Multiresistente Erreger bei Ukraine-Flüchtlingen

Niels Pfennigwerth
Nationales Referenzzentrum für gramnegative Krankenhauserreger
Ruhr-Universität Bochum

24. Februar 2022

How much of Ukraine does Russia control?

Source: Institute for the Study of War (as of 18:00 GMT, 26 February)

BBC

https://www.bbc.com/pidgin/60547606

https://www.bloomberg.com/news/articles/2022-03-07/poland-rolls-out-1-7-billion-package-to-help-ukrainian-refugees

https://www.bundeswehr.de

https://de.wikipedia.org/wiki/Landstuhl_Regional_Medical_Center

https://upload.wikimedia.org/wikipedia/commons/5/55/US_military_bases_in_Germany.png

Was bekannt war

Journal of Hospital Infection 112 (2021) 69–76

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Journal of Hospital Infection

journal homepage: www.elsevier.com/locate/jhin

Phenotypic and genotypic characterization of antibiotic resistance in military hospital-associated bacteria from war injuries in the Eastern Ukraine conflict between 2014 and 2020

V. Kondratiuk [a,*], B.T. Jones [b], V. Kovalchuk [c], I. Kovalenko [c], V. Ganiuk [d], O. Kondratiuk [e], A. Frantsishko [f]

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[b] Walter Reed Army Institute of Research, Multidrug-Resistant Organism Repository and Surveillance Network, Silver Spring, MD, USA
[c] Department of Microbiology, National Pirogov Memorial Medical University, Vinnytsia, Ukraine
[d] Intensive Care Unit (For Surgical Patients), National Military Medical Clinical Center 'Main Military Clinical Hospital', Kyiv, Ukraine
[e] Military Medical Clinical Center of Central Region, Ambulatory Clinic, Vinnytsia, Ukraine
[f] Laboratory Department (Microbiological) Clinic of Laboratory Diagnostics, National Military Medical Center "Main Military Clinical Hospital", Kyiv, Ukraine

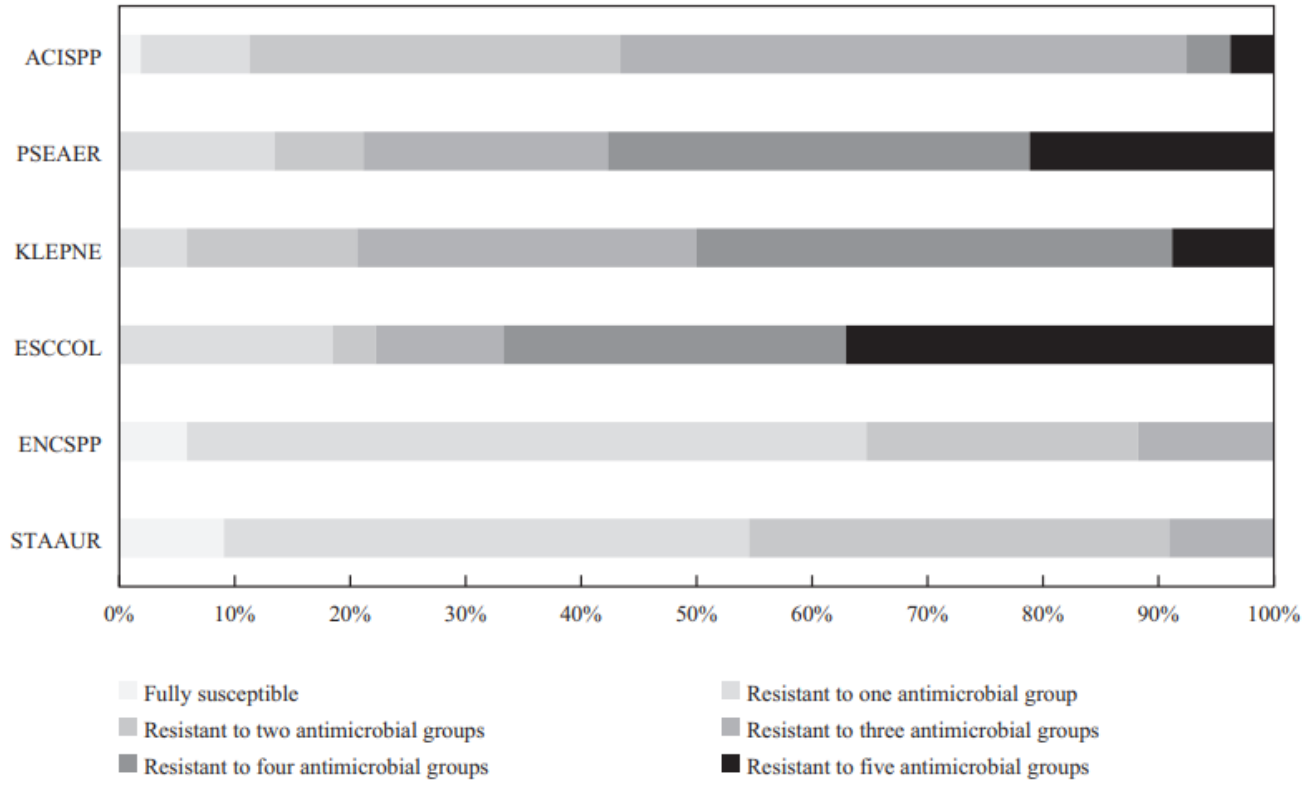

Figure 2. Distribution of isolates with co-resistance. ACISPP, *Acinetobacter* species; ENCSPP, *Enterococcus* species; ESCCOL, *Escherichia coli*; KLEPNE, *Klebsiella pneumoniae*; PSEAER, *Pseudomonas aeruginosa*; STAAUR, *Staphylococcus aureus*.

35-jähriger Kriegsverletzter (hospitalisiert in UK)

	*Klebsiella pneumoniae**	*Acinetobacter baumannii*	*Enterococcus faecalis*
Amoxicillin	>32 (R)	ND	S†
Co-amoxiclav	>32 (R)	ND	ND
Piperacillin–tazobactam	>64 (R)	ND	ND
Aztreonam	>16 (R)	ND	ND
Ceftazidime	>16 (R)	ND	ND
Ceftriaxone	>8 (R)	ND	ND
Cefiderocol	21 mm† (ATU)	14 mm†‡	ND
Imipenem	>8 (R)	>8 (R)	ND
Meropenem	>8 (R)	>8 (R)	ND
Amikacin	>16 (R)§	>16 (R)§	ND
Gentamicin	>4 (R)§	>4 (R)§	ND
Ciprofloxacin	>1 (R)	>1 (R)	ND
Levofloxacin	>2 (R)	>2 (R)	ND
Fosfomycin	>64 (R)	ND	ND
Eravacycline	2¶	0·5‡	ND
Tigecycline	20 mm†‖	0·5‡	0·125 (S)
Colistin	0·5; 2**	1 (S)§	ND
Co-trimoxazole	>4 (R)	>4 (R)	ND
Vancomycin	ND	ND	2 (S)

Data are minimum inhibitory concentration (mg/L) unless stated otherwise. ATU=area of technical uncertainty. EUCAST= European Committee on Antimicrobial Susceptibility Testing. ND=not determined. R=resistant. S=susceptible. *Producing New Delhi metallo-β-lactamase carbapenemases. †Disk-diffusion test conducted according to EUCAST Clinical Breakpoints v13.0. ‡No breakpoint. §According to EUCAST Guidance Document *EUCAST Breakpoints in Brackets*, 2021. ¶Breakpoint validated for *Escherichia coli* only. ‖Data for *E coli* and *Citrobacter koseri* only. **Two strains noted by reference laboratory.

