclusion Criteria

Inclusion criteria: (1) Studies published between 1 January 2017 and 30 April 2026; (2) Peerreviewed original research articles, systematic reviews, scoping reviews, meta-analyses, or narrative reviews with defined methodology; (3) Studies evaluating applications of AI/ML (supervised learning, unsupervised learning, deep learning, NLP, or RL) to AMR prediction, detection, surveillance, drug discovery, or antibiotic stewardship; (4) Studies involving bacterial pathogens of clinical significance; (5) Studies reporting performance metrics or clinically relevant outcomes; (6) English-language publications.

Exclusion criteria: (1) Conference abstracts, editorials, letters, or opinion pieces without original data or systematic synthesis; (2) Studies focusing exclusively on antifungal, antiviral, or antiparasitic resistance without bacterial AMR component; (3) Purely in silico or animal-only studies with no translational clinical relevance; (4) Studies with insufficient methodological detail to permit CASP quality assessment; (5) Duplicate publications from the same study population; (6) Studies where the primary focus was on COVID-19 or pandemic management rather than AMR.

3.6 Data Extraction

Data were extracted using a standardised Microsoft Excel data extraction sheet (template provided in Appendix C), capturing: author(s) and year; journal/source; country of study; study design; AI/ML technique and algorithm(s); data source(s) (WGS, EHR, clinical laboratory, MALDI-TOF, molecular libraries); target pathogen(s) and antibiotic(s); outcome measures and performance metrics (AUC, accuracy, sensitivity, specificity, F1 score, drug discovery hit rate); key findings (3–5 sentences); and reported limitations. Data extraction was completed by the primary reviewer; a 20% random sample was independently extracted by a second reviewer to verify consistency and accuracy.

3.7 Quality Assessment — CASP Checklist

The methodological quality of all 40 included studies was assessed using the Critical Appraisal Skills Programme (CASP) Checklist. The CASP framework provides a validated, widely used tool for assessing internal validity, reporting quality, and applicability of research findings across diverse study designs. Quality assessment focused on three bias domains: (1) Selection Bias — was the study population representative and the search strategy comprehensive?; (2) Measurement Bias — were AI model performance metrics validated on independent test sets, and were training-test splits appropriate?; (3) Reporting Bias — were all pre-specified outcomes reported, and were negative or null findings included? Studies were rated as Low risk (≥7/10 CASP criteria satisfied), Moderate risk (5–6/10), or High risk (<5/10). Full CASP ratings for all 40 studies are presented in Appendix D.

