Recent Advances in Medical Microbiology: Integrating Rapid Diagnostic Technologies and Precision Antimicrobial Therapies to Combat Antimicrobial Resistance

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Abstract

Background: Infectious diseases continue to cause illness and death around the world, and antimicrobial resistance (AMR) is a concern for the ability to treat. In 2021, bacterial AMR directly contributed to approximately 1.14 million deaths and was responsible for 4.71 million deaths, and the number of attributable deaths is expected to increase by 2050. Resistance is promoted by prolonged culture-based diagnostics, resulting in delayed targeted therapy.

Methods: A structured narrative search was done on PubMed-, Scopus- and Web of Science-indexed literature, primarily between 2023 and 2026. These terms were used in searching: molecular diagnostics, point-of-care testing, next-generation sequencing, artificial intelligence, bacteriophage therapy, antimicrobials, CRISPR-Cas, microbiome therapeutics, antimicrobial peptides, nanotechnology, stewardship, antimicrobials burden, AMR burden. Recent reviews, large analyses and authoritative global reviews were given priority.

Potential benefits: Molecular assays, multiplex platforms at the point of care, metagenomic and whole-genome sequencing, and AI-driven analysis can shorten pathogen and resistance detection from days to hours, promoting the selection of appropriate antimicrobials and the management of sepsis. Multidrug-resistant pathogens are targeted by precision approaches such as antimicrobial peptides, phage therapy, targeting with CRISPR and intervention in the microbiome and delivery with nanotechnology. Yet, there are challenges in the areas of standardization, regulation, cost, data integration, and equitable access.

Conclusion: The implementation of rapid genomic diagnostics coupled with targeted antimicrobial therapies presents a strong tool to combat AMR, but a coordinated investment, stewardship alignment, and a more innovative regulatory environment and One Health surveillance are needed to achieve this.

Keywords: Antimicrobial resistance; rapid diagnostics; precision medicine; molecular microbiology; antimicrobial stewardship; bacteriophage therapy; CRISPR-Cas; One Health

1. Introduction

1.1. Novelty and Scientific Contribution

Many previous reviews have already discussed the diagnostic component of the antimicrobial resistance (AMR) problem, mostly limited to molecular assays or a point-of-care platform, or the therapeutic aspect, mostly on a specific emerging platform, like bacteriophage therapy or antimicrobial peptides (AMP) (Kaprou et al., 2021). Fewer studies directly link the emergence of rapid diagnostics to parallel development of precision antimicrobial therapy in an integrated stewardship approach. This review aims to fill this gap, specifically by intentionally focusing on diagnostics and therapeutics as two sides of the same clinical decision pathway and not separate literatures.

The main achievement of this review is that it is described below.

- It integrates recent evidence (2023–2026) on the use of rapid diagnostic technologies such as molecular polymerase chain reaction (PCR) assays, point-of-care platforms, metagenomic and whole-genome next-generation sequencing (NGS), as well as emerging precision antimicrobial therapeutics, such as novel antimicrobial peptides, bacteriophage therapy, CRISPR-Cas resistance gene targeting, and microbiome-directed interventions.
- It directly addresses the role of speed and accuracy of diagnostics in relation to antimicrobial stewardship outcomes, based on recent network meta-analyses and reviews of the antimicrobial stewardship-focused literature on bloodstream infection management.
- It places the discussion in the most recent authoritative global context of the Bacterial Priority Pathogens List of WHO 2024 and the Global Burden of Disease (GBD) AMR mortality forecasts to 2050 to orient the framing of the review in the context of current global epidemiological trends of AMR rather than previous estimates.
- It identifies gaps in cross-cutting implementation, such as diagnostic standards, regulatory processes for living therapeutics, data interoperability, and access to diagnostic, that are common to otherwise very different technology streams (Marino et al., 2025).
- It offers a conceptual framework of integrated concepts that are linked together and can be used as a heuristic for clinical and policy audiences and not as a validated causal model (Virhia et al. 2024).

Together, these contributions aim not to offer an exhaustive account of all innovation and its implications for AMR, but to offer a single reference point for the clinical, microbiological, and health policy communities that will help them coordinate rather than work in parallel to meet the rapidly unfolding AMR crisis.

1.2. Overview of Medical Microbiology

Medical microbiology is the study of microorganisms which cause human disease, including bacteria, viruses, fungi and parasites, including their identification, characterization and clinical management (Frank, 2014). The discipline has evolved from a purely morphological and culture-dependent identification to molecular, genomic and, in recent years, computationally based diagnostic approaches in the last century. All of these transitions are prompted by a clinical need that has been present for many years: the need for the identification of the causative organism and its susceptibility to the antimicrobials, in time to impact antimicrobial treatment choices that drive patient outcomes. In this article, the current age of medical microbiology is dominated by the coming together of two very different areas: the speed at which molecular and genomic diagnostics can be performed, and precision-targeted antimicrobial therapeutics, both of which are discussed in great detail.

1.3. Global burden of infectious diseases

Infectious diseases remain a significant burden on health systems globally, and bloodstream infections and sepsis are an important part of this burden. Sepsis has been estimated to impact tens of millions of people every year, and delays in effective antimicrobial therapy have been shown to be associated with an increased risk of death for every hour that elapses after diagnosis (Kumar et al., 2024). The clinical urgency associated with sepsis and other serious bloodstream infections has turned how quickly and accurately the pathogen of the infection is identified into a key factor in patient survival, highlighting the clinical importance of the fast diagnostic tools outlined below in this review.

1.4. A new challenge facing the world today is antimicrobial resistance

Aslam et al. (2021) have reported that antimicrobial resistance (AMR) is one of the greatest threats to public health in the 21st century. In 2024, the GBD 2021 Antimicrobial Resistance Collaborators published the most comprehensive epidemiological assessment ever, which estimated that in 2021,

bacterial AMR was directly responsible for approximately 1.14 million deaths and indirectly responsible for an additional 4.71 million deaths. The same analysis estimated that annual mortality directly caused by AMR could reach 1.91 million by 2050, and the annual number of deaths associated with AMR could reach 8.22 million by 2050, with a total of over 39 million deaths from 2025-2050 (AMR, 2026). Importantly, the same study showed that a significant fraction of this projected mortality (92 million deaths between 2025 and 2050) could be prevented under a better-care scenario with better management of infections and greater access to antibiotics, demonstrating that the AMR mortality trend is not set in stone but is subject to intervention.

This load is not evenly distributed. The same GBD analysis predicted that the highest all-age AMR deaths by 2050 will be in South Asia and Latin America, and the burden of AMR-attributable deaths will be disproportionately high among adults aged 70 years and older, which will represent almost two-thirds of all-age AMR deaths by mid-century. Using region-level analyses, including the WHO Eastern Mediterranean Region, which includes Iraq, similarly shows significant AMR-attributable mortality and that rigorous, methodologically consistent time-trend data for the region are comparatively sparse compared to those in high-income settings, highlighting the need for surveillance and reporting at the regional level (Ahmed, 2026).

In this context, the World Health Organization released an updated version of the Bacterial Priority Pathogens List (BPPL) in 2024, which followed the 2017 version. In 2024, BPPL looked at 24 antibiotic-resistant bacterial pathogens, assigned them to a critical, high priority and medium priority tier, based on eight criteria, such as mortality, incidence, resistance trends, and treatability (WHO, 2026). Other Gram-negative bacteria also had the highest priority quartile with a composite priority score of 84% for carbapenem-resistant Klebsiella pneumoniae and rifampicin-resistant Mycobacterium tuberculosis. The 2024 list also included a number of pathogens that have been associated with community-acquired infection, notably fluoroquinolone-resistant Salmonella enterica serotype Typhi and Shigella species, which have recently been identified as a community problem as well as in primary care (Ranjan et al., 2026).

