KlebNET-GSP

LECTURE SERIES

Klebsiella pneumoniae Genomic Epidemiology and Antimicrobial Resistance

One Health genomic surveillance of *K. pneumoniae*

Marit Hetland, Stavanger University Hospital, Norway

Intended Learning Objectives

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Specific objectives of this session:

1. Understand why a One Health framework is important to combat AMR and its implications for public health responses
2. Learn about key findings from One Health studies of *K. pneumoniae*
3. Know about genomic methods to study *K. pneumoniae* in a One Health framework, including:

   3.1 SLs, AMR, and virulence gene profiling

   3.2 Pangenome analysis

   3.3 Genetic relatedness of clones

   3.4 Plasmid typing

   3.5 Genome-wide association studies

Outline

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This session consists of the following elements

1. One Health & why it matters for public health
2. Non-human reservoirs of *K. pneumoniae*
3. Studies of *K. pneumoniae* in a One Health context
4. Genomic approaches to *K. pneumoniae* surveillance

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What is One Health?

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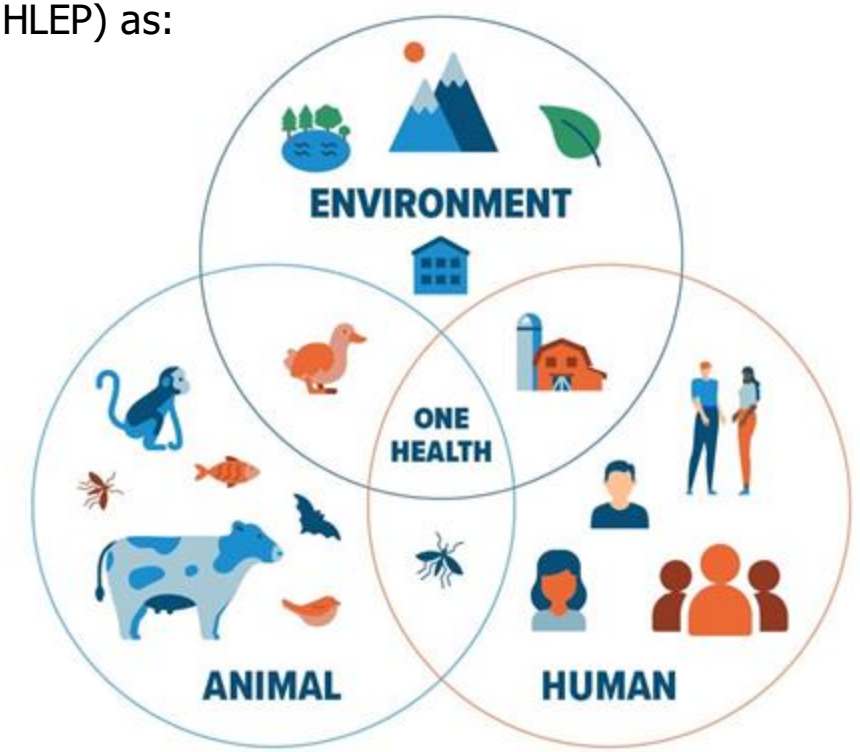
One Health has been defined by the One Health high-level expert panel (OHHLEP) as:

"One Health is an integrated, unifying approach that aims to sustainably balance and optimize the health of humans, animals, plants and ecosystems. It recognizes the health of humans, domestic and wild animals, plants and the wider environment (including ecosystems) are closely linked and interdependent.

The approach mobilizes multiple sectors, disciplines and communities at varying levels of society to work together to foster well-being and tackle threats to health and ecosystems, while addressing the collective need for clean water, energy and air, safe and nutritious food, taking action on climate change, and contributing to sustainable development."



One Health High-Level Expert Panel (OHHLEP), et al. 2022. PMID: 35737670
Image source: https://prezode.org/about/the-one-health

One Health prioritised in strategies against AMR

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ECDC One Health Framework

May 2024

One Health

Find out more about One Health – a key priority of the interim Australian Centre for Disease Control (CDC).

