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Emerging Resistance Patterns in Gastrointestinal Surgical Site Infections and Implications for Empirical Antibiotic Policy

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ABSTRACT

Background: Empirical antibiotic selection for gastrointestinal surgical site infection (SSI) is meant to be guided by resistance surveillance data, yet the mechanisms connecting local resistance trends to guideline revision and institutional prescribing policy remain poorly characterized.

Objective: This review examines, from a policy rather than a purely epidemiological standpoint, how current surgical prophylaxis and intra-abdominal infection guidelines incorporate resistance data, how regional and temporal variation in resistance drives divergence in local empirical policy, what antimicrobial stewardship programs have actually been shown to change, and where the evidence base for resistance-adjusted guideline recommendations remains thin.

Scope: Drawing on published guideline documents (including Surgical Infection Society, ASHP/IDSA/SHEA/SIS, NICE, and Italian national recommendations), country-level adaptation frameworks such as GRADE-ADOLOPMENT, antibiogram and surveillance studies, and stewardship intervention evaluations, this synthesis argues that guideline revision cycles generally lag the pace of local resistance change, that empirical algorithms calibrated in one resistance setting transfer poorly to others, and that stewardship programs demonstrably shift prescribing and specimen-collection behaviour but have been evaluated far less rigorously on whether they actually recalibrate empirical regimens against current local resistance data.

Conclusions: Closing the gap between resistance surveillance and empirical antibiotic policy for gastrointestinal SSI will require guideline frameworks that specify explicit, locally checkable resistance thresholds for recommendation revision, shorter and more routinized antibiogram-to-policy review cycles, and prophylaxis and treatment trials that prespecify resistant-organism infection as an outcome rather than treating it as an incidental subgroup finding.

Keywords: *antimicrobial stewardship; surgical antibiotic prophylaxis; antimicrobial resistance policy; gastrointestinal surgical site infection; empirical antibiotic therapy*

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Introduction

Every surgeon who opens an abdomen for a perforated diverticulum or a leaking anastomosis is, whether they think of it this way or not, making a policy decision in miniature. The choice of empirical antibiotic - piperacillin-tazobactam versus a carbapenem, the addition or omission of an agent aimed at vancomycin-resistant enterococci, the decision to keep prophylaxis to a single dose or extend it "just in case" - is supposed to be governed by a guideline. But guidelines are built from surveillance data that are, almost by definition, already a year or two old by the time they are synthesized, graded, and published, and the resistance landscape in gastrointestinal surgical site infection (SSI) has not been especially patient in the interval. Extended-spectrum beta-lactamase (ESBL)-producing Enterobacterales, carbapenem-resistant organisms, and multidrug-resistant Pseudomonas have moved from "consider in high-risk patients" to "expect in a meaningful minority" in many centres, and the empirical-therapy calculus that guidelines were written to standardize has become correspondingly harder to standardize - a shift consistent with the global estimate that bacterial antimicrobial resistance was directly implicated in more than a million deaths in a single year, with intra-abdominal and surgical infection among the syndromes most exposed to that burden [1].

This is not a new observation, and it is not one this journal is making for the first time. Two related reviews published in earlier issues of this journal have already mapped the epidemiology of multidrug-resistant organisms (MDROs) in gastrointestinal SSI broadly, and the pathogen-specific resistance patterns encountered in postbiliary infection more narrowly. Both are, in essence, epidemiological accounts: what organisms, what resistance mechanisms, what proportions. This review asks a different, and in some ways harder, question - not what the resistance data show, but what surgical and pharmacological policy is supposed to do with them. How does a stewardship committee, a hospital pharmacy and therapeutics group, or a national guideline panel translate a rising ESBL rate into a revised empirical regimen, and how confident should any of us be that the process by which that translation happens is actually evidence-based rather than habit dressed up as evidence?

