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Review Article

Artificial Intelligence in Antimicrobial Stewardship: Transforming Antibiotic Prescribing in the Digital Era

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Abstract

Background: Antimicrobial resistance (AMR) is a major global health threat, driven in part by inappropriate antibiotic prescribing, and clinical workload, workforce shortages, and fragmented data systems increasingly strain conventional antimicrobial stewardship (AMS). Artificial intelligence (AI) is proposed as a means of augmenting AMS by integrating heterogeneous clinical, microbiological, and pharmacy data. **Objective:** To critically synthesize the evidence for AI-enabled AMS across the antibiotic-prescribing pathway, appraise the maturity of that evidence, and identify the barriers separating algorithmic performance from clinical benefit. **Methods:** Narrative review. PubMed/MEDLINE, Google Scholar, and preprint/repository sources were searched for English-language records published between 2020 and 2026 using combinations of "artificial intelligence," "machine learning," "antimicrobial stewardship," "antibiotic prescribing," "clinical decision support," and "antimicrobial resistance," supplemented by hand-searching reference lists of identified reviews. Sources were prioritized by relevance and study type, with a preference for systematic reviews, meta-analyses, and primary clinical evaluations over case reports or non-peer-reviewed material. **Results:** AI applications span infection prediction, empiric antibiotic selection, resistance prediction, dose and duration optimization, and de-escalation. Predictive performance is often encouraging (pooled AUC $\approx$72% across 80 studies in one meta-analysis), but the evidence is dominated by small, single-center, retrospective studies with limited external validation; only a handful of prospective or randomized evaluations exist, and none demonstrate consistent, generalizable improvement in patient-level or stewardship outcomes. Explainability, workflow integration, alert fatigue, governance, and infrastructure and data representativeness, particularly in low- and middle-income countries (LMICs), remain unresolved and are rarely addressed jointly with model development. **Conclusions:** Current evidence supports AI as a promising but clinically unproven adjunct to AMS. The literature's emphasis on algorithmic accuracy over demonstrated clinical effectiveness means AI should not yet be treated as validated stewardship infrastructure; prospective, externally validated, multicenter evaluation, not further retrospective model-building, is the priority for the field.

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1. Introduction

Antimicrobial resistance (AMR) is a major and escalating threat to global health, driven substantially by inappropriate and excessive antibiotic use [1]. Inappropriate prescribing (unnecessary initiation, excessive spectrum, suboptimal dosing or duration, and failure to revise therapy as new evidence emerges) intensifies selection pressure for resistance and exposes patients to avoidable harm, including *Clostridioides difficile* infection and microbiome disruption [2].

Antimicrobial stewardship (AMS) programs exist to optimize antimicrobial use, but their effectiveness is constrained by shortages of specialist personnel, diagnostic uncertainty, fragmented clinical and microbiological information, and the sheer volume of decisions required before definitive culture results are available [3, 4]. Artificial intelligence (AI), encompassing machine learning, natural language processing, and predictive analytics, has been proposed to address these constraints by integrating large, heterogeneous datasets from electronic health records, laboratories, and pharmacy systems [5].

However, expanding technical capability should not be conflated with demonstrated clinical effectiveness. An algorithm's value in AMS depends not on predictive accuracy alone but on whether its recommendations measurably improve prescribing, integrate into real workflows, generalize across populations, and withstand the data-quality, bias, interpretability, and governance concerns that pervade clinical AI more broadly [6]. These concerns are amplified in low- and middle-income countries (LMICs), where the same infrastructural gaps that limit AI development also constrain its evaluation.

This review critically appraises the evidence for AI-enabled AMS across the antibiotic-prescribing pathway, asking not merely what AI can predict but whether predictive gains have translated into safer prescribing and better outcomes, and identifies the translational barriers and priorities that will determine whether that translation occurs.