Table: Selected antimicrobial susceptibility test data for organisms isolated from an infected war-related combat injury of the left lower leg in November, 2022, Ukraine

Pallet *et al.*, The Lancet Infectious Diseases 2023

ca. 55-jähriger Patient

Dnipro
↓
Kiev
↓
US-Hospital
Deutschland

Appendix Table 1. Antibiotic susceptibility data*

	MIC†				
	110606	110817	110818	110819	110821
Antibiotic	**PSA**	**PSA**	**PSA**	**ACB**	**KPN**
Amikacin	≥64	≥64	32	NA	≥64
Gentamicin	≥16	≥16	8	≥16	≥16
Tobramycin	≥16	≥16	≥16	≥16	≥16
Ampicillin/Sulbactam	NA	NA	NA	≥32	≥32
Cefazolin	≥64	≥64	≥64	≥64	≥64
Cefepime	≥32	≥32	≥32	NA	≥32
Cefotaxime	NA	NA	NA	≥64	≥64
Ceftazidime	≥64	≥64	≥64	≥64	≥64
Ceftazidime/Avibactam	>32	>32	32	32	>32
Ceftolozane/Tazobactam	>8	>8	>8	>8	>8
Imipenem	≥16	≥16	≥16	≥16	≥16
Meropenem	≥16	≥16	≥16	≥16	≥16
Piperacillin/Tazobactam	≥128	≥128	≥128	NA	≥128
Ticarcillin/Clavulanic Acid	≥128	≥128	≥128	NA	NA
Ciprofloxacin	≥4	≥4	≥4	≥4	≥4
Levofloxacin	≥8	≥8	≥8	4	≥8
Tetracycline	NA	NA	NA	2	≥16
Trimethoprim/Sulfameth	NA	NA	NA	≥320	≥320
Colisitin	2	1	1	≤0.25	16
Eravacycline	>8	8	>8	0.25	4
Imipenem	>16	>16	16	>16	>16
Imipenem/Relebactam	>16	>16	2	>16	>16
Meropenem	>8	>8	>8	>8	>8
Meropenem/Vaborbactam	>16	>16	8	>16	>6
Omadacycline	>8	>8	>8	2	>8
Plazomicin	>4	>4	4	>4	>4
Cefiderocol‡	20	21	24	20	8

* PSA, Pseudomonas aeruginosa; ACB, Acinetobacter baumannii, KPN, *Klebsiella pneumoniae*
† Interpretation is based on CLSI (2020) where available. Blue, Resistant; Yellow, Intermediate; Green, susceptible; Orange, Not Interpretable
‡ Performed by Disk diffusion; Results are the Zone of Inhibition expressed in millimeters (mm)

McGann *et al.*, Emerging Infectious Diseases 2023

ca. 55-jähriger Patient

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Cefepime	≥32	≥32	≥32	NA	≥32
Cefotaxime	NA	NA	NA	≥64	≥64
Ceftazidime	≥64	≥64	≥64	≥64	≥64
Ceftazidime/Avibactam	>32	>32	32	32	>32
Ceftolozane/Tazobactam					
Imipenem	**IMP-1**	**NDM-1**	**OXA-10**	**OXA-23**	**NDM-1**
Meropenem				**OXA-72**	**OXA-48**
Piperacillin/Tazobactam	≥128	≥128	≥128		
Ticarcillin/Clavulanic Acid	≥128	≥128	≥128		
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McGann *et al.*, Emerging Infectious Diseases 2023

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Cefepime	≥32	≥32	≥32	NA	≥32
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Ceftazidime	≥64	≥64	≥64	≥64	≥64
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+ *E. faecium* vanA

McGann *et al.*, Emerging Infectious Diseases 2023

Einsendescheine im NRZ

Quelle des Isolates
- ☐ Blutkultur
- ☐ Urin
- ☐ Sputum
- ☐ BAL o. Bronchialsekret
- ☒ Wundabstrich
- ☐ intraabdominale Probe
- ☐ Rektalabstrich,Stuhl
- ☐ Mund-/Rachenabstrich
- ☐ Sonstiges (bitte spezifizieren):

Schussverletzung

zum Zeitpunkt der Probenentnahme liegt Pat. auf:
- ☒ Intensivstation
- ☐ Normalstation
- ☐ ambulant/Notfallaufnahme
- ☐ unbekannt

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- ☐ Blutkultur
- ☐ Urin
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- ☒ Wundabstrich
- ☐ intraabdominale Probe
- ☐ Rektalabstrich,Stuhl
- ☐ Mund-/Rachenabstrich
- ☐ Sonstiges (bitte spezifizieren):

Wunde am Bein (Durchschuss durch Granatsplitter (Schuss Krieg)

zum Zeitpunkt der Probenentnahme liegt Pat. auf:
- ☐ Intensivstation
- ☐ Normalstation
- ☐ ambulant/Notfallaufnahme
- ☐ unbekannt

- ☐ Pat. bereits ≥ 2 d im jetzigen Krankenhaus
- ☐ Pat. < 2 d im jetzigen Krankenhaus

Weitere Angaben zum Patienten/ zur Infektion
- ☒ Isolat aus Infektionsprozess
- ☐ Isolat kolonisierend
- ☐ Isolat stammt aus Ausbruch

Krankenhausaufenthalt in letzten 6 Monaten:
- ☒ ja
- ☐ nein
- ☐ unbekannt

Auslandsaufenthalt in letzten 6 Monaten:
- ☐ nein
- ☐ unbekannt
- ☒ ja, mit Krankenhausaufenthalt (bitte spezifizieren):

Ukraine

- ☐ ja, ohne Krankenhausaufenthalt (bitte spezifizieren):

Weitere Angaben zum Patienten/ zur Infektion
- ☒ Isolat aus Infektionsprozess
- ☐ Isolat kolonisierend
- ☐ Isolat stammt aus Ausbruch

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- ☐ nein
- ☒ unbekannt

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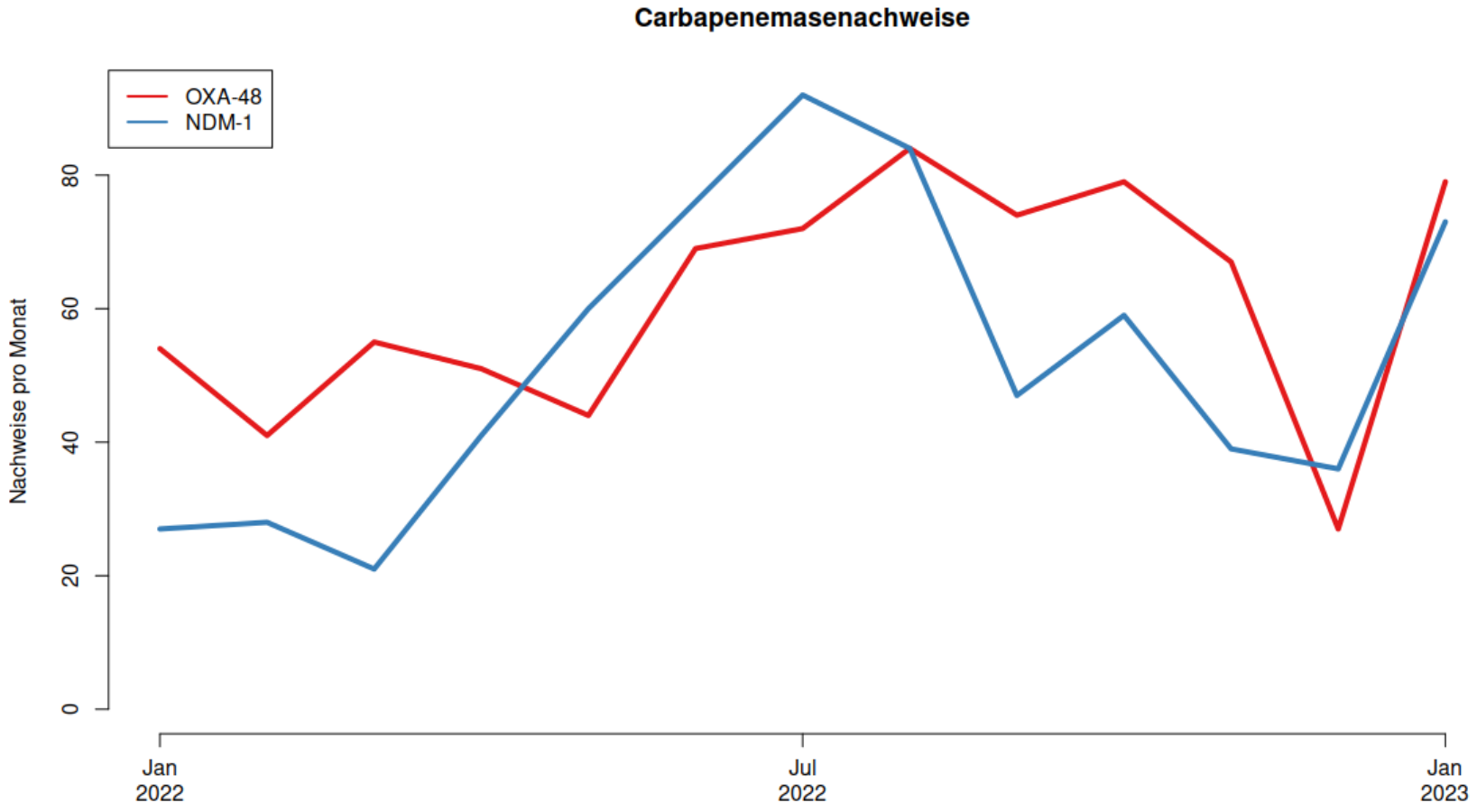
- ☐ nein
- ☐ unbekannt
- ☐ ja, mit Krankenhausaufenthalt (bitte spezifizieren):

