International Journal of Infectious Diseases 167 (2026) 108536

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

When the whole exceeds the sum of its parts: Squeezing greater cumulative benefit from cross-technology partnerships in bacterial infection

Francesca Saluzzo[1,2], Olof Lindahl[3], Leonid Chindelevitch[4], Till T Bachmann[5], Dominik M. Meinel[6], Cihan Papan[7], Konstantinos Mitsakakis[8,9], Valentina Di Gregori[10], Khine Swe Swe-Han[11], Kevin M. Krause[12], Betsy Wonderly Trainor[13], Nico T. Mutters[7], Volkan Özenci[14], Daniela Maria Cirillo[1,#,*], Chantal M. Morel[7,15,#]

[1] *IRCCS San Raffaele Scientific Institute, Milan, Italy*
[2] *CRIMEDIM - Center for Research and Training in Disaster Medicine, Humanitarian Aid and Global Health, Università del Piemonte Orientale, Novara, Italy*
[3] *Department of Business Studies, Uppsala University, Uppsala, Sweden*
[4] *MRC Centre for Global Infectious Disease Analysis, Faculty of Medicine, School of Public Health, Imperial College, London, United Kingdom*
[5] *Centre for Inflammation Research, University of Edinburgh, Edinburgh, United Kingdom*
[6] *Institute for Chemistry and Bioanalytics, University of Applied Sciences and Arts, Muttenz, Switzerland*
[7] *Institute for Hygiene and Public Health, University Hospital, Bonn, Germany*
[8] *Hahn-Schickard, Freiburg, Germany*
[9] *IMTEK–Department of Microsystems Engineering, Laboratory for MEMS Applications, University of Freiburg, Freiburg, Germany*
[10] *San Pier Damiano Hospital, GVM Care and Research, Faenza, Italy*
[11] *Medical Microbiology Department, Academic Complex, School of Laboratory Medicine and Medical Sciences, University of KwaZulu Natal, Durban, South Africa*
[12] *AN2 Therapeutics, Inc., Menlo Park, CA, USA*
[13] *Diagnostics Alliance, CARB-X, Boston, MA, USA*
[14] *Department of Laboratory Medicine, Karolinska Institute, Solna, Sweden*
[15] *KPM Centre for Public Management, University of Bern, Bern, Switzerland*

ARTICLE INFO

Article history:
Received 21 January 2026
Revised 9 March 2026
Accepted 14 March 2026

Keywords:
Antimicrobial resistance
Antibiotic-diagnostic co-development
Drug-diagnostic partnerships
Precision infection management

ABSTRACT

Objectives: Effective care for bacterial infections requires both new antibiotics (ABx) to address antimicrobial resistance (AMR) and appropriate diagnostics (Dx) to guide their use. Diagnostics are essential to identify pathogens, determine susceptibility, and support targeted prescribing, including ruling out unnecessary antibiotic use. However, diagnostics are undervalued in the current market, limiting their availability and integration with antibiotic development. To examine the interplay between antibiotics and diagnostics and assess the potential value of coordinated development and partnerships.

Methods: This paper analyses the antibiotic and diagnostic development landscape, focusing on market dynamics, regulatory frameworks, and collaboration models involving ABx developers, Dx developers, clinicians, and public-sector stakeholders.

Results: Antibiotics and diagnostics are rarely developed or introduced in parallel, and available diagnostics often fail to deliver treatment-focused or point-of-care–relevant results. This misalignment hampers the effective deployment of new antibiotics and weakens stewardship. Cross-technology partnerships can improve trial efficiency, enhance market valuation, and support more targeted antibiotic use. Key barriers include fragmented incentives, regulatory misalignment, and financial constraints.

* Corresponding author.
E-mail address: cirillo.daniela@hsr.it (D.M. Cirillo).
# Both authors contributed equally to the manuscript.

https://doi.org/10.1016/j.ijid.2026.108536

Conclusion: Better alignment between antibiotic and diagnostic development is critical to maximise clinical impact and support resistance monitoring. Public-sector support could help enable effective partnerships and improve patient outcomes.

Background

It is well known that both antibiotics (ABx) and diagnostics (Dx) are important to tackling the problem of growing antibacterial resistance and the loss of treatment efficacy. Yet the ability to do so hinges in many respects on their complementarity. According to the US Food and Drug Administration (FDA), a complementary diagnostic provides valuable information about whether a treatment might be beneficial, even if it is not required for the administration of the drug [1]. This differs from a companion diagnostic, which is required for the safe and effective use of a specific therapy and is typically approved alongside the drug.

In this context, the appropriate use of new antibiotics depends on the existence and availability of complementary microbiological tests to guide their use in everyday clinical practice and to monitor resistance levels, supporting related activities such as updating guidelines for presumptive treatment [2].

Two types of microbiological test results are crucial for treatment decision-making: 1) the species of the pathogen, and 2) its antibiotic susceptibility profile. The identification of the species can, at a high level, guide the choice of the appropriate antimicrobial and inform the spectrum of coverage needed. Antimicrobial susceptibility testing (AST) further narrows down the options by steering prescribing toward antibiotics that remain effective for the specific infection. AST also plays a key role in public health by monitoring resistance levels and supporting activities such as updating treatment guidelines. In cases of clinical urgency, guidelines for presumptive treatment, based on clinical symptoms alone, rely heavily on trends in susceptibility data. However, important limitations remain, particularly the lack of rapid phenotypic susceptibility tests that can be performed directly from patient samples such as whole blood. Current practices largely depend on slower culture-based methods or nucleic acid-based tests, which can only detect certain resistance-conferring genes, often providing incomplete results due to inconsistent concordance between genotypic and phenotypic findings.

These challenges are compounded by differences between the ABx and Dx markets across several dimensions. These differences impact their development, procurement, sales, and use, ultimately preventing the successful integration of both technologies in clinical practice.

The key characteristics of ABx and Dx are summarized in Table 1, focusing on key differences and similarities between the two markets.

This paper combines elements of literature-based analysis and policy-oriented discussion to examine how better coordination between antibiotic and diagnostic development could improve clinical, economic, and public health outcomes, using tuberculosis as an illustrative case study.

Exploring potential synergies in the co-development of ABx and Dx

Despite shared challenges, partnerships between antibiotic and diagnostic developers, referred to here as cross-technology partnerships (e.g., joint development agreements or strategic alliances), remain relatively rare [14]. One example of such a partnership is the use of bioMerieux' platform in the clinical trial of Entasis' latest drug combination against *Acinetobacter baumannii* complex [15]. Another example is the joint venture between Boehringer Ingelheim, Evotec, and bioMérieux in co-creating Aurobac Therapeutics specifically in the area of AMR [16]. However, such partnerships remain rare because of several reasons, summarized in Table 2.

