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Beyond Guideline-Concordant Antibiotic Selection: Integrating Rapid Diagnostics, PK/PD Target Attainment, Source Control, De-escalation, Treatment Duration, and Oral Step-Down in Antimicrobial Stewardship

Mark Anderson[1]*, Lisa Wong[2], Sarah Lee[1]

[1] Department of Antimicrobial Stewardship and Infectious Diseases, Faculty of Pharmacy, University of Florida, Gainesville, United States

[2] Department of PK/PD Optimization and Rapid Diagnostics, Faculty of Pharmacy, National University of Singapore, Singapore.

***E-mail** ✉ mark.anderson@ufl.edu

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ABSTRACT

Antimicrobial stewardship is often judged at the moment an antibiotic is selected: whether empirical coverage accords with guidance, whether the organism is susceptible, and whether therapy appears microbiologically appropriate. Yet treatment success and avoidable antimicrobial exposure are determined by a sequence of decisions that continues after initial prescribing. Diagnostic information becomes progressively more specific; pharmacokinetic and pharmacodynamic conditions may alter achieved exposure; source control can determine whether active antibiotics are sufficient; de-escalation becomes possible only when uncertainty falls; treatment duration must be actively reconsidered; and intravenous therapy may no longer be necessary once clinical and pharmacological conditions permit oral treatment. This For Debate article argues that stewardship should therefore be conceptualized as repeated evidence integration across the treatment course rather than as guideline-concordant antibiotic selection followed by passive continuation. The analysis distinguishes faster information from effective action, nominal susceptibility from exposure adequacy, antimicrobial activity from anatomical control, narrowing from indiscriminate spectrum reduction, shorter treatment from arbitrary stopping, and oral step-down from route substitution without eligibility assessment. A proposed adaptive stewardship decision architecture is developed in which diagnostic, pharmacological, anatomical, clinical and implementation information can reopen earlier treatment decisions as the patient's state changes. The framework is intentionally evidence-bounded. It does not imply that every patient should undergo every optimization step, that individual interventions have uniform clinical effects, or that an integrated architecture has been prospectively validated. Its purpose is to sharpen where stewardship decisions occur, why they remain conditional, and where failure to reassess can convert an initially reasonable antibiotic choice into progressively less appropriate treatment.

Keywords: Antimicrobial stewardship, Rapid diagnostics, Pharmacokinetics/Pharmacodynamics, Source control, De-escalation, Treatment duration

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Introduction

Why guideline-concordant antibiotic selection is not the endpoint of stewardship

The first stewardship error is conceptual: treating appropriateness as a property of the antibiotic selected rather than of the evolving treatment course. Contemporary work on antibiotic-prescribing indicators shows that appropriateness is assessed through multiple dimensions, including indication, spectrum, dose, route, duration and other decision attributes, rather than through agent identity alone [1]. This matters because the same regimen can move between defensible and indefensible states without the drug name changing. A broad empirical regimen

may be appropriate when severe infection is suspected and resistance is uncertain, yet become unnecessarily expansive once cultures, susceptibilities and clinical trajectory clarify the problem.

Contemporary US hospital data illustrate why initial spectrum must be interpreted as a provisional risk-management decision. Broad-spectrum empirical therapy remains common among patients treated for suspected community-onset sepsis, but population-level prescribing patterns cannot determine whether each individual exposure was necessary [2]. The stewardship question is therefore not simply whether broad treatment was justified at hour zero, but whether the justification still exists when better information becomes available. This distinction protects against two opposite errors: reflexively condemning broad empirical therapy in unstable patients and allowing the logic of early uncertainty to justify prolonged broad treatment after that uncertainty has diminished.

Continuation also has a patient-level cost. Antibiotic-associated adverse events are sufficiently frequent that exposure cannot be considered pharmacologically neutral once treatment no longer contributes meaningful benefit [3]. Avoidable days, excessive spectrum, unnecessary intravenous access and dosing that fails to account for changing physiology can each erode the net value of an initially sensible prescription.