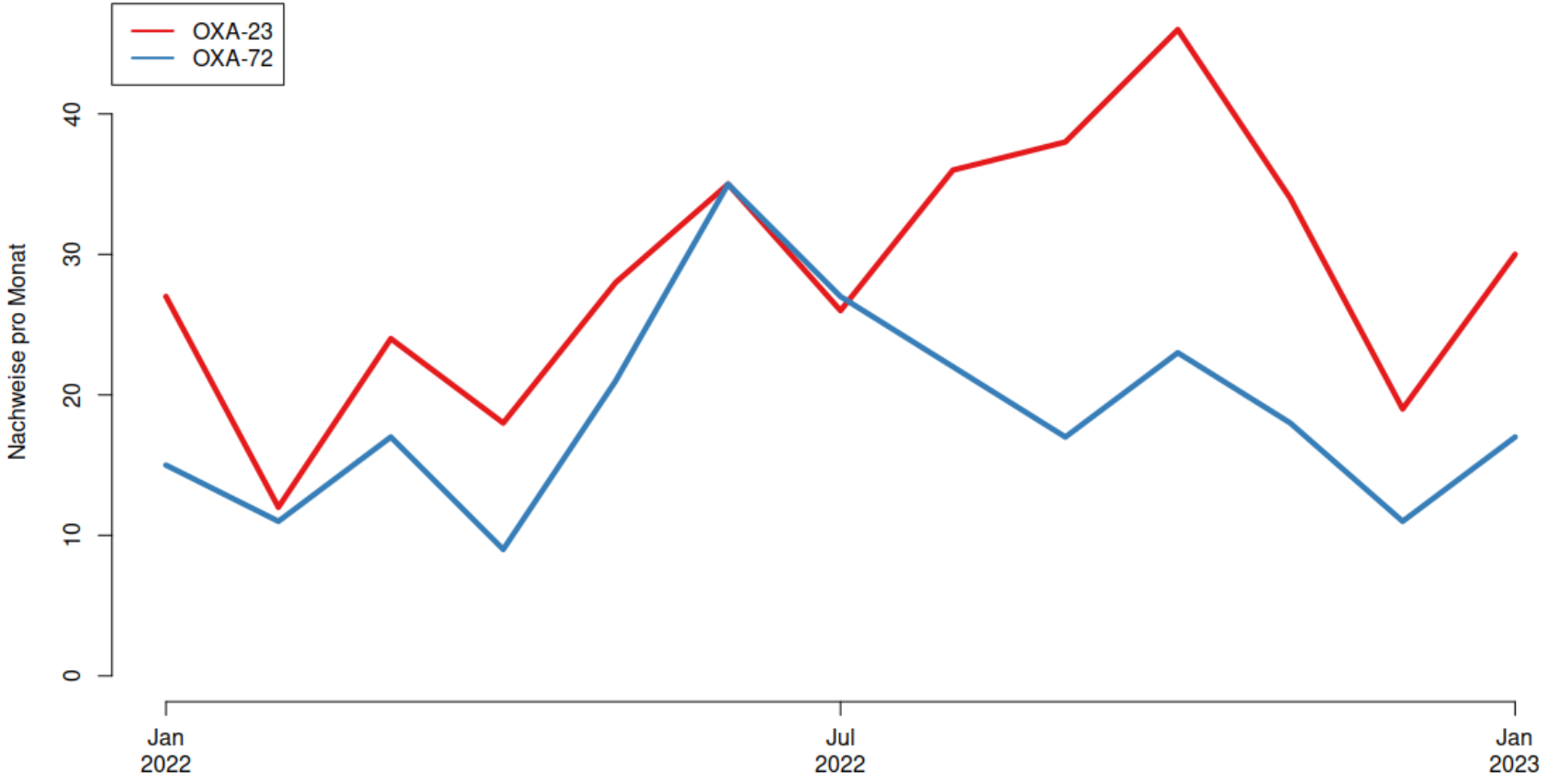
- ☒ ja, ohne Krankenhausaufenthalt (bitte spezifizieren):

Kriegsverletzung aus Ukraine – Krieg

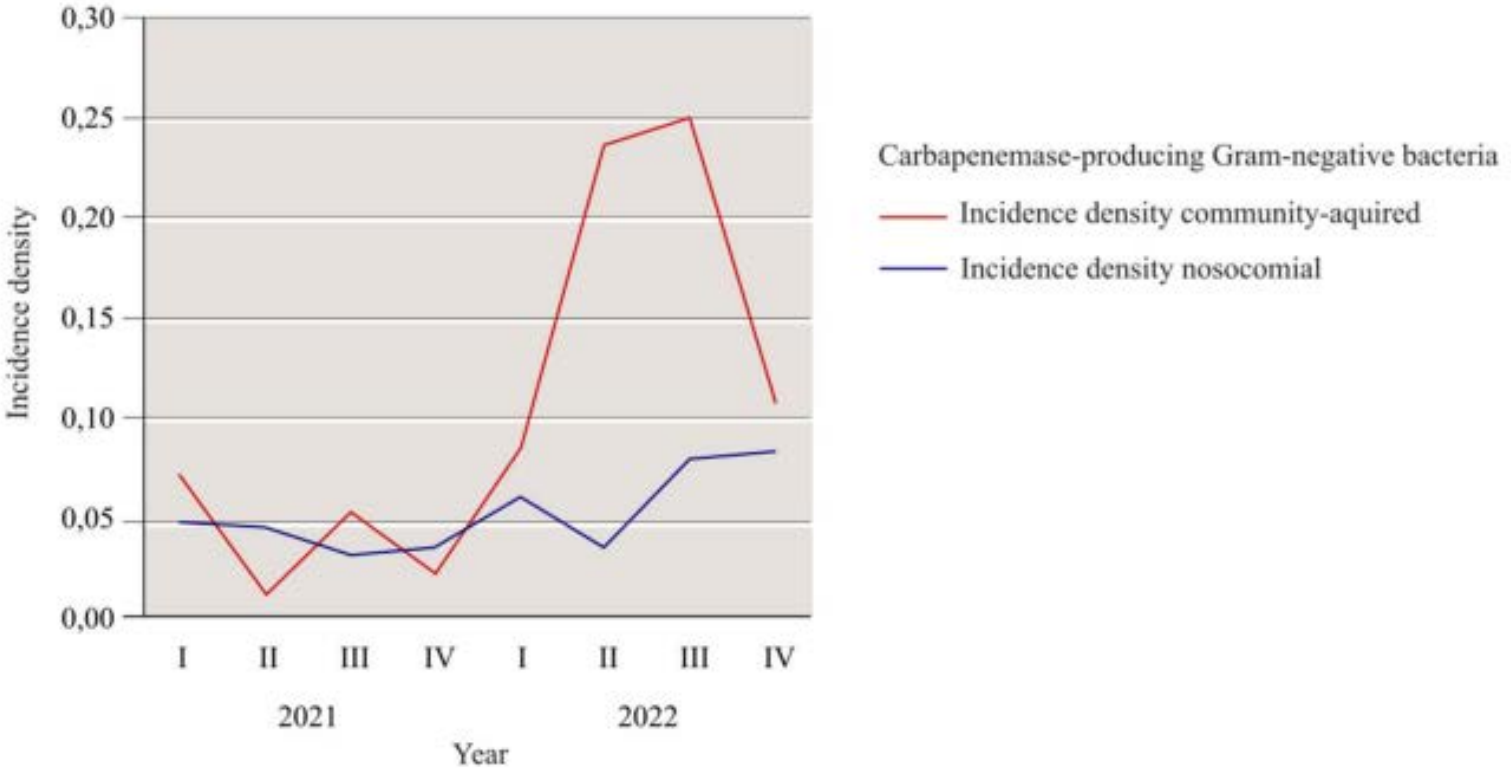
Enterobacterales – NDM-1 und OXA-48 (2022)