The honest answer, as this review will try to show, is "somewhat confident, with substantial gaps." Guideline bodies - the Surgical Infection Society (SIS), the American Society of Health-System Pharmacists (ASHP) working jointly with the Infectious Diseases Society of America (IDSA) and the Society for Healthcare Epidemiology of America (SHEA), national bodies such as the UK's National Institute for Health and Care Excellence (NICE), and multinational efforts such as Italy's antimicrobial-use optimization council - have all, over the past decade, revised or updated their recommendations at least partly in response to resistance trend data [2,3,4,5]. But the revision cycles are slow relative to how fast local antibiograms can shift, the underlying trial evidence for many "resistance-adjusted" recommendations is thin, and there is enormous unevenness in how much local resistance surveillance actually feeds back into local prescribing policy versus simply sitting in an annual antibiogram report that few clinicians read closely. This review synthesizes what is known about (1) the current guideline architecture for empirical antibiotic selection in gastrointestinal surgery and intra-abdominal infection, (2) how regional and temporal resistance variation is - and is not - driving divergence in local policy, (3) what stewardship programs have actually been shown to do to empirical prescribing once implemented, and (4) where the evidence base for guideline-setting itself remains thin. The aim is not another resistance surveillance summary but a critical look at the policy machinery that is supposed to sit downstream of that surveillance.

Guideline Frameworks for Empirical Antibiotic Selection in Gastrointestinal Surgery

The regulatory and professional-society landscape governing empirical antibiotic choice for gastrointestinal SSI and intra-abdominal infection is more fragmented than clinicians outside the field often assume. There is no single global guideline; instead there is a loose confederation of documents with overlapping but not identical scope, updated on different schedules, by different methodologies, and with different degrees of explicit attention to local resistance data.

The joint ASHP/IDSA/SHEA/SIS clinical practice guideline for antimicrobial prophylaxis in surgery remains the reference document for perioperative prophylaxis dosing, timing, and agent selection across surgical specialties, including colorectal and hepatobiliary procedures [2]. Its core recommendations - a beta-lactam-based regimen, usually cefazolin with or without metronidazole for colorectal cases, given as a single dose timed to incision - were built on a trial base assembled well before the current burden of ESBL-producing Enterobacterales in many surgical populations. The guideline does gesture toward local resistance patterns as grounds for deviation, but it does not operationalize how a service should decide when local ESBL prevalence has crossed a threshold that justifies routine departure from the standard regimen. That gap is, in a sense, the entire subject of this review.

Where prophylaxis guidance stops, treatment guidance for established intra-abdominal infection - which is what a genuinely infected gastrointestinal SSI usually becomes - picks up, and here the SIS has been the most active reviser. The 2024 update to the SIS guidelines on management of intra-abdominal infection explicitly widens its risk-stratification language around when empirical coverage for resistant Gram-negative organisms is warranted, reflecting an editorial judgment that resistance prevalence has shifted enough since the prior iteration to justify new recommendations rather than a re-endorsement of the old ones [3]. That the SIS felt compelled to revise a document this quickly, rather than waiting the customary five-to-seven-year interval typical for surgical infection guidelines, is itself informative about how the field currently perceives the pace of resistance change.

A parallel effort with a distinctly national flavour is the Italian council's 2024 recommendations on intra-abdominal infection, produced explicitly to adapt broader international guidance to Italy's own, comparatively high, burden of carbapenem-resistant Enterobacterales and to give clinicians algorithm-level guidance on when to escalate beyond standard empirical regimens [5]. This is a useful illustration of a broader pattern worth naming early: guideline panels increasingly recognize that a single globally applicable empirical algorithm is not defensible when the underlying resistance prevalence driving the algorithm's risk-benefit calculus varies by an order of magnitude between countries. The response has been a proliferation of national or regional adaptations rather than a single universal document, a pattern echoed by the UK's NICE update on surgical site infection prevention, which layers country-specific antimicrobial resistance surveillance data onto its recommendations for prophylaxis and treatment thresholds [4].

None of these documents, it is worth being blunt about, is built around gastrointestinal SSI as a freestanding entity in the way that, say, a diabetic foot infection guideline is built around its own clinical syndrome. Gastrointestinal SSI recommendations are instead scattered across the prophylaxis guideline, the intra-abdominal infection treatment guideline, and procedure-specific society statements, which is itself a policy-relevant observation: a clinician trying to decide on empirical coverage for a resistant-organism SSI after colorectal surgery is triangulating between at least two or three separate documents that were not written to be read together, and whose resistance-adjustment language does not always align.

