SYKEHUSET I VESTFOLD

What's going on with *Haemophilus influenzae?*

- Update on epidemiology and AST

Dagfinn Skaare MD PhD
Department of Microbiology / Infection Prevention and Control
Tønsberg, Vestfold, Norway
NordicAST Workshop May 13, 2026

Taxonomic changes

ORIGINAL RESEARCH article

Front. Microbiol., 31 March 2026

Sec. Infectious Agents and Disease

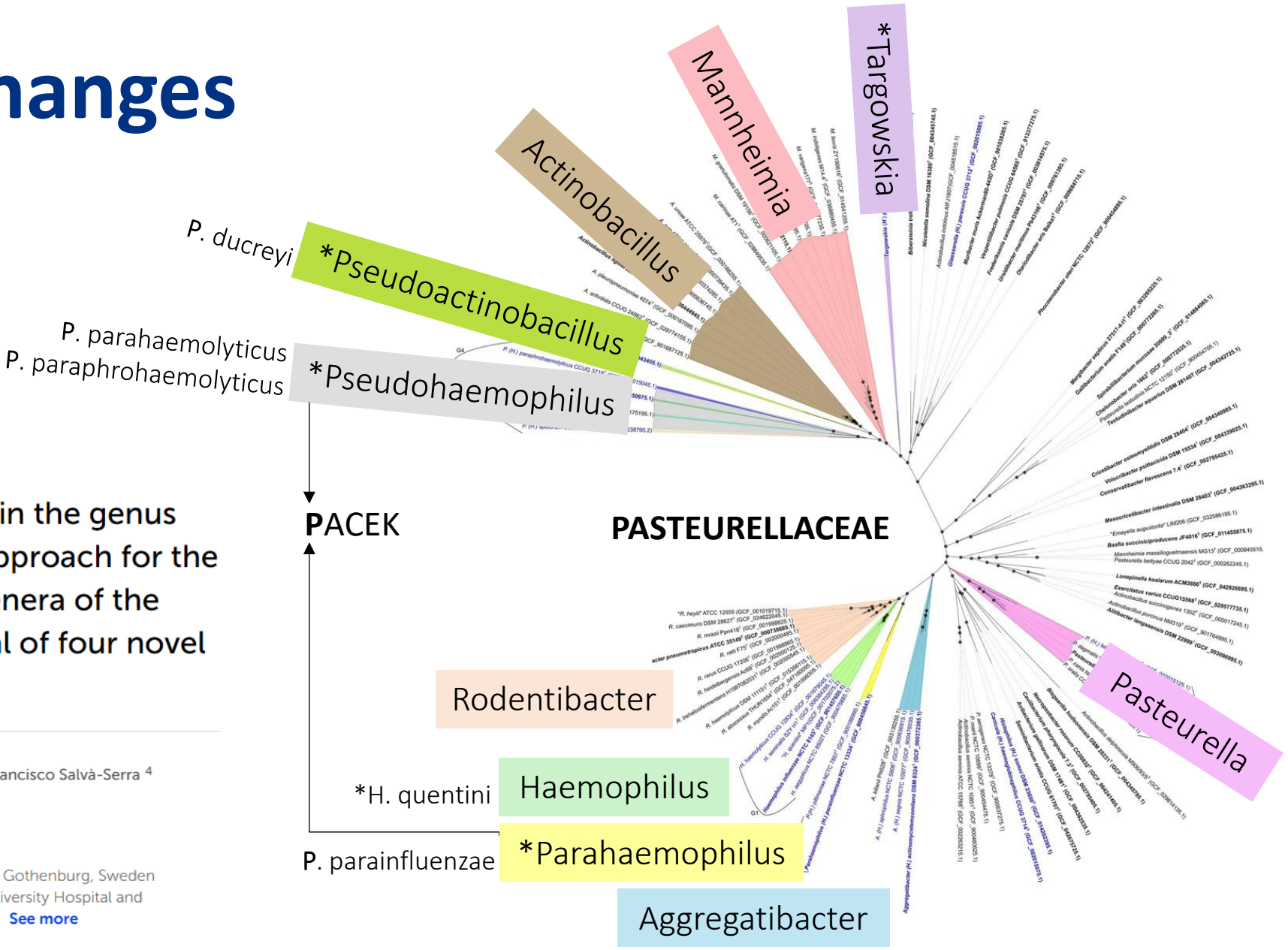
Volume 17 - 2026 | https://doi.org/10.3389/fmicb.2026.1798515

Resolving taxonomic uncertainties in the genus *Haemophilus*: a genomics-based approach for the reclassification of species within genera of the family *Pasteurellaceae* and proposal of four novel genera and one novel species

Guillem Segui [1,2*] Beatriz Piñeiro-Iglesias [1,2,3] Francisco Salvà-Serra [4]

Roger Karlsson [1,2,3,5] Edward R. B. Moore [1,2,3*]

1. Department of Clinical Microbiology, Sahlgrenska University Hospital, Gothenburg, Sweden
2. Culture Collection University of Gothenburg (CCUG), Sahlgrenska University Hospital and Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden See more



An under-recognised priority pathogen

Non-typeable *Haemophilus influenzae*, an under-recognised pathogen

Johan Van Eldere, Mary P E Slack, Shamez Ladhani, Allan W Cripps

Lancet Infect Dis 2014; 14: 1281–92

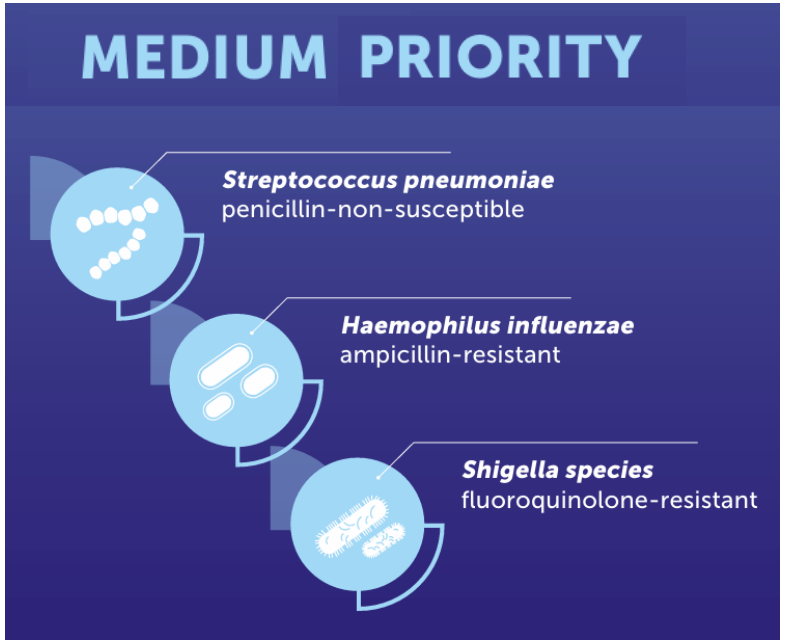
Published Online July 8, 2014 http://dx.doi.org/10.1016/S1473-3099(14)70734-0

Discovery, research, and development of new antibiotics: the WHO priority list of antibiotic-resistant bacteria and tuberculosis

Evelina Tacconelli, Elena Carrara, Alessia Savoldi*, Stephan Harbarth, Marc Mendelson, Dominique L Monnet, Céline Pulcini, Gunnar Kahlmeter, Jan Kluytmans, Yehuda Carmeli, Marc Ouellette, Kevin Outterson, Jean Patel, Marco Cavaleri, Edward M Cox, Chris R Houchens, M Lindsay Grayson, Paul Hansen, Nalini Singh, Ursula Theuretzbacher, Nicola Magrini, and the WHO Pathogens Priority List Working Group†*

Lancet Infect Dis 2018; 18; 318–27

Published Online December 21, 2017 http://dx.doi.org/10.1016/S1473-3099(17)30753-3



Van Eldere et al. Lancet Infect Dis 2014
Tacconelli et al. Lancet Infect Dis 2018

dagfinn.skaare@siv.no

WHO BPPL 2017

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Published Online July 8, 2014 http://dx.doi.org/10.1016/S1473-3099(14)70734-0

The WHO Bacterial Priority Pathogens List 2024: a prioritisation study to guide research, development, and public health strategies against antimicrobial resistance

Hatim Sati, Elena Carrara*, Alessia Savoldi, Paul Hansen, Jacopo Garlasco, Enrica Campagnaro, Simone Boccia, Juan Antonio Castillo-Polo, Eugenia Magrini, Pilar Garcia-Vello, Eve Wool, Valeria Gigante, Erin Duffy, Alessandro Cassini, Benedikt Huttner, Pilar Ramon Pardo, Mohsen Naghavi, Fuad Mirzayev, Matteo Zignol, Alexandra Cameron, Evelina Tacconelli, and the WHO Bacterial Priority Pathogens List Advisory Group†*

Lancet Infect Dis 2025; 25: 1033–43

Published Online April 14, 2025 https://doi.org/10.1016/S1473-3099(25)00118-5

[Van Eldere et al. Lancet Infect Dis 2014]
[Sati et al. Lancet Infect Dis 2025]

dagfinn.skaare@siv.no

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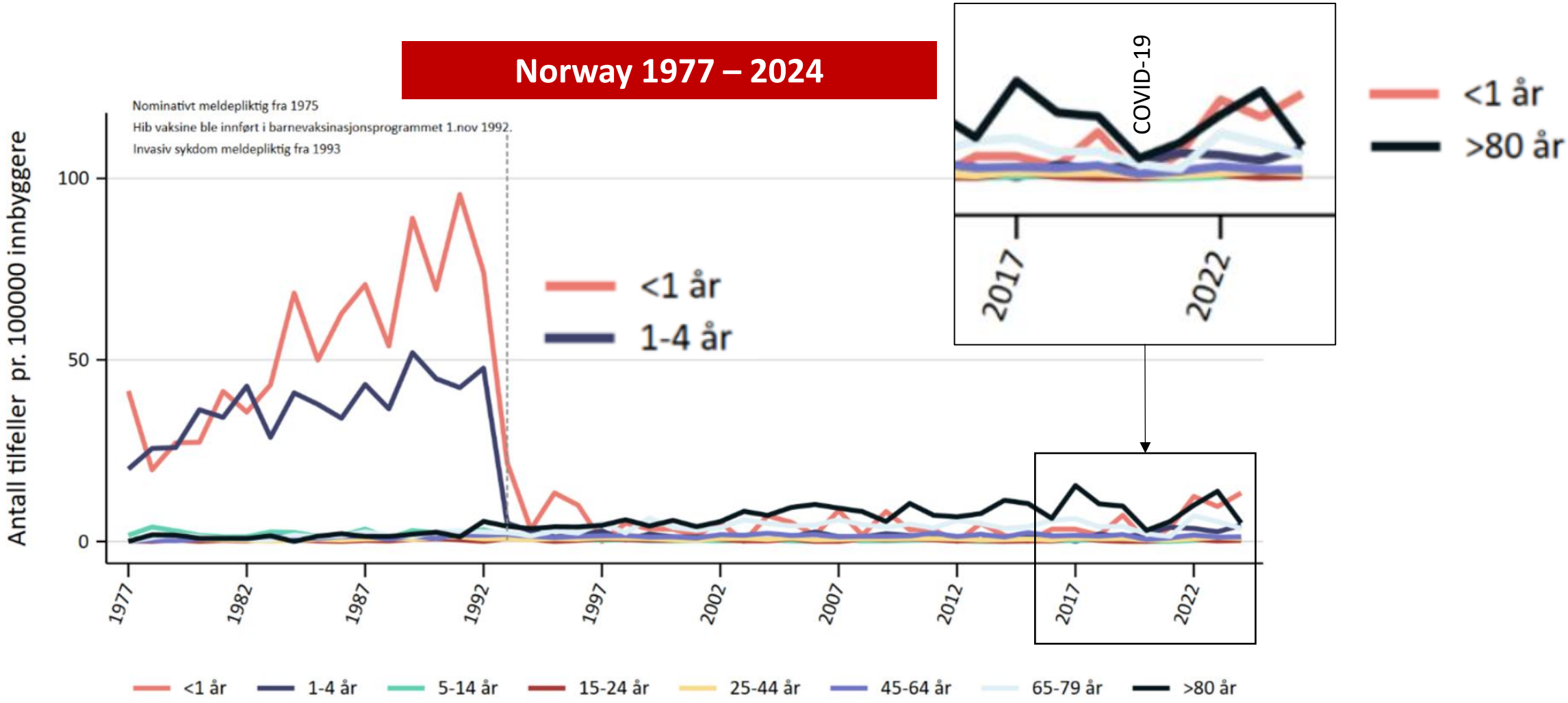
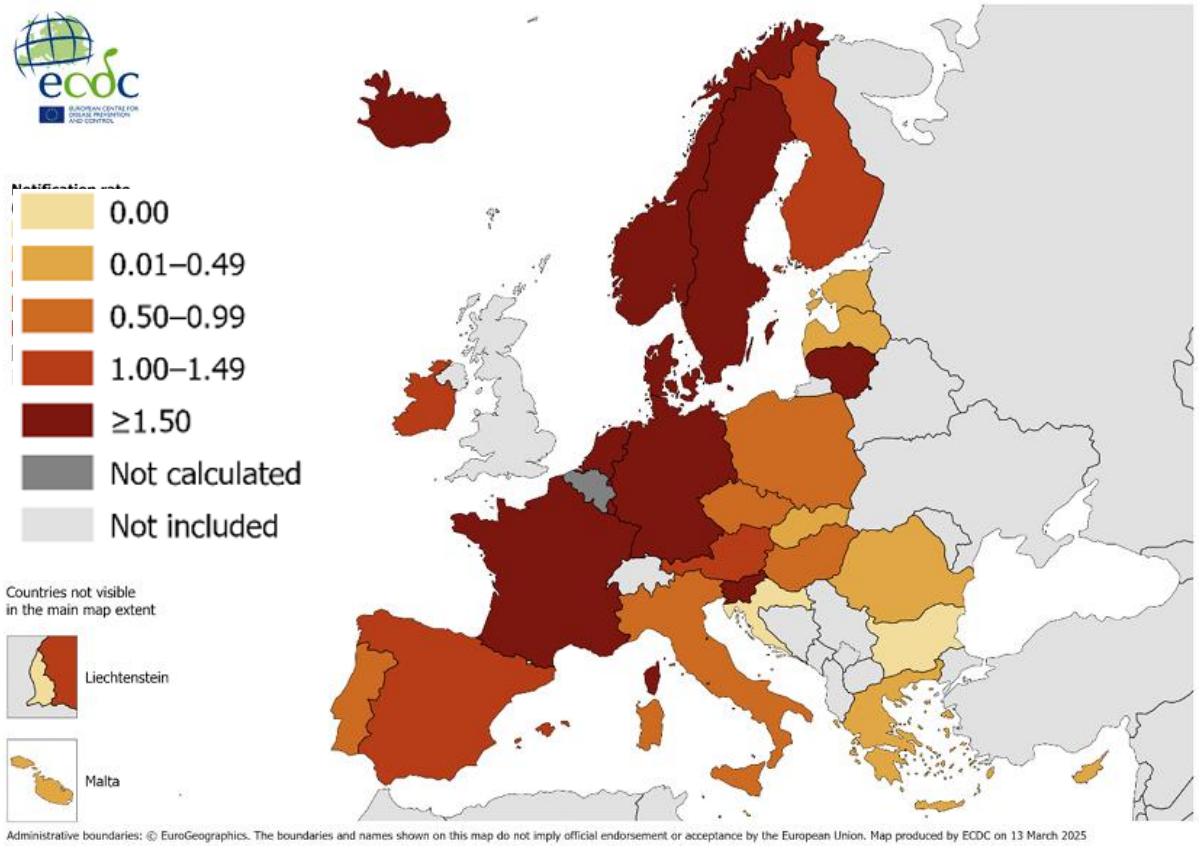
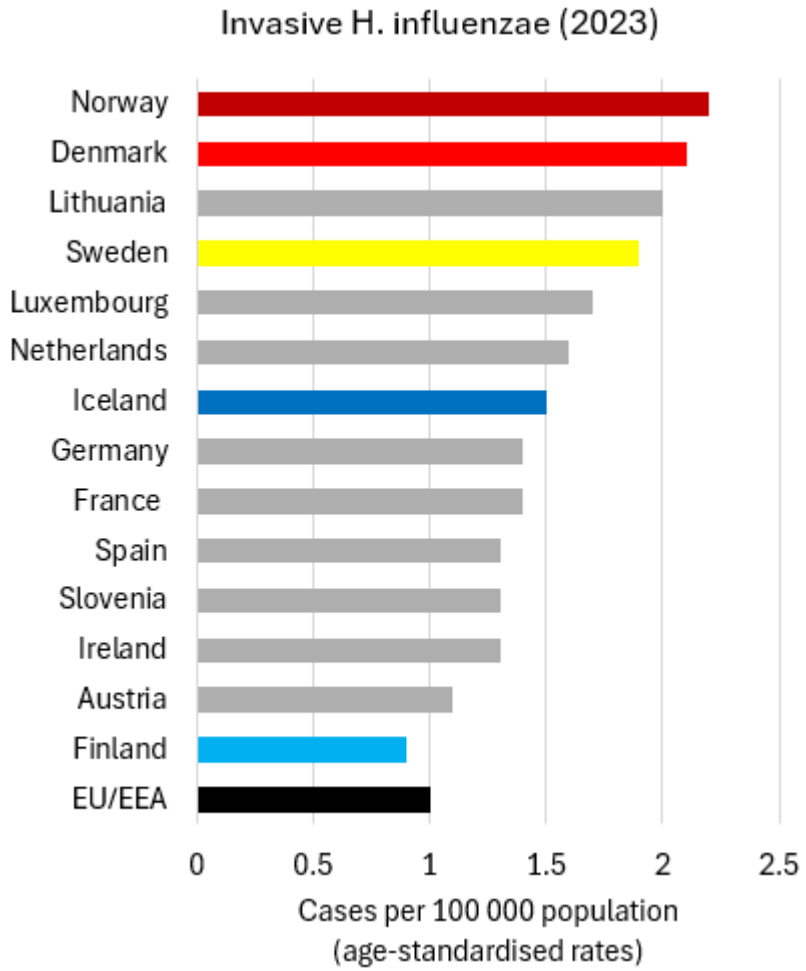
Invasive disease



