

Review Article

Extended-Spectrum Beta-Lactamase-Producing *Escherichia coli* in Healthcare Settings: Epidemiology, Risk Factors, Infection Control Strategies and Emerging Treatment Options

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ABSTRACT

Antimicrobial resistance continues to threaten effective infection management, with extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* emerging as a major antimicrobial-resistant pathogen in healthcare settings. The global expansion of these organisms is driven by antimicrobial selection pressure, mobile resistance determinants and transmission across healthcare, community and environmental reservoirs. This narrative review aimed to synthesise current evidence on the epidemiology, risk factors, transmission pathways, infection prevention strategies, antimicrobial stewardship approaches and emerging therapeutic options associated with ESBL-producing *E. coli* in healthcare environments.

A structured narrative review was conducted using literature published between January 2016 and June 2026 identified through PubMed, ScienceDirect, Dimensions and Google Scholar, alongside relevant reports from recognised public health organisations. Studies were selected based on their relevance to ESBL-producing *E. coli* epidemiology, clinical outcomes, transmission, prevention and treatment. A total of 29 publications were included and analysed through thematic synthesis.

The review identified ESBL-producing *E. coli* as a globally distributed antimicrobial-resistant organism, with healthcare populations experiencing substantial intestinal carriage and infection burden. Previous antibiotic exposure, prolonged hospitalisation, invasive devices, diabetes, chronic wounds and frequent healthcare contact were consistently identified as important factors associated with colonisation and clinical infection. Transmission was sustained through interactions between patients, healthcare workers, medical devices and environmental reservoirs. Antimicrobial stewardship, genomic surveillance, infection prevention measures and emerging approaches, including β -lactamase inhibitors, bacteriophage therapy and microbiome-based strategies, represent important areas for future control.

Overall, reducing the burden of ESBL-producing *E. coli* requires coordinated strategies integrating surveillance, responsible antimicrobial use, infection prevention and therapeutic innovation. However, progress remains limited by heterogeneous evidence, uneven surveillance capacity and restricted access to advanced diagnostic and treatment resources, particularly in resource-limited settings.

Keywords: ESBL-Producing *Escherichia coli*; Antimicrobial Resistance; Healthcare-associated Infections; Antimicrobial Stewardship; One Health

Introduction

Antimicrobial resistance (AMR) remains one of the most significant threats to global health because it reduces the effectiveness of antimicrobial agents that underpin the management of infectious diseases. The increasing prevalence of multidrug-resistant bacterial pathogens has complicated treatment decisions, increased healthcare costs, prolonged hospitalisation and contributed to adverse clinical outcomes worldwide [1]. Among resistant Gram-negative organisms, extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* has become a major concern because of its global distribution, ability to acquire and disseminate resistance determinants, and association with difficult-to-treat healthcare-associated infections. ESBL-producing *E. coli* produces enzymes capable of hydrolysing penicillins, third-generation cephalosporins and aztreonam, thereby limiting commonly used β -lactam therapies and increasing dependence on broader-spectrum antimicrobial agents [2].

The epidemiology of ESBL-producing *E. coli* has changed substantially over recent decades. Previously considered primarily a healthcare-associated pathogen, ESBL-producing *E. coli* is now detected across hospital, community and environmental settings. This expansion reflects the combined effects of antimicrobial selection pressure, movement of resistant clones, healthcare-associated transmission and exchange of resistance genes through mobile genetic elements. Recent surveillance studies demonstrate considerable geographical variation in ESBL-producing *E. coli* carriage and infection rates, influenced by antimicrobial consumption patterns, infection prevention capacity, diagnostic resources and surveillance infrastructure [3,4]. However, interpretation of these differences requires caution because regions with limited laboratory capacity may underestimate the true burden.

The global dissemination of ESBL-producing *E. coli* is strongly associated with transferable resistance genes, particularly *bla*CTX-M, *bla*TEM and *bla*SHV families. Among these, CTX-M enzymes, especially CTX-M-15, have become dominant among clinical isolates because of their association with successful bacterial lineages and plasmid-mediated transmission. These mobile resistance determinants frequently coexist with additional mechanisms affecting fluoroquinolones, aminoglycosides and other antimicrobial classes, contributing to multidrug-resistant phenotypes and further narrowing therapeutic options [2,5].

Healthcare settings remain important environments for ESBL-producing *E. coli* acquisition

and infection because they concentrate patients with increased susceptibility, intensive antimicrobial exposure and frequent contact with healthcare systems. Colonisation, particularly intestinal carriage, often precedes clinical infection and may persist unnoticed before progressing to urinary tract infections, bloodstream infections or wound infections. Urinary tract infections represent one of the most common clinical manifestations because of the organism's adaptation to urinary tract colonisation and infection. Patients with prolonged hospitalisation, invasive devices, diabetes, chronic wounds, advanced age and immunosuppression are particularly vulnerable because these conditions increase opportunities for bacterial persistence and invasion [6].

The spread of ESBL-producing *E. coli* within healthcare environments is not determined solely by patient susceptibility but also by interactions involving healthcare workers, medical devices and environmental reservoirs. Contaminated surfaces, shared equipment and inadequate infection prevention practices may facilitate transmission between patients, making control dependent on coordinated infection prevention measures, surveillance and antimicrobial stewardship rather than treatment interventions alone [7].

Although antimicrobial stewardship has become central to reducing ESBL dissemination, treatment of serious infections remains challenging. Carbapenems continue to provide reliable activity against many ESBL-producing *E. coli* isolates, but increasing reliance on these agents creates selective pressure for carbapenem-resistant organisms. Recent therapeutic developments, including β -lactam/ β -lactamase inhibitor combinations, rapid diagnostic approaches and non-antibiotic strategies, provide potential alternatives, although limitations related to resistance emergence, accessibility and clinical evidence remain [8].

Despite substantial progress in understanding ESBL-producing *E. coli*, important gaps remain in surveillance, prevention and treatment, particularly in low- and middle-income countries where antimicrobial resistance monitoring, molecular diagnostics and infection prevention infrastructure may be limited. Evidence from sub-Saharan Africa demonstrates considerable circulation of ESBL-producing *E. coli* and highlights the need for strengthened surveillance and context-specific control strategies [9].

Previous reviews have examined specific aspects of ESBL-producing *E. coli*, including resistance mechanisms, antimicrobial treatment or epidemiological distribution. However, an integrated

healthcare-focused synthesis linking global epidemiology, patient-related risk factors, transmission dynamics, infection prevention, antimicrobial stewardship and emerging therapeutic approaches remains valuable. Therefore, this narrative review aims

Methodology

This study employed a structured narrative review approach to synthesise and critically evaluate contemporary evidence on extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* in healthcare settings. A narrative review design was selected because it allows integration of diverse evidence sources, including epidemiological studies, molecular investigations, clinical research, infection prevention literature, antimicrobial stewardship studies and therapeutic guidance, to provide a comprehensive understanding of a complex antimicrobial resistance challenge. The review focused on the epidemiology, risk factors, transmission pathways, infection prevention strategies, antimicrobial stewardship interventions and emerging treatment options associated with ESBL-producing *E. coli*.

A comprehensive literature search was conducted using PubMed/MEDLINE, ScienceDirect, Dimensions and Google Scholar. Additional relevant publications were identified through screening reference lists of selected articles and searching grey literature sources from recognised public health organisations, including the World Health Organization (WHO) and Centers for Disease Control and Prevention (CDC). The final search was conducted on 6 June 2026, and publications published between January 2016 and June 2026 were considered to capture recent developments in antimicrobial resistance epidemiology, molecular surveillance, infection control practices and therapeutic advances.

The search strategy combined controlled vocabulary and free-text terms related to four main concepts: the organism, resistance mechanism, healthcare setting and clinical implications. The main search terms included "*Escherichia coli*", "*E. coli*", "extended-spectrum beta-lactamase", "ESBL-producing Enterobacterales", "healthcare-associated infection", "hospital-acquired infection", "risk factors", "urinary tract infection", "bloodstream infection", "wound infection", "environmental contamination", "infection prevention", "antimicrobial stewardship", "beta-lactamase inhibitors" and "carbapenem alternatives". Boolean operators (AND/OR) were used to combine search concepts. The search strategy adopted was:

("Escherichia coli" OR "E. coli") AND ("extended-spectrum beta-lactamase" OR ESBL) AND ("healthcare-

to provide a comprehensive analysis of ESBL-producing *Escherichia coli* in healthcare settings, with emphasis on current challenges, evidence-based control strategies and priorities for future research.

associated infection" OR hospital OR healthcare setting) AND (epidemiology OR risk factors OR transmission OR infection control OR treatment OR antimicrobial stewardship).

Studies were considered eligible when they provided relevant evidence on ESBL-producing *E. coli* among human populations, particularly within healthcare environments. Included evidence comprised hospital-based observational studies, multicentre surveillance studies, molecular epidemiological investigations, clinical outcome studies, systematic reviews, meta-analyses and evidence-based clinical guidelines. Studies addressing colonisation, healthcare-associated urinary tract infections, bloodstream infections, wound infections, invasive device-associated infections, antimicrobial resistance mechanisms and therapeutic approaches were prioritised.

Although the primary focus of the review was healthcare-associated ESBL-producing *E. coli*, selected community and environmental studies were included where they provided relevant information on colonisation reservoirs, transmission pathways or movement of resistant organisms into healthcare settings. This approach reflects the increasing recognition that ESBL-producing *E. coli* circulates across interconnected human, animal and environmental reservoirs. Studies were excluded when they were unrelated to ESBL-producing *E. coli*, lacked clinical or epidemiological relevance, focused exclusively on unrelated non-human populations, were conference abstracts without sufficient data or were unavailable in English.

