







Review

# Caught in the ESKAPE: Wildlife as Key Players in the Ecology of Resistant Pathogens in a One Health Context

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**Abstract:** The emergence of antimicrobial-resistant bacteria poses a significant global health challenge, with ESKAPE pathogens (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* spp.) playing a major role in multidrug-resistant infections. While traditionally associated with hospital settings, these bacteria have increasingly been detected in wildlife, suggesting a complex web of transmission between human, animal, and environmental reservoirs. Wildlife may act as both sentinels and reservoirs for resistant pathogens, contributing to their persistence and dissemination across ecosystems. This review explores the presence of ESKAPE bacteria in wild animals, examining their clonal lineages, resistance profiles, and virulence traits. Understanding how these pathogens circulate in natural environments is crucial for designing effective strategies to mitigate antimicrobial resistance. By adopting a One Health perspective—integrating human, animal, and environmental health—efforts to control ESKAPE bacteria can extend beyond clinical interventions to broader ecological and public health frameworks. Addressing this issue requires comprehensive surveillance, responsible antibiotic use, and policies aimed at reducing environmental contamination, ultimately safeguarding both biodiversity and global health.

**Keywords:** ESKAPE pathogens; antimicrobial resistance; wildlife; One Health; bacterial transmission; environmental reservoirs



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## 1. Introduction

The emergence and spread of antimicrobial-resistant bacteria is a growing global threat, with the ESKAPE pathogens (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* spp.) at the forefront. These pathogens are recognized for their ability to evade standard treatments,

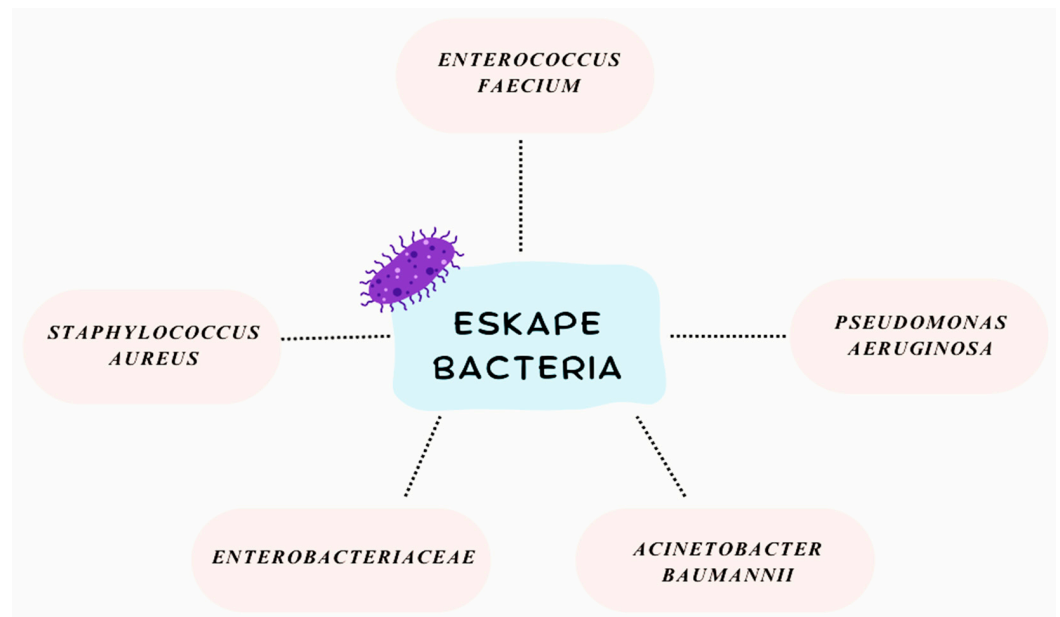
leading to difficult-to-manage infections, particularly in hospital settings where immunocompromised patients are most vulnerable [1,2]. Their name, “ESKAPE”, reflects their capacity to “escape” the effects of antibiotics through various mechanisms, including the rapid acquisition and dissemination of resistance genes and an array of virulence factors that enhance their ability to cause disease [1,3]. To contrapose the global menace posed by antimicrobial resistance, the World Health Organization (WHO) has assigned the pertinent bacterial pathogens into three categories of risk: critical, high, and medium priority. Remarkably, some constituents of the ESKAPE group are classified as extreme priority in relation to the threat that accompanies their infection such as carbapenem-resistant *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacteriaceae* [4]. The existence of these bacteria within wildlife underscores the necessity of knowing how these bacteria circulate within a One Health approach.

Initially considered a primarily clinical issue, ESKAPE bacteria have increasingly been detected outside hospital environments, appearing in agriculture, the community, and even natural ecosystems [5]. This wider distribution points to a complex web of transmission involving humans, animals, and the environment [5,6]. In this context, wild animals have emerged as unexpected reservoirs for ESKAPE pathogens [5,6]. As they interact with diverse habitats, from urban landscapes to remote wilderness areas, wildlife can become exposed to contamination from human activities, such as agricultural runoff, untreated sewage, and waste from healthcare facilities [7]. This ongoing environmental exposure suggests that resistance is not confined to anthropogenic settings but is also maintained and potentially amplified through natural reservoirs, creating a cycle of transmission that connects diverse ecosystems [7,8].

This review examines the presence of ESKAPE bacteria in wildlife and explores their role in the broader ecology of antimicrobial resistance. By investigating the clonal lineages, resistance profiles, and virulence traits of these pathogens in wild animals, we can gain insights into how resistance spreads and persists across different settings. Understanding these dynamics is essential for formulating strategies that extend beyond traditional clinical approaches to embrace a One Health perspective that recognizes the interconnectedness of human, animal, and environmental health. While previous reviews have explored antimicrobial resistance in wildlife, most have focused on specific bacterial groups or individual species. This review uniquely examines the ESKAPE group as a whole, assessing their presence in diverse wildlife hosts, their resistance profiles, and their potential role in resistance transmission. By integrating data across multiple bacterial species and ecological contexts, this work provides a broader understanding of how ESKAPE pathogens circulate in natural environments and their implications for One Health. Additionally, this review identifies gaps in the literature, highlighting areas where further research is needed to fully understand the role of wildlife in the ecology of antimicrobial resistance.

## 2. ESKAPE Bacteria

The ESKAPE group of bacteria—comprising *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* species—has gained notoriety in recent years as a leading cause of hospital-acquired infections worldwide (Figure 1). These pathogens are not only adept at evading the human immune system but also display a remarkable capacity to “escape” the effects of antibiotics, making them key drivers of antimicrobial resistance (AMR) [8,9]. Collectively, they are responsible for a significant proportion of difficult-to-treat infections, ranging from pneumonia and bloodstream infections to urinary tract and wound infections, particularly in immunocompromised patients or those undergoing invasive medical procedures [3,9].



**Figure 1.** ESKAPE bacterial group.

The threat posed by ESKAPE bacteria is twofold. On the one hand, their ability to rapidly acquire and share resistance genes—often through mobile genetic elements like plasmids, transposons, and integrons—means that even once-effective antibiotics can quickly lose their efficacy [2,10,11]. On the other hand, many of these bacteria possess an array of virulence factors, including toxins, enzymes, and biofilm-forming capabilities, which allow them to colonize host tissues, evade immune responses, and persist on medical devices such as catheters and ventilators [3,12]. This dual ability to resist treatment and cause severe disease complicates infection control efforts and has led to a growing reliance on last-resort antibiotics, which are themselves increasingly compromised [13]. Drugs such as carbapenems and colistin, once considered the final line of defense, are becoming less effective due to the spread of resistant strains like carbapenem-resistant *Klebsiella pneumoniae* and colistin-resistant *Acinetobacter baumannii* [11,14].

Originally recognized as a major issue within hospital settings, the reach of ESKAPE pathogens extends beyond clinical environments. These bacteria have been detected in community settings, agricultural contexts, and natural ecosystems, underscoring the interconnected nature of AMR [5,14,15]. The detection of multidrug-resistant ESKAPE strains in livestock, wildlife, and even water sources suggests that the problem is not confined to hospitals but is also driven by environmental factors and the widespread use of antibiotics in both human and veterinary medicine [5,16]. This highlights the need for a One Health approach that addresses antimicrobial resistance as a shared challenge across human, animal, and environmental health.

Efforts to combat ESKAPE bacteria require a comprehensive strategy that goes beyond the development of new antibiotics. It involves improved infection prevention and control measures, responsible antibiotic use in both healthcare and agriculture, and proactive surveillance to track emerging resistance trends [2,17]. Understanding the mechanisms through which these pathogens spread and persist in different settings is critical for developing sustainable solutions to curb their impact. As the global community grapples with the growing crisis of AMR, ESKAPE bacteria remain at the forefront of this struggle, serving as both a symbol of the challenges ahead and a call to action for coordinated, multi-disciplinary efforts.

### 2.1. *Staphylococcus aureus*

*S. aureus* is a versatile and opportunistic pathogen known for its ability to colonize a variety of hosts, from humans to animals, and its remarkable adaptability to different environments [18,19]. As a Gram-positive bacterium, it is commonly found on the skin and mucous membranes, where it often exists as a harmless commensal [19]. However, under certain conditions, such as breaches in the skin barrier or immunosuppression, *S. aureus* can shift from a benign colonizer to a formidable pathogen, causing a range of infections from superficial skin lesions to life-threatening conditions like sepsis, endocarditis, and pneumonia [20]. *S. aureus* success as a pathogen can be attributed to its extensive arsenal of virulence factors, which include surface proteins that facilitate adhesion to host tissues, enzymes that promote invasion and tissue destruction, and toxins that disrupt the immune response [21–23]. Among these, the production of staphylococcal enterotoxins, hemolysins, and leukocidins plays a significant role in the severity of infections [24,25]. Additionally, *S. aureus* is adept at forming biofilms, particularly on medical devices, which not only helps it evade the host's immune system but also significantly complicates treatment efforts [26,27]. The emergence of methicillin-resistant *Staphylococcus aureus* (MRSA) in the mid-20th century marked a significant turning point, transforming a once-treatable pathogen into a global public health threat. Today, MRSA is a major cause of hospital-associated (HA-MRSA) and community-associated (CA-MRSA) infections worldwide [28,29]. The ability of *S. aureus* to harbor resistance genes, such as *mecA* and *mecC*, which confer resistance to nearly all  $\beta$ -lactam antibiotics, underscores its resilience in the face of modern medicine [30,31]. The discovery of *mecC*-positive MRSA in both livestock and wildlife also highlights the broader environmental and zoonotic dimensions of *S. aureus* epidemiology [32]. The transmission dynamics of *S. aureus* are complex and multifactorial, involving not just person-to-person spread but also environmental reservoirs and animal hosts. Livestock-associated MRSA (LA-MRSA), particularly strains linked to clonal complex 398 (CC398), has demonstrated that farm animals can act as reservoirs for resistant strains, which can then spread to humans through direct contact or environmental contamination [33–35]. The detection of various *S. aureus* lineages in wildlife further expands this narrative, suggesting that these bacteria ecology extends well beyond human-associated settings [32]. Efforts to control *S. aureus* infections thus require a multifaceted approach, encompassing not only clinical interventions but also public health strategies that address the environmental and veterinary aspects of its transmission [36,37]. Understanding the interplay between human, animal, and environmental reservoirs is crucial for developing effective measures to combat this adaptable pathogen.

