AS2AMR/BIC2025

AMR in the Clinical Environment

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Each year, 4.3 million patients in hospitals in the EU are affected by healthcare-associated infections

- Pneumonia and LRTI (incl. COVID-19): 29.3%
- Urinary tract infections : 19.2%
- Surgical site infections : 16.1%
- Bloodstream infections : 11.9%

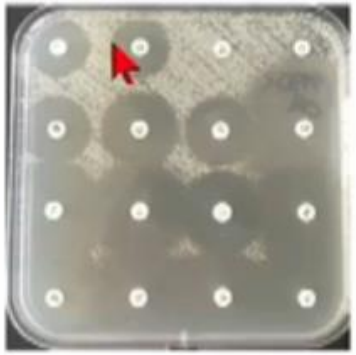
Micro-organisms involved	%	
Enterobacterales	**34.2%**	
E. coli		12.7%
K. pneumoniae		11.7%
Gram positive cocci	**26.9%**	
S. aureus		9%
Enterococci		10%
Other Gram negative bacilli	**12.9%**	
P. aeruginosa		7.9%
A. baumannii		3.2%
Anaerobes	**9.%**	
Fungi	**5.3%**	
Viruses	**10.3%**	
Others	**1.2%**	

LRTI: Low respiratory tract infections

https://www.ecdc.europa.eu/en/publications-data/PPS-HAI-AMR-acute-care-europe-2022-2023

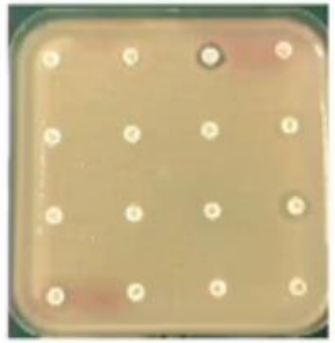
Multi-drug resistant key pathogens

ESBL-E: Extended-spectrum beta-lactamase-producing Enterobacterales



MRSA: methicillin-resistant *Staphylococcus aureus*

VRE: Vancomycin resistant Enterococci

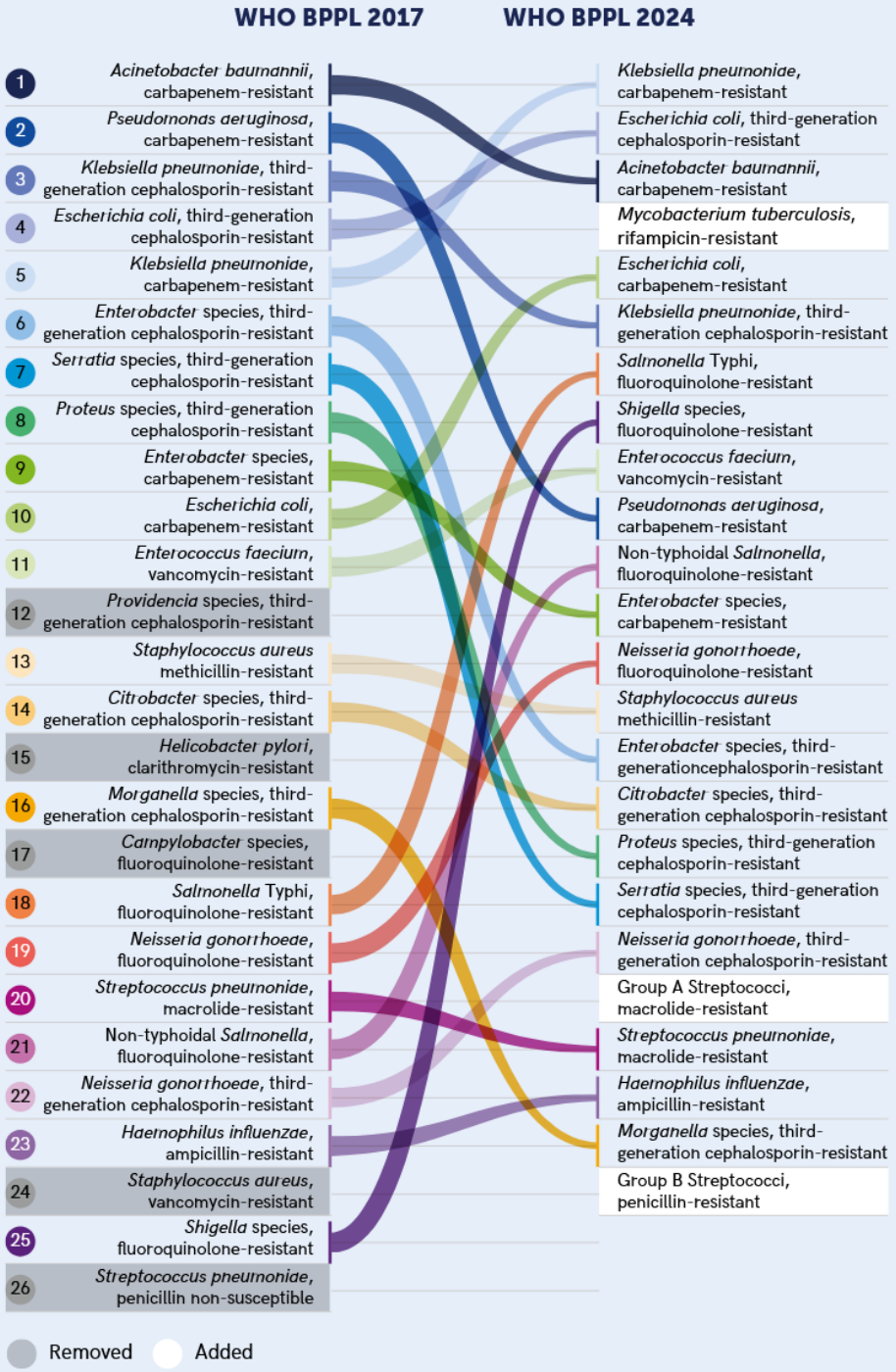


CPE: carbapenemase producing Enterobacterales

CPPA: Carbapenemase producing *Pseudomonas aeruginosa*

CRAB: Carbapenem resistant *Acinetobacter baumannii*

WHO Priority Pathogens



Source: WHO Bacterial Priority Pathogens List, 2024

AMR transmission in a One Health context: Plasmid mediated colistin resistance, *mcr*

Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study

Yi-Yun Liu, Yang Wang*, Timothy R Walsh, Ling-Xian Yi, Rong Zhang, James Spencer, Yohei Doi, Guobao Tian, Baolei Dong, Xianhui Huang, Lin-Feng Yu, Danxia Gu, Hongwei Ren, Xiaojie Chen, Luchao Lv, Dandan He, Hongwei Zhou, Zisen Liang, Jian-Hua Liu, Jianzhong Shen*