Study selection was performed in two stages. First, two authors independently screened the titles and abstracts of all identified records against the predefined eligibility criteria. Second, the full texts of potentially relevant publications were retrieved and assessed independently by the same two authors. Data extraction was then performed independently by the two authors using a standardised extraction template aligned with the objectives of the review. Disagreements at any stage of screening or extraction were first resolved through discussion between the two authors; where consensus could not be reached, a third author reviewed the publication and made the final decision. Publications were included when they contributed meaningful evidence to one or more review

domains. A total of 29 publications were included in the final narrative synthesis, and their characteristics are summarised in Table 1.

Because this study was designed as a structured narrative review rather than a systematic review, the number of records retrieved from each database, the number of duplicates removed and the number of records excluded at each screening stage were not formally logged during the search process. These figures therefore cannot be reported reliably, and a PRISMA flow diagram has not been provided; this is acknowledged as a limitation of the review (Section 8).

The reference list contains 38 sources because, in addition to the 29 included publications, nine further sources were cited to provide background information, definitions or policy and surveillance context (references 1, 5, 12, 18, 24, 31, 35, 36 and 38). These comprise four organisational reports and web resources from the WHO and CDC, and five publications addressing antimicrobial resistance in general, animal and environmental reservoirs of resistance, or genomic surveillance methods. These sources informed the framing and interpretation of the review but were not subject to data extraction and are therefore not counted among the included publications.

Information extracted from included studies included publication characteristics, geographical location, healthcare setting, study population, sample size, ESBL prevalence or carriage rates, resistance genes identified, associated risk factors, infection types, transmission mechanisms, infection prevention measures and treatment outcomes. Particular attention was given to molecular determinants including *bla*CTX-M, *bla*TEM and *bla*SHV because of their established contribution to the global dissemination of ESBL-producing *E. coli*.

The extracted evidence was analysed through thematic synthesis and organised into five major domains: global epidemiology and burden of ESBL-producing *E. coli*; patient-related and healthcare-associated risk factors; transmission dynamics and infection prevention strategies; antimicrobial stewardship and therapeutic approaches; and future research priorities. Findings were critically interpreted by comparing evidence across geographical regions and healthcare settings while considering differences in antimicrobial prescribing practices, diagnostic capacity, surveillance systems and infection prevention resources.

Table 1: Characteristics of Publications Included in the Narrative Synthesis (n = 29)

Ref.	Study (year)	Country / region	Study design	Population / setting	Key findings relevant to this review
2	Husna et al. (2023)	Global	Narrative review	ESBL enzymes in human, animal and environmental sources	Describes ESBL classes and mechanisms; CTX-M enzymes predominate, with plasmid-mediated spread and frequent co-resistance to other antimicrobial classes.
3	Ng et al. (2025)	Global (25 studies)	Systematic review and meta-analysis	13,901 community members and hospital inpatients (studies published 2021–2024)	Pooled faecal carriage of ESBL-producing <i>E. coli</i> 25.4% (community 23.4%; inpatients 27.7%), with the highest prevalence in Asian WHO regions.
4	Salman et al. (2024)	China	Narrative review	Human, animal and environmental sources	Summarises the epidemiological features and transmission dynamics of ESBL-producing <i>E. coli</i> across sectors in China.
6	Chaisaeng et al. (2024)	Northeastern Thailand	Laboratory characterisation study	Clinical Enterobacteriaceae isolates from two rural tertiary hospitals (2019–2020)	195 of 202 third-generation cephalosporin-resistant <i>E. coli</i> produced ESBL; phylogroup B2 predominated, with <i>bla</i> CTX-M (mainly CTX-M-15) in 83.6% of isolates.
7	Göpel et al. (2025)	Germany, France, Spain, Netherlands	Multicentre prospective cohort with WGS	299 residents of six long-term care facilities	Baseline ESBL-E colonisation 16.4%; associated with age ≥80 years, vascular disease, prior antibiotic use, lack of hand sanitiser and low nurse-to-resident ratio; acquisition linked to medical devices.

Ref.	Study (year)	Country / region	Study design	Population / setting	Key findings relevant to this review
8	Kayinamura et al. (2024)	Rwanda	Cross-sectional hospital study	Patients with clinical isolates at the University Teaching Hospital of Kigali	Substantial prevalence of ESBL-producing Enterobacteriaceae, including <i>E. coli</i> , with associated clinical implications in a resource-limited referral setting.
9	Olaitan et al. (2025)	Sub-Saharan Africa	Systematic review and meta-analysis (One Health)	Human, animal and environmental samples	Considerable circulation of ESBL-producing <i>E. coli</i> across One Health sectors; highlights the need for strengthened regional surveillance.
10	Bezabih et al. (2022)	Global	Systematic review and meta-analysis	Healthcare-associated and community populations	Pooled intestinal carriage 21.1% in healthcare settings vs 17.6% in community settings.
11	Al-Mustapha et al. (2025)	Global (ATLAS dataset)	Observational analysis of surveillance data	Clinical <i>E. coli</i> isolates in the ATLAS surveillance database	Describes the global distribution and incidence of multidrug-resistant and ESBL-producing <i>E. coli</i> ; identifies major surveillance gaps, notably in Africa.
13	Kazemi et al. (2025)	Guilan Province, Iran	Cross-sectional molecular study	Clinical <i>E. coli</i> isolates	Emergence of the ST131 clone carrying <i>bla</i> CTX-M genes among clinical isolates.
14	Nasher et al. (2018)	Sana'a, Yemen	Cross-sectional study	130 <i>E. coli</i> isolates from inpatients at two hospitals	33.8% of isolates were ESBL producers, documenting substantial hospital circulation in a setting with limited surveillance capacity.
15	Whelan et al. (2023)	Global	Narrative review	Uropathogenic <i>E. coli</i> (UPEC) infections	Explains the molecular basis of UPEC treatment challenges; ESBL production can lead to failure of empirical UTI therapy.
16	Agbo et al. (2025)	Enugu, Nigeria	Cross-sectional study	Patients with wound infections attending tertiary hospitals	Identifies ESBL-producing bacteria, including <i>E. coli</i> , among wound-infection isolates.
17	Ramatla et al. (2023)	Global	Systematic review and meta-analysis (One Health)	Human, animal and environmental samples	Co-existence of ESBL-producing <i>E. coli</i> and <i>K. pneumoniae</i> across sectors; supports a One Health control approach.
19	Larramendy et al. (2020)	Multinational	Systematic review	16 observational studies; 12,138 patients with community-acquired UTI	Previous antibiotic exposure was the most frequently reported risk factor; prior hospitalisation and recurrent UTI were also identified.
20	Goyal et al. (2019)	USA	Retrospective study	Patients with symptomatic community-acquired UTI	Recent antibiotic exposure and urinary catheterisation were associated with ESBL-producing Enterobacteriaceae UTI.

Ref.	Study (year)	Country / region	Study design	Population / setting	Key findings relevant to this review
21	Asmarawati et al. (2025)	Surabaya , Indonesia	Hospital-based observational study	224 hospitalised patients with <i>E. coli</i> bacteraemia (2022–2024)	Urinary source, prior antibiotic use and central venous catheter insertion independently predicted ESBL bacteraemia; ESBL infection associated with greater illness severity.
22	Vance et al. (2023)	USA	Retrospective matched observational study	150 adults with <i>E. coli</i> , <i>Klebsiella</i> spp. or <i>P. mirabilis</i> bacteraemia	Receipt of more than one antibiotic in the preceding 90 days was the only independent risk factor for ESBL bloodstream infection.
23	Gómez-Zorrilla et al. (2026)	Spain	Retrospective cohort study	Patients with bacteraemic <i>E. coli</i> UTI	ESBL production associated with prolonged hospitalisation, greater healthcare resource use and identifiable stewardship opportunities.
25	Tschudin-Sutter et al. (2017)	Europe	Point/counterpoint review	Hospitalised patients	Effectiveness of contact precautions is context-dependent; ESBL-producing <i>E. coli</i> contributes to transmission mainly through its high prevalence.
26	Singh et al. (2025)	India	Observational environmental sampling study	Surfaces and equipment in a tertiary care hospital	Hospital environment harboured antimicrobial-resistant Gram-negative bacteria, supporting environmental monitoring and cleaning.
27	Puspandari et al. (2025)	Jakarta, Indonesia	Genomic (WGS) study (preprint)	ESBL-producing <i>E. coli</i> from human, animal and environmental sources	Genomic evidence of likely transmission within and between One Health sectors.
28	Miftode et al. (2024)	Iași, Romania	Retrospective study	724 ESBL-E urine isolates (2016–2019), catheterised vs non-catheterised patients	Catheterisation associated with extensive drug resistance and lower susceptibility, including to carbapenems (59.6% vs 83.4%).
29	Beaumont et al. (2026)	Global	Narrative review	Community carriage and dissemination	Spread reflects antimicrobial exposure, bacterial evolution, healthcare practices and transmission across human, animal and environmental systems.
30	Baur et al. (2017)	Multinational	Systematic review and meta-analysis	Hospital inpatients	Antimicrobial stewardship reduced the incidence of infection and colonisation with antibiotic-resistant bacteria, including ESBL-producing Gram-negative bacteria.
32	Harris et al. (2018)	Nine countries (26 hospitals)	Open-label non-inferiority RCT (MERINO)	379 adults with ceftriaxone-resistant <i>E. coli</i> or <i>K. pneumoniae</i> bacteraemia	30-day mortality 12.3% with piperacillin–tazobactam vs 3.7% with meropenem; non-inferiority not demonstrated.
33	Tamma et al. (2024)	USA (IDSA)	Clinical practice guidance	Antimicrobial-resistant Gram-negative infections	Carbapenems preferred for ESBL-E infections outside the urinary tract; nitrofurantoin and TMP-SMX preferred for uncomplicated cystitis.