### 2.2. *Enterobacteriaceae*

*Enterobacteriaceae* are a diverse family of Gram-negative bacteria that inhabit a range of environments, including soil, water, and the gastrointestinal tracts of animals and humans [38]. While many members of this family play a role as commensals or environmental organisms, some, such as *Escherichia coli* and *Klebsiella pneumoniae*, can become opportunistic pathogens under certain conditions [39,40]. These bacteria are not only a significant cause of community and hospital-acquired infections, but they are also at the forefront of the global issue of antimicrobial resistance [41,42].

*Escherichia coli*, for instance, is a common inhabitant of the human gut, where it generally coexists harmlessly with the host [43]. However, certain strains have acquired virulence factors that enable them to cause a spectrum of infections, ranging from uncomplicated urinary tract infections (UTIs) to severe conditions like septicemia and meningitis [44,45]. Pathogenic *E. coli* strains are broadly classified into pathotypes based on their virulence mechanisms, with extraintestinal pathogenic *E. coli* (ExPEC) being a major contributor to

UTIs and bloodstream infections [46]. The increasing prevalence of multidrug-resistant *E. coli*, especially those producing extended-spectrum  $\beta$ -lactamases (ESBLs) such as *bla*<sub>CTX-M</sub>, poses a significant challenge for treatment, as these enzymes confer resistance to many  $\beta$ -lactam antibiotics, including third-generation cephalosporins [47]. Moreover, the spread of plasmid-mediated colistin resistance (*mcr* genes) raises concerns about the diminishing efficacy of last-resort treatments [48].

*Klebsiella pneumoniae* is another key member of the *Enterobacteriaceae* family that has emerged as a major public health threat, particularly in healthcare settings. Known for its characteristic thick polysaccharide capsule, which enhances its virulence and helps it evade the host immune system, *K. pneumoniae* is a leading cause of hospital-acquired pneumonia, bloodstream infections, and urinary tract infections [49,50]. The rise in carbapenem-resistant *K. pneumoniae* has added to the urgency of controlling its spread, as carbapenems are often the last line of defense against MDR Gram-negative infections [51]. The resistance is frequently mediated by carbapenemase enzymes, such as *KPC* (*Klebsiella pneumoniae* carbapenemase), *NDM* (New Delhi metallo- $\beta$ -lactamase), and *OXA-48*, which can be transferred between bacteria through mobile genetic elements, accelerating the dissemination of resistance [52,53].

Both *E. coli* and *K. pneumoniae* have demonstrated remarkable genetic plasticity, enabling them to adapt to different hosts and environments. This adaptability is facilitated by horizontal gene transfer (HGT), which allows for the acquisition of resistance genes and virulence factors from other bacteria [54]. The detection of MDR *Enterobacteriaceae* in animals, food, and the environment highlights the One Health aspect of AMR, where human, animal, and environmental health are interconnected [38,55]. Livestock, wildlife, and even companion animals can harbor and transmit resistant strains, potentially contributing to the spread of AMR through direct contact or environmental contamination [56,57].

*Enterobacter* species, although less commonly discussed than *E. coli* and *Klebsiella*, are significant contributors to the burden of hospital-acquired infections and antimicrobial resistance. These bacteria are naturally found in the environment, including water and soil, but can become opportunistic pathogens in vulnerable patients, causing respiratory, urinary, and bloodstream infections [58,59]. The clinical relevance of *Enterobacter* has been heightened by the emergence of multidrug-resistant (MDR) strains, often due to the production of AmpC  $\beta$ -lactamases and, more recently, carbapenemases. The ability of *Enterobacter* to upregulate these enzymes in response to antibiotic exposure makes treatment particularly challenging, often requiring the use of last-resort antibiotics such as carbapenems or colistin. Moreover, their capacity for acquiring resistance genes via horizontal gene transfer contributes to the broader dissemination of antimicrobial resistance across bacterial communities, highlighting the importance of monitoring and controlling *Enterobacter* as part of comprehensive AMR strategies [60,61].

Addressing the threat posed by *Enterobacteriaceae*, particularly *E. coli* and *K. pneumoniae*, requires a comprehensive approach that extends beyond the clinical setting. Strategies must include rigorous infection control measures in healthcare facilities, prudent antibiotic use in both human medicine and agriculture, and environmental monitoring to track the spread of resistance genes [62–64]. Understanding the intricate ecology of these bacteria, including their role in natural reservoirs, will be crucial for developing effective interventions to curb the tide of antimicrobial resistance.

### 2.3. *Acinetobacter baumannii*

*Acinetobacter baumannii* is a Gram-negative bacterium that has gained prominence as a formidable opportunistic pathogen, especially in healthcare settings [65]. Its natural habitat includes soil and water, where it can persist under harsh conditions, but it is in hospitals

where *A. baumannii* truly thrives, causing a range of infections such as ventilator-associated pneumonia, bloodstream infections, and wound infections in critically ill patients [66,67]. This adaptability is largely due to its remarkable ability to survive on various surfaces for extended periods, making it a notorious cause of hospital-acquired infections [68].

The pathogenicity of *A. baumannii* is bolstered by a suite of virulence factors that allow it to evade the host's immune response and adapt to different environments [69,70]. These include biofilm formation, which enhances its survival on medical devices, and an outer membrane that resists desiccation and antiseptics [71,72]. Furthermore, the bacteria's capacity for acquiring and integrating foreign DNA facilitates the rapid spread of resistance genes. This is particularly concerning with the emergence of carbapenem-resistant *A. baumannii* (CRAB), which has severely limited treatment options. Carbapenem resistance is often mediated by the production of carbapenem-hydrolyzing enzymes known as oxacillinases (OXA), such as *blaOXA-23*, *blaOXA-24/40*, and *blaOXA-58* [73,74]. The presence of these genes on mobile genetic elements like plasmids and transposons accelerates their spread within and between bacterial populations.

What makes *A. baumannii* especially challenging to control is its ability to rapidly develop resistance not just to carbapenems, but to multiple classes of antibiotics, including aminoglycosides, fluoroquinolones, and even polymyxins like colistin, which are considered last-resort treatments [75–77]. The emergence of colistin-resistant strains is alarming, as it leaves clinicians with very few therapeutic options [78,79]. Resistance mechanisms in *A. baumannii* often involve efflux pumps, enzymatic degradation, and modifications to target sites, reflecting the bacteria genetic versatility [80,81].

Beyond hospitals, the detection of *A. baumannii* in community settings and natural environments is increasingly reported, raising questions about the pathways through which this pathogen disseminates. Studies have found *A. baumannii* in diverse ecological niches, including wildlife, livestock, and aquatic environments [56,82,83]. These findings suggest that *A. baumannii* can persist outside clinical settings, potentially using environmental reservoirs to maintain a foothold from which it can re-enter healthcare facilities. Therefore, understanding their ecology, including the non-clinical reservoirs that may contribute to their persistence and transmission, will be crucial in formulating effective control measures. As such, *A. baumannii* remain a stark reminder of the challenges posed by antimicrobial resistance and the need for a coordinated One Health approach to tackle this global issue.

#### 2.4. *Pseudomonas aeruginosa*

*P. aeruginosa* is a Gram-negative bacterium that stands out for its adaptability and resilience across a wide range of environments, from soil and water to the human body. While it is typically found in natural settings such as rivers, lakes, and soil, it is also a notorious opportunistic pathogen, particularly in healthcare settings. It poses a significant threat to immunocompromised patients, where it can cause severe infections, including pneumonia, bloodstream infections, urinary tract infections, and chronic lung infections in individuals with cystic fibrosis [84–86].

The success of *P. aeruginosa* as a pathogen is largely due to its diverse arsenal of virulence factors and sophisticated regulatory networks that allow it to sense and adapt to different conditions [84,85]. These include the ability to form biofilms, which are complex communities of bacteria encased in a protective matrix that adhere to surfaces like medical devices and tissues. Biofilm formation not only helps *P. aeruginosa* evade the host immune response but also confers significant tolerance to antibiotics, complicating treatment. Moreover, the bacterium produces a variety of toxins and enzymes, such as elastases, exotoxins (e.g., ExoU and ExoS), and proteases, which contribute to tissue damage and impair host defenses [87–89].

Compounding its virulence is *P. aeruginosa*'s impressive ability to develop resistance to multiple classes of antibiotics [90]. This multidrug resistance (MDR) is driven by several mechanisms, including the overexpression of efflux pumps that expel antibiotics from the cell, enzymatic degradation of antibiotic molecules, and mutations in target sites that reduce drug binding. The emergence of carbapenem-resistant *P. aeruginosa* (CRPA) has become a global concern, as carbapenems are often used as last-resort antibiotics for treating MDR bacterial infections [91]. Resistance is frequently mediated by the production of carbapenemases, such as metallo- $\beta$ -lactamases (e.g., VIM and IMP), and loss of porins that decrease antibiotic uptake [17,92,93].

Beyond healthcare settings, *P. aeruginosa* is increasingly found in community and environmental contexts, including water sources, soil, and even in association with wildlife [94–96]. In aquatic environments, for example, *P. aeruginosa* can survive and persist, raising concerns about its role in the natural spread of resistance genes, which can be transferred to other bacteria via horizontal gene transfer [85,97].

To combat *P. aeruginosa*, a multifaceted approach is essential, combining the development of new therapeutic options with robust infection prevention measures, particularly in hospitals and long-term care facilities. Efforts to better understand its ecology, including the role of environmental reservoirs in sustaining and spreading resistant strains, are crucial for developing comprehensive strategies to curb the impact of this adaptable pathogen.

### 2.5. *Enterococcus* spp.

*Enterococcus* species, particularly *Enterococcus faecalis* and *Enterococcus faecium*, are important members of the gut microbiota in humans and animals, playing a largely commensal role [98]. However, they are also notorious as opportunistic pathogens capable of causing a variety of infections, including urinary tract infections, endocarditis, bacteremia, and wound infections [99]. These bacteria are well adapted to survive in harsh conditions, such as high salinity, a wide range of temperatures, and the presence of bile, which contributes to their persistence not only in the gut but also in hospital environments [98,100].

The shift from benign gut inhabitants to formidable pathogens is often associated with the acquisition of virulence factors that enhance their ability to colonize host tissues, evade immune defenses, and cause disease [98]. Virulence factors commonly found in pathogenic *Enterococcus* strains include surface adhesins like the enterococcal surface protein (*esp*), enzymes such as gelatinase (*gelE*) and hyaluronidase (*hyl*), and biofilm-forming capabilities that promote persistent infections, particularly on medical devices such as catheters and prosthetic valves [101,102].

Compounding their pathogenic potential is *Enterococcus*'s remarkable ability to develop resistance to a wide range of antibiotics, which is a major concern in healthcare settings. *Enterococcus faecium*, in particular, has emerged as a leading cause of hospital-acquired infections due to its high levels of resistance to multiple antibiotics, including aminoglycosides,  $\beta$ -lactams, and glycopeptides such as vancomycin [103,104]. The rise in vancomycin-resistant enterococci (VRE) poses a significant therapeutic challenge, as vancomycin is often used as a last-resort antibiotic for treating multidrug-resistant infections [105]. Resistance to vancomycin is typically mediated by the *vanA* and *vanB* gene clusters, which alter the bacterial cell wall target, reducing the efficacy of the antibiotic [106].

The ability of *Enterococcus* to acquire resistance genes through horizontal gene transfer is facilitated by the presence of mobile genetic elements like plasmids and transposons [107]. These elements can carry multiple resistance genes, allowing the bacteria to adapt rapidly to antibiotic pressures. The spread of resistance is further exacerbated by the environmental resilience of *Enterococcus*, which can survive in contaminated surfaces, water sources, and even in agricultural settings where antibiotics are used in livestock production [63,108].

