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"Comparative genomics of NDM-producing *Klebsiella pneumoniae* human High-Risk Clone ST307 in companion animals: a OneHealth perspective "

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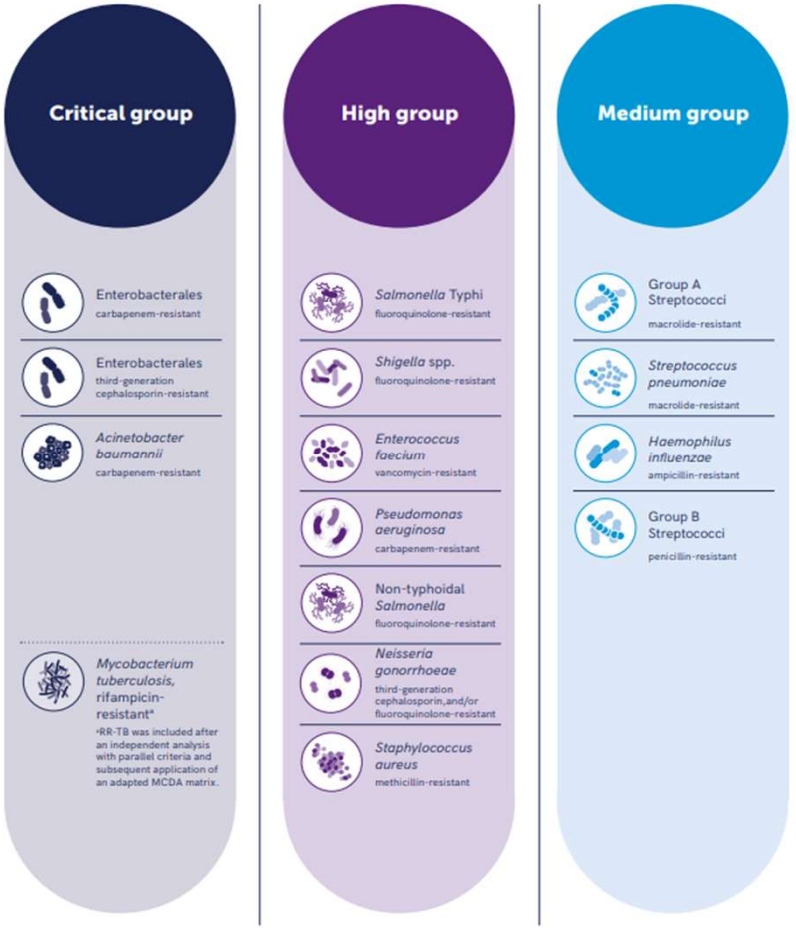
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Klebsiella pneumoniae

- Gram-negative, encapsulated, non-motile bacterium found in the environment, acting as a major opportunistic pathogen in livestock, companion animals and humans.

- It is a primary cause of pneumonia, sepsis, and UTIs in humans, severe acute mastitis in dairy cattle, reproductive tract infections in equines, and UTIs or pyogenic infections in companion animals

- Carbapenem-resistant *Klebsiella pneumoniae* is classified by WHO (2024) as one of the world's most critical pathogens for human health, with multidrug-resistant (MDR/ESBL) strains increasingly isolated in the veterinary sector