Ref.	Study (year)	Country / region	Study design	Population / setting	Key findings relevant to this review
34	Kortright et al. (2019)	Global	Narrative review	Phage therapy for antibiotic-resistant bacteria	Phage therapy offers pathogen specificity but faces regulatory, evidence-base and phage-resistance barriers.
37	Dyar et al. (2017)	Global	Narrative (conceptual) review	Antimicrobial stewardship programmes	Defines antimicrobial stewardship and emphasises multidisciplinary collaboration for responsible antimicrobial use.

Abbreviations: ESBL, extended-spectrum β -lactamase; ESBL-E, ESBL-producing *Enterobacterales*; IDSA, Infectious Diseases Society of America; RCT, randomised controlled trial; ST, sequence type; TMP-SMX, trimethoprim–sulfamethoxazole; UTI, urinary tract infection; WGS, whole-genome sequencing. The nine additional cited sources (references 1, 5, 12, 18, 24, 31, 35, 36 and 38) provided background context and were not subject to data extraction.

Epidemiology and Global Burden of ESBL-Producing *Escherichia coli* in Healthcare Settings

The epidemiology of extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* has changed considerably over the past decade, with these organisms expanding from predominantly healthcare-associated pathogens to globally distributed antimicrobial-resistant organisms found across healthcare, community and environmental reservoirs. This expansion is driven by antimicrobial selection pressure, movement of successful bacterial clones, healthcare-associated transmission and the acquisition of resistance determinants through mobile genetic elements. Consequently, ESBL-producing *E. coli* has become one of the most clinically significant antimicrobial-resistant *Enterobacterales* associated with healthcare burden, particularly among patients requiring prolonged medical care [10].

A major component of the global burden of ESBL-producing *E. coli* is intestinal colonisation, which serves as an important reservoir for subsequent infection and transmission. In a systematic review and meta-analysis, Bezabih et al. (2022) [10] reported a pooled intestinal carriage prevalence of 21.1% among healthcare-associated populations compared with 17.6% among community populations. These findings demonstrate that healthcare exposure increases the likelihood of ESBL carriage; however, colonisation should be distinguished from clinical infection because many individuals carrying ESBL-producing organisms remain asymptomatic while retaining the potential to transmit resistant strains or develop infection under favourable conditions.

The distribution of ESBL-producing *E. coli* varies considerably across geographical regions due to differences in antimicrobial consumption, infection prevention capacity, laboratory infrastructure and surveillance systems. Higher reported prevalence has been observed in regions where antibiotic regulation, diagnostic capacity and infection control resources are limited. However, comparisons between regions

require caution because variations in surveillance intensity and laboratory detection methods may influence reported estimates. In Africa, Al-Mustapha et al. (2025) [11] highlighted substantial circulation of ESBL-producing *E. coli* but also identified major surveillance gaps that limit accurate estimation of regional disease burden.

The global dissemination of ESBL-producing *E. coli* is strongly linked to the spread of transferable resistance genes, particularly *bla*CTX-M, *bla*TEM and *bla*SHV families. CTX-M enzymes, especially CTX-M-15, have become dominant globally because of their association with mobile genetic elements and successful bacterial lineages. These genetic elements frequently carry additional resistance determinants, contributing to multidrug-resistant profiles involving fluoroquinolones, aminoglycosides and other antimicrobial classes [2,5,12].

The emergence of high-risk clones has further accelerated global spread. Sequence type 131 (ST131) represents one of the most successful ESBL-producing *E. coli* lineages due to its association with urinary tract infections, bloodstream infections, CTX-M enzymes and persistence across healthcare and community environments. The ability of such clones to combine antimicrobial resistance with pathogenic characteristics has contributed significantly to the continued clinical impact of ESBL-producing *E. coli* [13].

Healthcare facilities remain important settings for ESBL acquisition and infection because they concentrate vulnerable patients, antimicrobial exposure and opportunities for transmission. Intensive care units, surgical wards and long-term care facilities are particularly affected because patients frequently experience prolonged admission, invasive procedures and device exposure [14]. Among clinical infections, urinary tract infections represent the most common manifestation of ESBL-producing *E. coli*, reflecting the organism's dominance among uropathogenic *E. coli*

and its ability to maintain urinary tract colonisation and infection potential despite acquisition of resistance traits. Whelan et al. (2023) [15] noted that ESBL-associated urinary infections create significant therapeutic challenges because empirical treatment may fail before resistance is recognised.

Beyond urinary infections, ESBL-producing *E. coli* contributes to bloodstream infections, postoperative infections and chronic wound infections, particularly among patients with diabetes, vascular disease and prolonged healthcare exposure. These infections are associated with delayed recovery, increased healthcare utilisation and greater antimicrobial requirements, demonstrating that ESBL production has important clinical consequences beyond laboratory resistance detection [16].

The epidemiology of ESBL-producing *E. coli* is further complicated by environmental and intersectoral transmission pathways. Resistant strains have been identified in healthcare environments, wastewater and

other ecological reservoirs, supporting the movement of resistance determinants between human, animal and environmental compartments. Ramatla et al. (2023) [17] emphasised that effective control requires a One Health approach integrating antimicrobial stewardship, environmental management, surveillance and infection prevention measures.

Overall, current evidence demonstrates that ESBL-producing *E. coli* represents a globally established antimicrobial resistance challenge sustained by genetic adaptability, healthcare-associated selection pressure and interconnected transmission networks. However, major knowledge gaps remain, particularly in low-resource settings where limited surveillance and molecular diagnostic capacity may underestimate the true burden. Strengthening genomic surveillance, improving infection prevention infrastructure and integrating healthcare-based interventions with broader One Health strategies remain essential priorities for reducing future impact.

Risk Factors and Clinical Significance of ESBL-Producing *Escherichia coli* Among Hospitalized Patients

The acquisition and clinical impact of ESBL-producing *Escherichia coli* among hospitalised patients result from interactions between bacterial characteristics, antimicrobial exposure, healthcare practices and host vulnerability. Although ESBL-producing *E. coli* may colonise individuals without causing immediate disease, hospitalised patients have increased risk of progression from colonisation to infection because of repeated antibiotic exposure, prolonged healthcare contact, invasive procedures and impaired host defence mechanisms.

The gastrointestinal tract represents the major reservoir of ESBL-producing *E. coli*, where resistant strains may persist before causing infection or facilitating transmission. The Centers for Disease Control and Prevention (CDC) (2025) [18] recognises that ESBL-producing Enterobacterales commonly colonise the gastrointestinal tract and may subsequently cause urinary tract infections, bloodstream infections, wound infections and other invasive diseases. Therefore, factors associated with increased carriage also represent important indicators of future infection risk.

Antibiotic Exposure and Selection Pressure

Previous antibiotic exposure remains one of the most consistently reported risk factors for ESBL-producing *E. coli* acquisition and infection. Antimicrobial use disrupts normal intestinal microbial communities, reducing competition and creating ecological conditions that favour expansion of resistant organisms. This effect is particularly relevant among

hospitalised patients who frequently receive broad-spectrum antibiotics for empirical treatment, surgical prophylaxis or recurrent infections.

Larramendy et al. (2020) [19], in a systematic review of ESBL-producing *E. coli* urinary tract infections, identified previous antibiotic exposure as the most frequently reported risk factor across 16 observational studies involving 12,138 patients. Similarly, Goyal et al. (2019) [20] found that recent antibiotic exposure was independently associated with community-acquired ESBL-producing Enterobacterales urinary tract infections. Together, these findings demonstrate that antimicrobial selection pressure contributes to ESBL emergence across both healthcare and community settings.

The association between antibiotic exposure and ESBL-producing *E. coli* is particularly important because repeated use of fluoroquinolones, third-generation cephalosporins and other broad-spectrum agents may promote persistent intestinal carriage. Consequently, antimicrobial stewardship remains essential for reducing unnecessary selection pressure and limiting subsequent resistant infections.

Prolonged Hospitalisation and Healthcare-Associated Exposure

Prolonged hospitalisation increases opportunities for acquisition of ESBL-producing *E. coli* through repeated exposure to antimicrobial therapy, healthcare workers, contaminated environments and invasive procedures. Patients in intensive care units, surgical wards and long-term care facilities are

particularly vulnerable because they often experience prolonged admissions, multiple interventions and greater dependence on medical devices.

Healthcare exposure also contributes to interfacility spread. Patients transferred between hospitals, rehabilitation centres and long-term care facilities may carry resistant organisms into new healthcare environments, reinforcing the need for coordinated surveillance and infection prevention strategies across healthcare networks.

Invasive Devices and Biofilm-Associated Infection

Invasive medical devices represent important risk factors because they bypass natural protective barriers and provide surfaces for bacterial attachment. Urinary catheterisation is particularly associated with ESBL-producing *E. coli* because catheter surfaces support biofilm formation, allowing bacteria to persist despite antimicrobial treatment and host immune responses.

Goyal et al. (2019) [20] identified urinary catheterisation as an important risk factor for ESBL-producing Enterobacterales urinary infections, particularly among patients with recurrent infections and previous antibiotic exposure. Similarly, Asmarawati et al. (2025) [21] reported that urinary tract infection, previous antimicrobial exposure and central venous catheter insertion were associated with ESBL-producing *E. coli* bloodstream infections among hospitalised patients.