This adaptability raises concerns about the dissemination of resistant *Enterococcus* strains from non-clinical settings to human populations, blurring the boundaries between hospital-acquired and community-associated infections.

In addition to healthcare environments, *Enterococcus* species have been increasingly detected in wildlife, livestock, and food products, highlighting their ecological versatility and the broader One Health implications [109–111]. The presence of VRE and multidrug-resistant strains in animals and the environment points to the interconnectedness of antimicrobial resistance across different sectors. Efforts to control the spread of resistant *Enterococcus* must therefore consider not only clinical interventions but also measures to reduce antibiotic use in agriculture and improve environmental management practices. Understanding the ecology and transmission dynamics of *Enterococcus* will be crucial in developing strategies to mitigate its impact as a pathogen and limit the spread of antimicrobial resistance.

### 3. ESKAPE Bacteria in Wildlife

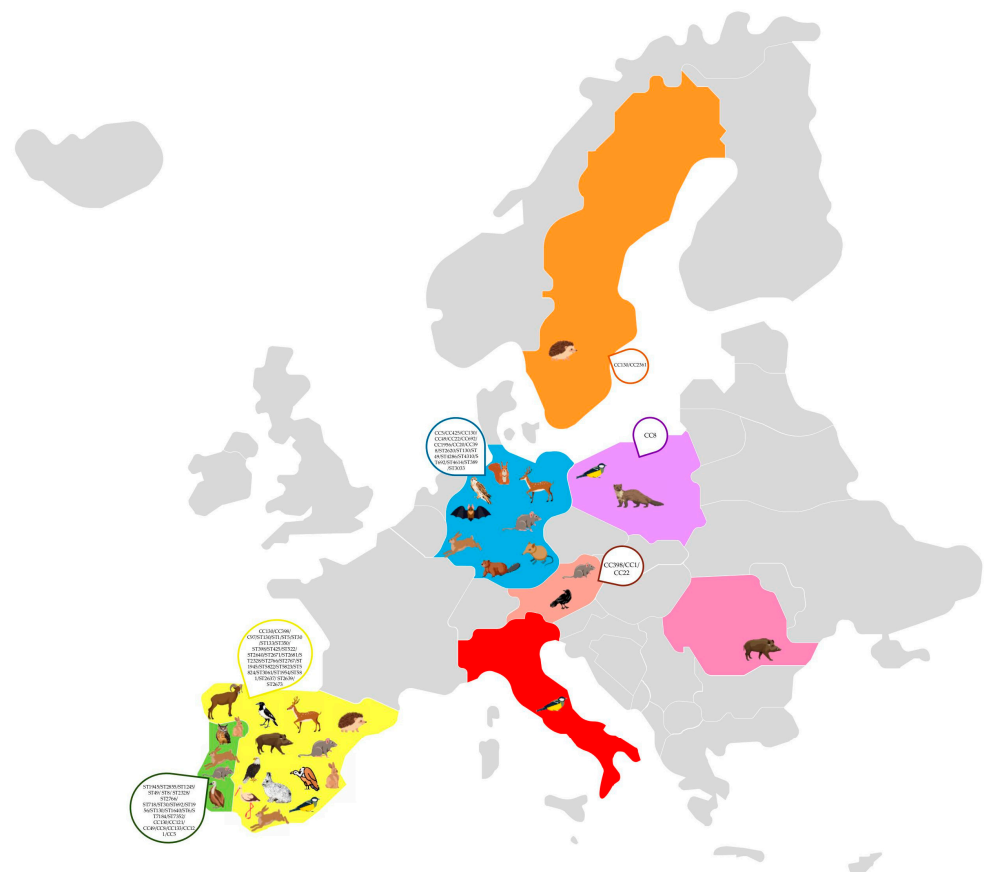
In recent years, it has become increasingly clear that the environment plays a crucial role in the ecology of pathogenic and antibiotic-resistant bacteria [112]. Wild animals, as they interact with habitats ranging from remote forests to urban and agricultural areas, are frequently exposed to contamination sources such as industrial effluents, hospital waste, and veterinary products [113,114]. This exposure means that wildlife can serve as unexpected reservoirs for pathogens of public health concern, including those within the ESKAPE group. These bacteria, known for their ability to evade antimicrobial treatments, are found not only in hospitals and farms but also among wildlife and in natural environments [115]. The detection of resistant strains in animals inhabiting natural ecosystems challenges the notion that resistance is solely a problem of anthropogenic settings, suggesting a continuous cycle of transmission between humans, domestic animals, wildlife, and the natural environment. Previous studies examined the resistome and the microbiome of migratory birds through metagenomic techniques and studied the resistance in *Escherichia coli* of wild birds [116,117]. Still, this review differs from the literature by presenting a more holistic approach to ESKAPE pathogens in the domain of wildlife and their clonally related lineages, resistance strategies, and possible dispersal mechanisms. This effort, which spans multiple species of bacteria and taxa of hosts, enhances the understanding of the spread of antimicrobial resistance in the world's ecosystems. This review provides a unique contribution to the field by consolidating data on ESKAPE pathogens in wildlife, offering a comparative perspective across different bacterial species and host taxa. Unlike previous studies that primarily address antimicrobial resistance trends in specific bacterial groups, our work synthesizes findings on all six ESKAPE pathogens, allowing for a more integrated understanding of their ecological and epidemiological significance. The identification of clonal lineages, resistance patterns, and transmission risks in wildlife underscores the importance of expanding surveillance efforts beyond clinical and agricultural settings. Future research should focus on genomic and functional studies to further elucidate the role of wildlife in AMR dissemination.

#### 3.1. *Staphylococcus aureus* and MRSA in Wild Animals

The detection of *S. aureus*, including methicillin-resistant *S. aureus* (MRSA), in wild animals across Europe highlights the potential role of wildlife as reservoirs and disseminators of antimicrobial resistance (Figure 2) [32]. Various studies have identified multiple clonal lineages, indicating a complex epidemiology with implications for both veterinary and human health (Table 1) [16,118–141]. The most frequently reported clonal complex in wildlife is CC130, particularly in association with the *mecC* gene, which confers methicillin

resistance. This clonal complex has been detected in numerous animal species, including rabbits, storks, hedgehogs, hares, rodents, and birds of prey, suggesting a widespread presence in different habitats [121,123,132,138,140,142]. In Spain and Portugal, for example, studies found *mecC*-positive MRSA belonging to ST130/CC130 in red deer, wild boars, and wild rodents, indicating that these animals may act as reservoirs for *mecC*-MRSA [118,137]. Similarly, in Sweden and Germany, *mecC*-carrying CC130 isolates have been found in a variety of wildlife, such as hedgehogs and rats, highlighting the geographical spread of this lineage across Northern and Central Europe [127,140].

Besides CC130, other clonal lineages have been detected in wild animals, demonstrating a diverse population structure of *S. aureus* in wildlife. For instance, CC425 has been identified in red deer in Germany [129]. Additionally, rare lineages such as ST2855 (CC121) and ST49 (CC49) have been reported in wild rodents and hares in Portugal, indicating the existence of localized clonal variants [122,137]. The resistance profiles of *S. aureus* isolates from wild animals exhibit variability, with many isolates displaying resistance primarily to  $\beta$ -lactam antibiotics due to the presence of the *mecA* or *mecC* genes. For instance, *mecC*-positive MRSA isolates frequently show resistance to penicillin and ceftiofur, while remaining susceptible to other antibiotic classes, reflecting the typical resistance pattern associated with *mecC*-carrying strains. In contrast, some isolates from wildlife, particularly those associated with CC398, exhibit broader resistance profiles, including resistance to tetracycline, erythromycin, and clindamycin, which may be linked to antibiotic use in livestock [120,127,132,135,139]. Several studies have reported the transmission of MRSA from animals to humans [143–145], with particular emphasis on *mecC*-MRSA, a strain predominantly found in animals but increasingly detected in human infections. These findings suggest the potential for zoonotic spillover, reinforcing the need for surveillance to understand transmission pathways and public health implications.



**Figure 2.** Molecular characteristics of *Staphylococcus aureus* clones in Europe.

**Table 1.** Animal species, location, and genetic lineages of *S. aureus* isolated from European wild animals.

Animal	Location	Clonal Lineages		SCCmec Type	agr Type	Resistance		Virulence		References
		MLST	spa Type			Phenotype	Genotype	IEC Types	Other Genes	
Red deer	Spain	CC130 ST130/CC130	t834; t1535 t843					E negative	<i>etd2</i> <i>seg, seh</i>	[118]
	Germany	CC425 ST1; ST5; ST30; ST133; ST350; ST398; ST425; ST522; ST2640; ST2671; ST2681	t15473 t098; t127; t11223; t548; t11210; t342; t2678; t11215; t571; t1077; t6386; t6909; t11208; t11212; t11228; t11231; t528; t1534; t3576; t742; t11211; t11226; t11233; t015; t11217							[129]
	Spain	ST130/CC130	t843					negative	<i>seg, seh</i>	[135]
Wild boars	Spain	ST130/CC130	t843					negative	<i>seg, seh</i>	[118]
	Romania					AUG, PEN				[136]
Wild rodents	Portugal	ST1945/CC130	t1525					E	<i>hld</i>	[137]
	Germany	CC130	t843					negative		[138]
Hedgehog	Spain	ST2328; ST2766; ST2767/CC130	t1535; t120; t12365; t12752; t9303; t3750; t12363; t12364						<i>mecC</i>	[135]
	Austria	CC398	t011						<i>mecA</i>	[139]
Rabbit	Spain	ST130/CC130	t843					negative	<i>seg, seh</i>	[118]
	Sweden	CC130; CC2361	t843; t10751; t978; t9111; t15312; t3391; t10893; t11015			CIP, DA, ERY, CN, KAN, TE				[140]
Rabbit	Spain	ST130/CC130 ST1945; ST5823/CC130	t843					negative negative	<i>seg, seh</i>	[141]
	Portugal	CC121	t272			Susceptible				[119]

Table 1. Cont.

Animal	Location	Clonal Lineages		SCCmec Type	agr Type	Resistance		Virulence		References
		MLST	spa Type			Phenotype	Genotype	IEC Types	Other Genes	
Mouflon	Spain	ST130/CC130	t843					negative	<i>seg, seh</i>	[141]
Hare	Spain	ST1945; ST5823/CC130						negative		[120]
	Germany	ST2620; ST130/CC130	t843; t10513; t3256; t4335							[121]
	Portugal	ST2855	t1190	III		PEN, FOX, ERY, DA, CN	<i>mecA,</i> <i>blaZ,</i> <i>ermC,</i> <i>ermB,</i> <i>mphC,</i> <i>aac(6')-Ie-</i> <i>aph(2'')-Ia</i>		<i>hla, hlb</i>	[122]
Stork	Spain	ST3061/CC130	t843					negative	<i>etd2</i>	[123]
	Italy					AMP, ENR, CIP				[124]
	Poland					MET	<i>mecA1/2,</i> <i>mecA3/4</i>			[125]
Wild birds	Italy					PIP, AMP, PEN, AUG, FOX, CAZ, CTR, CPD, IMI, CN, AK, S, AZ, TE, DO, CIP, DA, SXT, CHL, RD				[16]
	Spain					AMP, CIP, ERY, DA				[126]

Table 1. Cont.

