engineering proceedings

MDPI

Proceeding Paper

The Future Step in Antibiotic Stewardship: Is Artificial Intelligence a Real Solution? †

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† Presented at the International Conference on Electromagnetic Fields, Signals and BioMedical Engineering (ICEMS-BIOMED), Suceava, Romania, 7–9 May 2026.

Abstract

The problem of antimicrobial resistance (AMR) is a significant worldwide health risk, which is why experts are interested in using artificial intelligence (AI) or machine learning (ML) to employ antibiotics more wisely. Diagnostic, empiric antibiotic choices, dosing, and surveillance in stewardship programs are AI-driven promises to make the process straightforward. This narrative review is a synthesis of the recent evidence (within the last 10 years) on the use of AI in antibiotic stewardship. It analyzed the literature on AI-based diagnostic systems, prescribing decision-support systems, resistance prediction models, real-time surveillance systems, and dose algorithms. The use of AI tools by clinicians and stewardship programs must be approached with discretion and human supervision and assessment.

Keywords: AI; machine learning; antimicrobial use; stewardship programs; antimicrobial resistance

1. Introduction

The issue of antimicrobial resistance (AMR) is a worldwide problem, with millions of deaths each year being related to drug-resistant infections [1,2]. Conventional stewardship practices are based on culture-oriented diagnostics and diagnostic experts, which tend to result in delayed or excessive broad empiric therapy [3]. The opportunities brought by artificial intelligence (AI) and machine learning (ML) are due to the analysis of large, complex healthcare datasets to inform the use of antibiotics [4]. As an example, using ML algorithms, it becomes possible to analyze the laboratory or genomic data quickly and identify the pathogens and resistance genes, or comb through the electronic health records (EHRs) to determine which antibiotic is most likely to work [5]. In antibiotic stewardship programs (ASPs), AI may be used to aid activities like flagging inappropriate prescriptions, predicting organ-specific risks of resistance, and automating aspects of audit-and-feedback (e.g., by identifying hotspots of unnecessary broad-spectrum use) [6]. The latest reviews highlight the potential of AI in diagnostic, surveillance, and therapeutic decision-making. Genomic datasets can be used to reveal new patterns of resistance with the help of AI-enhanced surveillance systems [7]. In diagnostics, deep learning has been utilized including rapid pathogen identification (ID) and syndrome classification (e.g., differentiating between bacterial and viral infections). Notably, AI tools in ASPs are meant to support (not to substitute) clinical judgment [8,9]. This review analyzes the existing data

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Academic Editors: L. Dan Milici, Mihai Munteanu, Simona Miclăuș, Paul Bechet and Radu Ciorap

Published: 28 August 2026

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on AI in antibiotic stewardship, specifically its application in clinical settings, reported advantages, limitations/challenges, and considerations of its implementation. The primary research and systematic reviews during 2010–2026 were summarized, pointing out such examples and outlining the development of the field.

2. Materials and Methods

A targeted literature search was conducted in PubMed, PubMed Central, Web of Science and other databases for peer-reviewed studies (≥2015) and reviews on "AI or machine learning" and "antibiotic or antimicrobial stewardship." Keywords included "AI antibiotic stewardship," "machine learning resistance prediction," "decision support antibiotic," "AI dosing antibiotics," etc. Only studies with full-text availability (e.g., observational studies, quantitative studies, systematic reviews, and meta-analyses) were considered. Additionally, publications such as editorials, letters, author responses, and review articles were excluded, as were studies without accessible full texts. Emphasis was placed on recent systematic reviews, narrative reviews, and key primary studies. Relevant references from core articles were also scanned. Studies were categorized by application (diagnostics, prescribing decision support, resistance prediction, surveillance, dosing, and workflow automation).