These findings highlight the importance of device stewardship, including appropriate catheter use, infection prevention during insertion and early removal when devices are no longer required.

Diabetes and Chronic Disease Conditions

Underlying chronic diseases increase susceptibility to ESBL-producing *E. coli* infection by reducing host defence mechanisms and increasing healthcare exposure. Diabetes mellitus is particularly important because chronic hyperglycaemia impairs immune function, delays tissue repair and increases vulnerability to urinary and wound infections.

Patients with diabetes also frequently require repeated antimicrobial therapy and healthcare interventions, increasing opportunities for ESBL colonisation and infection. Other conditions, including chronic kidney disease, malignancy, neurological disorders and immunosuppression, similarly increase risk because they are associated with prolonged healthcare contact and invasive procedures. Vance et al. (2023) [22] found that, after multivariable adjustment, receipt of more than one antibiotic in the preceding 90 days was the only independent risk factor for bloodstream infection caused by ESBL-producing *E.*

coli, *Klebsiella* spp. or *Proteus mirabilis*, suggesting that the contribution of chronic disease may operate largely through greater antimicrobial and healthcare exposure.

Clinical Significance: Urinary Tract and Wound Infections

Urinary tract infections represent the most common clinical manifestation of ESBL-producing *E. coli*. This association reflects the predominance of *E. coli* among uropathogenic organisms and the ability of resistant strains to maintain characteristics required for urinary tract colonisation and invasion. However, ESBL-associated urinary infections present therapeutic challenges because commonly used empirical antibiotics may be ineffective before resistance is identified.

Larramendy et al. (2020) [19] identified previous antibiotic exposure, hospitalisation and recurrent urinary tract infections as important risk factors for ESBL-producing *E. coli* urinary infections. Furthermore, Gómez-Zorrilla et al. (2026) [23] reported that ESBL-producing *E. coli* bloodstream infections originating from urinary sources were associated with increased healthcare resource utilisation and prolonged hospitalisation.

Chronic wounds, particularly diabetic foot ulcers and pressure injuries, also provide favourable conditions for persistence of resistant organisms because of delayed healing, repeated antimicrobial exposure and prolonged healthcare contact. Although *E. coli* is not the dominant pathogen in all wound infections, its presence in chronic wounds is clinically relevant because resistant Gram-negative organisms may complicate treatment and contribute to prolonged infection.

Clinical Implications of Identified Risk Factors

Recognition of ESBL-producing *E. coli* risk factors is important for improving empirical treatment decisions and infection prevention planning. Patients with recent antibiotic exposure, prolonged hospitalisation, invasive devices, diabetes, recurrent urinary infections or chronic wounds represent populations where early consideration of ESBL risk may improve antimicrobial decision-making.

Overall, the available evidence indicates that ESBL-producing *E. coli* infections arise from the interaction between bacterial resistance mechanisms and healthcare-related pressures. Therefore, effective control requires simultaneous attention to antimicrobial stewardship, device management, chronic disease care, infection prevention practices and surveillance systems.

Healthcare Transmission Dynamics, Environmental Contamination and Infection Prevention Strategies

The dissemination of ESBL-producing *Escherichia coli* within healthcare settings results from interactions between colonised patients, antimicrobial pressure, healthcare practices and environmental reservoirs. Although resistance develops through acquisition of genetic determinants, sustained spread depends on opportunities for transmission within healthcare systems. Hospitals and long-term care facilities are particularly vulnerable because they contain patients with increased susceptibility to infection, frequent antimicrobial exposure and repeated contact with healthcare personnel and medical devices.

Transmission occurs through direct and indirect pathways. Direct transmission commonly

involves transfer through contaminated hands of healthcare workers, while indirect transmission occurs through contaminated equipment, medical devices and environmental surfaces. Importantly, transmission is not restricted to patients with active infection. Colonised individuals may serve as silent reservoirs, allowing ESBL-producing *E. coli* to circulate before clinical infection develops. The interaction between colonisation, environmental contamination and infection progression is illustrated in Figure 1, which demonstrates that interruption of multiple transmission points is required for effective control.

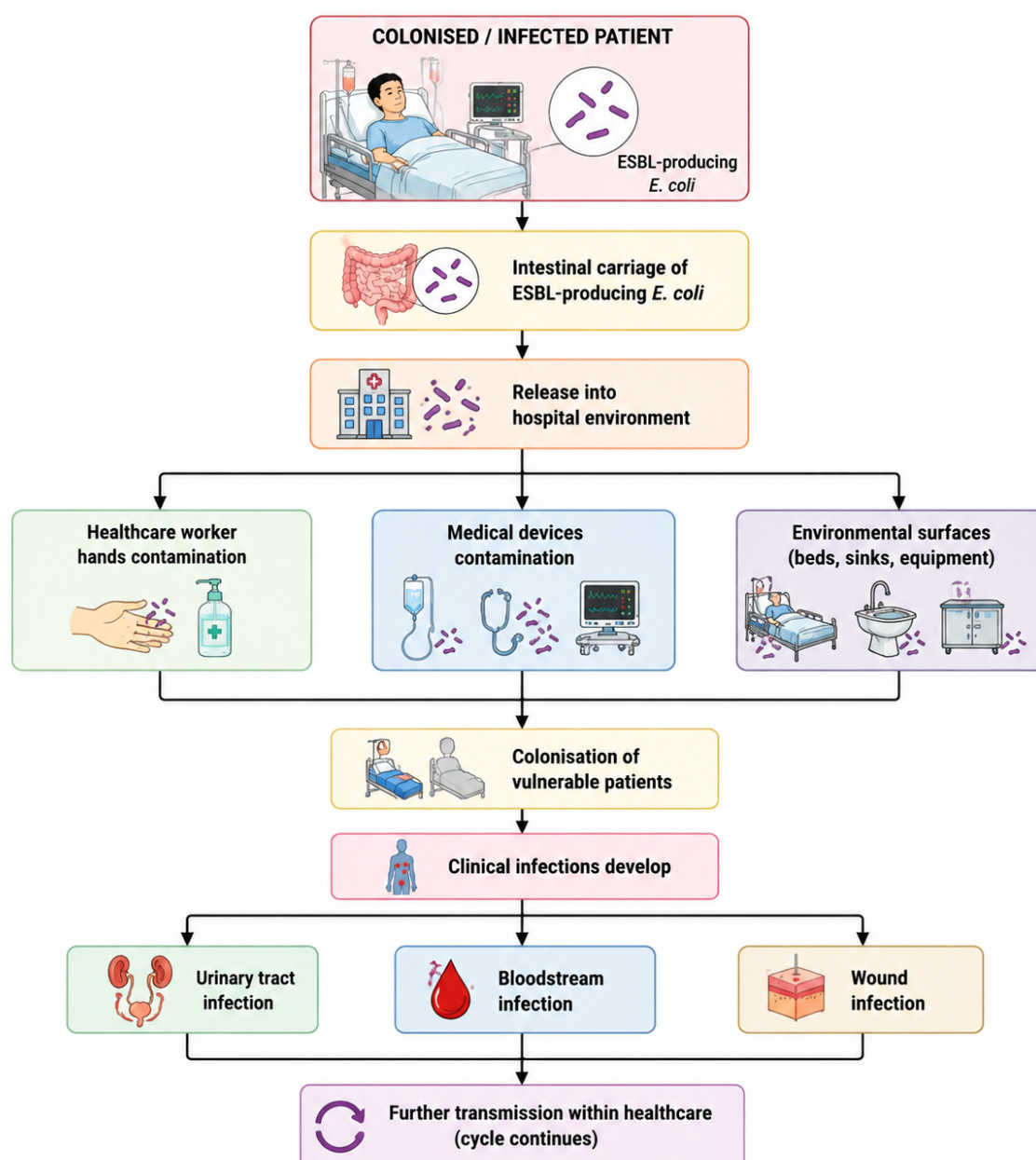


Figure 1: Transmission Cycle of ESBL-Producing *Escherichia coli* in Healthcare Settings

Figure 1 demonstrates that ESBL-producing *E. coli* transmission represents a continuous cycle involving intestinal carriage, contamination of healthcare environments, transfer through healthcare-associated pathways and development of clinical infection. Therefore, prevention strategies must target reservoirs, transmission routes and conditions that facilitate progression from colonisation to disease.

Healthcare Worker-Mediated Transmission

Healthcare workers represent a major pathway for movement of ESBL-producing organisms between patients. During routine care activities, resistant organisms may contaminate hands, gloves, clothing or shared equipment and subsequently transfer to other patients when infection prevention practices are inadequate.

Hand hygiene remains one of the most effective measures for reducing healthcare-associated transmission. The World Health Organization (WHO) (2017) [24] identifies hand hygiene as a fundamental component of infection prevention because healthcare worker hands can act as a bridge between colonised patients, infected patients and environmental surfaces. However, maintaining consistent compliance remains challenging, particularly in settings affected by high workload, limited staffing and inadequate infection prevention resources.

Tschudin-Sutter et al. (2017) [25] highlighted that ESBL-producing *E. coli* contributes substantially to healthcare transmission because of its high prevalence among patient populations, even when individual transmission efficiency may vary. This finding emphasises that infection control strategies must consider both transmissibility and prevalence when prioritising interventions.

Environmental Contamination and Healthcare Reservoirs

Environmental contamination contributes to ESBL persistence by providing additional reservoirs outside the patient. Frequently touched surfaces, medical equipment, sinks and patient-care areas may harbour resistant organisms and facilitate indirect transmission, particularly when cleaning practices are inconsistent.