Animal	Location	Clonal Lineages		SCCmec Type	agr Type	Resistance		Virulence		References
		MLST	spa Type			Phenotype	Genotype	IEC Types	Other Genes	
Red squirrel	Germany	ST49; ST4286; ST4310/CC49; CC22	t208; t307; t528			PEN, CHL, FQ	<i>blaZ</i> , <i>catpC221</i> , GyrA: Ser84Leu, GyrB: Leu469Val, GrlA: Ser80Phe		<i>lukM/lukF-P83</i> , <i>seg</i> , <i>sei</i> , <i>sem</i> , <i>sen</i> , <i>seo</i> , <i>seu</i>	[129]
Red kite	Germany	ST692/CC692	t14745							[129]
European beaver	Germany	ST4614/CC1956	t3058							[129]
Bat	Germany	ST389/CC20	t164						<i>seg</i> , <i>sei</i> , <i>sem</i> , <i>sen</i> , <i>seo</i> , <i>seu</i>	[129]
Wild Lagomorphs	Spain	ST1945; ST398; ST5822; ST5823; ST5824; ST1954/CC130; CC398		XI, V	III, I, II	PEN, FOX, ENR, TE	<i>mecA</i> , <i>mecC</i> , <i>blaZ</i> , SCC <i>mecXI</i> , SCC <i>mecV</i>	E		[120]
Wild rats	Germany	CC30; CC130; CC398	t685; t843; t011			PEN, MET	<i>mecA</i> , <i>mecC</i>			[127]



Table 1. Cont.

Animal	Location	Clonal Lineages		SCCmec Type	agr Type	Resistance		Virulence		References
		MLST	spa Type			Phenotype	Genotype	IEC Types	Other Genes	
Owl	Portugal	ST1245; ST49; ST8; ST2328; ST2766; ST718; ST30; ST692; ST1956; ST130; ST1640; ST6; ST7184; ST7352/CC130; CC49; CC8; CC133; CC121; CC130; CC5	t843; t208; t9811; t20169; t121; t3750; t12364; t11333; t9413; t1422; t20223; t9853; t16615; t2247; t2143	XI	III,II,I,IV	PEN, FOX, FA, CIP, TE, DA	<i>mecC</i> , <i>bla<sub>Z</sub>-SCCmecXI</i> , <i>bla<sub>Z</sub></i> , <i>tetK</i> , <i>ermA</i> , <i>mphC</i>	E, B	<i>hla</i> , <i>hly</i> , <i>etd2</i>	[128]
Wild raptors	Spain					AMP, AUG, NORF, CIP, ENR				[134]

Abbreviations: trimethoprim-sulfamethoxazole (SXT), ciprofloxacin (CIP), gentamicin (CN), streptomycin (S), tetracycline (TE), amoxicillin-clavulanic acid (AUG), enrofloxacin (ENR), doxycycline (DO), ampicillin (AMP), cefoxitin (FOX), imipenem (IMI), chloramphenicol (CHL), piperacillin (PIP), ceftriaxone(CTR), ceftazidime (CAZ), aztreonam (AZ), norfloxacin (NORF), clindamycin (DA), erythromycin (ERY), kanamycin (KAN), amikacin (AK), rifampicin (RD), cefpodoxime (CPD), fluoroquinolones (FQ), methicillin (MET), fusidic acid (FA), and penicillin (PEN).

In certain cases, multidrug-resistant MRSA strains have been identified. For example, wild birds in Portugal and red squirrels in Germany harbored isolates carrying both *mecA* and genes such as *ermB* (macrolide resistance) *tetK* (tetracycline resistance) and *catpC221* (chloramphenicol resistance), indicating exposure to diverse antimicrobial agents [128,129,133]. The pathogenic potential of *S. aureus* isolates from wildlife is underscored by the detection of multiple virulence genes. Common virulence factors include genes encoding for enterotoxins (*seg*, *seh*), leukocidins (*lukM/lukF-P83*), and hemolysins (*hla*, *hly*). For example, isolates from red deer in Spain have been found to carry the *seg* and *seh* genes, which encode staphylococcal enterotoxins implicated in food poisoning [118]. Similarly, strains isolated from red squirrels exhibited the presence of *lukM/lukF-P83*, which is known to enhance virulence in ruminants [129].

In addition to classical virulence genes, some wildlife-associated *S. aureus* strains possess unique adaptations. For instance, *etd2*, encoding an exfoliative toxin variant, has been found in strains from storks in Spain and owls in Portugal, suggesting the ability to colonize or infect avian hosts [123,128]. Additionally, some MRSA isolates from hedgehogs and rodents lacked certain immune evasion cluster (IEC) genes commonly found in human-adapted strains, potentially reflecting adaptations to the wildlife host [118,138].

### 3.2. Enterobacteriaceae in Wild Animals

The detection of *Enterobacteriaceae* in wild animals, especially antimicrobial-resistant strains, has significant implications for public health. These bacteria, which include pathogens such as *E. coli* and *K. pneumoniae*, are known for their ability to acquire and disseminate resistance genes, making them important indicators of environmental antimicrobial resistance. Studies across Europe have documented a diverse range of clonal lineages, resistance mechanisms, and virulence traits in *Enterobacteriaceae* isolated from wildlife, highlighting their role as potential reservoirs and sentinels for the spread of multidrug-resistant (MDR) bacteria [16,115,124,134,146–159] (Table 2). Various clonal lineages of *E. coli* have been reported in wild animals across Europe, with some lineages known for their relevance in human and animal infections. High-risk clones such as ST38, ST131, ST744, and ST410 have been identified in multiple studies [154,159]. For instance, ST38 and ST131, which are frequently associated with extraintestinal pathogenic *E. coli* (ExPEC) infections in humans, were found in gulls and other wild birds in Germany and Spain [154,159]. The presence of these lineages in wildlife suggests that wild birds may play a role in the environmental dissemination of ExPEC-related strains.

**Table 2.** Animal species, location, and genetic lineages of *Enterobacteriaceae* isolated from European wild animals.

Animal	Species	Location	Clonal Lineages		Resistance		Virulence	References
			MLST	Phenotype	Genotype			
Gulls	<i>E. coli</i>	France			<i>bla</i> <sub>VIM-1</sub>			[115]
		Germany	ST34; ST58; ST38; ST453; ST744; ST131; ST617; ST1598		<i>bla</i> <sub>CTX-M-14</sub> , <i>bla</i> <sub>CTX-M-15</sub> , <i>bla</i> <sub>CTX-M-55</sub> , <i>bla</i> <sub>CTX-M-27</sub> , <i>bla</i> <sub>CTX-M-32</sub>			[154]
		France	ST22; ST26; ST15		<i>bla</i> <sub>VIM-1</sub>			[155]
Apennine chamois	<i>E. coli</i>	Italy		AMP, CL,TE, CAZ, MRP	<i>bla</i> <sub>CMY2</sub> , <i>tetB</i> , <i>mcr-4</i> , <i>bla</i> <sub>TEM</sub> , <i>bla</i> <sub>CMY1</sub> , <i>bla</i> <sub>OXA-48</sub>			[156]

Table 2. Cont.

Animal	Species	Location	Clonal Lineages		Resistance Genotype	Virulence	References
			MLST	Phenotype			
Deer	<i>E. coli</i>	Italy		CL, TE, AMP, SXT	<i>bla</i> <sub>CMY2</sub> , <i>tetB</i> , <i>mcr-4</i> , <i>bla</i> <sub>TEM</sub> , <i>bla</i> <sub>CMY1</sub> , <i>bla</i> <sub>OXA-49</sub>		
		Italy		AMP, DA			[124]
Wild birds	<i>E. coli</i>	Italy		AMP, NFT, ENR, AK, DA	<i>bla</i> <sub>TEM</sub> , <i>sul3</i> , <i>int1</i> , <i>tetA</i>		
	<i>Escherichia fergusonii</i>			AMP, NFT, AK, DA			
	<i>Klebsiella oxytoca</i>			AMP, AUG, DA			
	<i>Escherichia albertii</i>			AMP, DA			
	<i>Salmonella enterica</i>			AMP, DA			
	<i>E. coli</i>	Italy		FOX, CPT, CTX, CAZ, AMP, AUG, CHL, AZ, NA, CIP, TE, SXT, CN			[157]
		Italy		AK, AUG, CL, TE, SXT, AUG, MAR, CTRX			[158]
	<i>Klebsiella</i> spp.	Italy		AMP, AUG, TE, PIP, SXT			[16]
	<i>Enterobacter</i> spp.	Italy		AMP, AUG, TE, PIP, SXT			
	<i>E. coli</i>	Spain	ST38; ST410; ST744		<i>bla</i> <sub>KPC-2</sub> , <i>bla</i> <sub>NDM-1</sub> , <i>bla</i> <sub>OXA-48</sub>		[159]
	<i>E. coli</i>	Ukraine			<i>bla</i> <sub>NDM-1</sub>		

Table 2. Cont.

Animal	Species	Location	Clonal Lineages		Resistance	Virulence	References
			MLST	Phenotype			
	<i>E. coli</i>	Greece		AMP, AUG, TCC, LEX, CLOT, CFP, TIO, CEQ, IMI, CN, FLU, ENR, MRB, SXT, N, TE	<i>bla</i> <sub>CTX-M-1</sub> , <i>bla</i> <sub>TEM</sub> , <i>bla</i> <sub>NDM</sub> , <i>bla</i> <sub>OXA-10</sub> , <i>aphA</i> , <i>aadA1</i> , <i>aadA2</i> , <i>ant(2)-Ia</i> , <i>qnrB</i> , <i>qnrS</i> , <i>sul1</i> , <i>sul2</i> , <i>dfrA5</i> , <i>dfrA12</i> , <i>mph</i> , <i>mrx</i> , <i>intI1</i>		[146]
	<i>E. coli</i>			T, CN, CIP, SXT, AMP, KAN, CHL	<i>tetA</i> , <i>sul2</i> , <i>sul3</i> , <i>bla</i> <sub>TEM</sub> , <i>aphA1</i> , <i>aadA</i> , <i>strA/strB</i>	<i>ompT</i> , <i>iss</i> , <i>cva/cvi</i> , <i>irp-2</i> , <i>iutA</i> , <i>papC</i> , <i>astA</i> , <i>tsh</i> , <i>iucD</i>	[147]
Rabbit	<i>E. coli</i>	Italy		AMP, AK, DA	<i>tetA</i> , <i>sul3</i> , <i>int1</i>		[124]
	<i>Enterobacter cloacae</i>			AMP, NFT, DA, SXT, TE			
Fox	<i>Klebsiella oxytoca</i>	Italy		AMP, DA			
Marten	<i>E. coli</i>	Italy		AMP, DA			
Wild boar	<i>Escherichia fergusonii</i>	Italy		AMP, DA			
Tortoise	<i>E. coli</i>	Italy		AMP, NFT, DA, SXT, TE	<i>bla</i> <sub>TEM</sub>		
	<i>Salmonella tennessee</i>			AMP, DA			
Turtle	<i>Klebsiella oxytoca</i>	Italy		AMP, DA			
	<i>Enterobacteriaceae</i>	Italy		AMP, SXT, TE, FOX, C, KAN, S, NA			[148]
Mouse	<i>E. coli</i>	Bulgaria		CN, TOB			[149]
	<i>Hafnia alvei</i>			AUG, AMP, CZ, LEX, CL			
	<i>Yersinia enterocolitica</i>			AUG, AMP, CZ, LEX			
	<i>Yersinia kristensenii</i>			AUG, AMP, TZP, CZ, CAZ, CXM, LEX, ERT			

Table 2. Cont.