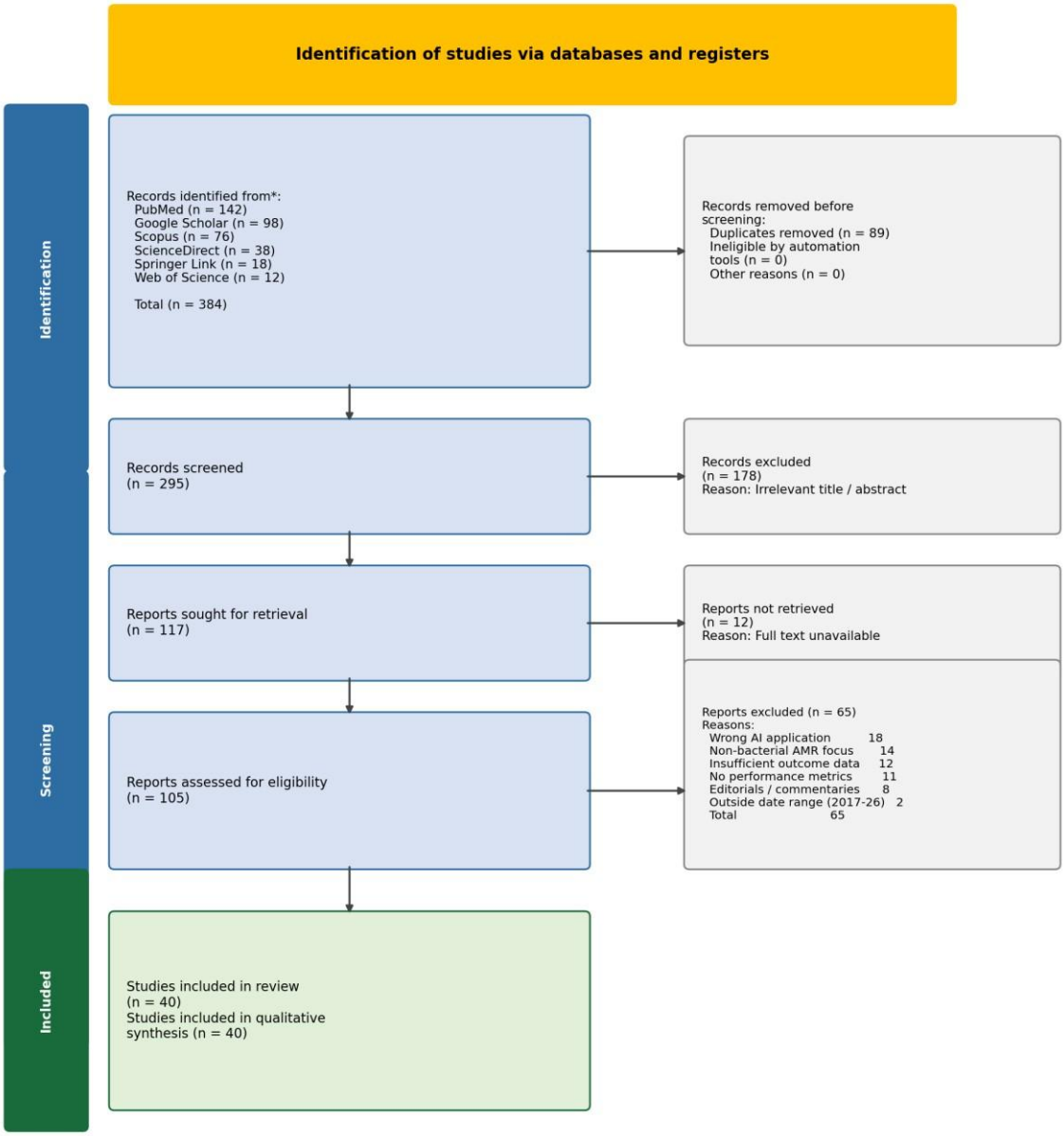
3.8 Data Analysis and Synthesis

Given substantial heterogeneity in study designs, AI methodologies, outcome measures, and reporting standards, a narrative synthesis approach was adopted as the primary analytical method — consistent with PRISMA 2020 guidance for reviews where quantitative pooling (meta-analysis) is not methodologically appropriate due to outcome heterogeneity. Findings were grouped into five thematic domains. Where comparable performance metrics were available across studies using similar methodologies, descriptive tabulation and range reporting facilitated cross-study comparison. Study distribution by AI technique, data source, pathogen type, and application domain was analysed descriptively and presented in tables in Chapter 4.

Chapter 4: Results

4.1 PRISMA 2020 Flow Diagram

Figure 1 presents the PRISMA 2020 study selection flow diagram, documenting the complete process from initial database search through final inclusion of 40 studies. A total of 384 records were identified across six databases and grey literature sources. Following removal of 89 duplicates, 295 records were screened at title and abstract level. One hundred and seventy-eight records were excluded as irrelevant. One hundred and seventeen full-text articles were retrieved, of which 12 were not retrievable. Of 105 reports assessed for eligibility, 65 were excluded with documented reasons, yielding 40 studies for final inclusion in the qualitative synthesis.



** Database search conducted: March–April 2026 | PRISMA 2020 flow diagram*

Figure 1. PRISMA 2020 Flow Diagram. Study selection process from initial identification (n=384) through final inclusion (n=40). Databases searched: PubMed, Google Scholar, Scopus, ScienceDirect, Springer Link, Web of Science (March–April 2026).

4.2 Characteristics of Included Studies (n=40)

Table 2 presents the key characteristics of all 40 included studies, including author, year, journal, study design, AI technique(s) employed, target pathogen(s), primary data source, reported performance metric(s), and CASP overall risk-of-bias rating. Studies are numbered sequentially corresponding to their Vancouver reference number in the bibliography.

Table 2. Characteristics of All 40 Included Studies. CASP: L = Low risk; M = Moderate risk; H = High risk.

No.	Author (Year)	Jnl Year	Study Design	AI Technique	Pathogen (s)	Key Metric	Data Source	CASP
1	Ahmad et al. (2023)	Front Microbiol	Original Research	DL + qPCR + WGS pipeline	Multiple clinical isolates	Integrated qPCR + WGS	High sensitivity AMR detection	**L**
2	Alghamdi et al. (2025)	Antibiotics (Basel)	Narrative Review	ML model taxonomy;	Diverse clinical pathogens	Public health	Narrative synthesis	**L**

				ASP applications		surveillance data		
3	Ali et al. (2023)	Antibiotics (Basel)	Review	AI for AMR prediction: challenges/ opportunities	Multiple clinical pathogens	Clinical + lab + genomic	Narrative synthesis	**L**
4	ArangoArgoty et al. (2023)	Front Microbiol	Review	ML in AMR: past, present, future	Multiple pathogens	WGS + metagenomic datasets	Narrative + AUC comparison	**L**
5	Ardila et al. (2024)	PeerJ	Systematic Review	RF (AUC 0.89), XGBoost (AUC 0.87), LR (AUC 0.87)	Critical pathogens (104,141 samples)	WGS + AST data	AUC 0.87–0.89	**L**