PRESS RELEASE | NOVEMBER 28, 2023

One Health Framework for Action Set to Enhance the Quality of Health Care Services Across Central Asia

Regjeringen.no

National one-health strategy against antimicrobial resistance 2024–2033

One Health prioritised in strategies against AMR

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Quadripartite Joint Secretariat on AMR

Food and Agriculture Organization of the United Nations

UN environment programme

World Health Organization

World Organisation for Animal Health
Founded as OIE

FAO, UNEP, WHO, and WOAH, 2022. https://doi.org/10.4060/cc2289en

Is One Health important?

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Global burden of bacterial antimicrobial resistance 1990–2021: a systematic analysis with forecasts to 2050

*GBD 2021 Antimicrobial Resistance Collaborators**

Deaths per year by 2050:
1.9M attributed to AMR
8.2M associated to AMR

Forecasting the Fallout from AMR: Averting the Health and Economic Impacts through One Health Policy and Investment

A policy brief from the EcoAMR series

Cost of AMR per year:
Currently: $66B USD (0.7% global expenditure)
By 2050: $159B USD (1.2%)

GBD 2021 Antimicrobial Resistance Collaborators, 2024. PMID: 39299261
World Organisation for Animal Health (WOAH), 2024. https://doi.org/10.20506/ecoAMR.3544

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Is One Health important for *K. pneumoniae* infections?

K. pneumoniae is a key AMR trafficker

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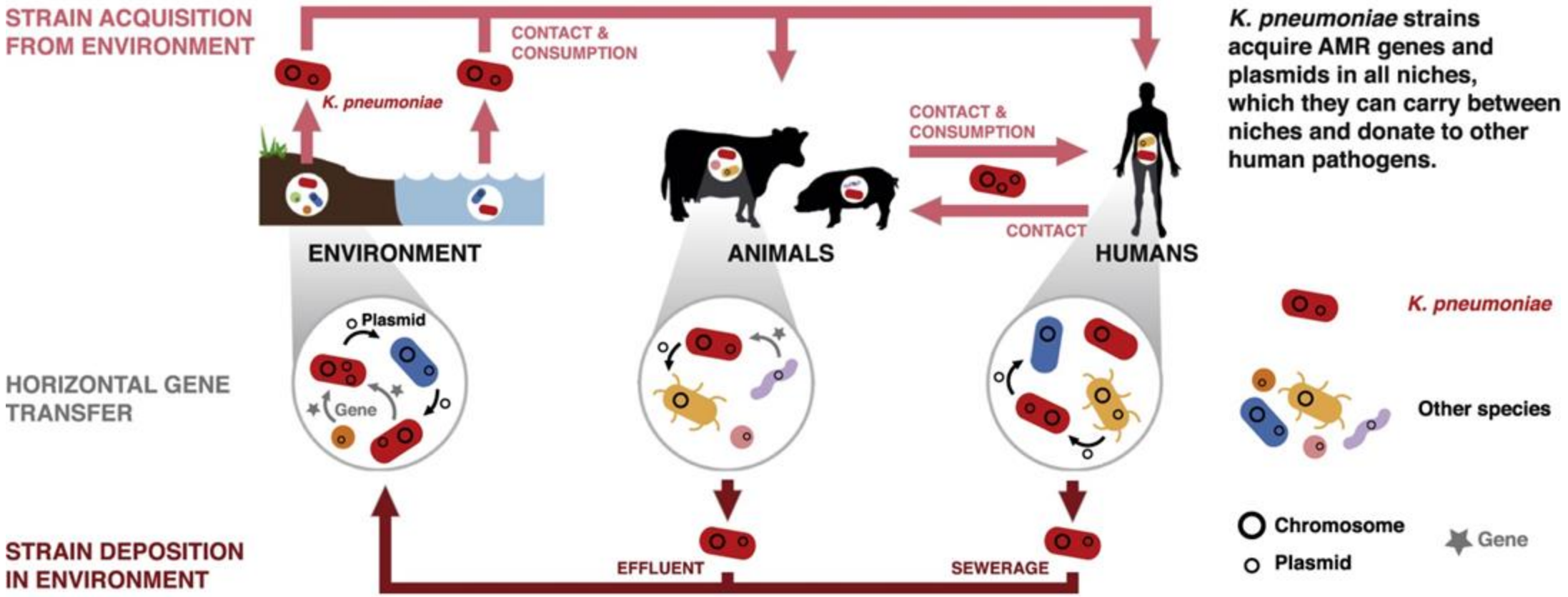