Animal	Species	Location	Clonal Lineages		Resistance Genotype	Virulence	References
			MLST	Phenotype			
Vole	<i>Serratia marcescens</i>			AUG, AMP, CZ, CXM, LEX, CL, NFT			
	<i>Enterobacter cloacea</i>			AUG, AMP, CZ, FOS			
	<i>Serratia liquefaciens</i>			FOS			
	<i>Serratia proteamaculans</i>			AUG, AMP, CZ, CXM, CL, NFT			
Wild mammals	<i>Enterobacteriaceae</i>	Italy		CN, S, TOB, IMI, MER, CTX, CTX/CA, CAZ, CAZ/CA, CHL, CIP, AZ, AML, AUG, AMP, NA, DO, TE, SXT			[150]
Wildlife	<i>Enterobacteriaceae</i>				<i>bla</i> <sub>EC</sub> , <i>bla</i> <sub>TEM-1</sub> , <i>bla</i> <sub>CARB</sub> , <i>bla</i> <sub>A</sub> , <i>bla</i> <sub>ATC-27</sub>		[151]
Gulls	<i>K. pneumoniae</i>	Germany	ST290		<i>bla</i> <sub>CTX-M-15</sub>		[154]
Wild birds		Spain	ST11		<i>bla</i> <sub>KPC-3</sub>		[159]
Wild raptors		Spain		AMP, AUG, PIP, CZOL, CROX, CTX, CTRX, CAZ, CLEX, AZT, NORF, CIP, ENR, CN, TOB, TE, DO, SXT, DA			[134]

Table 2. Cont.

Animal	Species	Location	Clonal Lineages		Resistance		Virulence	References
			MLST	Phenotype	Genotype			
Wild animals		Italy	ST133; ST301; ST5670; ST2217; ST200; ST162; ST4895; ST277; ST219; ST116; ST23; ST35; ST3071	AMP, FOX, BPR, ETP, W, CLO, TE, CZOL	<i>bla</i> <sub>SHV-75</sub> , <i>bla</i> <sub>SHV-27</sub> , <i>bla</i> <sub>SHV-11</sub> , <i>bla</i> <sub>SHV-1</sub> , <i>bla</i> <sub>SHV-65</sub> , <i>bla</i> <sub>OKP-A-2</sub> , <i>bla</i> <sub>SHV-33</sub> , <i>tetA</i> , <i>sul2</i> , <i>strA</i> , <i>strB</i>	<i>iuc1</i> , <i>iuc3</i> , <i>iro1</i> , <i>clb2</i> , <i>rmpA</i> , <i>ybt1</i> , <i>ybt5</i> , <i>ybt9</i> , <i>ybt16</i>	[152]	
		Portugal		AML, AUG, TIM, AZ, IMI, KF, FOS, FOX, CFP, CIP, S, E, C, SXT, TE	<i>bla</i> <sub>OXA-aer</sub> , <i>bla</i> <sub>TEM</sub> , <i>bla</i> <sub>SHV</sub>		[153]	

Abbreviations: trimethoprim-sulfamethoxazole (SXT), ciprofloxacin (CIP), gentamicin (CN), streptomycin (S), tetracycline (TE), amoxicillin-clavulanic acid (AUG), enrofloxacin (ENR), doxycycline (DO), ampicillin (AMP), ceftazidime (CAZ), aztreonam (AZ), norfloxacin (NORF), clindamycin (DA), ceftobiprole (BPR), trimethoprim (W), cloxacillin (CLO), (MER), cefotaxime-clavulanic acid (CTX/CA), ceftazidime-clavulanic acid (CAZ/CA), nalidixic acid (NA), colistin (CL), nitrofurantoin (NFT), cefalexin (LEX), piperacillin + tazobactam (TZP), kanamycin (KAN), amikacin (AK), neomycin (N), marbofloxacin (MRB), flumequine (FLU), cefquinome (CEQ), ceftiofur (TIO), and cefepime (CPT).

Similarly, ST744 and ST410, often linked to resistance to extended-spectrum  $\beta$ -lactamases (ESBLs) and carbapenemases, have been detected in wildlife species such as wild birds in Spain, indicating the wide distribution of these resistant clones [159]. The occurrence of diverse clonal lineages in various wildlife species suggests that these animals encounter different sources of contamination, including human sewage, agricultural runoff, and other environmental reservoirs.

*Klebsiella pneumoniae* in wild animals has also shown a concerning pattern of clonal diversity. High-risk clones such as ST11, ST307, and ST35, which are associated with healthcare-related infections in humans, have been isolated from wild animals in Spain and Italy [152,159]. For example, ST11, a notorious clone linked to carbapenem resistance, was found in wild birds, suggesting possible exposure to contaminated water bodies or food sources [159]. Additionally, other clones, such as ST290 in Germany and ST5670 in Italy, have been reported in various wild mammals and birds, further indicating the potential role of wildlife in the persistence and spread of these lineages [152,154]. The resistance profiles of *Enterobacteriaceae* isolated from wild animals exhibit a wide range of antimicrobial resistance, often mirroring the patterns observed in clinical and agricultural settings. Many isolates possess genes encoding for ESBLs, such as *bla*<sub>CTX-M</sub>, *bla*<sub>TEM</sub>, and *bla*<sub>SHV</sub>, which confer resistance to third-generation cephalosporins [124,146,147,153,154,156]. For example, studies in Germany have identified *E. coli* isolates from wild birds carrying *bla*<sub>CTX-M-15</sub> and *bla*<sub>CTX-M-55</sub>, two of the most prevalent ESBL genes worldwide [154]. These findings suggest that wild birds may act as vectors for the dissemination of ESBL-producing strains across different geographic regions.

In addition to ESBLs, carbapenem-resistant *Enterobacteriaceae* (CRE) have also been detected in wildlife. *E. coli*-carrying carbapenemase genes such as *bla*<sub>VIM-1</sub> and *bla*<sub>NDM-1</sub> have

been reported in aquatic birds and rodents in France, Greece, and Ukraine [115,146,155,159]. The detection of these resistance genes in wildlife is particularly concerning, as carbapenems are considered last-resort antibiotics for treating multidrug-resistant infections. The presence of CRE in wildlife habitats may be linked to the contamination of water bodies with untreated sewage or agricultural runoff.

Resistance to colistin, a last-resort antibiotic for treating multidrug-resistant *Enterobacteriaceae*, has also been documented. The mobile colistin resistance gene *mcr-4* was found in *E. coli* isolates from deer and apennine chamois in Italy, indicating the spread of plasmid-mediated colistin resistance in natural environments [156]. This highlights the potential for wildlife to serve as reservoirs for colistin-resistant bacteria, which can pose a significant challenge to public health.

*K. pneumoniae* isolates from wild animals have shown multidrug resistance, including resistance to  $\beta$ -lactams, aminoglycosides, fluoroquinolones, and tetracyclines. For instance, isolates from gulls and raptors in Spain harbored genes such as *bla*<sub>KPC-3</sub>, *bla*<sub>OXA</sub>, and *bla*<sub>CTX-M-15</sub>, indicating the presence of highly resistant clones [153,154,159]. The detection of carbapenemase-producing *K. pneumoniae* in wild birds suggests that these animals could facilitate the environmental spread of carbapenem-resistant strains.

The pathogenic potential of *Enterobacteriaceae* from wild animals is indicated by the presence of numerous virulence factors. In *E. coli*, common virulence genes include *ompT*, *iss*, *papC*, and *cva/cvi*, which are associated with ExPEC strains capable of causing urinary tract infections and sepsis in humans [160,161]. For instance, *E. coli* isolates from birds in Poland were found to carry combinations of these genes, suggesting that these strains could pose a zoonotic risk [147].

In *K. pneumoniae*, virulence factors such as siderophore genes (*ybt*, *iro*, *iuc*), which enhance iron acquisition, and capsular polysaccharide genes (*rmpA*, *rmpA2*), associated with hypervirulence, were detected in isolates from gulls and other birds [152]. These virulence traits, coupled with antibiotic resistance, indicate that wildlife-associated *K. pneumoniae* may have a significant pathogenic potential, similar to the strains found in human clinical settings. Numerous studies provide evidence of the transmission of *Enterobacteriaceae* from animals to humans, particularly in pets and food-producing animals, where close contact or the food chain facilitates dissemination [162–165]. However, transmission from wild animals to humans is less evident and much more challenging to trace. Despite this, it can still occur through direct contact with wildlife or indirectly via environmental contamination, such as through water sources, soil, or food products exposed to resistant strains.

### 3.3. *A. baumannii* in Wild Animals

The presence of *A. baumannii* in wild animals is a growing concern due to its potential role as a reservoir for multidrug-resistant strains that pose a significant risk to both veterinary and human health. However, studies of *A. baumannii* in wildlife are still very scarce [134,148,150,153,166–168] (Table 3). This opportunistic pathogen is known for causing healthcare-associated infections, and its detection in wildlife suggests that environmental transmission pathways could contribute to the spread of resistance genes [169,170]. Studies across Europe have identified various clonal lineages, resistance mechanisms, and virulence traits in *A. baumannii* isolated from different wild animal species.

**Table 3.** Animal species, location, and genetic lineages of *Acinetobacter baumannii* isolated from European wild animals.

Animal	Species	Location	Clonal Lineages	Resistance		Virulence	References
			MLST	Phenotype	Genotype		
Turtles	<i>A. baumannii</i>	Italy		AMP, SXT, TE, FOX, C, K, S, NA			[148]
Wild mammals		Italy		CN, S, TOB, IMI, MER, CTX, CTX/CA, CAZ, CAZ/CA, C, CIP, AZ, AML, AUG, AMP, NA, DO, TE, SXT			[150]
Wild raptors		Spain		AMP, AUG, CZOL			[134]
Wild animals		Portugal		AML, AUG, TIM, ATM, IMI, CLOT, FOS, FOX, CFP, CIP, S, E, C, SXT, TE			[153]
Goose			ST1447; ST836				[166]
White stork		Germany			bla <sub>OXA-314</sub> , bla <sub>OXA-71</sub> , bla <sub>OXA-95</sub> , bla <sub>OXA-378</sub> , bla <sub>OXA-64</sub>		
		Poland	ST1459; ST1458		bla <sub>OXA-93</sub> , bla <sub>OXA-374</sub> , bla <sub>OXA-314</sub> , bla <sub>OXA-67</sub> , bla <sub>OXA-375</sub> , bla <sub>OXA-376</sub> , bla <sub>OXA-377</sub> , bla <sub>OXA-388</sub> , bla <sub>OXA-378</sub> , bla <sub>OXA-379</sub> , bla <sub>OXA-65</sub> , bla <sub>OXA-380</sub> , bla <sub>OXA-381</sub> , bla <sub>OXA-382</sub> , bla <sub>OXA-383</sub> , bla <sub>OXA-389</sub> , bla <sub>OXA-384</sub> , bla <sub>OXA-390</sub> , bla <sub>OXA-69</sub> , bla <sub>OXA-51</sub> , bla <sub>OXA-338</sub> , bla <sub>OXA-429</sub> ,		[167]

Table 3. Cont.