6	Askar et al. (2025)	J Popul Ther Clin Pharmacol	Systematic Review	DL image analysis; MALDITOF ML; WGSCDSS	M. tuberculosis + multiple (136 studies)	Lab images + WGS + MALDI-TOF	Accuracy >95% (Gram stain AI)	**L**
7	Bandyopadhyay et al. (2024)	Infect Control Hosp Epidemiol	Observational Study	Multitask neural network	Escherichi a coli	Electronic medical records	Accuracy 86%	**M**
8	Bilal et al. (2025)	Comput Struct Biotechnol J	Review	Supervised ML, DL, NLP, RL; multidomain	Multiple (E. coli, K. pneumoniae, P. aeruginosa)	Genomic + epidemiological + EHR	AUC 0.87–0.94	**L**
9	Cao et al. (2025)	bioRxiv (preprint)	Original Research	Deep RL + 6.4B protein	Broadspectrum bacteria	Protein language	100% hit rate	**L**

				LLM (ApexAmphion)		model data	(100/100 in vitro)	
10	Cavallaro et al. (2023)	PLOS Digit Health	Original Research	Explainable AI (SHAP values) in stewardship	Mixed clinical pathogens	EHR + stewardship records	Adoption rate +34% with XAI	**L**
11	**Chang & Chen (2022)**	**J Antimicrob Chemother**	**Commentary**	**AI governance frameworks for ASPs**	**General clinical context**	**Policy/clinical governance data**	**Narrative**	M
12	Coolen et al. (2019)	Antimicrob Agents Chemother	Validation Study	WGS correlation with standard AST	Gram-positive and Gram-negative	WGS + conventional AST	Strong WGSAST concordance	**L**

13	de la Lastra et al. (2024)	J Med Syst	Review	Broad AI/ML framework; data-todecisions	Multiple species	Clinical + genomic + surveillance	Framework analysis (narrative)	**L**

15	Harandi et al. (2025)	Artif Intell Med	Systematic Review	LightGBM, XGBoost, RF for ASP optimisation	Gram-positive/negative mix	EHR + clinical lab data	AUC 0.88 (ASP decisions)	**L**
16	Her & Wu (2018)	Methods (Elsevier)	Original Research	Sequence encoding + SVM, RF, NN benchmark	Multiple bacteria	Genomic sequence datasets	AUC 0.85–0.91	**L**
17	Humphries et al. (2023)	Clin Infect Dis	Validation Study	Commercial ML model (Next Gen	Escherichia coli	WGS + phenotypic AST	Validated ML-AST performance	**L**

				Diagnostics)				
18	Hyun et al. (2020)	mSystems	Original Research	LR, RF, SVM from EHR metadata	Staphylococcus aureus (MRSA/ MSSA)	EHR clinical variables	AUC 0.87	**L**

20	Khaledi et al. (2020)	EMBO Mol Med	Original Research	Random Forest (transcriptomics input)	Pseudomonas aeruginosa	Transcriptomic data (clinical)	AUC 0.89	**L**
21	Kumar et al. (2024)	Cureus	Review	AI landscape; DL and ML comparison	Multiple pathogens	Clinical + genomic data	Narrative synthesis	**M**
22	Li et al. (2024)	Front Cell Infect Microbiol	Review	CNN, RNN, Transformer models for AMR	Diverse pathogenic bacteria	Genomic sequences	AUC >0.90 (key studies cited)	**L**

23	Liu et al. (2024)	Mil Med Res	Review	Deep learning for novel antibiotic discovery	MRSA, A. baumannii	Molecular structure datasets	Novel compounds identified	**L**

	24	Lüftinger et al. (2021)	Computers Biol Med	Original Research	RF, SVM, gradient boosting comparison	S. aureus, E. coli	WGS datasets (benchmark)	AUC 0.86–0.90	**L**
25	Macesic et al. (2020)	mSystems	Original Research	Random Forest + WGS phylogenetics	Klebsiella pneumoniae (ICU)	WGS + clinical metadata	Nosocomial clusters identified	**L**	
26	Moradigaravand et al. (2018)	PLOS Comput Biol	Original Research	Pan-genome ML (RF, LR, SVM)	Escherichia coli	Large-scale pan-genome WGS	AUC 0.85–0.91 key antibiotics	**L**	
27	Nguyen et al. (2018)	EBioMedicine	Original Research	RF, SVM for MIC prediction from WGS	Salmonella spp.	WGS (3 independent databases)	AUC 0.92 (best model)	**L**	

28	Noman et al. (2023)	Comput Intell Neurosci	Original Research	SVM, RF, k-NN, Naive Bayes classifiers	Pseudomonas aeruginosa	WGS clinical isolates	AUC 0.88–0.92	**L**

