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Exploring multidrug resistance patterns in community-acquired *E. coli* urinary tract infections with machine learning

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► To cite this version:

E. Hodbert, O. Leménand, R. Mpoyi, S. Thibaut, David Boutoille, et al.. Exploring multidrug resistance patterns in community-acquired *E. coli* urinary tract infections with machine learning. European Congress of Microbiology and Infectious Diseases, Apr 2024, Barcelone, Spain. hal-04687851

HAL Id: hal-04687851

<https://hal.science/hal-04687851v1>

Submitted on 4 Sep 2024

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Introduction

- **Multi-drug resistant (MDR) bacteria** cause infections with limited treatment options, resulting in aggravated morbidity and mortality¹
- **MDR often occur more frequently** than expected if resistance associations happened by chance²
- However, **clinically relevant antibiotic resistance patterns** remain relatively unexplored³
- **Machine learning approaches** have proved useful to investigate MDR patterns^{3,4}

Objective : identify and quantify resistance associations within isolates from community-acquired *E. coli* urinary tract infections (CA-*E. coli*-UTI)

Methods

- Data : antibiograms of **community-acquired *E. coli* urinary tract infections** collected by the French national surveillance system of antimicrobial resistance (PRIMO)
- Analyses conducted separately by
 - **Year** : 2018 to 2022
 - **Phenotype** : extended-spectrum beta-lactamase producing (ESBL) *E. coli* isolates distinguished from non-ESBL *E. coli* isolates
- **Identification of patterns with association rule mining** : machine learning technique used to discover interesting patterns between elements in a dataset
- **Evaluation of multiresistance patterns** with 2 measures of interest :
 - eSup \approx pattern frequency
 - cLift \approx strength of resistance associations between antimicrobials within the pattern
- **Pruning of patterns**, keeping those with higher eSup and cLift than expected if resistance associations were random (p -value ≤ 0.05)
- **Creation of graphical networks** by decomposing resistance patterns into nodes (antimicrobials) connected by edges (associations of resistances)

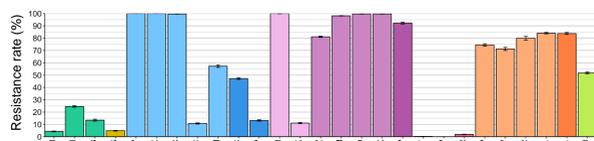
Descriptive results

Data description

	2018	2019	2020	2021	2022
Number of isolates	360 303	450 845	450 169	571 178	629 104
ESBL	10 152 (3%)	13 555 (3%)	13 267 (3%)	16 004 (3%)	18 642 (3%)
Non-ESBL	350 142 (97%)	437 272 (97%)	436 880 (97%)	555 132 (97%)	610 462 (97%)
Women	276 231 (84%)	356 020 (84%)	361 781 (84%)	457 828 (84%)	520 166 (84%)
Men	50 710 (16%)	66 006 (16%)	68 740 (16%)	85 457 (16%)	98 080 (16%)
Mean age	63	63	65	65	65

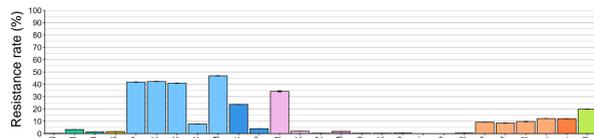
Prevalence of individual antimicrobial resistances in ESBL and non-ESBL *E. coli* isolates

ESBL *E. coli* (2022)



	AKN	GEN	TOB	FOS	AMP	AMX	TIC	MEC	TEM	AMC	TZP	CXM	FOX	CAZ	CFM	CRO	CTX	FEP	ERT	IMP	FUR	CIP	LEV	NOR	OFL	NAL	TSU
% tested	100%	95%	43%	92%	80%	99%	88%	89%	47%	98%	90%	8%	98%	96%	96%	100%	100%	27%	100%	27%	98%	40%	26%	16%	83%	44%	100%

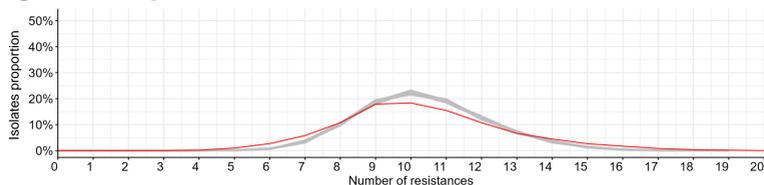
Non-ESBL *E. coli* (2022)