Animal	Species	Location	Clonal Lineages		Resistance	Virulence	References
			MLST	Phenotype			
		Poland			bla <sub>OXA-104</sub> , bla <sub>OXA-413</sub> , bla <sub>OXA-430</sub> , bla <sub>OXA-402</sub> , bla <sub>OXA-208</sub> , bla <sub>OXA-432</sub> , bla <sub>OXA-433</sub>		[167]
		Germany			bla <sub>OXA-378</sub> , bla <sub>OXA-374</sub>		
Lizard		Ukraine	ST1292	PEN, AUG, AMP, ERY, CN, TE, TIA, SPT, FFC, TUL, TIL, CLOT, TIO	bla <sub>OXA-132</sub>		[168]

Abbreviations: trimethoprim-sulfamethoxazole (SXT), ciprofloxacin (CIP), gentamicin (CN), streptomycin (S), tetracycline (TE), tiamulin (TIA), spectinoycin (SPT), tulathromycin (TUL), amoxicillin-clavulanic acid (AUG), penicillin (PEN), doxycycline (DO), ampicillin (AMP), ceftazidime (FOX), imipenem (IMI), florfenicol (FFC), nalidixic acid (NA), cefazolin (CZOL), cefotaxime (CTX), cephalotin (CLOT), erythromycin (ERY), tilmicosin (TIL), ceftiofur (TIO), amoxicillin (AML), ticarcillin/clavulanic acid (TIM), aztreonam (AZ), fosfomycin (FOS), cefoperazone (CFP), tobramycin (TOB), meropenem (MER), ceftazidime (CAZ), cefotaxime-clavulanic acid (CTX/CA), and ceftazidime-clavulanic acid (CAZ/CA).

The detection of *A. baumannii* in wildlife has been reported in several European countries, with varying clonal lineages indicating a broad genetic diversity [134,148,150,153,166–168]. However, high-risk clones such as ST2, ST25, and ST78, which are often associated with hospital outbreaks, were not detected in wild animals in those studies. *A. baumannii* clones ST1447 and ST836, which have been identified in geese in Germany, were first reported in Brazilian hospitals and in sewage water from a poultry slaughterhouse, respectively [166,171,172]. These findings highlight the potential for wildlife to harbor distinct *A. baumannii* strains not commonly found in clinical settings, possibly reflecting local adaptation or exposure to environmental sources of contamination. In Southern Europe, particularly in Italy, Spain, and Portugal, *A. baumannii* has been isolated from various wild animals, including turtles, raptors, and wild mammals, suggesting that wildlife in Mediterranean areas may act as a reservoir for specific *A. baumannii* genotypes, some of which may possess environmental origins [134,148,150,153]. The detection of these strains across different animal species and geographical regions points to the potential for cross-species transmission or shared environmental sources, such as water bodies or contaminated soils.

The antimicrobial resistance profiles of *A. baumannii* isolated from wild animals often indicate multidrug resistance (MDR), with resistance to  $\beta$ -lactams, aminoglycosides, fluoroquinolones, and tetracyclines being frequently observed. A significant concern is the detection of carbapenem-resistant *A. baumannii* (CRAB), as carbapenems are considered last-resort antibiotics for treating MDR bacterial infections [173,174]. Carbapenem resistance in wildlife-associated *A. baumannii* is often mediated by the presence of bla<sub>OXA</sub> genes, which encode carbapenem-hydrolyzing class D  $\beta$ -lactamases [166–168]. For instance, the bla<sub>OXA-314</sub> gene was detected in isolates from geese in Germany and from geese and white storks in Poland, indicating a geographically widespread distribution of these resistance genes in wildlife. The presence of these resistance genes suggests exposure to contaminated environments where antibiotics may be present, such as agricultural lands, wastewater discharge areas, or locations impacted by human activity. *A. baumannii* is

primarily known as a human pathogen associated with healthcare infections, but increasing evidence suggests its presence in animals, raising concerns about zoonotic transmission. Human-to-animal transmission has been documented, particularly in pets such as dogs and cats, where strains genetically similar to human clinical isolates have been identified. Animal-to-human transmission is less well understood but has been reported in livestock, where *A. baumannii* has been isolated from cattle and pigs, with potential transmission routes through direct contact or environmental contamination [175–178].

### 3.4. *P. aeruginosa* in Wild Animals

Studies in *P. aeruginosa* isolated from wild animals are also very scarce [95,124,134,136,148,179,180]. *P. aeruginosa* is a versatile opportunistic pathogen found in various environments and is a significant concern due to its ability to acquire multidrug resistance [181,182]. Although it is primarily associated with hospital-acquired infections, its presence in wildlife suggests that natural environments could serve as reservoirs or transmission pathways for resistant strains. Several studies suggest that *P. aeruginosa* can be transmitted between animals and humans, either through direct contact with infected animals or indirectly via contaminated environments, water, or food. While most cases in humans are linked to healthcare settings, evidence indicates zoonotic and reverse zoonotic transmission. For example, a study documented the transmission of a carbapenem-resistant *P. aeruginosa* strain (ST233, VIM-2 producer) between a dog, its owner, and their household environment. Additionally, poultry has been identified as a potential reservoir, with strains capable of infecting humans through foodborne exposure [96,183–185]. These findings highlight the need for surveillance and a One Health approach to monitor the spread of *P. aeruginosa* across human, animal, and environmental interfaces. Studies across Europe have reported various clonal lineages, resistance patterns, and virulence traits in *P. aeruginosa* isolates from wild animals, indicating a potentially significant role in the ecology of antimicrobial resistance (Table 4) [95,124,134,136,148,179,180].

**Table 4.** Animal species, location, and genetic lineages of *P. aeruginosa* isolated from European wild animals.

Animal	Species	Location	Clonal Lineages	Resistance		Virulence	References
			MLST	Phenotype	Genotype		
Wild birds	<i>P. aeruginosa</i>	Italy		AMP, AUG, NFT, ENR, CIP, DA, SXT			[124]
		England		CPT, CIP, LEV			[95]
Wild boars		Romania		AUG, FFC, CEP, PEN, TY			[136]
		Spain	ST1711; ST1648; ST2252; ST2194	DOR		<i>exlA</i> , <i>exoS</i> , <i>exoY</i> , <i>exoT</i> , <i>exoA</i> , <i>lasA</i> , <i>lasB</i> , <i>aprA</i> , <i>rhlAB</i> , <i>rhlC</i> , <i>rhlI</i> , <i>rhlR</i> , <i>lasI</i> , <i>lasR</i>	[179]

Table 4. Cont.

Animal	Species	Location	Clonal Lineages	Resistance		Virulence	References
			MLST	Phenotype	Genotype		
Turtles		Italy		AMP, SXT, TE, FOX, CHL, KAN, S, NA			[148]
Red deer		Portugal	ST274	IMI	<i>bla</i> <sub>PAO</sub> , <i>bla</i> <sub>PDC-24</sub> , <i>bla</i> <sub>OXA-486</sub> , <i>aph</i> (3')-IIb, <i>fosA</i> , <i>catB7</i>		[180]
Wild raptors		Spain		AMP, AUG, CZOL, CROX, CTAX, CTRX, CLEX, CLOT, TE, DO, SXT, DA			[134]

Abbreviations: trimethoprim-sulfamethoxazole (SXT), ciprofloxacin (CIP), streptomycin (S), tetracycline (TE), amoxicillin-clavulanic acid (AUG), enrofloxacin (ENR), clindamycin (DA), nitrofurantoin (NFT), penicillin (PEN), doxycycline (DO), ampicillin (AMP), kanamycin (KAN), ceftiofur (FOX), imipenem (IMI), levofloxacin (LEV), florfenicol (FFC), cephalexin (CEP), tylosin (TY), doripenem (DOR), nalidixic acid (NA), cefazolin (CZOL), cefuroxime (CROX), ceftriaxone (CTR), cephalexin (CLEX), and cephalotin (CLOT).

Among the collected studies, only two documented diverse clonal lineages of *P. aeruginosa* in wild animals. The globally prevalent high-risk clone ST274 and its associated clonal complex (CC274) are primarily linked to hospital environments and are frequently found colonizing cystic fibrosis patients across different regions [186]. Nevertheless, this high-risk clone has been identified in wild raptors in Spain, suggesting a possible spillover from human-impacted environments to wildlife. [179,180]. Additionally, novel lineages have been identified in wild animals, including ST1711 and ST2252 in Spain, which have not been commonly associated with human infections. *P. aeruginosa* ST1711 has been reported in non-clinical samples, while ST2252 has been identified in both non-clinical samples and among healthy animals also in Spain [179,187]. In some cases, the isolates showed a high degree of genetic diversity, indicating the presence of both well-known and novel clonal types circulating among various animal species. Geographically, *P. aeruginosa* has been reported in a wide range of habitats, including wetlands, forests, and coastal areas, where animals such as wild boars, turtles, and birds of prey reside [94,188]. The widespread detection across different ecosystems suggests that wildlife could play a role in the environmental dissemination of *P. aeruginosa*.

The antimicrobial resistance profiles of *P. aeruginosa* isolated from wild animals often reveal significant multidrug resistance, including resistance to  $\beta$ -lactams, aminoglycosides, fluoroquinolones, and carbapenems. Resistance to carbapenems, such as imipenem (IMI) and doripenem (DOR), is particularly concerning, as these antibiotics are used as last-resort treatments for serious *P. aeruginosa* infections [189,190]. Carbapenem resistance mechanisms in wildlife-associated isolates are often related to the production of  $\beta$ -lactamases, such as VIM, IMP, OXA, and GES metallo- $\beta$ -lactamases, as well as alterations in porin channels and efflux pump overexpression. For instance, carbapenem-resistant *P. aeruginosa* isolates from red deer in Portugal were found to carry *bla*<sub>OXA-486</sub> [180]. Resistance to other antibiotics, including fluoroquinolones (e.g., ciprofloxacin), aminoglycosides (e.g., gentamicin), and tetracyclines, has also been observed. In birds of prey from Spain and wild boars from Italy, *P. aeruginosa* isolates exhibited high resistance rates to aminoglycosides and

fluoroquinolones, possibly due to exposure to contaminated environments where these antimicrobials are present, such as agricultural runoff or water bodies affected by human waste [134,191].

The pathogenic potential of *P. aeruginosa* isolates from wild animals is underscored by the detection of various virulence factors, which contribute to the bacterium's ability to cause disease in humans and animals. Only one study reported the presence of virulence genes among *P. aeruginosa* from wild boars in Spain [179]. Virulence genes identified include those encoding exotoxins (*exoS*, *exoY*, *exoT*), elastases (*lasB*), and alkaline proteases (*aprA*), which are associated with tissue invasion and immune evasion [179]. The presence of quorum sensing systems, which regulate the expression of virulence factors, further indicates the pathogenic potential of these isolates. Genes like *lasI* and *rhlI* involved in quorum sensing were found in isolates from healthy animals, suggesting that these bacteria may coordinate virulence gene expression to adapt to different hosts or environmental conditions.

### 3.5. *E. faecium* in Wild Animals

*Enterococcus* spp., particularly *Enterococcus faecium* and *Enterococcus faecalis*, are commensal bacteria of the gastrointestinal tract in various hosts but can also act as opportunistic pathogens causing severe infections in humans and animals [98,192]. The detection of multidrug-resistant *Enterococcus* in wild animals suggests that wildlife may serve as reservoirs or vectors for the dissemination of resistance genes and virulent strains. Studies across Europe have identified diverse clonal lineages, resistance mechanisms, and virulence factors in *Enterococcus* isolates from wildlife, highlighting their significance in the One Health context (Table 5) [16,124,125,134,149,156,193–204].

**Table 5.** Animal species, location, and genetic lineages of *Enterococcus faecium* isolated from European wild animals.

