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Antimicrobial Stewardship in Emergency Departments: Strategies to Reduce Antibiotic Resistance and Enhance Clinical Outcomes

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Abstract

Antibiotic resistance constitutes a worldwide public health emergency with lasting implications on selective treatment regimens, increasing costs of health care, and overall patient morbidity and mortality. Rising rates of multidrug-resistant (MDR) bacteria, which are accelerated by inappropriate (or excessive) use of antimicrobials, pose an enormous threat to continued control over infections. Antimicrobial stewardship programs (ASPs) are new strategies that promote a balance between antibiotic prescribing optimization, prevention of emergent resistance, and clinical improvement. ASPs have been widely implemented in inpatient and outpatient settings, but have only been applied in hospital emergency departments (EDs). EDs frequently start antibiotic therapy and manage infections with an understanding of the dynamic nature of patient flow. This study analyzes the ED, pressures of MDR due to the increased frequency of extended-spectrum β-lactamase (ESBL) producing isolates, and current use of antibiotics (which can be inappropriate in 25–50% of presentations). We explore key measures of ASP and its impact on monitoring antimicrobial use and clinical outcomes and provide examples of evidence-based strategies tailored to the realities of ED practice. They entail multidisciplinary stewardship teams, quick diagnostic tests, culture follow-up programs, local resistance profiling, and targeted education. Although there is evidence for improved prescribing by ASPs, heterogeneity in interventions and outcome measures underscores the need for standard strategies. With the deployment of tailored ASPs, EDs can restrict MDR propagation, optimize patient care, and aid global resistance control programs.

Keywords: Antimicrobial stewardship, antibiotic resistance, emergency departments, multidrug-resistant organisms, rapid diagnostics

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1. Introduction

Antibiotic resistance is a global health crisis that cannot be conquered, as it poses significant strains on health care systems by complicating treatment regimens, increasing costs, and leading to notable patient morbidity and mortality (1). The emergence of multidrug-resistant (MDR) organisms, which can resist multiple classes of antibiotics, is a troubling development in the context of treatment options, greatly impacting the delivery of care (2). This trend is primarily associated with the over-use and indiscriminate prescribing of antimicrobials, stimulating the emergence and expansion of resistant bacterial isolates, thus perpetuating the strain of health care providers mainly related to the use of indiscriminate prescribing (3). Drivers like the misuse of broad-spectrum antibiotics, poor dosing, and wasteful viral infection prescribing exacerbate the problem, resulting in the spread of resistant pathogens that are even more difficult to treat (4). The implications are significant concerning longer hospital stays, higher treatment costs, and higher death rates, and this is particularly true for sensitive populations (i.e., elderly or immunocompromised) (5).

To address the growing risk of AMR with the rise of multidrug-resistant organisms, antimicrobial stewardship programs (ASPs) have been developed to optimize antibiotic prescribing patterns and improve clinical outcomes while reducing the risk of the development of resistance (3). ASPs seek to enhance antimicrobial stewardship by optimizing the selection of the correct drug, dose, and duration of antibiotic therapy for all patients in order to reduce adverse events and minimize antibiotic resistance (6). These interventions have (largely) been implemented in inpatient settings, including ICUs, hospital wards, and outpatient clinics, and have been effective in reducing inappropriate antibiotic overuse and controlling resistant pathogens (7). Their application in the hospital ED has gone unstudied, even though the role that these departments play within the healthcare system is crucial. EDs are the single largest entry point for a disproportionate percentage of hospital admissions, and up to 80% of inpatients can pass through these units, hence positioning them as an important point of interface between community and hospital care (8). This role of authority amplifies their influence on antibiotic prescribing, as decisions in the ED often dictate what occurs for future care in inpatient or outpatient settings (9).

EDs possess extremely unique challenges that make antimicrobial stewardship more difficult. The high volume of patients, broad spectrum of infections, and great time pressures create an environment where rapid decision-making is indicated, often leading to empirical prescribing without complete diagnostic information (10). ED visits, while episodic and time-limited, also create challenges for antimicrobial stewardship. Patients are more likely to be exposed to potentially inappropriate antibiotic therapy if they receive broad-spectrum antibiotics for a presumed, but subsequently unproven, bacterial infection, and doctors have very limited access to rapid microbiology test results in EDs (4). The range of clinical (community-acquired disease versus complicated hospital-acquired disease) and microbiological contexts (risk of transmission and dissemination of MDR pathogens within healthcare facilities) (11) creates a more comprehensive challenge to antimicrobial stewardship, as difficult decisions are often required. Further complicating decision-making are community-associated outbreaks of MDR disease, including attention to extended-spectrum beta-lactamase (ESBL)-producing Enterobacterias disease, which is typically resistant to first-line antibiotics (12).

