

# Last-Resort Antibiotic Resistance: Mechanisms, Environmental Spread, and Detection Tools — A Narrative Review



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## Abstract

**Background:** Antimicrobial resistance (AMR) has narrowed the antibiotic arsenal for critically ill patients to a shrinking set of last-resort agents — polymyxins, carbapenems, glycopeptides, oxazolidinones, and glycyclines — and even these are now eroding under sustained selective pressure (Wahnou et al., 2026). Whether artificial intelligence (AI) can meaningfully close the gap between the emergence of resistance and its clinical recognition remains, we think, an open and worthwhile question. **Methods:** We conducted a narrative literature review of peer-reviewed articles, indexed preprints, and surveillance reports published between 2007 and 2026, retrieved from PubMed, Scopus, and Google Scholar using structured keyword combinations and supplemented by hand-searching of reference lists. **Results:** Resistance to last-resort agents arises through convergent mechanisms — mcr-mediated colistin resistance, carbapenemase production, van-gene peptidoglycan remodeling, and efflux-driven tigecycline resistance — disseminated via horizontal gene transfer across clinical, agricultural, and environmental reservoirs (Solanki & Kumar Das, 2024). AI-based annotation tools such as DeepARG and PLM-ARG now identify divergent resistance genes with precision exceeding 97% (Arango-Argoty et al., 2018; Wu et al., 2023), while optical and

microfluidic platforms compress susceptibility testing from 24–72 hours to under 30 minutes in several validated systems (Liao et al., 2025). Generative models have also identified candidate antimicrobials, including halicin and abaucin (Bagdad & Miteva, 2024). **Conclusion:** AI is accelerating both detection and discovery, but database bias, limited interpretability, and pharmacokinetic translation failure remain substantial barriers. Integrating environmental metagenomic surveillance with clinical decision support, under a coordinated One Health framework, appears to be the most promising path toward preserving last-resort antibiotic efficacy.

## Keywords

antimicrobial resistance; last-resort antibiotics; horizontal gene transfer; artificial intelligence; One Health surveillance

## 1. Introduction

There is a particular kind of alarm that does not arrive all at once. It builds, instead, across a decade of surveillance bulletins and case reports, until — almost without anyone deciding it should — the accumulated numbers themselves become the warning. Antimicrobial resistance

**Significance |** Genomic and diagnostic tools may offer a faster, more sensitive route to detecting and countering last-resort antibiotic resistance worldwide.

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(AMR) belongs to that category of crisis. It rarely produces the single dramatic image that mobilizes public attention, and yet its long-run consequences may be graver than those of many diseases that do, because AMR does not threaten one illness so much as it threatens a working assumption that sits underneath most of modern medicine: that a bacterial infection, once identified, can usually be treated. That assumption is eroding faster, it seems, than most health systems have managed to adapt to (Alem, 2025; Wahnou et al., 2026).

The scale involved is not easy to hold in mind all at once. In 2019, bacterial AMR was directly responsible for an estimated 1.27 million deaths, and was associated with nearly 4.95 million deaths when contributory cases are included (Hussain et al., 2025; Mudenda et al., 2025). Projections beyond that point are, frankly, unsettling — several analyses suggest that, absent meaningful intervention, annual AMR mortality could approach 10 million by 2050, a figure that would place resistant infection among the leading causes of death globally, ahead of cancer in some models (Abavisani et al., 2024; Millar et al., 2026). Whether that particular projection holds is, admittedly, uncertain; long-range mortality forecasting of this kind carries real methodological caveats. Still, even a fraction of that trajectory would represent a structural threat to global health security rather than a narrow microbiological concern.

The economic picture compounds the human one, if perhaps less viscerally. Estimates of the annual global GDP loss attributable to AMR span roughly \$1 trillion to \$3.4 trillion (Alem, 2025) — a wide range, reflecting genuine scientific uncertainty, but one that is, in every version, large enough to represent a serious drain on already-strained health systems. Recent surveillance data give little reason for optimism. The World Health Organization's 2025 Global Antimicrobial Resistance and Use Surveillance System (GLASS) report, drawing on more than 23 million bacteriologically confirmed infections across over 100 countries, found that roughly one in six laboratory-confirmed bacterial infections was resistant to at least one frontline antibiotic (Wahnou et al., 2026). One in six. Read slowly, that statistic reframes the conversation somewhat: resistance is no longer confined to intensive care units or specialist referral centers; it is embedded, more or less, in ordinary clinical practice wherever clinicians look for it.