Antimicrobial-stewardship guidance correspondingly extends beyond drug selection toward reassessment, optimization and discontinuation decisions [4]. The argument advanced here goes further only in its organization: stewardship should be treated as a temporally linked set of conditional decisions. Selection opens the course; it does not complete it. The clinically relevant endpoint is sustained appropriateness as microbiological certainty, patient physiology, anatomical control, treatment response and discharge context change.

Rapid diagnostics and the timing of therapeutic reassessment

Rapid diagnostics alter the timing of available evidence, but they do not determine what clinicians do with that evidence. Across bloodstream-infection studies, the clinical contribution of rapid molecular diagnostics has been stronger when faster microbiological information is coupled with active antimicrobial-stewardship interpretation and response [5, 6]. This is more than an implementation detail. A result has no stewardship effect until it changes the probability assigned to competing explanations and prompts a defensible treatment decision. Identification without interpretation can accelerate certainty without accelerating action.

Newer rapid susceptibility platforms make this distinction particularly visible. In critically ill patients with Gram-negative bloodstream infection, implementation of rapid identification and susceptibility workflows has shortened the time to antibiotic optimization [7]. Such evidence supports an important process claim: shortening laboratory turnaround can create an earlier opportunity for escalation, narrowing or confirmation of treatment. It does not establish that all earlier results improve survival, nor that a laboratory metric should substitute for the patient's clinical state, infection source or available treatment options.

The FAST randomized trial provides the necessary counterweight. Faster antimicrobial-susceptibility testing for Gram-negative bacteraemia did not produce superiority on its patient-centred primary outcome despite providing susceptibility information sooner [8]. The appropriate interpretation is not that rapid AST lacks clinical value. Rather, diagnostic speed and therapeutic value occupy different causal positions. The former changes when information becomes available; the latter depends on whether that information identifies a meaningful treatment difference, reaches a clinician in time, is interpreted correctly and can be acted upon safely.

This has direct implications for stewardship design. Reassessment should be synchronized to clinically meaningful information arrivals rather than scheduled solely by elapsed time. A new species identification, resistance determinant or phenotypic susceptibility result may warrant reopening the empirical decision immediately. Conversely, absence of actionable new information should not force treatment change merely because a nominal “timeout” has arrived. Rapid diagnostics are therefore best understood as timing modifiers within a broader decision system: they can move the reassessment window forward, but they cannot determine the correct response in isolation.

PK/PD target attainment beyond nominal susceptibility

Microbiological susceptibility describes a relationship between an organism and antimicrobial concentration under defined testing conditions; it does not establish that the patient will achieve the exposure needed at the infected site. This distinction becomes especially important in critical illness, where altered volume of distribution, renal clearance, organ dysfunction, extracorporeal therapies and rapid physiological change can make standard

dosing an unreliable proxy for achieved exposure. Expert guidance on antimicrobial therapeutic drug monitoring therefore supports concentration-guided approaches for selected critically ill patients and agents where pharmacokinetic variability creates substantial uncertainty [9].

Yet the same evidential discipline that challenges nominal susceptibility must also constrain enthusiasm for precision dosing. In a multicentre randomized trial, model-informed precision dosing of β-lactams and ciprofloxacin improved the dosing process without demonstrating that such optimization automatically translated into superior clinical outcomes [10]. Exposure adequacy should therefore be treated as an important intermediate condition, not as a guaranteed surrogate for patient benefit. A pharmacologically elegant regimen can still fail because the infectious focus persists, treatment began too late, the host response dominates prognosis, or the selected PK/PD target does not fully capture clinically relevant exposure.

The continuous-infusion debate illustrates this problem. BLING III did not establish statistically significant superiority of continuous β-lactam infusion for its primary mortality outcome in critically ill patients with sepsis [11]. At the same time, a contemporaneous synthesis of randomized evidence was compatible with benefit from prolonged β-lactam infusion at the aggregate level [12]. These findings should not be forced into a binary verdict. Differences in populations, organisms, baseline exposure, drug selection and trial weighting can influence whether an exposure-optimizing strategy produces a detectable clinical advantage.