A. baumannii – OXA-23 und OXA-72 (2022)



Auch in Jena



Stein *et al*., Infection 2023

Table 1 Clinical data of the seven Ukrainian patients were collected. Patients #1–#4 were admitted as refugees, while patients #5–#7 were wounded soldiers

Patient-identifier	Admission date	Age, sex	Cause of admission	Sampling	Infection/colonization	Isolated pathogen	Carbapenemase
#1	March	76 years, female	Transfer from external hospital with known myeloproliferative disease	Stool	Colonization	*K. pneumoniae*	NDM-3
#2	April	54 years, female	Dialysis patient with acute hepatitis b	Urine	Colonization	*P. aeruginosa*	NDM-1
#3	August	3 years, male	Suspected obstructive sleep apnea syndrome with known mucopolysaccharidosis	Rectal swab Rectal swab	Colonization Colonization	*K. pneumoniae* *K. pneumoniae*	OXA-48 NDM-1
#4	September	49 years, female	Transfer from external hospital with liver cirrhosis	Urine Blood culture Rectal swab Ascites	Colonization Infection Colonization Infection	*K. pneumoniae* *K. pneumoniae* *K. pneumoniae* *K. pneumoniae*	NDM-1 NDM-1 NDM-1 NDM
#5	April	48 years, male	Direct transfer from Ukraine due to war injuries Wounded 04/2022 Multiple bony injuries of the lower extremities on both sides Urologic and abdominal injury from a bullet through the abdomen	Wound Blood culture Abdomen Rectal swab Rectal swab Urine	Infection Infection Infection Colonization Colonization Colonization	*P. aeruginosa* *K. pneumoniae* *A. baumannii* *E. coli* *K. pneumoniae* *K. pneumoniae*	IMP-34 NDM-1 OXA-72, -90 NDM-5 OXA-48 NDM-5, OXA-48
#6	June	47 years, male	Direct transfer from Ukraine due to war injuries Wounded 05/2022 Open fractures of the upper and lower extremities	Skin Skin	Colonization Colonization	*C. freundii* *P. aeruginosa*	NDM-1 IMP-34
#7	August	35 years, male	Direct transfer from Ukraine due to war injuries Wounded 05/2022 Mine injury with fractures of the lower extremities	Blood culture Catheter Catheter Rectal swab Rectal swab Rectal swab Deep wound Deep wound Deep wound	Infection Colonization Colonization Colonization Colonization Colonization Infection Infection Infection	*K. pneumoniae* *K. pneumoniae* *P. aeruginosa* *K. pneumoniae* *K. pneumoniae* *E. coli* *P. aeruginosa* *P. aeruginosa* *P. stutartii*	OXA-48 NDM-1 NDM-1 NDM-1, OXA-48 NDM-1, OXA-48 KPC-3 NDM-1 VIM-2 NDM

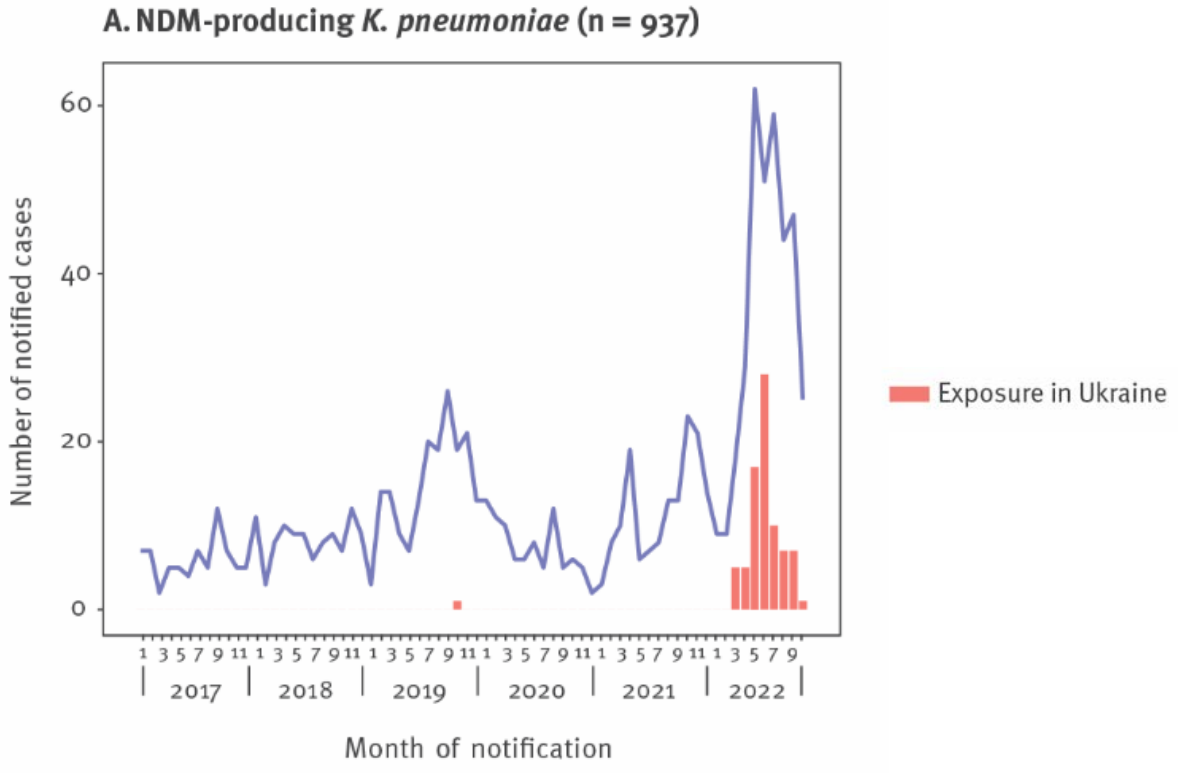
Stein *et al*., Infection 2023

Rapid communication

Open Access

Increase in NDM-1 and NDM-1/OXA-48-producing *Klebsiella pneumoniae* in Germany associated with the war in Ukraine, 2022

Mirco Sandfort[1,*], Jörg B Hans[2,*], Martin A Fischer[3,*], Felix Reichert[1], Martina Cremanns[2], Jessica Eisfeld[2], Yvonne Pfeifer[3], Annika Heck[1], Tim Eckmanns[1], Guido Werner[3], Sören Gatermann[2], Sebastian Haller[1,**], Niels Pfennigwerth[2,**]