1.5. Limitations of Conventional Microbiological Diagnostics

Traditional clinical microbiology has been based on the culture method, where a clinical specimen is cultured and then phenotypically identified and tested for antimicrobial susceptibility (Maurer et al., 2017). These methods continue to be the diagnostic standard in many hospitals and are clinically useful, but are time-limited: most bacterial cultures take 24-72 hours to deliver identification and susceptibility data, and slower-growing or fastidious bacteria can take much longer. Clinicians are often forced to start empiric broad-spectrum antimicrobial therapy, which is medically essential to avoid under-treatment of life-threatening infection, but one of the main contributors to selective pressure for resistant organisms. A key driver of the fast diagnostic technologies (discussed in Section 3 of this review) is the diagnostic-therapeutic mismatch, where there is a need for immediate treatment, but not enough organism-specific information is available.

1.6. Emergence of Precision Medicine in Infectious Diseases

While traditionally precision medicine is linked to oncology, it is generally defined as the customization of clinical approaches based on the unique genomic, molecular and/or phenotypic features of the individual and their disease process. But the same reasoning – the clearer you can describe the cause the more targeted and less harmful the intervention – is especially relevant for infectious disease. From a perspective of AMR, precision medicine suggests that the shift from "shotgun" or "one size fits all" empirical wide-spectrum antimicrobial prescribing to prescribing based on more rapidly available, organism- and resistance gene-specific diagnostic data, with the aim of using narrower-spectrum therapeutic modalities (bacteriophages, antimicrobial peptides, and

gene-edited antimicrobials, if applicable), rather than broad-spectrum therapy alone (Yaffe et al., 2025).

1.7. Aim and Scope of the Review

The purpose of this review is to critically synthesize recent literature on rapid diagnostic tools and precision antimicrobial therapeutics and to explore the potential role of combining these tools to enhance AMR stewardship and mitigate the clinical and public health impact of AMR. The review is based mainly on literature published from 2023 to 2026, with some studies cited that are fundamental to provide context and historical background. The literature search and source selection process for the identification of the studies discussed in this review is summarized as shown in Figure 1.

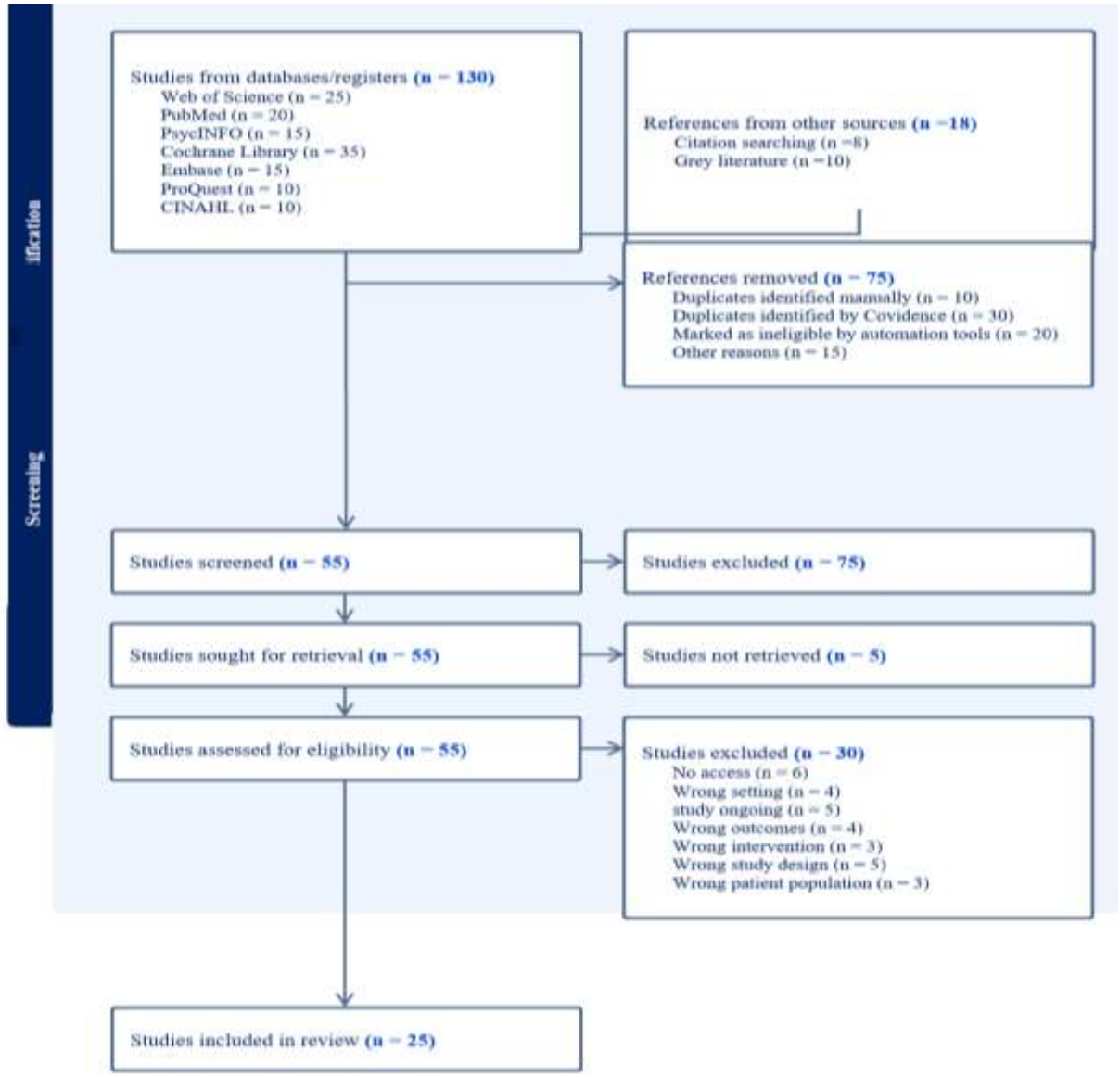

Figure 1. PRISMA

It should be emphasized that this review is not a systematic review with all the information that should be included in a PRISMA-compliant systematic review, including exhaustive multi-database searches, two independent reviewers screening all articles, and formal risk-of-bias scoring of all included articles. The eighteen key sources included for detailed synthesis (Figure 1) were included because they were deemed to be of methodological quality, recent and theme-relevant, and are representative of salient recent developments rather than a complete listing of published literature across this rapidly evolving field. For a comprehensive systematic evidence base on any one of the subtopics covered in this document, such as clinical trials of bacteriophages or antimicrobial mechanisms of CRISPR-Cas, readers are referred to the systematic reviews on these specific topics cited within each of the respective sections, some of which used a full PRISMA methodology.

This review is related to three research objectives and research questions, which are addressed below.

2. Research Objectives and Questions

Objective 1: To critically review recent developments in rapid diagnostic technologies and their implications for the detection of infectious diseases and clinical decision-making.

Research Question 1 (RQ1): What are the recent innovations in rapid diagnostic technologies which have changed the way microorganisms are detected and clinical decisions made in medical microbiology?

Objective 2: Evaluate new precision and targeted antimicrobial treatments of infectious diseases.

Research Question 2 (RQ2): What are the most promising targeted antimicrobial therapies available or being developed to treat infectious diseases?

Objective 3: To review the contribution of the application of advanced diagnostics and targeted therapeutics to antimicrobial stewardship and antimicrobial resistance mitigation.

Research Question 3 (RQ3): What can be done to enhance antimicrobial stewardship and decrease the emergence of antimicrobial resistance by combining rapid diagnostics and precision antimicrobial therapies?

3. Methodology

This review uses a structured narrative review design based on selected reporting principles from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines (Page et al., 2020) but does not meet the criteria to be considered a systematic review. The review is a structured synthesis of the existing literature and would have been a complete systematic review based on the dual independent screening of at least two reviewers, a pre-registered protocol, an exhaustive search of multiple databases with well-documented Boolean strings and a formal risk-of-bias assessment of each included study, had they been conducted.

3.1. Search Strategy

A multi-theme search was structured across PubMed/MEDLINE, Scopus, Web of Science, ScienceDirect and SpringerLink, with various combinations of the listed search terms (Table 1), mainly limited to publications between 2023 and 2026. A snowballing approach was also used to search reference lists of identified systematic reviews for additional relevant primary studies, and authoritative institutional sources, such as the World Health Organization and the Institute for

Health Metrics and Evaluation, were checked directly for the latest global estimates of the burden of AMR and the classification of priority pathogens.