15-20% in animals (Pigs/Chicken)
5-25% in food animal products
<1% in hospital patients

RAPID COMMUNICATIONS

Identification of a novel plasmid-mediated colistin-resistance gene, *mcr-2*, in *Escherichia coli*, Belgium, June 2016

BB Xavier [1,2,3], C Lammens [1,2,3], R Ruhal [1,2,3], S Kumar-Singh [1,3,4], P Butaye [5,6,7], H Goossens [1,2,3], S Malhotra-Kumar [1,2,3]

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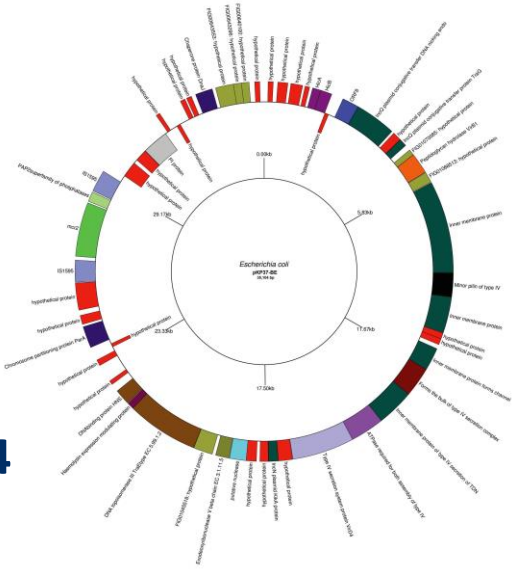
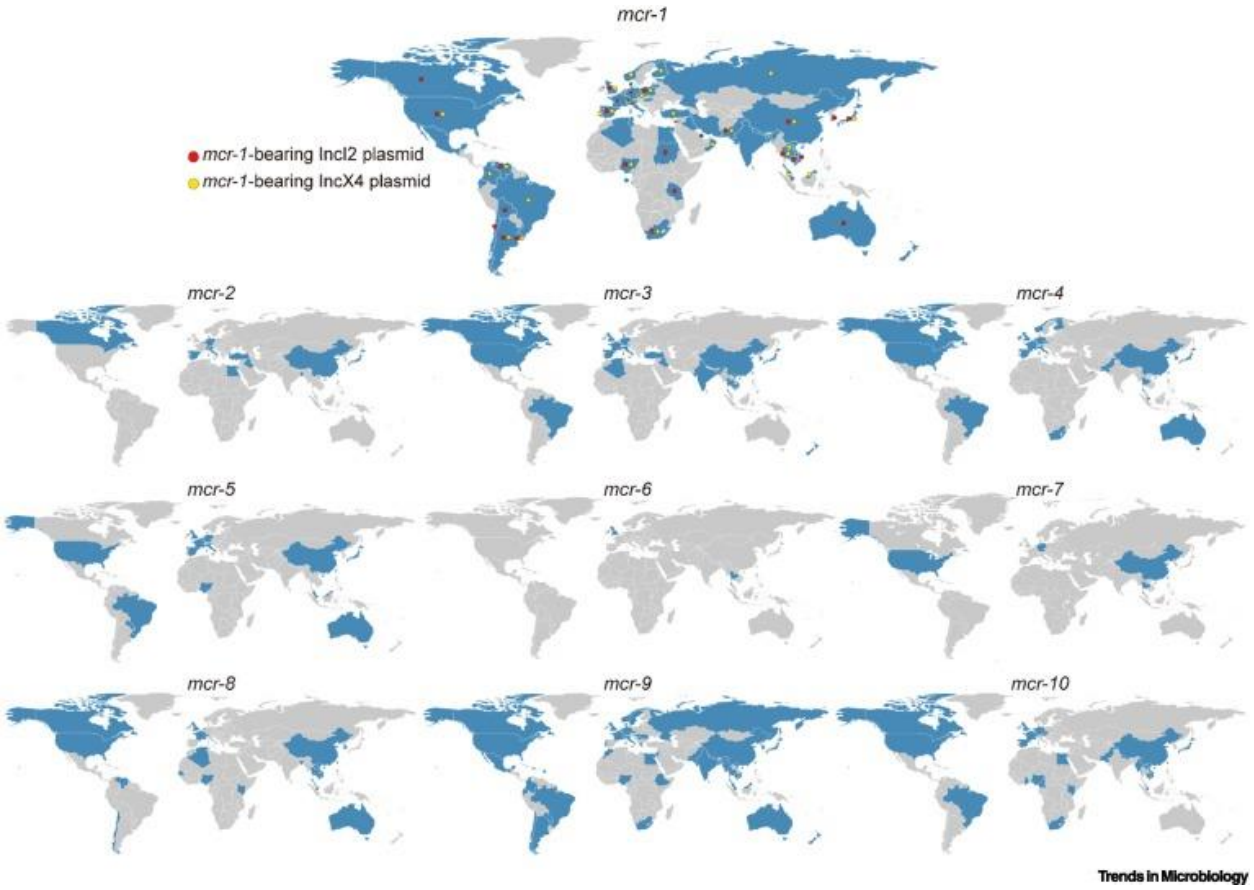
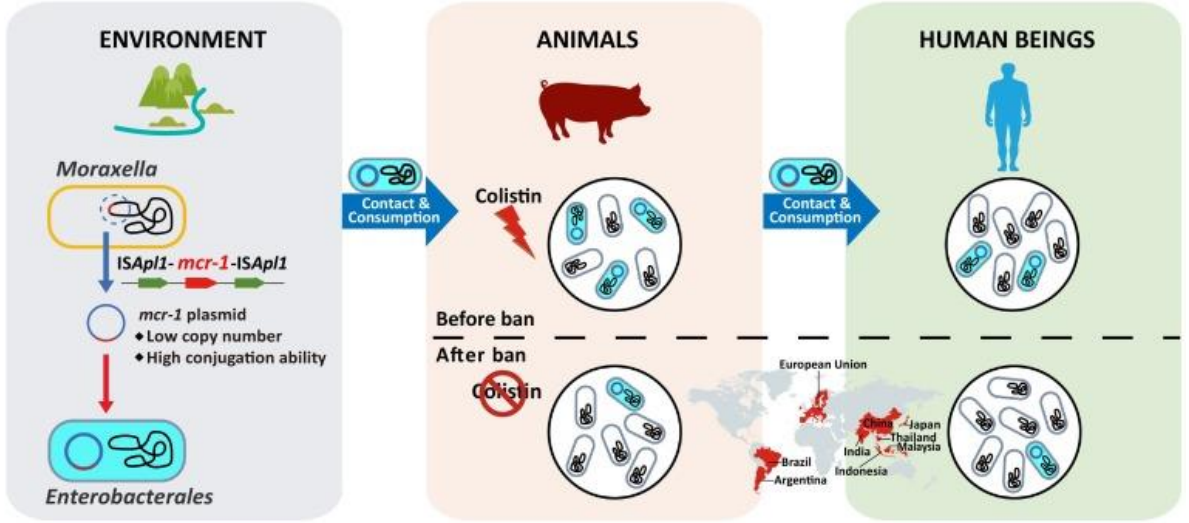