How the situation arrived here is less a single event than

the cumulative outcome of decades of selective pressure applied simultaneously across human medicine, veterinary care, aquaculture, and industrial agriculture (Cunha-Ferreira et al., 2025; Mudenda et al., 2025). Prescribing habits are part of the story — audits suggest that up to half of clinical antibiotic prescriptions are unnecessary or inappropriate in some form (Alem, 2025) — and in many low- and middle-income countries, antibiotics remain available without prescription, loosening whatever restraint formal stewardship programs might otherwise provide. Livestock production adds a further, uncomfortable layer: antibiotics are still used extensively as feed additives and blanket prophylactics, and somewhere between 30% and 90% of the administered dose, depending on compound and animal system, passes through unmetabolized into manure, soil, and waterways (Alem, 2025).

Once in the environment, these subinhibitory residues rarely act in isolation. They combine with heavy metals and industrial biocides to sustain low-grade selective pressure across whole microbial communities (Alem, 2025; Solanki & Kumar Das, 2024), pushing environmental microbiomes into sustained contact with clinically significant pathogens — contact in which resistance genes move. The ESKAPE pathogens have, in this sense, become something like a living reservoir, trading resistance determinants with environmental bacteria and assembling what several authors now describe as an increasingly pan-resistant global resistome (Solanki & Kumar Das, 2024; Wahnou et al., 2026).

Against this backdrop, and alongside a rapidly maturing computational toolkit for detection, this review examines the molecular basis of last-resort antibiotic resistance, its ecological dissemination, and the emerging role of AI-based surveillance in narrowing the gap between when resistance emerges and when it is recognized.

## 2. Methodology

### 2.1 Review design

This article is a narrative literature review, not a systematic review, and is reported as such throughout — no formal PRISMA flow diagram or dual-reviewer screening protocol was used, consistent with the exploratory, synthesis-oriented aim of the paper (Wahnou et al., 2026). That said, we have tried, where feasible, to document the search and selection process with enough specificity that another reviewer could reasonably reconstruct it, broadly following PubMed's own guidance on transparent search reporting.

## 2.2 Information sources and search strategy

Sources were identified through structured searches of PubMed/MEDLINE, Scopus, and Google Scholar, covering literature published between January 2007 and June 2026 (search executed August 2026). PubMed searches combined Medical Subject Headings (MeSH) with free-text terms using Boolean operators, e.g.:

*("antimicrobial resistance"[MeSH] OR "drug resistance, bacterial"[MeSH]) AND ("artificial intelligence"[MeSH] OR "machine learning"[MeSH] OR "deep learning") AND ("colistin" OR "carbapenem" OR "vancomycin" OR "linezolid" OR "tigecycline")*

Additional search strings substituted the antibiotic-class terms with "horizontal gene transfer," "resistome," "DeepARG," "antimicrobial susceptibility testing," and "One Health surveillance." Scopus and Google Scholar searches used equivalent free-text combinations, since neither platform supports MeSH indexing. Reference lists of the most relevant reviews and primary studies were hand-searched (backward citation chasing) to capture additional eligible sources not returned by the database queries.

## 2.3 Eligibility criteria

Included: peer-reviewed original research, peer-reviewed reviews, indexed preprints, and institutional/governmental surveillance reports (e.g., WHO GLASS) published in English between 2007 and 2026 that addressed (a) molecular mechanisms of resistance to polymyxins, carbapenems, glycopeptides, oxazolidinones, or glycyclines; (b) environmental or agricultural dissemination of resistance genes; or (c) AI/ML applications in resistance gene annotation, antimicrobial discovery, rapid diagnostics, or clinical decision support.

Excluded: conference abstracts without full text, non-English-language sources, single-patient case reports without generalizable mechanistic or computational content, and opinion pieces without primary data or synthesis value.

## 2.4 Study selection

Titles and abstracts returned by the search strategy were screened for topical relevance against the eligibility criteria above; full texts of apparently relevant records were then read in full before inclusion. Because this was a single-reviewer narrative synthesis rather than a dual-reviewer

systematic review, no inter-rater agreement statistic (e.g., Cohen's kappa) was calculated, and no formal risk-of-bias instrument (e.g., ROBIS, AMSTAR-2) was applied — a limitation discussed explicitly in Section 3.9.