This review integrates current evidence regarding ASP deployment in EDs to counter MDR bacterial threats, evaluate current antibiotic prescribing practices, and present necessary indicators for stewardship monitoring. It examines

evidence-based approaches to the unique operational challenges of EDs, including the use of rapid diagnostic technology, multidisciplinary team efforts, and specialty-specific education programs. In addressing these topics, this review provides recommendations to healthcare systems on how to develop effective ASPs in EDs, thus decreasing the risk of antibiotic resistance, enhancing patient care, and contributing to the global efforts to tackle this vital public health issue. The subsequent role addresses the specific aspects of multidrug-resistant (MDR) infection, antibiotic prescribing patterns, markers of monitoring, and successful stewardship programs, by providing a comprehensive road map that optimizes antibiotic usage in these high-risk settings.

2. The Increasing Threat of Multidrug-Resistant Bacteria in EDs

The increased prevalence of MDR bacteria poses significant challenges in EDs, where there is rapid decision-making and empirical antibiotic treatment because of uncertainty regarding diagnosis, time constraints, and inadequate access to contemporaneous microbiological data (4). EDs are also gateway points to the hospital system for patients, with approximately 80% of inpatients being admitted through these departments, raising the risk of introducing MDR pathogens into the hospital wards (8). The brief length of ED stays and elevated patient turnover exacerbate the challenge of infection control effectively, as empirical treatment initiated in the ED is prolonged within inpatient settings, influencing overall antimicrobial consumption (9). Epidemiological studies have revealed an astonishing increase in infections with bacteria producing extended-spectrum β-lactamase (ESBL), with a 53.3% increase in ESBL community-acquired infections reported in U.S. hospitals from 2012 to 2017 (5). Similarly, the European Centre for Disease Prevention and Control (ECDC) reported increasing resistance rates among *Escherichia coli*, *Klebsiella pneumoniae*, and *Acinetobacter* spp. strains from 2017 to 2021, as well as increasing vancomycin-resistant *Enterococcus faecium* and penicillin-resistant *Streptococcus pneumoniae* (13).

MDR bacteria in the EDs are most problematic in urinary tract infections (UTIs), as UTIs are one of the most common reasons for antibiotic prescriptions. A multicenter U.S. healthcare facility study reported 17% of ESBL-producing strains were derived from UTI samples, and that resistance was 32.3% to fluoroquinolones, 13.7% to gentamicin, and 1.3% to amikacin (14,15). A study of febrile patients with UTIs reported that 12.9% of infections were caused by MDR *E. coli*, *K. pneumoniae* or *Proteus mirabilis*, that discordant empirical therapy was initiated in 63% of patients, that mean differences in length of stay adjusted for confounding factors was 29.7 hours longer, and that there was a higher odds of 90-day mortality (12% versus 8% in controls (11). The increasing incidence of community-acquired MDR infections caused by ESBL-producing Enterobacterales is complicating empiric treatment because more frequently, these organisms are resistant to first-line antibiotics (12). Equally concerning, the movement of blaCTX-M genes to highly infectious plasmids has led to an escalation of ESBLs in the community, which creates a sizable burden to EDs (16). These trends underscore the urgent necessity for targeted ASP interventions in EDs to arrest the MDR infection tide, optimize empirical treatment, and stem the spread of resistant microbes in the healthcare environment.

3. Risk Factors and Challenges in Managing MDR Infections

The risk factors for these MDR infections need to be identified, as these will inform the use of empiric antibiotics in the ED, where treatment choices must be made with correct and timely decisions. All of the studies identified recent exposure to antibiotics, short time in the hospital, long-term care facility

residency, and age ≥65 and male gender as risk factors for ESBL-producing Enterobacterales infections (12,17). Other risk factors included recent exposure to resistant fluoroquinolone or ceftriaxone, and use of antibiotics in the 90 days before presentation (18). However, a major issue is that 34% of ESBL infections occur among individuals with no prior contact with healthcare, and it is difficult to predict resistance and select the correct empirical therapy (12). This uncertainty also tends to prompt ED physicians to prescribe broad-spectrum antibiotics, which in turn triggers the emergence of resistance and increases the risk of adverse effects (18).