- **Prevalence of *mcr-2* in porcine colistin-resistant *E. coli* (11/53) in Belgium was higher than that of *mcr-1* (7/53)**
- **1,617 bp phosphoethanolamine transferase harboured on a highly transferable IncX4 plasmid**
- **Shares ≈ 80% identity at protein level and 77% at nucleotide level with *mcr-1***

AMR transmission in a One Health context: *mcr* spread highlights the role of the plasmid backbone in aiding transmissibility and inter-species *transfer*



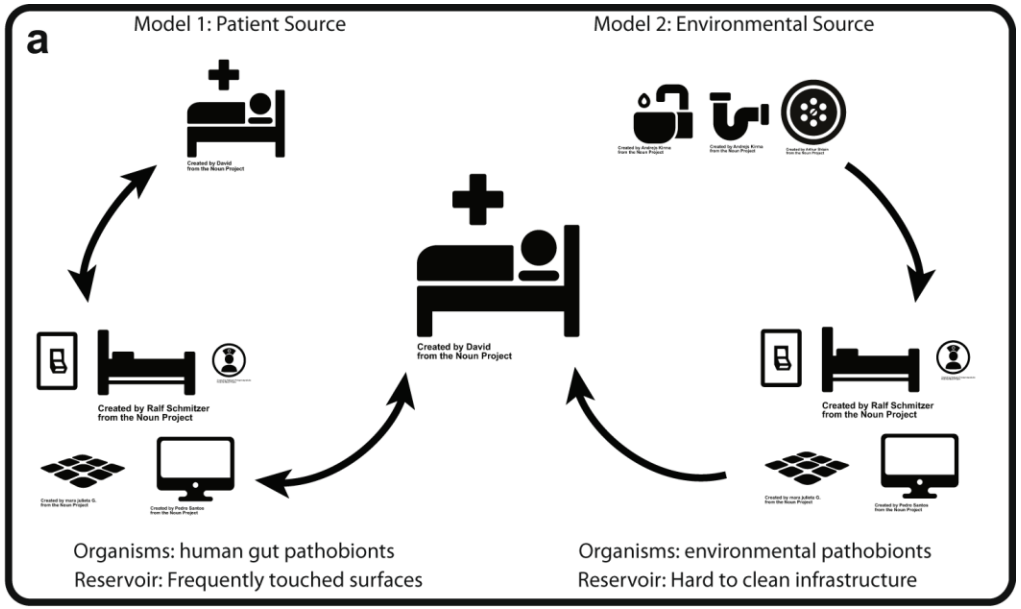


Liu et al, 2024., Trends in Microbiol.

A dynamic reservoir in the clinical environment: the patient

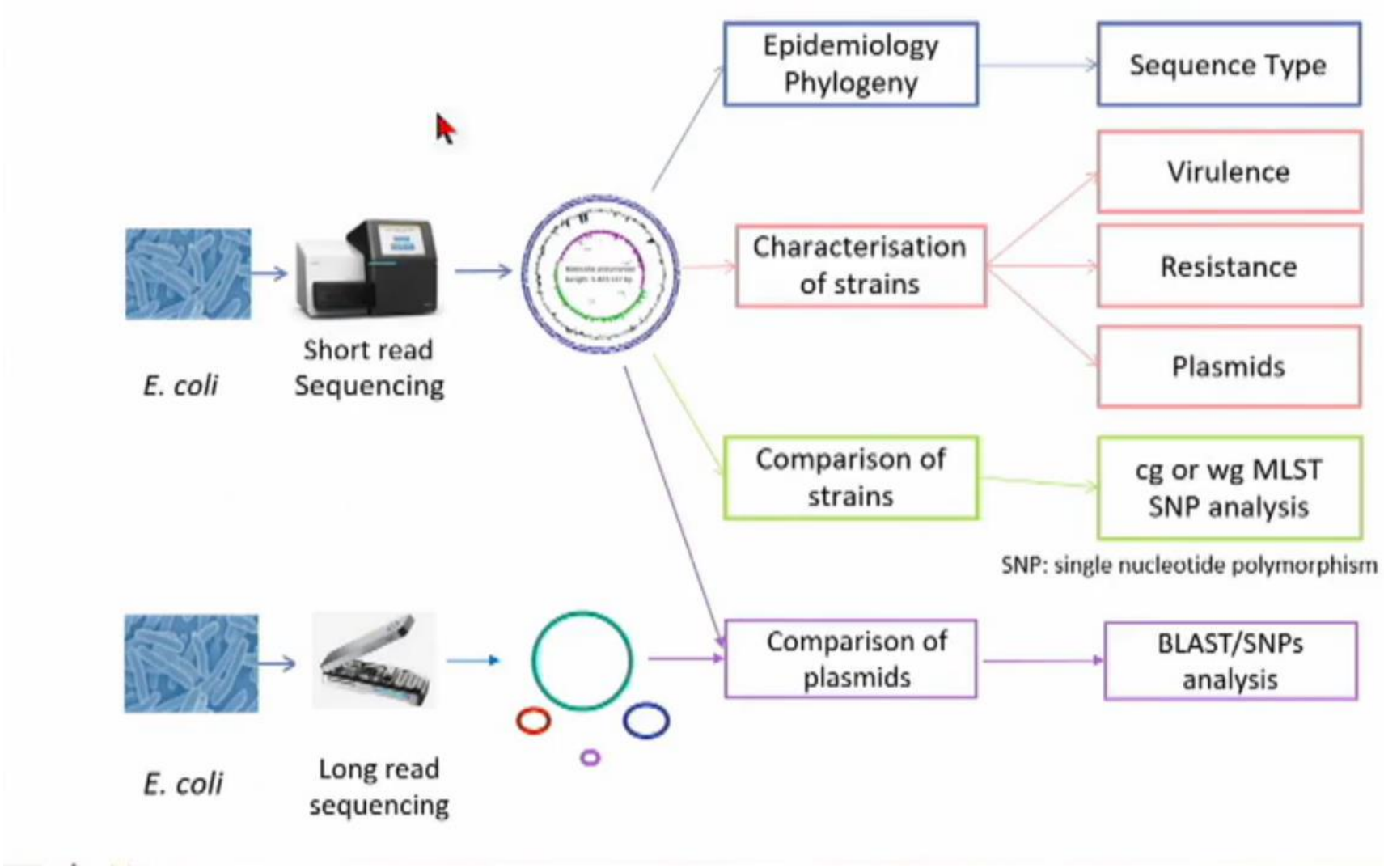
- Increasing intestinal colonization by ESBL-E. coli increased 3-fold from 7% in 2001-2005 to 25.7% in 2016-2020 among inpatients and 10-fold from 2.6% to 26.4% within community settings