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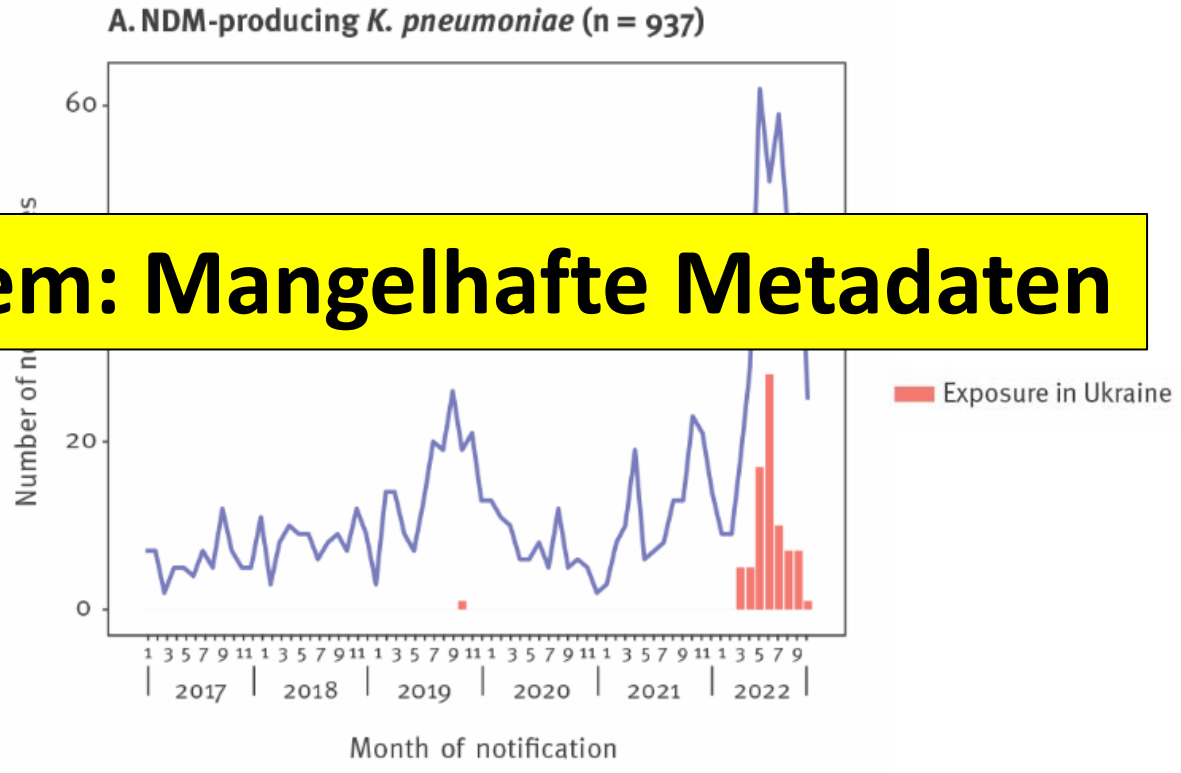
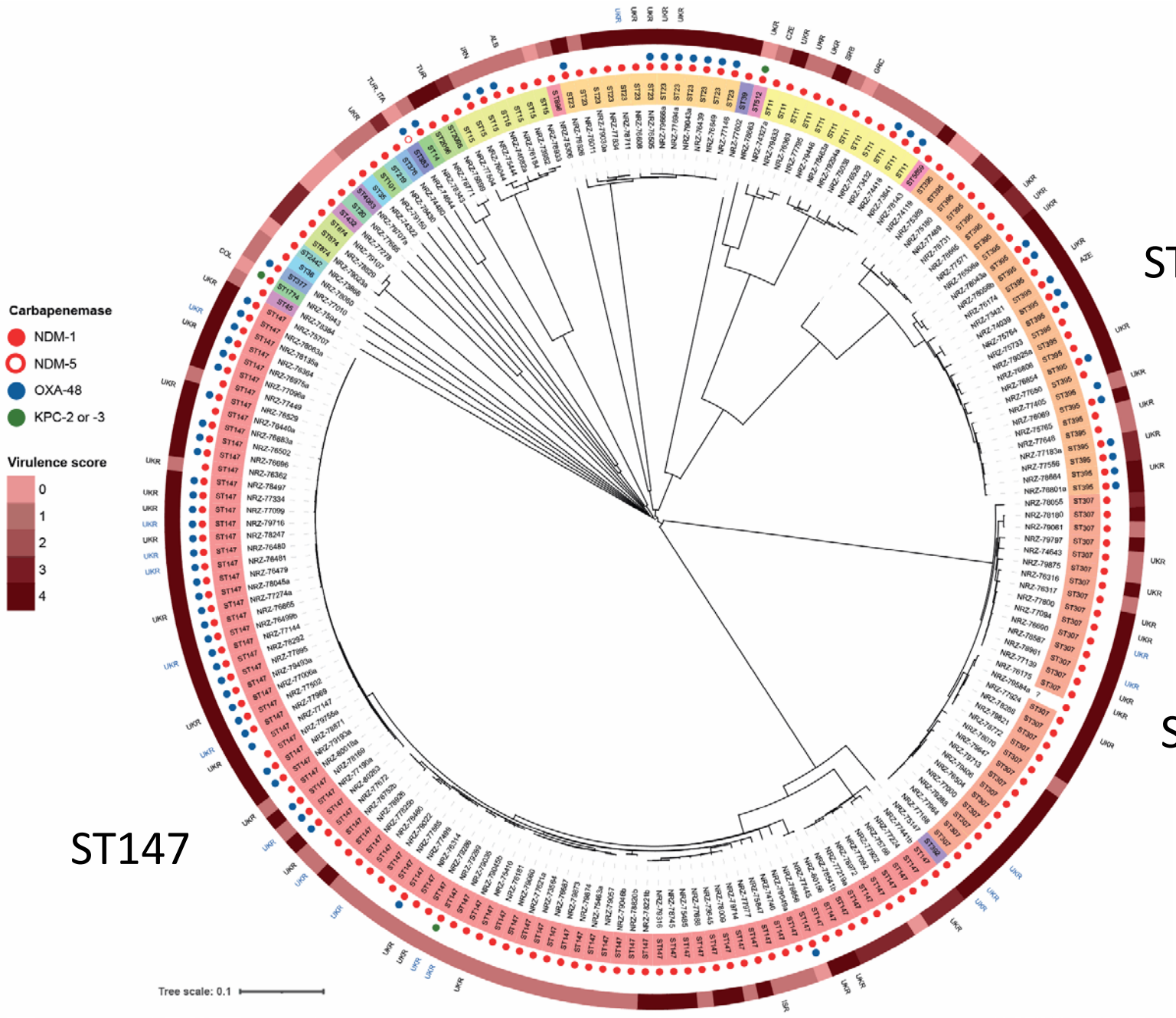


