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Review Article

Comparative Analysis of antimicrobial stewardship programs versus Standard Care in nosocomial infection

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Abstract

Background: Antimicrobial stewardship programs (ASPs) optimize antimicrobial selection, dosing, and duration while curbing the selective pressure that sustains multidrug-resistant organisms [1,2].

Objective: This analysis synthesizes evidence contrasting ASPs with standard, non-stewarded care in nosocomial infection, across use, resistance, *Clostridioides difficile* infection, length of stay, cost, and mortality.

Methods: We synthesized IDSA/SHEA guidance, policy frameworks, systematic reviews and meta-analyses, and comparative intervention studies addressing stewardship-supported versus standard prescribing for nosocomial infection.

Findings: Stewardship produced large reductions in inappropriate use and expenditure [9,13], a pooled ~50% reduction in *C. difficile* incidence [11], and no rigorous evidence of harm to mortality [14,25].

Conclusions: ASPs outperform standard care across outcome domains, with benefit tracking program intensity; multimodal strategies combining audit-and-feedback, preauthorization, and rapid-diagnostics-linked de-escalation should be prioritized over education-only models [2,15].

Keywords: antimicrobial stewardship; nosocomial infection; standard care; antimicrobial resistance; hospital-acquired infection

1. Introduction

Hospital-acquired, or nosocomial, infections remain a persistent threat to patient safety, and the antimicrobial agents used to treat them are simultaneously a principal driver of the resistant organisms that make those infections harder to cure. Antimicrobial stewardship programs (ASPs) were formalized as a structured institutional response, combining prospective audit and feedback, formulary restriction, prior-authorization, and de-escalation protocols to optimize antimicrobial selection, dosing, route, and duration while curbing the selective pressure that sustains multidrug-resistant organisms [1]. IDSA and SHEA jointly updated this guidance in a framework that remains the reference standard against which most program evaluations are measured [2], building on an earlier policy statement defining stewardship's institutional scope [3].

Standard care, in the comparative literature, denotes prescribing guided by individual clinician judgment without a dedicated stewardship team, audit-and-feedback loop, or restrictive formulary controls, though it may still include general infection-control measures. The comparison between ASP-supported prescribing and this baseline has been examined across surgical, medical, and intensive-care populations, and across outcomes from antimicrobial consumption and cost to *Clostridioides difficile* infection, resistance, length of stay, and mortality [4,5]. Early single-center studies suggested substantial reductions in inappropriate prescribing under stewardship oversight [6], motivating national mandates such as the U.S. requirement that acute-care hospitals maintain an ASP as a Medicare and Medicaid participation condition [7], alongside the World Health Organization's Global Action Plan on antimicrobial resistance [8].

Despite near-universal adoption, heterogeneity persists in how programs are implemented and how rigorously their effect on nosocomial infection outcomes, rather than

antimicrobial use metrics alone, has been measured. Reviews report consistent reductions in broad-spectrum consumption and cost, but more variable effects on mortality and length of stay depending on infection type and case mix [9,10]. This analysis synthesizes the evidence contrasting stewardship programs with standard care in nosocomial infection, examining appropriateness, resistance, length of stay, cost, and mortality, and what this implies for programs seeking to maximize benefit for hospital-acquired infection outcomes specifically.

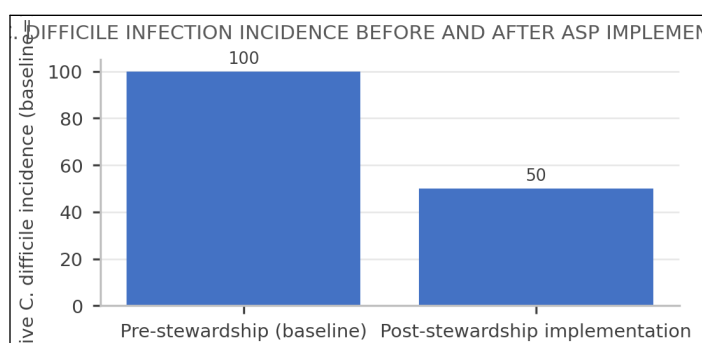


Figure 1: Relative incidence of *Clostridioides difficile* infection before and after antimicrobial stewardship program implementation, reflecting a pooled reduction of roughly 50% reported across institutions with an active program compared with pre-intervention or non-stewarded periods [11].

2. Methods

We synthesized peer-reviewed literature comparing stewardship implementation against standard prescribing in hospitalized patients with nosocomial infection: founding and updated IDSA/SHEA guidance [1,2,3]; policy mandates [7,8]; systematic reviews and meta-analyses of use, cost, resistance, *C. difficile*, length of stay, and mortality [9,11,12,13,14,15]; quasi-experimental studies across ICU, surgical, and medical wards [16,17,18,19,20]; multidrug-resistant organism outcomes [21,22,23]; evaluations of procalcitonin-guided therapy, rapid diagnostics, and audit-and-feedback [24,25,26,27,28]; and behavioral/health-economic analyses [29,30,31,4,5]. Evidence was organized around the outcome domains most consistently reported: use and appropriateness, resistance and *C. difficile*, clinical/economic outcomes, and implementation strategy.

