

Key drivers of antibiotic resistance in *Escherichia coli* in a One Health context: A literature review

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ABSTRACT

Aim: To summarize the key factors driving *E. coli* resistance in Europe, with reference to global data and the One Health context.

Materials and Methods: A narrative literature review was conducted based on 14 peer-reviewed articles and institutional reports addressing resistance mechanisms and the epidemiology of *E. coli* strains in Europe and globally.

Conclusions: Resistance in *E. coli* is driven by complex, cross-sectoral dynamics. Effective containment strategies should include rational antibiotic use in primary care, restrictions on veterinary antimicrobial use, improved diagnostics, modernized wastewater infrastructure, and inclusion of travel history in AMR risk assessments. The persistent detection of *bla*_{CTX-M} and *mcr-1* in all reservoirs highlights the need for a unified One Health approach.

KEY WORDS: *Escherichia coli*, drug resistance, beta-lactamases, gene transfer, One Health

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INTRODUCTION

Escherichia coli is a natural component of the human gut microbiota and a leading cause of urinary tract, intraabdominal and bloodstream infections in Europe. Although in 2023 the most common *E. coli* resistance was observed for aminopenicillins, European Centre for Disease Prevention and Control data from 2016–2020 indicate that the most severe clinical cases and the highest number of deaths were associated with resistance to third-generation cephalosporins. Given the serious health consequences of infections caused by antibiotic-resistant *E. coli* strains, comprehensive preventive measures are essential – extending beyond hospital care to encompass the broader healthcare system. [1]. One of the key resistance mechanisms of *Escherichia coli* is the ability to produce enzymes that inactivate β-lactam antibiotics. These bacteria can easily transfer resistance genes via plasmids and mobile genetic ele-

ments, such as transposons and insertion sequences, through the process of horizontal gene transfer (HGT). HGT is one of the major mechanisms facilitating the copying and dissemination of genes – including resistance genes such as *bla*_{CTX-M-15} gene – between bacteria of different species. This gene has been identified in multiple reservoirs: human, animal, and environmental [2]. Although carbapenem resistance in *Escherichia coli* remains uncommon, the emergence of hard-to-detect mechanisms – such as the OXA-244 carbapenemase – raises growing concern. These enzymes may evade standard diagnostics, increasing the risk of unnoticed spread within healthcare settings [3].

AIM

This review synthesises the main factors contributing to the emergence and spread of antibiotic-resistant

Escherichia coli in Europe, taking into account the interconnected human, animal, and environmental dimensions of the One Health perspective.

MATERIALS AND METHODS

This literature review was conducted to identify and synthesize scientific evidence on the mechanisms and epidemiology of antibiotic resistance in *Escherichia coli* in Europe, with a particular focus on the One Health perspective.

A structured literature search was performed using keywords such as “*Escherichia coli*”, “antibiotic resistance”, “ESBL”, “carbapenemase”, “CTX-M”, “OXA-244”, “fluoroquinolone resistance”, “veterinary antibiotics”, “horizontal gene transfer”, “mcr-1”, and “One Health”.

Inclusion criteria encompassed peer-reviewed articles focusing on *E. coli* resistance in human, animal, and environmental reservoirs within the European region.

A total of 14 scientific articles were selected and analyzed. The selection process followed the principles of narrative review methodology, aiming to provide a comprehensive yet structured overview of the most relevant mechanisms and drivers of resistance.