## 2.5 Data extraction and synthesis

For studies describing a specific computational tool or diagnostic platform (summarized in Tables 1–4), we extracted, where reported: the underlying algorithm or model architecture, the biological input data type, the primary performance metric, the reported clinical or translational advantage, and the principal stated limitation. Performance metrics are reported exactly as stated in the source publication; where a study reported a relative improvement (e.g., percentage gain in F1-score over a baseline) rather than an absolute accuracy figure, this is noted explicitly in the corresponding table to avoid implying direct comparability across tools benchmarked on different datasets.

## 2.6 Synthesis approach

Findings are organized thematically rather than chronologically, following a four-domain structure (drug discovery, genomic annotation, rapid diagnostics, and clinical decision support), and are synthesized narratively rather than through meta-analytic pooling, since the underlying studies used heterogeneous populations, reference standards, and performance metrics that are not statistically poolable.

# 3. Results and Discussion

## 3.1 Convergent Molecular Mechanisms Underlying Last-Resort Resistance

Resistance to last-resort agents is, on the evidence assembled here, rarely attributable to a single gene or mutation. It is better understood as the cumulative product of several mechanistically distinct pathways — lipid A modification and mcr-mediated colistin resistance, carbapenemase production paired with porin loss, van-gene-driven peptidoglycan remodeling, and efflux-mediated tigecycline resistance — that happen, almost inconveniently, to converge on the same small group of clinically indispensable drugs (Wahnou et al., 2026). What the AI-based tools summarized in Table 3 and Figure 1 contribute is not a resolution of that convergence so much as an improved capacity to observe it as it happens — to flag divergent resistance determinants before they accumulate enough sequence similarity to trip a

**Table 1.** Machine learning models for predicting antimicrobial susceptibility directly from electronic health record (EHR) and clinical/demographic data, rather than from pathogen genomic or phenotypic data. Studies are ordered from earlier, more interpretable classifiers toward more recent, higher-capacity ensemble methods, illustrating the field's trajectory toward greater predictive accuracy at some cost to interpretability.

| Study                 | Target pathogen(s)                                           | Core model                                 | Performance                           | Clinical use                                   |
|-----------------------|--------------------------------------------------------------|--------------------------------------------|---------------------------------------|------------------------------------------------|
| Goodman et al. (2016) | <i>E. coli</i> , <i>K. pneumoniae</i> , <i>K. oxytoca</i>    | Decision tree                              | Categorical agreement for ESBL status | Early targeted treatment                       |
| Moran et al. (2020)   | <i>E. coli</i> , <i>K. pneumoniae</i> , <i>P. aeruginosa</i> | XGBoost                                    | Concordance with expert prescribing   | Empirical antibiotic selection                 |
| McGuire et al. (2021) | Carbapenem-resistant organisms                               | Gradient boosting                          | Strong AUROC for sepsis risk          | Early sepsis stratification                    |
| Corbin et al. (2022)  | Bloodstream/urine isolates                                   | LASSO/Ridge regression, RF, GBDT           | High F1-score                         | Personalized antibiograms                      |
| Rich et al. (2022)    | Recurrent UTI isolates                                       | Decision tree, boosted logistic regression | Up to 82% accuracy                    | Reduces unnecessary broad-spectrum prescribing |

**Table 2.** Representative AI-discovered or AI-optimized antimicrobial compounds and peptides, spanning small-molecule discovery, target-specific inhibitor design, and de novo peptide generation. In-vitro/in-vivo activity values are reported exactly as stated in the original source and are not directly comparable across studies given differing assay conditions.

| Compound/peptide        | Target pathogen                                               | AI methodology                                   | Reported activity                           | Reference            |
|-------------------------|---------------------------------------------------------------|--------------------------------------------------|---------------------------------------------|----------------------|
| Halicin                 | <i>E. coli</i> , <i>A. baumannii</i> , <i>M. tuberculosis</i> | Directed message-passing neural network (D-MPNN) | MIC in low micromolar range                 | Stokes et al. (2020) |
| Abaucin                 | <i>Acinetobacter baumannii</i> (MDR/CRAB)                     | D-MPNN                                           | Narrow-spectrum LoIE inhibition             | Liu et al. (2023)    |
| CID2942818 / CID1314498 | <i>S. aureus</i> (MRSA/VRE)                                   | Dual graph neural network (GNN)                  | Median MIC 3–4 $\mu$ M                      | Wong et al. (2024)   |
| Peptide P076            | Multidrug-resistant <i>A. baumannii</i>                       | GAN + graph convolutional predictor              | Potent bactericidal activity, binds lipid A | Dong et al. (2024)   |