Problem: Mangelhafte Metadaten

cgMLST

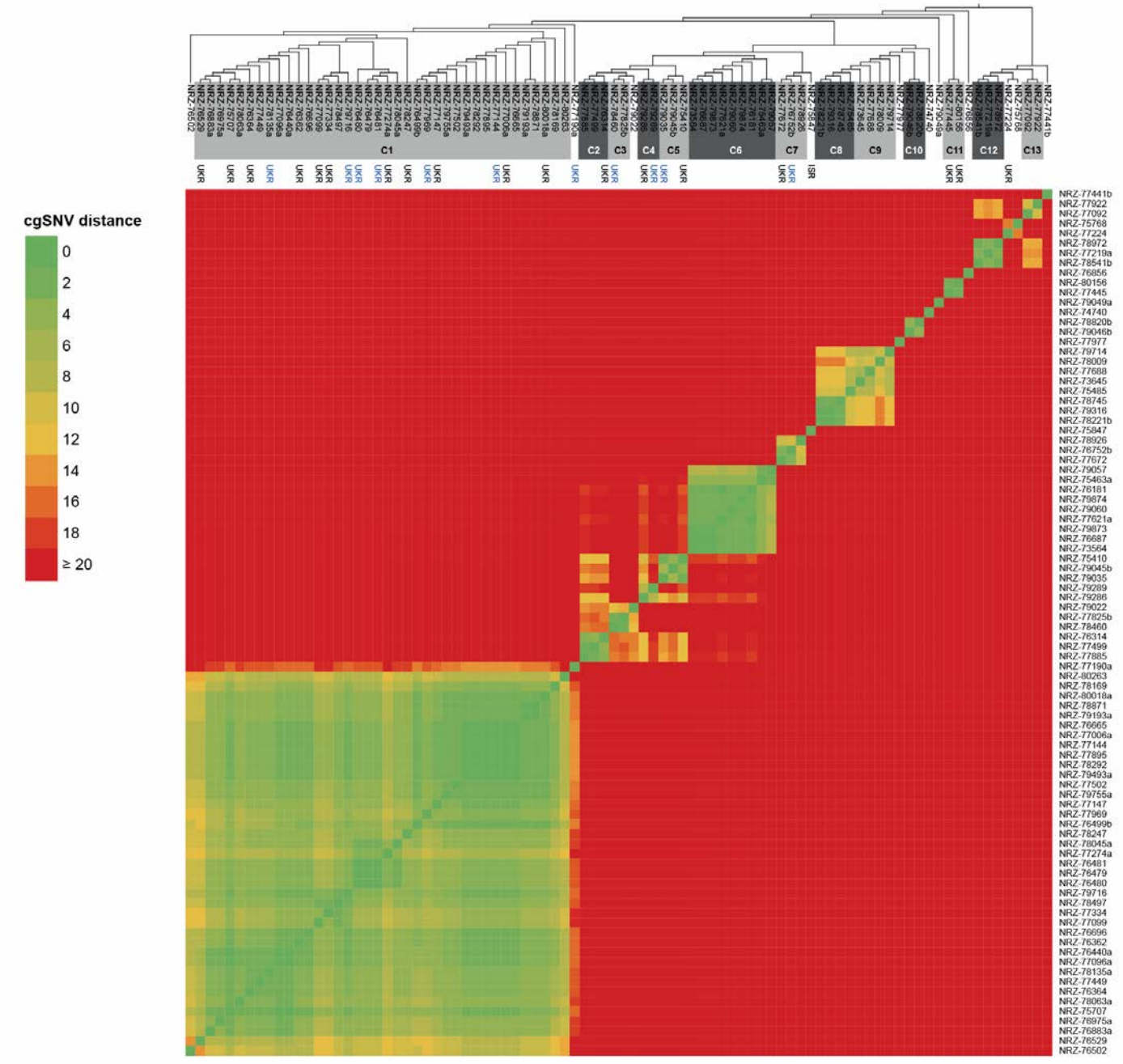


ST395

ST307

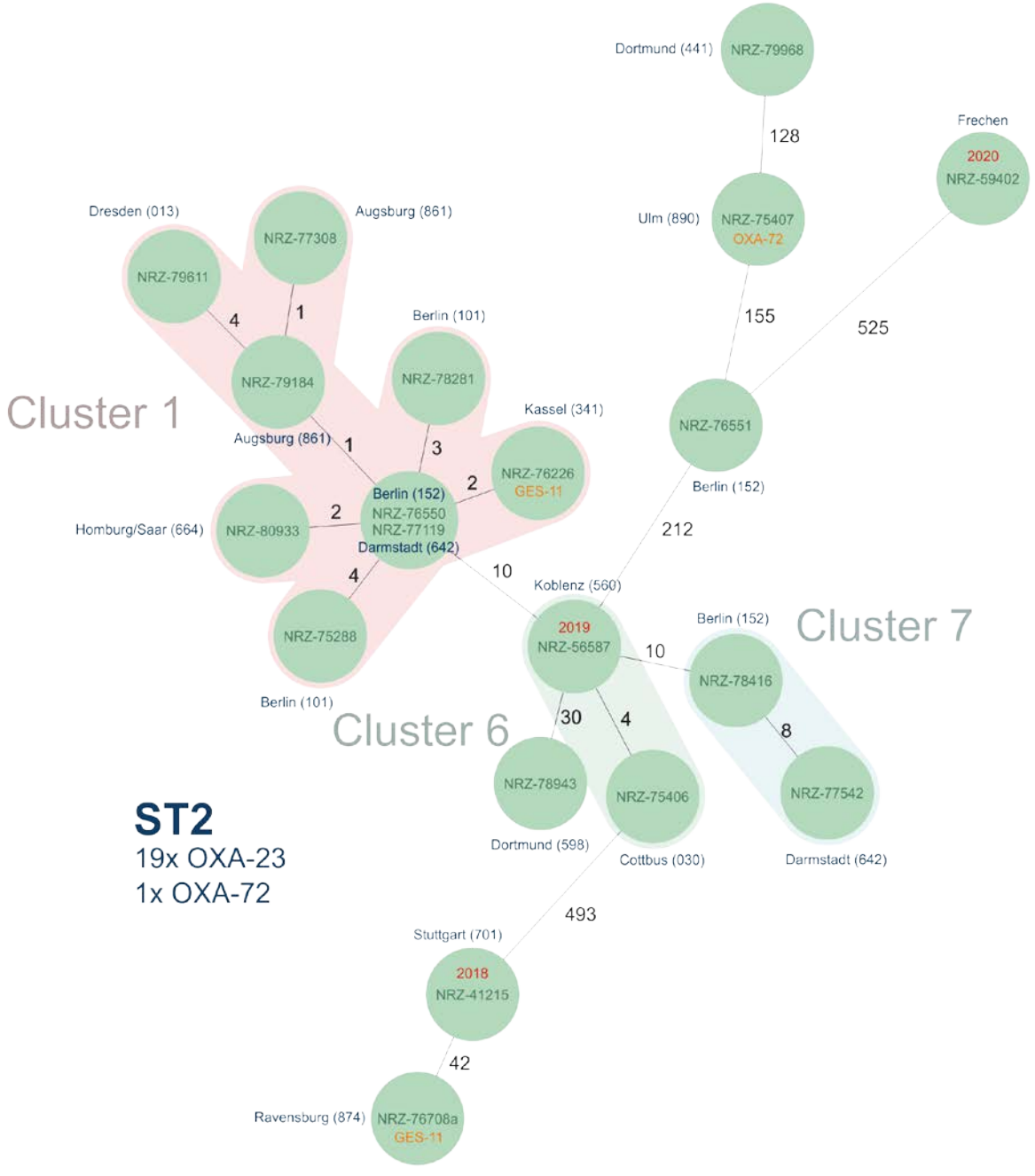
ST147

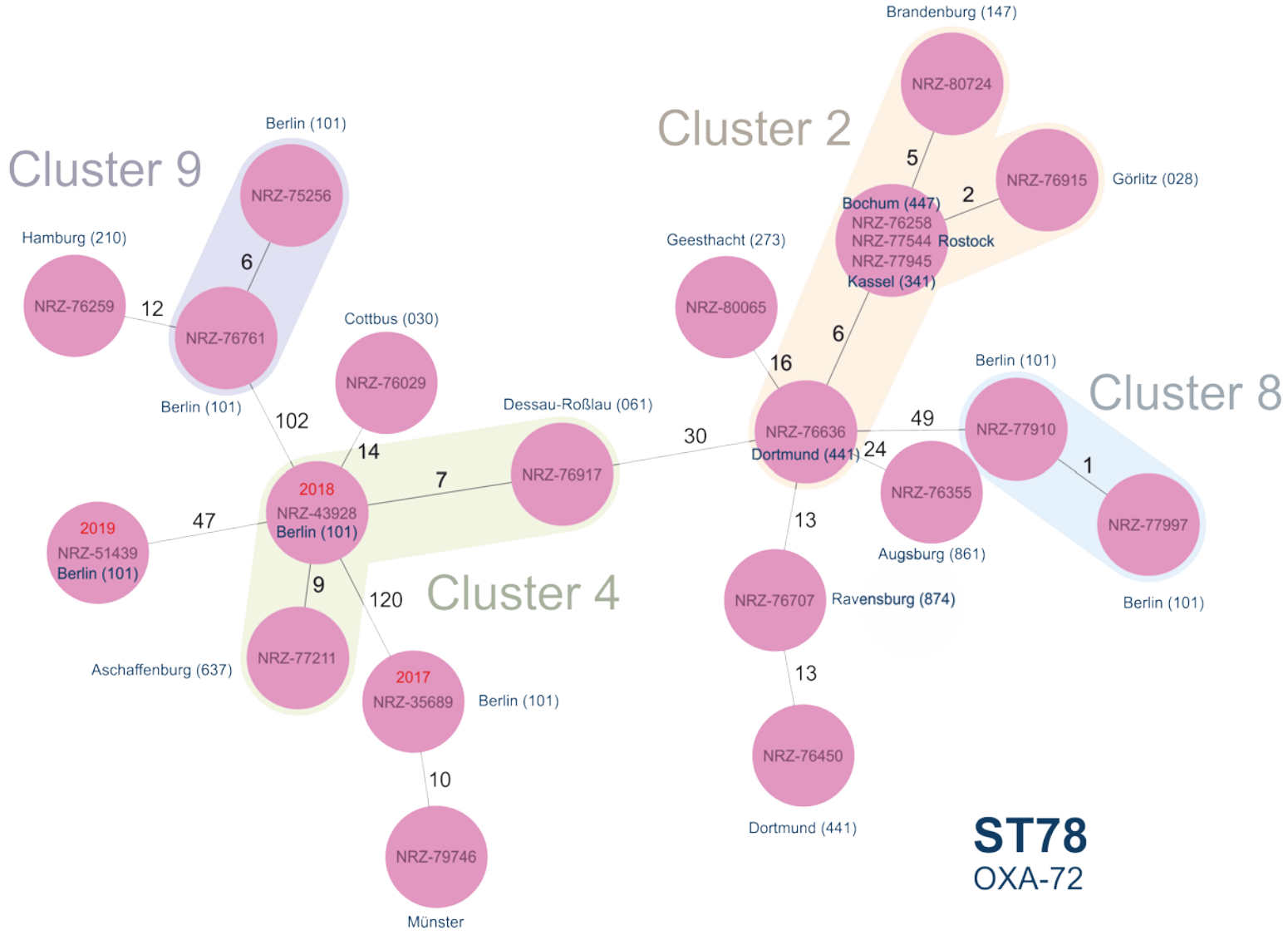
ST147 (cgSNV)