Operational dynamics within EDs present unique challenges in managing MDR infections. The high-pressure environment with high volumes of patients, short stays, and limited availability of real-time microbiological data is more likely to result in inappropriately empiric prescribing (10). Approximately 25–50% of ED antibiotic orders are inappropriately written, with common issues being the prescribing of broad-spectrum antibiotics for non-bacterial etiologies and failure to de-escalate therapy upon the receipt of subsequent culture data (19,20). The lack of ED-specific resistance patterns and feedback also makes stewardship harder, with clinicians having no local resistance pattern information available to help inform prescription choices (21). The transient character of ED patient visits also renders follow-up impossible, preventing the potential for modification of treatments in response to microbiological feedback (9). Innovations, such as artificial intelligence software, can predict resistance trends and guide prescribing decisions, but their use in ED operations remains limited (21). Dealing with these challenges requires new stewardship approaches that address the unique constraints of EDs and prioritize rapid diagnostics, data-guided prescribing, and robust follow-up mechanisms. Figure 1 represents the key challenges and risk factors of MDR infection in the ED.

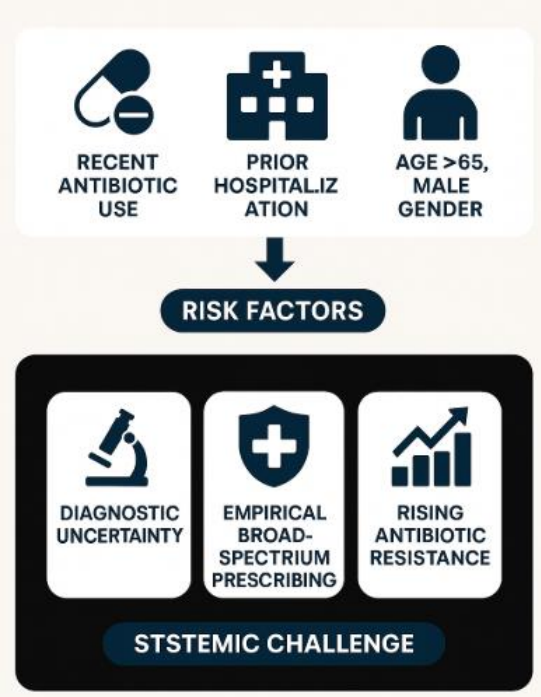

Figure. The key challenges and risk factors of MDR infection in the ED.

4. Antibiotic Prescribing Practices in Emergency Departments

EDs are central to the antimicrobial prescribing process, serving as a bridge between community and hospital care. Uncertainty related to diagnosis, pressure of time, and patient volumes make inappropriate prescribing a key reason for inappropriate antibiotic prescribing, and 25–50% of ED antibiotic prescribing is estimated as suboptimal (4,19). The most common mistakes are the use of antibiotics for viral infections, such as acute respiratory infections, the inappropriate use of broad-spectrum agents, and the lack of a change in therapy due to culture results (20). These practices not only promote resistance but also increase healthcare costs, prolong hospital stays, and result in increased risk of adverse drug events, including *Clostridioides difficile* disease (2). Inconsistency in inappropriate prescribing rates is the result of varying definitions and measurement tools used across studies, with varying rates for respiratory infections at 25% and UTIs at 50% reported (4,6).

The particular ED challenges add to the problem of inappropriate prescribing. Clinicians are often under time pressure to make rapid treatment decisions without having complete diagnostic data, leading to the use of broad-spectrum antibiotics for coverage against potential pathogens (9). As an example, in suspected sepsis, broad-spectrum agents like carbapenems are also widely utilized to cover for, but this can drive resistance if not also adjusted based on follow-up microbiological data (4). In addition, the lack of immediate feedback about prescribing patterns and geographic resistance levels prevents clinicians from making informed decisions (10). Educational courses, clinical decision support systems, and point-of-care testing devices have been proposed to combat these obstacles, but they are not utilized in EDs on a routine basis (3). Improving ED prescribing practice is a comprehensive approach that involves real-time diagnostic support, standardized protocols, and ongoing clinician education to reduce inappropriate use of antibiotics and the risk of resistance development.