For stewardship, the relevant conclusion is narrower but more useful. Susceptibility should trigger a second question: is the regimen likely to achieve appropriate exposure in this patient now? That question may justify dose adjustment, altered infusion, TDM or no change, depending on physiological instability, therapeutic window, assay availability and expected consequence of underexposure. PK/PD optimization is therefore neither an optional technical add-on nor a universally beneficial intervention. It is a conditional treatment decision whose value depends on the gap between nominal activity and credible patient-level exposure.

Source control as a determinant of antibiotic success

Antimicrobial stewardship can become distorted when every unfavourable trajectory is interpreted as evidence that the antibiotic is wrong. In infections sustained by an uncontrolled anatomical focus, microbiologically active therapy may remain insufficient because the biological problem is not purely pharmacological. Contemporary source-control literature shows substantial heterogeneity in how source control, timing and adequacy are defined across severe bloodstream-infection and critical-care studies [13]. That measurement problem matters: “source controlled” is not a uniform binary state, and an apparent treatment failure may reflect persistent infection burden that susceptibility testing cannot resolve.

Observational evidence nonetheless supports the clinical importance of timing. Among patients with sepsis requiring an intervention for source control, earlier intervention has been associated with improved survival [14]. Such data do not establish a universal causal deadline. Patients who can undergo earlier intervention may differ systematically from those whose procedures are delayed by diagnostic uncertainty, physiological instability, anatomical complexity or limited access to surgery or interventional radiology. The defensible conclusion is therefore that source-control timing is a major treatment variable, not that one fixed clock should govern every infection.

Secondary peritonitis provides a particularly clear hard case. Delayed or failed source control has been associated with worse outcomes in critically ill patients despite antimicrobial treatment [15]. Escalating antibiotic spectrum in this setting may be rational when new microbiological evidence indicates inadequate coverage, but escalation cannot be presumed to compensate for persistent contamination, an undrained collection or unsuccessful procedural control.

The same principle appears in *Staphylococcus aureus* bacteraemia, where management depends on identifying metastatic infection, removing infected devices when appropriate and defining complicated disease rather than selecting an active agent alone [16]. These syndrome-specific requirements should not be generalized mechanically to every bloodstream infection, but they expose a broader stewardship boundary: pharmacological adequacy and anatomical adequacy are analytically distinct.

Accordingly, source control should be assessed alongside—not after—antibiotic optimization. Persistent fever, bacteraemia or organ dysfunction should reopen at least two competing explanations: inadequate antimicrobial therapy and inadequate control of the infectious focus. Stewardship fails when the first explanation is repeatedly intensified while the second remains unexamined.

De-escalation as an evidence- and context-dependent decision

De-escalation is frequently described as an uncomplicated stewardship good, but the clinically relevant question is not whether narrower therapy is preferable in the abstract. It is whether uncertainty has fallen enough that broader coverage no longer protects against a plausible untreated pathogen. Contemporary target-trial emulation in adults hospitalized with community-onset sepsis suggests that selected patients meeting eligibility for day-4 de-escalation can undergo narrowing without a clear mortality penalty [17]. Because treatment selection remains observational, this evidence should support conditional safety rather than universal reassurance.

Randomized evidence strengthens that position within a defined microbiological setting. In the SIMPLIFY trial, structured de-escalation from antipseudomonal β-lactams in bloodstream infections caused by susceptible Enterobacterales was non-inferior for clinical cure compared with continued broader therapy [18]. The trial supports an actionable proposition: once the pathogen, susceptibility pattern and clinical circumstances satisfy defined conditions, spectrum can be narrowed without assuming that maximal breadth is inherently safer. It does not justify de-escalation before diagnostic clarification, in patients whose clinical deterioration raises concern for an unrecognized focus, or when polymicrobial or resistant infection remains plausible.

Resistance concerns also require careful directionality. A retrospective cohort of hospitalized patients with sepsis found that β-lactam de-escalation was associated with less subsequent Gram-negative resistance rather than more [19]. The study cannot establish that narrowing causally prevents resistance, but it challenges the argument that maintaining broader β-lactam exposure should be considered microbiologically conservative by default. Broader treatment can itself impose ecological selection pressure.