cgSNV distance
0
2
4
6
8
10
12
14
16
18
≥ 20
C1
C2
C3
C4
C5
C6
C7
C8
C9
C10
C11
C12
C13

Carbapenemase-positive *A. baumannii* aus der Ukraine

- 66 *A. baumannii*-Isolate sequenziert
  - ➢ 59 aus 2022
  - ➢ 7 Isolate aus vorherigen Jahren
- 65 Patienten mit Auslandsanamnese Ukraine
- 1 Patient mit Auslandsanamnese Polen
- Großteil der Isolate mit OXA-23 bzw. OXA-72
- Material: 30x wound, 11x rectal, 10x screening, 3x skin, 2x blood, 2x intraabdominal


Dortmund (441)
NRZ-79968
128
Frechen
2020
NRZ-59402
Ulm (890)
NRZ-75407
OXA-72
155
525
Dresden (013)
Augsburg (861)
NRZ-77308
NRZ-79611
4
1
Berlin (101)
NRZ-79184
NRZ-78281
Cluster 1
Kassel (341)
Augsburg (861)
1
3
NRZ-76551
NRZ-76226
GES-11
2
Berlin (152)
NRZ-76550
NRZ-77119
Darmstadt (642)
Berlin (152)
2
Homburg/Saar (664)
NRZ-80933
212
10
4
Koblenz (560)
NRZ-75288
Berlin (101)
2019
NRZ-56587
Berlin (152)
Cluster 7
10
NRZ-78416
Cluster 6
30
4
8
NRZ-78943
NRZ-75406
NRZ-77542
Dortmund (598)
Cottbus (030)
Darmstadt (642)
ST2
19x OXA-23
1x OXA-72
493
Stuttgart (701)
2018
NRZ-41215
42
Ravensburg (874)
NRZ-76708a
GES-11


Cluster 9
Cluster 2
Cluster 8
Cluster 4
Berlin (101)
NRZ-75256
6
Hamburg (210)
NRZ-76259
12
NRZ-76761
Berlin (101)
102
Cottbus (030)
NRZ-76029
14
2018
NRZ-43928
Berlin (101)
7
NRZ-76917
Dessau-Roßlau (061)
30
2019
NRZ-51439
Berlin (101)
47
9
NRZ-77211
Aschaffenburg (637)
120
2017
NRZ-35689
Berlin (101)
10
NRZ-79746
Münster
Brandenburg (147)
NRZ-80724
5
NRZ-76915
Görlitz (028)
2
Bochum (447)
NRZ-76258
NRZ-77544 Rostock
NRZ-77945
Kassel (341)
Geesthacht (273)
NRZ-80065
16
6
NRZ-76636
Dortmund (441)
49
Berlin (101)
NRZ-77910
24
NRZ-76355
Augsburg (861)
1
NRZ-77997
Berlin (101)
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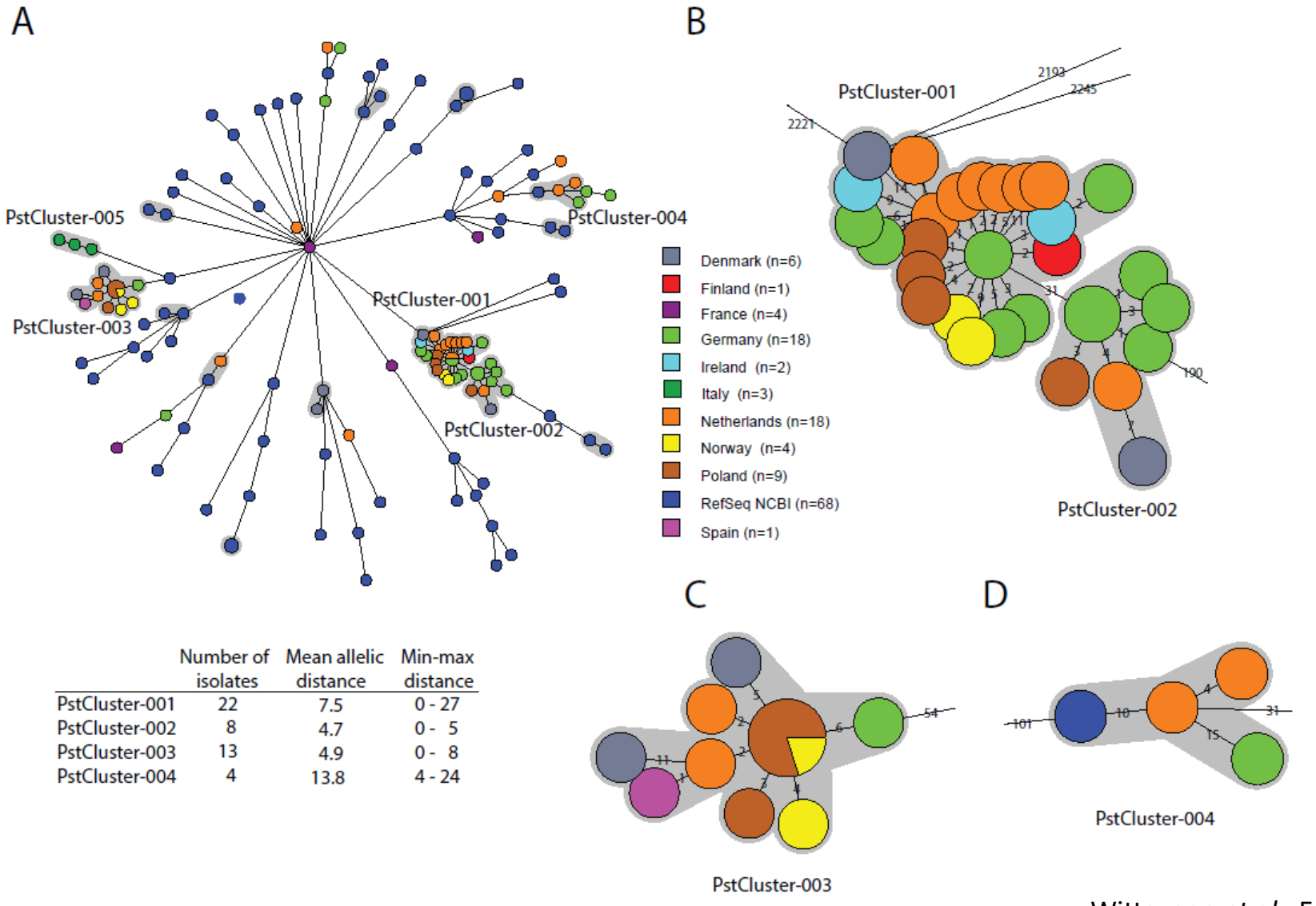
NRZ-76707
Ravensburg (874)
13
NRZ-76450
Dortmund (441)
ST78
OXA-72