Singh et al. (2025) [26] demonstrated that healthcare environments can contain antimicrobial-resistant Gram-negative bacteria capable of contributing to transmission networks, supporting the importance of environmental monitoring and effective cleaning programmes. Similarly, Puspadari et al. (2025) [27] used genomic analysis to demonstrate connections between ESBL-producing *E. coli* from human, animal and environmental sources, reinforcing the importance of integrated surveillance approaches.

These findings support a One Health perspective in which healthcare transmission is considered alongside broader environmental and community pathways. However, the relative contribution of environmental reservoirs to individual patient infections remains difficult to quantify and requires further genomic and epidemiological investigation.

Medical Devices and Transmission Risk

Medical devices provide important opportunities for ESBL-producing *E. coli* infection because they bypass natural protective barriers and support bacterial persistence. Urinary catheters are particularly relevant because they facilitate bacterial attachment and biofilm formation, allowing organisms to survive despite antimicrobial therapy.

Miftode et al. (2024) [28] highlighted that catheter-associated biofilms contribute to treatment difficulty and recurrent infection among patients with ESBL-producing Enterobacterales. Therefore, device stewardship remains an essential prevention strategy, requiring appropriate device indication, aseptic insertion practices, proper maintenance and early removal when clinical need has been resolved.

Infection Prevention and Control Strategies

Because ESBL-producing *E. coli* transmission involves multiple interconnected pathways, effective prevention requires a multimodal infection prevention and control approach. Single interventions are unlikely to achieve sustained reduction because transmission may continue through asymptomatic carriers, healthcare workers, devices and environmental reservoirs.

Core prevention measures include hand hygiene, contact precautions, environmental cleaning, surveillance and antimicrobial stewardship. Contact precautions involving gloves, gowns and dedicated equipment may reduce spread among colonised or infected patients. However, Tschudin-Sutter et al. (2017) [25] noted that the effectiveness of contact precautions depends on healthcare context and should be implemented alongside broader infection prevention measures.

Environmental cleaning programmes should include appropriate disinfectant use, regular auditing and staff training, particularly in high-risk areas such as intensive care units. Surveillance strategies may also support targeted interventions by identifying colonised patients who represent potential reservoirs. However, universal screening remains debated because of resource requirements, making targeted screening based on local epidemiology and patient risk factors a practical approach in many settings. Table 2 summarises the major interventions required to

interrupt ESBL-producing *E. coli* transmission pathways.

Table 2: Infection Prevention Strategies for Controlling ESBL-Producing *E. coli* Transmission

Intervention	Target pathway	Mechanism	Expected impact
Hand hygiene programmes	Healthcare worker-mediated spread	Reduces transfer of organisms between patients and surfaces	Decreases cross-transmission
Contact precautions	Direct patient contact	Limits movement of resistant organisms	Reduces healthcare-associated spread
Environmental cleaning	Surface and equipment contamination	Removes environmental reservoirs	Reduces indirect transmission
Device stewardship	Catheter-associated transmission	Minimises biofilm formation and bacterial entry	Reduces device-related infections
Surveillance screening	Undetected colonisation	Identifies high-risk carriers	Enables targeted prevention
Antimicrobial stewardship	Antibiotic-driven selection pressure	Reduces unnecessary resistance selection	Limits emergence of resistant strains

Challenges in Controlling Healthcare Transmission

Despite advances in infection prevention, controlling ESBL-producing *E. coli* transmission remains challenging because healthcare systems differ substantially in laboratory capacity, surveillance infrastructure and infection prevention resources. These limitations are particularly important in low- and middle-income countries, where inadequate diagnostic capacity, limited isolation facilities and unrestricted antibiotic availability may accelerate resistance dissemination.

Beaumont et al. (2026) [29] emphasised that ESBL-producing *E. coli* spread reflects interactions

between antimicrobial exposure, bacterial evolution, healthcare practices and transmission across human, animal and environmental systems. Therefore, sustainable control requires strategies adapted to local healthcare realities while incorporating antimicrobial stewardship, genomic surveillance, environmental management and One Health collaboration.

Overall, ESBL-producing *E. coli* transmission is maintained through a network of interconnected reservoirs and pathways. Effective prevention depends on coordinated interventions that reduce bacterial selection, interrupt transmission opportunities and strengthen healthcare systems' ability to detect and respond to resistant organisms.

Antimicrobial Stewardship and Emerging Therapeutic Approaches for ESBL-Producing *Escherichia coli*

The increasing prevalence of ESBL-producing *Escherichia coli* has complicated antimicrobial management because these organisms frequently exhibit resistance to multiple antimicrobial classes. Although carbapenems remain effective against most ESBL-producing strains, extensive reliance on these agents creates selective pressure for carbapenem-resistant Enterobacterales. Therefore, management requires a balance between providing effective treatment for infected patients and preserving antimicrobial effectiveness for future use.

Therapeutic decisions should be guided by infection severity, anatomical site, antimicrobial susceptibility results and patient-specific factors. The treatment approach differs substantially between uncomplicated urinary tract infections, complicated urinary infections, bloodstream infections and other

invasive diseases. Consequently, antimicrobial stewardship and development of alternative therapeutic strategies represent complementary approaches for reducing the clinical impact of ESBL-producing *E. coli*.

Antimicrobial Stewardship and Optimisation of Therapy

Antimicrobial stewardship is central to controlling ESBL-producing *E. coli* because antibiotic exposure remains one of the strongest drivers of resistance selection. Broad-spectrum antibiotics, particularly third-generation cephalosporins and fluoroquinolones, can disrupt intestinal microbial communities and favour persistence of resistant organisms.

Baur et al. (2017) [30], in a systematic review and meta-analysis, demonstrated that antimicrobial

stewardship interventions reduced antibiotic consumption and were associated with reductions in antimicrobial-resistant bacteria among hospitalised patients. These findings support stewardship approaches that combine evidence-based prescribing guidelines, prospective audit and feedback, antimicrobial de-escalation, rapid diagnostic support and clinician education.

Effective stewardship does not represent antibiotic restriction alone but involves ensuring that patients receive appropriate therapy at the correct dose, duration and timing. The World Health Organization (WHO) identifies antimicrobial stewardship as a core component of global antimicrobial resistance control because inappropriate antimicrobial use accelerates resistance development and threatens future treatment options [31].

Current Treatment Approaches According to Infection Type

For severe infections caused by ESBL-producing *E. coli*, particularly bloodstream infections and infections outside the urinary tract, carbapenems remain the preferred therapeutic option. Harris et al. (2018) [32], through the MERINO randomised clinical trial, demonstrated that piperacillin-tazobactam was associated with higher mortality compared with meropenem among patients with ceftriaxone-resistant *E. coli* and *Klebsiella pneumoniae* bloodstream infections. These findings support continued use of carbapenems as reliable therapy for serious ESBL-associated infections.

The Infectious Diseases Society of America (IDSA) 2024 guidance recommends carbapenems for severe ESBL-producing Enterobacterales infections while emphasising that treatment decisions should consider infection site, susceptibility results and clinical response [33]. However, preserving carbapenems remains essential because unnecessary exposure may accelerate the emergence of carbapenem-resistant organisms.

For uncomplicated cystitis caused by susceptible ESBL-producing *E. coli*, oral treatment options remain available. The IDSA guidance recommends nitrofurantoin and trimethoprim-sulfamethoxazole as preferred options when susceptibility is confirmed [33]. Fosfomycin may also be considered for uncomplicated urinary infections caused by susceptible *E. coli*, although its clinical role is limited by poor suitability for systemic infections.

Management of complicated urinary tract infections and pyelonephritis requires greater consideration because adequate tissue penetration and sustained antimicrobial activity are necessary. Oral agents should only be used when susceptibility and

clinical circumstances support their effectiveness. Patients with bloodstream infection, sepsis or other invasive infections generally require agents with reliable systemic activity, with carbapenems remaining the reference treatment for most severe ESBL-associated disease [33].

β -Lactam/Beta-Lactamase Inhibitor Combinations and Carbapenem-Sparing Strategies

Newer β -lactam/ β -lactamase inhibitor combinations have expanded therapeutic options for resistant Gram-negative infections by restoring β -lactam activity through inhibition of bacterial β -lactamases. However, their role in ESBL-producing *E. coli* infections requires careful interpretation because many of these agents were developed primarily for carbapenem-resistant organisms.

Agents such as ceftazidime-avibactam and meropenem-vaborbactam have important roles against selected resistant Gram-negative infections, particularly carbapenemase-producing Enterobacterales. However, current evidence does not support replacing carbapenems routinely for all ESBL-producing *E. coli* infections. The IDSA guidance recommends that these agents should be selected according to resistance mechanism, susceptibility profile and clinical context rather than used broadly as carbapenem alternatives [33].

Therefore, carbapenem-sparing strategies should focus on accurate diagnosis, susceptibility-guided therapy and stewardship principles rather than simply substituting newer agents.

Emerging Non-Antibiotic and Precision Therapeutic Approaches

The limitations of conventional antimicrobial therapy have encouraged investigation of alternative strategies targeting bacterial survival, colonisation and transmission. Bacteriophage therapy has received increasing attention because bacteriophages can selectively infect bacterial pathogens while potentially reducing disruption of normal microbiota.

Kortright et al. (2019) [34] reviewed the potential role of phage therapy against antimicrobial-resistant bacteria and highlighted advantages including pathogen specificity and adaptability. However, important challenges remain, including regulatory requirements, limited clinical trial evidence, difficulties in standardisation and the potential development of phage resistance.

Microbiome-based approaches are also being explored because intestinal colonisation frequently precedes ESBL-producing *E. coli* infection. Strategies such as microbiome restoration, probiotics and faecal microbiota transplantation may provide future opportunities for preventing resistant organism

expansion, although current evidence remains insufficient for routine clinical implementation.