De-escalation should therefore be framed as an evidence- and context-dependent reassessment rather than a ritual endpoint. The relevant inputs include microbiological confidence, current clinical stability, source-control status, likelihood of mixed infection, previous antimicrobial exposure and the consequences of being wrong in either direction. Narrowing too early can abandon necessary coverage; narrowing too late prolongs avoidable spectrum. The stewardship objective is not maximal de-escalation, but timely contraction of treatment when the residual uncertainty no longer justifies its broader cost. In the proposed treatment-course logic developed later, de-escalation is thus one revisable decision among several, not a stand-alone performance metric.

Treatment duration and the cost of automatic continuation

Duration is one of the clearest examples of how stewardship can fail after an initially correct prescription. Once a patient improves, continuation often feels safer than stopping because the harms of an unnecessary extra day are diffuse whereas relapse is salient. Contemporary randomized evidence challenges that asymmetry. In patients with bloodstream infection who met trial eligibility criteria, seven days of antibiotic treatment was non-inferior to fourteen days, and a subsequent meta-analysis of randomized Gram-negative bloodstream-infection trials likewise supported shorter treatment in appropriately selected patients [20, 21]. These findings do not establish a universal seven-day rule. They instead shift the burden of justification: extension beyond a supported shorter course should be linked to a clinical reason rather than inherited from habit.

That qualification is decisive. Deep or endovascular infection, inadequate source control, profound immunocompromise, persistent instability, unusual organisms, or other conditions excluded or under-represented in short-course trials may alter the duration decision. Duration is therefore not simply counted from the first dose. It depends on what infection is being treated, whether adequate control has been achieved, how the patient has responded, and whether new evidence has emerged that changes the original diagnosis.

A further timing problem is deciding when the duration clock meaningfully begins. Culture clearance, achievement of source control, restoration of stability and initiation of reliably active therapy may occur at different times. The available evidence does not justify collapsing those events into one universal starting point. In difficult infections, duration should therefore be anchored to the clinical question being answered rather than to an administratively convenient date.

Biomarker-guided stopping illustrates why “shorter” and “more individualized” are not synonymous. In ADAPT-Sepsis, procalcitonin- and C-reactive-protein-guided strategies did not behave as interchangeable decision tools [22]. A biomarker may contribute to reassessment, but it cannot independently determine whether a residual infectious focus, metastatic complication, or alternative diagnosis is present.

The stewardship failure is thus automatic continuation, not merely long treatment. Every additional day should remain an active decision. Stopping too early can expose a patient to relapse or uncontrolled infection; stopping too late adds treatment burden, adverse-event opportunity, ecological selection and transition-of-care complexity without assured benefit. A defensible duration decision therefore requires explicit reassessment of indication, source, response and residual uncertainty at the point when treatment would otherwise continue by default.

Oral step-down and the transition from intravenous therapy

Intravenous therapy is often treated as a marker of treatment intensity, yet route and antimicrobial adequacy are not equivalent. Recent randomized and synthesized evidence supports oral transition for selected, clinically stable patients with bloodstream infection when an active oral option is available and syndrome-specific eligibility conditions are satisfied [23–25]. That evidence includes Gram-negative bacteraemia and carefully selected low-risk *Staphylococcus aureus* bloodstream infection, but its restrictions are as important as its positive findings. It does not support indiscriminate oral conversion in patients with persistent instability, uncontrolled deep infection, unreliable absorption or a regimen incapable of achieving adequate exposure.

The stewardship question should therefore be framed as "what route can reliably deliver the required therapy now?" rather than "has the patient completed enough intravenous days?" This shifts attention toward oral bioavailability, dose, susceptibility, gastrointestinal function, drug interactions, adherence capability and the consequences of missed doses. It also keeps source control and clinical stability upstream of route selection. A patient whose source remains uncontrolled does not become a good oral-switch candidate simply because an active tablet exists.

Patient capability also belongs inside this decision. Oral therapy may be pharmacologically suitable yet practically fragile if medicines are unaffordable, unavailable, poorly understood, or unlikely to be taken consistently after discharge. Conversely, a reliable oral plan can reduce dependence on infusion services and vascular access. These are not arguments for privileging one route; they are reasons to distinguish theoretical oral activity from a route that can actually deliver treatment in the patient's post-hospital context.