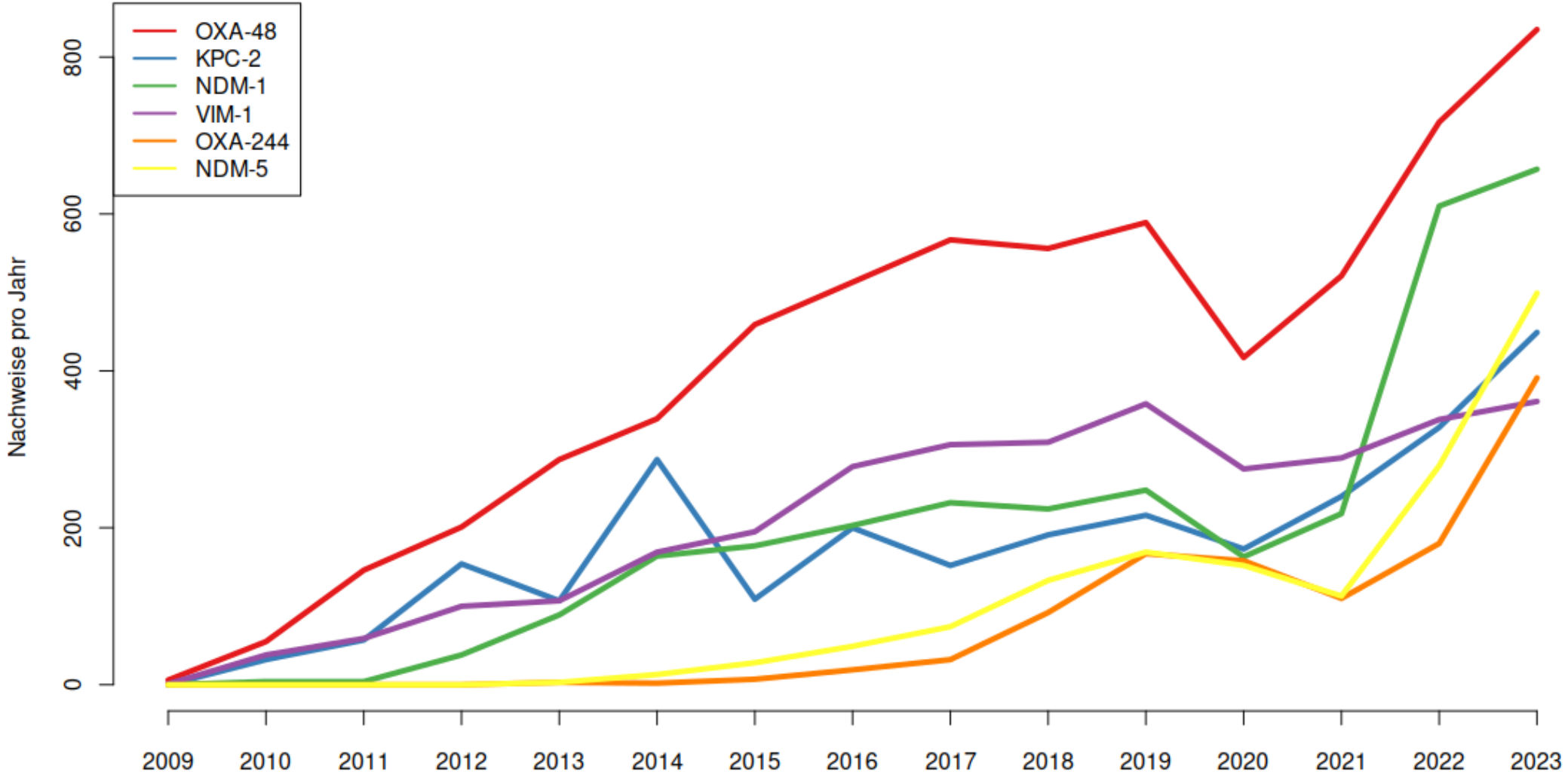
Providencia stuartii NDM-1



	Number of isolates	Mean allelic distance	Min-max distance
PstCluster-001	22	7.5	0 - 27
PstCluster-002	8	4.7	0 - 5
PstCluster-003	13	4.9	0 - 8
PstCluster-004	4	13.8	4 - 24

Witteveen *et al.*, Eurosurveillance 2024 (accepted)

Carbapenemasenachweise bei Enterobacterales
Daten des NRZ 2009-2023



Was es auch noch gibt: Multiresistente *Mycobacterium tuberculosis*

Tuberculosis profile: Ukraine

Population 2022: 40 million

Estimates of TB burden*, 2022

	Number	(Rate per 100 000 population)
Total TB incidence	36 000 (24 000-50 000)	90 (60-126)
HIV-positive TB incidence	7 900 (4 300-13 000)	20 (11-32)
MDR/RR-TB incidence**	12 000 (7 500-16 000)	30 (19-41)
HIV-negative TB mortality	2 300 (2 200-2 300)	5.7 (5.6-5.8)
HIV-positive TB mortality	3 400 (1 400-6 400)	8.7 (3.5-16)

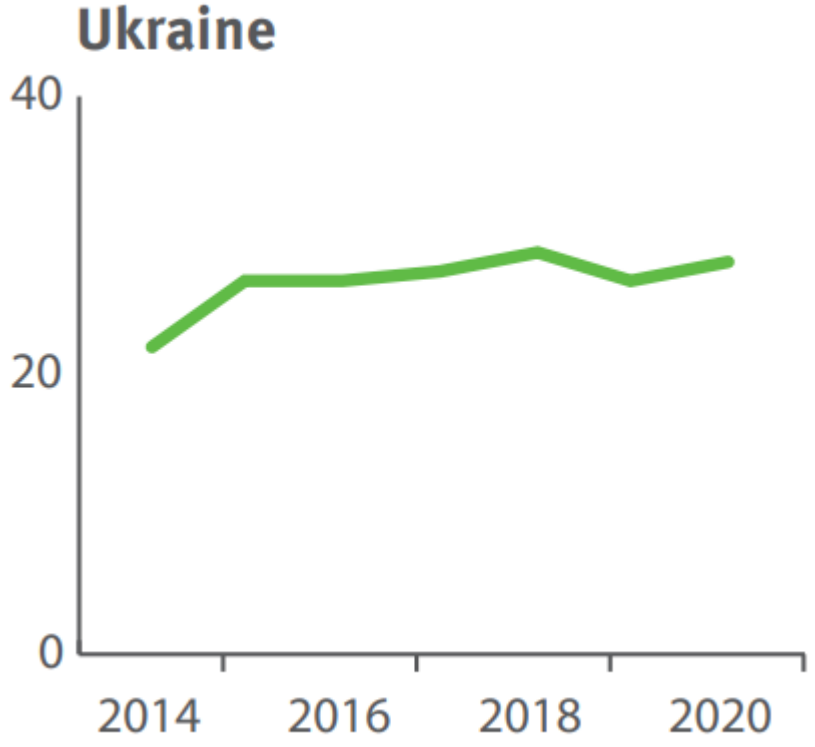
Estimated proportion of TB cases with MDR/RR-TB*, 2022

New cases	29% (29-30)
Previously treated cases	43% (42-44)

*** RR is TB resistant to rifampicin (R); MDR is TB resistant to R + isoniazid*

https://www.who.int/

ECDC tuberculosis surveillance



Was kann man tun?

- Sorgfalt bei Patienten aus der Ukraine
- Screening, Hygienemaßnahmen
- zeitnahe Meldung ans Gesundheitsamt (Metadaten!!!)
- Einsendung von Isolaten ans NRZ (Metadaten!!!)
- Wichtig: DEMIS-Meldungsbarcode

NRZ
Nationales Referenzzentrum
für gramnegative
Krankenhauserreger

Robert Koch-Instituts • Referenznetzwerk des

RUB

Vielen Dank!