2. Methods

This is a narrative, not systematic, review, and no formal protocol was registered. PubMed/MEDLINE, Google Scholar, and preprint or institutional-repository sources (e.g., ResearchGate) were searched for English-language literature published between 2020 and 2026, combining "artificial intelligence," "machine learning," "natural language processing," "large language model," or "clinical decision support" with "antimicrobial stewardship," "antibiotic prescribing," or "antimicrobial resistance." Reference lists of retrieved reviews were hand-searched for additional primary studies. Systematic reviews, meta-analyses, randomized or prospective evaluations, and major clinical guidelines were prioritized; case reports, non-peer-reviewed preprints, and general-purpose encyclopedic sources (e.g., StatPearls) were included selectively, chiefly for background or mechanistic context, and are identified as such where relevant. Because search terms and eligibility judgments were not independently verified by a second reviewer, this methodology description should be read as reconstructed for transparency rather than as a formally documented protocol.

3. From Rule-Based Stewardship to AI-Enhanced Decision Support

AMS decisions (whether infection is present, which pathogen is likely, how probable resistance is, and what regimen balances adequate coverage against unnecessary exposure) are made under uncertainty, often before microbiological confirmation [7, 8]. Established interventions (audit and feedback, restriction, guideline-based prescribing) remain effective but are resource-intensive, dependent on timely specialist review, and poorly suited to representing complex interactions among patient factors, prior exposure, and shifting local resistance patterns [9, 10].

Clinical decision support systems (CDSS) were the first computational response to this problem, but conventional CDSS apply predefined rules and thresholds that are transparent and consistent but static [11, 12]. AI-enhanced CDSS instead learn patterns from data, in principle enabling probabilistic, patient-specific outputs rather than fixed alerts [13, 14]. Table 1 summarizes this distinction, but it is worth stating plainly what the distinction does not imply: greater computational sophistication is not evidence of greater clinical value. A rule-based alert that a clinician trusts and acts on is more clinically useful than a probabilistic model whose output is ignored. The relevant empirical question, addressed in Sections 5–6, is whether AI-enhanced systems outperform established rule-based stewardship where it matters: prescribing quality and patient outcomes, not just discrimination statistics.

Two structural dependencies qualify this potential. First, AI-enhanced CDSS are only as useful as their integration with electronic health records (EHRs); interoperability across EHR, pharmacy, and laboratory systems remains a practical bottleneck rather than a solved prerequisite [15]. Second, model performance is bounded by training-data quality and representativeness [5, 16], a limitation that recurs, more acutely, in the LMIC discussion in Section 7. Both dependencies mean that "AI-enabled" and "clinically validated" are not synonyms, a distinction this review treats as central rather than incidental.

Table 1: Traditional versus AI-Enhanced Clinical Decision Support Systems (CDSS)

Characteristic	Traditional CDSS	AI-Enhanced CDSS
Decision principle	Rule-based, fixed thresholds	Data-driven, pattern recognition
Adaptability	Static; requires manual rule changes	Potentially adaptive; retrainable
Interpretability	Generally transparent	Often opaque, depending on model
Principal limitation	Poor handling of complex interactions	Dependent on data quality, validation, interpretability

Adapted conceptually from [13].

4. Applications Across the Prescribing Pathway: What the Evidence Actually Supports

AI has been proposed across the full antibiotic-prescribing pathway Figure 1, but the maturity of evidence varies sharply by application, and reviewing them together rather than in isolation exposes a consistent pattern: prediction tasks are comparatively well studied, while intervention tasks, the applications with the most direct stewardship payoff, are not.

Prediction-stage applications (distinguishing bacterial from non-bacterial infection, and estimating resistance risk before susceptibility results return) have the largest evidence base. Models integrating symptoms, vital signs, and laboratory values can discriminate bacterial from viral infection better than any single variable [17], and resistance-prediction models integrating prior cultures, exposure history, and local epidemiology show similarly encouraging discrimination [18, 19]. But this is also where the limits are clearest: performance degrades when models trained in one institution or period are applied elsewhere, because resistance epidemiology is neither static nor geographically uniform [20], a validation problem, not a modeling one, and one that most published models do not test for.