Conversely, continued intravenous therapy has its own burdens. Vascular access can complicate mobility, discharge and outpatient management, and intravenous treatment can prolong dependence on institutional infrastructure when an effective oral regimen is feasible. These considerations do not prove that oral therapy is superior; they establish that route is itself a stewardship decision with patient-level and system-level consequences.

The most difficult cases expose why a route rule cannot stand alone. Low-risk trial eligibility may not capture patients with metastatic infection, endovascular disease, malabsorption, unstable physiology or uncertain adherence. In such settings, maintaining intravenous therapy may be appropriate even when oral susceptibility appears favourable. Oral step-down should therefore occur when pharmacological feasibility, clinical stability, source adequacy and patient capability converge. The appropriate endpoint is not early oral therapy, but timely removal of an intravenous requirement that no longer contributes necessary therapeutic assurance.

Integrating stewardship decisions across the treatment course

The preceding domains should not be implemented as six independent checklists. Their value lies in the way each changes the interpretation of the others. A rapid susceptibility result may support de-escalation, but persistent shock or an uncontrolled focus may delay narrowing. Source control may permit a shorter course, while deteriorating renal function may reopen dosing. Clinical stability may make oral therapy reasonable, but only after the organism, regimen and infection source have been reassessed. Stewardship therefore requires decision continuity rather than a sequence of isolated interventions.

Implementation evidence shows why the existence of a reassessment point is insufficient. Prospective audit and feedback can create an active opportunity for clinicians and stewardship teams to reconsider treatment and, in a pragmatic cluster-randomized trial, altered antimicrobial decision-making in its study context [26]. By contrast, an electronic antibiotic timeout did not reliably increase treatment modification simply by generating an alert [27]. The distinction is between a checkpoint and an effective reassessment process: the latter requires clinically relevant evidence, timely interpretation, a feasible action and responsibility for acting.

The same issue appears at discharge. A stepped-wedge cluster-randomized evaluation of stewardship review before discharge produced mixed effects, including improvement in prescribing quality for reviewed cases without

a corresponding reduction in aggregate discharge antibiotic use [28]. Stewardship success therefore depends on what outcome is being optimized and on the workflow through which recommendations reach prescribers and patients.

A checkpoint register should not be mistaken for a fixed timetable. The same patient may revisit one checkpoint several times while never requiring another. The ordering is driven by information and clinical change: new renal dysfunction can reopen exposure after de-escalation, while newly recognized metastatic infection can reopen source, duration and route simultaneously.

Table 1 makes the treatment-course implication explicit by aligning each checkpoint with the evidence that should dominate it, the action being reconsidered and the next reason to reopen the decision.

Table 1. Antimicrobial-course checkpoints that require different stewardship decisions

Checkpoint	Dominant evidence	Decision option	Stewardship objective	Premature/ late risk	Next reassessment
Empirical start	Syndrome, severity, resistance risk	Start/withhold; select spectrum	Prevent untreated severe infection	Under-coverage / excess breadth	Microbiology or clinical change
Microbiology update	Identification and AST	Escalate, confirm, narrow	Match credible pathogen	Incomplete-data action / delayed optimization	Final AST and response
Exposure review	Physiology, renal function, concentrations	Adjust dose/infusion; TDM	Secure plausible exposure	Toxicity or underexposure	Physiological change
Source review	Imaging, procedures, persistence	Drain/remove/ investigate	Control ongoing focus	Unsafe intervention / missed source	Post-control response
Directed therapy	AST, stability, source status	De-escalate/retain breadth	Remove unjustified spectrum	Premature narrowing / excess exposure	Complication assessment
Duration/ route	Response, source, oral feasibility	Stop/extend; switch route	Limit unnecessary days/IV use	Relapse / prolonged burden	Discharge or new evidence

AST, antimicrobial susceptibility testing; IV, intravenous; PK/PD, pharmacokinetic/pharmacodynamic; TDM, therapeutic drug monitoring.