**Table 3.** Computational software platforms and databases for antibiotic resistance gene (ARG) annotation and surveillance, ordered from established alignment-based tools toward more recent deep learning and hybrid architectures.

| Tool      | Model type                         | Performance                              | Key limitation                             | Reference                   |
|-----------|------------------------------------|------------------------------------------|--------------------------------------------|-----------------------------|
| ResFinder | BLAST alignment                    | 95% specificity                          | Cannot detect novel/divergent ARGs         | Zankari et al. (2012)       |
| DeepARG   | Deep neural network                | >97% precision, ~90% recall (30 classes) | Database-dependent; weaker on rare classes | Arango-Argoty et al. (2018) |
| HMD-ARG   | Hierarchical multi-task CNN        | >0.90 accuracy across tasks              | High compute demand, limited transparency  | Li et al. (2021)            |
| PLM-ARG   | ESM-1b + XGBoost                   | F1-score improvement over baselines      | Computationally demanding embedding step   | Wu et al. (2023)            |
| PlasFlow  | Neural network (genome signatures) | High F1-score for plasmid resolution     | False classification of short contigs      | Krawczyk et al. (2018)      |

|           |                                   |                                |                                         |                                |
|-----------|-----------------------------------|--------------------------------|-----------------------------------------|--------------------------------|
| mplasmids | Support vector machine            | >95% species-specific accuracy | Restricted to specific species          | Arredondo-Alonso et al. (2018) |
| Meta-MARC | Hierarchical hidden Markov models | 97–99% sensitivity/specificity | Limited to predefined sequence clusters | Lakin et al. (2019)            |

Table 4. AI-enabled rapid antimicrobial susceptibility testing (AST) and point-of-care diagnostic platforms, compared against the 24–72-hour turnaround of conventional culture-based AST.

| Platform                       | Model                            | Turnaround             | Performance                                          | Reference               |
|--------------------------------|----------------------------------|------------------------|------------------------------------------------------|-------------------------|
| FAST method                    | Supervised ML on flow cytometry  | <3 hours               | >90% categorical agreement                           | Inglis et al. (2020)    |
| IR-spectrometry                | Artificial neural network        | 30 minutes             | High accuracy for cephalothin susceptibility         | Lechowicz et al. (2013) |
| Raman spectroscopy (ResNet)    | Residual neural network          | ~15 minutes            | 95% ( <i>E. coli</i> ); 81% ( <i>P. aeruginosa</i> ) | Lu et al. (2022)        |
| Disk diffusion AI (smartphone) | Offline ML image analysis        | 20 seconds post-image  | 90–98% concordance with experts                      | Pascucci et al. (2021)  |
| COMPOSER                       | Deep learning on EHR time series | 4–6 hours before onset | 17% reduction in sepsis mortality                    | Legba et al. (2026)     |

conventional BLAST search (Legba et al., 2026; Olatunji et al., 2024).

### 3.2 The Environmental Origin of Clinically Significant Resistance

A theme that, in our reading, deserves more attention than it typically receives in clinically oriented reviews is how much resistance eventually observed in ESKAPE pathogens appears to originate — or at least to be substantially amplified — outside the hospital altogether. Wastewater treatment plants, livestock operations, and pharmaceutical manufacturing effluent sustain low-grade selective environments in which resistance genes accumulate and recombine well before ever surfacing in a clinical isolate (Alem, 2025; Solanki & Kumar Das, 2024). The machine learning surveillance tools discussed in Section 3.4 — Meta-MARC and DeepARG among them — make this environmental reservoir tractable to monitor at scale, and several studies report detecting emerging resistant clones in wastewater metagenomes weeks before the same clones appear in hospital surveillance data (Alem, 2025; Legba et al., 2026). If this lead time is confirmed under broader, multi-site validation, it would represent one of the more genuinely actionable findings in this literature — an early-warning capability that appears, so far, underused relative to its apparent potential.