Rapid molecular diagnostics represent another important advancement because early identification of ESBL-associated resistance mechanisms may allow

faster optimisation of antimicrobial therapy. Integrating molecular diagnostics with stewardship programmes may reduce inappropriate broad-spectrum antibiotic use and improve treatment precision.

Table 3. Current and Emerging Therapeutic Options for ESBL-Producing *E. coli*

Treatment option	Main clinical role	Advantages	Limitations
Carbapenems	Severe infections, bloodstream infections and invasive disease	Strong clinical evidence and reliable activity	Selection pressure for carbapenem resistance
Nitrofurantoin	Uncomplicated cystitis	Effective oral option for susceptible isolates	Not suitable for systemic infection
Trimethoprim-sulfamethoxazole	Susceptible urinary infections	Oral treatment option	Resistance limits use
Fosfomycin	Selected uncomplicated urinary infections	Maintains activity against some resistant isolates	Limited systemic application
β -lactam/ β -lactamase inhibitors	Selected resistant Gram-negative infections	Target resistance mechanisms	Many established roles are for CRE rather than ESBL
Bacteriophages	Experimental resistant infections	High bacterial specificity	Limited clinical evidence

Table 3 summarises current and emerging treatment approaches and highlights the need to balance effective therapy for ESBL-producing *E. coli* infections with preservation of future antimicrobial options.

Overall, management of ESBL-producing *E. coli* requires an integrated therapeutic approach combining

antimicrobial stewardship, susceptibility-guided treatment, appropriate use of existing agents and continued investigation of innovative strategies. While newer therapies provide important opportunities, strengthening stewardship and diagnostic capacity remains essential for sustaining long-term control of ESBL-associated infections.

Future Perspectives, Research Gaps and Global Response Priorities in Controlling ESBL-Producing *Escherichia coli*

The continued global spread of ESBL-producing *Escherichia coli* demonstrates that antimicrobial resistance remains an evolving challenge influenced by bacterial adaptation, antimicrobial consumption, healthcare practices and ecological connectivity. Although substantial progress has been made in understanding ESBL epidemiology, transmission and treatment, important gaps remain in surveillance capacity, infection prevention implementation, therapeutic innovation and global coordination. Future control strategies must therefore move beyond isolated hospital-based interventions and integrate microbiological, clinical, environmental and policy approaches.

Strengthening Surveillance and Genomic Monitoring

Accurate surveillance remains fundamental for understanding ESBL-producing *E. coli* distribution, identifying emerging resistance patterns and guiding

public health responses. However, surveillance capacity remains uneven, particularly in low- and middle-income countries where limited laboratory infrastructure, inadequate molecular testing and inconsistent reporting systems may underestimate the true burden.

The World Health Organization (WHO), through the Global Antimicrobial Resistance and Use Surveillance System (GLASS), has promoted standardised approaches for monitoring antimicrobial resistance trends and antimicrobial consumption. However, implementation continues to face challenges related to laboratory capacity, funding and data integration [35].

Traditional antimicrobial susceptibility testing provides essential clinical information but offers limited insight into transmission pathways and resistance evolution. Whole-genome sequencing (WGS) provides additional resolution by identifying resistance

genes, tracking high-risk clones and linking isolates across transmission networks. Rogers et al. (2021) [36] highlighted that genomic approaches can strengthen antimicrobial resistance surveillance by providing information beyond conventional laboratory methods, particularly for outbreak investigation and monitoring of resistant lineages.

For ESBL-producing *E. coli*, genomic surveillance is particularly relevant because successful clones such as ST131 and mobile resistance elements contribute significantly to global dissemination. Expanding access to genomic technologies, particularly in resource-limited settings, will therefore be important for developing targeted interventions.

Improving Infection Prevention Through Context-Specific Strategies

Future infection prevention strategies should recognise that ESBL-producing *E. coli* transmission occurs through multiple interconnected pathways involving patients, healthcare workers, devices and environmental reservoirs. Therefore, interventions should be adapted according to local epidemiology, healthcare infrastructure and available resources.

Important priorities include improving identification of high-risk colonised patients, strengthening environmental hygiene, promoting device stewardship and ensuring consistent implementation of standard infection prevention measures. However, the value of universal screening remains uncertain because resource requirements may limit feasibility in many healthcare settings. Future research should therefore determine which patient populations and healthcare environments benefit most from targeted screening approaches.

Environmental transmission also requires further investigation. Although resistant organisms have been detected in healthcare environments and other ecological reservoirs, the contribution of specific environmental sources to individual patient infections remains incompletely understood. Combining environmental sampling with genomic epidemiology may provide clearer evidence regarding when environmental interventions produce meaningful reductions in transmission.

Optimising Antimicrobial Stewardship and Therapeutic Innovation

Antimicrobial stewardship remains a central component of ESBL control, but future programmes must become more integrated with diagnostic technologies and local resistance surveillance. Effective stewardship requires more than reducing antibiotic use; it requires timely identification of resistant infections, optimisation of therapy and avoidance of unnecessary broad-spectrum exposure.

Dyar et al. (2017) [37] emphasised that successful antimicrobial stewardship depends on multidisciplinary collaboration involving clinicians, pharmacists, microbiologists, infection prevention teams and healthcare administrators. Future programmes should therefore incorporate rapid diagnostics, electronic prescribing systems and institution-specific resistance data to improve treatment precision.

Therapeutic innovation also remains an important research priority. While β -lactamase inhibitor combinations have expanded options for resistant Gram-negative infections, emerging approaches such as bacteriophage therapy and microbiome-based interventions require further clinical evaluation before routine application. Kortright et al. (2019) [34] highlighted the potential of phage therapy against antimicrobial-resistant bacteria but noted that regulatory challenges, limited clinical evidence and phage resistance remain barriers to widespread implementation.

One Health Integration and Global Collaboration

The control of ESBL-producing *E. coli* requires recognition that resistance transmission extends beyond healthcare facilities. Resistant organisms and resistance genes circulate between humans, animals and environmental systems, creating interconnected pathways that cannot be addressed through hospital interventions alone.

The One Health approach provides a framework for integrating human health, veterinary practices and environmental management. Larsson et al. (2018) [38] highlighted that antimicrobial resistance has important environmental dimensions, including antibiotic residues, wastewater contamination and ecological dissemination of resistance determinants.

Future global responses should therefore include stronger antimicrobial regulation, responsible antibiotic use in agriculture, improved wastewater management, international data sharing and coordinated surveillance systems. Such approaches are particularly important for ESBL-producing *E. coli* because of its ability to move between healthcare, community and environmental reservoirs.

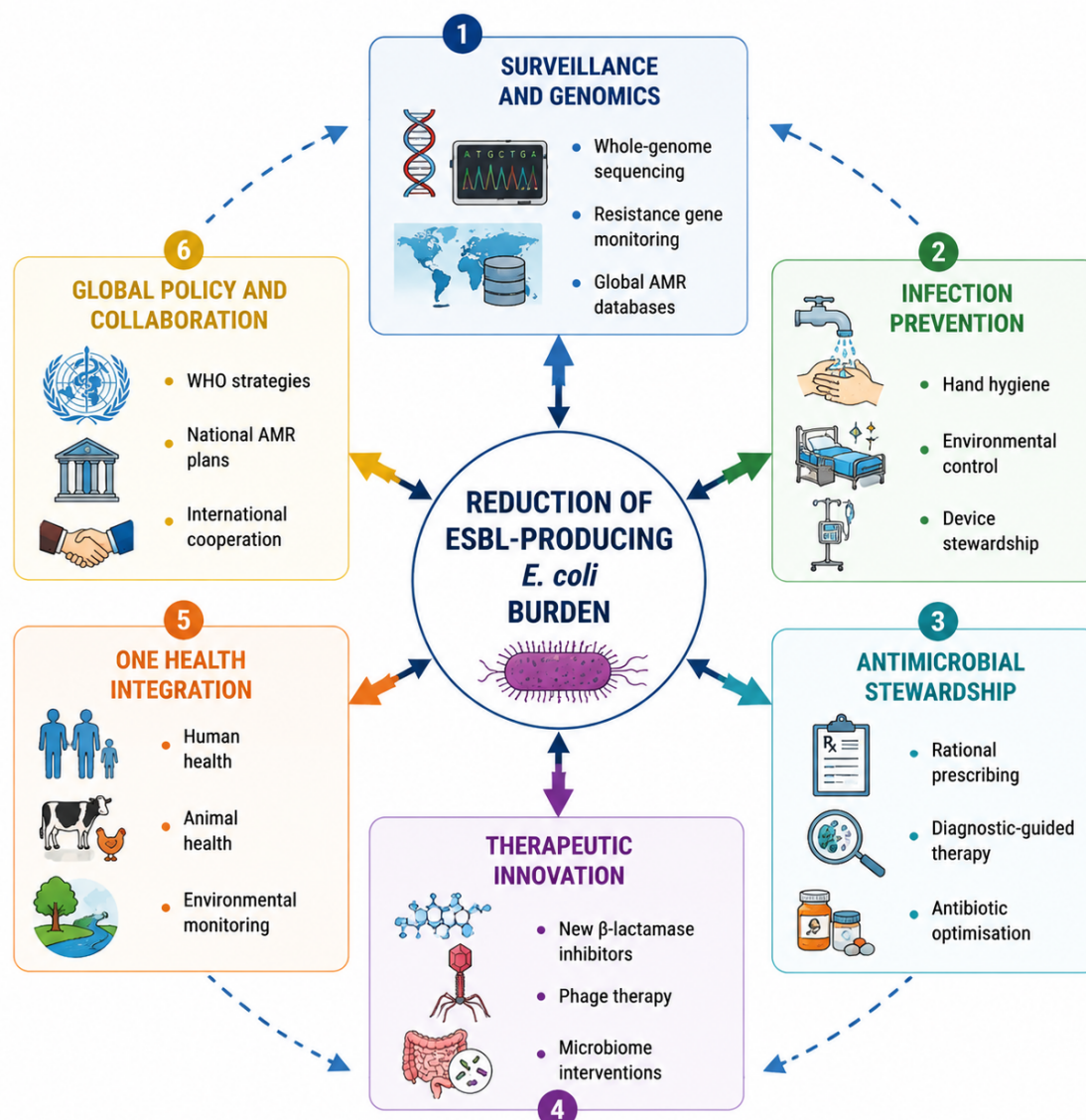


Figure 2: Integrated Framework for Future Control of ESBL-Producing *E. coli*

Figure 2 illustrates that reducing the burden of ESBL-producing *E. coli* requires coordinated action across surveillance, infection prevention, antimicrobial stewardship, therapeutic innovation, One Health integration and global policy rather than reliance on a single intervention.