First and foremost, the lack of attractiveness of ABx development overall affects this process, as well as the extreme financial challenges for any ABx developer to even make it through clinical trials [17]. Co-developing ABx and Dx might increase both the investment and the associated risk more than a future possible return of investment.

On a practical level, several challenges are also faced in creating partnerships between these two very different types of healthcare-related fields. Both ABx and Dx research require heterogenous research groups and while there is some overlap, the primary areas of expertise differ. For ABx development, typically chemistry and biochemistry are the primary areas of expertise involved, while Dx development requires engineering, biology, and software, expertise. For this reason, groups like CARB-X try to include both ABx and Dx expertise in meetings with the ABx companies as they move through the portfolio in order to discuss the ABx companies' diagnostic strategy for clinical trials and market entry.

Timing is also crucial in such partnerships and does not easily align. While a partnership could start early on (see Figure 1 [18] for an idealised timeline), this does not happen in practice.

Broth microdilution-based minimum inhibitory concentration (MIC) testing assays are typically developed during the preclinical phase and then validated during the clinical phase [19]. However, these tests are difficult to implement in every day clinical routine, so other testing devices are often needed to support the clinical phase of ABx development (e.g., disk diffusion tests, E-tests or automated MIC tests). Nonetheless, at early stages of ABx development it is still unclear whether the drug will eventually reach the market. Such test development is often initiated (and sometimes financed) by the ABx company, as it remains risky for Dx developers. A further relationship dynamic that would need to be accounted for is that Dx companies rarely have sufficient resources or capacities to supply clinical sites globally, so they would rely on ABx companies to supplement the cost of such capital goods.

Moreover, combined development also requires the partnering firms to be able to cooperate and accept that they are not free to change their development focus or timelines as they normally might. Even a nonexclusive partnership may, to some degree, limit the flexibility of the respective partners. These collaboration constraints are further compounded by broader economic barriers affecting both antibiotics and AMR diagnostics, including reimbursement limitations, financial silo effects, and market pressures. Selected examples of these economic challenges are summarised in Table 3.

Potential for gains to be reaped through partnerships

Nevertheless, the potential for benefits from partnerships between ABx and Dx development is considerable, even where they remain nonexclusive.

Table 1
ABx and Dx differences and similarities in market potential, market launch and adoption, development costs and timeline, regulatory requirements, reimbursement policies, and public sector support.

Category	ABx characteristics	Dx characteristics	Key similarities and differences
Market potential	2021 ABx market: $38 billion USD [3]	2021 Dx market for infectious diseases: $28 billion USD (half from immunodiagnostics) [3]	**Similarities:** Both have substantial market sizes. **Differences:** The ABx market is slightly larger, but Dx is growing rapidly.
Cost and development timeline	Over $1 billion USD ~12.5 years [4]	$50-100 million USD 7-10 years [4]	**Differences:** ABx development is significantly more expensive and takes longer compared to Dx.
Regulatory requirements	Extensive safety and efficacy trials: preclinical, three phases of clinical trials, pharmacovigilance, pediatric studies, and postapproval resistance monitoring.	Focus on validation of accuracy, sensitivity, specificity, reproducibility, robustness, positive/negative predictive value, and regulatory certification (IVDR, FDA, etc.). The implementation of the IVDR introduces additional requirements that may affect smaller diagnostic developers and development timelines.	**Similarities:** Both require rigorous regulatory approval. **Differences:** ABx focus on clinical safety and efficacy, while Dx focus on analytical performance validation and evolving regulatory frameworks (e.g., IVDR), which may influence development timelines.
Reimbursement policies	Requires inclusion on formularies, guidelines, and cost-effectiveness demonstration for Multi Drug Resistant (MDR) pathogens.	Requires proof of clinical utility and cost-effectiveness [5]. Long-term public health benefits remain undervalued.	**Similarities:** Both face challenges in proving cost-effectiveness and securing reimbursement. **Differences:** ABx requires integration into stewardship frameworks, while Dx reimbursement depends on proving added clinical value versus the standards of care.
Public sector support	Need support through incentive programs [6] and pipeline coordinators (e.g., CARB-X, GARDP, AMR Action Fund, PLATINEA [7], INCATE, NIAID, IMI ENABLE [8,9]). Major funding to offset high R&D costs [10,11].	Limited support. Since 2017, only 7% of AMR R&D funding has gone to diagnostics [6]. Supported by initiatives like Longitude Prize, FIND, JPIAMR, WHO EDL, IMI ValueDx, CARB-X, and BARDA.	**Differences:** ABx received substantially more funding and incentives than Dx, which remains underfunded.
Market launch and adoption	High clinical trial failure rates and development costs. Sales impacted by stewardship measures and restrictions on broad use. Uncertain profitability [12,13].	Faces low reimbursement rates and slow adoption in healthcare settings. Market entry was hindered by regulatory delays and pricing models. Historically lack of proper dissemination of Dx importance to healthcare providers [12,13].	**Similarities:** Because of different challenges both ABx and Dx face uncertainty in market entry, profitability, and adoption.

Acronyms: IVDR: *In Vitro* Diagnostic Regulation; FDA: Food and Drug Administration; PLATINEA: PLATform för INnovation av Existerande Antibiotika; INCATE: Incubator for Antibacterial Therapies in Europe; R&D: research and development; CARB-X: Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator; GARDP: Global Antibiotic Research and Development Partnership; AMR: Antimicrobial resistance; FIND: Foundation for Innovative New Diagnostics; JPIAMR: Joint Programming Initiative on Antimicrobial Resistance; NIAID: National Institute of Allergy and Infectious Diseases; BARDA: Biomedical Advanced Research and Development Authority; WHO EDL: World Health Organization model list of essential *in vitro* diagnostics; HTA: Health Technology Assessment.