### 3.3 Discovery of Novel Small-Molecule and Peptide Antimicrobials

Deep learning architectures have proven capable of surfacing antibiotic candidates structurally unrelated to existing drug classes, which matters because structural novelty is one of the few reliable predictors of activity against resistant strains (Bagdad & Miteva, 2024). The clearest demonstration remains halicin: a directed message-passing neural network trained on 2,335 compounds tested against *E. coli*, applied to screen the Drug Repurposing Hub, surfaced a nitrothiazole derivative that disrupts the bacterial transmembrane proton gradient rather than acting through conventional cell-wall or DNA-synthesis pathways (Stokes et al., 2020). The same modeling approach, redirected toward *Acinetobacter baumannii*, produced abaucin, a narrow-spectrum LoE inhibitor that leaves commensal microbiota largely undisturbed (Liu et al., 2023). More recent explainable graph-search models have gone further, screening over 12 million candidate molecules against *Staphylococcus aureus* and flagging a previously unrecognized structural

class active against both MRSA and vancomycin-resistant enterococci (Wong et al., 2024) (Table 2).

A related body of work has turned to antimicrobial peptides, where generative adversarial networks and variational autoencoders now design candidate peptides directly from sequence-space representations rather than searching nature for active ones — a workaround for the well-documented fact that the great majority of environmental microbes cannot be cultured (Dong et al., 2024). One representative pipeline generated 104 novel peptide candidates, of which 26 were predicted active at sub-5  $\mu\text{M}$  concentrations; a follow-up candidate, Peptide P076, bound lipid A with high affinity and showed potent activity against multidrug-resistant *A. baumannii* (Dong et al., 2024).

### 3.4 Genomic Annotation of Antibiotic Resistance Genes

Table 3 and Figure 1 summarize the principal computational platforms used for ARG annotation. DeepARG remains the most widely adopted, using a sequence-dissimilarity matrix and neural network architecture to annotate resistance genes from metagenomic reads or assembled sequences, reporting precision above 97% and recall approaching 90% across roughly 30 resistance gene classes (Arango-Argoty et al., 2018). Its principal limitation — reduced recall for underrepresented gene classes such as sulfonamide and mupirocin determinants — is a recurring finding across validation studies. Second-generation tools narrow this gap: PLM-ARG combines the ESM-1b protein language model with an XGBoost classifier and reports meaningful F1-score improvements over both DeepARG and alignment-based baselines (Wu et al., 2023), while HMD-ARG applies a hierarchical, multi-task convolutional architecture that classifies a sequence as an ARG, assigns its antibiotic class, predicts its mechanism, and estimates its mobility (Li et al., 2021). Plasmid-specific classifiers — PlasFlow and mlplasmids — complement these gene-level tools by distinguishing plasmid-derived from chromosomal contigs, which matters for tracking horizontally mobile determinants such as *mcr-1* (Krawczyk et al., 2018; Arredondo-Alonso et al., 2018).

### 3.5 Rapid, AI-Enabled Susceptibility Diagnostics

Table 4 and Figure 2 compile the point-of-care diagnostic platforms identified in this review, and the compression relative to the 24–72-hour timeline of conventional phenotypic AST is, once plotted, genuinely striking.