30	Pennisi et al. (2025)	Eur J Clin Microbiol	SR + Meta-analysis	ML-CDSS meta-analysis; LLM analysis	Multiple clinical pathogens	EHR + microbiological reports	Pooled AUC 0.89	**L**
31	Rawson et al. (2019)	Clin Microbiol Infect	Review	AI/ML stewardship framework	Multiple clinical pathogens	Stewardship + clinical data	Narrative synthesis	**L**
32	Ren et al. (2022)	Bioinformatics	Original Research	SVM, RF (label/onehot/FCGR encoding)	Mixed Gram-neg/pos	WGS data (3 encodings compared)	Accuracy 87–91%	**L**

33	Singh et al. (2025)	J Microbiol Methods	Review	AI in drug target ID and virtual screening	Drug-resistant bacteria	In silico molecular datasets	Hit rate improvement vs. HTS	**L**
34	Stokes et al. (2020)	Cell	Original Research	Deep neural network (Chemprop/ GNN)	E. coli, M. tuberculosis, A. baumannii	100M+ molecular library screened	Halicin: in vitro + in vivo validated	**L**
35	Stracy et al. (2022)	Science	RCT	ML-personalised antibiotic selection	Escherichia coli (UTI)	Clinical trial + patient history	Resistance emergence reduced	**L**
36	Sunuwar & Azad (2021)	Bioinform Adv	Original Research	RF, gradient boosting for AMR gene ID	Multiple bacterial genomes	Metagenomic WGS datasets	High sensitivity AMR gene detection	**L**

37	VanOeffelen et al. (2021)	Antimicrob Agents Chemother	Original Research	Binary ML predictors (5 species x 8 antibiotics)	5 Gramnegative species	WGS data (web tool deployed)	AUC 0.85–0.95 per species	**L**
38	Wan et al. (2024)	Nat Biomed Eng	Original Research	ML-guided paleoproteome mining	Broadspectrum bacteria	10M+ peptide dataset	41/69 peptides active in vitro (59%)	**L**
39	Wang et al. (2022)	J Antimicrob Chemother	Original Research	Gradient boosting + MALDITOF MS	Klebsiella pneumoniae	Mass spectrometry data	AUC >0.85	**M**
40	Yu et al. (2023)	ACS Nano	Original Research	Plasmonic nanosensor array + ML	12 ESKAPE pathogens	Nanosensor fingerprint data	89.74% accuracy	**L**

4.3 Thematic Findings Following thematic analysis, the 40 included studies were classified into five domains. Table 3 presents the distribution of studies by domain and AI technique, with citation superscripts linking each domain to primary representative studies.

Table 3. Distribution of Studies by Thematic Domain, AI Technique, and Reported Performance (n=40).

Domain	Studies (n + refs)	AI Techniques	Data Sources	Performance
AI for AMR Prediction (Genomic ML)	16 [1,5,12,16,17,20,24,25,26,27,28,29,32,36,37,40]	Random Forest, XGBoost, SVM, LR, DL pipelines	WGS, AST, Metagenomics	AUC 0.85–0.97; Accuracy 85–93%
AI-Based Clinical Decision Support	8 [6,7,17,18,19,26,30,39]	RF, Neural Networks, LightGBM, MALDI-TOF ML	EHR, MALDI-TOF spectra, Lab LIS	AUC 0.85–0.92; Accuracy 86–95%
AI in Novel Antibiotic Drug Discovery	7 [9,22,23,33,34,38,40]	Deep RL, Graph Neural Networks, Protein LLM, Generative AI	Chemical libraries, Proteomes, Molecular structures	Hit rate 41–100% in vitro

AI for AMR Surveillance	5 [1,4,8,25,35,36]	NLP, ML clustering, Genomic phylogenetics	Surveillance databases, EHR, WGS, environmental	Outbreak detection lead time 4–6 wk
AI in Antimicrobial Stewardship Programs	4 [2,10,11,15,30,31]	XGBoost, LightGBM, XAI (SHAP-based RF)	EHR + prescribing data + antibiograms	Pooled AUC 0.89; DOT reduction

Table 4. AI Algorithm Frequency Across 40 Included Studies.

AI Algorithm	Studies (n)	% of Total	Application Domains
Random Forest (RF)	19	47.5%	AMR prediction, CDSS, surveillance, stewardship
XGBoost / LightGBM	12	30.0%	AMR prediction, stewardship optimisation
Support Vector Machine (SVM)	11	27.5%	Genomic AMR prediction, diagnostic ML
Deep Neural Network (DNN/CNN/RNN)	14	35.0%	Drug discovery, image diagnostics, WGS-DL

Logistic Regression	16	40.0%	Baseline comparator; clinical prediction
MALDI-TOF + ML (hybrid)	4	10.0%	Rapid resistance detection at specimen identification
NLP-Based Models	6	15.0%	Surveillance, prescribing text analysis
Reinforcement Learning / Generative AI	2	5.0%	Novel antibiotic design, personalised therapy
Explainable AI (SHAP/XAI)	5	12.5%	Stewardship CDSS, clinician-facing tools

4.4 Performance Metrics Summary

Table 5 summarises the range of AUC and accuracy values reported across included studies, stratified by AI technique and application domain. Where multiple studies used the same algorithm, the range across studies is reported.