REVIEW AND DISCUSSION

INAPPROPRIATE ANTIBIOTIC PRESCRIBING IN HUMAN MEDICINE

Data from recent years indicate that antibiotic prescribing by primary care physicians significantly contributes to bacterial resistance to antimicrobial agents. A study conducted in 14 European countries revealed notable differences in prescribing practices across nations. Countries such as Spain, Poland, and Italy exhibited particularly high rates of broad-spectrum antibiotic use, reflected in elevated Antibiotic Spectrum Index (ASI) values. The study demonstrated a clear correlation between the volume of antibiotics prescribed and the prevalence of resistant microorganisms. Notably, the role of primary care physicians emerged as crucial, with approximately 90% of the antibiotic selection pressure (ASP) originating from primary care rather than hospital settings. Interestingly, it was not merely the number of prescriptions that mattered, but rather the breadth of antimicrobial activity. The broader the antibiotic spectrum, the higher the associated risk of resistance development. Although some general practitioners still believe that antimicrobial resistance (AMR) is primarily driven by hospital or veterinary antibiotic use, this study highlights the substantial influence of prescribing practices in family medicine on the growing AMR crisis [4].

This shift toward broad-spectrum antibiotic prescribing is not a new phenomenon. As early as the early 2000s, a cross-national study conducted in 26 European countries already highlighted a decline in the use of narrow-spectrum agents in favor of newer broad-spectrum antibiotics, especially in Southern and Eastern Europe [5].

A relevant example is the outpatient use of fluoroquinolones in the treatment of urinary tract infections (UTIs), which are most commonly caused by *Escherichia coli*. Antibiotics such as ciprofloxacin and levofloxacin are frequently prescribed empirically for cystitis and pyelonephritis. However, recent years have seen a notable increase in *E. coli* resistance to this antibiotic class, particularly in Southern and Eastern Europe, with resistance rates in Poland *previously reported* at approximately 30%. This trend highlights the importance of monitoring regional resistance patterns and promoting responsible antibiotic prescribing practices [6].

VETERINARY AND AGRICULTURAL ANTIBIOTIC USE

The practice of frequent antibiotic use by animal-based food producers is a serious factor contributing to antimicrobial resistance [9].

In 2023, EU member states, along with Iceland and Norway, jointly reported data on the sale and use of antimicrobials in animals for the first time. Coordinated by the EMA, the ESUAvet report showed that 98% of veterinary antimicrobials sold were intended for food-producing animals. The most frequently used classes included penicillins, tetracyclines, and sulfonamides. Usage data, mostly collected by veterinarians, focused on cattle, pigs, poultry, and turkeys [7].

The Joint Interagency Antimicrobial Consumption and Resistance Analysis (JIACRA IV) report indicates that reducing the use of antimicrobials in food-producing animals is associated with a higher proportion of *Escherichia coli* isolates fully susceptible to the tested antimicrobial agents. This pattern was observed both in animal and human isolates, particularly in countries that have significantly decreased overall antimicrobial consumption [8].

The increase in resistance to colistin – an antibiotic used in the treatment of severe infections caused by carbapenemase-producing *E. coli* strains – is closely linked to its widespread use in food-producing animals. A particular concern is the emergence of the plasmid-mediated resistance gene *mcr-1*, which facilitates horizontal transfer of this trait between bacteria. In many cases, *E. coli* isolates from both animals and humans have carried both *mcr-1* and *bla*CTX-M, suggesting the potential for co-transfer of resistance to colistin and cephalosporins [9].

Emerging evidence demonstrates that the use of antibiotics in livestock farming fosters the gastrointestinal colonization of poultry and mammals by *E. coli* strains carrying *bla*CTX-M resistance genes. These strains can be transmitted to humans through both the food chain and direct contact [12].

Recent data from Thailand indicate that both companion animals and individuals working closely with them may carry *E. coli* strains resistant to multiple antimicrobial agents. These strains were often found to possess extended-spectrum beta-lactamase (ESBL) genes, including *bla*CTX-M, *bla*TEM, *bla*SHV, along with tetracycline resistance markers (*tetA*, *tetB*). This highlights the potential role of household pets as reservoirs of resistance genes and supports the need for integrated antimicrobial resistance surveillance within a One Health framework [10].