Research Gaps and Future Priorities

Despite advances in ESBL research, several important questions remain unresolved. Future investigations should focus on:

- I. Expanding genomic and epidemiological surveillance in underrepresented regions.
- II. Defining effective and resource-appropriate strategies for identifying ESBL-colonised patients.
- III. Developing affordable rapid diagnostic tools suitable for diverse healthcare settings.

- IV. Evaluating long-term outcomes and cost-effectiveness of antimicrobial stewardship programmes.
- V. Establishing stronger clinical evidence for emerging therapies, including phage-based and microbiome interventions.
- VI. Clarifying the contribution of environmental reservoirs to healthcare-associated transmission.

Addressing these gaps requires collaboration between microbiologists, clinicians, epidemiologists, policymakers and public health organisations. Ultimately, controlling ESBL-producing *E. coli* will depend on sustained integration of surveillance, prevention, responsible antimicrobial use and therapeutic innovation across healthcare and wider ecological systems.

Limitations of the Review

This narrative review has several methodological limitations that should be considered when interpreting its findings. Although multiple databases, including PubMed, ScienceDirect, Dimensions and Google Scholar, were searched, relevant studies indexed in other databases may have been missed. Furthermore, restricting the search period to publications from 2016 to 2026 and excluding non-English articles may have limited inclusion of potentially relevant evidence. In addition, because the numbers of records retrieved from each database and excluded at each screening stage were not formally logged, a PRISMA flow diagram could not be provided, which limits the reproducibility of the study selection process.

The heterogeneity of the included literature represents another important limitation. The reviewed studies differed considerably in study design, healthcare settings, geographical regions, patient populations, laboratory methods and outcome definitions, making direct comparison of findings challenging. In addition, because this study adopted a narrative synthesis approach, no quantitative meta-analysis was performed, limiting the ability to estimate pooled effect sizes for identified risk factors, transmission pathways or treatment outcomes.

Conclusion

ESBL-producing *Escherichia coli* has evolved into a globally distributed antimicrobial resistance challenge sustained by bacterial adaptation, antimicrobial selection pressure and interconnected transmission pathways across healthcare, community and environmental settings. This review demonstrates that healthcare environments remain important reservoirs, where antibiotic exposure, prolonged hospitalisation, invasive devices and patient vulnerability contribute to both intestinal carriage and progression to clinical infection. The evidence further shows that urinary tract infections, bloodstream infections and wound infections represent major clinical manifestations, while transmission is maintained through interactions involving patients, healthcare workers, medical devices and environmental reservoirs.

Importantly, effective control of ESBL-producing *E. coli* requires more than therapeutic

Selection bias may also have influenced the evidence included in this review because studies reporting substantial ESBL-producing *E. coli* burdens, outbreaks or clinically important findings are more likely to be published and identified during literature searches. Additionally, evidence from low- and middle-income countries remains relatively limited, partly due to gaps in surveillance infrastructure and molecular diagnostic capacity, which may result in underrepresentation of resistance patterns in these settings.

Finally, the findings of this review highlight an important evidence gap regarding the relative contribution of different transmission reservoirs and the long-term effectiveness of emerging interventions. While healthcare-associated factors, antimicrobial stewardship and infection prevention strategies are consistently recognised as important, uncertainties remain regarding optimal screening approaches, environmental transmission pathways and the clinical role of newer therapeutic options. Future multicentre studies using standardised methodologies and stronger genomic surveillance approaches are required to address these gaps.

advances alone. Antimicrobial stewardship, infection prevention, genomic surveillance and appropriate diagnostic capacity must operate together to reduce transmission and preserve available treatment options. However, the available evidence remains limited by variation in study designs, surveillance capacity and geographical representation, particularly in resource-limited settings. Therefore, future efforts should prioritise standardised surveillance systems, context-specific infection prevention strategies, improved access to molecular diagnostics and further evaluation of emerging therapies. A coordinated One Health approach integrating human, animal and environmental perspectives will be essential for addressing the continuing global burden of ESBL-producing *E. coli*.

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References

1. Patra M, Gupta AK, Kumar D, Kumar B. Antimicrobial resistance: a rising global threat to public health. *Infect Drug Resist.* 2025;18:5419-37. doi:[10.2147/IDR.S530557](https://doi.org/10.2147/IDR.S530557)
2. Husna A, Rahman MM, Badruzzaman ATM, Sikder MH, Islam MR, Rahman MT, et al. Extended-spectrum β -lactamases (ESBL): challenges and opportunities. *Biomedicines.* 2023;11(11):2937. doi:[10.3390/biomedicines11112937](https://doi.org/10.3390/biomedicines11112937)
3. Ng RWY, Yang L, Lau SH, Hawkey P, Ip M. Global prevalence of human intestinal carriage of ESBL-producing *E. coli* during and after the COVID-19 pandemic. *JAC Antimicrob Resist.* 2025;7(1):dlaf001. doi:[10.1093/jacamr/dlaf001](https://doi.org/10.1093/jacamr/dlaf001)
4. Salman S, Umar Z, Xiao Y. Current epidemiologic features and health dynamics of ESBL-producing *Escherichia coli* in China. *Biosaf Health.* 2024;6(1):40-9. doi:[10.1016/j.bsheal.2024.01.002](https://doi.org/10.1016/j.bsheal.2024.01.002)
5. Ribeiro LF, Nespolo NM, Rossi GAM, Fairbrother JM. Exploring extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* in food-producing animals and animal-derived foods. *Pathogens.* 2024;13(4):346. doi:[10.3390/pathogens13040346](https://doi.org/10.3390/pathogens13040346)
6. Chaisaeng S, Chopjitt P, Kasemsiri P, Putthanachote N, Boueroy P, Takeuchi D, et al. High prevalence of ESBL-producing *E. coli* phylogroup B2 clinical isolates in northeastern Thailand. *BMC Microbiol.* 2024;24(1):425. doi:[10.1186/s12866-024-03582-0](https://doi.org/10.1186/s12866-024-03582-0)
7. Göpel S, Guther J, Gladstone BP, Conzelmann N, Bunk S, Terzer T, et al. Drivers of extended-spectrum β -lactamase (ESBL)-producing Enterobacterales colonization among residents of long-term care facilities: a European multicentre prospective cohort study. *J Hosp Infect.* 2025;157:67-74. doi:[10.1016/j.jhin.2024.12.010](https://doi.org/10.1016/j.jhin.2024.12.010)
8. Kayinamura MP, Muhirwa A, Kamaliza AC, Bigirimana Y, Rutare S, Hahirwa I, et al. Prevalence of extended-spectrum beta-lactamase-producing Enterobacteriaceae and associated clinical implications at the University Teaching Hospital of Kigali in Rwanda. *Am J Trop Med Hyg.* 2024;111(3):565-8. doi:[10.4269/ajtmh.23-0605](https://doi.org/10.4269/ajtmh.23-0605)
9. Olaitan MO, Orababa OQ, Shittu RB, Obunukwu GM, Kade AE, Arowolo MT, et al. Prevalence of ESBL-producing *Escherichia coli* in sub-Saharan Africa: a meta-analysis using a One Health approach. *One Health.* 2025;20:101090. doi:[10.1016/j.onehlt.2025.101090](https://doi.org/10.1016/j.onehlt.2025.101090)
10. Bezabih YM, Bezabih A, Dion M, Batard E, Teka S, Obole A, et al. Comparison of the global prevalence and trend of human intestinal carriage of ESBL-producing *Escherichia coli* between healthcare and community settings: a systematic review and meta-analysis. *JAC Antimicrob Resist.* 2022;4(3):dlac048. doi:[10.1093/jacamr/dlac048](https://doi.org/10.1093/jacamr/dlac048)
11. Al-Mustapha AI, Muasa B, Adetunji V, Awoyale OD, Adesiyun IM, Adesiji YO, et al. Global distribution and incidence of multidrug resistant and ESBL producing *Escherichia coli*: an observational study of the ATLAS dataset. *Clin Epidemiol Glob Health.* 2025;35:102150. doi:[10.1016/j.cegh.2025.102150](https://doi.org/10.1016/j.cegh.2025.102150)
12. Madenci EÇ, Hassan F, Türkyılmaz MK, Türkyılmaz S. Molecular epidemiology of ESBL-producing *Escherichia coli* causing clinical and subclinical bovine mastitis: associations between multidrug resistance, virulence genes, and phylogroups. *Vet Res Commun.* 2026;50(4):274. doi:[10.1007/s11259-026-11214-3](https://doi.org/10.1007/s11259-026-11214-3)
13. Kazemi S, Mojtahedi A, Hosseini F. Emergence of *Escherichia coli* sequence type 131 clone carrying blaCTX-M genes in Guilan Province, Northern Iran. *Microbiol Spectr.* 2025;13(10):e02270-24. doi:[10.1128/spectrum.02270-24](https://doi.org/10.1128/spectrum.02270-24)