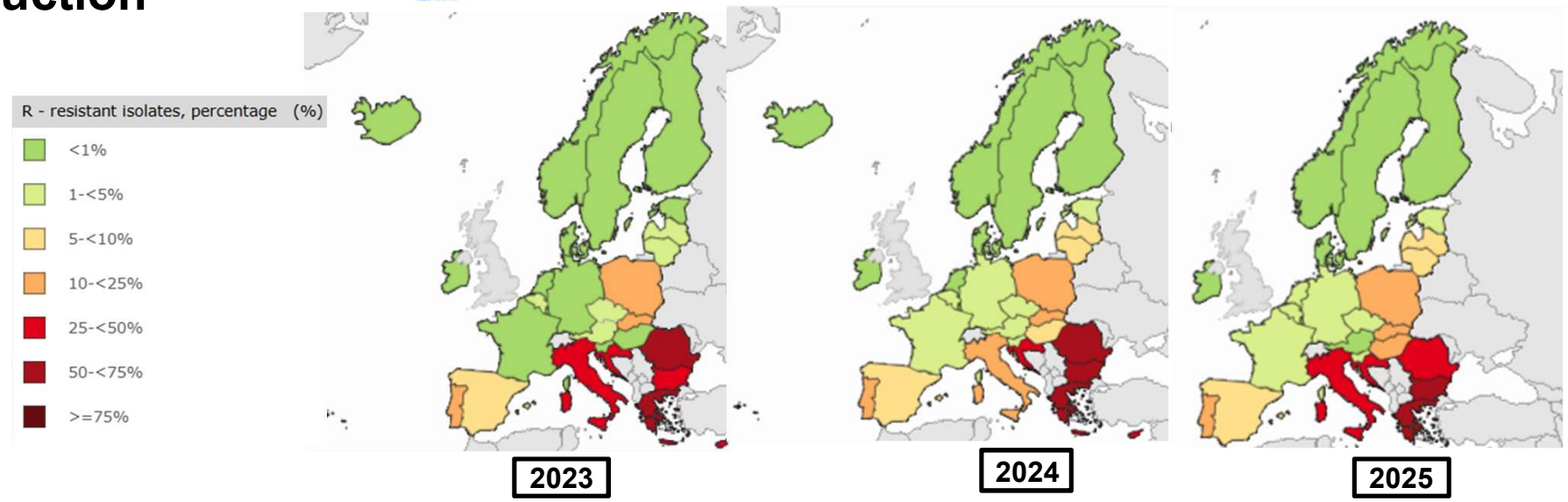


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Introduction

Surveillance Atlas of Infectious Diseases



- Italy is one of the countries with the highest percentage of Carbapenem-resistant *K. pneumoniae*

- Carbapenems have never been registered as VMPs in animals, and have recently been prohibited in the veterinary sector (EU Implementing Regulation 2022/1255).

- Carbapenemase-producing Enterobacterales have been increasingly reported in Europe in food-producing and companion animals.

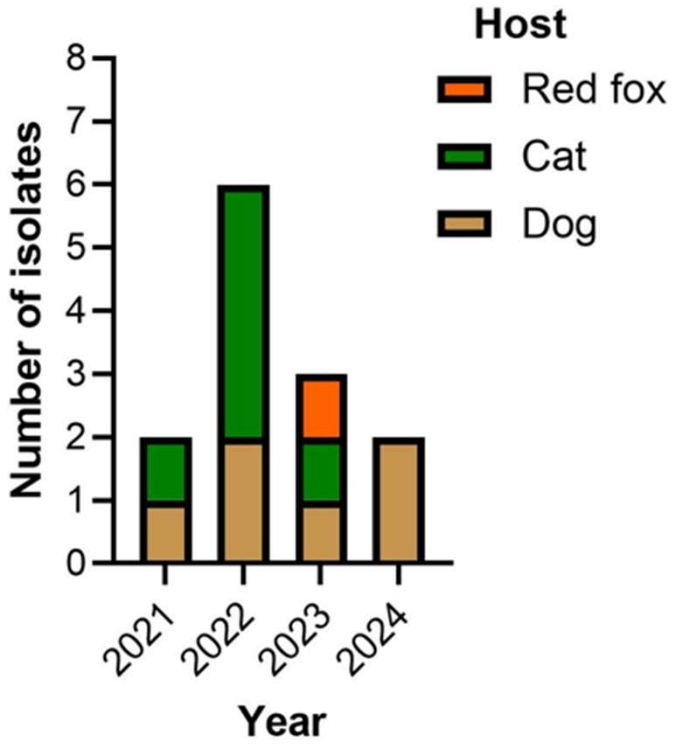
- Historically, in the human sector, carbapenem resistance *K. pneumoniae* has been dominated by KPC-producing ST512. Recently, an epidemiological shift toward other STs and alternative carbapenemases has been observed.



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Isolate Collection



13 Carbapenem resistance *Klebsiella pneumoniae*:

- 12 Isolates recovered from clinical samples and post-mortem examinations of dogs and cats in Northern and Central Italy.
- 1 Isolate recovered from a necropsied red fox in Northern Italy.

Questions:

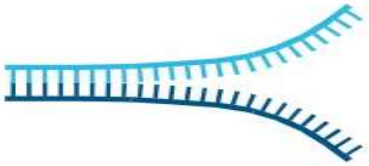
- **Which carbapenemases are involved and where?**
- **Which Sequence Types (STs) are driving this resistance?**



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AIMS



Identify high-risk *Klebsiella pneumoniae* clones circulating in Italy among our isolates and to track the mobile genetic elements involved in the spread of antibiotic resistance



In-depth genomic plasmids characterization of the isolates to investigate their relationship with human health and resistance towards novel human drugs