3. AI Technologies Relevant to Stewardship

Machine learning (ML) is an algorithm-based approach (e.g., decision trees, random forests, gradient boosting, neural networks) to identify patterns in large datasets. Deep learning (DL) (deep neural networks, CNNs) is particularly good at feature extraction from complex data such as genomics and images. ML and DL have already found applications in healthcare, where they assist in diagnosis (e.g., pneumonia detection on X-rays), genomic analyses, and personalized therapy prediction [10]. ML models can be used in stewardship to forecast antimicrobial resistance or optimal empiric decisions based on patient factors, local epidemiology, and the microbiology history. As an example, ML-based patient-specific resistance predictions in the form of antimicrobial-specific antibiograms have been trained to predict resistance in specific patients and across major antibiotics [11,12]. Neural networks can also learn trends in complex data (e.g., ICU time-series) to inform dosing changes or sepsis. Natural Language Processing (NLP) techniques can be used to extract pertinent information in clinical notes and guidelines to aid in decision-making, and Large Language Models (LLMs) (e.g., GPT-4, BERT) are able to provide a summary of the literature or suggest treatment recommendations based on textual queries. Early research suggests that LLMs generally fail at answering open-ended infectious disease queries; ChatGPT has been shown to make more than 30% errors on complicated cases [13]. The DeepSeek models are comparable to those of ChatGPT, with DeepSeek-V3 outperforming it in certain performance metrics [14]. LLMs can offer general knowledge or education, but the existing evidence indicates that they do not have any reliable, evidence-based clinical accuracy when not overseen by experts. Proper engineering in a timely manner can improve this, yet LLMs are not tested on frontline stewardship decisions [15]. Clinical Decision Support Systems (CDSSs) are AI-based systems integrated into electronic health records (EHRs) or ordering systems to provide real-time advice (e.g., highlighting narrower-spectrum agents or notifying professionals of IV-to-oral switching opportunities) [16]. Predictive analytics is the application of patient data to predict (e.g., risk of resistant infection). As one example, ML algorithms could be used to predict inpatients with the likelihood of contracting drug-resistant pathogens, which trigger more focused empiric therapy [17]. It is also possible to combine patient microbiology (e.g., blood culture results) and clinical data with AI to recommend the optimal antibiotic without final sensitivities [18]. AI (convolutional neural network—CNN) has the potential to differentiate between bacterial and viral infections

on a chest radiograph or CT scan and, therefore, potentially lower the use of unnecessary antibiotics in viral pneumonia [19,20]. Although imaging AI is yet to find substantial application in stewardship, proof-of-concept experiments indicate that DL can recognize features (e.g., pneumonia patterns) more quickly and reliably than humans. This helps indirectly in stewardship by enlightening clinicians about the situations in which they are unlikely to need antibiotics. AI can reduce time to identification and resistance profiles by many factors, with rapid pathogen sequencing [21]. Antibiotic susceptibilities can be predicted with the use of ML models that run on genomic or transcriptomic data. As an illustration, merging genomic data with ML (like in the system used by Arkstone) provided accurate, consensus-driven recommendations in just a few hours (n = 17–29)—orders of magnitude quicker than standard culture susceptibility [22]. This can be done by using such tools to speed up the de-escalation of broad antibiotics. AI can also be used to analyze host and microbiome genomics to forecast infection risk or tailor antibiotic dosage in the future [23]. In addition to radiology, AI used in new diagnostics (e.g., blood-based markers, point-of-care tests) may identify bacterial vs. non-bacterial infection in minutes, informing the need to use antibiotics [24]. Microscopy images (e.g., Gram stain or urine sediment) can also be further automated using deep learning, which can be used to further automate rapid diagnostics [25]. In short, AI involves various technologies, including the older models based on ML classification/regression and the newer models based on LLMs, which are being considered to assist with smarter antimicrobial use. Initial uses include ML-based decision support (resistance prediction and optimal therapy), whereas the tools based on LLMs are still under experimentation in stewardship.