Animal	Species	Location	Clonal Lineages	Resistance		Virulence	References
			MLST	Phenotype	Genotype	Other Genes	
Apennine chamois	<i>E. faecium</i>	Italy	LNZ, QD, TEIC, TE, VAN		<i>msrC</i> , <i>tetB</i> , <i>cfrD</i>		[156]
		Italy	QD, VAN, LNZ		<i>msrC</i> , <i>cfrD</i>	<i>gelE</i> , <i>efa</i>	
Deer	<i>E. faecium</i>	Italy	QD				
		Italy	QD		<i>msrC</i>	<i>gelE</i>	
Wild birds	<i>E. faecium</i>	Italy	NFT, SXT				[124]
		Poland	VAN, TEC		<i>vanA</i> , <i>vanB</i>		[125]
		Italy	PEN, ERY, DO, TE				[16]
		Italy	RD, C, LZD, F, W, N, CN, S, KE, CIP, ENR, TEC, VAN, ERY, QD, DA, OX, AUG, AMP, TE, TIG		<i>aac(6')</i> -Ie- <i>aph(2'')</i> -Ia, <i>ant(6)</i> -Ia, <i>aac(6')</i> -Ii, <i>tetM</i> , <i>tetL</i> , Int-Tn		[201]

Table 5. Cont.

Animal	Species	Location	Clonal Lineages	Resistance		Virulence	References
			MLST	Phenotype	Genotype	Other Genes	
		Slovakia		AMP, ERY, TE	<i>ermB</i> , <i>mefA</i> , <i>tetM</i> , <i>tetL</i> , <i>vanC</i>		[202]
		Poland	ST2340; ST2341; ST2342; ST121; ST32; ST22; ST2067; ST54; ST241	QD, CL, CIP, ERY, CN, TE	<i>aac(6')-Ii</i> , <i>aacA-ENT1</i> , <i>aph(2'')-Ih</i> , <i>aph(3')-IIIa</i> , <i>spw</i> , <i>Isa(E)</i> , <i>Inu(B)</i> , <i>msr(C)</i> , <i>erm(B)</i> , <i>tetM</i> , <i>tetL</i> , <i>fexA</i> , <i>catA8</i> , <i>dfrE</i> , <i>sat4</i>		[203]
		Germany	ST121			<i>ptsD</i> , <i>orf1481</i> , IS16, <i>sgrA</i> , <i>hyl</i> , <i>acm</i> , <i>fms20</i> , <i>fms14</i> , <i>ebpA</i> , <i>fms16</i>	[204]
		Slovakia	ST917; ST6			<i>ptsD</i> , <i>orf1481</i> , IS16, <i>sgrA</i> , <i>ecbA</i> , <i>acm</i> , <i>fms20</i> , <i>fms14</i> , <i>ebpA</i> , <i>fms16</i>	
		Czech Republic	ST92			<i>fms20</i> , <i>fms14</i> , <i>ebpA</i> , <i>fms16</i>	
		Portugal	ST18; ST448; ST139/CC17; CC5	AMP, S, KAN, TE, ERY, QD, CIP, VAN, TEI	<i>vanA</i> , <i>erm(B)</i> , <i>tet(M)</i> , <i>aph(3')</i> , <i>ant(6')</i> , <i>vat(E)</i> , <i>aac(6')</i>	<i>esp</i> , <i>hyl</i>	[200]
		Poland	ST1266; ST1272; ST17; ST1267; ST1271; ST957; ST32; ST683; ST1203; ST1270; ST429; ST29; ST636; ST512; ST70; ST1268; ST1269/CC17	LNZ, ERY, CIP, TE, DO, S, KAN, CN, PEN, AMP	<i>erm(B)</i> , <i>msr(A/B)</i> , <i>tetM</i> , <i>tetL</i> , <i>ant(6)-Ia</i> , <i>aph(3')-IIIa</i> , <i>aph(2'')-Id</i> , <i>pbp5</i> , Int-Tn		[193]

Table 5. Cont.

Animal	Species	Location	Clonal Lineages	Resistance		Virulence	References
			MLST	Phenotype	Genotype	Other Genes	
		Poland				<i>ebpA, ebpC, srt, ace, agg, asa1, efaAfm, gelE, sprE, fsrA, fsrB, fsrC, cpd, cob, ccf</i>	[194]
Mouse		Bulgaria		FOX, CPT, CIP, CN, ERY, FA, SXT			[149]
Wild animals		Italy		VAN, TE, ERY, CN, CIP	<i>tetM, tetL, ermB, msrA/B, msrC, aac(6)-Ii, ant(4')-Ia, int-Tn</i>	<i>efaAfm, gelE, esp, ace, orf1481, ptsD, sgrA</i>	[195]
Wild mammals		Spain		QD, AUG, CL, CIP, ERY, CN, S, TE			[196]
		Slovakia		AMP, ERY, TE, VAN	<i>ermB, mefA, tetM, tetL, vanC</i>		[202]
Red foxes		Latvia		CIP, DA, ERY, QD, TE	<i>aac(6')-I, ant(6)-Ia, spw, tetM, tetL, lsaA, lsaE, msrC, lnuB, lnuG</i>		[197]
Wildlife		Poland		S, CN, KA, CIP, ENR, ERY, TE, AMP, PEN, CHL	<i>aac(6')-Ie-aph(2')-Ia, aph(3')-IIIa, ant(6)-Ia, ermB, msrA, ermA, tetL, tetM, tetK, tetO, tndX, Int-Tn, ant(9)-Ia, aph(2')-Ic, catA8, catA7, catA9</i>		[198]

Table 5. Cont.

Animal	Species	Location	Clonal Lineages	Resistance		Virulence	References
			MLST	Phenotype	Genotype	Other Genes	
		Poland	ST8, ST12, ST18, ST21, ST22, ST32, ST56, ST190, ST241, ST264, ST370, ST502, ST640, ST666, ST668, ST887, ST901, ST907, ST944, ST1144, ST1230, ST1607			<i>efaA</i> , <i>ccf</i> , <i>gelE</i> , <i>efaA</i> , <i>cpd</i> , <i>cylB</i> /1	[199]
Wild raptors		Spain		CLEX, DA			[134]

Abbreviations: trimethoprim-sulfamethoxazole (SXT), ciprofloxacin (CIP), streptomycin (S), gentamicin (CN), tetracycline (TE), amoxicillin-clavulanic acid (AUG), quinupristin/dalfopristin (QD), teicoplanin (TEIC), tigecycline (TIG), vancomycin (VAN), enrofloxacin (ENR), chloramphenicol (CHL), cephalixin (CLEX), clindamycin (DA), linezolid (LNZ), nitrofurantoin (NFT), teicoplanin (TEC), penicillin (PEN), erythromycin (ERY), doxycycline (DO), rifampicin (RD), trimethoprim(W), neomycin (N), cephalothin (KF), oxacillin (OX), ampicillin (AMP), kanamycin (KAN), cefepime (CPT), fusidic acid (FA) and colistin (CL).

The genetic diversity of *Enterococcus* [109] isolates from wild animals is considerable, with various clonal lineages commonly associated with human and veterinary infections. In Europe, CC17, a high-risk lineage associated with hospital-acquired infections, has been frequently identified in wild birds and mammals, indicating that these animals could act as reservoirs for lineages typically associated with human clinical settings [193,200]. In addition to CC17, other clonal lineages such as ST121, ST32, and ST448 have been reported in wild animals. For instance, ST121 and ST32 were detected in wild birds in Germany and Poland, suggesting potential transmission or environmental contamination linked to agricultural activities or human waste [203,204]. ST448, associated with multidrug resistance, was found in wild partridges in Portugal, indicating that wildlife in various ecological niches can harbor diverse *Enterococcus* lineages.

Geographically, *Enterococcus* isolates from wildlife have been reported across a wide range of habitats, from forested areas and rural landscapes to urban environments. Studies have documented the presence of *Enterococcus* in species such as birds, rodents, foxes, and wild boars across countries including Spain, Italy, Poland, Slovakia, and the Czech Republic. This widespread distribution indicates that wild animals living in different environments are exposed to factors that promote the acquisition and spread of *Enterococcus* strains [200,205].

The antimicrobial resistance patterns of *Enterococcus* isolates from wild animals often reflect significant multidrug resistance, with resistance to antibiotics such as glycopeptides (e.g., vancomycin), aminoglycosides (e.g., gentamicin), tetracyclines, macrolides (e.g., erythromycin), and  $\beta$ -lactams (e.g., ampicillin). The detection of vancomycin-resistant

enterococci (VRE) in wildlife is of particular concern, as vancomycin is a last-resort antibiotic for treating MDR *Enterococcus* infections [206]. Vancomycin resistance in *Enterococcus* is usually mediated by the presence of *vanA* or *vanB* gene clusters, which encode enzymes that alter the bacterial cell wall to reduce vancomycin binding [207]. Several studies have reported the presence of *van* genes in *E. faecium* isolates from wild birds and mammals in Poland, Portugal, and Slovakia [125,200,202]. In addition to glycopeptide resistance, *Enterococcus* isolates from wild animals often exhibit resistance to other antibiotics. Resistance genes such as *ermB* (macrolides), *tetM* and *tetL* (tetracyclines), *aac(6′)-I* and *ant(6)-Ia* (aminoglycosides), and *pbp5* ( $\beta$ -lactams) have been commonly detected. For example, Red foxes in Latvia harbored *Enterococcus* strains resistant to macrolides, tetracyclines, and lincosamides, and rodents in Bulgaria carried *E. faecium* showing resistance to ciprofloxacin, aminoglycosides, macrolides, and trimethoprim-sulfamethoxazole [149,197]. The presence of these resistances suggests that wildlife is exposed to environments contaminated with antibiotic residues, which may select for resistance. The detection of multidrug resistance, including combinations of vancomycin resistance and resistance to other antibiotic classes, poses a significant risk for the transfer of resistance genes across different reservoirs, including humans, animals, and the environment.

Virulence factors in *Enterococcus* species contribute to their ability to cause infections in humans and animals. These factors include genes encoding for surface adhesins, biofilm formation, and extracellular enzymes [208,209]. In wildlife-associated isolates, common virulence genes include *esp* (enterococcal surface protein), *gelE* (gelatinase), *asa1* (aggregation substance), *efaA* (endocarditis antigen), and *hyl* (hyaluronidase). The presence of the *esp* gene, which is associated with biofilm formation and colonization of host tissues, has been frequently reported in *E. faecium* isolates from wild animals, including wild birds in Portugal and several wild mammals in Italy [195,200,210]. The ability to form biofilms enhances the persistence of these bacteria in the host and environment, potentially facilitating transmission and colonization of new hosts [208,209]. The detection of *gelE* and *asa1* in *Enterococcus* isolates from wildlife further indicates a potential for pathogenicity. For example, several studies reported the presence of *gelE* and *asa1* in *E. faecalis* isolates from Apennine chamois and deer in Italy, as well as several animal species in Poland [156,194,199], suggesting that these strains could pose a risk for causing opportunistic infections. Additionally, the presence of *hyl*, found in some VRE isolates from wild birds in Portugal, suggests an enhanced ability to degrade host tissues and evade immune responses [200]. The genetic adaptability of *Enterococcus* is often facilitated by horizontal gene transfer (HGT), which allows for the acquisition of antibiotic resistance genes and virulence factors. Mobile genetic elements such as plasmids, transposons, and integrative conjugative elements play a key role in the dissemination of resistance genes across different bacterial populations [211–213]. In wildlife-associated *Enterococcus*, several studies have documented the presence of mobile genetic elements carrying resistance genes. For example, the *Tn1546* transposon, which carries the *vanA* gene cluster, has been found in VRE isolates from wild birds in Portugal [200]. Similarly, conjugative plasmids carrying multiple resistance genes, including *ermB*, *aac(6′)-I*, and *tetM*, have been identified in *E. faecium* and *E. faecalis* from wild mammals in Poland and the Czech Republic [125,204]. The detection of these elements highlights the potential for wildlife to contribute to the spread of resistance genes through HGT. Evidence of human-to-animal and animal-to-human transmission has been reported, particularly in companion animals and livestock [199,214–216]. Pets, such as dogs and cats, have been found to carry strains genetically similar to those isolated from hospitalized patients, suggesting possible bidirectional transmission. In livestock, *E. faecium* has been detected in farm animals, particularly in those exposed to antibiotics, raising concerns about its potential spread to humans through direct contact or the food chain. The increasing

detection of VRE in non-human hosts highlights the importance of surveillance and a One Health approach to mitigate its spread across human, animal, and environmental interfaces.