- Parallel increased incidence of ESBL-E infections from 2012 to 2017 by 53.3% (from 37.55 to 57.12 77 cases per 10,000 hospitalizations), primarily attributed to an increase in community-acquired infections

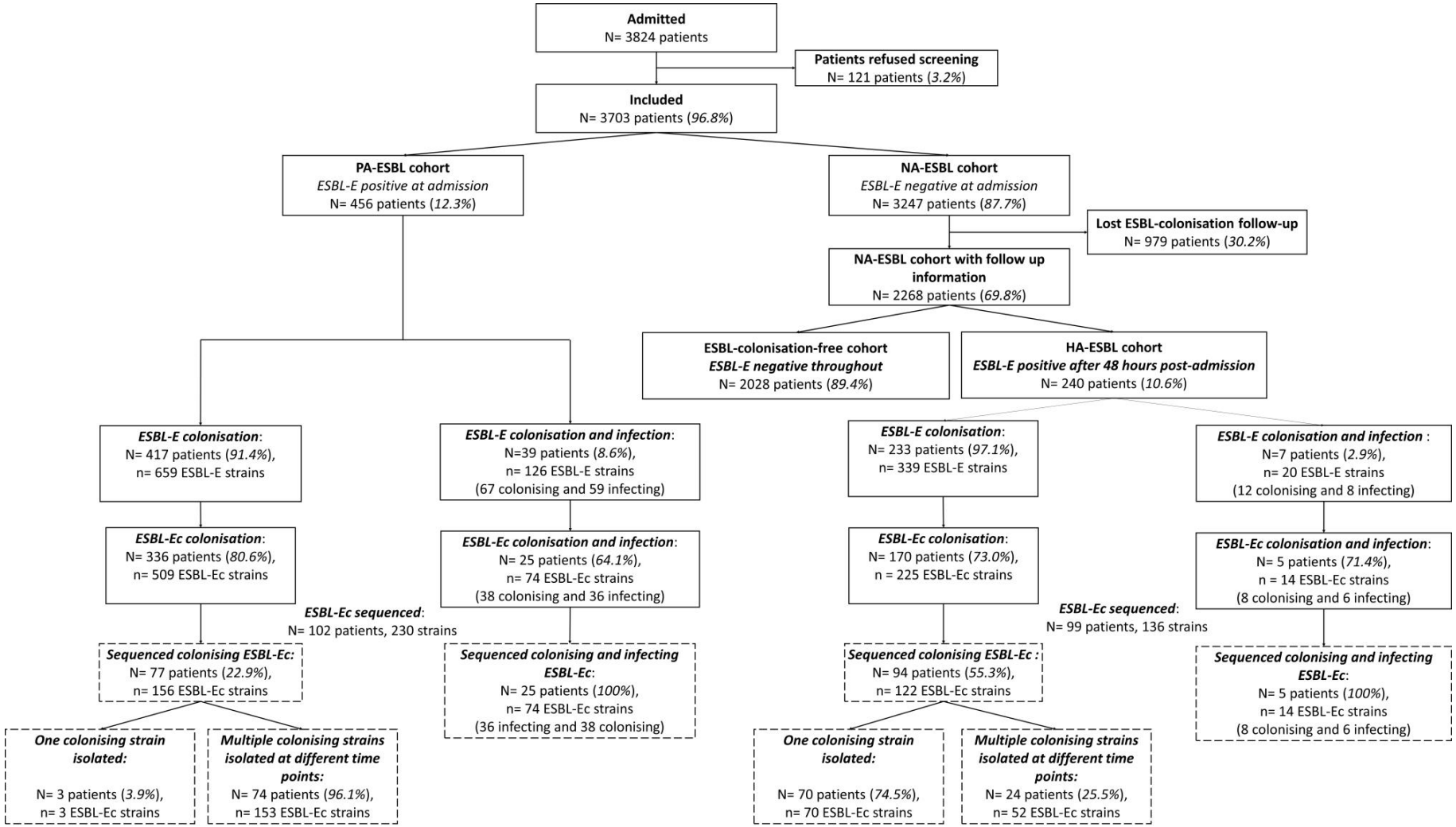


Sukhum et al, 2022., Comms. Medicine

New tools: 3rd generation sequencing



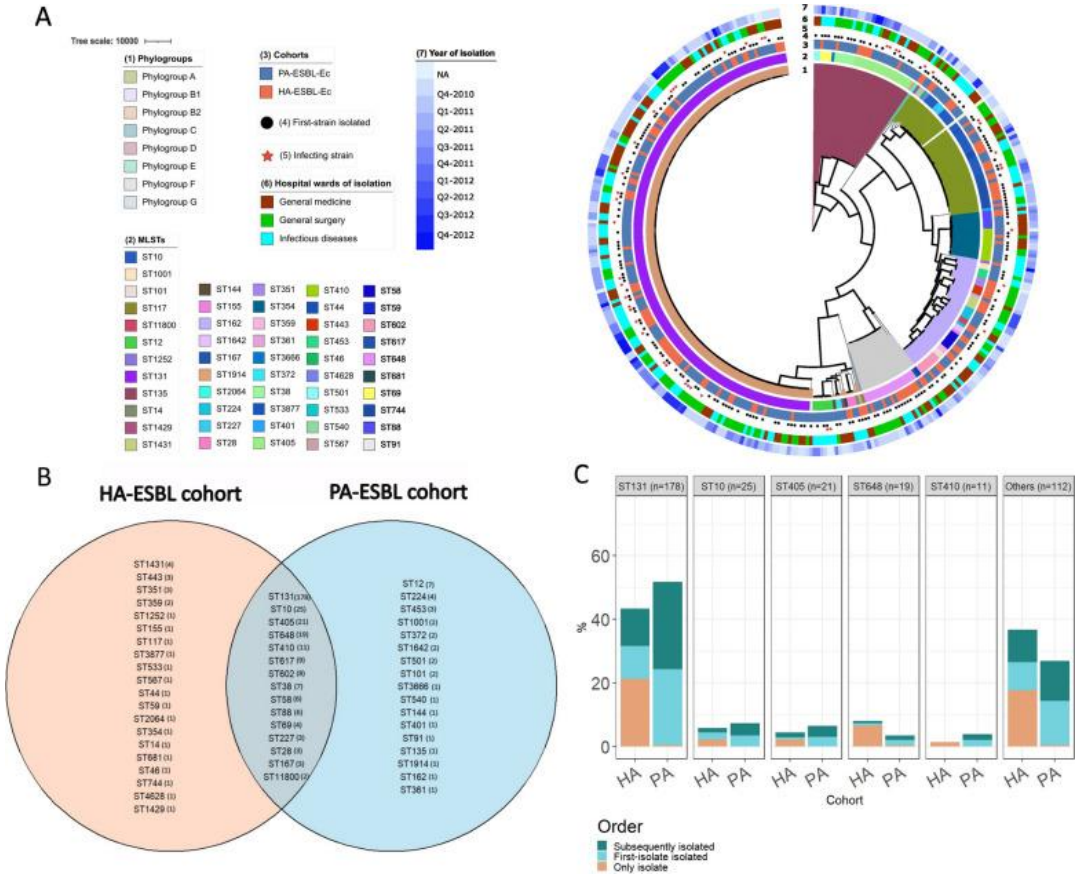
Tracing carriage, acquisition, and transmission of ESBL-producing Escherichia coli over two years in a tertiary care hospital