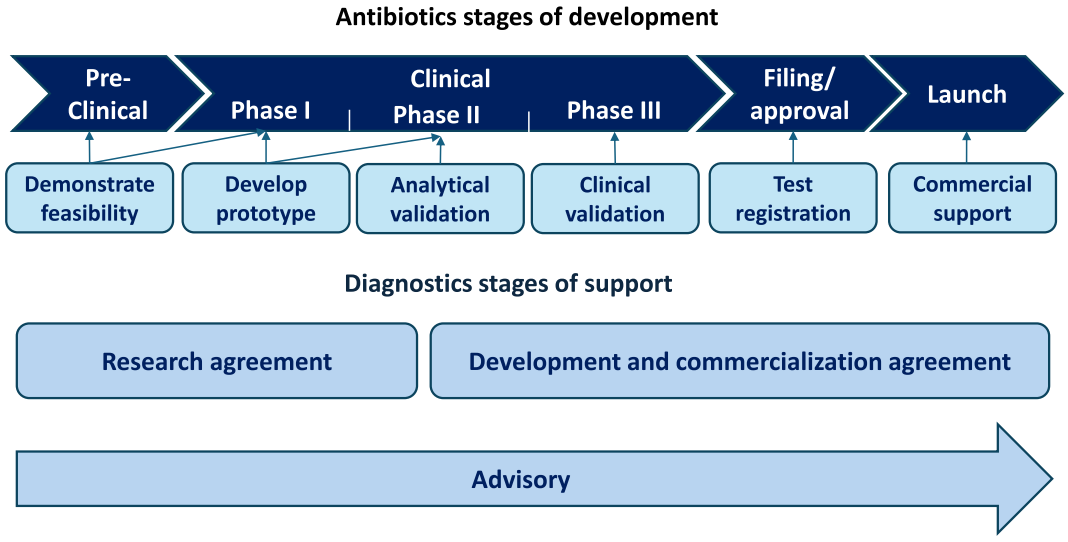

Figure 1. Antibiotics and diagnostics stages of development. Adapted from [8].

Table 2
Challenges in ABx and Dx co-development.

Challenge	Details
Financial aspect	Considering the current overall healthcare market, ABx and Dx co-development increases the required investment, elevates the associated risk and offers limited potential financial future returns.
Heterogeneity of the development groups	Primary areas of expertise within these groups differ. ABx: chemistry and biochemistry Dx: engineering, biology, and software expertise.
Timing	The development timelines are crucial in ABx and Dx partnerships and do not easily align between them.
Test development dynamics	Development of "commercial" Dx tests during ABx clinical validation is risky as it is still uncertain if the drug will be put on the market.
Equipment challenges	Dx companies rarely have sufficient capacities/resources to supply clinical sites globally, so they may rely on ABx companies to supplement the cost of such capital goods.
Flexibility in development	Combined development reduces flexibility in Dx and ABx development. Partners may face timeline and investments constraints.

In its latest Strategic Plan for addressing AMR, the World Health Organization (WHO) states that efforts to develop new antibacterial agents must be accompanied by parallel efforts to ensure universal access to tools for preventing, diagnosing, and treating infections, in order to mitigate AMR's impact on public health and the economy [27].

Thus, the co-existence and co-availability of the respective "complementary" products is required to achieve gains. These gains are primarily foreseen in four areas summarized in Figure 2.

Gains from partnership during drug development

Phase III clinical trials are one of the most expensive stages of developing new drugs. Introducing rapid point of care (POC) pathogen identifying Dx early in the ABx clinical trial process has the potential to help rule out patients who are unlikely to have the bacterial infection in question, thereby increasing the efficiency of the study [28]. This is especially important for pathogen specific clinical trials or trials for narrow spectrum antibiotics.

More precise enrolment can reduce the required sample size. Enrolling fewer patients per site allows allocation of resources to other sites, and potentially shorten the duration of the overall trial. Such efficiencies of course translate into considerable savings for the antibiotic developers.

Availability of supporting Dx may also strengthen the engagement of those involved at the clinical trial sites as it becomes clearer whether a patient may benefit from being enrolled. This can be especially important in clinical studies for indications with polymorbid patients (e.g., with hospital-acquired pneumonia or sepsis) to avoid adding one or several study drugs on top of the standard of care. This is very important given the vulnerability of this target population [28].

Naturally, as Rex and colleagues warn, Dx "do not create cases" [29]. If an infection is rare, it is still going to take a lot of patients to find the right ones to enrol in an antibiotic trial.

Using an idealised example, Tait and colleagues previously estimated that doubling the proportion of patients that are recruited into a trial and are likely to be infected by a pathogen sensitive

Table 3
Economic barriers affecting AMR diagnostics and antibiotics that may hinder coordinated development and market uptake.

Economic dimension	AMR diagnostics	Antibiotics
Reimbursement and market access challenges		
Core reimbursement problem	Systematic undervaluation: existing HTA/reimbursement frameworks fail to capture broader societal and population-level benefits of diagnostics [20,21]	Low revenue from low-volume use: novel antibiotics intentionally held in reserve. Peak annual revenues for several recently approved antibiotics have remained below US$100 million, limiting expected returns [11,22]
Financial silo effects	Diagnostic costs fall on one budget (e.g., laboratory) while benefits (e.g., reduced hospitalisations, narrower antibiotic use) accrue elsewhere in the system. For example, rapid diagnostics combined with antimicrobial stewardship reduced hospital costs for bloodstream infections from US$78,991 to US$52,693 per hospitalization [23,24]	Hospital pharmacy budgets disincentivise use of costlier novel antibiotics even when clinically superior; diagnosis-related group bundling compresses margins [25].
Competing with generics	A generic antibiotic course may cost less than the diagnostic test itself, leading payers to favour empirical prescribing over testing [21]	Generic antibiotics dominate the market (~81% of global antibiotic sales), creating a low-price benchmark that undermines the commercial case for novel agents [20,26]
Value Assessment and Cost-Offset Evidence		
Proposed value frameworks	STRIDES framework: seven AMR-specific value elements for diagnostics (Spectrum, Transmission, Research, Insurance, Diversity, Enablement, Stewardship) [20].	STEDI framework (OHE/Towse et al.): captures Spectrum, Transmission, Enablement, Diversity, and Insurance value of antimicrobials [26]
Commercial viability	Numerous recent failures. Case example: **T2 Biosystems (2006–2025)** developed FDA-cleared rapid sepsis diagnostics but ultimately ceased operations after failing to compete with larger firms and achieve sustainable market uptake.	Multiple small antibiotic developers have filed for bankruptcy despite achieving FDA approval for their products (e.g., **Achaogen, Melinta, Nabriva**), highlighting structural weaknesses in the antibiotic market [22].
Externality problem	Public benefits (reduced transmission, longer antibiotic lifespans, reduced healthcare burden) are not internalised by purchasers; costs are borne individually while benefits are societal [21].	Similar externality: new antibiotics preserve treatment options for future patients, but this insurance value is not captured in current pricing systems, creating a free-rider problem across countries [22].