3.1. Eligibility Criteria

Sources would be included if they fulfilled the following criteria:

- From a peer-reviewed journal or published as an official report from a recognized global health organization (e.g., WHO, GBD/IHME).
- Directly relevant to rapid diagnostic technologies, precision antimicrobial therapeutics, antimicrobial stewardship or global AMR epidemiology.
- Had a true bibliographic record including a digital object identifier, PubMed identifier or equivalent that allows readers and editors to independently verify the record.

Sources that were excluded included those that were not peer-reviewed, preprints presented as primary evidence, did not provide enough methodological detail to determine their relevance, or were not verifiable independently.

Table 1. Summary of Methodological Parameters

Parameter	Detail
Review design	Structured narrative literature review, informed by PRISMA reporting principles where applicable, but not a full systematic review with formal dual screening and meta-analysis
Databases consulted	PubMed/MEDLINE, Scopus, Web of Science, ScienceDirect, SpringerLink (via web-based search and citation tracking)
Search period	Primary focus 2023-2026; key foundational sources from earlier periods included for historical context
Search themes	Global AMR burden; molecular and point-of-care diagnostics; metagenomic/whole-genome sequencing; AI in clinical microbiology; bacteriophage therapy; CRISPR-Cas antimicrobials; microbiome therapeutics; antimicrobial peptides; nanotechnology-based antimicrobials; antimicrobial stewardship; WHO Bacterial Priority Pathogens List
Inclusion criteria	Peer-reviewed articles; English language; systematic reviews, meta-analyses, large observational studies, and authoritative global health reports; verifiable bibliographic record
Exclusion criteria	Non-peer-reviewed preprints presented as primary evidence; sources lacking sufficient methodological detail; unverifiable or non-retrievable records
Sources retained for detailed synthesis	18 key sources (see References), supplemented by a narrative discussion of additional contextual literature identified during searching

3.2. Approaches to Synthesis

Findings are presented as themes, grouped into the four substantive areas of the research objectives of the review: rapid diagnostic technologies (Section 5); precision antimicrobial

therapeutics (Section 6); antimicrobial stewardship and antimicrobial resistance mitigation (Section 7); and cross-cutting research gaps (Section 8), rather than by the narrative. Systematic reviews and large observational studies from the last few years are given the highest priority as the most recent evidence within each domain, with single primary studies cited to support any specific mechanism or finding where a systematic synthesis was not found.

4. Evolution of Medical Microbiology

4.1. Historical Development

The modern era of medical microbiology began in 1928 with the discovery of penicillin, and the discovery of streptomycin and other early antibiotics during the 1940s, which made once-fatal bacterial infections treatable (History, 2023). Over the next few decades, the field evolved from accurately describing the phenotypic culture-based identification of a pathogen to methods that could interrogate the genetic material of a pathogen directly. In 1977, Sanger sequencing was invented, and in 1983, the polymerase chain reaction (PCR) was invented (PCR, 2026). With the sequencing of the first complete bacterial genome in the mid-1990s and the introduction of next-generation sequencing (NGS) platforms in the mid-2000s onward, the resolution with which pathogens and their resistance determinants could be characterized was further expanded. The discovery of CRISPR-Cas9 genome editing in 2012 provided a whole new therapeutic direction (Eid & Mahfouz, 2016) (as explained in detail in Section 6.4), and the COVID-19 pandemic from 2020 onwards was a significant enabler for PoC molecular diagnostics in many health systems. These and other selected milestones are shown in a timeline in Figure 2, below, and are relevant to the themes discussed in this review.

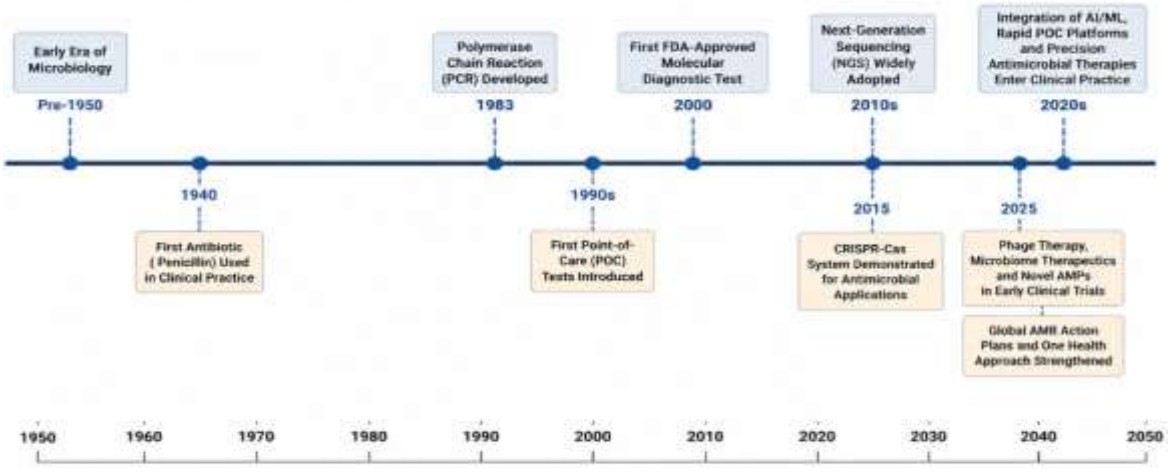

Figure 1 Timeline of selected major advances in medical microbiology, molecular diagnostics and precision antimicrobial therapy.

4.2. Traditional Diagnostic Approaches

Traditional clinical microbiological diagnosis includes the sequential process of specimen collection, culture on selective/non-selective media, phenotypic identification (based on colony morphology, Gram stain and biochemical tests), and if bacterial growth is achieved, antimicrobial susceptibility testing (using disk diffusion or broth microdilution). More recently, matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) has been added to

many clinical laboratories as an additional hurdle on the way to organism identification following colony growth, greatly reducing the time required after the growth of the organism, without replacing the need for the initial culture.

4.3. Limitations of Conventional Microbiology

The one major drawback of culture-based diagnosis is time; most bacterial pathogens need from one to three days for the culture to grow and yield an identifiable product, and antimicrobial susceptibility testing requires a further 12 to 18 hours. For organisms that grow slowly or are fastidious, such as some mycobacteria, it may last a few weeks. Another disadvantage is sensitivity; for example, false-positive culture results may be obtained due to prior antibiotic treatment, low organism load, and the presence of non-culturable pathogens or intracellular pathogens; this is especially important in the setting of culture-negative sepsis, where the organism may not be detected despite a high clinical suspicion of infection.

4.4. Transition toward Precision Microbiology

All of these constraints have led to a long-term trend toward more information available in a clinically relevant timeframe, and more specifically to information about the organism and resistance genes, in a time frame that is hours, rather than days. This shift in diagnostics has, in turn, enabled a shift in therapeutics, which has been from the broad-spectrum, empirical antimicrobial treatment to the more narrowly targeted, precision-guided therapeutic treatment outlined in Section 6. This double shift, in the diagnosis and in the therapy, is the analytical core of the review.

4.5. New technologies for rapid diagnosis of disease

Four interrelated areas of rapid diagnostic technology—molecular (PCR-based) diagnostics, next-generation sequencing, point-of-care platforms, and artificial intelligence-assisted interpretation—are examined in this section to address Research Objective 1 and Research Question 1. A summary of these technologies is presented in Table 2, and each is then discussed in turn.