Nguyen et al, 2024, Genome Medicine

High prevalence of nosocomial acquisition of ESBL-E in a non-ICU setting

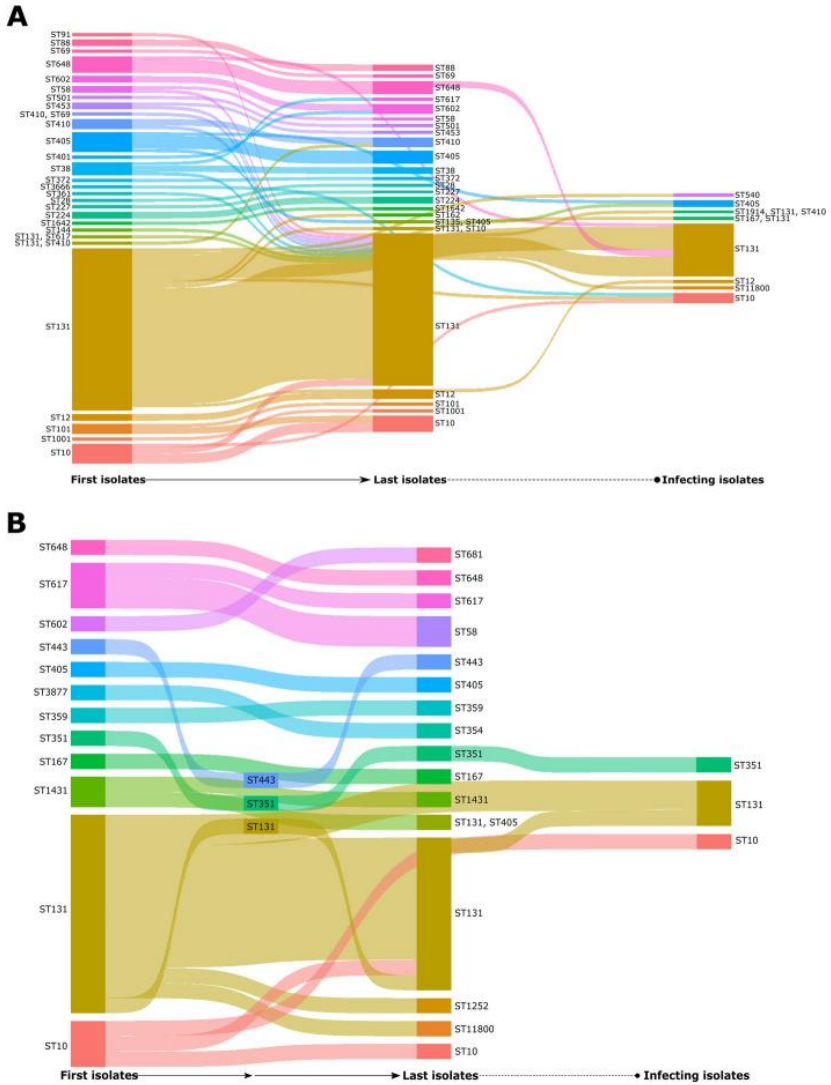
- 12.3% (456/3703) patients were ESBL-positive-at-admission (**PA-ESBL**).
- 10.6% (240/2268) ESBL-negative-at-admission (**NA-ESBL**) patients with follow-up samples acquired ESBL-E (**HA-ESBL**), with an incidence density rate of 7.96 cases/1000 patient-day, notably higher in patients receiving antibiotics ($P < 0.001$).



Nguyen et al, 2024, Genome Medicine

Tracing carriage, acquisition, and transmission of ESBL-producing Escherichia coli over two years in a tertiary care hospital