Regional and Temporal Variation in Resistance and Its Policy Consequences

If guidelines were only ever applied in the population from which their evidence was drawn, the mismatch between guideline vintage and current resistance prevalence would matter less. But surgical antibiotic guidelines circulate globally, often adopted with only minor local annotation, and the resistance prevalence against which their empirical recommendations are implicitly calibrated varies enormously by geography and by year.

Guideline and policy frameworks bearing on empirical antibiotic selection for gastrointestinal surgical site infection, compared by scope, mechanism for incorporating resistance data, and revision cadence.

Framework (reference)	Primary scope	Mechanism for local resistance adaptation	Revision cadence to date	Key limitation for empirical GI-SSI policy
ASHP/IDSA/SHEA/SIS surgical antimicrobial prophylaxis guideline (Bratzler et al. 2013)	Perioperative prophylaxis agent, dose, timing across surgical specialties	General instruction to consider local resistance; no explicit threshold specified	No comprehensive update since 2013	Underlying trial base predates current ESBL/CRE prevalence in many surgical populations
Surgical Infection Society intra-abdominal infection guideline, 2024 update (Huston et al. 2024)	Empirical and definitive treatment of established intra-abdominal infection	Expanded risk-stratification language for resistant Gram-negative coverage	Updated ahead of typical 5-7 year cycle in response to perceived resistance shift	Risk-stratification criteria not tied to a quantified local resistance threshold
Italian council recommendations on intra-abdominal infection (Viale/Sartelli et al. 2024)	National adaptation of intra-abdominal infection management	Explicit algorithmic escalation keyed to national carbapenem-resistant Enterobacterales burden	Single national iteration to date	Model not yet generalized to other national settings with different resistance profiles
NICE surgical site infection prevention and treatment guideline (Leaper et al. 2019)	SSI prevention and treatment, UK national scope	Layers UK-specific AMR surveillance onto prophylaxis/treatment thresholds	Periodic exceptional surveillance review	National scope limits direct transferability to higher-resistance-burden settings
GRADE-ADOLOPMENT country-level adaptation framework (Carrara et al. 2024)	Adaptation of international MDR Gram-negative treatment guidance to country level	Formal re-grading of recommendations against local epidemiology and stewardship capacity	Applied to a limited set of pathogen-drug combinations so far	Resource-intensive; not yet routinized as standing guideline-maintenance practice

Antibiogram-based studies make the scale of this variation concrete. A four-year antibiogram analysis of priority pathogens from a single tertiary centre found resistance trends among Enterobacterales and non-fermenters shifting meaningfully within the observation window itself, to the point that recommendations for empirical coverage that were reasonable at the study's outset were no longer clearly reasonable by its end - a finding the authors used explicitly to argue for antibiogram review cycles shorter than the multi-year intervals typical of formal guideline revision [6]. A similarly instructive exercise from a teaching hospital in Ghana describes the practical difficulty of building a local antibiogram robust enough to inform prescribing policy in a setting with limited microbiology capacity, and is candid about how much of empirical prescribing in that context still runs on regional or imported guidance rather than truly local data [7]. A broader systematic review and meta-analysis of antibiotic resistance across the Middle East and Southern Asia likewise documents resistance prevalence for key Gram-negative pathogens that is substantially higher, and considerably more heterogeneous between neighbouring countries, than the ranges implicit in most internationally authored empirical guidance [8].

The consequence of this variation for policy is not subtle: a single empirical algorithm calibrated to, say, North American or Western European resistance prevalence will systematically under-treat resistant-organism gastrointestinal SSI in settings where ESBL or carbapenemase prevalence is substantially higher, while the reverse recommendation - broad, carbapenem-forward empirical coverage as a universal default - would represent significant antimicrobial overuse in lower-prevalence settings and accelerate the very resistance the policy is meant to manage. This is precisely the tension that motivated the GRADE-ADOLOPMENT framework for adapting international guidance on multidrug-resistant Gram-negative infection to country-level resistance data, which formalizes a process for taking an international evidence synthesis and re-weighting its recommendations against local epidemiology, local antimicrobial stewardship capacity, and local drug availability rather than adopting the source guideline unmodified [9]. It is a methodologically serious attempt to solve a problem that most surgical prophylaxis guidance has, so far, only gestured at.