4. AI vs. Traditional Stewardship Approaches

Conventional ASPs (audit/feedback, preauthorization) can generally decrease inappropriate utilization and quantity of antibiotics by up to 20–30 percent in intervention wards [26–28]. Similar or even larger effects have been demonstrated by AI-augmented CDSSs. The INSPIRE trials reported further 11–28% relative decreases in extended-spectrum antibiotic days beyond the baseline stewardship [29–31]. One of the predecessors of modern AI was the Clinical Decision Support (CDS), which reduced the confirmed diagnosis time and hospitalization days [32]. These results indicate that ML-based interventions may be enhanced when overlayed with routine stewardship. Guidelines and patient data are directly integrated into AI tools, and frequently have high concordance with expert recommendations [33]. Conversely, manual audit is based on human examination, and AI is able to use the rule in a consistent and alert–fatigued manner. No population-level decrease in resistance due to AI stewardship has been demonstrated as it needs long-term massive surveillance. Nevertheless, AI tools ought to contribute to decreasing resistance development by cutting down on unneeded broad-spectrum consumption. Conventional ASPs have been associated with the stabilization of or the reduction in resistance among hospitals. The quantitative effect of AI is yet to be determined. Most importantly, there is no evidence of adverse outcomes as AI-guided prescribing increases [34]. Bolton et al. discovered no patient safety measure was worsened by the introduction of an AI CDSS; clinicians were able to ignore bad advice [35]. The INSPIRE data did not indicate any increase in ICU transfers [29–31]. Furthermore, accelerated optimal therapy (with the help of AI) will enhance performance with severe infections (indirectly supported by sepsis AI research) [36]. Conventional stewardship also demonstrates no or a positive influences on outcomes. So far AI seems to be at least as safe as more traditional methods as long as it is properly validated. There are few formal cost-effectiveness studies of AI in stewardship. Nevertheless, the saving of broad-spectrum antibiotic days and hospital stay by even a fraction will pay off investment in AI tools. As an example, the saving of approximately

700 IV days/year would probably reduce costs and complications [4]. AI can have initial software expenditure and data infrastructure, but it can decrease clinician workload (less manual audit). The conventional programs necessitate constant personnel (pharmacists, epidemiologists). An essential gap in research is economic evaluations. The AI interventions will mostly be implemented into the current workflow (EHR alerts or dashboards), which may be more effective than manual audits that are time-consuming. According to Bolton et al., clinicians found the AI CDSS helpful (TAM scores were around 3.8/5 for ease-of-use) [35]. Nonetheless, it is important to lean on explanations and trust, as in the study, most clinicians seldom sought the rationale of the AI (9% of the decisions) and embraced the AI advice mainly when it was based on evidence and was user-friendly [35]. Cultural change is needed in traditional stewardship, but AI tools have special obstacles. To conclude, AI systems can help to improve or even speed up the old-fashioned metrics of stewardship, but direct comparisons with the traditional ASPs are not possible. They are to be regarded as complementary: risk stratification and alerts can be automated with the help of AI, whereas stewardship teams should have oversight and contextually judge.

5. Benefits of AI in Antibiotic Stewardship

AI has a number of tangible advantages for antibiotic stewardship initiatives. AI algorithms are able to reveal complicated trends and hidden risk factors that may be overlooked by human analysis. The meta-analysis study by Pinto et al. (2025) discovered that ML was more effective than conventional analyses in terms of sensitivity and negative predictive value (NPV) because fewer resistant cases were neglected [34]. Better diagnostic and predictive accuracy aids in better matching therapy to patient needs. Data are processed by automated tools, which do not become tired. As an example, a pharmacist AI rule engine can screen all inpatient orders in real time, unlike human pharmacists who cannot cover all cases [36]. By reducing unnecessary broad-spectrum prescribing (e.g., saving 28% in the INSPIRE trial) and streamlining audits (Goodman et al.'s ~50% work reduction), AI frees up stewardship resources for high-value tasks and enables truly personalized antibiograms and dosing [29,37,38]. Instead of using hospital-wide statistics, ML models can estimate risk on a personalized basis (e.g., by the co-morbidities and previous cultures of a patient) [39]. This results in safer empiric therapy. An example is the OPTIVAN vancomycin model that varies dose based on the pharmacokinetics of a particular patient [39]. AI models are able to constantly consume incoming lab results and identify outbreaks or trends in resistance earlier than manual systems [40]. Detection of increasing AMR in near real time and alerting stewardship teams enables quicker action (e.g., changing hospital formularies). Interpretable models (such as the SHAP-based model proposed by Cavallaro and the decision trees proposed by Yang) can be used to uncover why a recommendation is given [9,41]. This will not only create clinician trust but also have the potential to inform a provider about risk factors of resistance, strengthening good prescribing behavior.