3. Results

Antimicrobial use and prescribing appropriateness

The most consistent, largest-magnitude effect across the stewardship literature is reduced antimicrobial consumption and improved prescribing appropriateness relative to standard care. Davey and colleagues' Cochrane review found stewardship interventions significantly increased compliance with prescribing policy and reduced duration of therapy without evidence of harm, across dozens of studies from multiple countries [9]. Prospective audit-and-feedback, reviewed by an infectious-diseases-trained pharmacist or physician within 48-72 hours, produced particularly large reductions in broad-spectrum use in the wards studied by Standiford and colleagues [16] and the community-hospital cost analysis by Malani and colleagues [17]. Fridkin and colleagues' national evaluation found hospitals with structured stewardship reported substantially lower rates of inappropriate use for common nosocomial syndromes than facilities without formal programs [10], a pattern Ohl and Luther situate within the broader institutional architecture required to sustain such gains [18].

Table 1: Core antimicrobial stewardship strategies and their relative evidence strength versus standard, unsteiwared prescribing, per IDSA/SHEA implementation guidance [2,1].			
Strategy	Mechanism	Relative evidence strength	Representative effect vs standard care
Prospective audit and feedback	Post-prescription review with real-time modification	Strong	Large reduction in inappropriate broad-spectrum use [16]
Preauthorizati on / formulary restriction	Restricts access to targeted agents at order entry	Strong	Reduced broad-spectrum consumption, variable resistance impact [2]
Rapid diagnos tics-linked de-escalation	Pathogen ID/susceptibility shortens time to optimal therapy	Moderate -strong	Lower mortality, shorter antibiotic exposure [26]
Passive education / guideline dissemination alone	Didactic materials without audit or restriction	Weak	Small or non-significant reduction, approximates standard care [28]

Resistance and *Clostridioides difficile* infection

Reductions in resistant-organism and *C. difficile* rates are reported less uniformly than reductions in consumption, but the direction of effect consistently favors stewardship. Feazel and colleagues' meta-analysis found a pooled reduction in incident *C. difficile* infection of roughly 50% among institutions with an active program compared with pre-intervention or non-stewarded periods [11]. Baur and colleagues, in a meta-analysis spanning multidrug-resistant Gram-negative organisms, found stewardship associated with significant reductions in resistant-organism and *C. difficile* incidence, larger in intensive-care than general-ward settings [12]. Carbapenem-resistant Enterobacteriaceae outbreaks investigated after stewardship gaps illustrate the converse: lapsed oversight has repeatedly been implicated as a contributing factor in outbreak reports from tertiary and long-term-care facilities [21,22], a vulnerability Rice's "no ESKAPE" analysis traces directly to selective pressure from unmanaged use [23]. Rapid diagnostic-linked de-escalation, layered onto stewardship, shortened time to optimal therapy and was associated with lower mortality and resistant-organism acquisition in bloodstream-infection cohorts [26,27].

Length of stay, cost, and mortality

Effects on length of stay, cost, and mortality are the least uniform outcomes, though the balance of evidence favors stewardship or shows no significant harm. Karanika and colleagues' meta-analysis of clinical and economic outcomes found consistent reductions in antimicrobial expenditure, generally 19-40% institution-wide, alongside a modest but significant reduction in length of stay, with no evidence of increased mortality from stewardship-driven de-escalation [13]. Schuts and colleagues similarly reported reduced mortality or no significant difference in most included studies, with none reporting worse mortality under stewardship [14]. Procalcitonin-guided algorithms for antibiotic discontinuation, examined in the PRORATA trial by

Bouadma and colleagues and the subsequent SAPS trial by de Jong and colleagues, reduced antibiotic exposure days without increasing mortality relative to standard care, and in the latter reduced it, suggesting structured de-escalation can improve rather than merely preserve safety [24,25]. Health-economic modelling, including Nathwani and colleagues' systematic review and Dik and colleagues' cost-minimization model, estimates favorable cost-effectiveness across hospital sizes, driven primarily by reduced drug expenditure and shorter stay in nosocomial-infection subpopulations [15,20]. Cosgrove's analysis of resistance and outcomes, and Kollef's review of empirical therapy, together frame why the appropriateness gains above translate into the downstream signals summarized here [4,5].

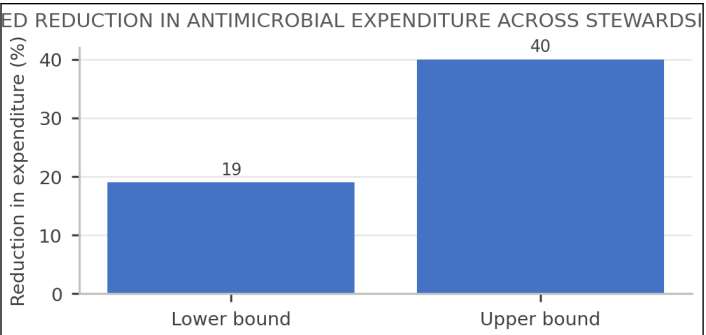


Figure 2: Reported range of institution-wide reduction in antimicrobial expenditure attributable to hospital-based antimicrobial stewardship programs relative to standard, non-stewarded prescribing, drawn from a systematic review and meta-analysis of clinical and economic outcomes [13].