Genes first detected in *K. pneumoniae* include: ***qnrAB*** **TEM** **KPC** **OXA-48** **SHV-2** ***mcr-1*** **CTX-M** **NDM** **CMY-1**

Wyres & Holt, 2018. PMID: 29723841

K. pneumoniae is a key AMR trafficker

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- *K. pneumoniae* can colonise humans and animals, and has been isolated from several environmental sources

- Large accessory genome and ecological range, ability to move between ecological niches and adapt – often exchanging DNA with other bacterial species (including AMR)

- Can then "traffic" the acquired AMR genes into healthcare settings, where they can further spread in the hospital environment and among people, or to other bacterial hosts, ultimately cause opportunistic infections, that are becoming increasingly difficult to treat with accumulating AMR

- It goes both ways; *K. pneumoniae* spills back to the environment from humans, e.g. through wastewater

Wyres & Holt, 2018. PMID: 29723841

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K. pneumoniae is (nearly) everywhere we look

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Human

- Infection
- Colonisation (12.4-87.7%)

Animals (wild & domestic)

- Pigs
- Broiler
- Turkey
- Cattle
- Horses
- Cats
- Wild boar
- Dogs
- Elephants
- Dolphins
- Catfish
- Mussels
- Oysters
- Scallops
- Prawns
- Flies

Ready-to-eat food

- Retail meat
- Cheese
- Lettuce
- Chili
- Bananas

Environment

- Hospital surfaces
- Fresh water
- Seawater
- Soil
- Sediments
- Influent and effluent wastewater

- **Examples; not a complete list**
- **Carriage rates vary**
- **Some carry AMR but not all**

References:
Calland et al, 2023. PMID: 37858320
Crippa et al, 2023. PMID: 37414963
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Ludden et al, 2020. PMID: 30840764
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We find *K. pneumoniae* in non-human sources…
but does it matter for human health?

We find *K. pneumoniae* in non-human sources… but does it matter for human health?

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Two examples:

- AMR genes can emerge in the environment or in animals and move to humans: the colistin resistance gene *mcr-1*
- Animal reservoirs as a source of virulence traits: the pig-associated siderophore *iuc*3

Liu, et al. 2016. PMID: 26603172
Crippa et al, 2023. PMID: 37414963
Gibbon et al, 2025. https://doi.org/10.1101/2024.01.05.574329

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A large-scale genomic snapshot of *Klebsiella* spp. isolates in Northern Italy reveals limited transmission between clinical and non-clinical settings

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Check for updates

Harry A. Thorpe[1], Ross Booton[2], Teemu Kallonen[3], Marjorie J. Gibbon[4], Natacha Couto[4], Virginie Passet[5], Sebastián López-Fernández[5], Carla Rodrigues[5], Louise Matthews[6], Sonia Mitchell[6], Richard Reeve[6], Sophia David[7], Cristina Merla[8], Marta Corbella[8], Carolina Ferrari[8], Francesco Comandatore[9], Piero Marone[8], Sylvain Brisse[5], Davide Sassera[10,12], Jukka Corander[3,11,12] & Edward J. Feil[4,12]

Limited Transmission of *Klebsiella pneumoniae* among Humans, Animals, and the Environment in a Caribbean Island, Guadeloupe (French West Indies)

Alexis Dereeper,[a] Gaëlle Gruel,[a] Matthieu Pot,[a] David Couvin,[a] Elodie Barbier,[b] Sylvaine Bastian,[c] Jean-Christophe Bambou,[d] Moana Gelu-Simeon,[e] Séverine Ferdinand,[a] Stéphanie Guyomard-Rabenirina,[a] Virginie Passet,[f] Frederic Martino,[g] Pascal Piveteau,[h] Yann Reynaud,[a] Carla Rodrigues,[f] Pierre-Marie Roger,[i,j] Xavier Roy,[k] Antoine Talarmin,[a] Benoit Tressieres,[l] Marc Valette,[g] Sylvain Brisse,[f] Sébastien Breurec[a,c,j,l]

Population structure and antimicrobial resistance among *Klebsiella* isolates sampled from human, animal, and environmental sources in Ghana: a cross-sectional genomic One Health study