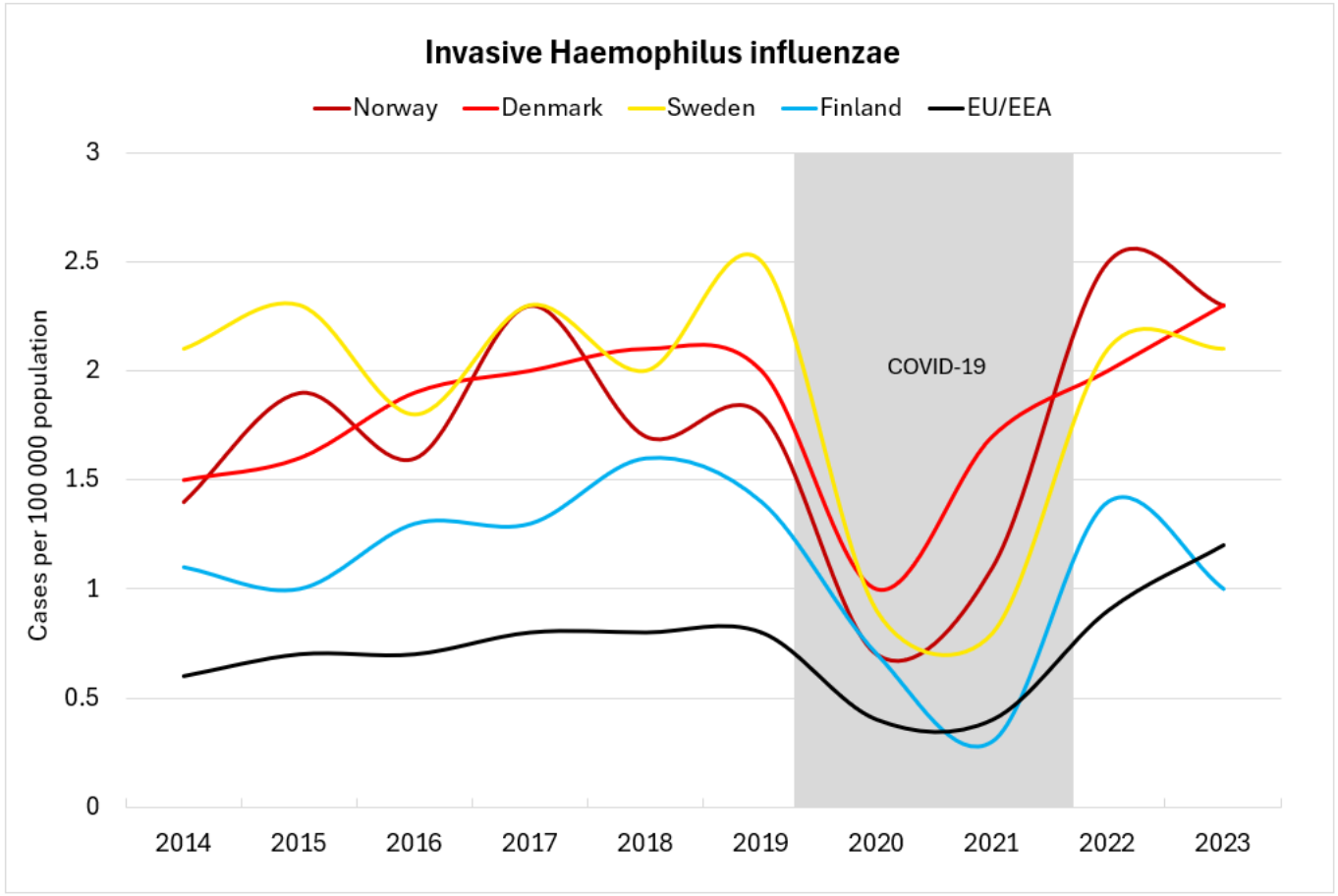
Invasive disease

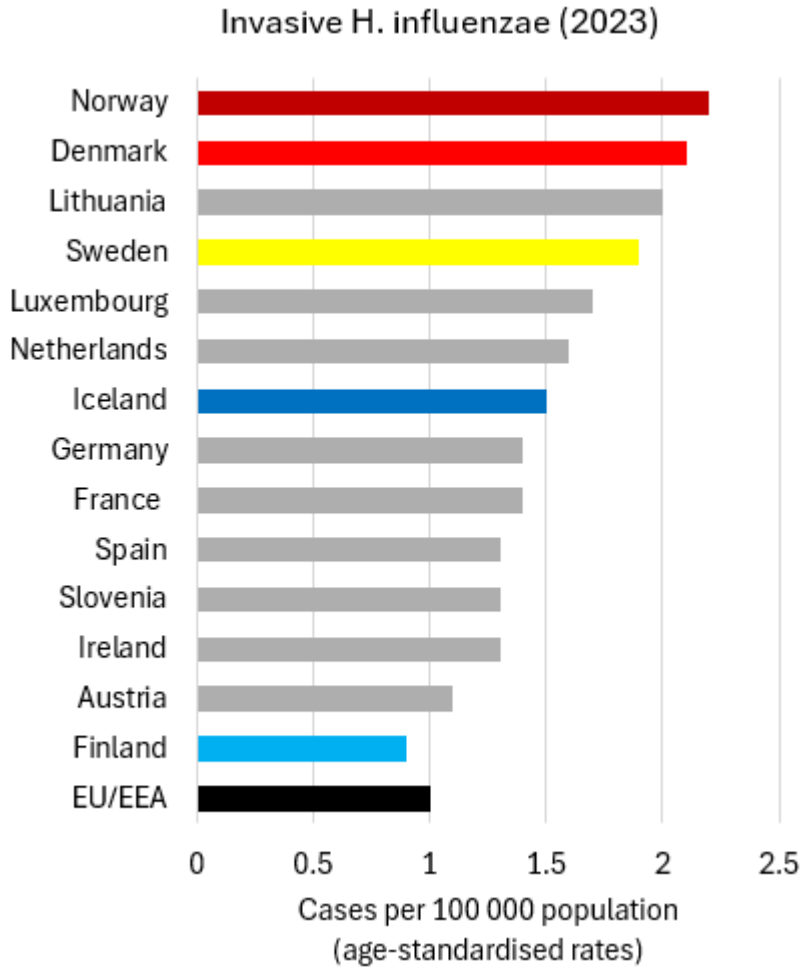
Figure 1. Confirmed Haemophilus influenzae disease cases per 100 000 population by country, EU/EEA, 2023



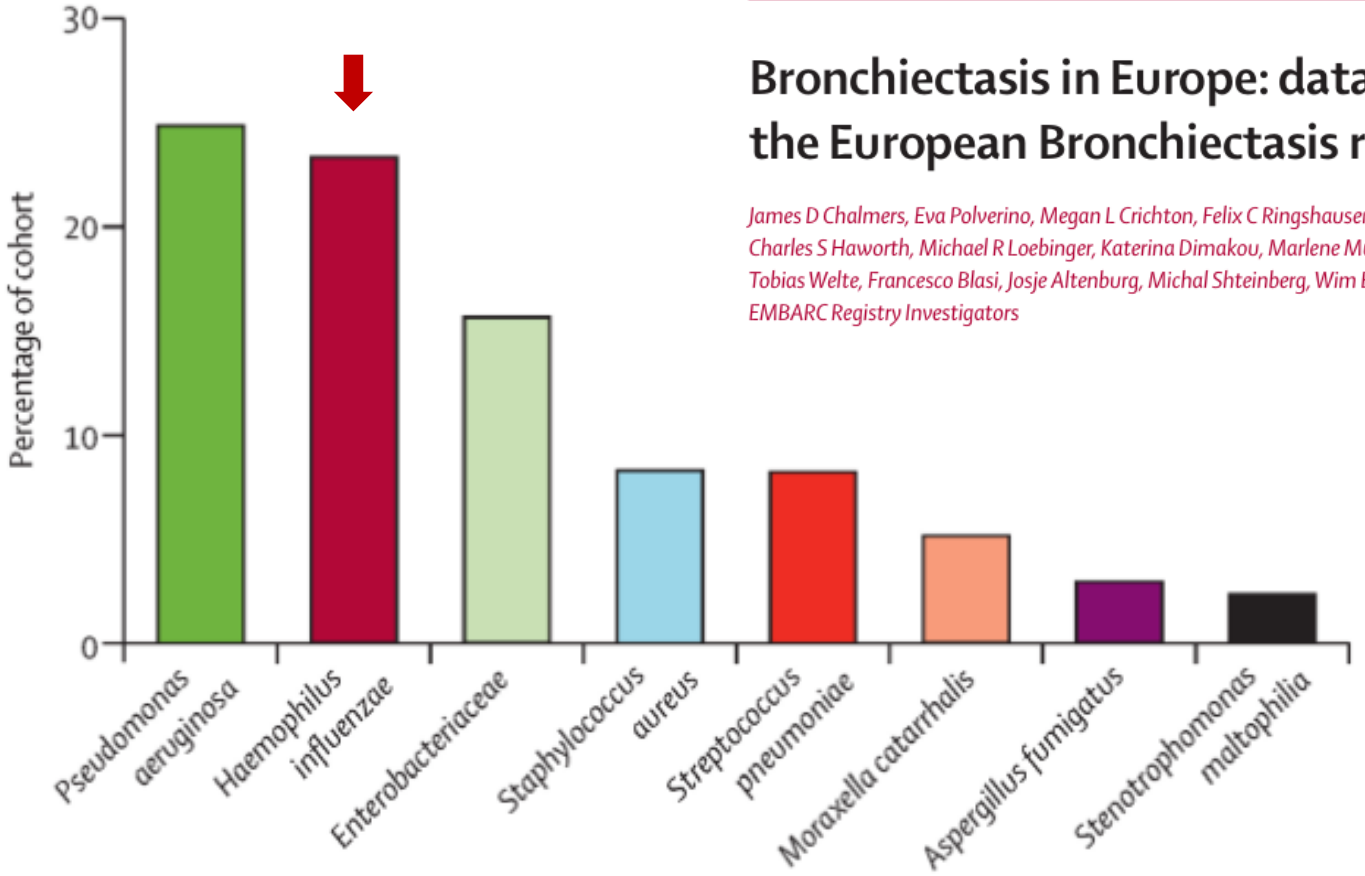


Invasive disease





Bronchiectasis



Bronchiectasis in Europe: data on disease characteristics from the European Bronchiectasis registry (EMBARC)

James D Chalmers, Eva Polverino, Megan L Crichton, Felix C Ringshausen, Anthony De Soyza, Montserrat Vendrell, Pierre Régis Burgel, Charles S Haworth, Michael R Loebinger, Katerina Dimakou, Marlene Murris, Robert Wilson, Adam T Hill, Rosario Menendez, Antoni Torres, Tobias Welte, Francesco Blasi, Josje Altenburg, Michal Shteinberg, Wim Boersma, J Stuart Elborn, Pieter C Goeminne, Stefano Aliberti, on behalf of the EMBARC Registry Investigators

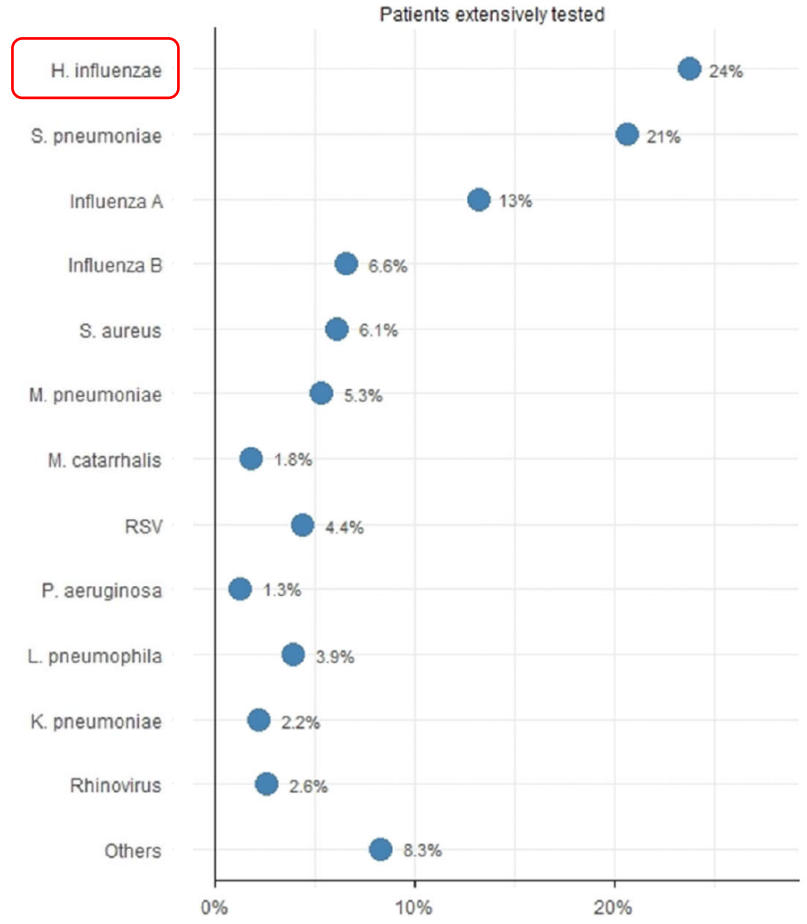
Lancet Respir Med 2023; 11: 637–49

Published Online April 24, 2023 https://doi.org/10.1016/S2213-2600(23)00093-0

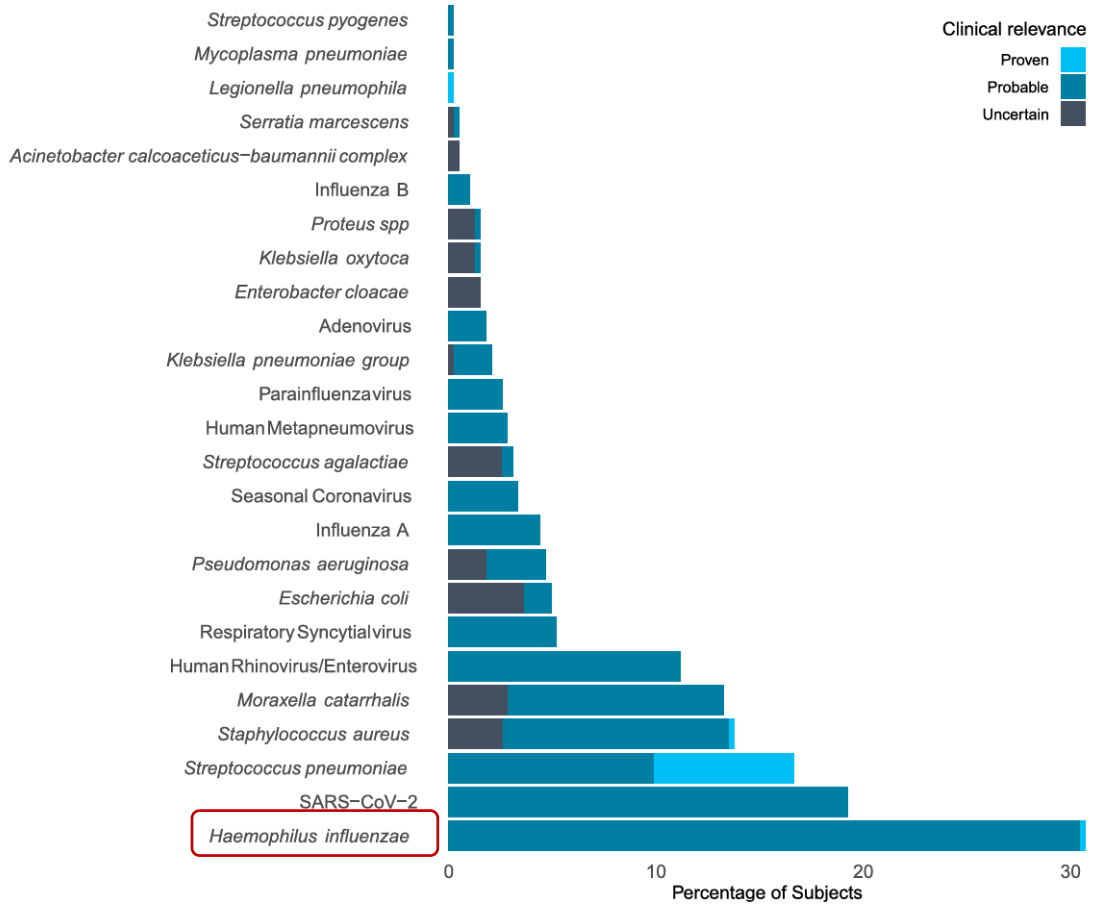
Pseudomonas aeruginosa *was far more common in southern Europe whereas* **Haemophilus influenzae** *was more common in the UK and northern and western Europe.*

Community-acquired pneumonia

Denmark 2017 – 2019 (n = 315)



Norway 2020 – 2023 (n = 384)



Fally et al. Infect Dis 2020
Markussen et al. Int J Infect Dis 2024

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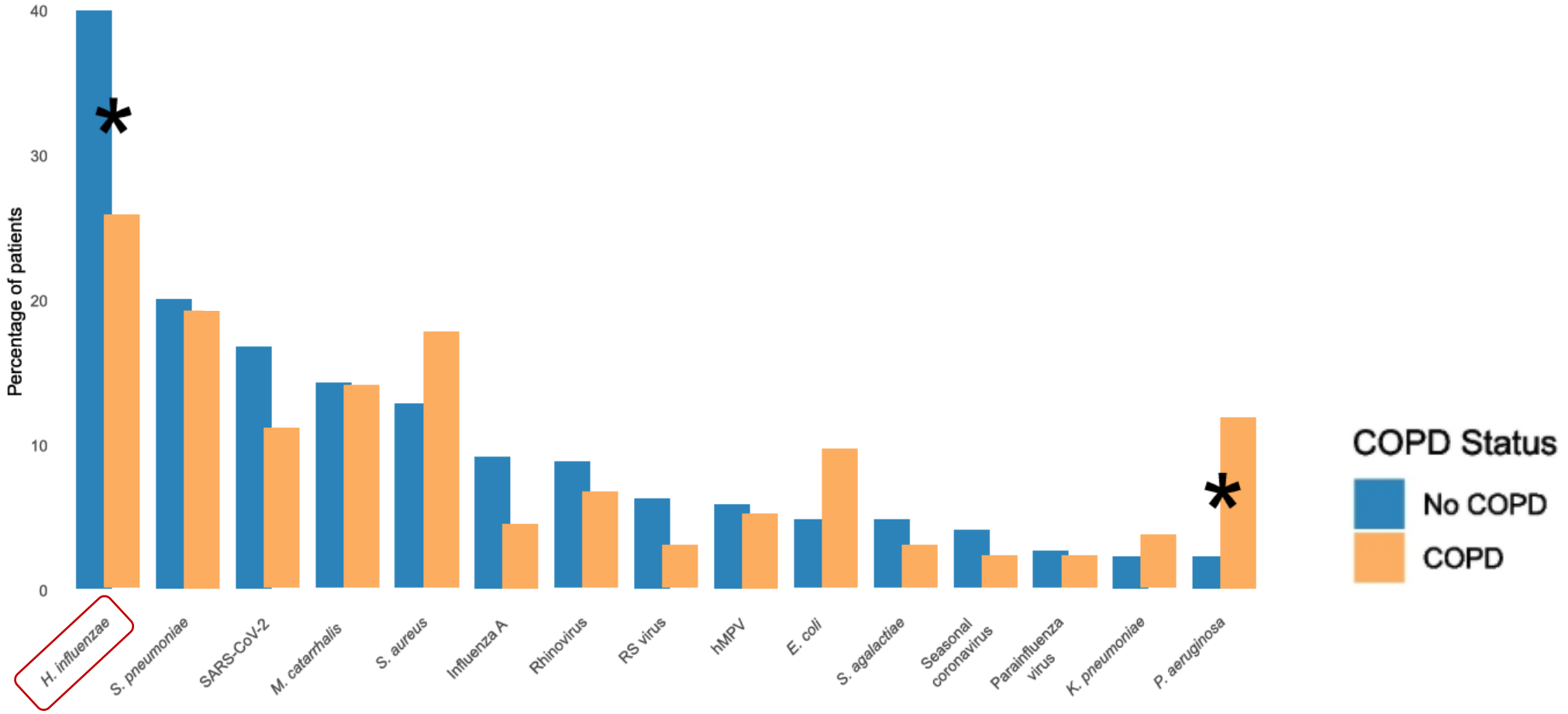
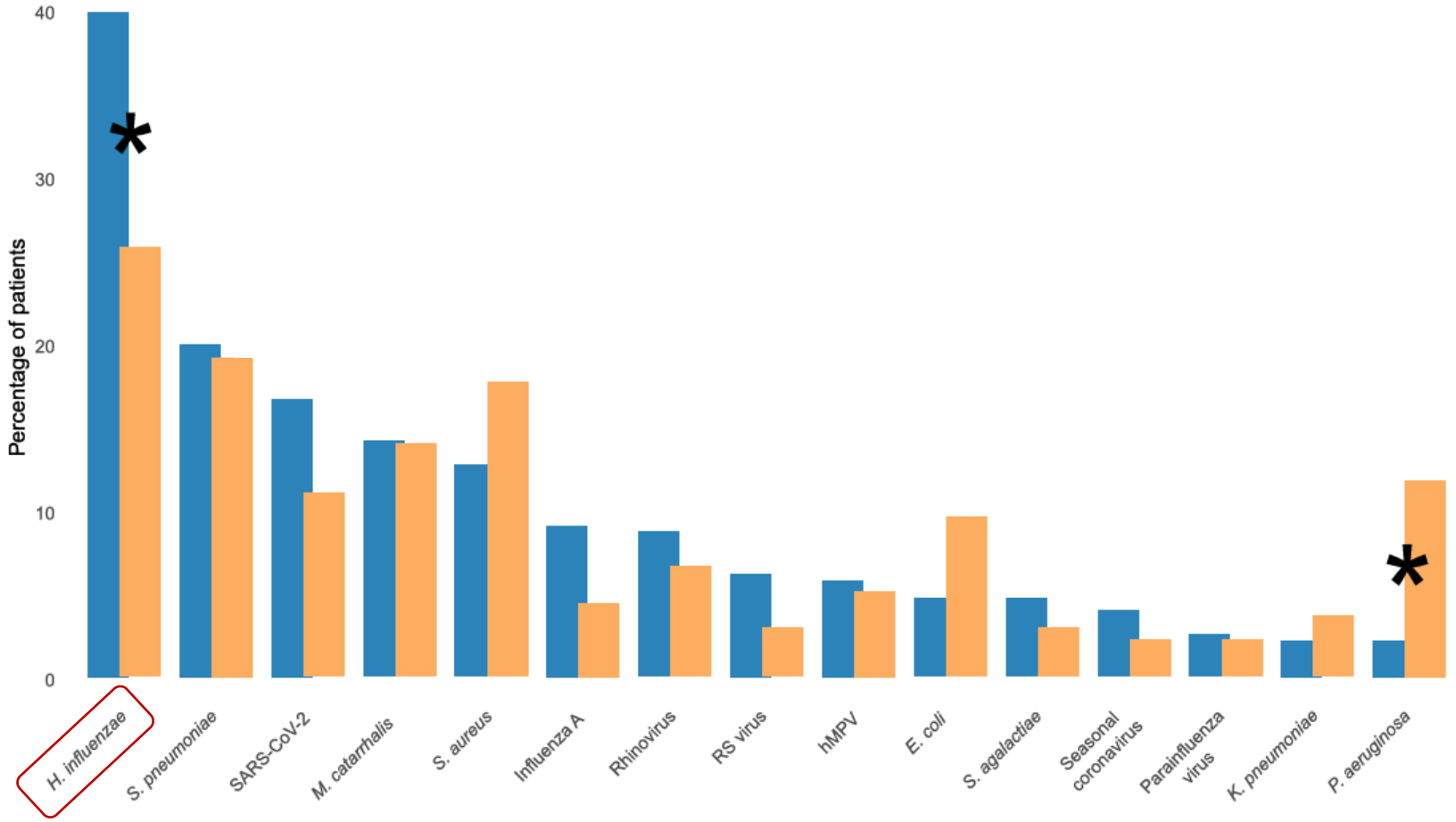
Community-acquired pneumonia