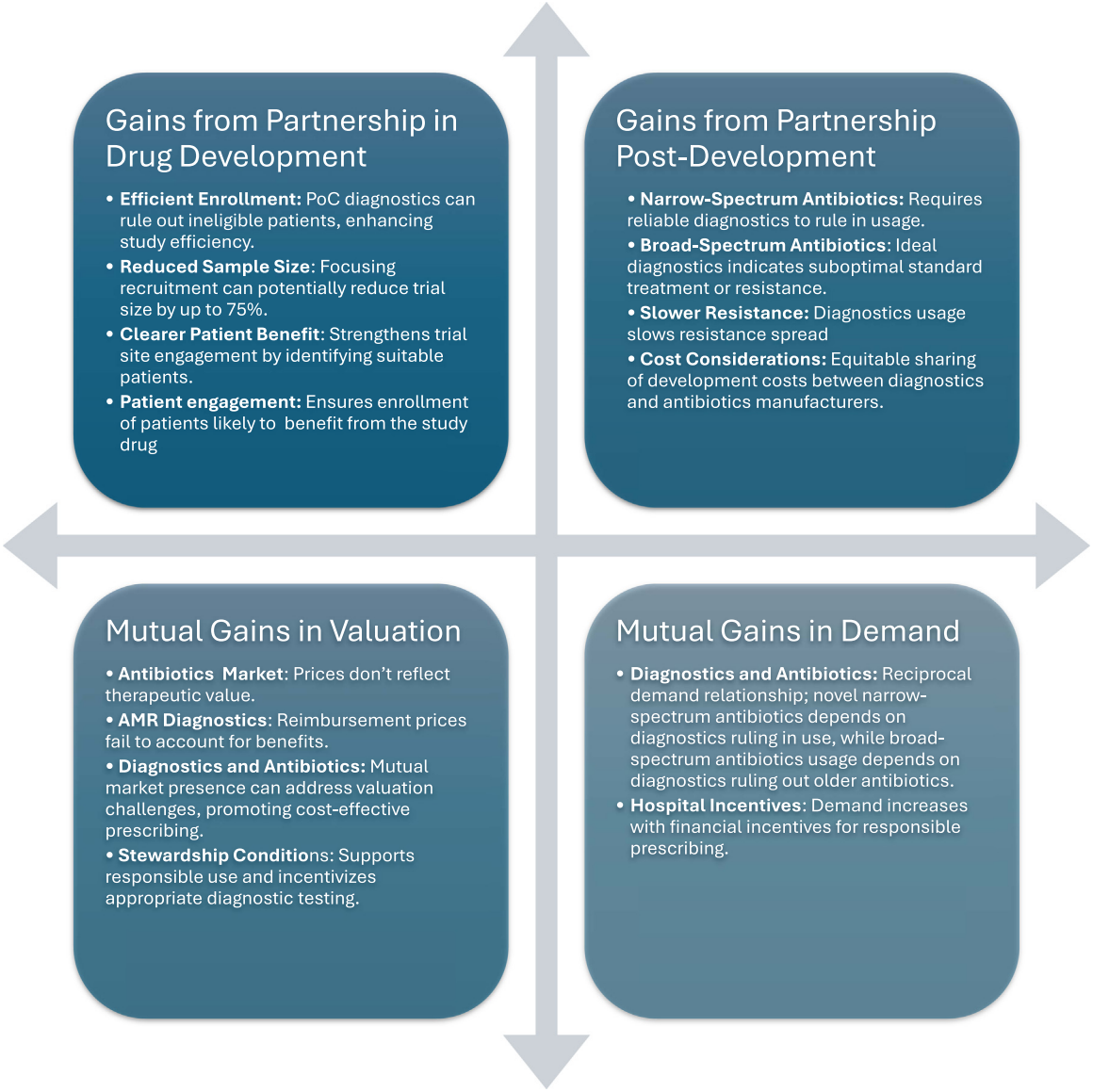

Figure 2. Gains of coexistence and co availability of complementary antibiotics and diagnostics. Acronyms: PoC: point of care; AMR: antimicrobial resistance.

to the experimental drug, can theoretically reduce the trial sample size by as much as 75% [30]. Although in practice the difference between "Modified Intention to Treat" (mITT) and "Intention to Treat" group (ITT) is not this large in most clinical trials. A real-life example of such savings comes from the partnership between Entasis and bioMerieux' Biofire® FilmArray® Pneumonia Panel for the former's sulbactam-durlobactam Phase III trial. According to Entasis CEO declarations during the 2022 National Academies meetings, this partnership resulted in savings of "millions." This also translated to gains for the public sector given its financial support to the market [31].

Nonetheless, it is also important to note that inclusion of a Dx in a therapeutic clinical study can complicate the protocol. If a Dx reveals a resistant infection, the patient may be excluded from the trial to avoid ineffective treatment in the control group. In such cases, alternative study designs, like those without a comparator group, may be needed. These designs must be supported by robust historical control data and are often part of a broader set of studies focused on noninferiority to fully assess the safety of a novel ABx.

Indeed, physicians should only enrol patients who they think can benefit equally from the study drug and the comparator drug [29]. Ruling out patients in this way could theoretically make it longer to find enrollable patients. However, in also being able to demonstrate susceptibility, the Dx reinforces the physician's intention of enrolling only patients with susceptible infections and reduces risks for the enrolled patient. The latter could ultimately bolster patient willingness to be enrolled.

Gains from partnership postdevelopment

Once new ABx and Dx reach the market, important synergies may emerge, enabling the use of novel antibiotics only when appropriate and reducing unnecessary use of broad-spectrum drugs. Quantitative evidence from hospital implementation studies illustrates the economic value of aligning diagnostics with antibiotic use. For example, the use of MALDI-TOF MS with stewardship reduced mean hospital costs from $78,991 to $52,693 per hospitalization in patients with bloodstream infections [23]. Similarly, another analysis reported lower hospital costs per episode ($42,580 vs $45,019), corresponding to savings of about $2439 per infection and approximately $2.34 million annually [24]. These findings highlight how coordinated deployment of diagnostics and

antibiotics can generate measurable health-system efficiencies in addition to improving clinical management.

Moreover, on a societal level, the expanded use of Dx should translate to slower emergence and spread of resistance over time and faster cure for patients. However, one complication with such partnerships is the cost consideration that must be equitably shared between the Dx and ABx manufacturers so that risk, economic benefit, and utility of each party are factored into the development costs share that they each incur.

Mutual gains in valuation

Both the ABx market and the AMR Dx market suffer from incomplete valuation as their price does not reflect the value that they offer [32,33]. In the case of ABx, generics costing only a few USD are used to treat many of the infections seen within health services. Even treatments for complicated infections remain low-cost in comparison to other classes of drugs.

AMR Dx are usually purchased/reimbursed at prices of standard supplies or accessory technologies [34]. Prices fail to account for the fact that these Dx provide a multitude of benefits. Historically, prices have resembled those of simple consumables rather than specialised devices delivering clinical and long-term value. Furthermore, microbiology laboratory budgets do not grow with the introduction of a new diagnostic despite the health and related cost benefits that follow from faster and more accurate results [35].

There are some changes now being seen with the introduction of molecular diagnostics, especially where the inability to compare them to existing diagnostics allows them to bypass the historical coding procedures that drive down reimbursement prices. This is especially important in markets like the US where reimbursement levels are often "cross-walked" or simply matched to levels previously set for older technologies [36].