Treatment-stage applications (empiric agent selection, dose optimization, duration, and de-escalation) are more numerous in the literature than they are validated. Empiric-selection models risk a specific, under-acknowledged failure mode: optimizing for treatment adequacy alone systematically favors broader-spectrum agents, which is precisely the outcome stewardship exists to prevent [21, 22]. Dosing models incorporating renal function and pharmacokinetic variability are conceptually the strongest use case for individualization [23], yet none of the cited work compares AI-supported dosing against standard pharmacokinetic/pharmacodynamic monitoring in a prospective trial. Duration-and de-escalation-support tools show plausible mechanisms for shortening courses once culture data return [24–26], but the evidence here is almost entirely retrospective and process-oriented (e.g., time-to-de-escalation) rather than outcome-oriented.

Surveillance-stage applications, flagging inappropriate prescriptions for stewardship review, reframe the value proposition from "automating a decision" to "triaging attention," which is a lower evidentiary bar and the one AI is closest to meeting: several tools can prioritize higher-risk prescriptions for human review at scale [27, 28], without requiring the model itself to be correct about every case.

Taken together, the pathway-wide picture is one of uneven maturity rather than uniform promise: prediction is ahead of intervention, and process metrics are ahead of patient outcomes. That asymmetry, not the number of proposed applications, should set expectations for near-term clinical adoption.