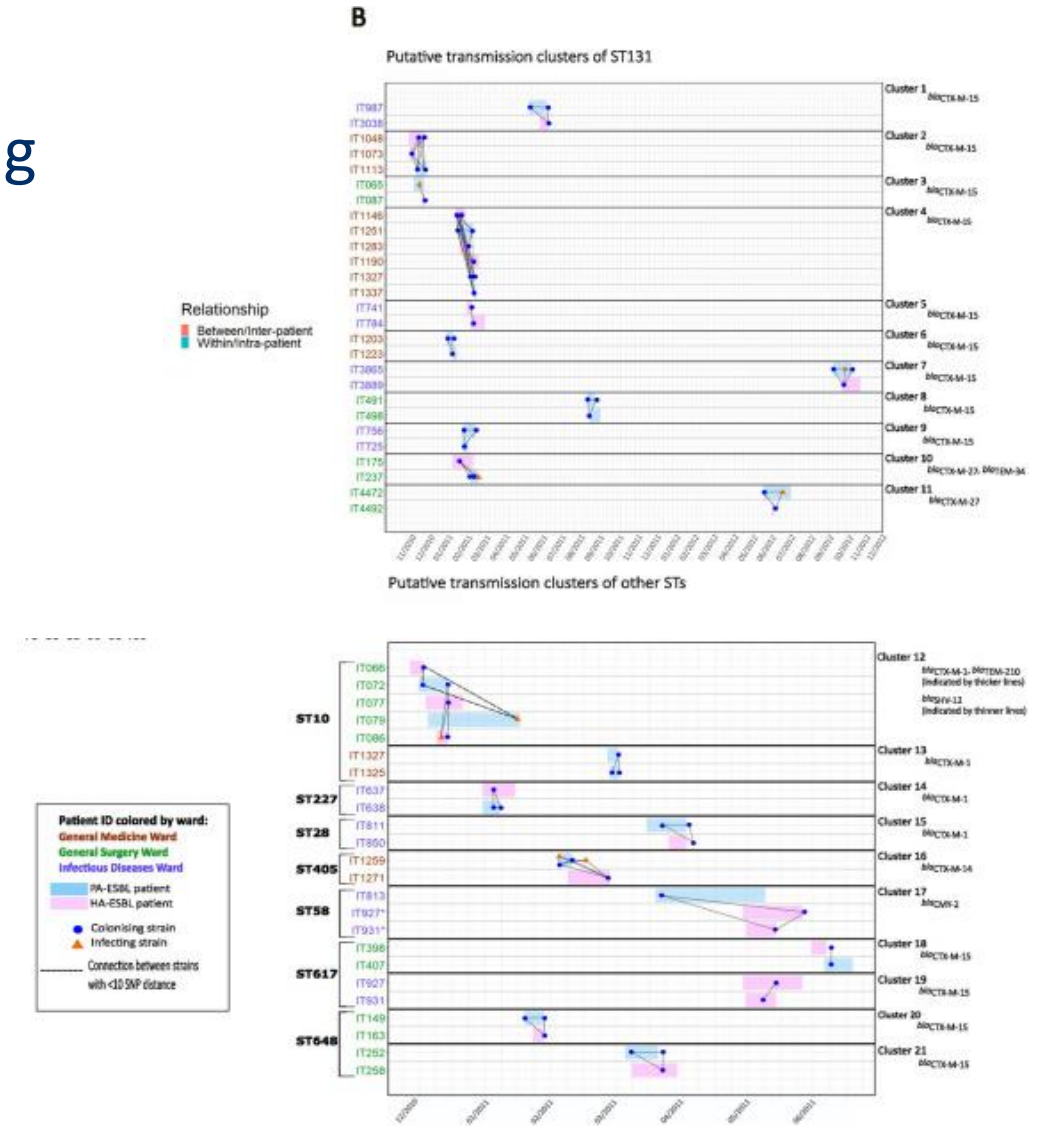
- PA- and HA-ESBL patients developed significantly more ESBL-E infections than ESBL-free patients ($P < 0.001$).
- Sequenced ESBL-Ec showed high clonal diversity dominated by the multidrug-resistant and highly virulent ST131 clade, C2/H30-Rx
- Among ESBL-Ec infections, 60% (18/30) were endogenous.



Nguyen et al, 2024, Genome Medicine

Patient-to-patient putative clonal transmissions at the ward level in both cohorts

- Putative transmission clusters identified among ST131 and other STs by SNP distance ≤ 10
- Supported by strong epidemiological links: patients stayed in the same wards (represented by the colours of patient ID) and with overlapping periods of hospitalisation durations represented by blue and pink bars for PA- and HA-ESBL patients, respectively
- Direct between-patients transmission clusters (*n* = 21) involved 23.9% (48/201) of patients



Nguyen et al, 2024, Genome Medicine

Risk factors for AMR gut colonization of neonates

Horizon 2020 Programme

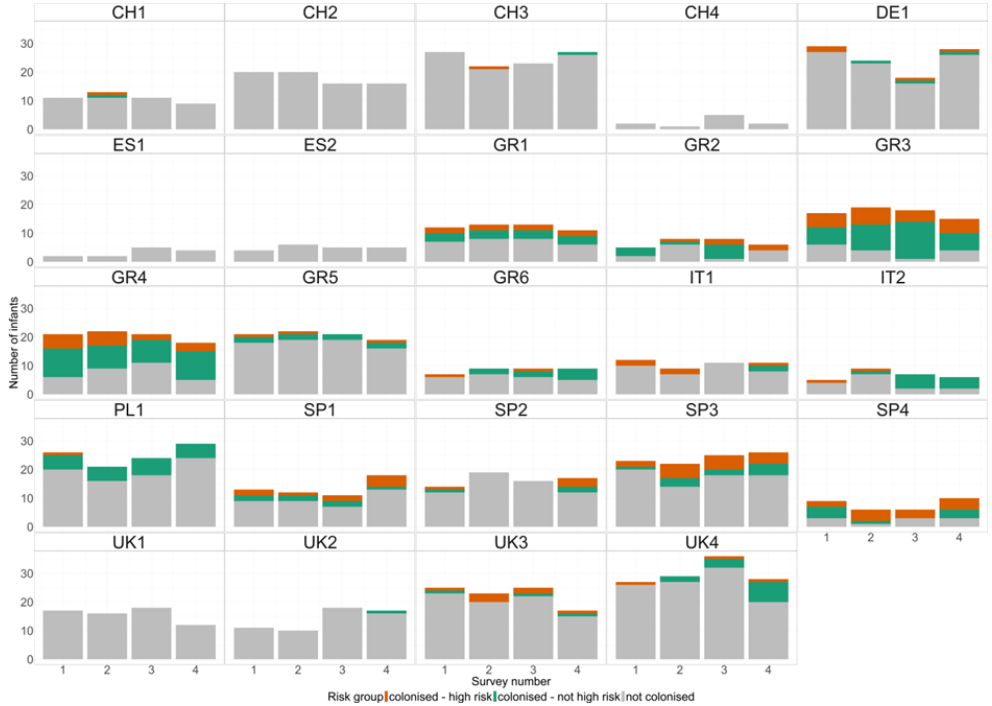
- Infants on neonatal units are at risk of severe bacterial infections, particularly those born at <32 weeks
- Infants colonised by resistant bacteria have an increased risk of sepsis
- 24 sites in 8 countries conducted 4 cross-sectional surveys in a one-month period and collected clinical data, stool samples
- Stool samples were analysed by PCR
- Gene targets of interest in stool samples
  - Carbapenem resistance: blaKPC, blaNDM, blaVIM, blaIMP, blaOXA-48
  - Extended-spectrum beta-lactamase: blaCTX-M group1, blaCTX-M group9
  - Vancomycin resistance: vanA, vanB

NeoIPC

Risk factors for AMR gut colonization of neonates

Horizon 2020 Programme

- Resistant bacterial colonisation was low overall (20%, 301/1447 samples)
- Significant variation between units and countries ($p<0.001$)
- Both low- and high-risk infants were colonised
- Unit-level IPC interventions target both direct and indirect effects of colonisation regardless of risk status
- Interventions focusing only on infants at high risk of sepsis will miss significant resistant bacterial colonisation in low-risk infants



NeoIPC

Contamination of inanimate surfaces as a source of HAI

- Inanimate surfaces may be contaminated by a range of HAI pathogens
- This contamination plays a role in acquisition of HAI via direct or indirect contact with contaminated surfaces
- Contamination with clinically relevant pathogens may persist for several months
- Duration of contamination is influenced by several factors
- 20% of HAI outbreaks can be attributed to an environmental source

How long do nosocomial pathogens persist on inanimate surfaces?