Mutual presence on the market may provide both ABx and related Dx an opportunity to rectify some of these valuation/pricing challenges.

Importantly, new Dx, in addition to patient- and pathogen-specific data, provide an opportunity to re-frame ABx within the broader framework of infection management based on multiple data points and a careful, targeted approach to treatment. This could provide the context needed to move beyond the era of widespread use of unsustainably inexpensive ABx and toward a "precision medicine" approach to managing infection, where side-effects to the patient and curbing resistance over time are prioritized. Notably, this process triggers spending outside of the diagnosis-related groups (DRGs), allowing for higher reimbursement for Dx [37].

Finally, for both ABx and Dx, the prospect of their future mutual presence in the market could lower the uncertainty surrounding sales, which in turn should make more developers interested in undertaking their development.

Mutual gains in demand

Dx intended to help combat AMR are often not taken up swiftly or broadly once they are produced and approved for the market [38]. While they could improve patient care, hospitals face financial disincentives to purchase them. Demand for such Dx is likely to increase if cost becomes secondary to larger, systemic incentives for more responsible prescribing. As mentioned above, the use of a novel narrow-spectrum antibiotic as first-line treatment is entirely dependent on it being ruled in by a rapid Dx, if it can get on the hospital formulary. As for new broad-spectrum antibiotics, it is unlikely that they will be used unless there is a diagnostic capable of ruling out the use of the standard, older antibiotic. The demand relationship is likely to be reciprocal: demand of any new ABx is likely to increase when a complementary Dx is available and demand for a new Dx is likely to increase demand for the associated new ABx. In microeconomics these are thus considered "complementary" goods.

Table 4
Risks of introducing new drugs without accompanying diagnostics: The case of TB.

New drugs are badly needed to shorten and improve (e.g., reduce side effects) TB treatment. After decades of stagnation, new drugs have emerged and have been included in the treatment regimen recommended by WHO for drug-resistant TB. These include the following: **Bedaquiline:** Introduced in 2012 for extensively drug-resistant tuberculosis cases, bedaquiline is now a core drug for rifampicin-resistant TB. It was introduced without access to the compound to set up an "in house" AST for the majority of National Reference Laboratories. A provisional Critical Concentration (CC) was endorsed by WHO in 2018, yet no endorsed molecular tests are available. The WHO has evaluated targeted next-generation sequencing (tNGS) as a basis for testing for bedaquiline and other new drugs in 2023, leading to a rapid communication [41]. The slow rollout of phenotypic testing seems likely to have led to an inappropriate use of this drug severely affecting clinical outcomes and increasing drug resistance, jeopardising future use. After only a decade of use, alarming rates of resistance are emerging [42]. **Delamanid:** Approved by the European medical Agency (EMA) in 2014 and immediately evaluated by the WHO, which issued a rapid communication in the same year, revised in 2017 in light of new data. With few exceptions, the drug has not been made available to reference laboratories. Access to the compound is currently very limited, and a provisional CC has been released by WHO in 2018. No rapid and accessible molecular tests have been developed. Resistance has been reported in cases never exposed to the drug [43]. **Pretomanid:** This is the latest TB drug to be approved (in 2019 by the FDA and in 2020 by the EMA) and it is part of the core recommended treatment for rifampicin-resistant TB. It belongs to the same class as delamanid, with a partial overlap of drug resistance determinants. Only in 2024, CC has been endorsed by WHO [41]. Very few labs have access to the drug, and those that do, have it mainly for research purposes [44].. As such, this drug will be provided without any capacity to test for susceptibility nor perform surveillance.

Dangers in "going alone"

It must be emphasised that if relevant Dx are not brought to market or made available alongside new ABx, the risk of driving AMR without noticing is high, which will eventually devalue the underlying investments and put patient health at risk once again. The case of drugs for tuberculosis (TB) provides a good example of the risks taken when new ABx are launched without accompanying Dx (Table 4) [39,40].

It should be noted that the newer TB drugs were brought to market since the early 2010s with a firm understanding from the TB community of the diagnostic requirements that were needed for their appropriate use. The Target Regimen Profiles published more recently, in 2023, by the WHO include specific and detailed recommendations to avoid the mistakes of the past, when the requirements for the monitoring of resistance of new drugs were largely ignored [45].

A second relevant example refers to cefiderocol, in this case the challenges in making available susceptibility testing tools, which highlights the need for early collaboration between pharmaceutical companies, diagnostic experts, and regulatory bodies. This siderophore-conjugate cephalosporin, approved by the FDA and EMA between 2019 and 2020 for hospital-acquired, ventilator-associated, and healthcare-associated pneumonia and complicated urinary tract infections, targets multidrug-resistant Gram-negative organisms such as *Pseudomonas aeruginosa, Acinetobacter baumannii*, and *Klebsiella pneumoniae* [46]. Its iron transport mechanism

complicates susceptibility testing, and standard methods such as broth microdilution and disk diffusion may not adequately capture its activity, leading to discrepancies, particularly for *A. baumannii* [47,48]. Although the developer later collaborated with the Clinical and Laboratory Standards Institute (CLSI) to establish breakpoints and testing methods, this occurred after market introduction, contributing to delays and unresolved testing challenges [47,49].

The case for a greater public sector role in facilitating partnerships

The reasons for encouraging partnership and co-launch of associated ABx and Dx are numerous from the perspective of both financial efficiency and clinical care. From the perspective of traditional economics, the public sector would benefit from playing a facilitating role. The externalities associated with infectious bacterial diseases, especially those affected by resistance, mean that society also reaps positive externalities when they are tackled more efficiently. In the case of technologies for the management of bacterial infection there is much to gain from encouraging the production of new ABx before resistance renders all of our therapeutic options obsolete (keeping in mind that it generally takes more than 12 years after the completion of basic research to get new therapies on the market). There is also much to gain from encouraging the production of technologies that improve the way these new therapies are used.

Given what is at stake, direct incentivization of such partnerships is arguably justified. As stressed by Tait and colleagues in the context of AMR technologies, the state has historically had a role in shaping technology trajectories and creating new markets, thereby generating economic activity that would not otherwise have taken place and opening up new areas that private investors can subsequently move into [30].

Public sector support for co-development partnerships could correct strategic oversight by governments across the world who may encourage the development of new drugs without ensuring their responsible use. Many National Action Plans on AMR state an explicit commitment to using ABx solely when justified by Dx tests, yet there is no clear strategy for getting there or accountability systems to track progress [50]. A strategy could be introducing Dx-guided therapy prioritizing those ABx that are at greatest risk of misuse and/or those which are last-line therapies and need to be preserved.