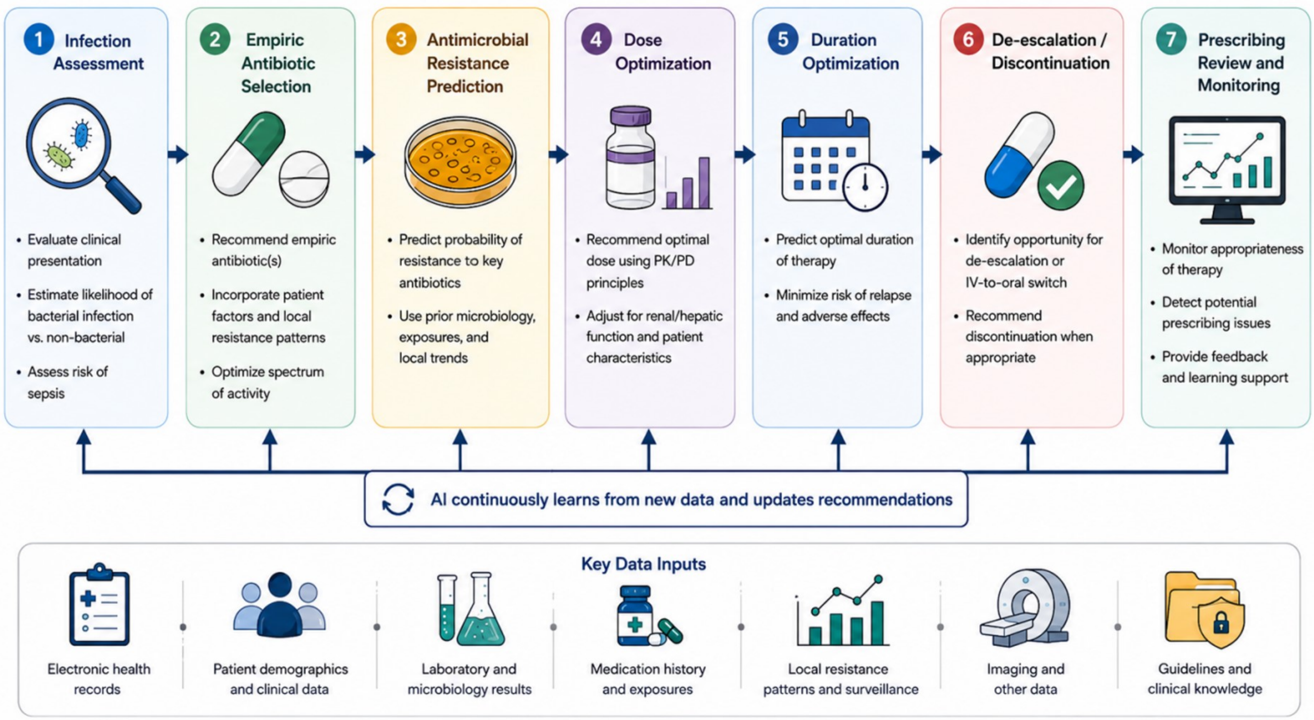

Figure 1: AI-enabled decision support mapped across the antibiotic-prescribing pathway (infection assessment, empiric selection, resistance prediction, dose/duration optimization, de-escalation, and prescribing review), integrating EHR, microbiology, pharmacy, and surveillance data. AI is intended to complement, not replace, clinical judgment

5. Current Evidence: A Critical Appraisal

The evidence base has grown quickly but remains shallow relative to its breadth of claims. A 2023 systematic review screening 3,692 records found only five studies meeting eligibility for AI applications in antibiotic prescribing specifically, evidence that the field's apparent volume of publications does not yet translate into a comparable volume of rigorous, prescribing-focused evaluations [29]. By 2025, a larger meta-analysis pooling 80 studies reported respectable aggregate discrimination (AUC $\approx$72%, accuracy 75%, sensitivity 77%, specificity 74%) [30], and a parallel synthesis linked ML-based CDSS to improved resistance prediction and antimicrobial-use optimization, though with variable sensitivity–specificity trade-offs across models [31]. Table 2 summarizes these findings; read together rather than individually, they show a field with real, moderate, but plateauing predictive performance, not one accelerating toward clinical reliability.

Three critical qualifications temper this picture. First, technical performance and clinical effectiveness are different levels of evidence: a model can achieve strong discrimination and still fail to change prescribing if its output is poorly timed, poorly integrated, or simply disregarded [32], and almost none of the studies synthesized above measured prescribing behavior or patient outcomes rather than model accuracy. Second, the evidence is methodologically heterogeneous enough (different populations, algorithms, outcome definitions) that pooled estimates likely overstate what any single deployed model would achieve in a new setting [33]. Third, large language models represent the least mature and most safety-sensitive branch of this literature: a 2025 review of six LLM evaluations in antimicrobial therapy found genuine promise for accessible decision support alongside real concerns about prescribing errors, meaning LLMs are further from clinical readiness than the ML-based CDSS discussed above, not merely a variant of them [34, 35].

The honest summary is not that AI "shows promise" (nearly every technology under early study can claim that) but that the evidence to date establishes predictive feasibility without establishing clinical benefit, and multidisciplinary evaluation combining physicians, pharmacists, microbiologists, and data scientists is a prerequisite for closing that gap rather than an optional refinement [36].

Table 2: Selected Evidence for AI in Antimicrobial Stewardship

Study	Scope	Main Finding	Key Limitation
Amin et al. [29]	Systematic review; 5/3,692 records	ML identified inappropriate use	Minimal prescriber involvement or cross-setting testing
Pennisi et al. [30]	Meta-analysis; 80 studies	Pooled AUC ≈72%	Heterogeneous, mostly retrospective
Bosetti et al. [31]	Systematic analysis	AMR prediction, use optimization	Variable sensitivity/specificity
AlGain et al. [34]	Systematic review; 6 LLM studies	LLMs feasible but error-prone	Limited validation, safety concerns

6. Translational Barriers

Five barriers recur across this literature, and they are not independent: each compounds the others, which is itself the central translational problem.

Data quality and representativeness are foundational: models trained on incomplete microbiological records or non-representative populations inherit and can amplify those gaps rather than correct for them [37, 38], and because resistance epidemiology shifts with antimicrobial use and outbreaks, yesterday's representative dataset is not guaranteed to represent tomorrow's patients. Interpretability compounds this: complex models that cannot explain their outputs make it harder for clinicians to catch exactly the data-quality failures just described, creating a genuine risk of automation bias (accepting algorithmic output without adequate scrutiny) that is arguably more dangerous in antimicrobial prescribing than in lower-stakes domains, because an erroneous recommendation can directly delay effective treatment or broaden unnecessary exposure [39, 40].