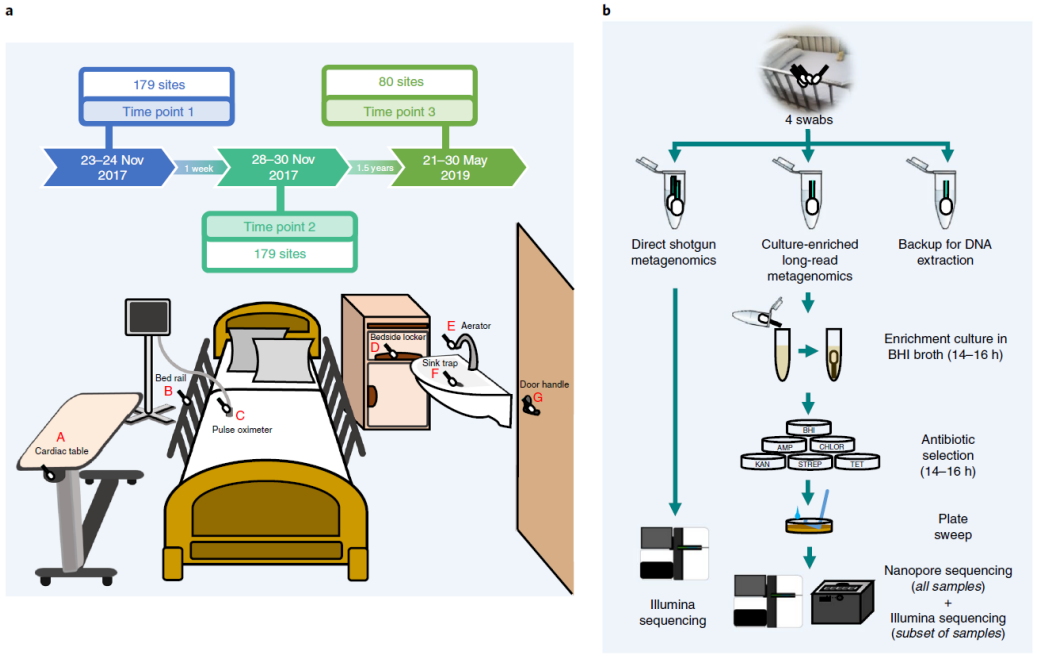
Table 1: Persistence of clinically relevant bacteria on dry inanimate surfaces.

Type of bacterium	Duration of persistence (range)
Acinetobacter spp.	3 days to 5 months
Bordetella pertussis	3 – 5 days
Campylobacter jejuni	up to 6 days
Clostridium difficile (spores)	5 months
Chlamydia pneumoniae, C. trachomatis	≤ 30 hours
Chlamydia psittaci	15 days
Corynebacterium diphtheriae	7 days – 6 months
Corynebacterium pseudotuberculosis	1–8 days
Escherichia coli	1.5 hours – 16 months
Enterococcus spp. including VRE and VSE	5 days – 4 months
Haemophilus influenzae	12 days
Helicobacter pylori	≤ 90 minutes
Klebsiella spp.	2 hours to > 30 months
Listeria spp.	1 day – months
Mycobacterium bovis	> 2 months
Mycobacterium tuberculosis	1 day – 4 months
Neisseria gonorrhoeae	1 – 3 days
Proteus vulgaris	1 – 2 days
Pseudomonas aeruginosa	6 hours – 16 months; on dry floor: 5 weeks
Salmonella typhi	6 hours – 4 weeks
Salmonella typhimurium	10 days – 4.2 years
Salmonella spp.	1 day
Serratia marcescens	3 days – 2 months; on dry floor: 5 weeks
Shigella spp.	2 days – 5 months
Staphylococcus aureus, including MRSA	7 days – 7 months
Streptococcus pneumoniae	1 – 20 days
Streptococcus pyogenes	3 days – 6.5 months
Vibrio cholerae	1 – 7 days

Kramer et al, 2006, BMC Infectious Dis.

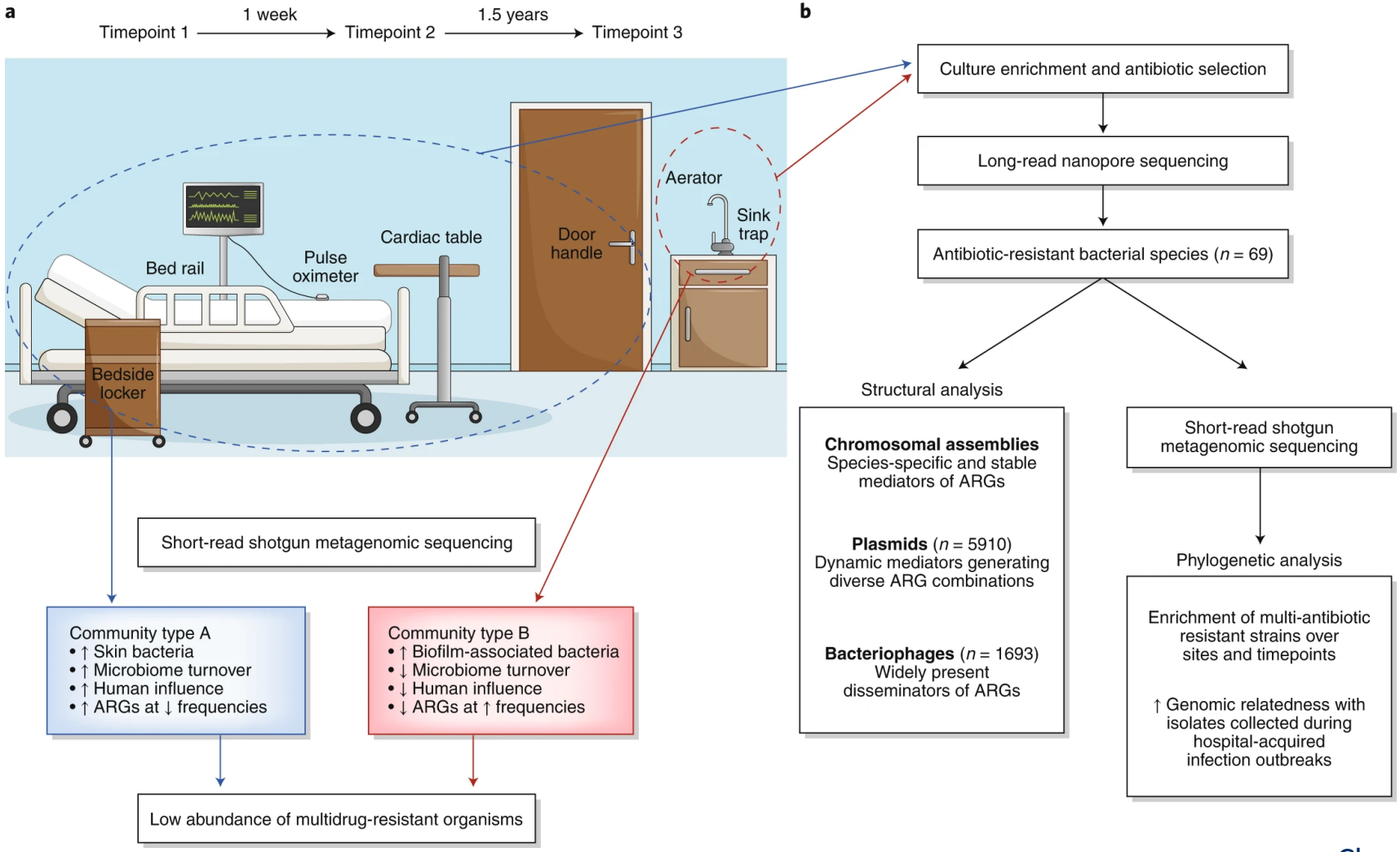
Cartography of opportunistic pathogens and AMR genes in a tertiary hospital environment