Temporal variation compounds the regional picture. Guideline-concordant prophylaxis studied in real-world colorectal surgery practice in Thailand found that adherence to a guideline-recommended regimen was associated with lower SSI rates overall, but also noted that the "recommended regimen" itself required local adaptation to account for resistance patterns that had shifted since the source guideline's underlying evidence was collected [10]. Put differently: guideline concordance is being used as a quality metric even in settings where the guideline being measured against may already be lagging local epidemiology, which risks rewarding adherence to a target that is itself out of date. A comparable microbiologic evaluation of colorectal SSI isolates undertaken specifically to inform local prophylaxis recommendations reached a similar conclusion from the opposite direction - that the organisms actually recovered from infected surgical sites at a given institution diverged enough from the assumptions built into national prophylaxis guidance to warrant a locally tailored regimen rather than uncritical adoption of the national default [11].

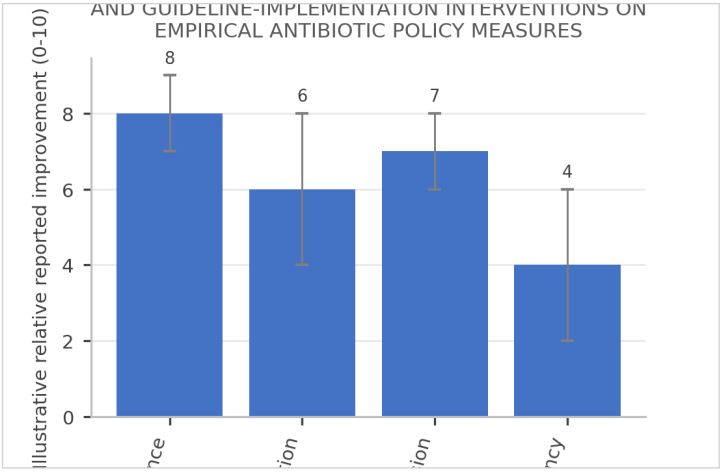
Retrospective description of prescribing behaviour in critically ill surgical patients with intra-abdominal infection adds a further wrinkle: even where clinicians are aware of elevated local MDRO risk, prescribing patterns for empirical therapy do not always track that risk in a linear or fully rational way, with some high-risk patients under-treated and some low-risk patients over-treated relative to what a strict risk-stratified algorithm would recommend [12]. This is a reminder that policy documents are necessary but not sufficient; translating a resistance-adjusted algorithm into bedside practice depends on clinician awareness of the local data the algorithm is supposed to be built on, which is a stewardship and implementation problem as much as a guideline-writing one.

Antibiotic Stewardship Programs and Their Measured Effect on Empirical Policy

Antimicrobial stewardship programs (ASPs) are, in principle, the

mechanism by which resistance surveillance data is supposed to reach the bedside faster than the multi-year guideline revision cycle allows. The IDSA/SHEA guideline on implementing an ASP lays out the structural elements - dedicated leadership, prospective audit with feedback, formulary restriction and preauthorization, and facility-specific treatment recommendations tied to local antibiograms - that are meant to let an institution adjust its own empirical policy faster than any external body could revise a published guideline [13]. The relevant question for this review is how well that mechanism actually performs when the goal is specifically adjusting empirical therapy for gastrointestinal surgical infection in response to rising resistance, rather than antimicrobial stewardship in general.

Illustrative synthesis of the reported direction and approximate magnitude of effect of antimicrobial stewardship and guideline-implementation interventions on measures relevant to empirical antibiotic policy for gastrointestinal surgical/intra-abdominal infection, drawn from the intervention studies reviewed (Xia et al. 2025; Sefah et al. 2024; Tanyakul et al. 2026; Dodoo et al. 2023).



