

Impact of the Ukrainian war on CPE in the Nordic countries

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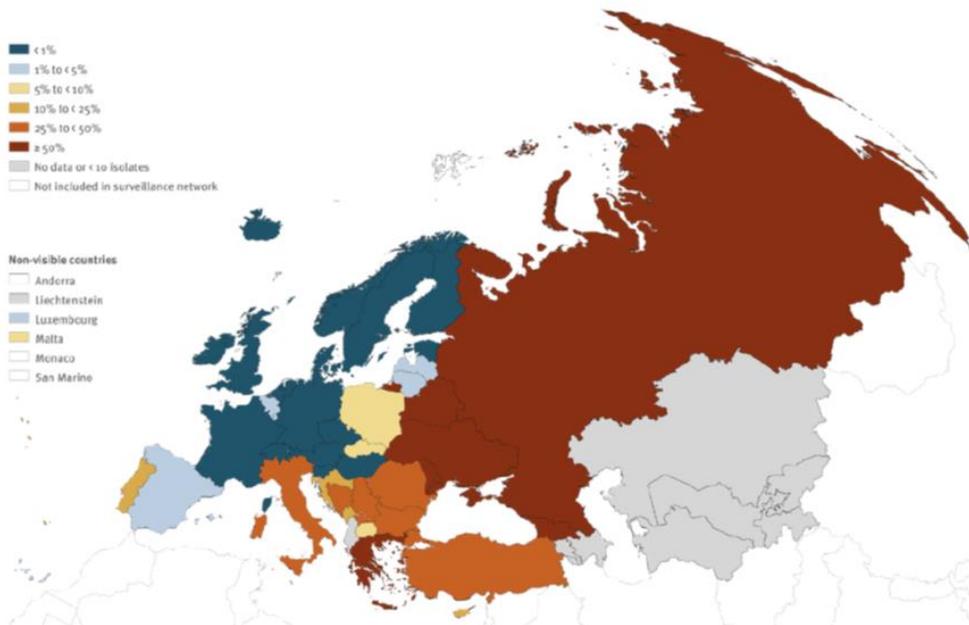
Norwegian National Advisory Unit on Detection of Antimicrobial Resistance

University Hospital of North Norway

AMR in Ukraine



Fig. 5 *K. pneumoniae*: percentage of invasive isolates resistant to carbapenems (imipenem/meropenem), by country/area, WHO European Region, 2020



	2018		2019		2020	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
<i>E. coli</i>	18	0	31	6.5	45	4.4
<i>K. pneumoniae</i>	37	43.2	67	61.2	99	53.5
<i>P. aeruginosa</i>	10	100	16	56.7	27	70.4
<i>Acinetobacter</i> spp.	28	75	44	72.7	48	77.1



Epidemiology of healthcare-associated infections and mechanisms of antimicrobial resistance of responsible pathogens in Ukraine: a multicentre study

A. Salmanov^{a,*}, D. Shcheglov^b, O. Svyrydiuk^b, I. Bortnik^b, M. Mamonova^c, S. Korniyenko^d, V. Rud^e, V. Artyomenko^d, M. Gudym^b, R. Maliarchuk^f, T. Bondar^c