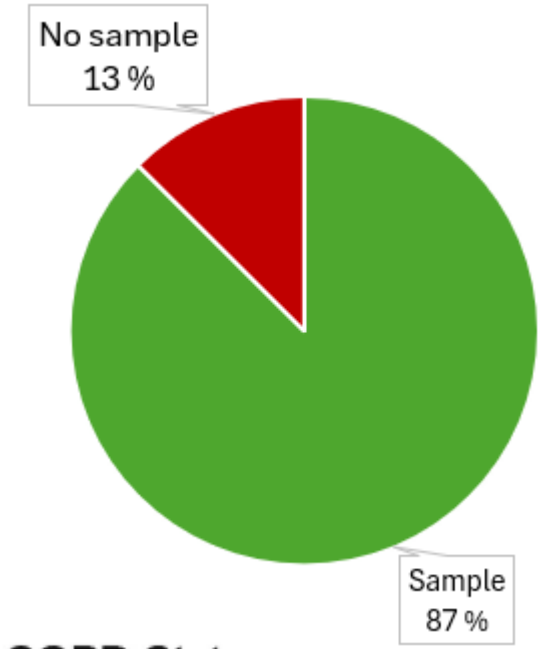
Norway 2019 – 2023 (n = 412)



Community-acquired pneumonia

Norway 2019 – 2023 (n = 412)



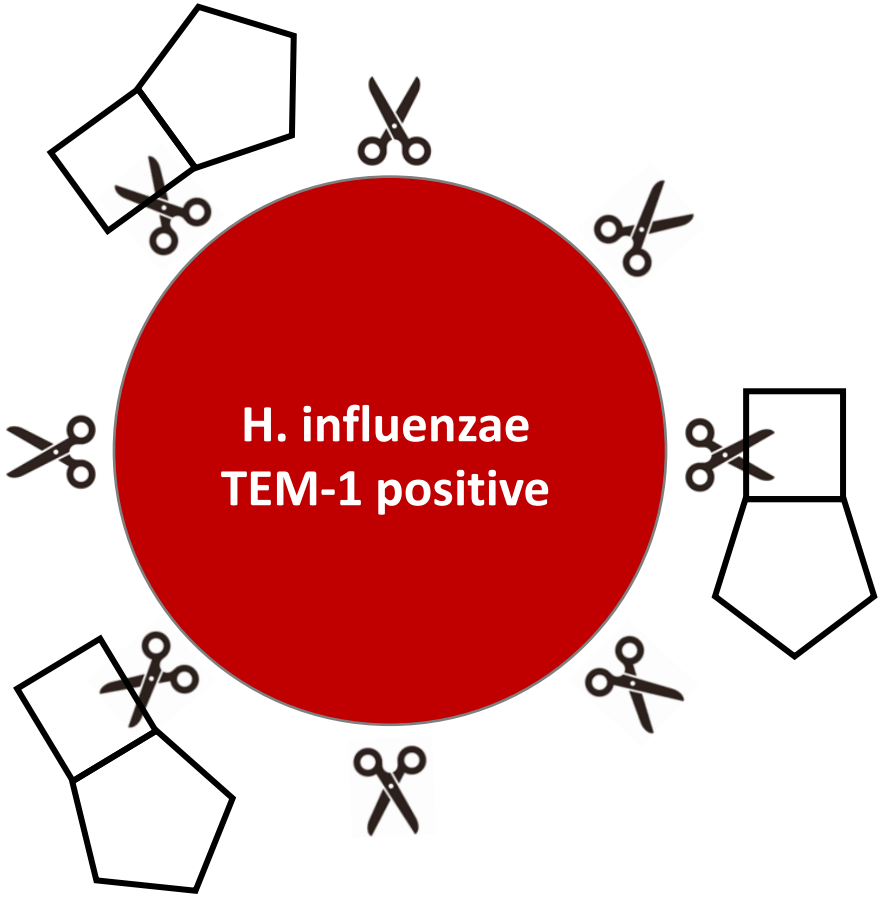


Beta-lactam resistance

TABLE 1. *Beta-lactamase production by ampicillin-resistant Haemophilus influenzae as determined by a rapid capillary tube method*

No. of strains	Type	Susceptibility		Beta-Lactamase (Capillary tube test)
		MIC[a] (μg/ml)	Interpretation	
2	b	0.06	Susceptible	–[b]
4	b	0.12	Susceptible	–
4	b	0.25	Susceptible	–
4	b	0.50	Susceptible	–
2	b	8	Resistant	+
8	b	16	Resistant	+
4	b	32	Resistant	+
1	b	64	Resistant	+
3	Not b	8	Resistant	–, –, +
2	Not b	64	Resistant	+

[a] MIC, Minimal inhibitory concentration.
[b] – indicates negative test and + indicates positive test for beta-lactamase production.



Thornsberry & Kirven AAC 1974

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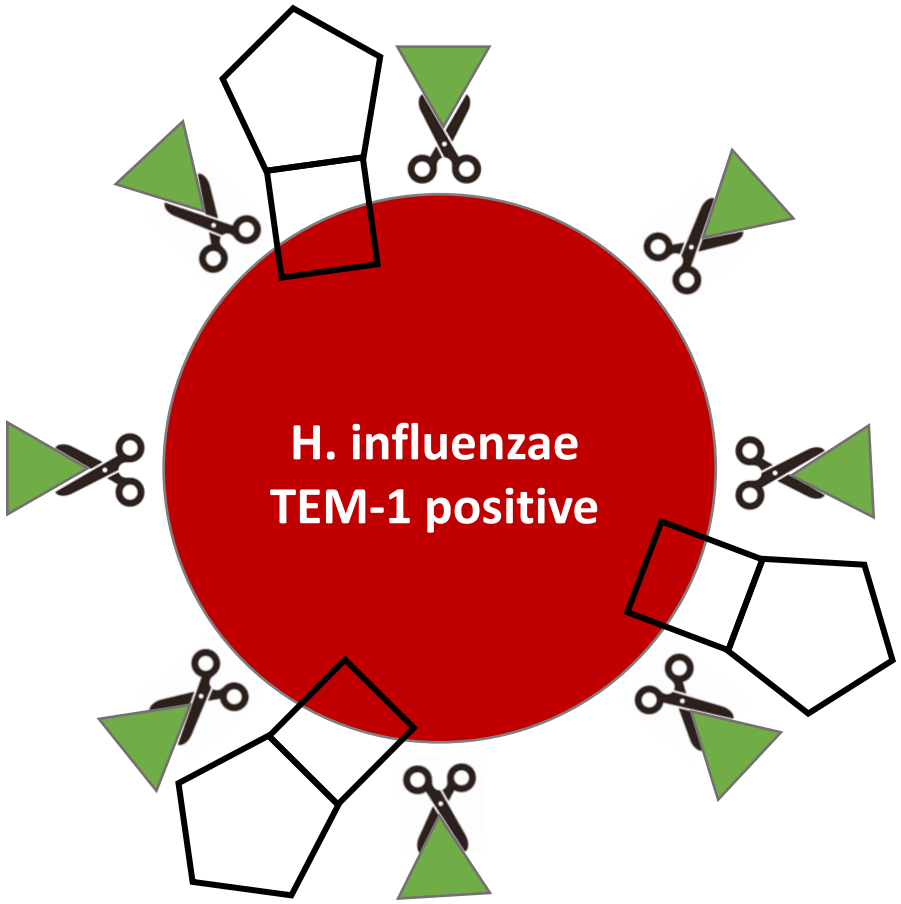

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BLNAR

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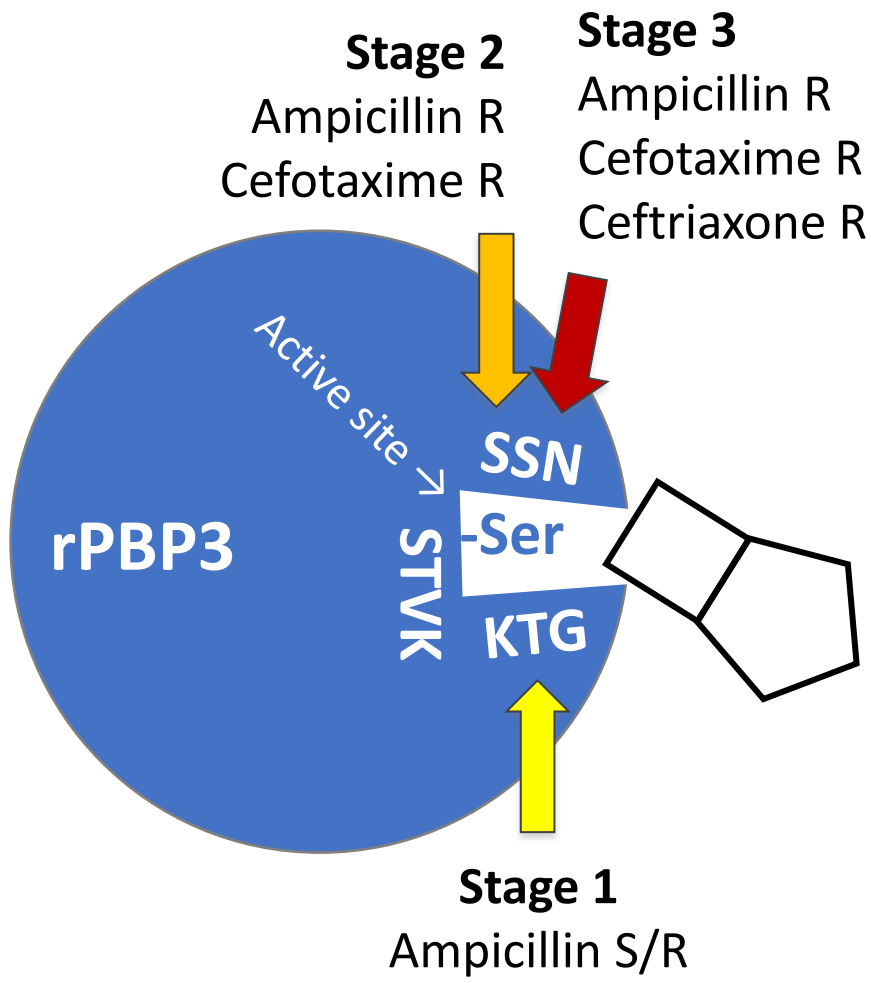
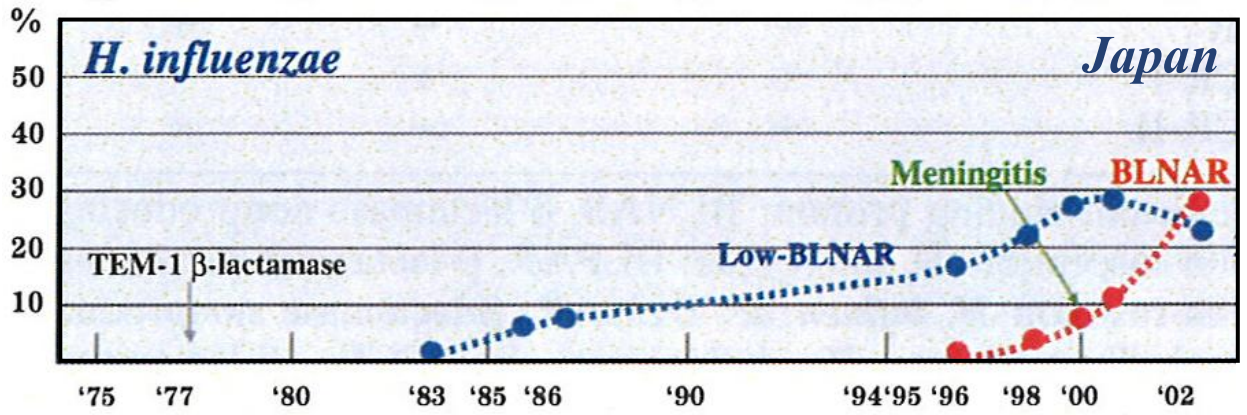
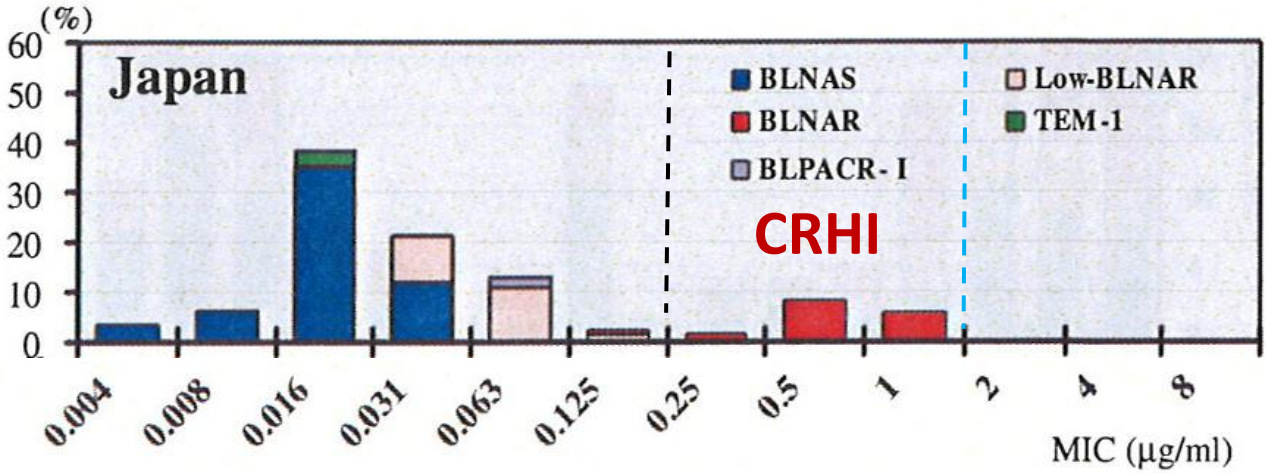