Implementation strategy and program structure

The magnitude of stewardship's benefit depends heavily on which core strategies a program deploys; the updated IDSA/SHEA guideline ranks prospective audit-and-feedback and preauthorization as the interventions with the strongest evidence base, ahead of passive education alone [2]. Programs relying solely on didactic education produced substantially smaller reductions in inappropriate prescribing than multimodal programs, including Filice and colleagues' decision-support evaluation [28] and Charani and colleagues' review of behavior-change strategies [6].

Behavioral-economics-informed interventions, such as accountable-justification prompts embedded in prescribing workflow, produced meaningful reductions in inappropriate broad-spectrum prescribing when layered onto stewardship infrastructure, in Meeker and colleagues' cluster-randomized trial [29] and Gerber and colleagues' pediatric outpatient trial [30]. Pharmacist-led, ICU-embedded models produced larger relative reductions in device-associated antimicrobial days and lower mortality than ward-based programs without dedicated ICU liaison staffing [19,31], underscoring that "stewardship" versus "standard care" is itself heterogeneous depending on intensity and setting.

Table 2: Representative comparative studies of antimicrobial stewardship versus standard care by outcome domain.			
Study	Design / setting	Comparison	Reported outcome
[11]	Meta-analysis , multi-institution	Stewardship vs pre-intervention/standard care	~50% reduction in C. difficile infection incidence
[13]	Meta-analysis , hospital-based programs	Stewardship vs standard care	19-40% reduction in antimicrobial expenditure; reduced length of stay
[24]	Multicentre RCT (PRORATA), ICU	Procalcitonin-guided vs standard-duration therapy	Reduced antibiotic exposure days, no mortality increase
[29]	Cluster-randomized trial, primary care	Accountable justification prompt vs usual prescribing	Reduced inappropriate broad-spectrum prescribing

4. Discussion

The literature supports a clear conclusion for the outcome most directly under a program's control: antimicrobial consumption and prescribing appropriateness, where structured programs outperform standard care by a wide, reproducible margin across settings and designs [9,10,16]. Evidence is directionally favorable but more heterogeneous for *C. difficile* incidence and multidrug-resistant organism acquisition, where pooled estimates are large but individual effect sizes vary with case mix and program intensity [11,12]. Clinical outcomes

further downstream, length of stay, cost, and mortality, show the most heterogeneity, though no rigorous comparative study demonstrates worse mortality under stewardship, and several show improvement with structured de-escalation such as procalcitonin-guided algorithms [13,14,25].

This gradient, strong proximal effects on prescribing behavior, moderate downstream effects on resistance and *C. difficile*, and never clearly harmful distal clinical effects, suggests that measured benefit over standard care is contingent on which interventions a program deploys: passive education alone approximates standard care in effect, whereas multimodal programs combining audit-and-feedback, preauthorization, and rapid-diagnostics-linked de-escalation approximate the larger effects reported in the strongest studies [2,28,26,6,29]. The persistence of carbapenem-resistant organism outbreaks in institutions with weak or lapsed oversight argues the comparison is not merely academic [21,22]. Health-economic analyses reinforce that benefit is realized efficiently, driven by reduced drug expenditure and shortened stay within nosocomial-infection populations [15,20,4].

Limitations temper these conclusions. Most comparative studies are before-after or quasi-experimental rather than randomized, so secular trends in infection control, diagnostics, or case mix may contribute to observed differences independent of stewardship [23]. Heterogeneity in how "standard care" is defined across studies complicates direct comparison in pooled meta-analytic estimates [9,12]. Publication and reporting biases favoring positive findings cannot be excluded given strong institutional incentives to demonstrate value under mandates such as the CMS Conditions of Participation and the WHO Global Action Plan [7,8].

5. Conclusion

Across use, resistance and *C. difficile* incidence, and clinical and economic outcomes, the evidence favors

antimicrobial stewardship programs over standard, unstewarded prescribing for nosocomial infection, with the strongest benefit in prescribing appropriateness and consumption, a moderate but consistent benefit in resistant-organism and *C. difficile* rates, and no rigorous evidence of harm on length of stay, cost, or mortality [13,14,15]. Benefit magnitude tracks program intensity, with multimodal strategies outperforming passive-education-only approaches that more closely resemble standard care [2,28,26,30,31]. Given the near-universal policy mandate and the consistent direction of evidence, institutions managing nosocomial infection should prioritize evidence-supported core strategies over minimal or purely educational models, and should measure programs against nosocomial-infection-specific clinical endpoints, not consumption metrics alone [1,3,20].

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