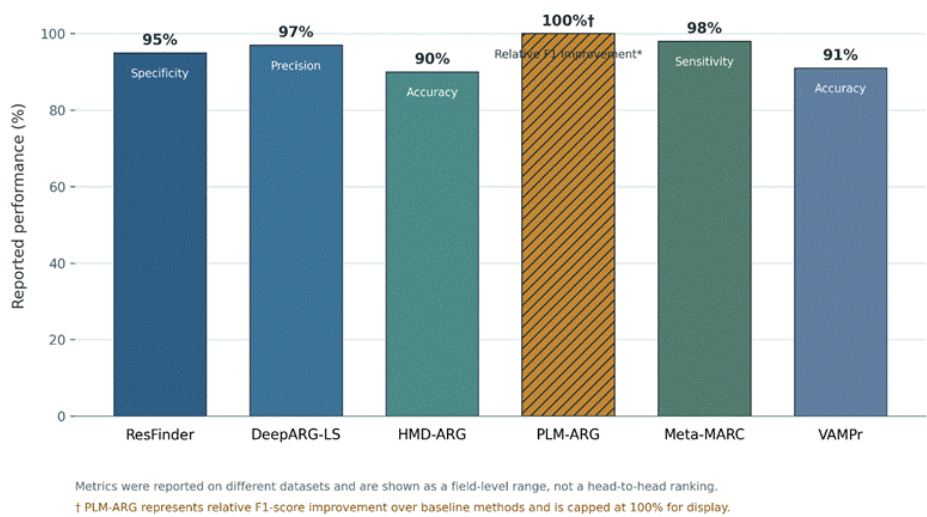


Figure 1. Reported performance of representative AI/ML-based antibiotic resistance gene (ARG) annotation tools. Bars summarize the single best-reported performance metric (precision, recall, accuracy, sensitivity, or F1-score) for six tools — ResFinder, DeepARG-LS, HMD-ARG, PLM-ARG, Meta-MARC, and VAMPr — as detailed in Table 3. Because each tool was benchmarked on a different dataset, against different resistance gene classes, and using different reference metrics, the bars are not directly comparable to one another; they illustrate the range of reported performance across the field rather than a head-to-head ranking. The PLM-ARG bar reflects a relative F1-score improvement over baseline methods rather than an absolute accuracy value, and has been capped for display purposes. All values are drawn from the source literature synthesized in this review; no independent benchmarking was performed.

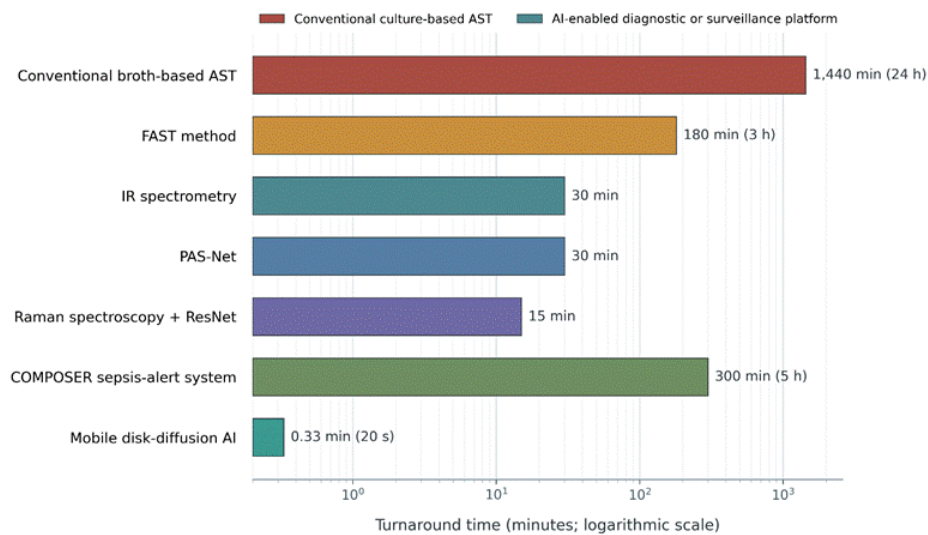


Figure 2. Turnaround time of AI-enabled diagnostic and surveillance platforms relative to conventional culture-based antimicrobial susceptibility testing (AST). Horizontal bars, plotted on a logarithmic minute scale, compare reported turnaround times for seven approaches — conventional broth-based AST, the FAST method, IR-spectrometry, PAS-Net, Raman spectroscopy with ResNet, the COMPOSER sepsis-alert system, and mobile disk-diffusion AI — as summarized in Table 4. The chart is intended to convey the order-of-magnitude compression these platforms achieve relative to the ~24-hour benchmark of traditional culture-based AST, from roughly 15 minutes for Raman-based classification down to 20 seconds for mobile image-based disk-diffusion reading. Reported times reflect single validation studies performed under specific experimental conditions and may not generalize across all clinical specimen types, bacterial species, or resource settings.

Acoustic-enhanced flow cytometry (the FAST method) produces reliable susceptibility profiles from positive blood cultures in under three hours (Inglis et al., 2020); infrared spectroscopy coupled with an artificial neural network classifies cephalothin susceptibility in uropathogenic *E. coli* within 30 minutes (Lechowicz et al., 2013); and confocal Raman spectroscopy combined with a residual neural network classifies resistant bacterial species within roughly 15 minutes, at accuracies approaching 95% for *E. coli* though notably lower — around 81% — for *P. aeruginosa* (Lu et al., 2022). At the system level, the COMPOSER model, trained on electronic health record time series, flags the likely emergence of sepsis caused by resistant pathogens four to six hours ahead of standard clinical criteria, associated with a 17% reduction in in-hospital mortality in the reporting study (Legba et al., 2026).