The evidence here is more encouraging on process measures than on the harder question of whether stewardship demonstrably closes the gap between local resistance data and empirical prescribing. An interrupted time series analysis of an ASP intervention found measurable increases in pre-therapy pathogen detection specimen submission and shifts in antimicrobial use following the intervention, alongside a documented reduction in the recovery of certain resistant pathogens over the study period - a result consistent with the idea that structured stewardship activity can move both prescribing behaviour and, eventually, local resistance prevalence, though the causal chain between the two is not fully disentangled in a single-centre before-after design [14]. A systematic review focused specifically on stewardship interventions targeting appropriate use of surgical antimicrobial prophylaxis in low- and middle-income countries found a broadly consistent direction of effect - improved concordance with recommended prophylaxis choice, dose, or duration across the included studies - but flagged substantial heterogeneity in intervention design, outcome definition, and duration of follow-up, which makes it difficult to say with confidence which specific stewardship components are doing the work [15].

What is less well demonstrated, across this literature, is stewardship's effect on the specific decision this review is concerned with: empirical antibiotic selection at the point of surgical infection, adjusted explicitly for locally rising resistance. Most published stewardship evaluations measure guideline concordance or overall antimicrobial consumption as their primary outcome, which is a reasonable and tractable metric, but it is a different question from whether the empirical regimen a stewardship program is enforcing concordance with has itself been recalibrated to current local resistance data. A program can achieve excellent compliance with an empirical algorithm that is, unbeknownst to the auditors, already several resistance-prevalence-percentage-points out of date. This is not a criticism of the stewardship literature so much as an observation about what it has, and has not yet, been designed to measure.

Evidence Gaps in Guideline-Setting for Resistant-Organism Gastrointestinal SSI

Stepping back from individual interventions, several structural gaps in how the evidence base for guideline-setting is assembled become visible, and they matter more for empirical policy than any single new resistance study would.

The first is a straightforward surveillance-infrastructure problem. A review of antimicrobial resistance surveillance in low- and middle-income countries described the available data as, in the authors' own phrase, a "scattered picture" - fragmented across institutions with inconsistent laboratory capacity, non-standardized reporting, and limited representativeness at the national level [16]. Guideline panels that want to write resistance-adjusted recommendations for these settings are, in effect, being asked to synthesize evidence from a surveillance system that was never built with guideline synthesis in mind. This is a genuine methodological bind rather than a matter of insufficient effort: you cannot GRADE the certainty of evidence for a resistance threshold that is itself measured inconsistently across the studies being pooled.

The second gap concerns how, and whether, resistance surveillance is formally incorporated into evidence-based practice guideline methodology at all. A comparative review of antibiotic prescribing guidelines across countries found wide variation not just in the empirical recommendations themselves but in whether local resistance data were explicitly cited as the rationale for a given recommendation or simply assumed as background context, with many guidelines offering little transparency about how a specific resistance threshold translated into a specific empirical-agent recommendation [17]. Where that translation logic is not made explicit, it becomes very difficult for a downstream user - a hospital pharmacy committee trying to decide whether its own resistance data justify deviating from the national guideline - to know whether their local numbers actually cross whatever threshold the original panel had implicitly in mind.

Third, and perhaps most consequential for low-resource surgical settings specifically, is what has been termed the evidence-to-policy gap: even where resistance data exist and are of reasonable quality, the pathway from surveillance report to an actual, implementable change in institutional or national empirical antibiotic policy is often informal, under-resourced, and dependent on individual champions rather than a defined process [18]. Data sitting in a laboratory information system or an annual antibiogram PDF does not automatically become a revised order set; someone has to notice the trend, have the authority to act on it, and navigate whatever approval process governs changes to formulary or protocol. The GRADE-ADOLOPMENT framework represents one serious attempt to formalize that translation step for a defined class of infections [9], but it remains a resource-intensive process that has, to date, been applied to a

limited number of pathogen-drug combinations rather than routinized as a standing element of hospital guideline maintenance.

Fourth, there is a comparative-effectiveness gap specific to prophylaxis regimen choice under rising resistance. The most rigorous recent synthesis of antibiotic prophylaxis strategies in colorectal surgery, a systematic review and network meta-analysis, was able to rank regimens on SSI outcomes but noted that few of the underlying trials were designed or powered to detect differential effectiveness against resistant-organism SSI specifically, since resistant-organism infection was rarely a prespecified outcome in the original prophylaxis trials [19]. In practical terms, this means that when a guideline panel wants to recommend an alternate prophylaxis regimen on the grounds that it offers better coverage against locally prevalent resistant organisms, it is often reasoning from mechanism and observational cohort data - such as the earlier-cited microbiologic evaluations of resistant SSI isolates [11] - rather than from head-to-head randomized comparisons targeting that specific question. That is not necessarily the wrong basis for a recommendation, but it is a weaker evidentiary basis than guideline methodology committees generally prefer to acknowledge in their grading of recommendation strength, and it partly explains why so many resistance-adjusted prophylaxis recommendations across these documents are graded as conditional or weak rather than strong.