Jessica K Calland, Kaisa Haukka, Stephen W Kpordze, Atanyiwoen Brusah, Marta Corbella, Cristina Merla, Ørjan Samuelsen, Edward J Feil, Davide Sassera, Akosua B Karikari, Courage K S Saba*, Harry A Thorpe*, Jukka Corander**

A One Health Study of the Genetic Relatedness of *Klebsiella pneumoniae* and Their Mobile Elements in the East of England

Catherine Ludden,[1,2,a] Danesh Moradigaravand,[3,a] Dorota Jamrozy,[2] Theodore Gouliouris,[4,5,6] Beth Blane,[4] Plamena Naydenova,[4] Juan Hernandez-Garcia,[7] Paul Wood,[8] Nazreen Hadjirin,[7] Milorad Radakovic,[7] Charles Crawley,[5] Nicholas M. Brown,[5,6] Mark Holmes,[7] Julian Parkhill,[2] and Sharon J. Peacock[1,2,4,5]

A genome-wide One Health study of *Klebsiella pneumoniae* in Norway reveals overlapping populations but few recent transmission events across reservoirs

Marit A. K. Hetland, Mia A. Winkler, Håkon P. Kaspersen, Fredrik Håkonsholm, Ragna-Johanne Bakksjø, Eva Bernhoff, Jose F. Delgado-Blas, Sylvain Brisse, Annapaula Correia, Aasmund Fostervold, Margaret M. C. Lam, Bjørn-Tore Lunestad, Nachiket P. Marathe, Niclas Raffelsberger, Ørjan Samuelsen, Marianne Sunde, Arnfinn Sundsfjord, Anne Margrete Urdahl, Ryan R. Wick, Iren H. Löhr & Kathryn E. Holt

Limited Evidence of Spillover of Antimicrobial-Resistant *Klebsiella pneumoniae* from Animal/Environmental Reservoirs to Humans in Vellore, India

Jobin John Jacob[1] · V. Aravind[1] · Benjamin S. Beresford-Jones[2] · Y. Binesh Lal[1] · Chaitra Shankar[1] · M. Yesudoss[1] · Fiza Abdullah[1] · T. Monisha Priya[1] · Sanika Kulkarni[1] · Stephen Baker[2] · Balaji Veeraraghavan[1] · Kamini Walia[3]

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Key findings from One Health *K. pneumoniae* studies

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- *K. pneumoniae* is «everywhere»
- But AMR *K. pneumoniae* is largely concentrated in human clinical isolates, particularly ESBLs and carbapenemases
- No carbapenemases found in non-clinical settings in large snapshot studies from Italy[1] or Ghana[2], or nationwide study from Norway[4] – but carbapenemases have been found in (a few) animal and environmental *K. pneumoniae* samples elsewhere (including India[4], China, Brazil, Canada[5])
- Hypervirulence-associated clones found mainly in human settings (patients, colonisation or hospital environment), except 2 in dogs[6], 1 cow & 1 pig[5]
- Animals, particularly pigs, reservoirs for virulence factors (*iuc*3[1,3] and *iuc*5[3])

1) Thorpe et al, 2022. PMID: 36411354
2) Calland et al, 2023. PMID: 37858320
3) Hetland, et al. 2025. PMID: 40296028
4) Jacob et al, 2024. PMID: 39531180
5) Huang et al, 2025. PMID: 40890500
6) Dereeper et al, 2022. PMID: 36094181

Key findings from One Health *K. pneumoniae* studies

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- Genetic relatedness: Strain-sharing is more common within humans (especially in hospitals) than across niches, but occasional cross-niche transmission does occur [1,2]
- Overlap in gene pools: Large SL and pangenome overlap seen across niches, but also across countries (Norway and Ghana) [2,3]
- Cross-niche spread appears constrained more by geography and exposure patterns than by intrinsic *K. pneumoniae* barriers
- Geographic, socio-economic and cultural factors affect the amount of cross-niche transmission [4] – it is important to monitor *K. pneumoniae* in multiple settings
- Is *K. pneumoniae* food-borne? Several studies implicate food sources (as well as companion animals[1]) as potential routes of human acquisition of *K. pneumoniae* – this warrants surveillance [5,6]

1) Thorpe et al, 2022. PMID: 36411354
2) Hetland, et al. 2025. PMID: 40296028
3) Calland et al, 2023. PMID: 37858320
4) Subbiah et al, 2020. PMID: 31932601
5) Zamudio et al, 2025. PMID: 40889870
6) Crippa et al, 2023. PMID: 37414963