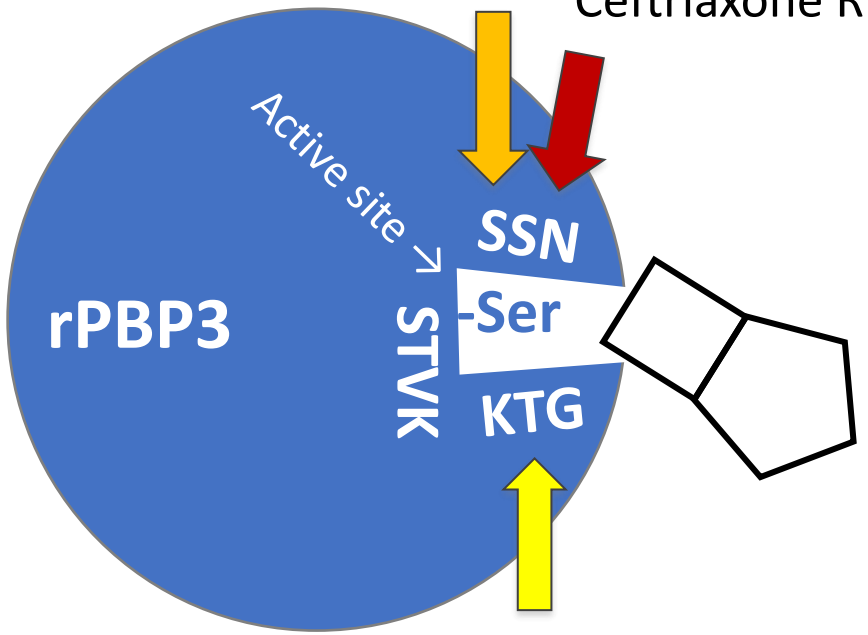
Beta-lactam resistance





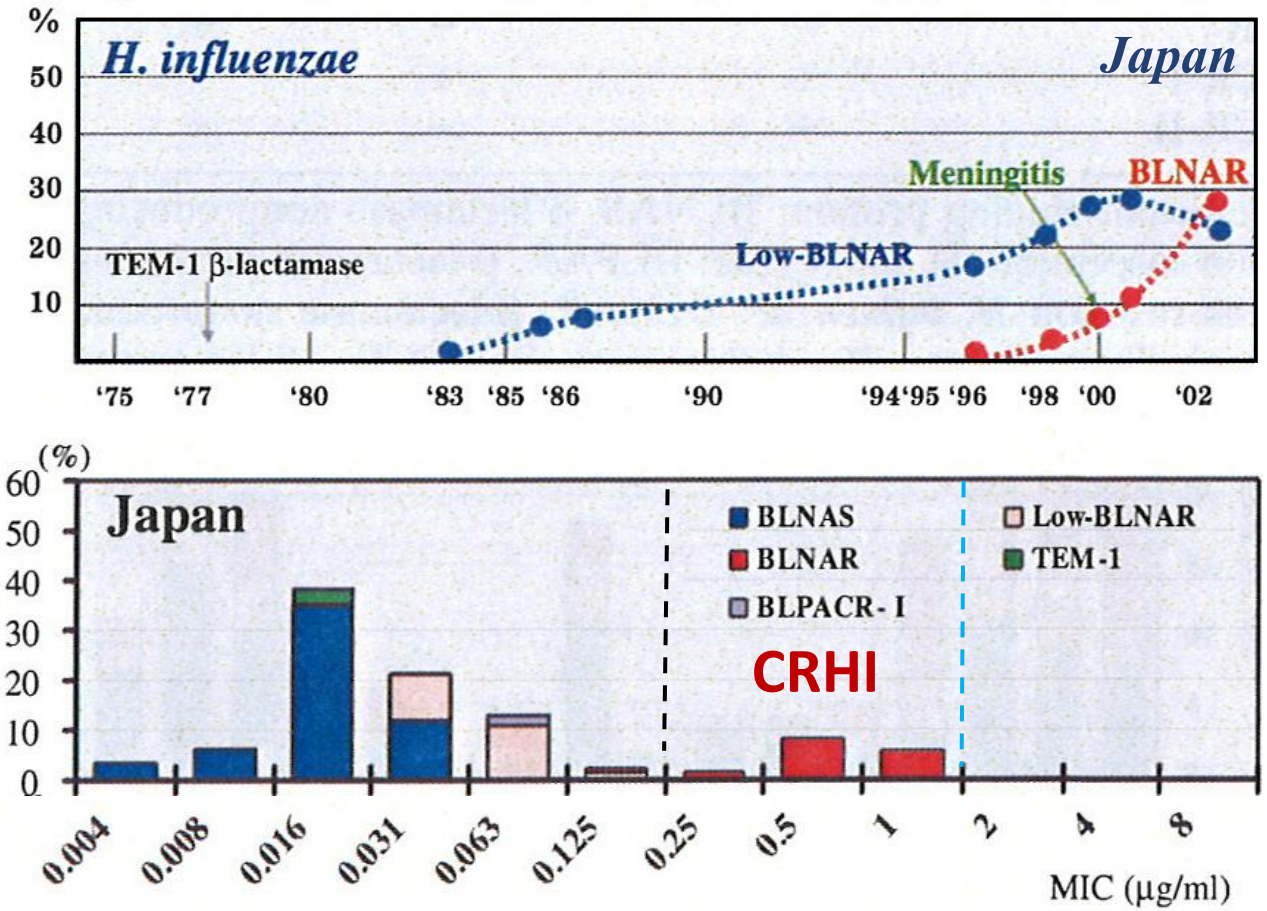
Stage 2
Ampicillin R
Cefotaxime R

Stage 3
Ampicillin R
Cefotaxime R
Ceftriaxone R

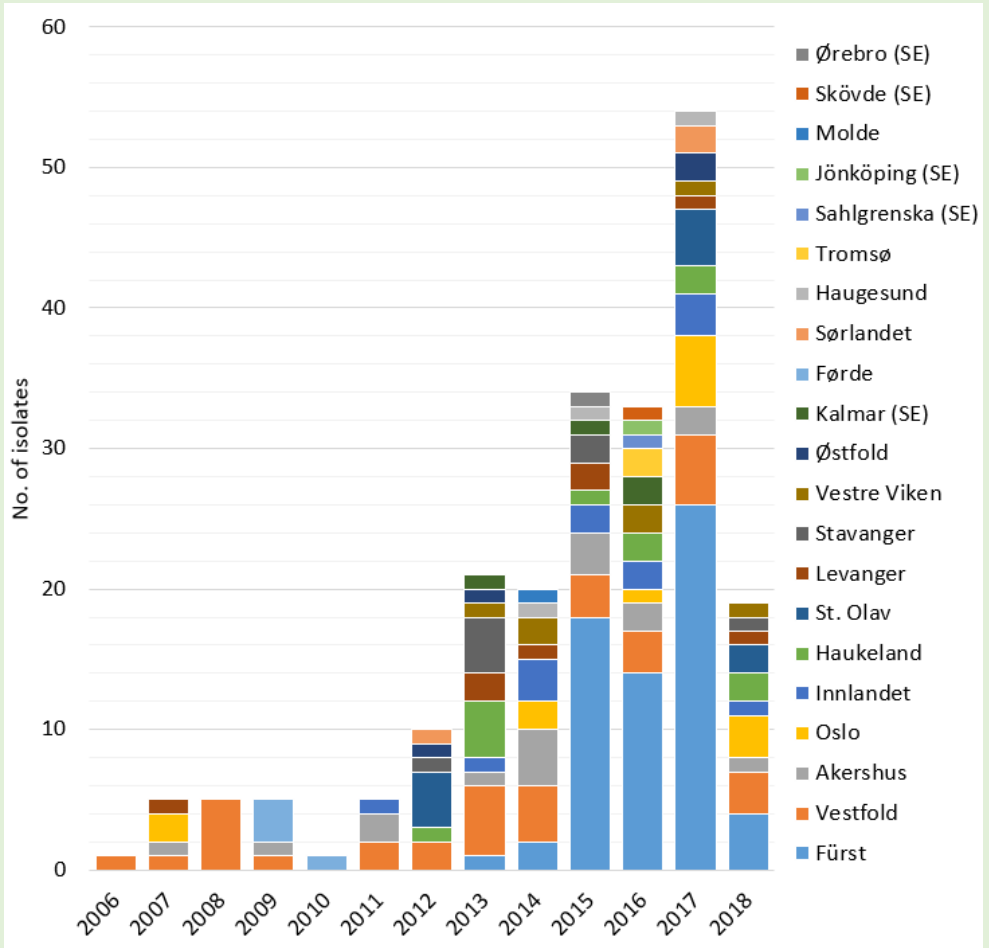


Stage 1
Ampicillin S/R

Beta-lactam resistance



CTX-R by gradient MIC (n = 213)

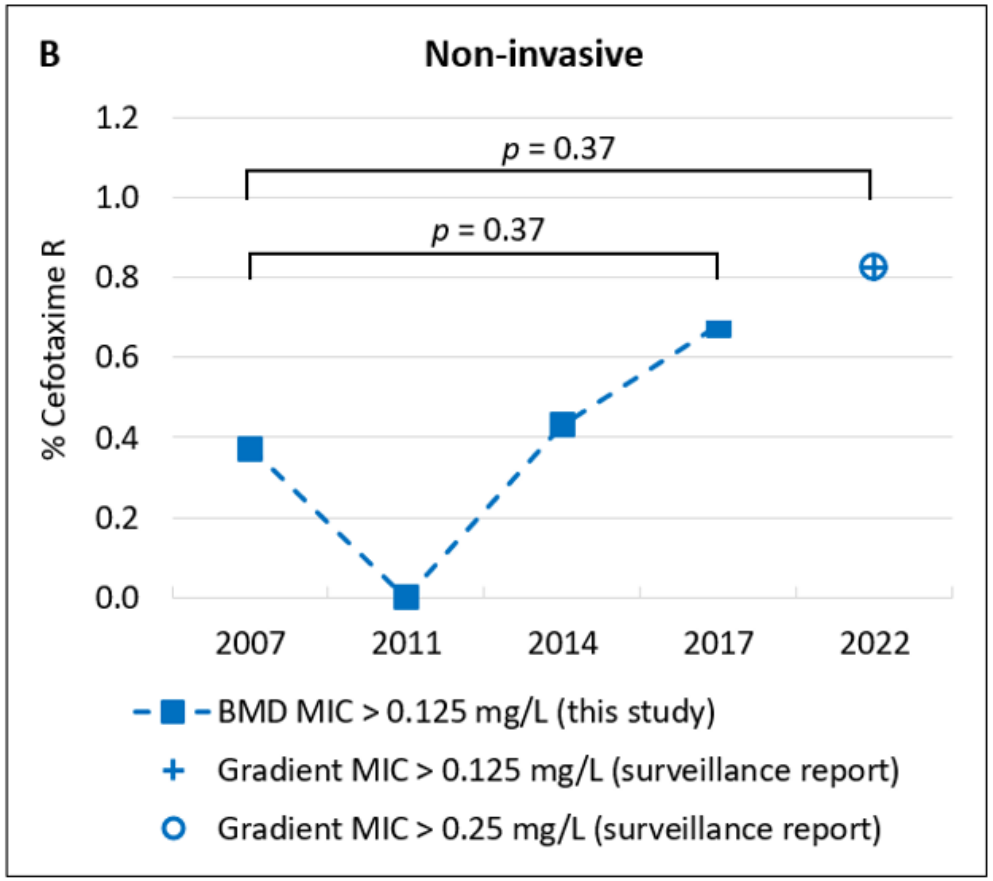


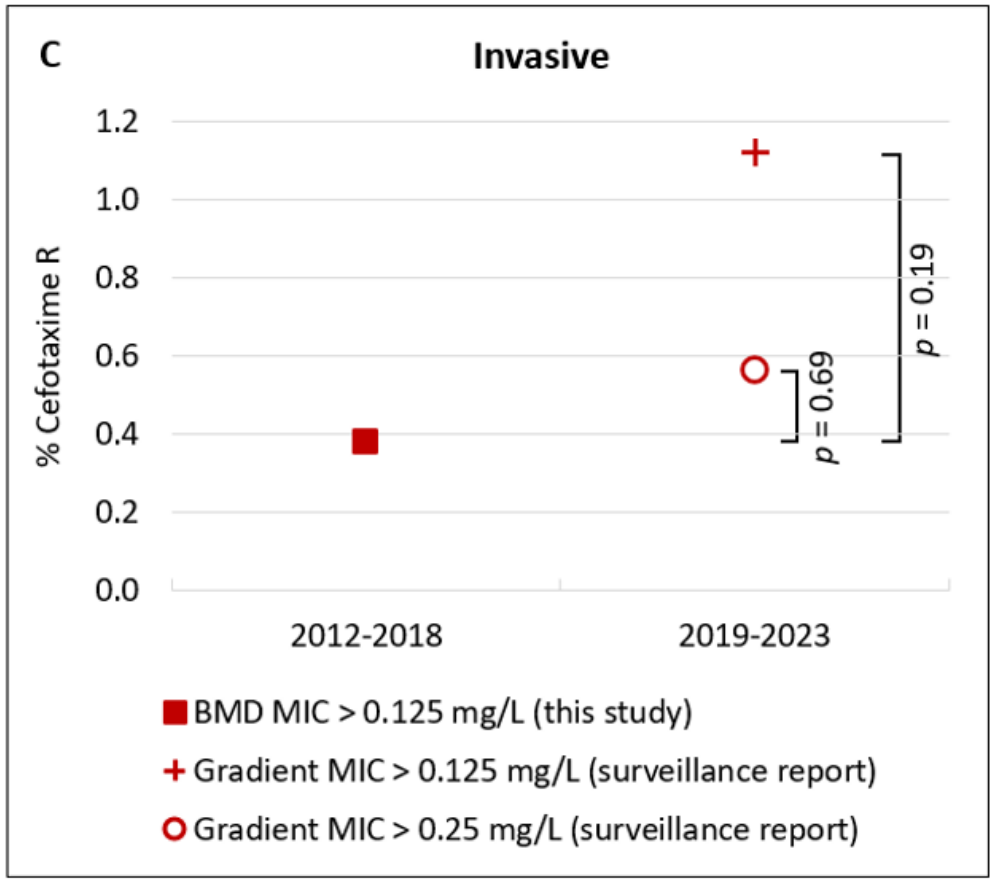
Ubukata J Infect Chemother 2003

Gradient tests overcalls cefotaxime MIC

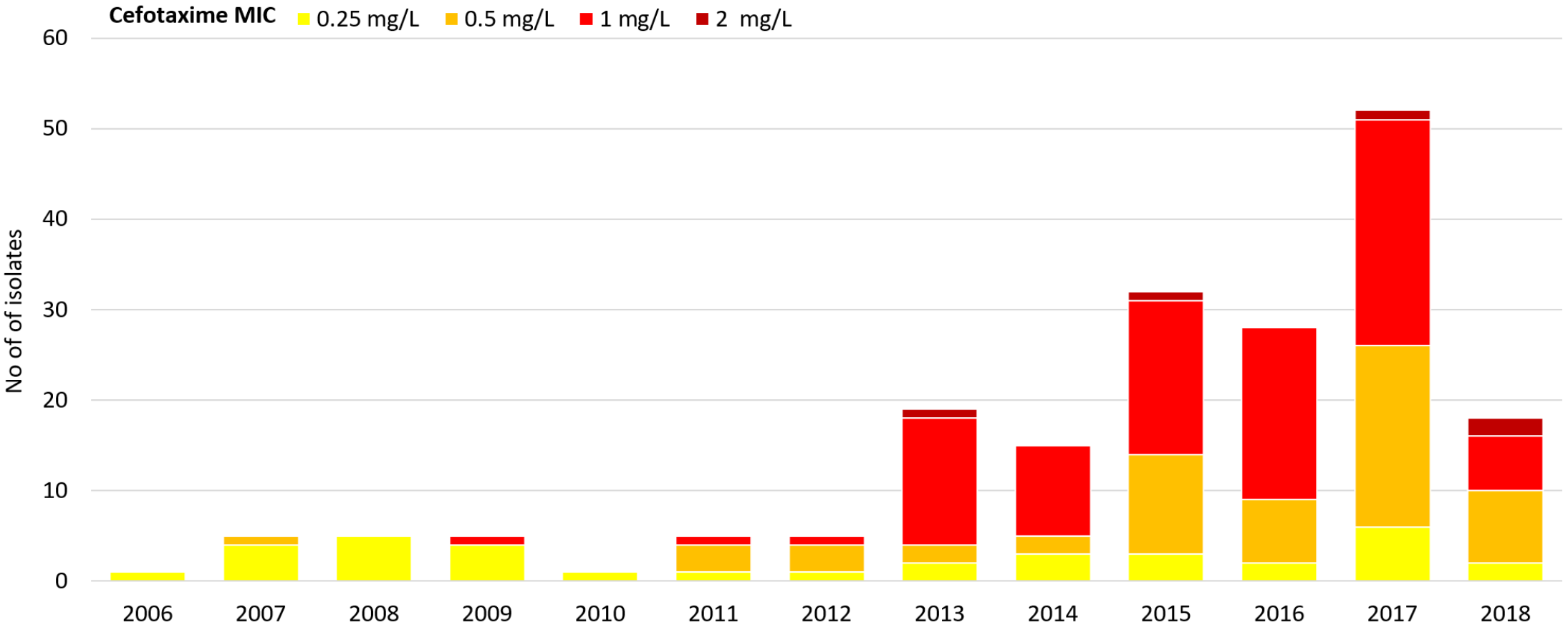
Cefotaxime gradient MIC (mg/L)	No. of isolates	Cefotaxime broth microdilution (BMD) MIC (mg/L)					Falsely resistant	
		0.125	0.25	0.5	1	2	No. of isolates	%
4	2	-	-	1	-	1	-	-
2	60	-	-	10	49	1	-	-
1	65	-	-	24	39	2	-	-
0.5	28	-	6	17	4	1	-	-
0.25	56	20	29	5	2	-	20	35.7%
No. of isolates	211	20	35	57	94	5	20	9.5%
%	100.0%	9.5%	16.6%	27.0%	44.5%	2.4%		

Non-significant increase in CRHI prevalence





Significant increase in resistance levels



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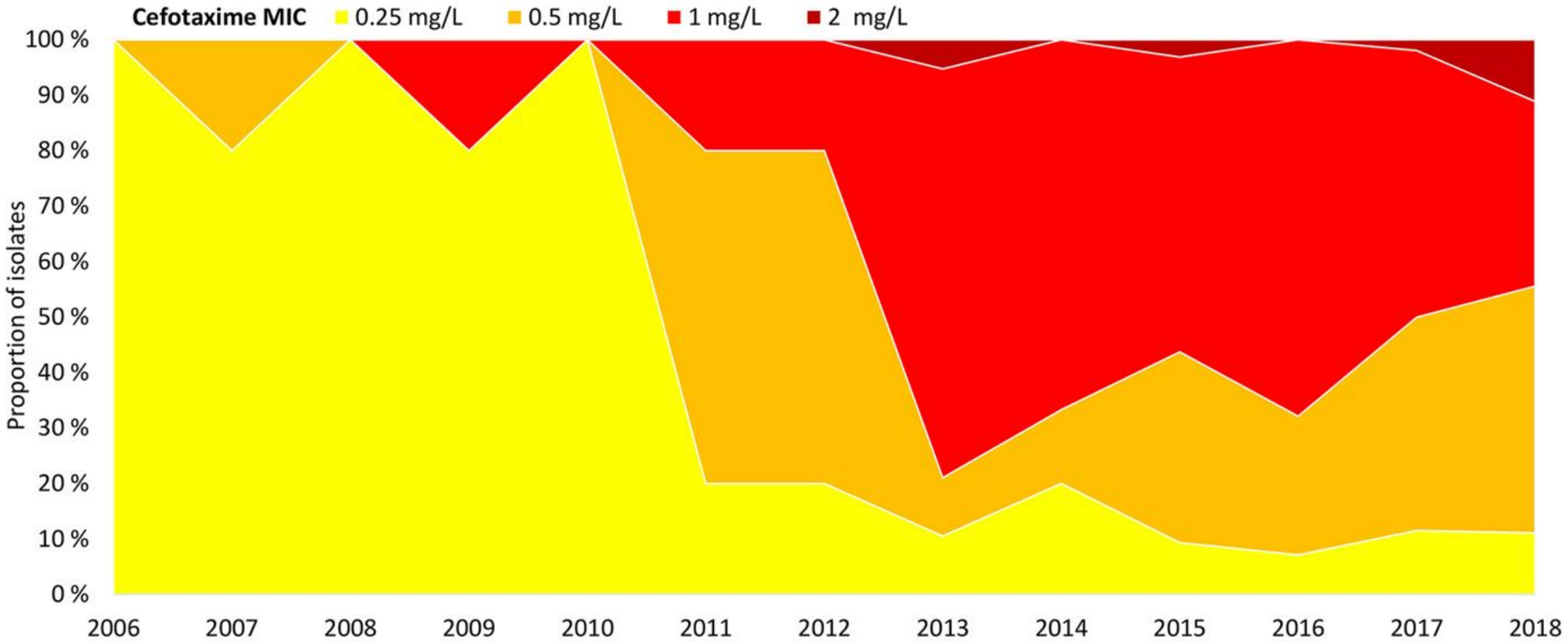