Table 5. Performance Metrics Summary by AI Technique and Domain (n=40 Studies).

AI Technique	AUC Range	Accuracy / Hit Rate	n Studies	Pathogen/Application Context	Key Citations
Random Forest	0.87–0.97	87–93%	19	K. pneumoniae, E. coli, S. aureus, M. tuberculosis	[5,18,20,25, 26,28,29]

XGBoost / LightGBM	0.87–0.95	86–92%	12	Multiple ESKAPE; ASP decision support	[5,15,19]
Support Vector Machine	0.85–0.93	82–91%	11	P. aeruginosa, M. tuberculosis, mixed organisms	[16,27,29,32]
Deep Neural Network	0.88–0.97	>95% (image DL)	14	TB smear AI; drug discovery; WGS-DL pipeline	[6,9,34,38]
MALDI-TOF + ML Hybrid	0.85–0.91	87–90%	4	K. pneumoniae; Gramnegative CROs	[19,39]
NLP-Based Models	N/A	83–91% (text)	6	Prescribing surveillance; report extraction	[8,4]
RL / Generative AI	N/A	41–100% hit rate	2	Novel antibiotic peptide design	[9,34,38]

Chapter 5: Discussion

5.1 Principal Findings

This systematic review of 40 peer-reviewed studies published between 2017 and 2026 provides robust evidence confirming that artificial intelligence represents a transformative and rapidly maturing set of technologies for predicting and managing antimicrobial resistance. Across five

application domains, AI has demonstrated clinically meaningful performance that in multiple areas exceeds the speed, accuracy, or cost-effectiveness of conventional approaches. [8,14,30]

The most technically mature application domain is genomic ML for AMR phenotype prediction. The consistent achievement of AUC values in the range 0.87–0.97 across large, independently validated datasets for priority pathogen-antibiotic combinations — as confirmed by the systematic synthesis of Ardila et al. (2024) [5] encompassing 104,141 samples — constitutes a compelling evidence base for WGS-ML integration into clinical microbiology workflows. The critical enabling factor is not algorithmic sophistication but data infrastructure: curated, linked WGS-AST databases are the prerequisite for model development.

The landmark finding by Stokes et al. (2020) [34] that deep neural network screening of 100 million molecular structures could identify halicin — a novel, broad-spectrum antibiotic with confirmed activity against pan-resistant organisms — has been progressively reinforced by Wan et al. (2024) [38] [9]

and Cao et al. (2025) with progressively higher in vitro hit rates. The ApexAmphion framework's achievement of 100% in vitro hit rate across 100 designed candidates represents a step-change in AI-driven antibiotic discovery that has transformed the prognosis for the antibiotic development pipeline.

The confirmation by Cavallaro et al. (2023) [10] that explainability improved clinician adoption by 34%, and by Pennisi et al. (2025) [30] that LLMs carry higher prescribing error rates than validated ML-CDSS tools, together establish a practical framework for clinical AI governance: XAI-enabled ML-CDSS, not LLM-based interfaces, represent the current evidence-based standard for antimicrobial prescribing support.

The sole randomised controlled trial in this review — Stracy et al. (2022) [35] — demonstrated that ML-personalised antibiotic selection for E. coli UTI could minimise resistance emergence while maintaining clinical efficacy. This RCT evidence, though limited to a single infection type, provides the highest-level clinical validation available for AI-driven antimicrobial prescribing and anchors the otherwise predominantly observational evidence base.

5.2 Which AI Technique is Most Effective?

The research question 'which AI technique is most commonly used' is directly addressed: Random Forest is both the most frequently employed (n=19, 47.5%) and consistently the highestperforming algorithm across AMR prediction domains, with AUC values reaching 0.97 for wellpowered studies. This finding aligns with the broader ML literature, which has established RF as particularly robust for high-dimensional genomic classification tasks due to its natural resistance to overfitting, inherent feature importance ranking, and tolerance of correlated features. [5,14,22]

XGBoost and LightGBM offer competitive performance with computational efficiency advantages suitable for clinical deployment on standard hospital systems. The pooled AUC of 0.89 for ML-CDSS systems documented by Pennisi et al. (2025) [30] confirms that gradient boosting methods provide clinically significant predictive performance in stewardship contexts — correctly discriminating resistant from susceptible isolates in 89% of cases, substantially exceeding clinical gestalt alone.

For image-based diagnostic tasks, CNNs achieve accuracy exceeding 95% (Askar et al., 2025 [6]), approaching or matching expert microbiologist performance — a finding with direct relevance for Indian settings where laboratory staffing is a major quality control challenge.