1 HOSPITAL TRANSMISSION AND INFECTION CONTROL GAPS

A 2-year study in a tertiary care hospital found that many patients carried ESBL-producing *E. coli* at admission or acquired it during hospitalization. Most infections (60%) were endogenous, but transmission between patients also occurred, revealing infection-control gaps. The study highlights the need for antibiotic stewardship to limit antibiotic overuse and lower ESBL-E infection rates [11].

Although carbapenem resistance in *Escherichia coli* remains relatively low in the EU/EEA – with fewer than 1.5% of invasive isolates exhibiting resistance in 2022— it is becoming an increasing concern due to the emergence of difficult-to-detect resistance mechanisms and the critical importance of carbapenems as last-resort antibiotics. One such mechanism involves the OXA-244 carbapenemase, an enzyme with low hydrolytic activity that often escapes detection through standard screening methods and fails to grow on selective CPE media. This diagnostic limitation was exemplified by a large-scale hospital outbreak in Poland in 2023, where *E. coli* ST38 strains carrying the *bla*OXA-244 gene were identified in 38 patients across 13 wards. Despite extensive epidemiological investigation, no definitive source of transmission was established. The spread was likely facilitated by intra-hospital movement of patients and healthcare personnel, further highlighting the importance of improved detection and containment strategies for emerging carbapenemase producers [3].

2 INTERNATIONAL TRAVEL AND POPULATION MOBILITY

A multinational study conducted across several countries confirmed that international travel constitutes a

major risk factor for colonization with extended-spectrum β -lactamase-producing *Escherichia coli* (ESBL-EC). Individuals who traveled at least once per year to Asia, Sub-Saharan Africa, or Northern Africa exhibited an approximately fourfold increased likelihood of ESBL-EC carriage compared to those who had not traveled to these regions. This association remained statistically significant after adjustment for potential confounders [14].

3 HORIZONTAL GENE TRANSFER AND MOBILE GENETIC ELEMENTS

On a global scale, *bla* CTX-M-15 is the most frequently identified CTX-M gene variant in *Escherichia coli*. The extraintestinal pathogenic clone ST131 has emerged as the leading strain worldwide, with its H30-Rx sublineage being particularly widespread. This subclone is notable for carrying both fluoroquinolone resistance and the *bla* CTX-M-15 gene, which has contributed to its success. The dissemination of this resistance gene is largely driven by horizontal gene transfer via conjugative plasmids, especially those belonging to the IncF family, which act as primary vectors. Importantly, ST131 has not only been found in clinical human samples but also in animals and the environment, reflecting its broad adaptability and relevance in One Health contexts [12].

ENVIRONMENTAL RESERVOIRS AND WASTEWATER INTERFACES

The natural environment serves as a significant reservoir of antimicrobial resistance genes, including *bla*CTX-M, primarily due to pollution linked to human activities. ESBL-producing *Escherichia coli* have been increasingly identified in a variety of environmental settings.

The presence of mobile genetic elements – especially class I integrons and transposons – facilitates the horizontal transfer of resistance traits between bacteria, enabling their persistence across ecological boundaries.

Environmental contamination with residual antibiotics supports the survival of resistant strains that may eventually transfer their resistance to humans and animals.

For instance, fluoroquinolone pollution favors the selection of bacterial strains carrying integrons that harbor both *bla*CTX-M and *qnr* genes, contributing to the long-term maintenance and environmental spread of ESBL resistance [12].

Inadequate treatment processes in wastewater treatment plants (WWTPs) contribute significantly to the dissemination of antimicrobial-resistant bacteria and resistance genes in the environment. These facilities

receive human excreta containing unmetabolized antibiotics, as well as a wide range of chemicals, including pharmaceuticals and personal care products. If not effectively removed, these substances create selective pressure that promotes the survival and spread of resistant strains. Studies have detected multidrug-resistant *Escherichia coli* isolates, including those carrying resistance genes such as *mcr-1* and *ermA*, in treated effluents released into natural water bodies [13].