We find *K. pneumoniae* in non-human sources… but does it matter for human health? Yes

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- **The biggest AMR burden is in healthcare settings:** but non-human sources can act as reservoirs for new resistance or virulence traits
- **Rare spillovers can have big impacts:** even infrequent introductions from animals, food, or the environment can establish in humans and persist as public health problems
- **Colonisation often precedes infection:** preventing transmission and colonisation from the food chain may reduce disease burden and mortality

Implications for public health responses

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- **Surveillance should go across sectors:** Extend beyond hospitals to include animals, food, and the environment
- **Policies must tackle antibiotic use everywhere:** Regulate use in livestock, agriculture, and wastewater to prevent AMR emergence and spillover
- **Mitigation requires research and coordination:** Study AMR/virulence evolution outside hospitals and align policy across human, animal, and environmental health

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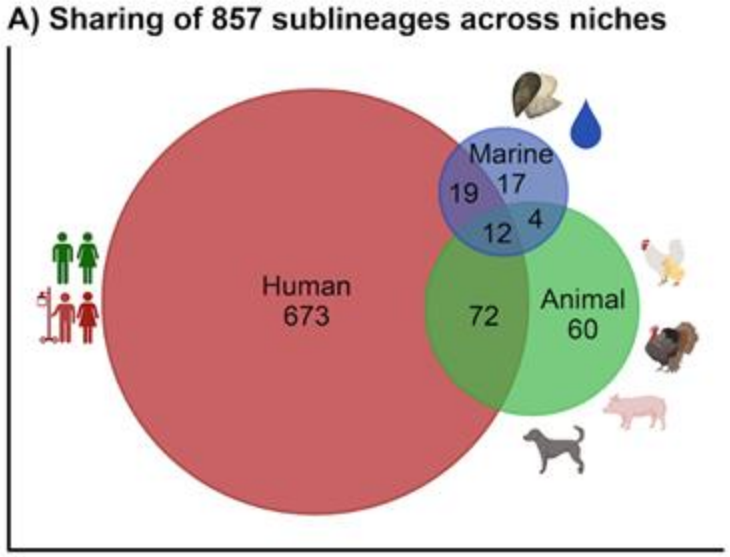
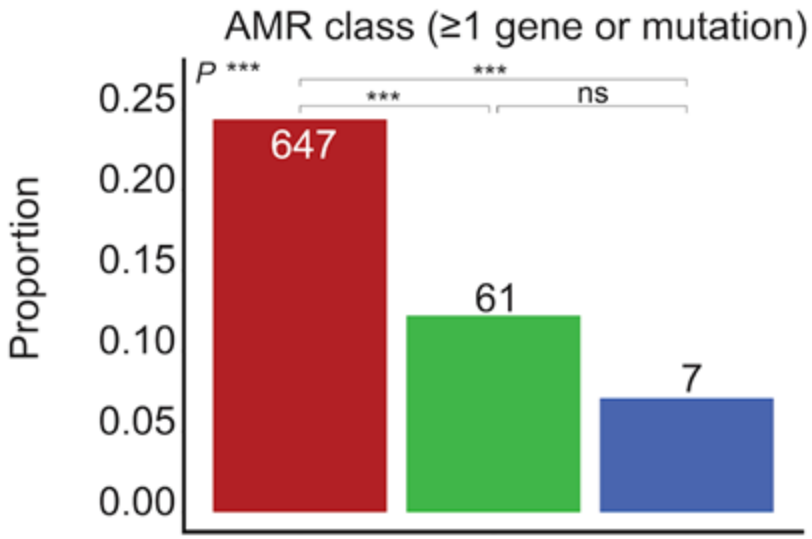
SLs, AMR, and virulence gene profiling

- Do the populations (SLs, MDR/Hv clones) overlap?
- Diversity measures (e.g. Simpson's diversity) to compare populations