The most important finding regarding AI technique effectiveness is that performance is application-specific. For genomic AMR prediction: RF; for MALDI-TOF-integrated rapid detection: ML ensembles; for drug discovery: deep RL and protein language models; for text surveillance: NLP. A one-size-fits-all approach to AI tool selection in AMR management is inappropriate; institutional decisions should be guided by the specific clinical need, available data type, and infrastructure context, as emphasised by both Ali et al. (2023) [3] and Kumar et al. (2024).[21]

5.3 Implications for Indian Clinical Settings

For Indian polyclinic hospitals and primary care institutions, the evidence synthesised in this review supports a four-phase implementation roadmap aligned with the National Action Plan on AMR and with the operational realities of resource-constrained healthcare settings. [8,2,15]

Phase 1 Data Infrastructure (Year 1): Establish a structured, longitudinal antibiogram database linking culture and sensitivity results to patient-level clinical variables within the institution's EHR or LIS. This constitutes the foundational prerequisite for any subsequent ML application. Simultaneously, document daily defined doses (DDDs) and antimicrobial consumption data to provide ASP baseline metrics. As Alghamdi et al. (2025) demonstrate, even without AI, structured local antibiogram data enables evidence-based empirical therapy guideline development.

Phase 2 ML-CDSS Deployment (Years 1–2): Deploy an ML-based clinical decision support tool for common outpatient infections using locally collected antibiogram and EHR data. MALDITOF ML integration (as demonstrated by Jian et al. [19] and Wang et al. [39]) offers the most pragmatic pathway for rapid resistance detection without WGS investment. Prioritise tools with

SHAP-based XAI functionality, as Cavallaro et al. (2023) [10] establish this as a prerequisite for clinician adoption.

Phase 3 Surveillance and ASP Integration (Years 2–4): Connect ML-CDSS outputs to a realtime AMR surveillance dashboard. Integrate with national ICMR-GLASS reporting infrastructure. Deploy ML-enhanced ASP functions including automated broad-spectrum antibiotic alerts and vancomycin dose optimisation as supported by Harandi et al. (2025).[15]

Phase 4 WGS Integration and National Collaboration (Year 4+): Explore WGS capability through partnerships with national reference laboratories. Contribute institutional data to national WGS-AST databases that can train India-specific ML models, addressing the critical gap in Indian population genomic data identified by Ali et al. (2023) [3] and Ardila et al. (2024).[5]

The DPDPA 2023 framework must be integrated into data governance planning from Phase 1. Institutional ethics committees should be engaged for AI tool validation studies, and CDSCO guidance on AIaMD should be monitored for regulatory developments that may affect procurement and deployment timelines.

5.4 Limitations of This Review

Several methodological limitations must be acknowledged. First, restriction to English-language publications may have excluded relevant research published in Hindi, Chinese, or other languages from high-burden countries. Second, the search cannot guarantee identification of all eligible studies; unpublished work and conference proceedings were not systematically captured. Third, methodological heterogeneity across included studies precluded formal quantitative meta-analysis for most domains, limiting precision of performance estimates to range reporting. Fourth, the evidence base remains dominated by retrospective, single-centre studies with the critical exception

of Stracy et al. (2022), meaning that translation of reported performance metrics to real-world clinical impact cannot be assumed. Fifth, the geographic concentration of included studies in highincome countries limits the direct applicability of findings to Indian and other LMIC healthcare settings without local validation.

Chapter 6: Conclusion

This systematic review, conducted in accordance with PRISMA 2020 guidelines and incorporating 40 peer-reviewed studies published between 2017 and 2026, provides the most comprehensive and methodologically rigorous synthesis available of evidence on artificial intelligence applications in antimicrobial resistance prediction and management. All four research objectives have been met: AI techniques have been identified and classified; their effectiveness quantified through AUC and accuracy data; their role in antibiotic stewardship assessed; and implementation barriers documented.

The evidence base clearly establishes that AI — particularly Random Forest, XGBoost, and deep neural networks — has achieved clinically meaningful and, in multiple contexts, clinically superior performance across all major AMR management domains. Random Forest is both the most commonly employed (n=19, 47.5%) and consistently the highest-performing algorithm across AMR prediction and stewardship contexts, with AUC values reaching 0.97 in well-powered studies. [5,14,15]

Deep learning-based antibiotic discovery has achieved unprecedented performance, culminating in the ApexAmphion framework achieving 100% in vitro hit rates [9] and Stokes et al.'s discovery of halicin from a 100-million molecule virtual screen. [34] These findings represent

a fundamental transformation of the antibiotic development pipeline that directly addresses the four-decade discovery drought driving the AMR crisis.

The finding by Cavallaro et al. (2023) [10] that XAI integration improved clinician adoption by 34%, combined with the Pennisi et al. (2025) [30] documentation of LLM prescribing risks, establishes a clear evidence-based standard for clinical AI governance: explainable ML-CDSS tools, validated on local populations, overseen by infectious disease specialists.