Finally, existing broad surgical prophylaxis reviews tend to synthesize guideline recommendations, prescribing pattern surveys, and resistance trend data side by side without a clear framework for reconciling them when they point in different directions, which is itself a symptom of the underlying problem rather than a solution to it [20]. Bringing prescribing-pattern evidence, antibiogram evidence, and guideline text into the same document is a useful first step, but it does not, on its own, tell a hospital committee what to do when its local antibiogram diverges sharply from the assumptions embedded in the national or international guideline it is otherwise obligated to follow.

Discussion: Toward Adaptive, Locally Calibrated Empirical Policy

Taking the evidence above together, a coherent - if not entirely comfortable - picture of the current state of empirical antibiotic policy for gastrointestinal SSI emerges. The major guideline bodies are aware that resistance has shifted meaningfully since their foundational documents were written, and several have responded with genuine revisions rather than cosmetic updates [3,5,4]. But the revision cadence remains slower than the pace of local resistance change documented in single-institution antibiogram studies [6], the underlying trial evidence for many resistance-adjusted recommendations is thinner than guideline grading language sometimes implies [19], and the mechanisms by which local surveillance data are supposed to feed back into local prescribing policy are inconsistent, under-formalized, and heavily dependent on institutional stewardship maturity [13,15,14].

A few directions seem worth taking seriously by hospitals and guideline bodies alike, without pretending any of them is a complete fix. Shortening the interval between antibiogram review and empirical-policy reassessment - moving from an annual ritual that few clinicians consult to a standing item on a stewardship committee's agenda with an explicit trigger threshold for policy reconsideration - would address some of the temporal lag documented above, though it requires stewardship infrastructure that many hospitals, particularly in lower-resource settings, do not yet have [7,16]. Making explicit, in guideline text itself, the resistance-prevalence threshold at which a recommendation should be reconsidered locally - rather than a vague instruction to "consider local resistance patterns" - would give hospital committees something concrete to check their own data against, an approach the GRADE-ADOLOPMENT framework begins to formalize but that most surgical prophylaxis documents still lack [9,2]. And building resistant-organism SSI as a prespecified outcome into future prophylaxis and treatment trials, rather than treating it as a post hoc subgroup finding in observational cohorts, would give the next generation of guideline revisions a stronger evidentiary footing than the current one has [19,11].

None of this is a call for uniform global escalation of empirical coverage, which would be both clinically unjustified in lower-resistance settings and actively harmful from a stewardship standpoint. It is, instead, an argument for building the feedback loop between surveillance and policy more deliberately than it currently exists - closing, or at least narrowing, the evidence-to-policy gap that the low- and middle-income country literature has documented most starkly [18] but that, on the evidence reviewed here, is not confined to any one income setting or region.

Conclusion

The empirical antibiotic dilemma in gastrointestinal surgical site infection is not primarily a knowledge problem in the sense of lacking resistance data - antibiograms, surveillance reports, and cohort studies of resistant-organism SSI are, if anything, proliferating. It is a translation problem: getting that data, in a timely and locally relevant way, into the guidelines and institutional protocols that actually govern what a surgeon reaches for at three in the morning when a patient develops a fever on postoperative day six. Current guideline frameworks have made real, if uneven, progress toward resistance-adjusted empirical recommendations, and stewardship programs have demonstrated genuine ability to shift prescribing behaviour and specimen-collection practice. What remains underdeveloped is the formal, routine mechanism connecting the two - a standing process by which a rising local ESBL rate or an emerging carbapenemase cluster is expected, as a matter of institutional policy rather than individual initiative, to trigger reconsideration of the empirical regimen. Building that mechanism, and generating the trial evidence to support the recommendations it produces, is the unfinished business this review has tried to describe.

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