5. Critical Indicators for Monitoring ASPs in EDs

Effective ASPs in EDs are premised on standardized indicators to monitor antimicrobial use, resistance, and clinical outcomes. A systematic review conducted by Losier et al. grouped ED ASP indicators into four broad categories: antimicrobial consumption, microbiological findings, process measurements, and clinical outcomes (22). However, the variation of the indicators across the studies makes program comparison and assessment difficult, given that institutions use various metrics and definitions (22). Antimicrobial prescription is traditionally measured in the form of the proportion of patients who receive antibiotics or DDD per 1,000 patients, but informatics assistance to precisely observe such data in EDs is non-existent in the majority of hospitals (10). The lack of robust data systems prevents the determination of the size of antibiotic use and the impact of stewardship interventions (9).

Certain antibiotics should be given priority for monitoring since they are among those that contribute to resistance development. Carbapenems and fluoroquinolones, which are cross-resistance causators, and aminoglycosides, which are nephrotoxic and ototoxicity causators, are some of the most significant targets for stewardship (1). The WHO's AWaRe classification, which grades antibiotics into Access, Watch, and Reserve categories based on their resistance risk, provides a practical guideline for prioritizing less resistance-prone agents in EDs (1). Syndrome-related markers, such as the proportion of pneumonia cases treated with quinolones or the proportion of skin and soft tissue infections with anti-MRSA coverage, can guide specific interventions and indicate where to target improvement (22,23). Clinical outcomes, such as reduced ED revisits, quicker hospitalization, and

reduced infection-related death, are central to the measurement of ASP effect but are challenging to quantify due to the transient nature of ED patient visitations and limited post-discharge follow-up (20). Leveraging electronic health records and standardization of indicators across institutions can enhance the capacity to evaluate the effectiveness of ASP and drive antimicrobial use improvement (24).

6. Strategies for Successful Antimicrobial Stewardship in the ED

Requesting ASPs to operate in EDs necessitates strategies intending to address the unique operational challenges of EDs, including high patient turnover, constrained time, and uncertainty of diagnostics. We introduce below primary interventions to maximize antimicrobial use.

A successful stewardship program in EDs requires an interprofessional ASP team consisting of emergency physicians, infectious disease clinicians, pharmacists, microbiologists, and nurses (3). A pharmacist is the primary steward and, as such, will play an important role in reviewing antibiotic regimens, optimizing dosing, and tracking the metrics of stewardship. There is evidence to suggest that a pharmacist can improve prescription appropriateness and clinical outcomes through interventions (25). In a study by Losier et al., ED ASPs with the participation of pharmacists reduced inappropriate antibiotic use by 20% (22). Involvement with hospital administrators, infection preventionists, and information technology personnel ensures that stewardship activities in ED operations align with real-time data capture and feedback (6). Appointment of an ED physician as the ASP leader is imperative in the coordination of activities, clinicians' participation, and mutual feedback between the stewardship staff and frontline staff (3). Nurses' participation in culture collection and patient education contributes to the effectiveness of ASPs, offering a comprehensive approach to stewardship (26).

RDTs are critical to enable the rapid identification of pathogens and resistance in EDs to allow for targeted therapy within a few hours (4). Multiplex PCR, immunoassays, mass spectrometry, and nucleic acid amplification have shown promising results in the identification of pathogens in bloodstream, respiratory, and urinary tract infections (27). A meta-analysis and systematic review by Timbrook et al. found that RDTs were associated with a decreased risk of mortality in bloodstream infections (OR, 0.64; 95% CI, 0.51–0.79) when the RDT was combined with ASP (4). The application of RDTs is, however, reliant on multidisciplinary interpretation and application in stewardship protocols since their application autonomously confers minimal gains (27). While empathics can improve quality of care, based on the principles of EBM, EDs may be an effective means of better stewardship of resources, also. Point-of-care rapid molecular diagnostic tests of respiratory infections can identify bacterial and viral pathogens and reduce the inappropriate use of antibiotics (7). Novel technologies may allow for even faster and easier detection of pathogens, such as CRISPR-based diagnostics and next-generation sequencing; however, to date, we have not fully explored the costs and clinical utility of such tools (28).