Specifically, the public sector could support ABx-Dx partnerships in several ways summarized below:

- De-risk co-development of ABx and Dx by taking on some of the development costs, e.g., by issuing forgivable loans
- De-risk such co-development by offering revenue-boosting rewards, e.g., innovation prizes or market entry rewards that account for the extra cost of Dx development
- Offer procurement guarantees (with conditions to minimise market distortion) to help set a revenue floor and reduce the uncertainty surrounding the partnership
- Provide institutional support for partnership formation and maintenance
- Make ABx market entry contingent on an approved Dx strategy that supports responsible use of the ABx at launch (while also helping to address the challenges mentioned above to minimize the strict requirements for ABx developers)
- Make reimbursement of the new ABx contingent on empirical data provided by a diagnostic test
- Address ABx and Dx together as part of a coherent package within important documents (Essential Medicines and Diagnostics lists) and contexts (Global Health Assembly)

De-risking or incentivizing co-development of ABx and Dx by taking on some of the developmental costs would likely decrease many of the hurdles which are currently hindering the start of ABx and Dx collaborations (timeline mismatches, risk of market failure of ABx, etc., as stated above). Funding to integrate new ABx onto new and existing AST panels, for example, could significantly de-risk this activity for the Dx company and expedite market uptake of ABx while also establishing a truly collaborative foundation that can be built upon.

Conclusions

Both ABx and Dx are needed to help tackle resistance. Both are undervalued in the current market environment, and this contributes to their underproduction and undermines optimal patient care. Encouraging relationships between developers of ABx and complementary Dx would achieve gains for both parties, increasing efficiency of trials and improving valuation. The success of such partnerships could be assessed through indicators such as improved efficiency in clinical trial enrolment, the availability of complementary diagnostics at the time of antibiotic launch, and more appropriate antibiotic use in clinical practice.

Crucially, complementary Dx would support the appropriate use of both narrow-spectrum ABx and broad-spectrum ones as well. Overall, such partnerships have clear advantages for public health.

Given the important and increasing support for the development of new and much needed ABx, and the role that Dx play in preserving any new ABx that are developed, explicit action is needed to address both simultaneously through partnerships. Left to themselves these partnerships rarely materialize. Greater public sector support could help overcome the obstacles preventing partnerships, and such support would be both economically and strategically justified.

Authors contributions

Francesca Saluzzo: Conceptualization (supporting); Visualization and figures (lead); writing—review and editing (lead). **Olof Lindahl:** Conceptualization (supporting); writing—original draft (equal); writing—review and editing (equal). **Leonid Chindelevitch:** Project administration (lead); Conceptualization (supporting); writing—original draft (equal); writing—review and editing (equal). **Till T. Bachmann:** Conceptualization (supporting); writing—original draft (equal); writing—review and editing (equal). **Dominik M. Meinel:** Conceptualization (supporting); writing—original draft (equal); writing—review and editing (equal). **Cihan Papan:** Conceptualization (supporting); writing—original draft (equal); writing—review and editing (equal). **Konstantinos Mitsakakis:** Conceptualization (supporting); writing—original draft (equal); writing—review and editing (equal). **Valentina Di Gregori:** Conceptualization (supporting); writing—original draft (equal); writing—review and editing (equal). **Khine Swe Swe-Han:** Conceptualization (supporting); writing—original draft (equal); writing—review and editing (equal). **Kevin M. Krause:** Conceptualization (supporting); writing—original draft (equal); writing—review and editing (equal). **Betsy Wonderly Trainor:** Conceptualization (supporting); writing—original draft (equal); writing—review and editing (equal). **Nico T. Mutters:** Conceptualization (supporting); writing—original draft (equal); writing—review and editing (equal). **Volkan Özenci:** Conceptualization (supporting); writing—original draft (equal); writing—review and editing (equal). **Daniela Maria Cirillo:** Conceptualization (co-lead); writing—original draft (equal); writing—review and editing (lead). **Chantal M Morel:** Conceptualization (lead); writing—original draft (lead); writing—review and editing (equal).

Funding

This work has been developed in the context of the project Bench, Bedside, Business, and Beyond: innovative solutions for AMR diagnostics (B2B2B AMRDx). The project is funded by the Joint Programming Initiative on Antimicrobial Resistance (JPIAMR) 2022 call "Diagnostics and Surveillance Networks." Grant Reference Number: JPIAMR_NC_2022-008.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: JPIAMR (via the UK MRC) has provided funding for the B2B2B network, which has been actively involved in the discussions surrounding this manuscript and contains 9 out of its 15 authors.

CMM and OL contribution was supported by the Swedish Research Council (under grant number 2019-00,313), as was VO (under grant number 2019-00315), all under the frame of the Joint Programming Initiative for Antimicrobial Resistance (Grant Reference Number JPIAMR2019-094). LC acknowledges funding from the MRC Centre for Global Infectious Disease Analysis (reference MR/R015600/1), jointly funded by the UK Medical Research Council (MRC) and the UK Foreign, Commonwealth & Development Office (FCDO), under the MRC/FCDO Concordat agreement and is also part of the EDCTP2 programme supported by the European Union.

Acknowledgments

With thanks to Pete Dailey, independent consultant to CARB-X for review of the manuscript.

CARB-X is funded in part with federal funds from the U.S. Department of Health and Human Services (HHS); Administration for Strategic Preparedness and Response; Biomedical Advanced Research and Development Authority (BARDA) under agreement number 75A50122C00028 and by awards from Wellcome (WT224842), Germany's Federal Ministry of Education and Research (BMBF), the Global Antimicrobial Resistance Innovation Fund (GAMRIF), the Public Health Agency of Canada (PHAC), the Bill & Melinda Gates Foundation, and the Novo Nordisk Foundation. The U.S. National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH) in HHS, provides support in the form of in-kind services through access to a suite of preclinical services for product development. The content of this publication is solely the responsibility of the authors and does not necessarily represent the official views of any CARB-X funders.

References

[1] Dailey PJ, Elbeik T, Holodniy M. Companion and complementary diagnostics for infectious diseases. *Expert Rev Mol Diagn* 2020;**20**:619–36. doi:10.1080/14737159.2020.1724784.

[2] Schmitz JE, Stratton CW, Persing DH, Tang YW. Forty years of molecular diagnostics for infectious diseases. *J Clin Microbiol* 2022;**60**. doi:10.1128/JCM.02446-21.

[3] Skyquest. Global infectious disease diagnostics market 2024. https://www.skyquestt.com/report/infectious-disease-diagnostics-market [accessed 6 August 2024].

[4] Wouters OJ, McKee M, Luyten J. Estimated research and development investment needed to bring a new medicine to market, 2009-2018. *JAMA* 2020;**323**:844–53. doi:10.1001/JAMA.2020.1166.

[5] Miller MB, Atrzadeh F, Burnham CAD, Cavalieri S, Dunn J, Jones S, et al. Clinical utility of advanced microbiology testing tools. *J Clin Microbiol* 2019;**57**. doi:10.1128/JCM.00495-19.