Global phylogenetic analysis of *K. pneumoniae* ST307

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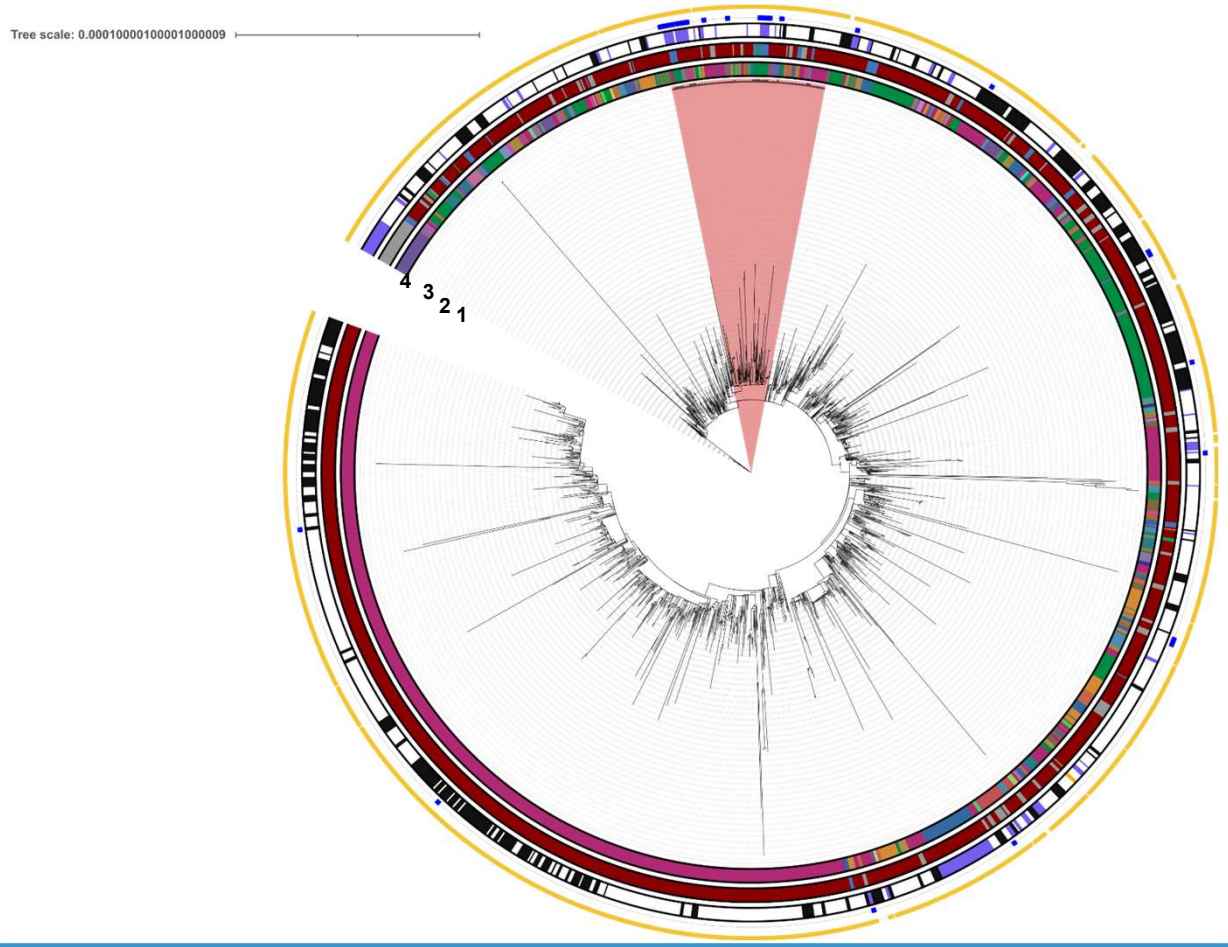
- 1,633 ST307 genomes were included in the global phylogenetic analysis:
- 13 animal-derived isolates (this study)
- 9 genomes from the NRL-AR, IZSLT internal database
- 1,611 publicly available genomes (BIGSdb-Pasteur: 1,574; NCBI: 37)

- The 13 animal-derived ST307 isolates showed high genetic relatedness, despite different hosts, geographical origins, and sampling years (2021-2024).

- Close phylogenetic relationships were observed with ST307 genomes from other countries, including human-derived isolates.

- WGS analysis identified two plasmids: IncX3 and pKpN (a IncFIB(K) plasmid harbouring several virulence cluster genes), in all 13 animal-derived ST307 isolates.

- All 13 isolates carried the bla_{NDM-5} gene on an identical conjugative 45,122 bp IncX3 plasmid.





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Conclusions

- High genomic relatedness: The 13 animal derived *K. pneumoniae* ST307 isolates showed high genetic similarity despite originating from different animal hosts, geographical locations, and sampling years, clustering with human and international ST307 genomes.

- All 13 isolates carried an identical 45,122-bp IncX3 plasmid harbouring $bla_{\text{NDM-5}}$, a plasmid replicon relatively uncommon in the global ST307 population, and representing the first identification of an IncX3-borne $bla_{\text{NDM-5}}$ plasmid in *K. pneumoniae* ST307 in Italy.

- Companion animals may act as reservoirs of human-associated *K. pneumoniae* ST307 lineages and mobile resistance determinants, with potential for further dissemination across bacterial lineages with One Health implications.

- Animal-derived pKpN plasmids retained five putative virulence-associated clusters, including the Fec-like iron transport system, highlighting the persistence of these determinants in companion animals in Italy and their potential contribution to reduced cefiderocol susceptibility under specific genetic backgrounds.



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Thank you for your attention!

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