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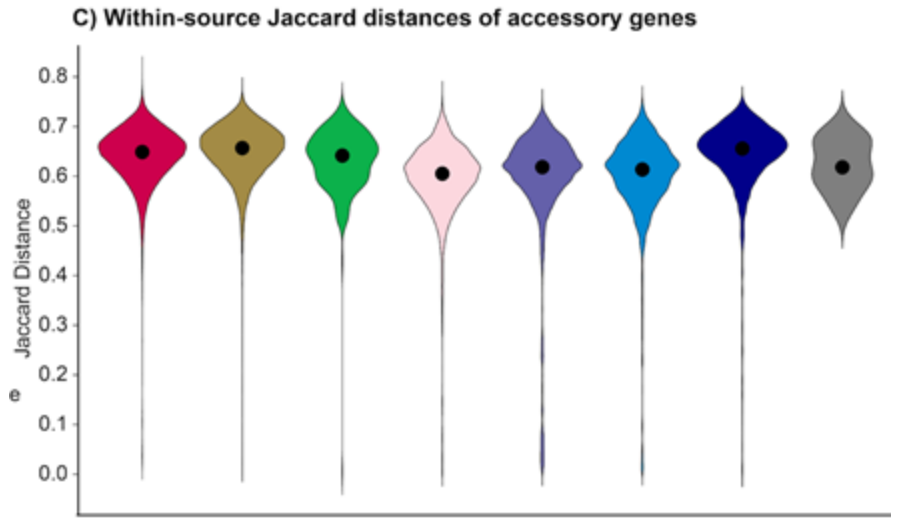
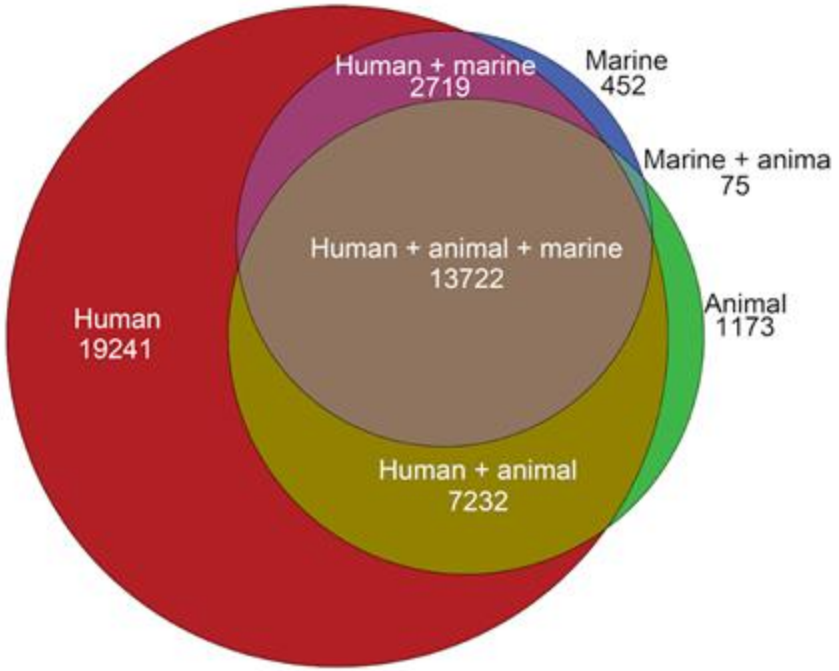
- Estimate rates of gene gain/loss
- Measure gene content similarity (e.g. Jaccard distances)





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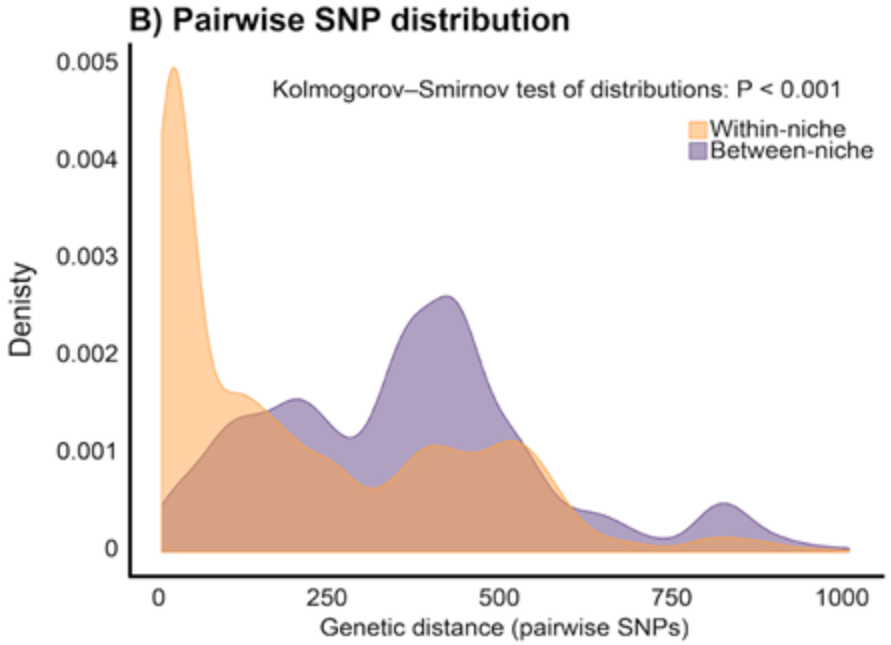
Genetic relatedness of clones