6. Limitations and Challenges

Despite advantages, AI tools will have to address challenges before they can be used in a wide range of clinical applications. Numerous ML models are based on extensive retrospective data. These data are subject to fluctuations in quality: gaps in fields, coding mistakes and variations in measurement can distort model training. To illustrate this, when an EHR database is not reporting some infections, an ML model can underpredict those cases [42]. The heterogeneity of results of the studies (different hospitals, disease mix) makes it difficult to compare them directly [43]. In the absence of quality representative data (both outpatient and pediatric settings), models face the risk of low generalizability. Patterns of historical care, trained in the model, could be biased (e.g., socioeconomic or racial

differences). Few studies have focused on fairness in antibiotic AI, and any implementation must ensure the absence of unequal performance among subpopulations. Black-box models (e.g., deep neural nets) may be highly accurate, but provide no information to users about the process behind how they arrive at their predictions. This opaqueness causes clinical denial and poses accountability questions. The regulatory agencies are also cautious of opaque AI as well. The integration of such technology into hospital IT systems is not easy. Even at the moment, there is a risk of alert fatigue: excessive amounts of AI warnings or improperly tuned prompts can be disregarded [44]. Effective algorithms can be of little use unless human factors are carefully designed and trained. There should be transparency, validation and compliance with medical device regulations. Privacy of data (particularly in the case of genomic or inter-institutional data-sharing) should be ensured. The creation and sustenance of AI tools need knowledge in data science, informatics infrastructure, and ongoing updates. These resources may not be available in smaller hospitals or low-resource settings. Collaborations (e.g., with academic centers) or cloud-based applications may work; however, sustainability is an issue.

7. Conclusions

AI and ML are rapidly gaining traction in antibiotic stewardship, with promising applications across the workflow from diagnosis to dosing. Studies have shown that AI systems can match or improve upon conventional care in predicting resistance and guiding therapy, while saving resources (e.g., reducing pharmacy reviews) and potentially improving patient safety. The technology enables personalized, data-driven decision-making, a major advancement over one-size-fits-all antibiograms. However, the current evidence is preliminary. Most studies are single-center or retrospective, and real-world implementation has been limited. Challenges of data quality, bias, interpretability, and integration into busy clinical workflows must be addressed before AI can be a standard stewardship tool. Ethical and regulatory frameworks are lagging behind the technology. In the near term, stewardship programs should consider pilot projects where AI augments (not replaces) human expertise. Clinicians must remain the final arbiters, using AI recommendations as one input.

Author Contributions: Conceptualization, O.A.C.-S., methodology, O.A.C.-S. and R.F.; formal analysis, O.A.C.-S. and R.F. investigation, O.A.C.-S. and R.F.; resources, O.A.C.-S. and R.F.; writing—original draft preparation, O.A.C.-S. and R.F.; writing—review and editing, O.A.C.-S. and R.F.; visualization, O.A.C.-S. and R.F. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: No new data were created or analyzed in this study. Data sharing is not applicable to this article.

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript: AI—Artificial Intelligence; CDSS—Clinical Decision Support System; AMR = Antimicrobial Resistance; ASP—Antibiotic Stewardship Program; Clinical Decision Support—CDS; CNN—Convolutional Neural Network; CPOE—Computerized Provider Order Entry; DL—Deep Learning; ED—Emergency Department; EHR—Electronic Health Record; ICU—Intensive Care Unit; LLM—Large Language Model; MDRO—

Multidrug-Resistant Organisms; ML—Machine Learning; NLP—Natural Language Processing; NPV—Negative Predictive Value.

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