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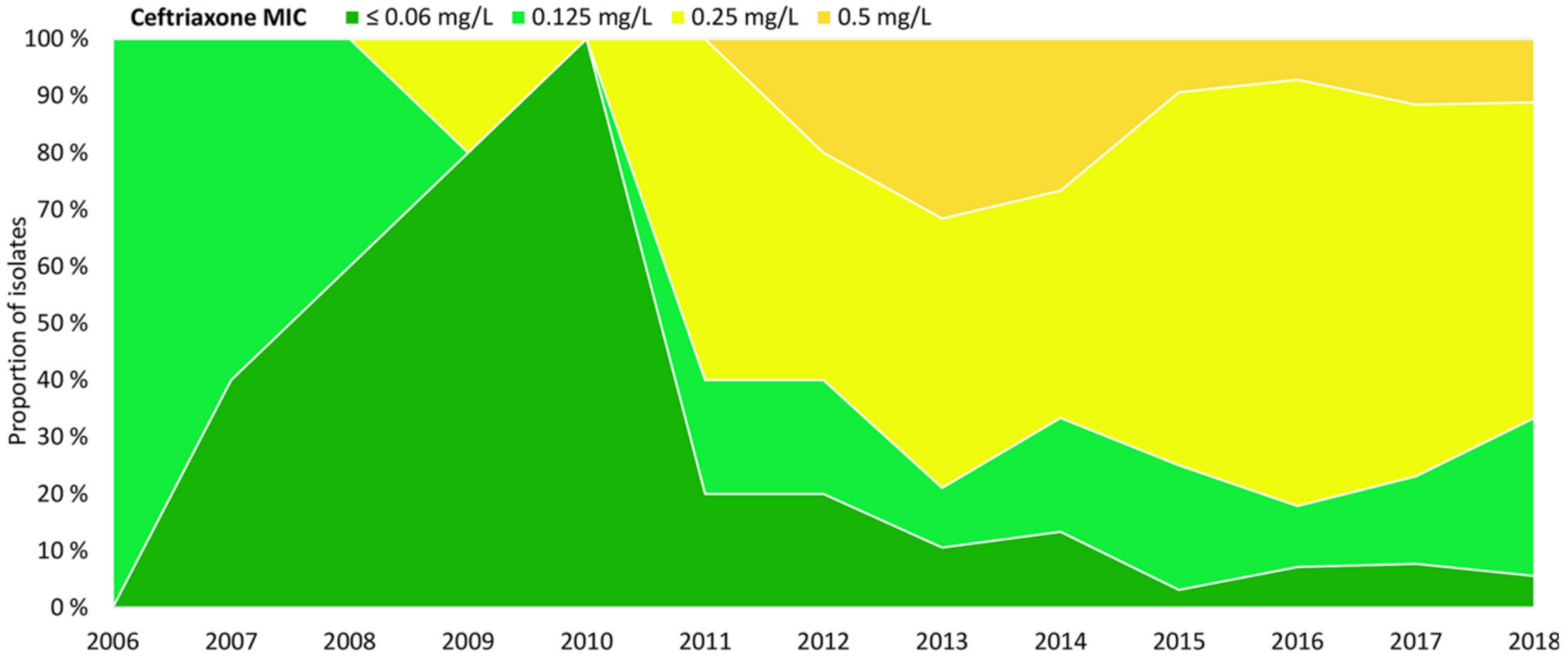
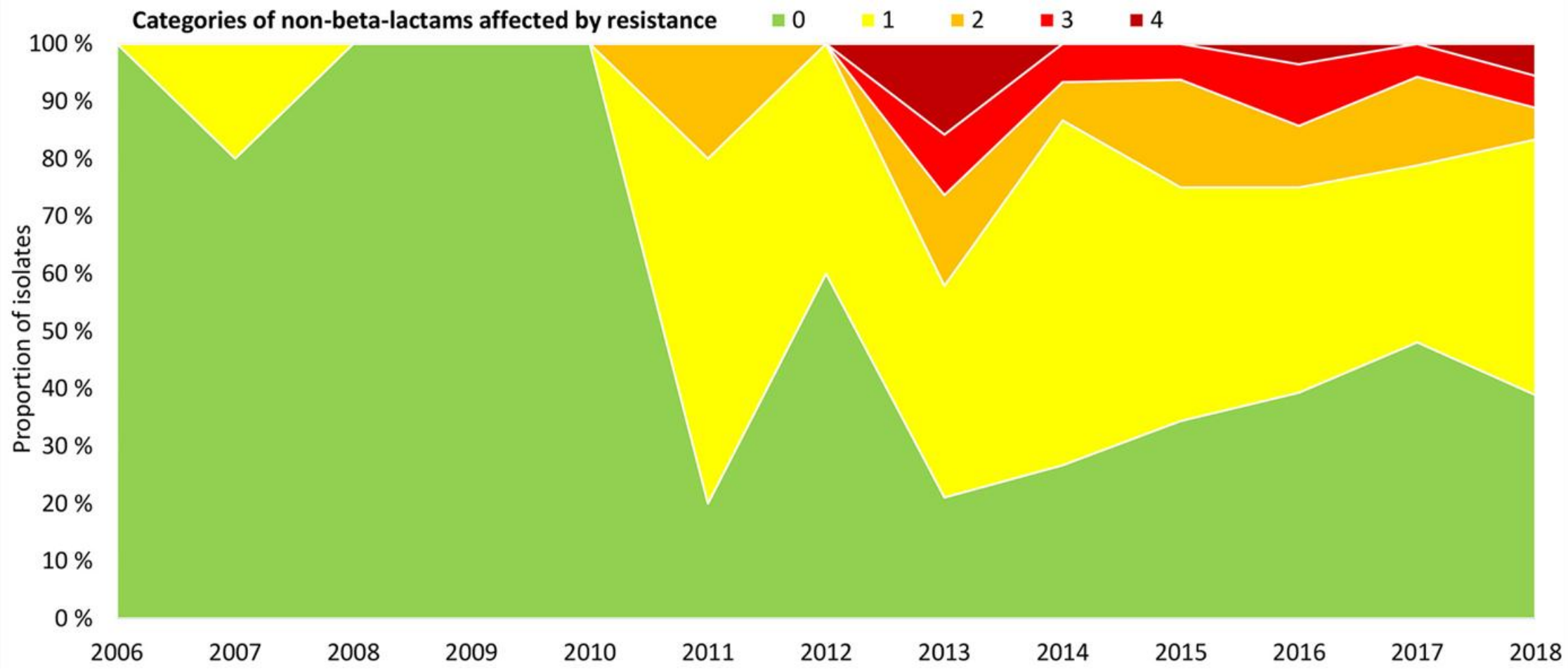
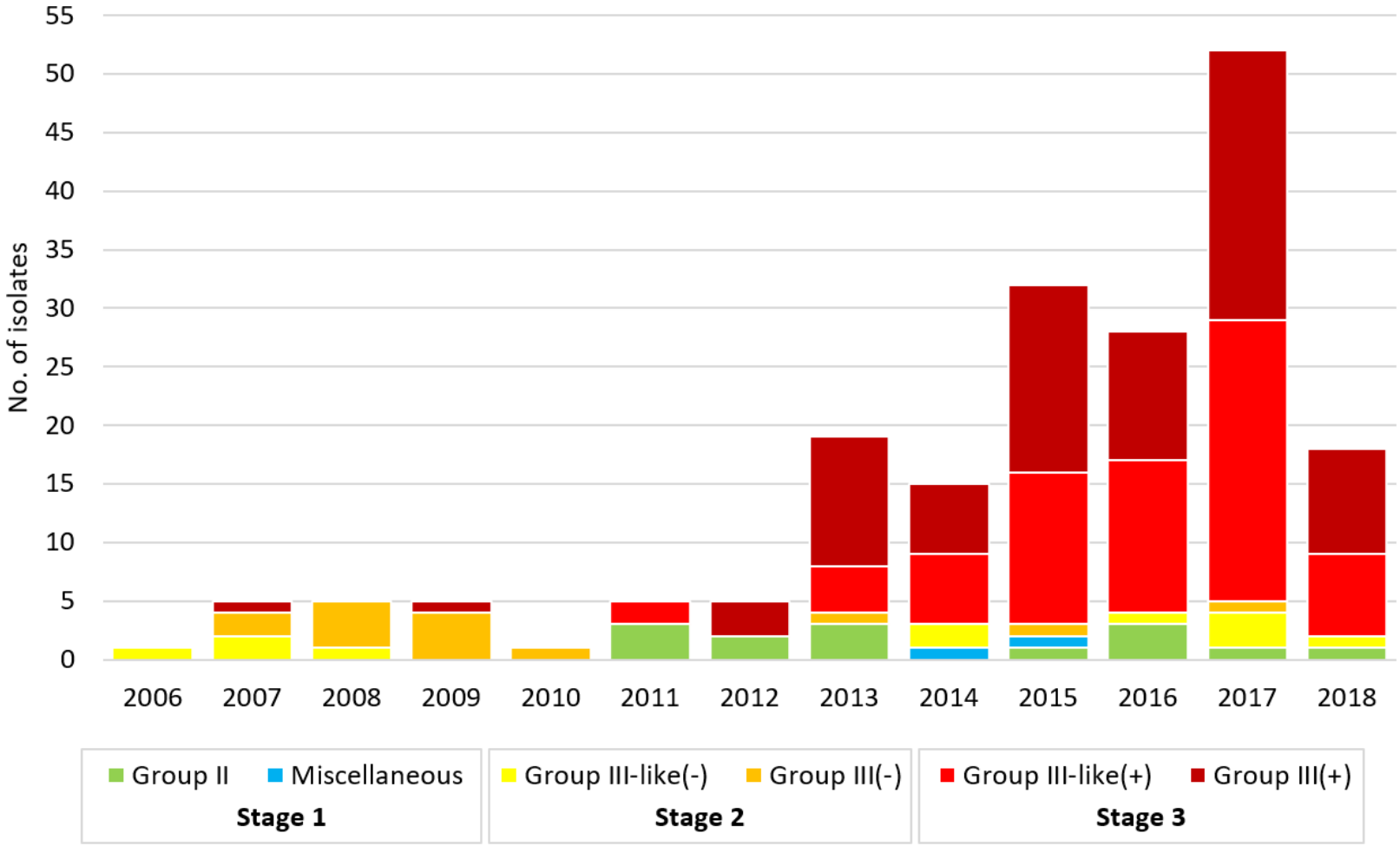
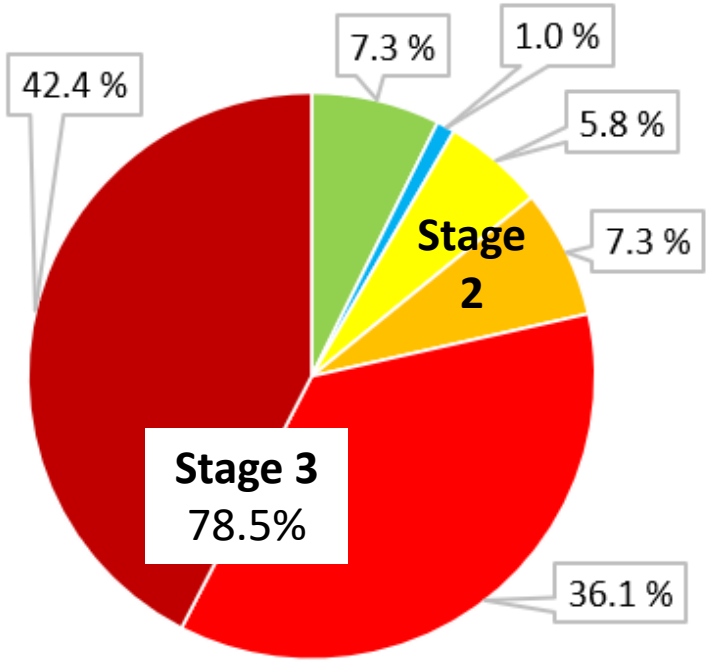