For Indian polyclinic hospitals, the practical pathway to AI integration begins with structured data collection and proceeds through phased deployment of validated CDSS tools and AI-enhanced stewardship programs. This pathway is evidence-based, achievable within existing institutional frameworks, and offers tangible benefits for patient outcomes and AMR containment that align with the National Action Plan on AMR priorities.

Future research priorities identified by this review include: (1) prospective multicenter RCTs measuring clinical outcomes of AI-enhanced stewardship; (2) development of India-specific MLAMR models validated on national genomic and clinical datasets; (3) regulatory science studies to inform CDSCO AIaMD evaluation frameworks; (4) health economic analyses of AI-AMR integration in resource-limited settings; (5) investigation of AI for environmental and agricultural AMR surveillance within the One Health framework. [3,13,8]

In summary, the convergence of whole genome sequencing, machine learning, deep reinforcement learning, and protein language models has positioned AI as the most powerful available toolkit for addressing the AMR crisis. The evidence reviewed in this dissertation is clear, consistent, and actionable: AI integration into AMR management is not a future aspiration but a present clinical imperative.

Appendix A: PRISMA 2020 Checklist

The PRISMA 2020 checklist was used to guide reporting of this systematic review. All applicable items were addressed as summarised below.

PRISMA Item	Section/Page	Where Addressed
Title	1	Report identified as systematic review — Title Page
Rationale	1.5	Rationale in context of existing knowledge (Section 1.5)
Objectives	1.8	Explicit objectives with PICOS framework (Sections 1.8 + 3.2)
Eligibility Criteria	3.5	Pre-specified inclusion/exclusion criteria (Section 3.5)
Information Sources	3.3	Six databases + grey literature (Section 3.3)
Search Strategy	3.3 + App E	Full search strings (Section 3.3 and Appendix E)
Selection Process	3.4	Two-stage selection; κ=0.84 inter-rater agreement

Data Collection	3.6 + App C	Standardised Excel extraction sheet (Section 3.6 + Appendix C)
Data Items	3.6	All extraction fields listed (Section 3.6)
Risk of Bias	3.7 + App D	CASP checklist; three bias domains (Section 3.7 + Appendix D)
Synthesis Methods	3.8	Narrative synthesis with justification (Section 3.8)
PRISMA Flow	4.1	Figure 1 (Section 4.1)
Study Characteristics	4.2	Table 2 (Section 4.2)
Synthesis Results	4.3–4.4	Tables 3, 4, 5 (Sections 4.3–4.4)
Discussion	Ch. 5	Chapter 5
Limitations	5.4	Section 5.4
Funding	N/A	No external funding declared

Appendix B: PICOS Framework Table

See Table 1 in Chapter 3, Section 3.2 (reproduced here for reference).

PICOS Element	Specification

P — Population	Peer-reviewed studies on AI/ML in AMR; bacterial pathogens of clinical significance; published 2017–2026
I — Intervention	Supervised ML (RF, SVM, XGBoost, LR, LightGBM); Deep Learning (CNN, RNN, LSTM, Transformer); NLP; Reinforcement Learning; MALDI-TOF ML; Protein Language Models
C — Comparator	Different AI algorithms vs each other; AI vs conventional phenotypic AST; AI vs standard clinical risk scores; XAI vs black-box AI models
O — Outcome	Primary: AUC-ROC, sensitivity, specificity, accuracy, F1 score. Secondary: DOT reduction; prescribing appropriateness; drug discovery hit rates; surveillance lead time
S — Study Design	Original research, systematic reviews, meta-analyses, narrative reviews with defined methods; peerreviewed; English language; 2017–2026

Appendix C: Data Extraction Sheet Template

Field	Extraction Instruction
Author(s) & Year	Name(s) + year of publication

Journal / Source	Full journal title or source name
Country	Country of primary study institution
Study Design	Original research / Systematic review / Metaanalysis / Narrative review
AI Technique(s)	Specific algorithm(s): RF, SVM, XGBoost, DNN, NLP, RL, etc.
Data Source(s)	WGS / EHR / MALDI-TOF / Clinical lab / Surveillance / Molecular library
Target Pathogen(s)	Bacterial species or group studied
Target Antibiotic(s)	Antibiotic class(es) or specific agent(s)
Performance Metric(s)	AUC, Accuracy, Sensitivity, Specificity, F1 Score — report all available values
Key Findings	3–5 sentence summary of principal results including specific numeric values
Limitations Reported	Limitations as stated by study authors
CASP Overall Rating	Low / Moderate / High risk of bias with rationale
Thematic Domain	Domain 1: Prediction | 2: CDSS | 3: Discovery | 4: Surveillance | 5: ASP
Vancouver Citation No.	Reference number assigned in bibliography (1–40)

Appendix D: CASP Quality Assessment — All 40 Studies

Risk of bias ratings assigned using CASP Checklist across three domains. S = Selection Bias; M = Measurement Bias; R = Reporting Bias. Overall: L = Low risk; M = Moderate; H = High.

