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When Faster Diagnosis Is Not Enough: Bringing Diagnostic Stewardship into Antimicrobial Stewardship

Luca Mezzadri[1,2], Paolo Bonfanti[1,2]
[1]School of Medicine and Surgery, University of Milano-Bicocca, Milan, Italy;
[2]Infectious Diseases Unit, Fondazione IRCCS San Gerardo dei Tintori, Monza, Italy.

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Antimicrobial resistance (AMR) remains one of the most urgent global health challenges. In 2021, an estimated 4.71 million deaths were associated with bacterial AMR, including 1.14 million directly attributable to resistance, with projections exceeding 8 million annually by 2050 [1].

The widespread and often inappropriate use of antibiotics across human medicine, animal health, and food production has been a major driver of this trend [2]. At the healthcare level, AMR is associated with increased mortality, prolonged hospital stays, and substantial economic burden [3].

In this context, antimicrobial stewardship (AMS) programs are central to improving antibiotic use and limiting selective pressure [4]. Over the past decade, stewardship efforts have focused on optimizing empiric therapy, promoting early de-escalation, and shortening treatment duration when appropriate [5]. More broadly, AMS aims to ensure that patients receive the most appropriate therapy at each stage of infection [6].

In practice, however, these principles are not always easy to apply. A recent case illustrates this well. A patient presented with fever and focal neurological deficits; and imaging scans revealed a brain abscess requiring prompt surgical drainage. Empirical broad-spectrum therapy was initiated, covering streptococci anaerobes. Microbiological cultures subsequently identified penicillin-susceptible *Streptococcus intermedius*, a typical oral pathogen and a well-recognized cause of brain abscess. From a microbiological perspective, de-escalation to a narrow-spectrum anti-streptococcal penicillin would have appeared appropriate. However, current European guidelines recommend maintaining anaerobic coverage in this setting, particularly when a contiguous or odontogenic source is suspected, given the often polymicrobial nature of these infections and the risk of under-detection of anaerobes in routine cultures [7]. This example highlights the limits of relying on microbiological results alone and the need to interpret them within the broader clinical context.

In this context, the expansion of rapid diagnostic technologies has reshaped the landscape. Molecular assays, syndromic panels, and rapid phenotypic susceptibility platforms now allow earlier identification of pathogens and resistance mechanisms [8]. In bloodstream infections, these tools can shorten the time to active therapy and reduce unnecessary exposure to broad-spectrum antibiotics [9].

Yet, the impact of these tools on clinical outcomes remains uncertain. A large multinational randomized clinical trial, published very recently, evaluating rapid Antimicrobial Susceptibility Testing (AST) directly from positive blood cultures in patients with Gram-negative bacteraemia did not demonstrate superiority over standard AST for patient-centred outcomes, with a 48.8% probability that patients in the rapid testing group would achieve a more desirable DOOR outcome than those in the standard group. At the same time, rapid AST was associated with improvements in process-of-care measures, including a shorter time to antibiotic modification (median 22 vs 36 hours) [10].

Corresponding author
Paolo Bonfanti
E-mail: paolo.bonfanti@unimib.it

This reflects an increasingly consistent finding. Rapid diagnostics tend to improve process-related outcomes - such as time to optimal therapy, appropriateness of prescribing, and reduction of unnecessary antibiotic exposure - while their effect on endpoints such as mortality, length of stay, and cost-effectiveness, is less consistent across settings [11]. Similar considerations apply to other diagnostic platforms. Syndromic panels for meningitis and encephalitis, for example, may reduce unnecessary antiviral use in selected populations, but their impact on antibiotic use and length of stay remains variable [12]. Overall, robust evidence demonstrating consistent improvements in clinical outcomes and healthcare costs is still limited.

In this context, the concept of diagnostic stewardship becomes essential. Diagnostic stewardship goes beyond the interpretation of test results and includes decisions about which test to perform, in which patient, and at what time. It also involves avoiding unnecessary testing and limiting the use of complex diagnostic panels outside appropriate clinical contexts [13, 14]. This is particularly relevant in the setting of rapid diagnostics. For example, the indiscriminate use of syndromic panels in low-pretest probability settings may generate results that are difficult to interpret and do not meaningfully change management. Moreover, given the cost and complexity of many rapid diagnostic tools, appropriate patient selection is critical to ensure real clinical and economic value.

A key implication is that the effectiveness of rapid diagnostics depends not only on the technology itself, but on how it is implemented. Their impact is greatest in settings where structured AMS programs are already in place and able to act on the information provided [11]. This highlights the importance of the organizational dimension, such as real-time communication between microbiology laboratories and clinicians, availability of expert interpretation, audit and feedback mechanisms, and clearly defined therapeutic pathways.

In this context, randomized trials are currently underway to better assess the impact of rapid diagnostic platforms when combined with antimicrobial stewardship interventions in serious Gram-negative infections [15].

The diagnostic pipeline continues to evolve. Emerging approaches, including direct-from-blood assays and metagenomic techniques, aim to further shorten the time to pathogen identification and potentially bypass conventional culture [16]. In parallel, the use of artificial intelligence in clinical practice is becoming increasingly common. Machine learning models have shown promising performance across several areas of AMS, including antibiotic selection, dose optimization, and adherence to stewardship principles. However, a key limitation remains their reliance on training data and when applied to external datasets from epidemiologically distinct settings, model performance often declines [17, 18]. As with other diagnostic innovations, their clinical value will depend on how effectively they are integrated into clinical workflows and stewardship frameworks.

In conclusion, the central challenge of antimicrobial stewardship remains unchanged: ensuring the appropriate and judicious use of antibiotics to address the threat of AMR.

Advances in diagnostic technologies provide important opportunities, but their impact ultimately depends on their implementation in routine practice by clinicians, highlighting their persisting central role in clinical decision-making.

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