...and multidrug resistance

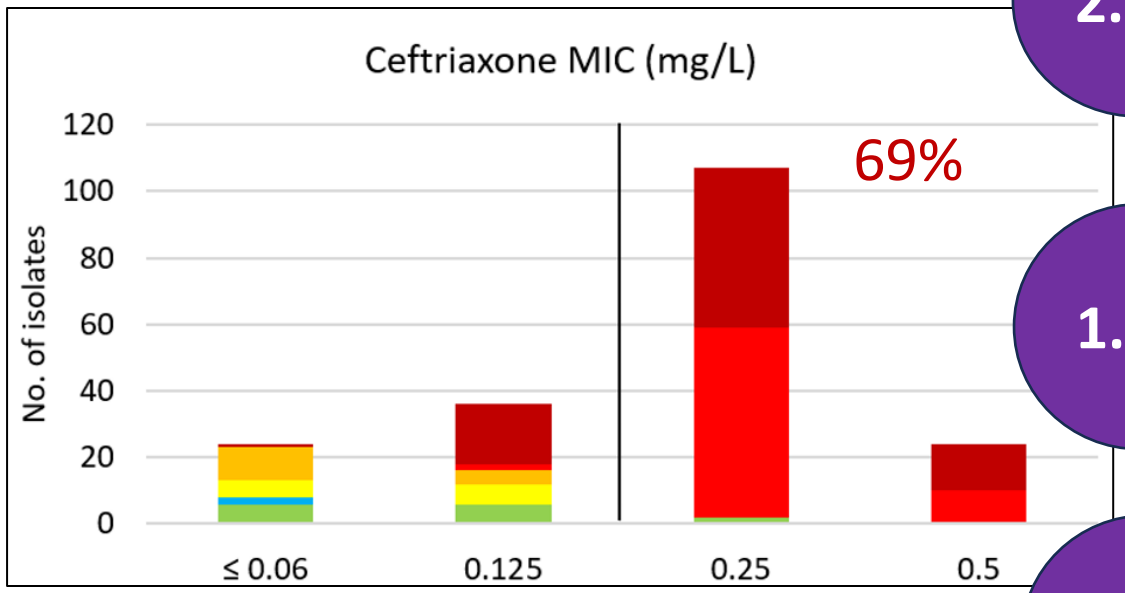


rPBP3 genotype shift

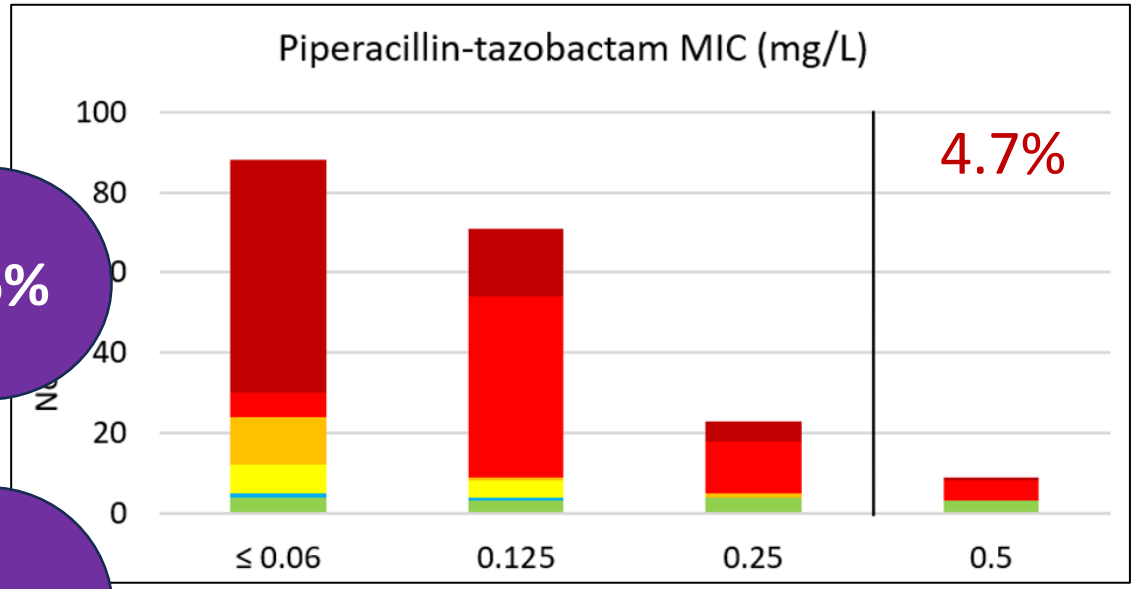




Cross-resistance

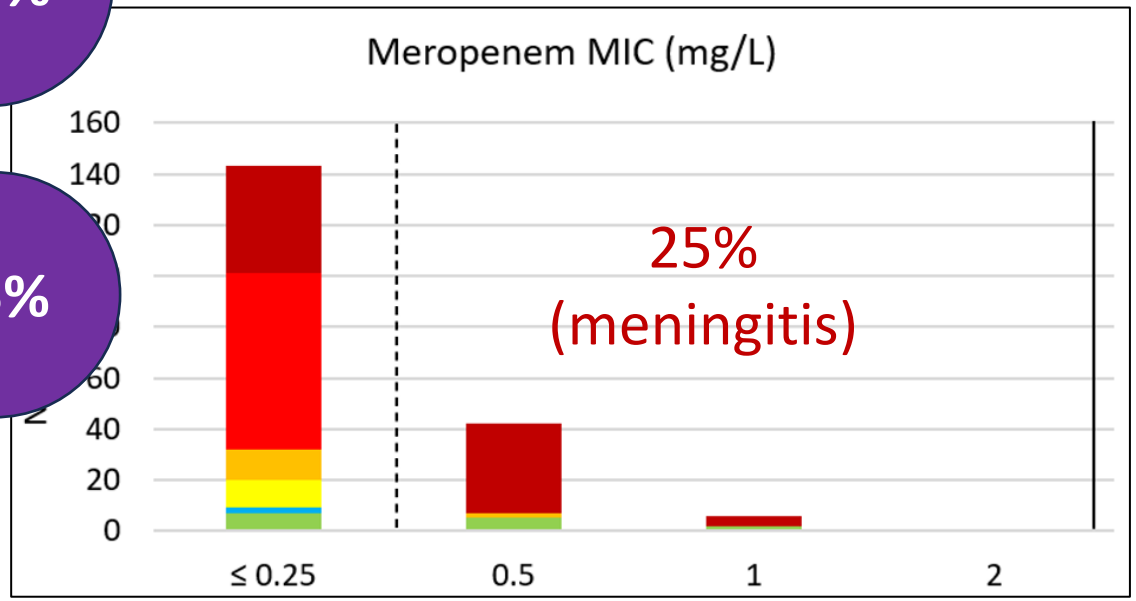


2.6%

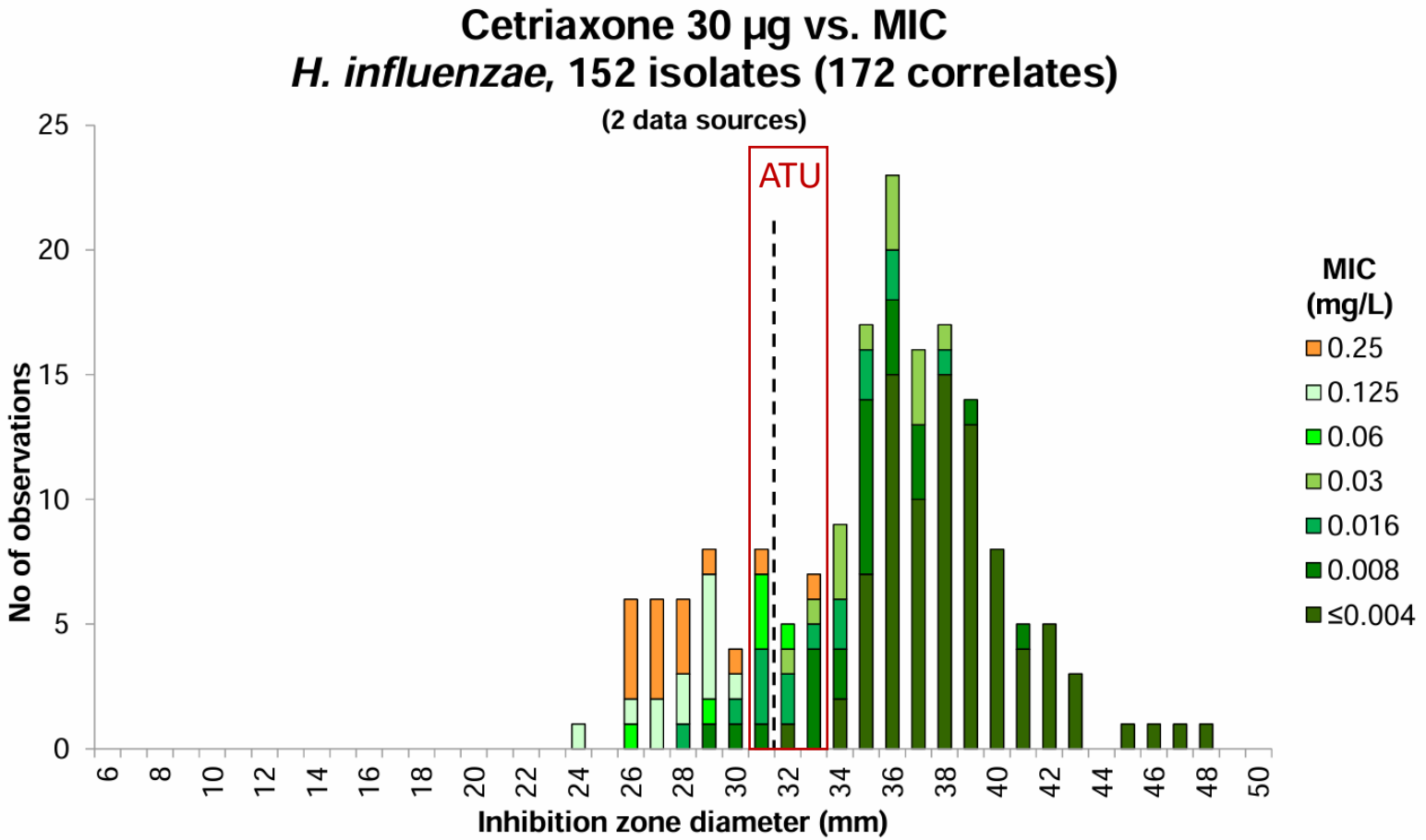


1.0%

15%



AST challenges



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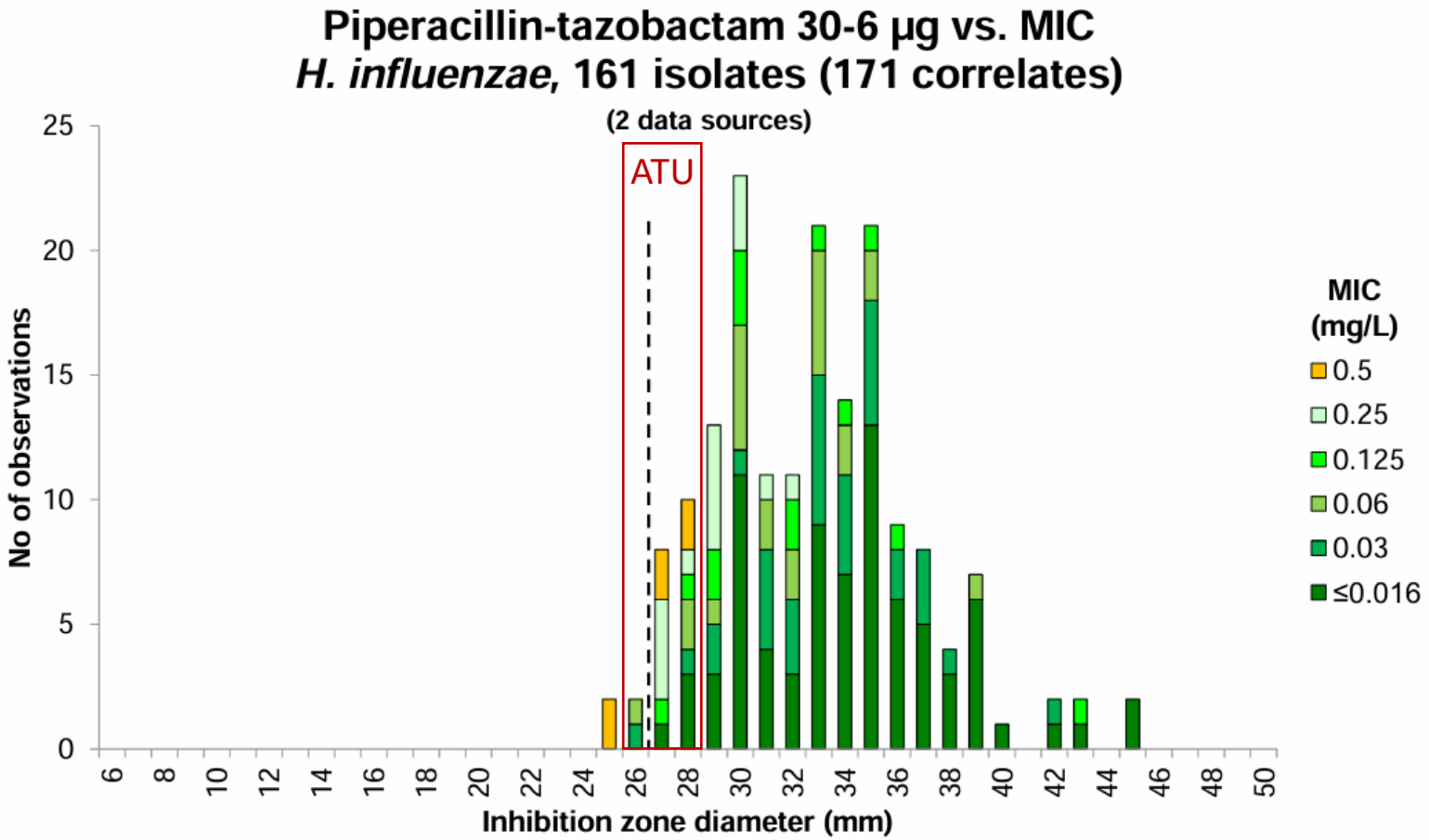
AST challenges



Warnings

Concerning antimicrobial susceptibility testing product

Discover More

EUCAST European Committee on Antimicrobial Susceptibility Testing

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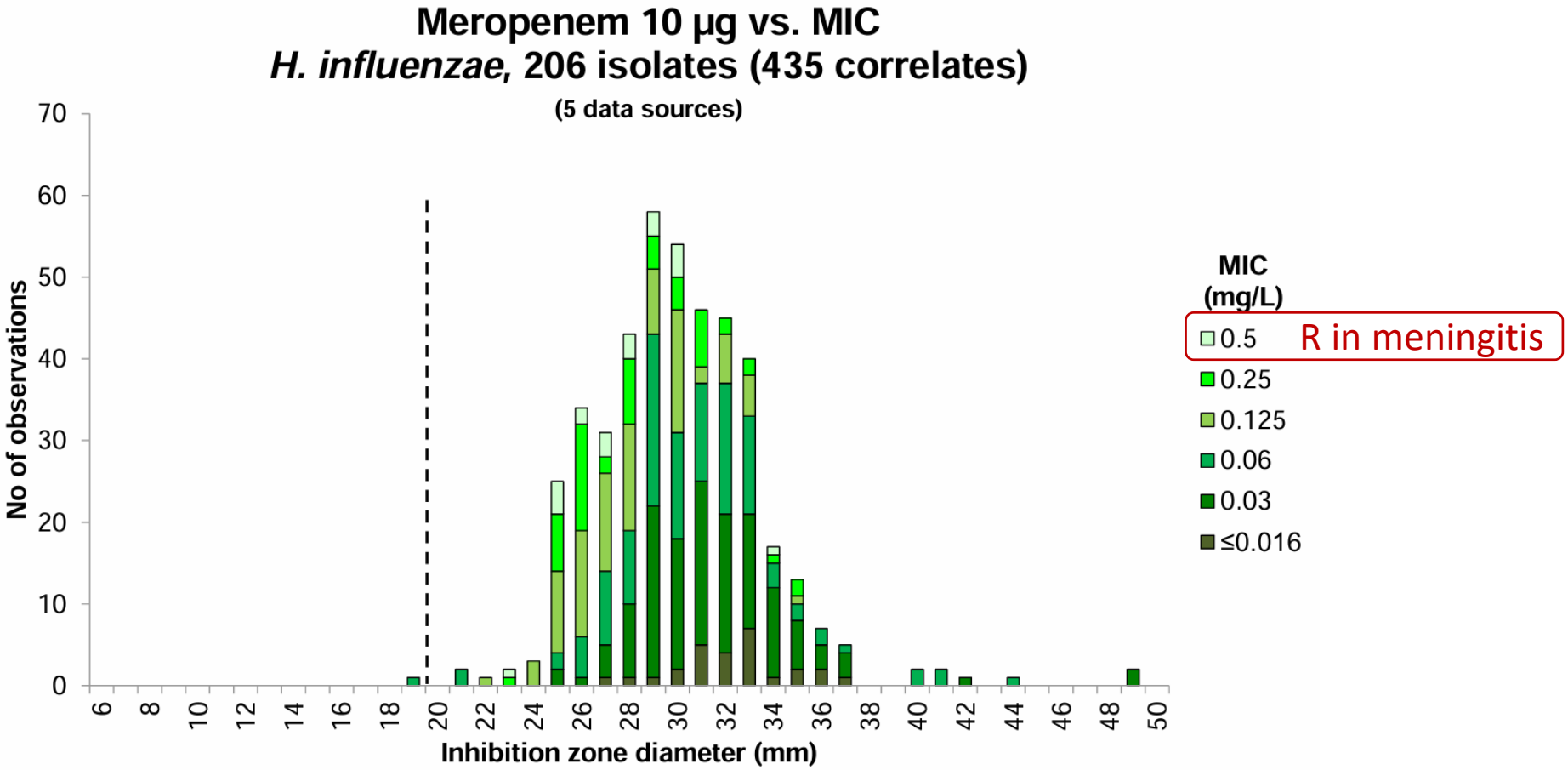
Warnings against piperacillin-tazobactam gradient tests from two manufacturers removed

01 April 2020 | Bacteria

Note. The new Etest and MTS for piperacillin-tazobactam are valid only for *Enterobacterales, Pseudomonas aeruginosa* and *Acinetobacter* - and should not be used with other bacteria, such as *Bacteroides* or *Haemophilus* without having confirmed with the manufacturers.

AST challenges



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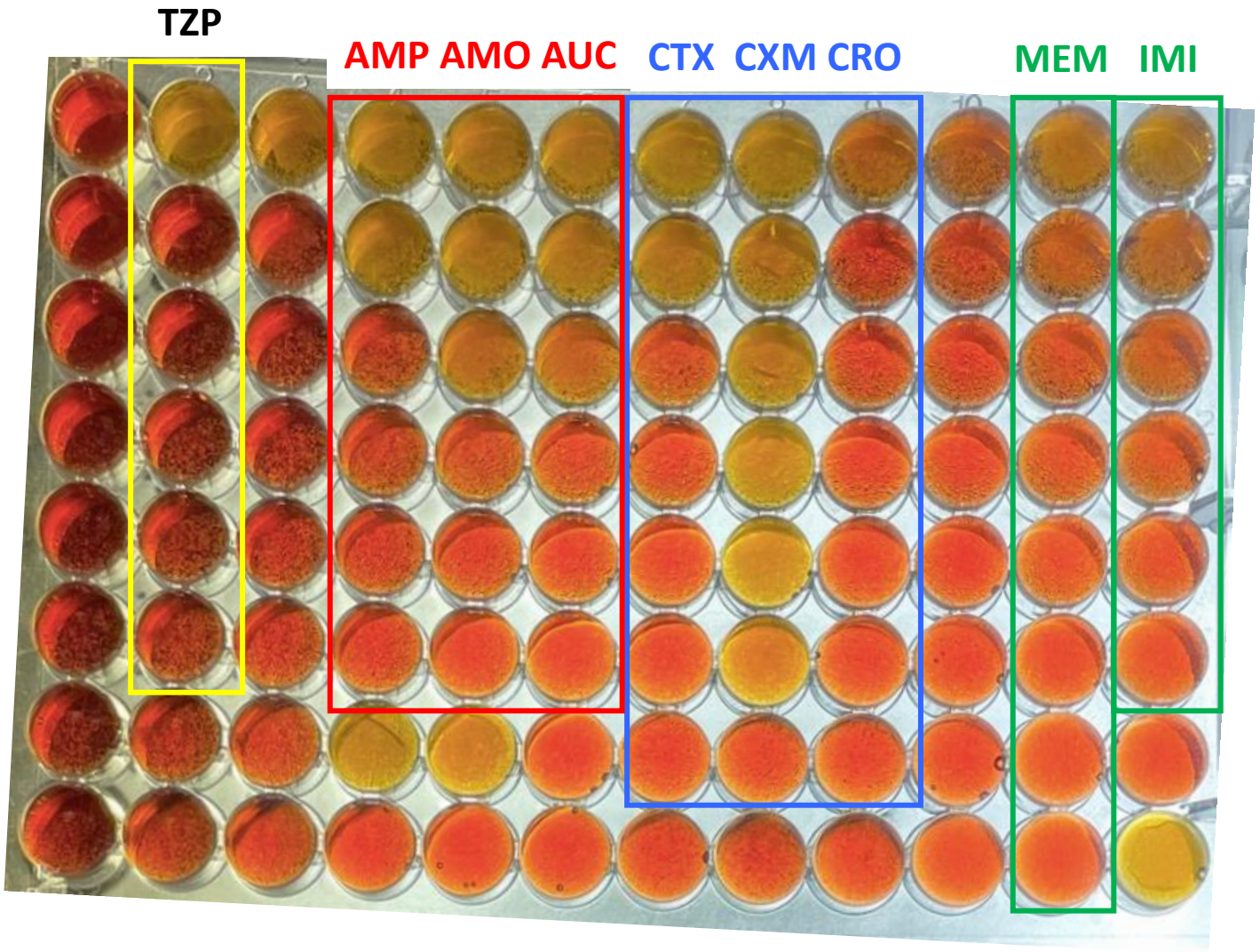
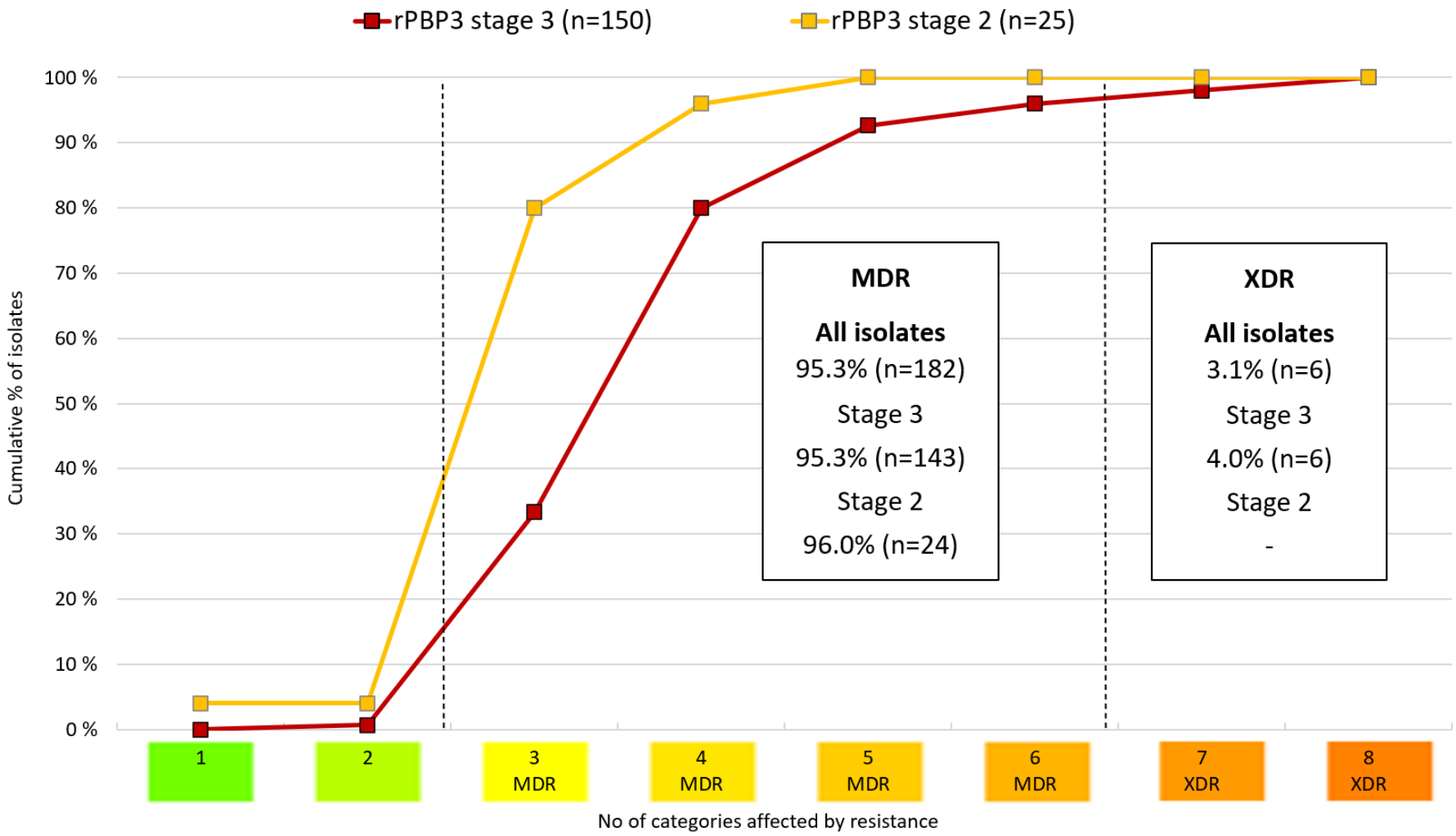
The optimal solution: BMD!