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

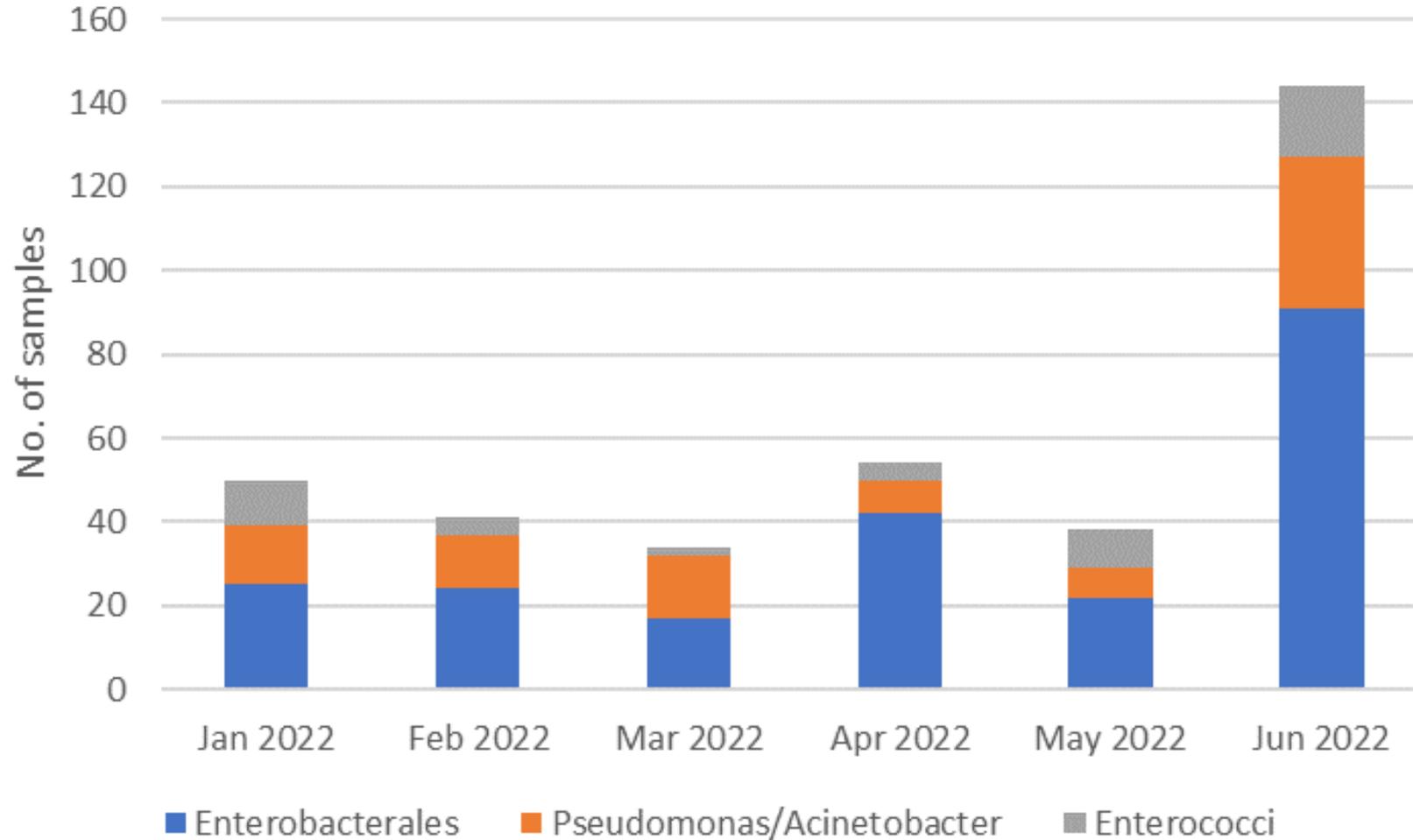
V. Kondratiuk^{a,*}, B.T. Jones^b, V. Kovalchuk^c, I. Kovalenko^c, V. Ganiuk^d, O. Kondratiuk^e, A. Frantsishko^f

- 2019-2021 – 17 regional hospitals
 - MRSA: 41%
 - VRE (*E. faecium*): 12%
 - 3GC-R *Enterobacterales*: 48%
 - CR non-fermenters: 71%