Post-discharge culture follow-up programs are a cornerstone of ED ASPs since empirical treatments can be adjusted based on microbiological results. Post-discharge culture follow-up programs have been proven to reduce ED revisits, healthcare costs, and the misuse of antibiotics for the treatment of diseases such as UTIs and bacteremia (26). Dumkow et al. documented a 30% reduction in ED returns after implementing a culture follow-up program for UTIs by pharmacist follow-up and patient education (26). Follow-up is effective only when there are strong systems in place for culture result tracking, communication with outpatient providers, and prompt adjustment of treatment (20). Challenges include a lack of adequate resources for follow-up

due to the unpredictable nature of ED patient presentation, which can complicate communication with patients' post-discharge (9). Integration of electronic health records and telehealth platforms would enhance the practicability of culture follow-up programs and provide continuity of care in addition to maximizing antimicrobial therapy (10).

Access to ED-specific resistance patterns and antimicrobial use information is necessary to guide empirical treatment and identify inappropriate prescribing habits (10). ED-specific antibiograms can guide the creation of guidelines, while consumption data highlight education intervention opportunities (20). This generation is challenging since ED data needs to be separated from hospital-wide data, duplicated and removed, and data accuracy verified (9). Talan et al. pointed out ED-specific antibiograms to be crucial in guiding empirical treatment of UTIs due to widespread ESBL-producing strains (14). Regular updating of resistance profiles and consumption rates, supported by informatics tools, can enhance the precision of prescribing decisions and enable targeted stewardship interventions (24).

Clinician and patient education are key to stimulating effective antibiotic use. While repeated educational sessions are modestly successful in the long run, extensive interventions with guidelines, audits, and clinical decision support systems have shown enhanced success (29). For instance, Buising et al. experienced a significant increase in guideline-consistent prescribing following the introduction of electronic decision support tools (OR, 1.99; 95% CI, 1.07–3.69) (29). Patient education, for instance, leaflets and social campaigns regarding the right use of antibiotics in the treatment of respiratory infections, might reduce inappropriate prescriptions as well as enhance public awareness (30-32). Education of the clinician in accurate microbiological sample collection and source control is equally relevant, with these behaviors improving diagnostic quality and patient outcomes (3). Multidimensional strategies, like regular feedback and active education, are required for sustaining behavioral change in prescribing behavior (32-35).

Biomarkers like procalcitonin (PCT) may guide antibiotic prescribing by discriminating between bacterial vs. viral infection, with a reduction of unnecessary antibiotic use. A meta-analysis by Schuetz et al. demonstrated that antibiotic exposure in EDs decreased from 8.1 to 5.7 days with PCT-guided algorithms (7). Furthermore, Mathioudakis et al. identified that antibiotic prescribing for chronic obstructive pulmonary disease exacerbations fell through PCT-guided protocols (32). However, variable results across studies reveal that biomarkers have to be used in combination with ASP guidance to exert the maximum impact because standalone usage may not lead to significant prescribing behavior change (35-39). Biomarker testing has to be deployed carefully as part of ED routines enabled by clinician education and audit-driven feedback (20).

Restriction of availability of broad-spectrum antibiotics, such as carbapenems and fluoroquinolones, in the ED can restrict unwise utilization and preserve their efficacy (40,41). Interventions like preauthorization by infectious disease specialists have been employed in some centers, but effectiveness is undermined by infrastructural challenges and inconsistent clinician uptake (10). Antibiotic cycling, which has also been proposed, has shown limited utility in preventing resistance, and its use among high-risk patients continues to be controversial (42-45). Formulary restrictions must be balanced against the need to ensure timely access to successful therapy for serious infections, such as sepsis (40-43) **(**Figure 2**).**

Figure 2. ASP intervention strategies tailored to emergency departments.

7. Results of ED-Based ASPs

There is poor evidence of ED ASP effectiveness, with single-center descriptive studies predominant and lacking the power of clinical outcome evaluation and resistance patterns (22,46-48). Respiratory infection and UTI interventions have yielded mixed outcomes. Angoulvant et al. reported improved pediatric respiratory infection prescribing trends following guideline implementation, with the elimination of 15% of inappropriate antibiotic use (36). On the other hand, Akenroye et al. did not see any reduction in the prescription of antibiotics for bronchiolitis following the introduction of the protocol, indicating the need for more intense interventions (37). Multimodal interventions that include education, audit, and decision support have been more successful with increased concordance to guidelines reported as much as 40% in UTIs (49-52). Hecker et al. studied fluoroquinolone prescribing for uncomplicated cystitis and found rates dropped by 30% following intensive educational sessions and guideline changes (38). Borde et al. also studied cephalosporin use in EDs and similarly found a significant reduction from implementing an ASP in combination with education and ID consulting (39). These studies tell us that interdisciplinary continued education is required to affect clinically meaningful change in prescribing practices and ultimately impact patient care in the ED.