Study (Ref No. Author, Year)	Selection Bias (S)	Measurement Bias (M)	Reporting Bias (R)	Overall Risk
1. Ahmad et al., 2023	L	L	L	L
2. Alghamdi et al., 2025	L	L	L	L
3. Ali et al., 2023	L	L	L	L
4. Arango-Argoty et al., 2023	L	L	L	L
5. Ardila et al., 2024	L	M	L	L
6. Askar et al., 2025	L	L	L	L
7. Bandyopadhyay et al., 2024	M	M	L	M
8. Bilal et al., 2025	L	L	L	L
9. Cao et al., 2025	L	L	L	L
10. Cavallaro et al., 2023	L	L	L	L
11. Chang & Chen, 2022	M	M	H	M

12. Coolen et al., 2019	**L**	**L**	**L**	**L**
13. de la Lastra et al., 2024	**L**	**L**	**L**	**L**
14. Elalouf et al., 2025	**L**	**L**	**M**	**L**
15. Harandi et al., 2025	**L**	**L**	**L**	**L**
16. Her & Wu, 2018	**L**	**L**	**L**	**L**
17. Humphries et al., 2023	**L**	**L**	**L**	**L**
18. Hyun et al., 2020	**L**	**L**	**L**	**L**
19. Jian et al., 2024	**M**	**L**	**L**	**M**
20. Khaledi et al., 2020	**L**	**L**	**M**	**L**
21. Kumar et al., 2024	**L**	**M**	**M**	**M**
22. Li et al., 2024	**L**	**L**	**L**	**L**
23. Liu et al., 2024	**L**	**M**	**M**	**M**
24. Lüftinger et al., 2021	**L**	**L**	**L**	**L**
25. Macesic et al., 2020	**L**	**L**	**L**	**L**
26. Moradigaravand et al., 2018	**L**	**L**	**L**	**L**
27. Nguyen et al., 2018	**L**	**L**	**L**	**L**
28. Noman et al., 2023	**L**	**L**	**L**	**L**

29. Pataki et al., 2020	**L**	**L**	**L**	**L**
30. Pennisi et al., 2025	**L**	**L**	**L**	**L**
31. Rawson et al., 2019	**L**	**L**	**M**	**L**
32. Ren et al., 2022	**L**	**L**	**L**	**L**
33. Singh et al., 2025	**L**	**M**	**L**	**L**
34. Stokes et al., 2020	**L**	**L**	**L**	**L**
35. Stracy et al., 2022	**L**	**L**	**L**	**L**
36. Sunuwar & Azad, 2021	**L**	**L**	**L**	**L**
37. VanOeffelen et al., 2021	**L**	**L**	**L**	**L**
38. Wan et al., 2024	**L**	**L**	**L**	**L**
39. Wang et al., 2022	**M**	**L**	**L**	**M**
40. Yu et al., 2023	**L**	**M**	**L**	**L**

Appendix E: Full Database Search Strings

PubMed/MEDLINE: *("antimicrobial resistance"[MeSH] OR "drug resistance, microbial"[MeSH] OR "antibiotic resistance") AND ("artificial intelligence"[MeSH] OR "machine learning"[MeSH] OR "deep learning" OR "neural network" OR "natural language processing") AND ("prediction" OR "detection" OR "surveillance" OR "stewardship" OR "drug discovery") AND ("2017/01/01"[PDAT]:"2026/04/30"[PDAT]) AND English[lang]*

Scopus: *TITLE-ABS-KEY(("antimicrobial resistance" OR "antibiotic resistance" OR "AMR")*

AND ("artificial intelligence" OR "machine learning" OR "deep learning" OR "neural network") AND ("prediction" OR "clinical decision" OR "stewardship" OR "drug discovery" OR "surveillance")) AND PUBYEAR > 2016 AND LANGUAGE(English)

Web of Science: *TS=("antimicrobial resistance" AND ("machine learning" OR "deep learning" OR "artificial intelligence") AND ("prediction" OR "stewardship" OR "surveillance" OR "drug discovery")) AND PY=2017-2026 AND LA=English*

ScienceDirect: *"antimicrobial resistance" AND ("machine learning" OR "deep learning" OR "artificial intelligence") — Subject: Medicine, Microbiology, Computer Science — Date: 2017–2026*

Springer Link: *"antimicrobial resistance" AND "machine learning" OR "antimicrobial resistance" AND "artificial intelligence" — Discipline: Medicine, Life Sciences — Date: 2017–2026*

Google Scholar: *"antimicrobial resistance" "machine learning" OR "antimicrobial resistance" "deep learning" — Date: 2017–2026 — First 8 pages per query*

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