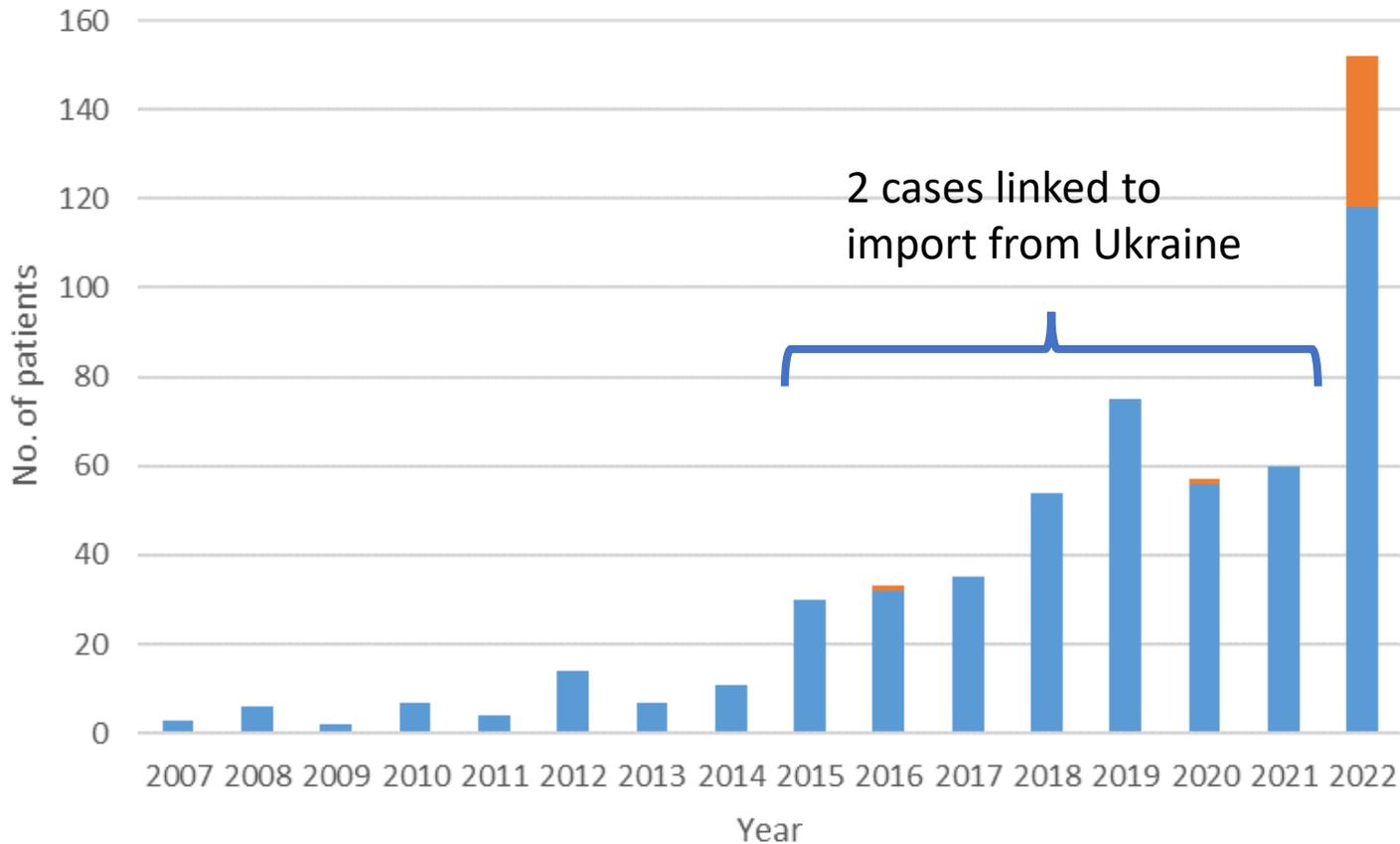
- 2014-2020 – 4 military hospitals

- Carbapenem-resistance:
 - *A. baumannii*: 68%
 - *P. aeruginosa*: 56%
 - *K. pneumoniae*: 33%
 - *E. coli*: 43%

What happened in Norway - June 2022



Impact on CPE Norway – 2007-2022

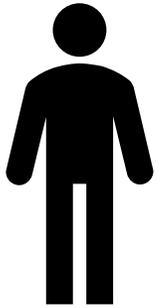


■ Ukraine

- >150% increase from 2021
- 2022:
 - Ukraine: 22% of cases

Important – Ukraine is not solely responsible for the increase in CPE!