Clinical validation is the sharpest gap: most models are evaluated retrospectively on the data they were built from, not prospectively on the patients they would actually inform, and the field has not yet produced the multicenter or randomized evidence needed to close that gap [41]. Workflow integration and alert fatigue are practical rather than statistical problems, but no less consequential: a validated model that arrives through a separate platform, or that fires too often to be trusted, will be ignored regardless of its accuracy [42, 43]. Finally, governance (data privacy, cybersecurity, and accountability when an algorithm-supported decision contributes to harm) is frequently treated as a deployment afterthought rather than a design requirement, despite involving unresolved questions of whether responsibility sits with clinicians, institutions, or developers [44–46].

None of these barriers is primarily technical in the sense of requiring a better algorithm. They are evaluative, organizational, and governance barriers, which is precisely why continued investment in model development without matched investment in prospective validation and implementation science will not resolve them.

7. Resource-Limited Settings: A Sharper Version of the Same Problem

Every barrier above is amplified, not merely repeated, in low- and middle-income countries (LMICs), where inappropriate antimicrobial use already coexists with limited microbiological diagnostics, incomplete surveillance, and thin stewardship infrastructure [47, 48]. This creates a genuine paradox: settings with the least specialist capacity to buffer AI's current limitations are also those where extending decision-support capacity would plausibly matter most [49].

Two consequences follow, and both argue against simply exporting models built elsewhere. First, models developed on high-income-country data do not transfer reliably to settings with different disease epidemiology, antimicrobial availability, and resistance profiles; this is the same external-validity problem raised in Section 5, but with fewer local resources available to detect or correct it before harm occurs [50, 51]. Second, the infrastructure prerequisites (reliable connectivity, EHR systems, and technically trained staff) are themselves unevenly available, meaning implementation questions cannot be separated from equity questions [52, 53].

Mobile and cloud-based tools, federated approaches to model development, and governance frameworks built for local regulatory and consent contexts are the most frequently proposed responses [54–56], but proposals of this kind considerably outnumber evaluations of them. Absent deliberate local validation and context-specific design, AI-enabled stewardship risks reproducing, under a technological label, the same resource disparities it is meant to help close [57, 58].

8. Priorities Going Forward

The field's stated priorities- real-time integration, personalized dosing, resistance-surveillance linkage, explainable AI, and federated learning [59–63]- are all reasonable extensions of current work, which is exactly the problem: they extend model capability rather than address the clinical-validation gap identified in Sections 5–6. Large language models illustrate this tension most sharply: genuinely promising for synthesizing clinical documentation, but the least validated and most safety-sensitive application discussed in this review, and one that should not be allowed to advance on enthusiasm alone [64].

If this review has one methodological recommendation, it is a reordering of priorities rather than an additional item on the list: prospective, externally validated, multicenter studies (measuring prescribing appropriateness, antimicrobial consumption, and patient outcomes, not discrimination statistics) should take precedence over further retrospective model development [65]. Explainability and equitable, LMIC-inclusive design [66] are necessary companions to that agenda, not substitutes for it.

9. Conclusion

AI has genuine, well-documented potential to make antimicrobial stewardship more individualized and data-informed across the prescribing pathway. But the evidence synthesized here supports a specific and more modest claim than the literature's enthusiasm often implies: AI has demonstrated predictive feasibility, not clinical effectiveness, and the two should not be conflated in how this technology is described to clinicians, institutions, or funders [67, 68].

Closing that gap requires prospective multicenter validation, transparent and interpretable models, workflow-level implementation research, resolved governance, and locally validated, affordable design, especially in LMICs [69], ahead of further algorithmic refinement. Until that evidence exists, AI is best positioned as an adjunct that augments antimicrobial stewardship expertise, not as validated stewardship infrastructure in its own right.

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