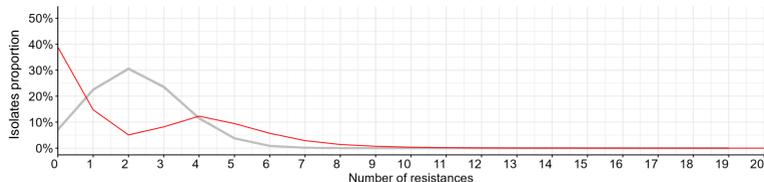
	AKN	GEN	TOB	FOS	AMP	AMX	TIC	MEC	TEM	AMC	TZP	CXM	FOX	CAZ	CFM	CRO	CTX	FEP	ERT	IMP	FUR	CIP	LEV	NOR	OFL	NAL	TSU
% tested	100%	97%	49%	98%	80%	97%	90%	95%	51%	99%	95%	9%	98%	95%	94%	100%	100%	17%	100%	18%	97%	35%	20%	15%	83%	47%	100%

Testing the independence of individual resistances

ESBL *E. coli* (2022)



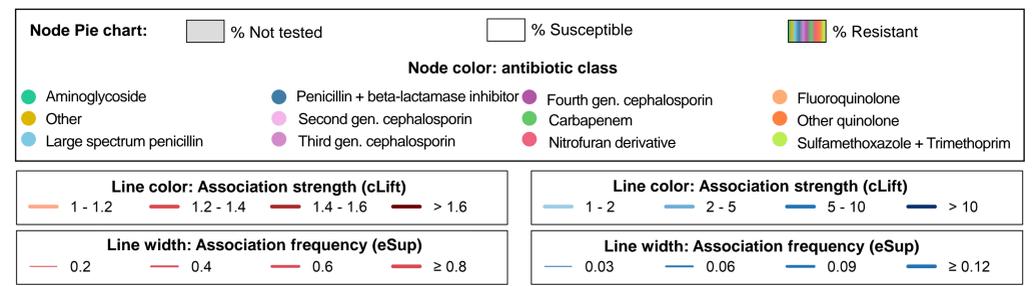
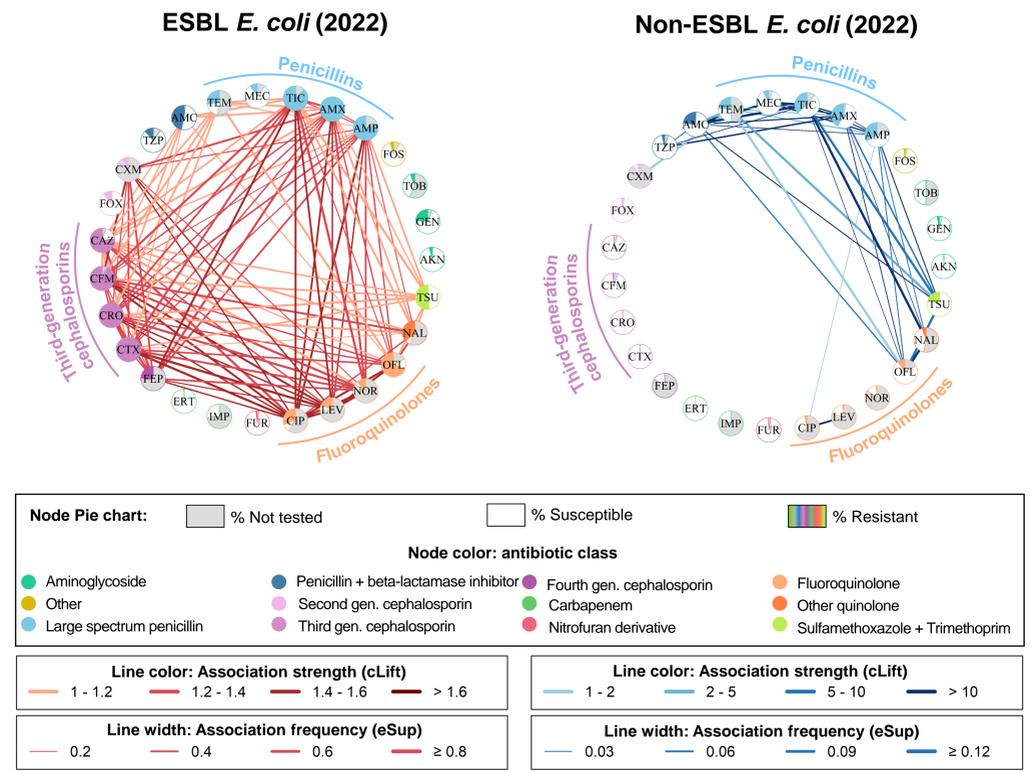
Non-ESBL *E. coli* (2022)