[6] World Health Organization *Incentivising the Development of New Antibacterial Treatments: 2023 Progress Report By The Global AMR R&D Hub and WHO - Global AMR R&D Hub*; 2023.

[7] Baraldi E, Lindahl O, Savic M, Findlay D, Årdal C. Antibiotic pipeline coordinators. *J Law Med Ethics* 2018;**46**:25–31. doi:10.1177/1073110518782912.

[8] Ciabuschi F, Baraldi E, Lindahl O. Joining forces to prevent the antibiotic resistance doomsday scenario : the rise of international multisectoral partnerships as a new governance model. *Acad Manag Pers : AMP* 2020;**34**(4):458–79.

[9] Baraldi E, Ciabuschi F, Kronlid C, Lindahl O. Managing interorganizational interactions for social impact: a study of two antibiotics R&D networks. *J Bus Res* 2022;**141**:264–78. doi:10.1016/J.JBUSRES.2021.12.027.

[10] Morel C, Mossialos E. Stoking the antibiotic pipeline. *BMJ* 2010;**340**:1115–18. doi:10.1136/BMJ.C2115.

[11] Outterson K, Rex JH. Global pull incentives for better antibacterials: the UK leads the way. *Appl Health Econ Health Policy* 2023;**21**:361–4. doi:10.1007/S40258-023-00793-W.

[12] Årdal C, Findlay D, Savic M, Carmeli Y, Gyssens I, Laxminarayan R, et al. DRIVE-AB report: Revitalizing the antibiotic pipeline, stimulating innovation while driving sustainable use and global access – Final text, executive summary, https://drive-ab.eu/wp-content/uploads/2018/01/DRIVE-AB-Final-Report-Jan2018.pdf; 2018.

[13] Stern S, Rentmeister H, Grosch B, Director M. Breaking through the wall: A call for concerted action on antibiotics research and development – Follow-up report for the German GARD initiative, full report, https://www.bundesgesundheitsministerium.de/fileadmin/Dateien/5_Publikationen/Gesundheit/Abschlussberichte/GUARD_Follow_Up_Report_Full_Report_final.pdf; 2017.

[14] Davis JC, Furstenthal L, Desai AA, Norris T, Sutaria S, Fleming E, et al. The microeconomics of personalized medicine: today's challenge and tomorrow's promise. *Nature Reviews Drug Discovery* 2009;**8**:279–86. doi:10.1038/nrd2825.

[15] National Academies of Sciences, Engineering, and Medicine; Health and Medicine Division; Board on Health Sciences Policy; Board on Global Health; Forum on Microbial Threats; Forum on Medical and Public Health Preparedness for Disasters and Emergencies; Forum on Drug Discovery, Development, and Translation; Shore C., Forstag E.H., editors. Accelerating the Development and Uptake of Rapid Diagnostics to Address Antibiotic Resistance: Proceedings of a Workshop. Washington (DC): National Academies Press (US); 2023. 4, Incentives at the Intersection of Drug Development and Complementary Diagnostics. Available from: https://www.ncbi.nlm.nih.gov/books/NBK593548/

[16] Boehringer Ingelheim. Joint venture to fight antimicrobial resistance 2022. https://www.boehringer-ingelheim.com/science-innovation/human-health-innovation/joint-venture-fight-antimicrobial-resistance [accessed 9 August 2024].

[17] Anderson M, Panteli D, van Kessel R, Ljungqvist G, Colombo F, Mossialos E Challenges and opportunities for incentivising antibiotic research and development in Europe. The Lancet Regional Health - Europe 2023;33:100705. https://doi.org/10.1016/J.LANEPE.2023.100705.

[18] Welcher R. Use of companion diagnostics (CDx) and predictive biomarkers for cancer targeted therapy: clinical applications in precision medicine. *Predictive Biomarkers in Oncology: Applications in Precision Medicine* 2018:539–51. doi:10.1007/978-3-319-95228-4_49/TABLES/2.

[19] Schön T, Werngren J, Machado D, Borroni E, Wijkander M, Lina G, et al. Multicentre testing of the EUCAST broth microdilution reference method for MIC determination on mycobacterium tuberculosis. *Clin Microbiol Infect* 2021;**27**:288.e1–288.e4. doi:10.1016/J.CMI.2020.10.019.

[20] Fong H, Bray G, Hampson G, Steuten L Taking STRIDES: the value of diagnostics against AMR - OHE 2025. https://www.ohe.org/publications/taking-strides-the-value-of-diagnostics-against-amr/ [accessed 7 March 2026].

[21] Morel C, McClure L, Edwards S, Goodfellow V, Sandberg D, Thomas J, et al. Overview of the diagnostic market. In: *Ensuring innovation in diagnostics for bacterial infection: Implications for policy*. Brussels, Belgium: European Observatory on Health Systems and Policies; 2016. p. 13–25.

[22] Outterson K. Estimating the appropriate size of global pull incentives for antibacterial medicines. *Health Aff (Millwood)* 2021;**40**:1758–65. doi:10.1377/hlthaff.2021.00688.

[23] Perez KK, Olsen RJ, Musick WL, Cernoch PL, Davis JR, Peterson LE, et al. Integrating rapid diagnostics and antimicrobial stewardship improves outcomes in patients with antibiotic-resistant gram-negative bacteremia. *Journal of Infection* 2014;**69**:216–25. doi:10.1016/j.jinf.2014.05.005.

[24] Patel TS, Kaakeh R, Nagel JL, Newton DW, Stevenson JG. Cost analysis of implementing matrix-assisted laser desorption ionization-time of flight mass spectrometry plus real-time antimicrobial stewardship intervention for bloodstream infections. *J Clin Microbiol* 2016;**55**:60–7. doi:10.1128/JCM.01452-16.

[25] Vogler S, Habimanaa K, Fischer S, Haasis MA Novel policy options for reimbursement, pricing and procurement of AMR health technologies - global AMR R&D hub 2021. https://globalamrhub.org/publications/novel-policy-options-for-reimbursement-pricing-and-procurement-of-amr-health-technologies/ [accessed 7 March 2026].

[26] Rothery C, Woods B, Schmitt L, Claxton K, Palmer S. FRAMEWORK FOR VALUE ASSESSMENT OF NEW ANTIMICROBIALS: Implications of alternative funding arrangements for NICE Appraisal. *The University of Sheffield. Report*; 2024. https://doi.org/10.15131/shef.data.25219094.v1.

[27] World Health Organization. *Antimicrobial resistance: Accelerating national and global responses: WHO strategic and operational priorities to address drug-resistant bacterial infections in the human health sector*; 2024. p. 2025–35 https://apps.who.int/gb/ebwha/pdf_files/WHA77/A77_5-en.pdf.