The proposed adaptive stewardship decision architecture

The synthesis proposed here treats the current antimicrobial plan as a revisable treatment state rather than a fixed prescription. The state comprises at least spectrum, exposure strategy, source-control status, intended duration and route. Different evidence streams update different parts of that state asynchronously. Microbiological information can reopen spectrum decisions [5]. Physiological change can reopen exposure decisions [9]. Persistent infection can reopen source-control assessment [13]. Clinical response and source adequacy can reopen duration [20], while stability and pharmacological feasibility can reopen route [23].

This structure matters because later decisions depend on combinations of evidence rather than on a compulsory sequence. De-escalation may require microbiological confidence plus clinical stability; shorter duration becomes more defensible after source control and response are established; oral step-down depends on both therapeutic feasibility and patient capability. Conversely, failure in one domain can block progress in another. An undrained focus can justify postponing duration closure, and unstable physiology can make an otherwise active oral regimen insufficiently reassuring.

The architecture also includes an implementation boundary. A decision opportunity becomes clinical action only when information is available, interpreted, communicated and operationally feasible. Active stewardship review can support that translation [26], whereas a passive alert may fail to do so [27]. Discharge creates another boundary because prescribing decisions cross teams, settings and accountability structures [28].

This proposed architecture therefore makes no claim that integration itself improves outcomes. Its testable proposition is narrower: making dependencies and reopening criteria explicit may produce more coherent reassessment than treating each stewardship intervention as a separate endpoint. That proposition requires

prospective comparison, process evaluation and external validation across different infection syndromes and stewardship capacities.

Figure 1 therefore depicts stewardship as an asynchronous evidence field in which treatment decisions can be revised, deferred or reopened rather than completed once and forgotten.

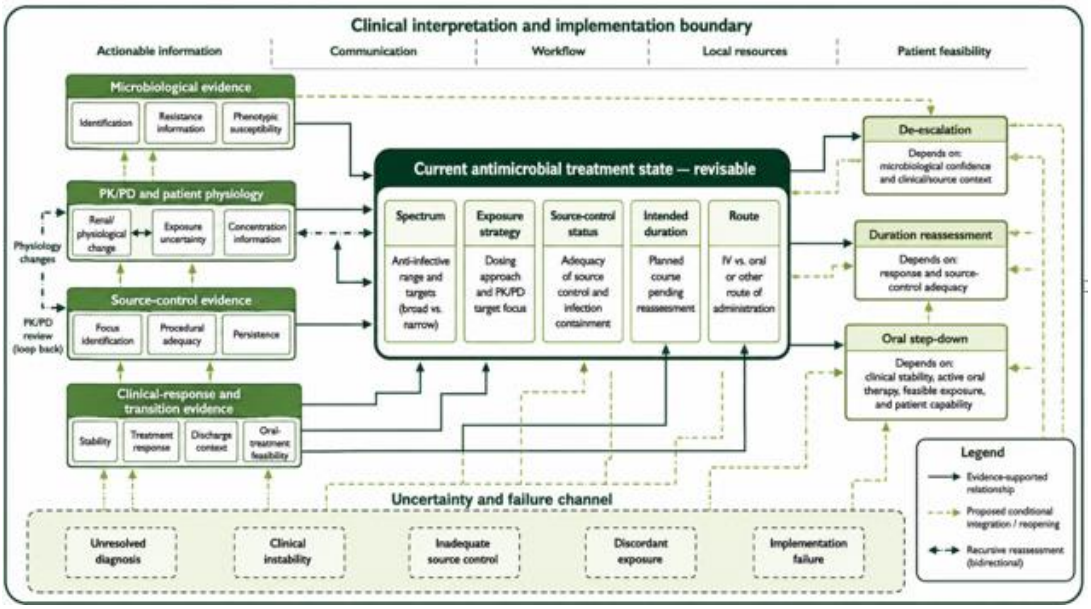

Figure 1. Antimicrobial treatment remains revisable as diagnostic, exposure, source, response, and transition evidence changes

Contentious trade-offs and boundary conditions

The strongest argument for an adaptive approach is also its principal limitation: more opportunities to optimize create more opportunities to act on incomplete evidence. Faster susceptibility information may reduce uncertainty sooner, yet FAST shows that faster data do not guarantee a better patient-centred outcome [8]. Precision dosing can improve the plausibility of exposure without guaranteeing clinical benefit [10]. Even prolonged-infusion evidence requires interpretation across a large trial with a non-significant primary mortality result and a meta-analysis compatible with aggregate benefit [11]. The debate should therefore resist converting intermediate-process improvement into assumed patient benefit.