4.6. Molecular Diagnostics

Polymerase chain reaction (PCR) based assays continue to be the most common molecular diagnostic tool employed in clinical microbiology, due to their analytical sensitivity/specificity and the ability to be used in centralized laboratory and, more recently, point-of-care workflows. Multiplex PCR panels, which test a clinical specimen for a specific list of pathogens and resistance features, are especially useful in syndromic settings like suspected bloodstream infection, respiratory infection and suspected sex transmission infection, where one can't simply guess the cause of the infection based on the clinical picture (Dunbar et al., 2022). Recent literature reviews show that such panels take only about 45 to 90 minutes to identify pathogens and to profile the resistance genes, compared to the 24–72-hour time required for culture-based methods. In addition to being able to detect pathogens and resistance genes, new platforms based on microfluidics and bacterial cells in droplets are also accelerating the traditional 24 or more hours of phenotypic antimicrobial susceptibility testing (AST) to results that are comparable to those of the minimum inhibitory concentration (MIC) in just 30 to 120 minutes. However, this is especially useful for novel or heterogeneous resistance phenotypes that are not necessarily detected by genotypic (resistance gene-based) assays, because phenotypic testing directly tests the growth response of the organism to the antimicrobial agent, rather than relying on genetic markers.

4.7. Next-Generation Sequencing (NGS)

Leading-edge sequencing technologies have pushed molecular diagnostics beyond just identifying pathogens and into deep pathogen characterization without any hypotheses. Metagenomic next-generation sequencing (mNGS) sequences all nucleic acid present in a clinical specimen without the need for pathogen-specific primers or probes and is a method capable of detecting the presence of bacteria, viruses, fungi and parasites all from a single sample (Chiu & Miller, 2019). It is an unbiased approach of great clinical importance in immunocompromised patients, where the spectrum of possible infecting organisms can be wider than in immunocompetent patients, as well as in culture-negative sepsis, where a causative organism is not identified by culture despite a high clinical suspicion.

There has been a growing number of studies investigating the use of mNGS for the detection of antimicrobial resistance genes. Today, curated databases of resistance genes are available for microbial and resistance gene detection within open-access bioinformatics pipelines, like the CZ ID AMR module, as part of a single cloud-based workflow for both clinical and environmental AMR surveillance. Clinical studies have also shown that NGS resistance gene detection can be clinically useful and have a clinically acceptable concordance when compared to conventional PCR-based resistance gene detection, but can also aid in pathogen identification in addition. In addition, whole-genome sequencing (WGS) of cultured bacterial isolates remains the best single-strain-level surveillance and outbreak investigation tool and is a complementary approach to the more timely culture-independent findings from mNGS.

4.8. Point-of-Care Diagnostics

Point-of-care (POC) diagnostics seek to provide clinically relevant information in an environment beyond the traditional centralized laboratory—at the bedside, in primary care, or in resource-challenged field environments (Plebani et al., 2024). The market for POC infectious disease diagnostics is currently worth USD 53 billion and will nearly double by 2033, indicating continued clinical and commercial investment in this technology category. Modern POC platforms are increasingly integrating nucleic acid amplification testing (NAAT) along with microfluidics for sample handling, and some incorporate isothermal amplification chemistries that require less equipment than conventional thermal cycling and can provide results in about 15 to 60 minutes, depending on the assay and specimen type, in a sample-to-answer format.

Such multiplex molecular POC panels can detect a large panel of viral, bacterial and fungal pathogens as well as relevant resistance genes such as mecA (methicillin resistance), blaNDM and blaKPC (carbapenem resistance), and vanA/B (vancomycin resistance) in syndromic panels used for sepsis, respiratory infection and sexually transmitted infection. There have been some clear examples in the literature of the clinical utility of this approach, such as in the use of rapid diagnostics in the management of bloodstream infections, where systematic reviews and network meta-analyses have established that the use of rapid diagnostics when integrated within a structured programmed for antimicrobial stewardship has a measurable impact on increasing the proportion of patients receiving timely, organism-targeted antimicrobial therapy, though evidence on the impact on mortality outcomes is less consistent when only rapid diagnostics were used (not within the context of a structured programmed for antimicrobial stewardship). This discovery is explained in more detail in Section 7.

4.9. Artificial Intelligence in Diagnostics

Artificial Intelligence (AI), which includes machine learning (ML), deep learning (DL) and CNN approaches, has been transitioning from experimental research tools and is now starting to

become an integral part of clinical microbiology workflows as an analytical layer. More comprehensive reviews have recently been published for the timeframe 2018-2024, which cover applications in virology (e.g., optimization of workflows in COVID-19 reverse transcription PCR), parasitology (e.g., automatic detection of malaria parasites from blood smear images) and bacteriology (e.g., image-based automatic counting of colonies and automatic interpretation of the Gram stain). These have highlighted the fact that there remain a number of prerequisites for widespread clinical adoption, including robust prospective clinical validation, consideration of data heterogeneity, and model interpretability.

An important and previously mentioned application is the use of AI in combination with matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS), which has been demonstrated to speed up the identification of microbes and profile for antimicrobial resistance. The application of AI-assisted approaches is also being explored upstream of diagnosis by identifying the most effective solutions for antimicrobial stewardship decision support and downstream of diagnosis by both inappropriate prescription detection and support of antibiotic selection, using supervised algorithms. However, a recent survey of clinical microbiology laboratories across Italy revealed that, while many laboratories (about a quarter) stated they were interested in AI or ML, only a small proportion (around three per cent) had a trained data scientist available for routine use, suggesting there remains a significant gap between AI/ML research and implementation in clinical practice.

Table 2. Comparative Summary of Rapid Diagnostic Technologies

Technology	Typical Turnaround Time	Key Strengths	Key Limitations
Multiplex / real-time PCR panels	45-90 minutes for pathogen ID plus key resistance genes	High analytical sensitivity; simultaneous detection of multiple targets, including resistance genes (e.g., mecA, blaNDM, blaKPC, vanA/B)	Limited to pre-selected targets; cannot detect novel or unanticipated organisms
Point-of-care (POC) platforms / microfluidic devices	15-60 minutes, sample-to-answer	Decentralised testing, usable in resource-limited and outpatient settings, supports immediate clinical decisions	Generally narrower test menus than laboratory-based platforms; quality assurance and connectivity challenges in some settings
Metagenomic next-generation	Same-day to ~24-48 hours depending on workflow	Unbiased, hypothesis-free detection of virtually any pathogen,	Higher cost; requires bioinformatics expertise; turnaround still slower than

sequencing (mNGS)		including rare or atypical organisms; simultaneous resistome profiling	targeted PCR/POC platforms
Whole-genome sequencing (WGS) of cultured isolates	Typically, 1-3 days (culture-dependent)	High-resolution strain typing; detailed resistance and virulence gene characterization; strong utility for outbreak surveillance	Dependent on prior culture; not a true rapid bedside test
AI-assisted interpretation (imaging, MALDI-TOF, multi-omics)	Adds minutes; embedded within existing platform workflows	Improves consistency and speed of image/spectral interpretation; supports automated resistance prediction from genomic and phenotypic data	Requires robust validation; data heterogeneity and interpretability remain open challenges

In combination, the technologies described in this section show that a diagnostic-therapeutic mismatch that occurs historically, when definitive microbiological information is not available until after the initial treatment has been begun, is becoming more manageable. The final challenge (Section 8) is not so much technical as it is technological standardization, cost and equitable distribution across health systems of different resource levels.

5. Advances in Precision Antimicrobial Therapies

The five domains of precision antimicrobial therapeutics under preclinical and clinical development are addressed in this section, which corresponds to the five categories of antimicrobials that align with Research Objective 2 and Research Question 2. A comparative summary is included at the end of the narrative discussion in Table 3.

This section outlines general principles for precision antimicrobial therapy. This Section aims to provide principles of precision antimicrobial therapy.

Precision antimicrobial therapy means that the choice of antimicrobial agents is made using more than just syndromic, empirical estimates; it also relies on information provided by diagnostic testing, including organism-specific and resistance-gene-specific test data, which can be provided by the technologies reviewed in Section 5. In practice, this could refer to the choice of an existing class of antibiotic once genotypic or phenotypic susceptibility results are available, or deployment of a new therapeutic modality that is developed to have a more restricted spectrum of activity than traditional broad-spectrum antibiotics. The five modalities discussed in this section are largely in this latter category, and all have similar conceptual aims of minimizing the collateral selection

pressure of populations of commensal and environmental bacteria that is inevitable from broad-spectrum antibiotic use, while still achieving clinical cure of the intended target infection.