- Repeated sampling (up to 1.5 years apart) of 179 sites associated with 45 beds
- Both shotgun metagenomics and culture enriched long read metagenomics was performed
- Phylogenetics identified a few multidrug-resistant strains as being widely distributed and stably colonizing across sites.
- Comparisons with clinical isolates indicated that such microbes can persist in hospitals for extended periods (>8 years), to opportunistically infect patients



Chng et al, 2024, Nature Medicine

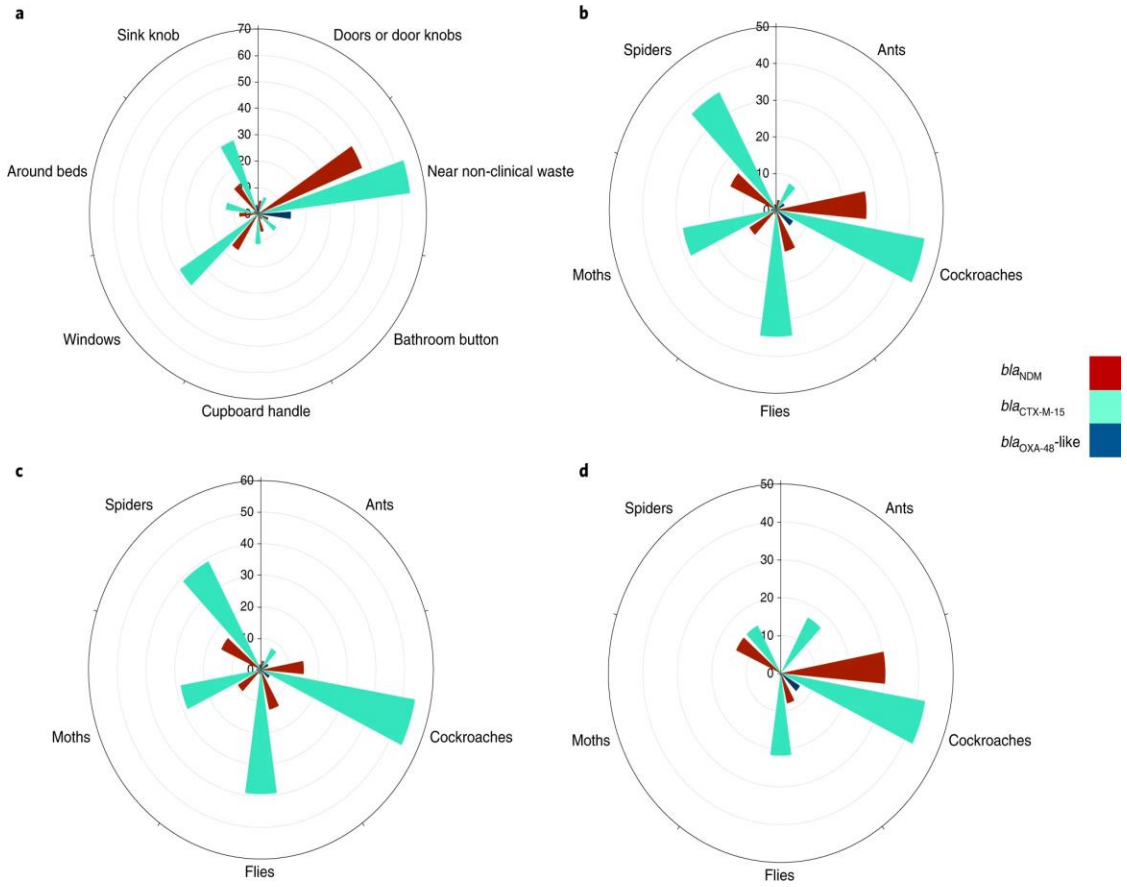
Uncovering hidden antimicrobial resistance patterns within the hospital microbiome



Chng et al, 2024, Nature Medicine

Unusual reservoirs of AMR in a LMIC setting

- Samples from surgical site infections (SSIs), hospital surfaces (HSs) and arthropods (summer and winter 2016) were investigated to gauge the incidence and transmission of AMR pathogens in a public hospital in Pakistan
- *bla*$_{NDM}$ was most commonly detected, with 15.5%, 15.1% and 13.3% of samples positive in SSIs, HSs and arthropods, respectively



Hassan et al, 2021, Nature Microbiology

Conclusions

- Healthcare systems differ in the type and abundance of AMR pathogens and therefore also the environmental niches that need to be screened
- LMIC settings might have local reservoirs relevant to the climate, and other socioeconomic differences
- Mapping the spread of multidrug-resistant organisms within healthcare systems will remain an important pillar of the global effort to reduce the spread of AMR in this most important setting

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