14. Nasher S, Alsharapy S, Al-Madhagi A, Zakham F. Epidemiology of extended-spectrum β -lactamase producing *Escherichia coli* from hospital settings in Yemen. J Infect Dev Ctries. 2018;12(11):953-9. doi:[10.3855/jidc.10560](https://doi.org/10.3855/jidc.10560)
15. Whelan S, Lucey B, Finn K. Uropathogenic *Escherichia coli* (UPEC)-associated urinary tract infections: the molecular basis for challenges to effective treatment. Microorganisms. 2023;11(9):2169. doi:[10.3390/microorganisms11092169](https://doi.org/10.3390/microorganisms11092169)
16. Agbo IU, Udeani TK, Ngwu AM. Prevalence of extended spectrum beta-lactamase producing bacteria in patients with wound infections attending tertiary hospitals in Enugu, Nigeria. South Asian J Res Microbiol. 2025;19(2):1-13. doi:[10.9734/sajrm/2025/v19i2416](https://doi.org/10.9734/sajrm/2025/v19i2416)
17. Ramatla T, Mafokwane T, Lekota K, Monyama M, Khasapane G, Serage N, et al. "One Health" perspective on prevalence of co-existing extended-spectrum β -lactamase (ESBL)-producing *Escherichia coli* and *Klebsiella pneumoniae*: a comprehensive systematic review and meta-analysis. Ann Clin Microbiol Antimicrob. 2023;22(1):88. doi:[10.1186/s12941-023-00638-3](https://doi.org/10.1186/s12941-023-00638-3)
18. Centers for Disease Control and Prevention. ESBL-producing Enterobacterales [Internet]. Atlanta (GA): CDC; 2025 [cited 2026 Jun 6]. About ESBL-producing Enterobacterales. Available from: <https://www.cdc.gov/esbl-producing-enterobacterales/about/index.html>
19. Larramendy S, Deglaire V, Dusollier P, Fournier JP, Caillon J, Beaudeau F, et al. Risk factors of extended-spectrum beta-lactamases-producing *Escherichia coli* community acquired urinary tract infections: a systematic review. Infect Drug Resist. 2020;13:3945-55. doi:[10.2147/IDR.S269033](https://doi.org/10.2147/IDR.S269033)
20. Goyal D, Dean N, Neill S, Jones P, Dascomb K. Risk factors for community-acquired extended-spectrum beta-lactamase-producing Enterobacteriaceae infections—a retrospective study of symptomatic urinary tract infections. Open Forum Infect Dis. 2019;6(2):ofy357. doi:[10.1093/ofid/ofy357](https://doi.org/10.1093/ofid/ofy357)
21. Asmarawati TP, Widyatama FS, Notobroto HB, Nasronudin N, Sugai M, Kuntaman K. Risk factors and clinical impact of extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* bacteremia among hospitalized patients. Antibiotics (Basel). 2025;14(9):882. doi:[10.3390/antibiotics14090882](https://doi.org/10.3390/antibiotics14090882)
22. Vance MK, Cretella DA, Ward LM, Vijayvargiya P, Garrigos ZE, Wingler MJB. Risk factors for bloodstream infections due to ESBL-producing *Escherichia coli*, *Klebsiella* spp., and *Proteus mirabilis*. Pharmacy (Basel). 2023;11(2):74. doi:[10.3390/pharmacy11020074](https://doi.org/10.3390/pharmacy11020074)
23. Gómez-Zorrilla S, Rodríguez-Cabalé G, López Montesinos I, Alanti SS, Franquet A, Pascual-Aranda M, et al. ESBL-producing *Escherichia coli* bacteraemic urinary tract infections: clinical and economic burden and antimicrobial stewardship opportunities in a retrospective cohort study. Int J Antimicrob Agents. 2026;67(6):107787. doi:[10.1016/j.ijantimicag.2026.107787](https://doi.org/10.1016/j.ijantimicag.2026.107787)
24. World Health Organization. Evidence of hand hygiene as the building block for infection prevention and control [Internet]. Geneva: WHO; 2017 [cited 2026 Jun 6]. Available from: <https://www.who.int/publications/i/item/WHO-HIS-SDS-2017.7>
25. Tschudin-Sutter S, Lucet JC, Mutters NT, Tacconelli E, Zahar JR, Harbarth S. Contact precautions for preventing nosocomial transmission of extended-spectrum β -lactamase-producing *Escherichia coli*: a point/counterpoint review. Clin Infect Dis. 2017;65(2):342-7. doi:[10.1093/cid/cix258](https://doi.org/10.1093/cid/cix258)
26. Singh KV, Puraswani M, Ningombam A, Ashita A, Thomas JM, Ambashta NK, et al. Environmental sampling reveals reservoirs of antimicrobial resistance in a tertiary care Indian hospital: an observational study to strengthen infection control practices. IJID Reg. 2025;17:100782. doi:[10.1016/j.ijregi.2025.100782](https://doi.org/10.1016/j.ijregi.2025.100782)
27. Puspadari N, Pratama R, Goodman R, Suandy I, Efadeswarni E, Febriana T, et al. Genomic investigation of ESBL-producing *Escherichia coli* reveals likely transmission within and between One Health sectors in Jakarta, Indonesia.

- Research Square; 2025. doi:[10.21203/rs.3.rs-7825238/v1](https://doi.org/10.21203/rs.3.rs-7825238/v1)
28. Miftode IL, Vâță A, Miftode RȘ, Parângă T, Luca MC, Manciu C, et al. The impact of urinary catheterization on the antibiotic susceptibility of ESBL-producing Enterobacterales: a challenging duo. *Antibiotics* (Basel). 2024;13(5):462. doi:[10.3390/antibiotics13050462](https://doi.org/10.3390/antibiotics13050462)
 29. Beaumont AL, Danjean M, Jacquier H, Boyd A, Jaspard M, Royer G, et al. Dissemination of ESBL-producing *Escherichia coli* and carriage in the community worldwide: epidemiology, transmission pathways, molecular insights, and practical aspects. *Clin Microbiol Rev*. 2026;e00274-25. doi:[10.1128/cmr.00274-25](https://doi.org/10.1128/cmr.00274-25)
 30. Baur D, Gladstone BP, Burkert F, Carrara E, Foschi F, Döbele S, et al. Effect of antibiotic stewardship on the incidence of infection and colonisation with antibiotic-resistant bacteria and *Clostridium difficile* infection: a systematic review and meta-analysis. *Lancet Infect Dis*. 2017;17(9):990-1001. doi:[10.1016/S1473-3099\(17\)30325-0](https://doi.org/10.1016/S1473-3099(17)30325-0)
 31. World Health Organization. Global antibiotic resistance surveillance report 2025 [Internet]. Geneva: WHO; 2025 [cited 2026 Jun 6]. Available from: <https://www.who.int/publications/i/item/9789240116337>
 32. Harris PNA, Tambyah PA, Lye DC, Mo Y, Lee TH, Yilmaz M, et al. Effect of piperacillin-tazobactam vs meropenem on 30-day mortality for patients with *E coli* or *Klebsiella pneumoniae* bloodstream infection and ceftriaxone resistance: a randomized clinical trial. *JAMA*. 2018;320(10):984-94. doi:[10.1001/jama.2018.12163](https://doi.org/10.1001/jama.2018.12163)
 33. Tamma PD, Heil EL, Justo JA, Mathers AJ, Satlin MJ, Bonomo RA. Infectious Diseases Society of America 2024 guidance on the treatment of antimicrobial-resistant gram-negative infections. *Clin Infect Dis*. 2024;ciae403. doi:[10.1093/cid/ciae403](https://doi.org/10.1093/cid/ciae403)
 34. Kortright KE, Chan BK, Koff JL, Turner PE. Phage therapy: a renewed approach to combat antibiotic-resistant bacteria. *Cell Host Microbe*. 2019;25(2):219-32. doi:[10.1016/j.chom.2019.01.014](https://doi.org/10.1016/j.chom.2019.01.014)
 35. World Health Organization. Global Antimicrobial Resistance and Use Surveillance System (GLASS) [Internet]. Geneva: WHO; [cited 2026 Jun 6]. Available from: <https://www.who.int/initiatives/glass>
 36. Rogers LA, Strong K, Cork SC, McAllister TA, Liljebjelke K, Zaheer R, et al. The role of whole genome sequencing in the surveillance of antimicrobial resistant *Enterococcus* spp.: a scoping review. *Front Public Health*. 2021;9:599285. doi:[10.3389/fpubh.2021.599285](https://doi.org/10.3389/fpubh.2021.599285)
 37. Dyar OJ, Huttner B, Schouten J, Pulcini C. What is antimicrobial stewardship? *Clin Microbiol Infect*. 2017;23(11):793-8. doi:[10.1016/j.cmi.2017.08.026](https://doi.org/10.1016/j.cmi.2017.08.026)
 38. Larsson DGJ, Andremont A, Bengtsson-Palme J, Brandt KK, de Roda Husman AM, Fagerstedt P, et al. Critical knowledge gaps and research needs related to the environmental dimensions of antibiotic resistance. *Environ Int*. 2018;117:132-8. doi:[10.1016/j.envint.2018.04.041](https://doi.org/10.1016/j.envint.2018.04.041)