5.1. Novel Antimicrobial Agents and Antimicrobial Peptides

Antimicrobial peptides (AMPs) are short, mostly cationic and amphipathic, molecules with a historically low potential to induce resistance as compared to conventional antibiotics that disrupt bacterial membranes or interfere with intracellular processes (Annunziato & Costantino, 2020). Computational tools and artificial intelligence (AI) have spurred the recent acceleration of discovery efforts; mines of the human proteome, the human gut microbiome and bacteriophage-derived peptidoglycan hydrolases have yielded thousands of new candidates for AMPs, with some computational approaches generating databases of millions of predicted antibacterial peptides for downstream experimental validation. Several of the AI-discovered or AI-optimized candidates have proven to be effective against multidrug-resistant and ESKAPE (Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa and Enterobacter species) pathogens in preclinical models, with the AI-identified peptides being identified using large-scale screening pipelines that evaluate hundreds of millions of candidate sequences through a protein language model.

5.2. Bacteriophage Therapy

Bacteriophages are viruses that target and kill certain strains of bacteria, and they have been brought back to the clinical arena in the wake of the decline in the efficacy of antibiotics (Subramanian, 2024). In 2025, a systematic review using PRISMA methodology of clinical trials that used phage therapy identified 11 trials eligible for analysis that showed a generally favorable safety profile with phage-antibiotic combination therapy being more effective than antibiotic therapy alone in several cases, across oral, intravenous and topical routes of administration. A separate, larger systematic review and meta-analysis, which included 130 studies and 1,115 patients identified from more than 16,000 studies that were screened, also found evidence for the efficacy and safety of customized and non-customized phage therapy and reported a range in clinical and microbiological response rates among the small number of RCTs conducted to date. A larger systematic review and meta-analysis of customized and non-customized phage therapy, which included 130 studies and 1,115 patients from over 16,000 studies screened, also found evidence for efficacy and safety signals and reported a range of clinical and microbiological response rates among the limited number of RCTs conducted to date. Within the small number of clinical trials related to bacteriophages registered on ClinicalTrials.gov as of early 2025, over half were sponsored by pharmaceutical companies or academic institutions, suggesting an emerging but developing clinical trial stream. Applications include recurrent urinary tract infection, prosthetic joint infection, chronic non-healing wounds and infections associated with biofilm formation, and one mini-review of wound and prosthetic joint infections indicated that 91% of the studies analyzed were successful.

5.3. CRISPR-Based Antimicrobials

The CRISPR-Cas gene editing technology provides a programmable approach to directly target and inactivate the genetic underpinning of antimicrobial resistance, instead of using a separate antimicrobial compound that acts indirectly to overcome resistance. When a 2025 systematic review was conducted, using the PRISMA guidelines and limited to studies published between 2014 and June 2024, only 48 studies were found that met the inclusion criteria and described the use of CRISPR-Cas9, CRISPR-Cas12a and CRISPR-Cas3 systems to target resistance genes to carbapenems, cephalosporins, methicillin, macrolides, vancomycin, colistin and fosfomycin,

respectively. The delivery of CRISPR-Cas machinery into target bacteria, a key translational hurdle for the technology, has been achieved in vitro with a number of systems, including bacteriophages, nanoparticles, electro-transformation and conjugative plasmids, all with measurable efficacy in vitro and some in vivo. In addition to directly destroying resistance genes, the ability of the CRISPR-Cas systems to degrade mobile genetic elements like resistance plasmids, thus reducing the horizontal spread of resistance determinants within and between bacterial populations, and the capacity of the CRISPR-Cas systems to engineer beneficial bacterial strains with increased colonization resistance against pathogenic species have been explored.

5.4. Microbiome-Based Therapeutics

Microbiome-directed therapeutics involve approaches that remove multidrug-resistant organisms (MDROs) indirectly by restoring a competitive and diverse gut microbiome that provides colonization resistance, which is the indirect effect of killing the resistant organism, rather than by direct killing. FMT has already been recommended in guidelines for the treatment of recurrent C. difficile infection, and several recent studies have added MDROs of special concern on the WHO critical priority list to the list of conditions that are treatable with FMT: extended-spectrum beta-lactamase-producing Enterobacterales (ESBL-E), carbapenemase-producing Enterobacterales (CPE) and vancomycin-resistant enterococci (VRE). A recent mechanistic study published in Science Translational Medicine showed that FMT can decrease the burden of antimicrobial resistance genes by strain replacement, and the abundance of resistance genes was measurable in the gut even within 7 days of transplantation and in the nasal microbiome by Day 56, indicating that interventions directed to the gut could affect the reservoirs of antimicrobial resistance genes beyond the GI tract. The clinical case-control evidence also demonstrated a reduction in MDRO associated UTI and bloodstream infections following FMT, but the field still has some standardization challenges, such as screening, variable engraftment rates and the most appropriate clinical endpoint (e.g. durable eradication versus a reduction in the risk of infection) to assess therapeutic efficacy.

5.5. Nanotechnology-Enabled Antimicrobials

Nanotechnology-based antimicrobial approaches involve the use of engineered nanocarriers, including metallic, polymeric, lipid-based, metal-organic framework, carbon and hybrid nanostructures, which can be used to deliver conventional antibiotics and novel antimicrobial agents like peptides with enhanced delivery, biofilm penetration and target specificity (Malook et al., 2026). Nanocarriers have the potential to increase antimicrobial activity in several ways, such as increasing solubility and penetration into tissues, drug release in response to infection, and direct antimicrobial action against the efflux pump-mediated resistance system of bacteria. Preclinical applications reported include improved efficacy of antibiotics against multidrug-resistant Klebsiella pneumoniae, using nanoparticles in the clearance of biofilm-forming Staphylococcus aureus, and graphene oxide-based adjuvant strategies being studied against drug-resistant Mycobacterium tuberculosis. Although there are many preclinical studies, the translation of nanotechnology-based antimicrobials to the clinic is still in its early stages, and long-term biodistribution, safety, and scalable manufacturing have yet to be addressed.

Table 3. Comparative Summary of Precision Antimicrobial Therapies

Modality	Mechanism	Stage of Clinical Development	Key Limitations
Novel antimicrobial peptides (AMPs)	Broad-spectrum membrane disruption or intracellular targeting; AI/deep learning-assisted discovery from natural and synthetic peptide libraries	Preclinical to early clinical; AI-discovered candidates validated in vitro against MDR/ESKAPE pathogens	Stability, manufacturing cost, and potential toxicity at scale remain key translational barriers
Bacteriophage therapy	Lytic bacteriophages selectively infect and destroy specific bacterial strains, including biofilm-embedded organisms	Multiple completed and ongoing clinical trials and case series (over 20 registered trials as of early 2025); systematic reviews report favourable safety profiles	Strain specificity complicates standardized production; regulatory pathways for personalized phage cocktails remain underdeveloped
CRISPR-Cas antimicrobials	Programmable targeting and elimination of specific resistance genes (e.g., blaNDM, blaKPC, mcr-1) or resistance plasmids can resensitize bacteria to existing antibiotics	Predominantly preclinical (in vitro and animal models); delivery via phage, nanoparticle or conjugative plasmid vectors under active investigation	In vivo delivery efficiency, off-target effects, and regulatory/ethical pathways for gene-editing antimicrobials remain unresolved
Microbiome-based therapeutics (FMT, probiotics)	Restoration of competitive gut microbiota to displace multidrug-resistant organism (MDRO) colonization and reduce resistance gene (resistome) burden	Established for recurrent Clostridioides difficile infection; emerging clinical evidence for MDRO decolonization (ESBL-E, CPE, VRE)	Variable engraftment; donor screening and standardization challenges; evidence for sustained MDRO eradication is still developing
Nanotechnology-enabled antimicrobials	Metallic, polymeric, lipid-based and hybrid nanocarriers enhance drug delivery, penetrate biofilms, and can bypass efflux-pump-mediated resistance	Extensive preclinical evidence across multiple nanoparticle classes; limited clinical-stage translation to date	Long-term safety, biodistribution and large-scale manufacturing reproducibility require further study

When taken together, these five therapeutic approaches reflect a space that's rapidly shifting and maturing with some evidence already emerging from clinical trials, and others in the early stages

in the preclinical arena but progressing at a vigorous pace. The following section explores how these therapeutic innovations contribute to the diagnostic innovations discussed in Section 5, and how they affect the course of antimicrobial resistance (AMR) and antimicrobial stewardship (AMS).