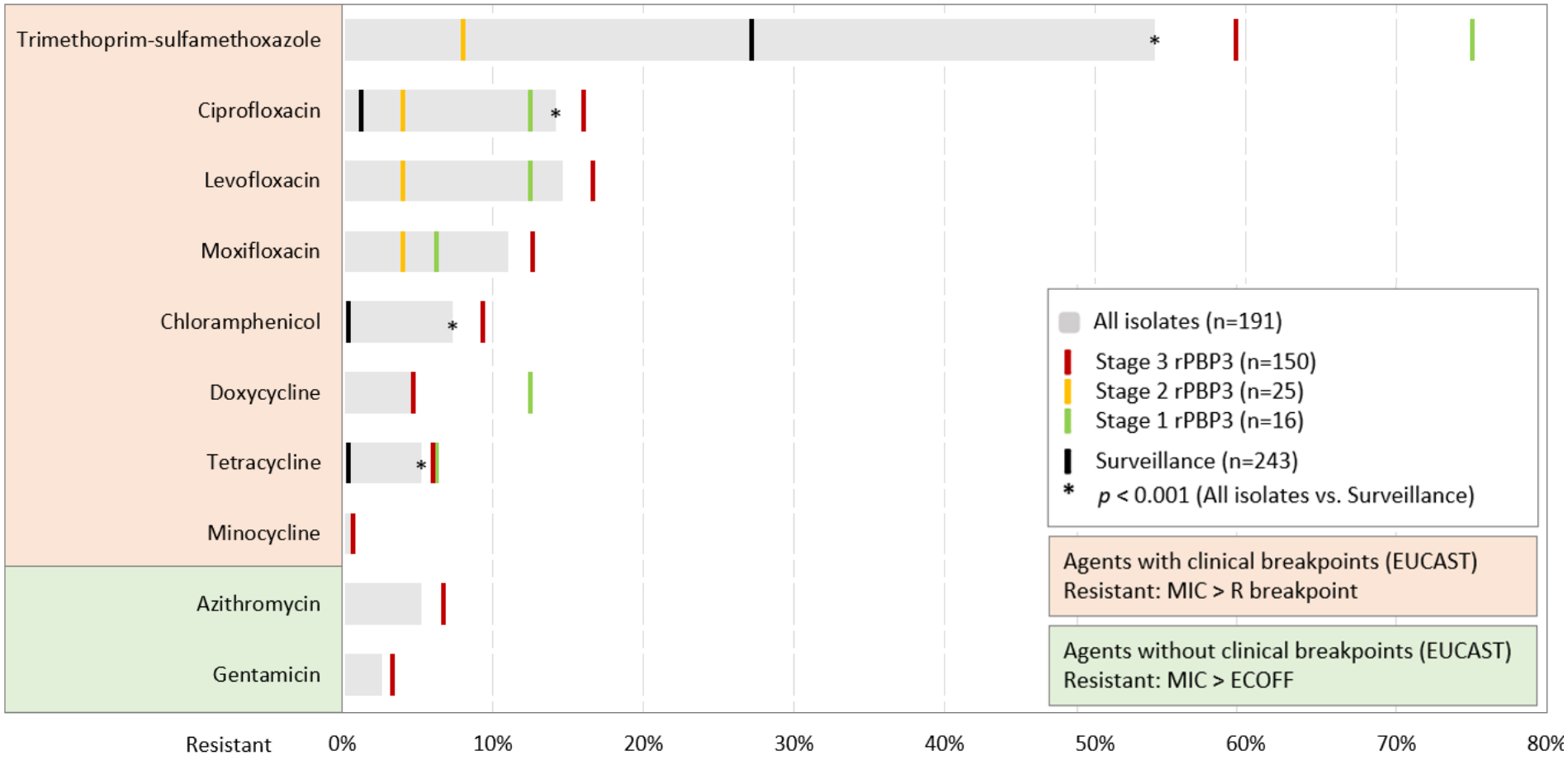


MH-F Broth (Liofilchem) EWC Diagnostics

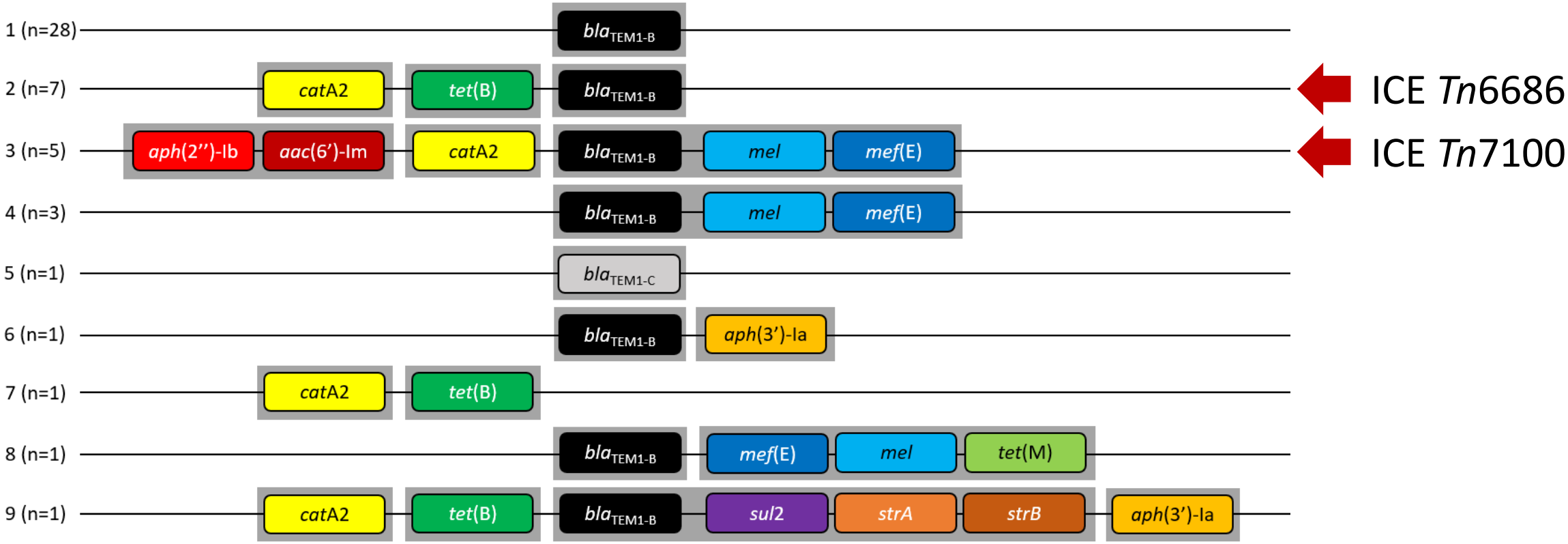
Multidrug resistance



Non-beta-lactam co-resistance

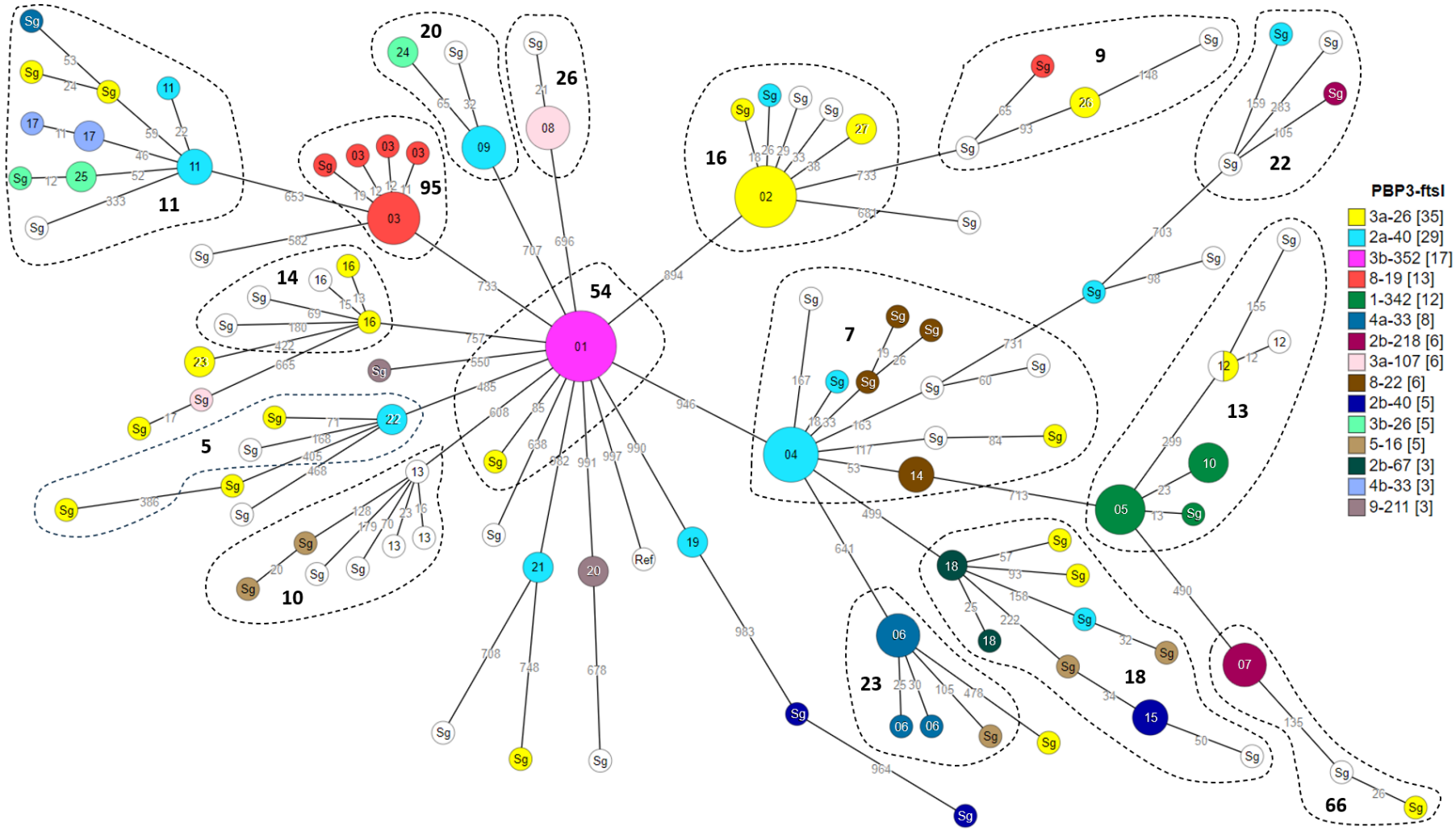


Transferable resistance gene profiles

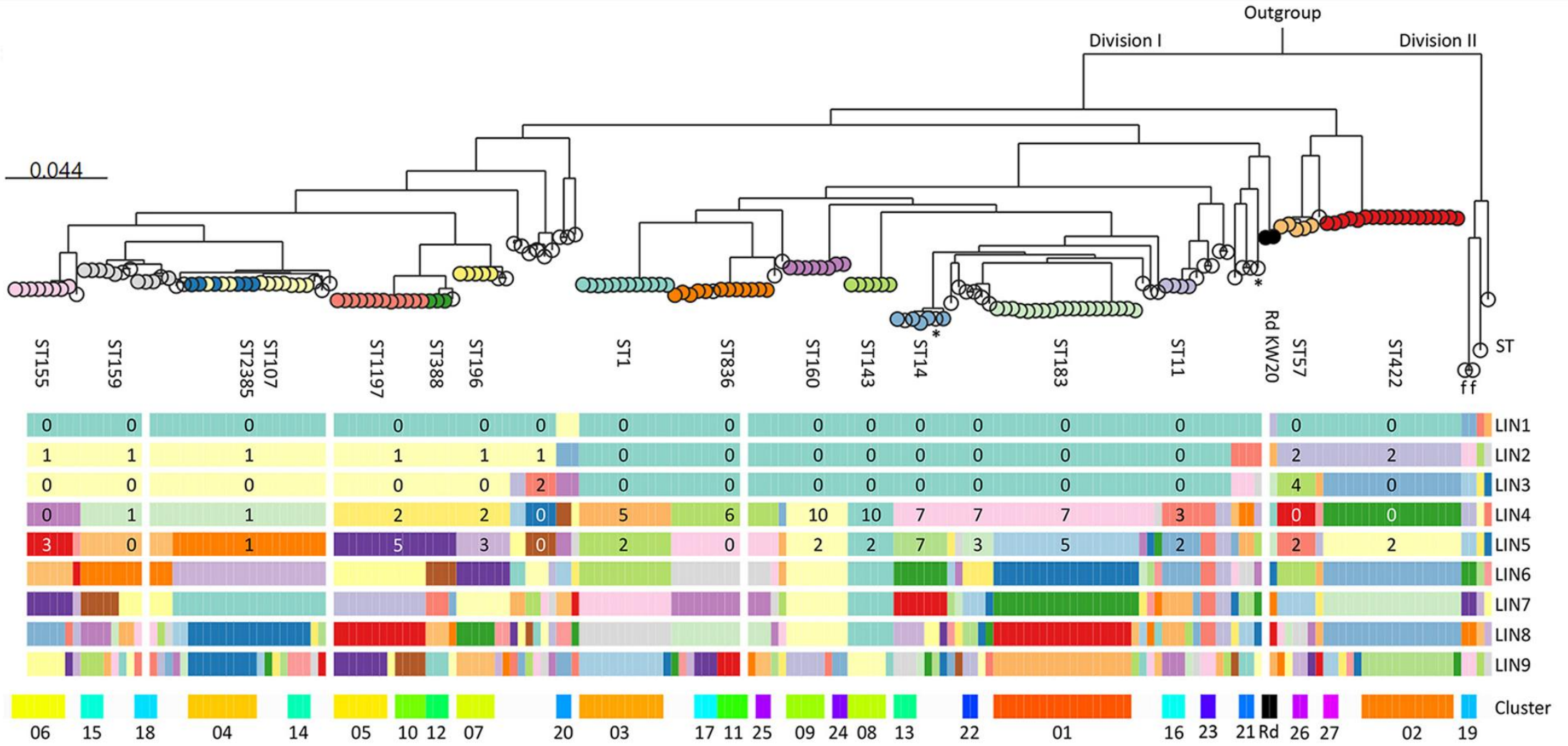


Hegstad et al. mSphere 2020, Johannessen et al. Front Microbiol 2022

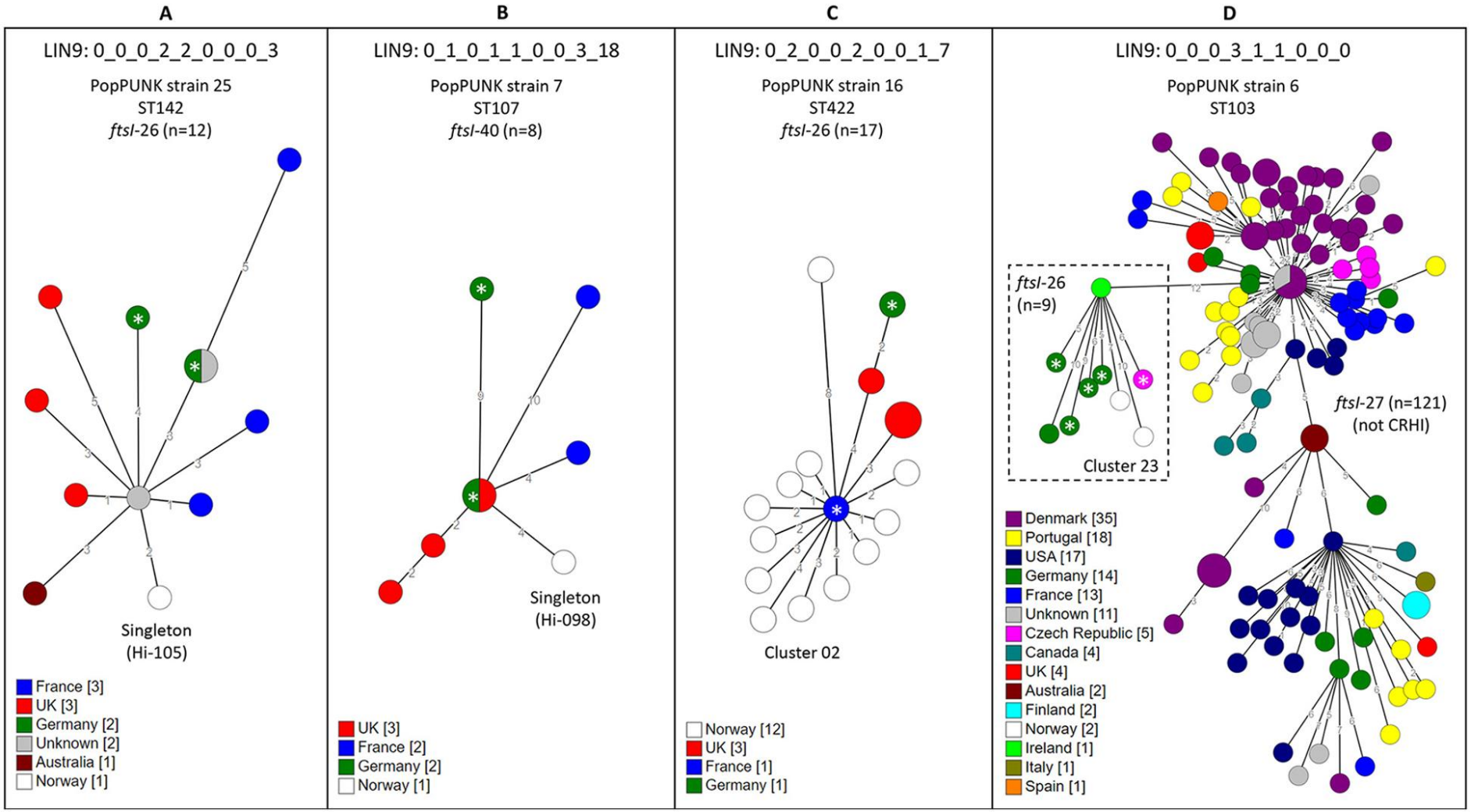
Epidemic *ftsI* alleles



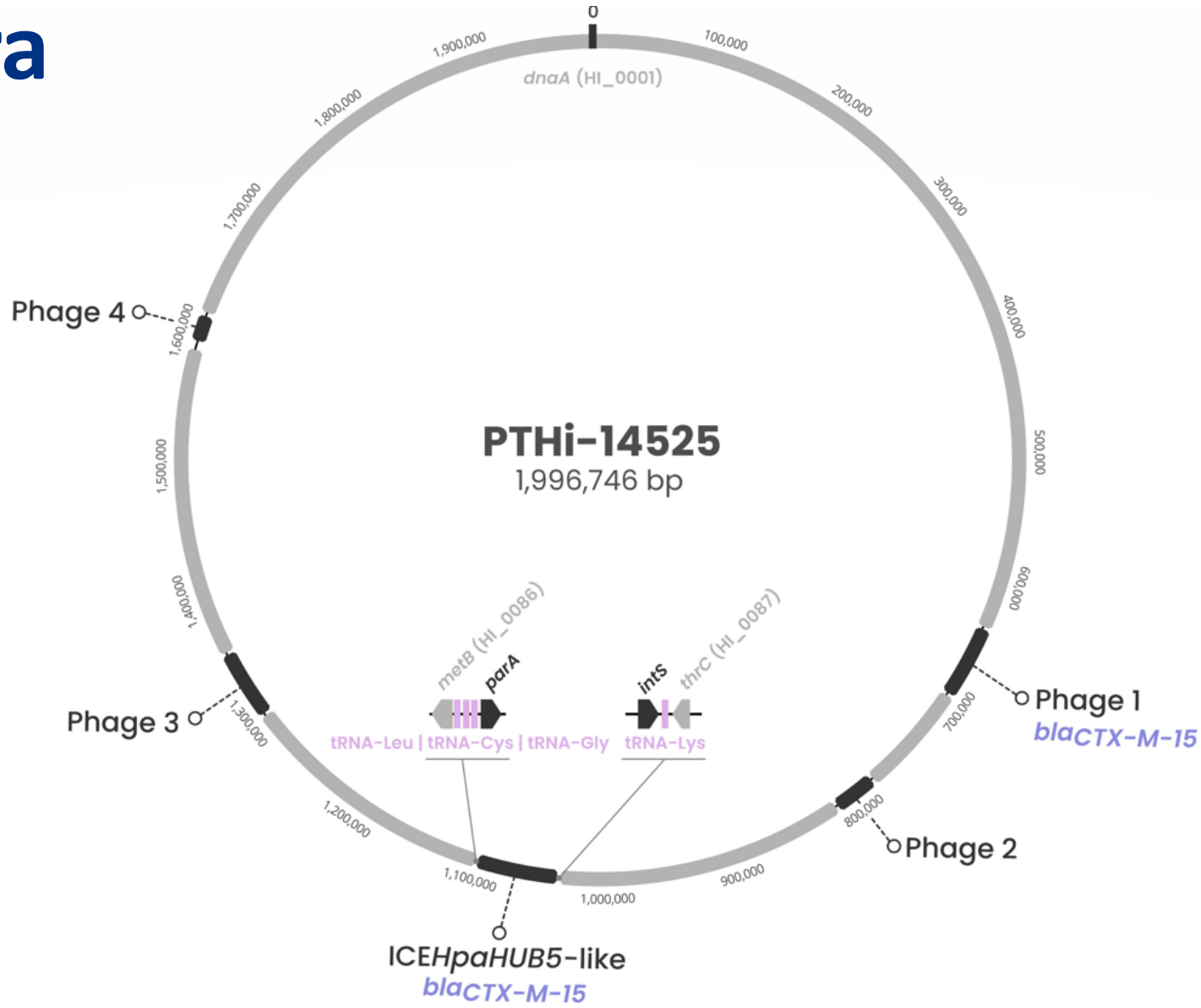
Polyclonal expansion



International clones



A new era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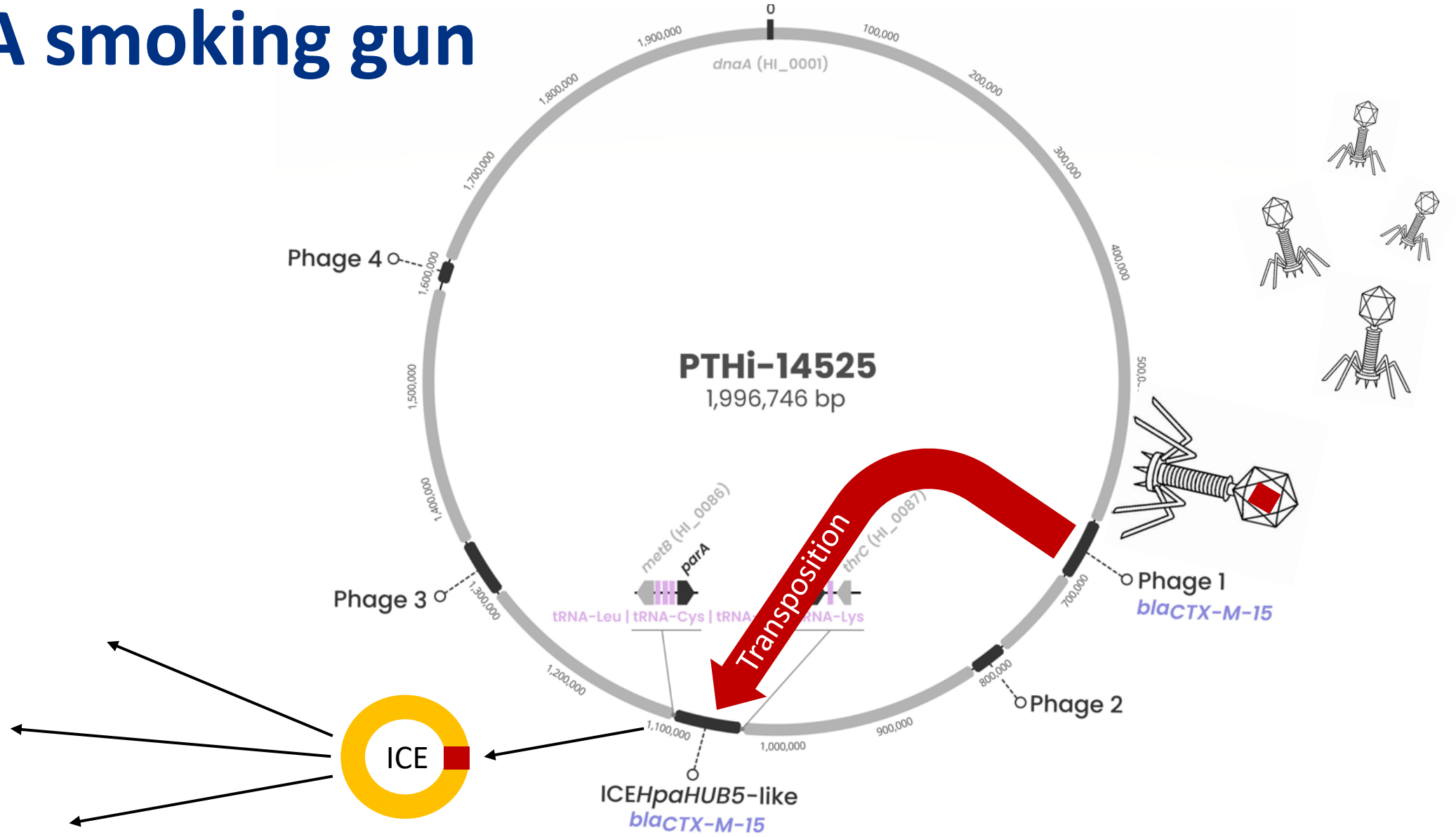
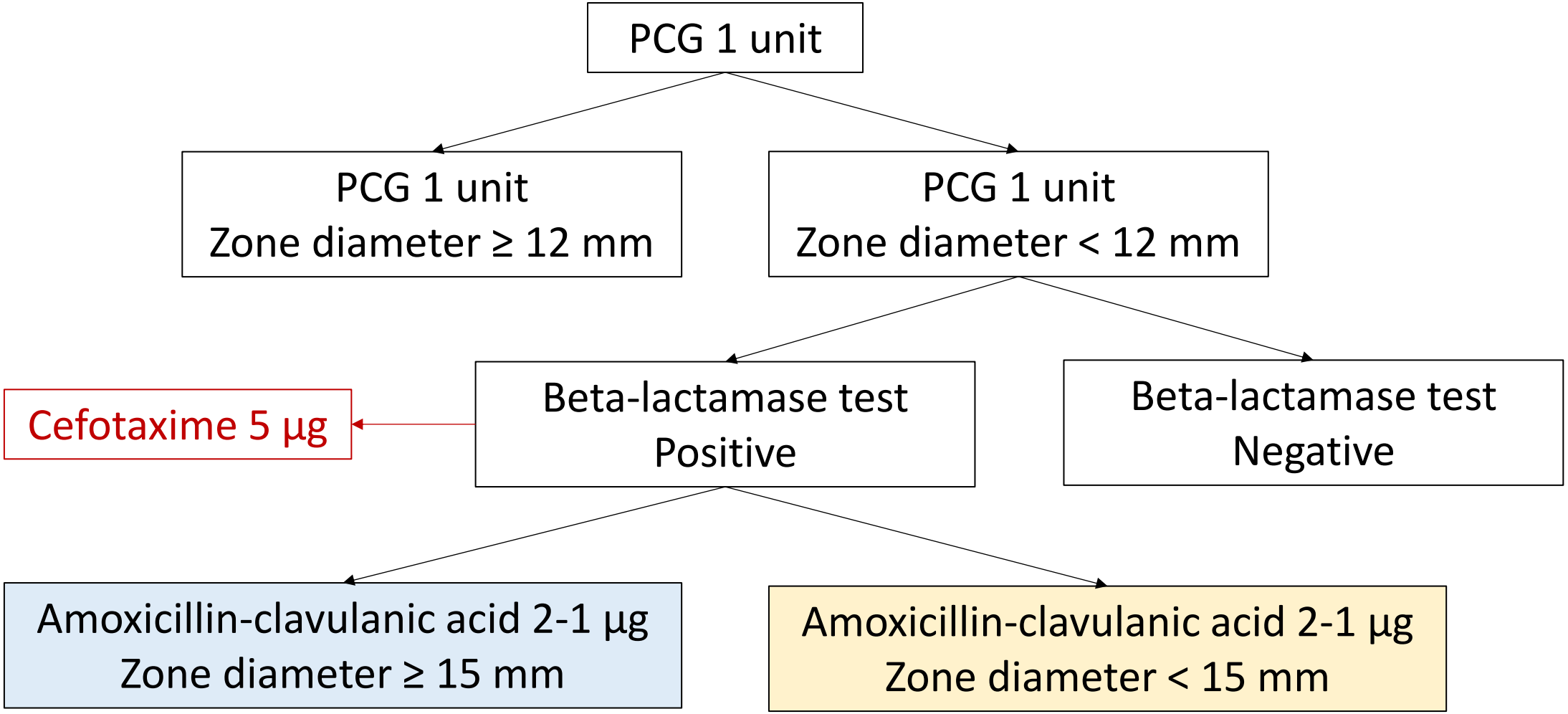
1,900,000
dnaA (HI_0001)
PTHi-14525
1,996,746 bp
metB (HI_0086)
parA
tRNA-Leu | tRNA-Cys | tRNA-Gly
intS
thrC (HI_0087)
tRNA-Lys
Phage 1
blaCTX-M-15
Phage 2
Phage 3
Phage 4
ICEHpaHUB5-like
blaCTX-M-15

A smoking gun

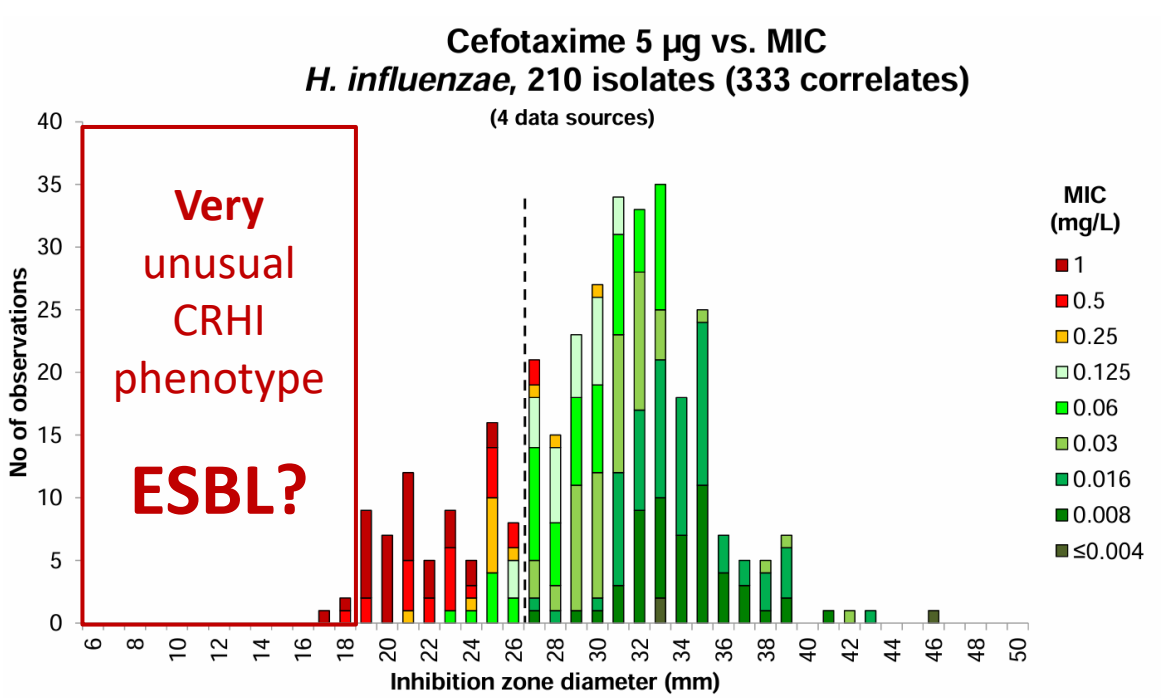


Screening algorithm

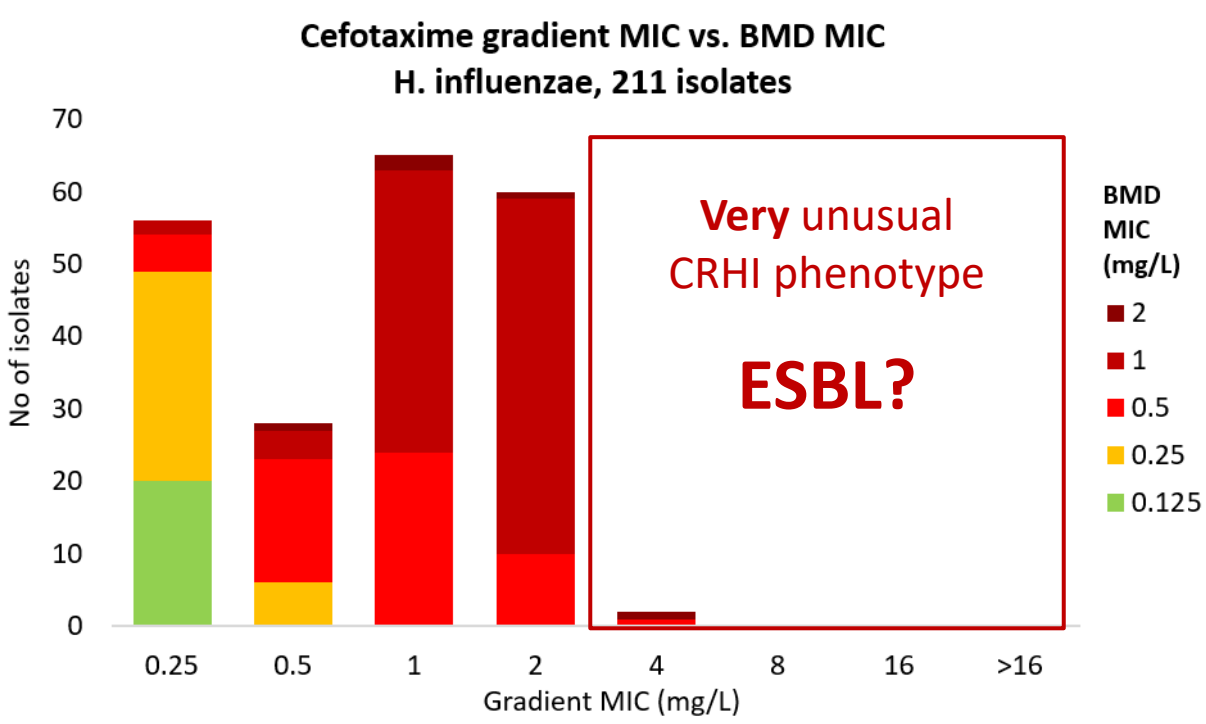


When to consider specific ESBL testing

Liberal: Beta-lactamase positive AND resistance to any third-generation cephalosporin
Stringent: Beta-lactamase positive AND high-level cefotaxime resistant (CTX5 zone < 19 mm OR MIC > 2 mg/L)
Consider clinical importance (e.g. IPC) and epidemiologic risk factors (e.g. recent travels to Iberian peninsula)



Data from EUCAST: Haemophilus influenzae



Data from Skaare et al. Front Microbiol 2025

First report of ESBL H. influenzae – implications for the laboratory?

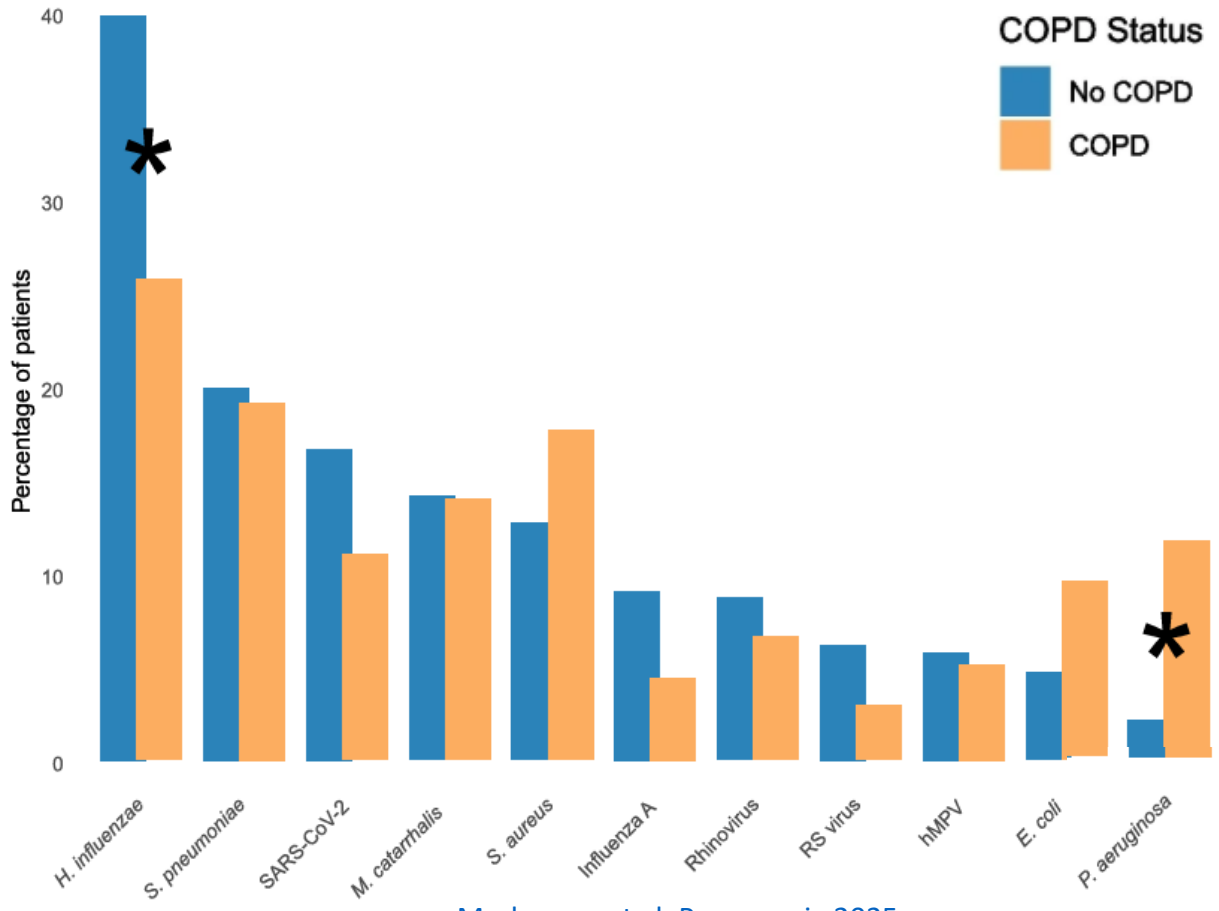
A. ESBL Hi are unlikely to become successful – no need to worry