Source control creates a different trade-off. Earlier intervention is associated with better outcomes, but procedural feasibility, diagnostic certainty and patient stability can determine when intervention is possible [14]. De-escalation similarly balances two errors: narrowing while important uncertainty remains versus preserving broad exposure after its justification has disappeared [17]. Evidence supporting structured narrowing in selected bloodstream infection does not erase the hard cases excluded from those studies.

Duration and route decisions are likewise conditional. Seven-day therapy is supported for selected bloodstream infections [20], but an endovascular or uncontrolled focus may require a different strategy. Low-risk *Staphylococcus aureus* bacteraemia can be studied for oral transition under restrictive eligibility [24], yet that should not be translated into routine early oral treatment for complicated disease. Patient-level absorption, adherence capability, drug interactions and access also matter even when microbiology appears favourable.

Implementation is the final boundary. An electronic timeout can exist without changing prescribing [27], and discharge stewardship can improve selected aspects of appropriateness without reducing total antibiotic use [28]. More stewardship infrastructure is therefore not automatically more effective stewardship.

Table 2 makes these controversies explicit by identifying what evidence would discriminate between competing actions rather than pretending that each domain has a single universally correct answer.

Table 2. Adjudicating recurrent stewardship controversies when competing priorities remain plausible

Contested decision	For action	Against action	Evidence discriminator	Patient/source condition	Defensible uncertainty

Act on rapid result	Earlier targeting	Result may not alter care	Actionable AST plus clinical consequence	Instability/resistance risk	Speed is not outcome
Intensify PK/PD	Reduce underexposure	Complexity may not improve outcome	Exposure uncertainty	Variable physiology	Target attainment is not sufficient
De-escalate now	Reduce spectrum	Residual uncertainty	Reliable microbiology plus stability	Controlled focus	Narrow only when breadth loses justification
Shorten duration	Reduce exposure	Relapse risk	Response and source adequacy	No unsupported deep-focus extrapolation	Short-course evidence is population-specific
Switch orally	Remove IV burden	Exposure/adherence concerns	Active oral regimen plus stability	Controlled source, feasible oral delivery	Eligibility remains conditional

AST, antimicrobial susceptibility testing; IV, intravenous; PK/PD, pharmacokinetic/pharmacodynamic.

Conclusion

Guideline-concordant antibiotic selection is necessary stewardship, but it is not sufficient stewardship. The treatment course continues to generate information that can alter the meaning of the original prescription. Rapid diagnostics may move microbiological certainty forward; PK/PD assessment can expose a gap between nominal susceptibility and achieved exposure; source control can determine whether antimicrobial activity is enough; de-escalation becomes defensible only as uncertainty falls; duration must be actively justified rather than inherited; and oral step-down depends on both pharmacological feasibility and the patient's clinical and practical capacity to transition.

The central contribution of this For Debate article is therefore a proposed shift in the unit of stewardship from the antibiotic selected to the sequence of revisable decisions that constitutes treatment. The proposed adaptive architecture does not claim prospective validation, universal effectiveness or implementation readiness. Its component evidence arises from different syndromes, populations, methods and health-system settings, and several crucial relationships remain conditional or observational. A technically superior diagnostic, dosing method, alert or stewardship process may fail to improve the outcome that ultimately matters.

The practical implication is not that every patient requires every stewardship intervention. It is that every continuing treatment plan should remain open to revision when new evidence changes the balance of benefit, harm and uncertainty. Future evaluation should test whether linking these decisions prospectively improves clinically meaningful outcomes over existing stewardship practice, while preserving syndrome-specific safety, patient heterogeneity, implementation feasibility and local resource constraints. Until then, the architecture should be used as an explicit reasoning model: a way to identify which decision remains unresolved, what evidence would change it, and when apparent antibiotic failure may actually reflect failure elsewhere in the treatment system.

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