6. Antimicrobial Resistance and Stewardship

This section directly reflects Research Objective 3 and Research Question 3 by exploring the influence of the diagnostic and therapeutic innovations that were discussed in Section 5 and Section 6 on measurable antimicrobial stewardship outcomes and places this in the context of the global AMR trend data.

6.1. Global AMR Trends

According to the latest comprehensive global analysis of bacterial AMR, some 1.14 million people died directly from the effects of bacterial AMR in 2021; another 4.71 million deaths were attributed to the effects of AMR in 2021, but not necessarily directly related to it. These figures for 2021 are shown in Figure 3, Panel A, along with the 2050 projections under the reference scenario (in which annual attributable mortality is estimated to be 1.91 million and annual AMR-associated mortality 8.22 million). Panel B shows the specific growth trends of two resistance phenotypes (deaths directly due to MRSA and deaths due to carbapenem-resistant Gram-negative infections) between 1990 and 2021, with deaths directly due to MRSA more than doubling (from ~ 57,000 to 130,000 per year) and deaths due to carbapenem-resistant Gram-negative infections increasing by more than 200% (from ~ 127,000 to 216,000 deaths per year) over the same time period, driven by the especially rapid rise of Gram-negative resistance.

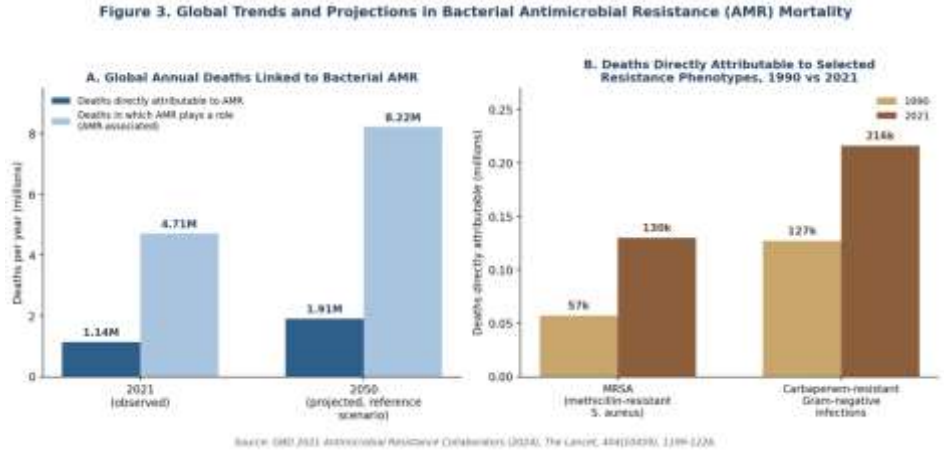

Figure 2 Global trends and projections in bacterial antimicrobial resistance (AMR) mortality. Source: GBD 2021 Antimicrobial Resistance Collaborators (2024), The Lancet, 404(10459), 1199-1226.

These trends are not consistent across the country. The highest projected all-age AMR mortality rates by 2050 are also in South Asia and Latin America and the Caribbean, and the WHO Eastern Mediterranean Region (Eastern Mediterranean Region, including Iraq and neighboring countries) was identified as an area of significant and potentially under-represented AMR burden because of the relatively limited longitudinal surveillance data compared with high-income regions.

6.2. Mechanisms of Resistance

There are several overlapping molecular mechanisms that underlie bacterial antimicrobial resistance: enzymatic inactivation of antimicrobials (e.g. beta-lactamases and carbapenems encoded by blaNDM, blaKPC and blaOXA-48 genes, respectively), modification of the drug target site (e.g. mecA gene, which encodes the alteration of penicillin-binding proteins associated with methicillin resistance), decreased membrane permeability, active efflux pump-mediated drug exclusion, and protection of the bacteria in a biofilm when drug penetration and host immune clearance are limited. Several of the resistance determinants discussed in this article are carried on mobile genetic elements such as plasmids, transposons and integrons that allow horizontal gene transfer from one bacterial species to another and are one of the major ways in which resistance is distributed within and between clinical and environmental bacterial populations and which several Therapeutic modalities listed in Section 6 specifically target.

6.3. Impact of Diagnostics on Stewardship

There is a large and growing body of evidence that supports the association between rapid diagnostic deployment and process measures of antimicrobial stewardship. The clinical benefit of rapid diagnostics was greatest when integrated into a structured antimicrobial stewardship programmed (ASP) as opposed to when RDTs were used in isolation, while evidence on the use of RDTs alone showed more limited and inconsistent clinical benefits in the management of bloodstream infections in 2024, as reported by a systematic review and network meta-analysis. A complementary systematic review in 2025 on the integration of rapid diagnostic tests (RDTs) within antimicrobial stewardship programmed (AMSP) reached the same conclusion, namely that the clinical impact of RDTs is greatest when they are paired with sound stewardship response plans and are not seen as an intervention in lieu of stewardship infrastructure.

In the case of sepsis, this is especially critical and has been linked to a 6 to 10% increased risk of death for every hour of delay in proper antibiotic treatment. Rapid diagnostic testing coupled with timely ID consultation has been shown to be part of a practical stewardship strategy, whereby speed of diagnosis can lead to improved targeting of antibiotic therapy without delaying the urgent treatment of septic patients in the ICUs.

6.4. Precision Therapy and Resistance Reduction

The precision therapeutic modalities examined in Section 6 include various mechanisms to reduce resistance, but with differing approaches. Bacteriophage and CRISPR-Cas-based therapeutics target the resistant organism or its resistance determinant, while microbiome-based therapeutics target the ecological niche available for the defense by MDROs, and in the case of FMT, the total burden of antimicrobial resistance (AMR) genes, measurably reduced after shifting the bacterial flora; nanotechnology-based delivery systems enhance the efficacy of existing or novel antimicrobial agents, which minimizes the dose and duration of exposure for clinical cure, and consequently the selection pressure on bacterial populations. These therapeutic advances are taken together with rapid diagnostics to follow a logical stewardship pathway: better diagnosis means better treatment which, in turn, means less antimicrobial exposure that will select for antimicrobial resistance.

6.5. One Health Approaches

Resistant microorganisms, resistance genes and antimicrobial residues can spread among human, animal and environmental reservoirs and occur outside of clinical settings, and the One Health approach is designed to bring together surveillance and intervention efforts across these sectors to prevent or slow the emergence and spread of antimicrobial resistance. A recent

perspective on a recent WHO Bacterial Priority Pathogens List from a One Health perspective noted that while the list serves as an effective evidence-based roadmap to guide research and development and infection control measures in humans – including vaccines and water, sanitation & hygiene (WASH) programmed – priorities in the list are predominantly human-based and therefore rather under-represented are agriculture and environmental drivers of AMR, as well as the Global AMR surveillance infrastructure, which is biased towards high income countries with laboratory networks. The enhancement of cross-sectoral surveillance is thus highlighted as one of the priorities, particularly in areas with relatively sparse integrated human-animal-environmental AMR data, such as Iraq.