B. ESBL screening should be included in the Hi test algorithm from 2027

C. ESBL Hi are likely all over the place – I will start screening tomorrow

Summary

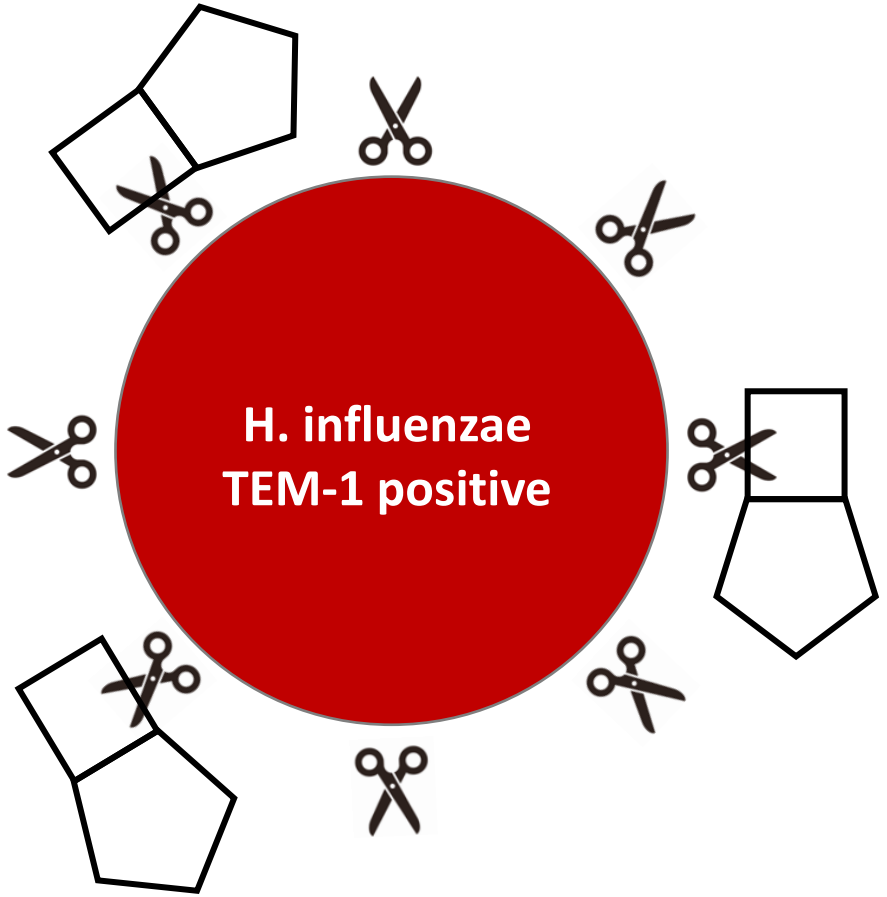
Haemophilus influenzae
is an underestimated
cause of deep infection
in the respiratory tract
COPD exacerbation
meningitis and pneumonia
You should use a beta-lactam
You should use a beta-lactam



Markussen et al. Pneumonia 2025

Summary

Way back in the 1970s
the narrow-spectrum beta-lactamase
TEM-1 came from E. coli
and spread with great success
by horizontal transfer
of ICEs and small plasmids
Breaking down ampicillin
Breaking down amoxicillin

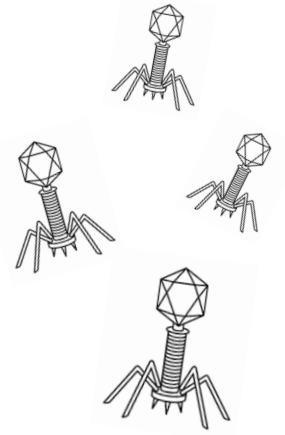


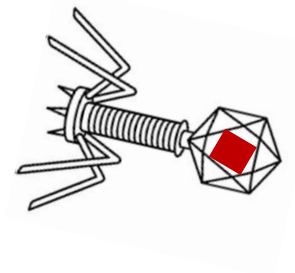
Summary

Chromosomal alterations	…
in PBPs may cause resistance	…
with variable profiles	Cefotaxime-resistant
that include cephalosporins	**CRHI!**
Beta-lactamase inhibitors	…
do not reverse resistance	…
You must test the drug you need	You must test the drug you need
You must test the drug you need	You must test the drug you need

Summary

In the current 2020s	…
a new era has begun	…
with CTX-M-15	Cefotaxime-resistant
right next to a smoking gun	**ESBL!**
Acquired by transduction	…
transposed to a nearby ICE	…
Breaking down cefotaxime	Breaking down cefotaxime
Breaking down ceftriaxone	Breaking down ceftriaxone





Summary

Never ever underestimate

Haemophilus influenzae

What happens in the future?

We'll have to wait and see

Transduction, transformation

Conjugation and mutations

Will it be a superbug?

Will it be a superbug?

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