#### 4. Implications for One Health

The presence of ESKAPE bacteria in wild animals has critical implications for public health, veterinary medicine, and ecosystem integrity. These bacteria, known for their role in hospital-acquired infections and multidrug resistance, are increasingly found in wildlife, raising concerns about the broader environmental dynamics of antimicrobial resistance and the potential risks posed to humans and domestic animals. The detection of diverse resistant and virulent strains across various wildlife species and geographical locations underscores the interconnectedness of human, animal, and environmental health, emphasizing the need for a One Health approach to combatting AMR [16].

Wild animals are often exposed to contaminated environments, which can act as reservoirs for resistant bacteria and antimicrobial residues [217]. Habitats near urban centers, agricultural areas, or water bodies impacted by human activities frequently harbor high levels of contaminants, including antibiotics and resistant bacteria shed by humans or livestock [217,218]. For example, surface waters polluted with untreated sewage, agricultural runoff, or waste from pharmaceutical production can serve as hotspots for the spread of resistant bacteria across different species [219]. Wild birds, rodents, and aquatic mammals that frequent these areas can acquire and carry ESKAPE bacteria, effectively acting as vectors that facilitate the movement of resistance genes across ecological boundaries. The evidence of ESKAPE pathogens, such as carbapenem-resistant *Acinetobacter baumannii* and ESBL-producing *Enterobacteriaceae*, in wildlife highlights the permeability of barriers between natural and human-impacted environments [56,217]. The presence of bacteria in wild animals suggests a bidirectional flow of resistance genes between wildlife and anthropogenic sources. While some strains found in wildlife may be of environmental origin, others share clonal lineages with human clinical isolates, indicating possible spillover from healthcare settings or animal husbandry practices. Such findings suggest that natural habitats are not isolated reservoirs but rather part of a complex web of transmission pathways that include human, animal, and environmental interfaces [220,221].

Wild animals can serve as sentinels for monitoring the spread and emergence of antimicrobial resistance. Species that live in close proximity to human activity, such as birds of prey, scavengers, and small mammals, are particularly useful indicators of environmental AMR levels because of their exposure to diverse sources of contamination [128]. The detection of methicillin-resistant *Staphylococcus aureus* (MRSA) in hedgehogs and other mammals, for instance, indicates the widespread nature of *mecC*-mediated resistance beyond clinical settings. The persistence of MRSA in natural populations suggests that resistant strains can thrive outside of traditional reservoirs, further complicating efforts to contain AMR. In the case of carbapenemase-producing *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*, their detection in gulls and other migratory birds provides evidence of the potential for long-distance transmission of resistant bacteria. Migratory species can disseminate AMR genes across continents, contributing to the global spread of resistance [222,223]. The identification of high-risk clones in wildlife emphasizes the relevance of including wild animal populations in AMR surveillance programs. These programs should not only focus on the pathogens commonly associated with human health but also account for the broader environmental and ecological drivers of resistance.

The spread of AMR is not limited to the movement of resistant bacterial strains but is also driven by horizontal gene transfer, facilitated by mobile genetic elements such as plasmids, transposons, and integrons [224,225]. Wildlife-associated ESKAPE bacteria often harbor resistance genes on mobile elements, which can be transferred across different bac-

terial species and genera. The detection of plasmid-mediated colistin resistance (*mcr* genes) in *Enterobacteriaceae* from deer and wild boars, as well as the presence of carbapenemase genes (*bla*<sub>OXA</sub>, *bla*<sub>NDM</sub>) in *Acinetobacter baumannii* from birds and mammals, suggests that natural environments provide a setting for the exchange of genetic material that enhances bacterial adaptability. The role of wildlife as reservoirs for resistance genes extends beyond individual bacterial species; it involves a network of genetic exchanges that can have significant consequences for public health. In particular, the combination of multidrug resistance and virulence factors in wildlife-associated strains raises concerns about the potential emergence of highly pathogenic, resistant bacteria [118,226]. The presence of conjugative plasmids carrying multiple resistance genes, such as *ermB*, *aac(6′)-Ii*, *vanA*, and *tetM*, in *Enterococcus* spp. from wild mammals, points to the complexity of the resistance gene pool circulating in natural environments. This gene pool is not static but dynamic, continuously shaped by selective pressures such as antibiotic use, ecological interactions, and environmental factors. The risk levels associated with antimicrobial resistance in wildlife vary depending on factors such as bacterial species, resistance mechanisms, and ecological interactions. High-risk resistance genes, such as those encoding carbapenemases (*bla*<sub>KPC</sub>, *bla*<sub>NDM</sub>, *bla*<sub>OXA</sub>), vancomycin resistance (*vanA*, *vanB*), and extended-spectrum β-lactamases (*bla*<sub>CTX-M</sub>), have been identified in ESKAPE bacteria isolated from wild animals. These genes are particularly concerning due to their association with multidrug-resistant infections in humans. However, the mere presence of a resistance gene does not always indicate immediate clinical relevance, as some may remain unexpressed under natural conditions. The expression of antimicrobial resistance genes can be influenced by environmental stressors, antibiotic exposure, and genetic regulation mechanisms. Silent resistance genes may still play a critical role in AMR dissemination, as they can be activated under selective pressure or transferred to other bacteria via horizontal gene transfer. This highlights the need for further studies evaluating not only the genetic presence of resistance determinants but also their phenotypic expression and potential impact on human and animal health.

The detection of ESKAPE bacteria in wildlife has direct implications for zoonotic transmission and human health risks. While the majority of studies focus on livestock and domestic animals as potential sources of resistant pathogens, wildlife represents a less controlled, yet equally significant, reservoir. The movement of wild animals into human-dominated landscapes, whether through natural migration, habitat encroachment, or attraction to urban food sources, increases the likelihood of direct or indirect transmission of resistant bacteria to humans and domestic animals [227,228]. For instance, scavenging species like foxes, raccoons, and vultures, which feed on waste or carcasses, can act as vectors for resistant bacteria that originate from agricultural or urban settings [128]. The risk extends to the transmission of virulent strains with enhanced pathogenicity. Wildlife-associated isolates of *P. aeruginosa*, for example, often carry virulence genes such as *exoS* and *lasB*, which can increase their capacity to cause severe infections in immunocompromised hosts [229]. Likewise, *E. faecium* strains from wild animals that carry biofilm-associated genes may have an enhanced ability to colonize medical devices or persist in hospital environments [210]. The combination of antimicrobial resistance and virulence traits in ESKAPE pathogens from wildlife thus represents a dual threat, complicating infection control and treatment strategies.

Addressing the implications of ESKAPE bacteria in wild animals requires an integrated One Health approach that combines efforts from human medicine, veterinary science, and environmental management [223,230]. Surveillance of antimicrobial resistance should not be confined to clinical settings but should include a broader range of ecosystems, recognizing the interconnectedness of different AMR reservoirs. Such integrated surveillance would enable earlier detection of emerging resistance patterns, providing critical data for guiding

policy decisions and mitigating the spread of AMR. Efforts to reduce environmental contamination with antibiotics and resistant bacteria are also essential. This includes better management of agricultural practices to limit the use of antibiotics in livestock, improving wastewater treatment to prevent the release of resistant bacteria into natural water bodies, and implementing regulations on the disposal of pharmaceutical waste [231,232]. Wildlife rehabilitation centers, zoos, and conservation programs should also incorporate AMR monitoring to ensure that released animals do not inadvertently contribute to the spread of resistance. Lastly, public awareness and education about the risks of AMR should extend beyond healthcare and agriculture to include the role of wildlife and natural ecosystems. Understanding that antimicrobial resistance is not confined to hospitals or farms but is a broader environmental issue can help garner support for policies aimed at addressing AMR on a global scale. The challenge of ESKAPE bacteria in wild animals exemplifies the need for a comprehensive and multidisciplinary approach to effectively tackle antimicrobial resistance in the One Health framework. Finding ESKAPE pathogens in wildlife poses a risk for their potential spread to humans, whether by direct contact with animals or through contaminated environments. Wildlife can serve as reservoirs, aiding in the maintenance and dissemination of these bacteria in natural ecosystems from where they may eventually be transmitted to people via food, water, or other vector species. This reiterates the need for an integrated multisectoral approach that incorporates monitoring and evaluation activities regarding the health of humans, animals, and the environment. In addition, integrating results with the WHO list of prioritized pathogens associated with antimicrobial resistance makes it possible to evaluate risks and produce comprehensive solutions with increased precision. Although earlier studies contributed useful information regarding the resistome of certain wildlife species like migratory birds, this review places ESKAPE pathogens in a wider context. By integrating information from different host species and resistance patterns, our study demonstrates that the circulation of antimicrobial resistance is more complex than clinical and agricultural environments. This point reinforces the need for more comprehensive surveillance systems that cover various wildlife reservoirs and their relationships with human and ecosystem health.

## 5. Conclusions

The detection of ESKAPE bacteria in wildlife underlines the complexity of antimicrobial resistance as a global issue that transcends healthcare settings. The evidence of diverse resistant strains across different animal species and geographic regions highlights the interconnected nature of human, animal, and environmental health. Wild animals, whether as reservoirs, sentinels, or vectors, play a significant role in the ecology of antimicrobial resistance. They are not only exposed to resistance genes through environmental contamination but can also contribute to their dissemination across ecological boundaries, potentially spreading resistance to human populations.

The findings suggest that controlling ESKAPE pathogens requires a comprehensive and multidisciplinary approach. Surveillance efforts must expand beyond hospitals to encompass broader environmental contexts, including wildlife and natural ecosystems. The inclusion of wild animals in AMR monitoring programs can provide valuable insights into emerging resistance patterns and help guide targeted interventions. This approach, combined with strategies to reduce environmental contamination, such as better management of antibiotic use in agriculture and improvements in wastewater treatment, can help to mitigate the spread of resistance.

Ultimately, addressing the challenges posed by ESKAPE bacteria in wildlife is not just about protecting animal health; it is about safeguarding public health and ensuring the sustainability of ecosystems. The One Health approach emphasizes that tackling antimicro-

bial resistance must involve coordinated efforts across human medicine, veterinary science, and environmental management. As our understanding of the dynamics of resistance continues to evolve, it becomes increasingly clear that efforts to curb the tide of antimicrobial resistance must consider the full spectrum of reservoirs and transmission pathways that extend well beyond the walls of hospitals. This review highlights the importance of evaluating AMR risk levels by considering both genetic detection and functional expression of resistance genes. While some antimicrobial resistance genes remain unexpressed in wildlife isolates, they may still pose a future threat due to their potential activation under selective pressure. Future research should focus on transcriptomic and proteomic analyses to determine gene expression patterns in different environmental contexts. Implementing a One Health surveillance approach that integrates genomic and phenotypic resistance data is essential for predicting and mitigating the spread of AMR across ecological boundaries.

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