Table 4. Advantages and Limitations of Emerging Technologies

Technology / Modality	Principal Advantages	Principal Limitations
Multiplex PCR / POC platforms	Rapid (15-90 min) organism and resistance gene detection; supports immediate stewardship decisions	Limited to pre-specified targets; cannot detect novel pathogens or untested resistance mechanisms
Metagenomic / whole-genome sequencing	Unbiased pathogen detection; comprehensive resistome and strain-level data; valuable for outbreak surveillance	Higher cost and bioinformatics burden; turnaround still slower than targeted POC assays
AI-assisted interpretation	Improves consistency and throughput of image/spectral analysis; embedded resistance prediction	Requires extensive validation; data heterogeneity; limited trained-personnel availability in many laboratories
Bacteriophage therapy	High specificity; favourable safety profile in trials to date; effective against biofilm-associated infection	Strain specificity complicates production standardization; an underdeveloped regulatory pathway
CRISPR-Cas antimicrobials	Directly eliminates resistance determinants; can resensitize bacteria to existing antibiotics	Predominantly preclinical; in vivo delivery efficiency and regulatory pathway remain unresolved
Microbiome therapeutics (FMT)	Established efficacy for recurrent C. difficile; emerging evidence for MDRO decolonization	Variable engraftment; donor standardization; uncertain durability of resistome reduction
Nanotechnology-enabled antimicrobials	Enhanced biofilm penetration; can bypass efflux-pump resistance; broad applicability across nanocarrier classes	Limited clinical-stage translation; long-term safety and manufacturing reproducibility unresolved

7. Research Gaps and Current Challenges

While significant advancements have been made in the diagnostic and therapeutic areas examined in Sections 5 and 6, there are certain areas that crosscut the entire literature and merit specific attention by researchers, clinicians and policy makers.

7.1. Diagnostic Challenges

The lack of standardization: bioinformatics pipelines for metagenomic sequencing and artificial intelligence-based interpretation of sequencing data can differ significantly between laboratories and platforms and can make it difficult to compare these studies with others.

Costly equipment: The new molecular sequencing technology and multiplex platforms are expensive and need a dedicated team to maintain them, making their use outside of highly-resourced laboratories difficult.

Accessibility is also limited in resource-limited contexts: while point-of-care platforms are clearly meant to address this challenge, the same WHO Bacterial Priority Pathogens List process highlighted that there are still substantial data and surveillance gaps in a number of regions in the world, suggesting that while diagnostic inventions exist, diagnostic deployment is not evenly distributed.

7.2. Therapeutic Challenges

Uncertainty around approval pathway: Several modalities reviewed in Section 6 have the potential for approval pathway uncertainty due to existing pharmaceutical regulatory frameworks, which are designed primarily for small-molecule drugs, not fully adapted to personalized bacteriophage cocktails or gene-editing antimicrobials.

There is limited long-term clinical evidence: Although the clinical evidence is limited, there is still meaningful evidence in the form of randomized controlled trials for bacteriophage therapy and microbiome-based therapeutics compared to conventional antibiotics; and for CRISPR-Cas antimicrobials and Nanotechnology-enabled delivery systems, the evidence is mainly preclinical.

In some preclinical and clinical situations, resistance to phages has been noted (although in a manner comparable to antibiotic resistance), leading to the possibility that multiple-agent therapies (such as phage-antibiotic or phage cocktail therapies) may eventually be more resistant to the evolution of resistance than phage therapy.

7.3. Data Challenges

AI-assisted resistance prediction models are constrained by the challenge of integrating laboratory data, which includes genomic, phenotypic and clinical outcome data, from a variety of hospital information systems to allow for the training and validation of models at scale.

AI validation challenges: As mentioned in other sections, a survey of 2025 clinical microbiology laboratories showed that while there was a strong interest in the development of AI/ML tools, few were deployed in the lab, and only a small number of the respondents had access to trained data scientists to develop these tools to a level where they can be used in routine clinical practice.

MRD interoperability issues: there are currently regional inequalities in the availability of interoperability in the global AMR surveillance infrastructure, including the WHO Global Antimicrobial Resistance and Use Surveillance System (GLASS), with laboratory networks and data reporting capacity being stronger in high-income settings compared to many LMIC settings, including parts of the Eastern Mediterranean Region.

In total, these difficulties imply that the primary obstacle to achieving the maximum value of the technologies discussed in this article is now less a scientific question of feasibility, and more a question of standardization, regulatory adaptation, data infrastructure and global deployment – at least for equitable access.

7.4. Proposed Integrated Framework

In this section, we propose a conceptual framework that combines the evidence in Sections 5-8 into one pathway that reinforces each other: rapid diagnostic deployment, precision treatment selection, targeted antimicrobial therapy, antimicrobial stewardship and AMR reduction. The framework, as presented in Figure 4, will be used as a heuristic device throughout this review to organize the relationships described and is in no way an empirically supported causal model, the strength of the individual links (e.g., rapid diagnostics and stewardship outcomes) will vary in the evidence base.

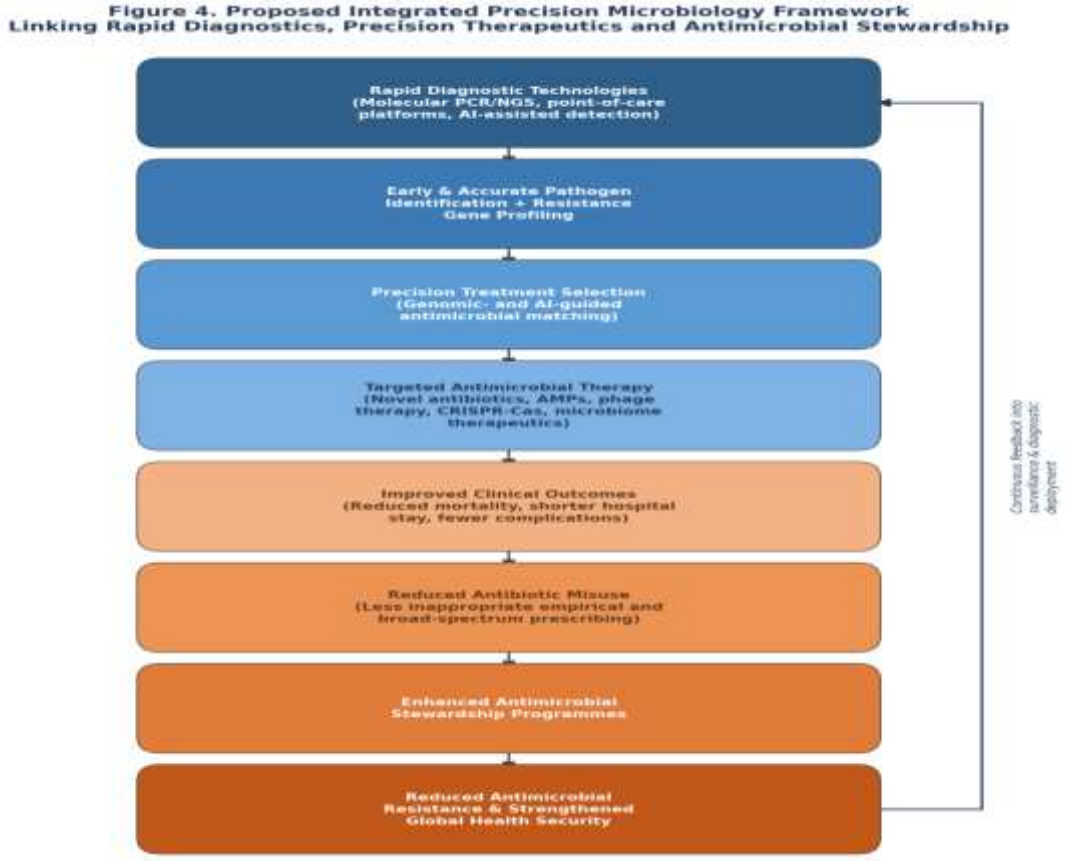

Figure 3 Proposed integrated precision microbiology framework linking rapid diagnostics, precision therapeutics and antimicrobial stewardship

The framework starts with rapid diagnostic technologies (Section 5) that allow identification of the pathogen at an early stage, and with good accuracy, as well as the resistance gene profiling. Precision treatment selection informed by genomic or AI-assisted decision support (Section 5.4), which involves a more targeted approach to therapy, either by using a relatively small number of conventional antibiotics or by using one of the precision modalities reviewed in Section 6, if applicable, follows this diagnostic output and guides clinicians towards more targeted antimicrobial therapy. Targeted therapy has been linked to better clinical results such as decreased mortality,

shorter hospital stays, and less antibiotic overuse due to an organism-matched, more narrow-spectrum approach to treatment, replacing unnecessary broad-spectrum empirical treatment. Together, these two downstream effects support improved AMSPs (as discussed in Section 7.3), which are most effective when used in combination with rapid diagnostic testing, and will help to lower antimicrobial resistance and improve global health security. As illustrated on the right of Figure 4, the resistance data and the outcome data from this pathway should also feed into the continuous prioritization and optimization of deployment of diagnostics and surveillance, as laid out in the One Health surveillance principles in Section 7.5, in a functioning health system.