[28] Morel C., McClure L., Edwards S., et al., editors. Ensuring innovation in diagnostics for bacterial infection: Implications for policy [Internet]. Copenhagen

(Denmark): European Observatory on Health Systems and Policies; 2016. (Observatory Studies Series, No. 44.) 11, Co-development of antibiotics and diagnostics for bacterial infection. Available from: https://www.ncbi.nlm.nih.gov/books/NBK447308/

[29] Rex J H, Outterson K. Clinical trial designs for non-traditional antibiotics, https://carb-x.org/wp-content/uploads/2018/06/RF-2018-06-14-Rex-Outterson-Duke-Margolis-Non-traditional-antibiotic-intro-.pdf; 2018.

[30] Tait J, Bruce A, Mittra J, Purves J, Scannell J. *Independent review on antimicrobial resistance: Regulation–innovation interactions and the development of antimicrobial drugs and diagnostics for human and animal diseases (Main report*. Innogen Institute; 2014. https://amr-review.org/sites/default/files/AMR_Final_Report_141214.pdf.

[31] Global AMR R&D Hub. *Dynamic Dashboard* 2023. https://dashboard.globalamrhub.org/ [accessed 6 August 2024].

[32] The Review on Antimicrobial Resistance. Rapid diagnostics: Stopping unnecessary use of antibiotics, https://amr-review.org/publications/rapid-diagnostics-stopping-unnecessary-use-of-antibiotics/; 2015.

[33] Jessup A, Wong H-H, Sertkaya A, Eyraud J, Birkenbach A, Franz C, et al. *Analytical Framework for Examining the Value of Antibacterial Products*. Eastern Research Group, Inc; 2014. https://aspe.hhs.gov/reports/analytical-framework-examining-value-antibacterial-products.

[34] Vogler S, Habimana K, Fischer S, Alexander M. Novel policy options for reimbursement, pricing and procurement of AMR health technologies: Final report commissioned by the Global AMR R&D Hub, https://globalamrhub.org/wp-content/uploads/2023/09/GOe_FP_AMR_Report_final-1.pdf; 2021.

[35] Price CP, McGinley P, John AS. What is the return on investment for laboratory medicine? The antidote to silo budgeting in diagnostics. *British Journal of Health Care Management* 2020;**26**. doi:10.12968/BJHC.2019.0075/ASSET/IMAGES/LARGE/BJHC.2019.0075_T01.JPEG.

[36] Sireci AN, Patel JL, Joseph L, Hiemenz MC, Rosca OC, Caughron SK, et al. Molecular Pathology Economics 101: an overview of Molecular diagnostics coding, coverage, and reimbursement: a report of the association for molecular pathology. *J Mol Diagn* 2020;**22**:975. doi:10.1016/J.JMOLDX.2020.05.008.

[37] Chen YJ, Zhang XY, Yan JQ, Xue-Tang Qian MC, Ying XH. Impact of diagnosis-related groups on inpatient quality of health care: a systematic review and meta-analysis. *Inquiry* 2023;**60**:1–16. doi:10.1177/00469580231167011.

[38] Hays JP, Mitsakakis K, Luz S, van Belkum A, Becker K, van den Bruel A, et al. The successful uptake and sustainability of rapid infectious disease and antimicrobial resistance point-of-care testing requires a complex 'mix-and-match' implementation package. *European Journal of Clinical Microbiology and Infectious Diseases* 2019;**38**:1015–22. doi:10.1007/S10096-019-03492-4.

[39] Saluzzo F, Maria Cirillo D. Mind the gap. Rolling out new drug resistant tuberculosis regimens with limited diagnostic tools. *J Clin Tuberc Other Mycobact Dis* 2023;**32**. doi:10.1016/J.JCTUBE.2023.100350.

[40] Saluzzo F, Yerlikaya S, Dorman SE, Eisenach K, Farhat MR, Ismail N, et al. Future-proofing tuberculosis therapy: framework for concurrent drug and resistance testing development. *Lancet Infect Dis* 2025;**0**:2025. doi:10.1016/S1473-3099(25)00547-X.

[41] World Health Organization *WHO operational handbook on tuberculosis: module 3: diagnosis: rapid diagnostics for tuberculosis detection, 3rd ed*; 2024.

[42] Chesov E, Chesov D, Maurer FP, Andres S, Utpatel C, Barilar I, et al. Emergence of bedaquiline resistance in a high tuberculosis burden country. *European Respiratory Journal* 2022;**59**. doi:10.1183/13993003.00621-2021.

[43] Nguyen TVA, Anthony RM, Cao TTH, Bañuls AL, Nguyen VAT, Vu DH, et al. Delamanid resistance: update and clinical management. *Clinical Infectious Diseases* 2020;**71**:3252–9. doi:10.1093/CID/CIAA755.

[44] Friesen I, Saluzzo F, Groenheit R, Aubry A, Anthony R, Niemann S, et al. Re: "availability of drugs and resistance testing for BPaLM regimen for rifampicin-resistant tuberculosis in Europe" by Lange et al. *Clin Microbiol Infect* 2024;**30**:1204–6. doi:10.1016/J.CMI.2024.06.001.

[45] World Health Organization. Target regimen profiles for tuberculosis treatment, 2023. https://www.who.int/publications/i/item/9789240081512 [accessed 9 August 2024].

[46] Simner PJ, Patel R. Cefiderocol antimicrobial susceptibility testing considerations: the Achilles' Heel of the Trojan Horse? *J Clin Microbiol* 2020;**59**:e00951-20. doi:10.1128/JCM.00951-20.

[47] Simner PJ, Palavecino EL, Satlin MJ, Mathers AJ, Weinstein MP, Lewis JS, et al. Potential of inaccurate cefiderocol susceptibility results: a CLSI AST Subcommittee advisory. *J Clin Microbiol* 2023;**61**. doi:10.1128/JCM.01600-22.

[48] Massol J, Dinh A, Jeannot K, Duran C, Bouchand F, Potron A, et al. Should we, and how to, optimize cefiderocol administration during severe nosocomial pneumonia due to carbapenem-resistant Acinetobacter baumanii? A viewpoint. *J Glob Antimicrob Resist* 2024;**38**:140–5. doi:10.1016/J.JGAR.2024.05.014.

[49] CLSI. AST News Update 2023: The latest on testing cefiderocol 2023. https://clsi.org/about/blog/ast-news-update-june-2023-the-latest-on-testing-cefiderocol/ [accessed 19 November 2024].

[50] World Health Organization. Library of AMR national action plans 2024. https://www.who.int/teams/surveillance-prevention-control-AMR/national-action-plan-monitoring-evaluation/library-of-national-action-plans [accessed 9 August 2024].