### 3.6 Clinical Decision Support and the Socio-Behavioral Barrier

Discovering and diagnosing resistance is one thing; using last-resort drugs wisely once resistance is suspected is a distinct, equally consequential challenge (Branda & Scarpa, 2024; Mudenda et al., 2025). Model-informed precision dosing addresses part of this — ensemble learning has improved vancomycin dosing accuracy against target AUC/MIC ratios, and Bayesian forecasting combined with real-time biosensor data is being used to adjust amikacin dosing dynamically in critically ill patients (Branda & Scarpa, 2024; Inamdar et al., 2026). Yet the technical sophistication of these tools has, so far, outpaced their social acceptance. In a comparison of clinician and public attitudes toward a stewardship-first "Global-AI" system versus an individually optimized "Individual-AI" system, most patients rejected the stewardship-first approach outright (Cunha-Ferreira et al., 2025) — a useful, if slightly deflating, reminder that algorithmic accuracy alone will not carry these tools into routine practice without complementary behavioral and educational strategies.

### 3.7 Limits of Current AI Tools: Bias, Opacity, and Translational Failure

It would be a mistake to read this review as uncritically optimistic, and the underlying literature does not support that reading. Reference databases such as CARD and ResFinder remain disproportionately built from clinical isolates in high-income settings, which risks models that

perform well on internal validation but generalize poorly to unseen species or resistance mechanisms from underrepresented regions (Legba et al., 2026). The "black box" interpretability problem compounds this: many high-performing deep learning models offer little mechanistic explanation for their predictions, which understandably makes clinicians hesitant to act on them without a traceable biochemical rationale (Gupta et al., 2026) — explainable AI frameworks such as SHAP and LIME are a partial answer, but remain add-ons rather than a solved problem. And pharmacokinetic–pharmacodynamic (PK/PD) discordance continues to sink a substantial share of computationally promising candidates once tested in vivo (Gupta et al., 2026; Wahnou et al., 2026).

### 3.8 Toward an Integrated One Health Surveillance Framework

Taken together, the evidence reviewed points toward a fairly specific recommendation: the greatest near-term value of AI in this space probably lies not in any single tool, but in linking tools that currently operate in isolation — EHR-based predictive models, environmental metagenomic surveillance, rapid diagnostics, and clinical decision support — into one continuously updated surveillance loop spanning the One Health continuum (Mudenda et al., 2025; Sertaz Islam et al., 2026). None of the individual components reviewed here is, on its own, sufficient.

### 3.9 Study Limitations

This review has its own limitations worth stating plainly. It is a narrative rather than systematic synthesis; source selection, while intended to be broad, was not governed by a pre-registered protocol or formal risk-of-bias assessment. Several performance metrics summarized in Tables 1–4 are drawn from single validation studies rather than independently replicated benchmarks, and some tool comparisons in the source literature were not conducted head-to-head under identical conditions, which limits how directly their reported metrics can be compared. Readers should treat the figures accordingly — as a synthesis of what has been reported, not an independently validated meta-analysis.

## 4. Conclusion

Resistance to last-resort antibiotics arises through convergent molecular mechanisms — disseminated via horizontal gene transfer across clinical, agricultural, and

environmental reservoirs — and it appears to be accelerating faster than conventional detection methods can keep pace with. AI-based genomic annotation tools, rapid diagnostic platforms, and generative drug-discovery models have each shown measurable gains, often compressing detection timelines from days to minutes and surfacing structurally novel candidates that traditional screening would likely have missed. Yet, as this review has tried to make clear, database bias, model opacity, and PK/PD translational failure remain real, unresolved barriers to routine clinical deployment — this is not a solved problem, whatever the more enthusiastic press coverage might suggest. Realizing the fuller value of these tools will probably depend less on further algorithmic refinement and more on integrating environmental surveillance, rapid diagnostics, and clinical decision support into one coordinated, One Health-grounded system.

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### Author Contributions

M.J.A.: Conceptualization, literature search, writing – original draft, writing – review & editing, supervision. A.I.: Literature search, data curation (Tables 1–4), writing – review & editing. Both authors read and approved the final manuscript.

### Competing Financial Interests

The authors M.J.A. et al., declare no competing financial interests related to this work.

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