7.5. Future Directions

Based on the gaps that were identified in Section 8 and the integrated framework proposed in Section 9, several emerging areas of research seem to be particularly promising to advance the next development steps in this field.

Microbiology assisted by Artificial Intelligence (AI): continued development of validated and prospectively tested AI models for pathogen identification, resistance prediction and discovery of antimicrobial peptides, with concurrent efforts on building laboratory data science capacity to deploy these routinely.

Real-time genomic surveillance: increasing the capacity and number of regions participating in sequencing-based surveillance, especially where underrepresented within global AMR genomic databases, to enable more rapid outbreak detection and better estimation of the global trend of resistance.

Digital health integration: improved linkage of rapid diagnostic outputs with EHR and clinical decision-making systems for greater reliability and speed of stewardship action to diagnosis.

Nanotechnology-based antimicrobials: further translation of the nanocarrier-based delivery systems for antimicrobials from preclinical to clinical experimentation, emphasizing long-term safety and manufacturing scalability.

CRISPR diagnostics and therapeutics: continued development of both CRISPR based diagnostics assays (e.g., CRISPR-Cas13-based nucleic acid detection) and CRISPR-Cas antimicrobial delivery systems, which have been predominantly preclinical to date, as reviewed in Section 6.4.

Personalized infectious disease management: the progressive merging of host genomic, microbiome and pathogen genomic data to enable individualized antimicrobial selection, which is the logic of precision medicine introduced in Section 2.5, extended to the field of infectious diseases.

One Health surveillance systems: improved integration of human, animal and environmental AMR surveillance data, as identified in Section 7.5, between the current human-centric focus of surveillance systems and the cross-sectoral nature of AMR emergence and spread.

Global AMR monitoring networks: scaling up and harmonization of AMR monitoring networks, including GLASS, and prioritizing participation and laboratory capacity in underrepresented areas, including parts of the Eastern Mediterranean Region.

8. Discussion

8.1. Comparison to the Next Review(s)

The body of literature on antimicrobial resistance that already exists has been primarily focused on either the innovation of diagnostics or the innovation of therapeutics, with separate reviews

covering the field of molecular diagnostics, the role of AI in microbiology, for example, or bacteriophage therapy or CRISPR-Cas antimicrobials providing important contributions to their individual fields but not explicitly linking them to the other (Wu et al., 2025). The primary value of this review, as described in Section 1, is that it takes these as a single, interdependent pathway: diagnostic speed and effectiveness lead to the right deployment of precision therapeutics, and precision therapeutics bring meaning to the more detailed diagnostic information that rapid technologies are now providing. Faster diagnostics, or narrower-spectrum therapeutics, alone would not be expected to make a meaningful difference to the AMR trajectory outlined in Section 7.1, and together, they would be much more promising if they were part of a structured stewardship programmed, as the evidence reviewed in Section 7.3 indicates they need to be.

The evidence provided in this article clearly points to a practice implication for practicing clinicians: the use of the rapid diagnostic test is best maximized when integrated within a structured response protocol, akin to those which characterize a well-developed antimicrobial stewardship programmed. The evidence presented in Section 7.3 strongly suggests that investment in rapid diagnostic infrastructure should be used in conjunction with investment in stewardship personnel and stewardship protocols – but not as a replacement for maximizing clinical benefit.

8.2. Cost-Effectiveness Considerations

While the details of an economic assessment are not included in the scope of this narrative review, the literature reviewed here indicates a recurring concern about the cost of the initial technology investment, the operating cost of a rapid diagnostic and precision therapeutic technology, and the savings that could be achieved downstream with that investment, through lower length of hospital stay, lower complication rates, and lower use of broad-spectrum antimicrobials. As observed in Section 5.3, the point-of-care (POC) diagnostics market is expected to grow from around USD 53 billion in 2024, and this cost-benefit judgment, at least in aggregate, is reflected in the growth of the market. Formal cost-effectiveness evidence for many of the precision therapeutics reviewed in Section 6, however, remains relatively underdeveloped and represents an important area for future health economic research.

8.3. Policy Implications

In 2024, the WHO Bacterial Priority Pathogens List was discussed in Sections 2.3 and 7.5 and was to be used as an evidence-based prioritization tool to guide research and development funding efforts toward the pathogens of greatest clinical concern, with carbapenem-resistant Klebsiella pneumoniae and related Gram-negative organisms listed in the highest-priority tier. The policy implication from this review is to consider funding and regulatory attention in addition to the priority pathogens themselves to the technology categories for diagnostics and therapeutics that will be most likely to deliver clinical impact from priority-setting. The One Health critique in Section 7.5 also indicates that policies that focus on human clinical outcomes may, if they do not complement agricultural and environmental policies, not adequately target the upstream drivers of the resistance burden that the clinical technologies are trying to address.

Future Implementation Challenges

The challenge of moving technology from capability to clinical deployment in an equitable and standardized way, which is outlined in Section 8, was identified across this review. This challenge is especially relevant for the WHO Eastern Mediterranean Region (EMR), where this review highlighted the relative lack of longitudinal AMR data and a lack of multi-sectoral One Health

integration compared to high-income countries, highlighting a need for capacity building in addition to ongoing technological advancement in this region.

9. Conclusion and Recommendations

9.1. Conclusion

The current review has explored the latest developments in rapid diagnostic technologies, ranging from molecular PCR-based assays, point-of-care platforms, next-generation sequencing and AI-driven interpretation, through to new precision antimicrobial therapeutics such as novel antimicrobial peptides/peptides of natural origin, bacteriophage therapy, microbiome-directed, nanotechnology-driven drug delivery. The evidence presented here highlights the growing interdependence of these two domains: the speed and resolution of the diagnostic process become increasingly relevant for the ability of precision therapeutics to be precisely targeted and the precision therapeutics provides practical utility in the context of the more detailed organism and resistance-gene specific information provided by rapid diagnostics. Together, this combination may have the potential to make a positive impact on the trajectory of the global burden of AMR, estimated at 1.91 million deaths per year by 2050, without intervention.

9.2. Recommendations

For Researchers:

Perform multi-centre validation of AI-driven Dx and resistance prediction tools, focusing on prospective clinical validation, rather than retrospective proof-of-concept analysis.

Establish standardized bioinformatics and reporting procedures for detecting resistances by metagenomic sequencing, which will enable comparability between studies and external validation.

Support the incorporation of evidence from randomized controlled trials for bacteriophage therapy, antimicrobial agents based on CRISPR-Cas and microbiome-based therapeutics, with the inclusion of encouraging, but still comparatively limited, clinical evidence reported in Section 6.

For Clinicians:

Make use of rapid diagnostic technologies when available and incorporated into standard antimicrobial stewardship programs, rather than as stand-alone tests as supported by evidence in Section 7.3.

Closely follow local antimicrobial resistance surveillance data to guide empirical antibiotic selection until diagnosed.

For Policymakers:

Provide enabling support to innovation funding for diagnostic and precision therapeutic technologies, acknowledging the complementary role they can play in AMR mitigation, not as substitutes for each other.

Optimize equitable access to rapid diagnostic infrastructure, especially in areas under-represented in global surveillance and technology deployment, such as parts of the Eastern Mediterranean Region.

Improve AMR monitoring systems under a One Health approach, drawing on data from human, animal and environment, in accordance with the gaps identified in Section 7.5.

These recommendations collectively support this review's key conclusion: that the prevention and mitigation of AR must go beyond the development of diagnostics and therapeutics and be purposefully and strategically integrated into enhanced stewardship and surveillance frameworks.

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