8. Conclusion

Hospitals, pharmacies, and EDs potentially provide avenues for combating antimicrobial resistance by addressing prescribing in acute care and initiating antibiotic therapy. The features of EDs uniquely position them to require modified interventions for successful ASPs, including multidisciplinary teams, rapid diagnostics, subsequent culture sampling, local resistance patterns, and contextually relevant education. Although the evidence suggests that ASPs can improve prescribing practice and reduce inappropriate antibiotic use, the different interventions and outcomes show that there is a need for standardization. Developing robust, evidence-based ASPs that can integrate into ED practice will

help health systems to stop the spread of MDR bacteria, improve patient outcomes, and contribute to the global fight against antibiotic resistance.

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إدارة المضادات الحيوية في أقسام الطوارئ: استراتيجيات للحد من مقاومة المضادات الحيوية وتحسين النتائج السريرية

الملخص

تمثل مقاومة المضادات الحيوية حالة طوارئ صحية عالمية ذات تداعيات طويلة الأمد على بروتوكولات العلاج الانتقائي، وزيادة تكاليف الرعاية الصحية، وارتفاع معدلات المراضة والوفيات بين المرضى. وتشكل المعدلات المتزايدة للبكتيريا متعددة المقاومة(MDR) ، والتي تتفاقم بسبب الاستخدام غير المناسب (أو المفرط) للمضادات الحيوية، تهديداً كبيراً للسيطرة المستمرة على العدوى. تعد برامج إدارة المضادات الحيوية (ASPs) استراتيجيات حديثة تهدف إلى تحقيق توازن بين تحسين وصف المضادات الحيوية، ومنع ظهور المقاومة، وتعزيز النتائج السريرية. وعلى الرغم من تطبيق برامج إدارة المضادات الحيوية على نطاق واسع في الأقسام الداخلية والعيادات الخارجية، فإن تطبيقها في أقسام الطوارئ (EDs) لا يزال محدوداً. غالباً ما تكون أقسام الطوارئ هي نقطة البداية لعلاج العدوى بالمضادات الحيوية، حيث تواجه تحديات فريدة بسبب الطبيعة الديناميكية لتدفق المرضى. تستعرض هذه الدراسة دور أقسام الطوارئ في مواجهة ضغوط زيادة مقاومة المضادات، لا سيما مع ارتفاع معدلات العزلات المنتجة لأنزيمات بيتا-لاكتاماز واسعة الطيف(ESBL) ، فضلاً عن أنماط الوصف الحالية للمضادات الحيوية (والتي قد تكون غير مناسبة في 25-50% من الحالات). كما نستكشف أهم مقاييس برامج إدارة المضادات وتأثيرها على مراقبة استخدام المضادات والنتائج السريرية، ونقدم أمثلة على استراتيجيات قائمة على الأدلة مصممة خصيصاً لبيئة أقسام الطوارئ. تشمل هذه الاستراتيجيات فرقاً متعددة التخصصات لإدارة المضادات، واختبارات تشخيصية سريعة، وبرامج متابعة المزارع البكتيرية، وتحديد أنماط المقاومة المحلية، بالإضافة إلى التوعية المستهدفة. وعلى الرغم من وجود أدلة على تحسين وصف المضادات من خلال برامج الإدارة، فإن الاختلاف في التدخلات ومقاييس النتائج يؤكد الحاجة إلى وضع استراتيجيات موحدة. ومن خلال تطبيق برامج إدارة المضادات المصممة خصيصاً لأقسام الطوارئ، يمكن الحد من انتشار البكتيريا متعددة المقاومة، وتحسين رعاية المرضى، ودعم الجهود العالمية للسيطرة على مقاومة المضادات الحيوية.

الكلمات المفتاحية: إدارة المضادات الحيوية، مقاومة المضادات الحيوية، أقسام الطوارئ، الكائنات متعددة المقاومة، التشخيص السريع