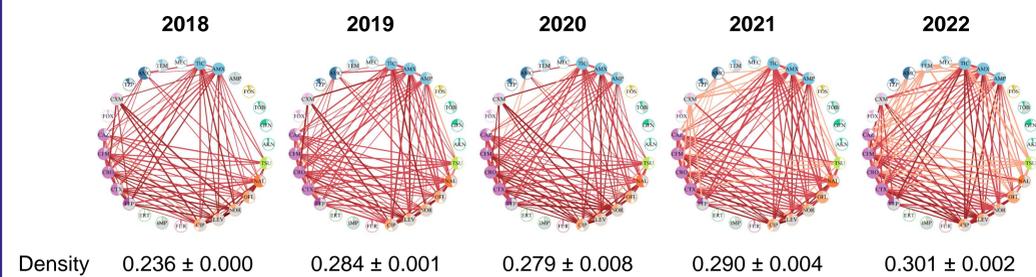
- Red curve : distribution the number of resistances per isolate in observed data
- Grey curves : distribution of the number of resistances per isolate in data simulated under the hypothesis that resistance associations occur randomly

→ The observed distribution of the number of resistances per isolate differs from what would be expected if resistance associations were random in non-ESBL *E. coli* isolates ($p < 0.10$)

Resistance associations networks have higher density for ESBL *E. coli* than non-ESBL *E. coli*

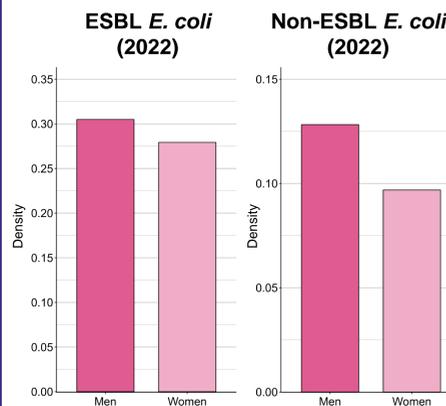


ESBL *E. coli* network density increases over time

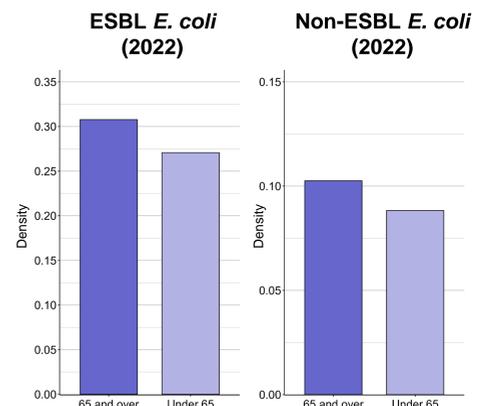


Network density differs by age and gender

Network density is higher for men



Network density is higher for people aged 65 and over



- Higher network density = more associations of antibiotic resistance
- Main difference : cefuroxime (CXM) involved in more resistance patterns in men and individuals over 65

Conclusion

- **ESBL *E. coli* shows a higher number of resistance associations** compared to non-ESBL *E. coli*
- Resistance associations in **ESBL *E. coli* increase from 2018 to 2022**
- **Men and people aged 65 and over show a higher number of resistance associations**, with a significant proportion of additional associations involving **CXM**
- Future work could investigate the potential linkage between these phenotypic resistance associations and genetic coresistance mechanisms

References

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Acknowledgments : This work was conducted as part of the COMBINE research program, which benefitted from a government grant managed by the Agence Nationale de la Recherche under the Programme France 2030 with the reference ANR 22 PAMR 0003