- Pairwise SNP distances within vs between niches
- Apply thresholds to define potential strain-sharing
- Quantify how many strains show cross-niche relatedness



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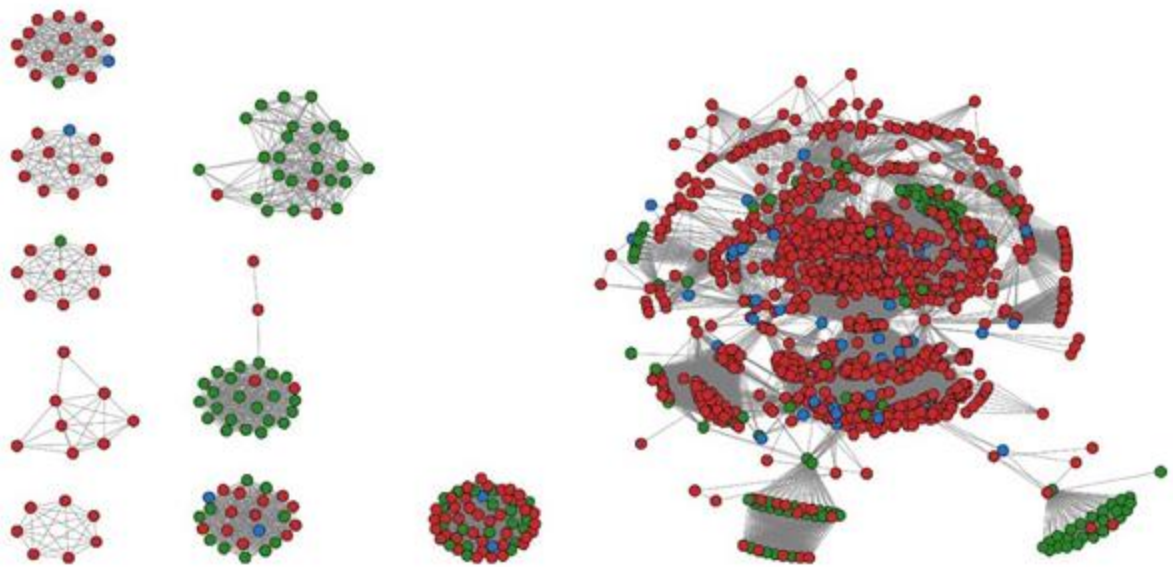
- Cluster plasmids to track movement of AMR/virulence genes



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Genome-wide association studies (GWAS)

- Test for associations between genetic variants and traits of interest (e.g. niche, AMR, virulence)

Considerations when interpreting genomic surveillance data

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- **Context matters**: When, where, and how samples are collected affects interpretation
- **Genomes alone can’t prove transmission**: Must be paired with epidemiological data
- **Directionality cannot be inferred & Identical strains may reflect unsampled hosts or a common source**
- **Beware of bias and limits**: Incomplete or uneven sampling and genomic resolution can obscure the true picture

In summary

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List of learning points in this session:

- One Health studies show that clinically relevant *K. pneumoniae* mostly transmits in healthcare settings; but even rare spillover events can have major public health impacts

- AMR *K. pneumoniae* is a One Health challenge: tackling it requires cross-sector surveillance, responsible antibiotic use, and coordinated policy

- Genomic tools are powerful, but must be paired with epidemiological context to understand transmission

References

Calland et al, 2023. PMID: 37858320

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