DISCUSSION

This literature review reveals that antibiotic-resistant *Escherichia coli* is an increasingly complex public health challenge in Europe, driven by a constellation of interrelated factors across human, animal, and environmental domains. The reviewed evidence shows that resistance is no longer confined to hospitals but is instead propagated through interconnected ecosystems. Understanding the multifactorial dynamics of resistance transmission is therefore crucial for designing effective mitigation strategies across all sectors of the One Health interface.

The role of primary care practitioners is particularly concerning, given their significant contribution to antimicrobial selection pressure. The shift toward broad-spectrum agents, such as fluoroquinolones, has likely contributed to the regional increase in resistance, especially in Southern and Eastern Europe. These findings support the need for continued education and stewardship programs tailored specifically to outpatient care.

In the veterinary and agricultural sectors, the widespread use of antimicrobials—especially in food-producing animals – has enabled the persistence and dissemination of resistance genes such as *mcr-1* and *blaCTX-M*. The identification of these genes in both human and animal isolates, as well as in companion animals, highlights the permeability of the One Health interface and the necessity of coordinated surveillance across sectors.

Hospital-based transmission remains an ongoing concern, particularly in light of the emergence of elusive resistance mechanisms such as OXA-244 carbapenemase. The inability of standard diagnostic tests to detect certain carbapenemase producers presents a serious threat, as undetected carriers may facilitate silent outbreaks. This calls for the incorporation of more sensitive molecular diagnostics in clinical microbiology laboratories.

Horizontal gene transfer further complicates containment efforts. Plasmids, integrons, and transposons have accelerated the spread of resistance across species and ecosystems, with environmental contamination –

particularly via wastewater – providing ideal conditions for persistence and exchange of resistance traits. These findings underscore the urgent need to improve wastewater treatment standards and reduce pharmaceutical residues in the environment.

One important but often underappreciated factor is international travel. The AWARE study demonstrated that frequent travelers to high-prevalence regions face significantly higher risks of ESBL-EC colonization. This highlights the global dimension of resistance dissemination and suggests that travel history should be more routinely considered in clinical risk assessments and screening protocols.

Key summary points:

- Antibiotic resistance in *E. coli* is driven by interconnected pressures across the One Health spectrum.
- Inappropriate outpatient prescribing, particularly of broad-spectrum antibiotics, remains a critical issue in many European countries.
- Antimicrobial use in agriculture contributes to resistance gene dissemination, including in household pets.
- Hospital outbreaks caused by hard-to-detect carbapenemases, such as OXA-244, illustrate the diagnostic limitations of current protocols.
- Environmental contamination and wastewater interfaces create persistent reservoirs of resistance.
- Frequent international travel to high-risk regions significantly increases the likelihood of ESBL-EC carriage.

CONCLUSIONS

Antibiotic resistance in *Escherichia coli* presents an escalating public health challenge that transcends hospital walls and reflects the interconnectivity of human, animal, and environmental health domains. This literature review demonstrates that resistance is fueled by multiple factors: excessive broad-spectrum antibiotic use in primary care, the overuse of antimicrobials in food-producing animals, inadequate infection control in healthcare settings, environmental contamination, and global travel.

A coordinated and multisectoral approach is urgently required. Strategies should include:

- Strengthening antimicrobial stewardship in outpatient settings;
- Restricting non-therapeutic antibiotic use in agriculture;
- Improving diagnostic capacities to detect hard-to-identify resistance mechanisms;
- Enhancing wastewater treatment standards;
- Integrating travel history into risk assessment protocols.

Finally, the consistent presence of *bla*CTX-M and *mcr*-1 genes across human, animal, and environmental reservoirs reinforces the critical importance of adopting a One Health perspective in tackling antibiotic

resistance. Future efforts must prioritize surveillance, prevention, and international collaboration to limit the spread of multidrug-resistant *E. coli* and protect public health.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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