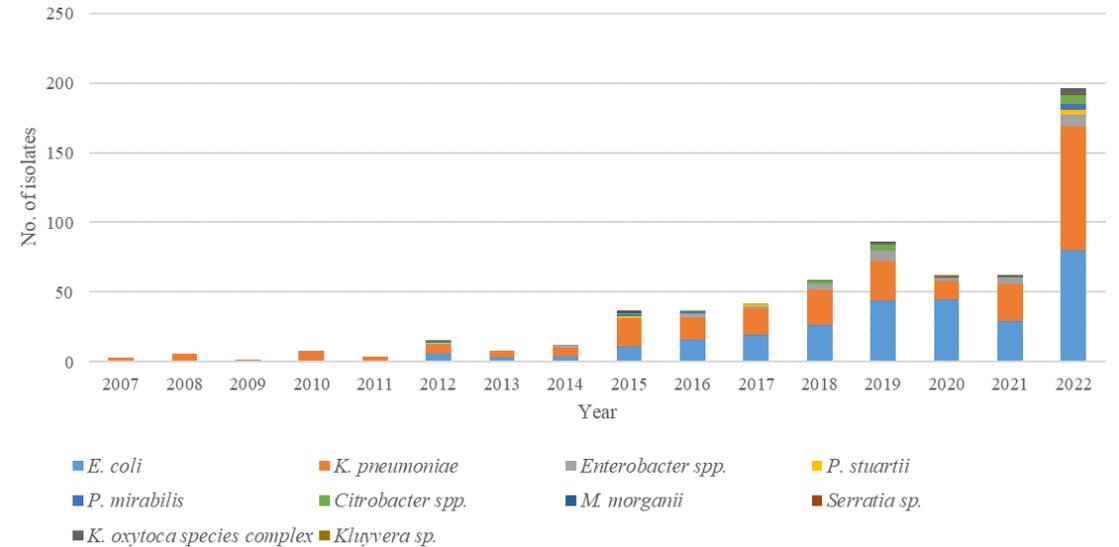
Not only one CPE/CPO/MDR



- *E. coli* ST156, NDM-5
- *K. pneumoniae* ST395, NDM-5 + OXA-232
- *K. pneumoniae* ST147, NDM-1 + OXA-48
- *K. pneumoniae* ST147, NDM-1
- *P. aeruginosa* ST1047, IMP-1
- *A. baumannii* ST400, (GES-11)

- *E. faecium* ST117, VanA

2-6 CPE/Ukrainian patient



- 216% increase 2021->2022
- 37% -> Ukraine

- 51% of *K. pneumoniae* -> Ukraine
- 18% of *E. coli* -> Ukraine

MDR/XDR/PDR

K. pneumoniae bla_{NDM-1} + bla_{OXA-48}

Antibiotika	2
Amikacin	R
Meropenem+Vaborbactam	R
Avibaktam+Ceftazidim	R
Ceftolozan+Tazobaktam	R
Aztreonam	R
Cefiderocol	R
Cefotaksim	R
Cefoksitin	-
Ceftazidim	R
Ciprofloksacin	R
Eravasyklin	-
Kolistin	R
Cefepim	R
Cefepim (ESBL)	-
Cefepim + Klavulansyre (ESBL)	-
Ertapenem	R
Fosfomycin	-
Gentamicin	R
Imipenem	R
Imipenem+Relebaktam	R
Meropenem	R
Nitrofurantoin	-
Piperacillin+Tazobaktam	R
Temocillin	R
Tigesyklin	-
Tobramycin	R
Trimetoprim+Sulfametoksazol	R

E. coli bla_{NDM-1}

Resistenstabell	1
Amikacin	R >128
Meropenem+Vaborbactam	R 16
Avibaktam + Ceftazidim	R >32
Ceftolozan+Tazobaktam	R >16
Aztreonam	R >32
Cefiderocol	R
Cefotaksim	R >16
Cefoksitin	>32
Ceftazidim	R >32
Ciprofloksacin	R >16
Eravasyklin	R 2
Kolistin	S 2
Cefepim	R >16
Cefepim (ESBL)	>16
Cefepim + Klavulansyre (ESBL)	>4
Ertapenem	R >4
Fosfomycin	R 64
Gentamicin	R >128
Imipenem	R 16
Imipenem+Relebaktam	R >8
Meropenem	R >16
Nitrofurantoin	S <16
Piperacillin+Tazobaktam	R >32
Temocillin	R >256
Tigesyklin	R 2
Tobramycin	R 128
Trimetoprim+Sulfametoksazol	R >16

Norge har for dårlig antibiotikaberedskap

Per Espen Akselsen
Arnfinn Sundsfjord
Kristian Tonby



Når vi har tatt imot krigsofre fra Ukraina, har vi sett at vi er godt rustet til å gi avansert medisinsk og kirurgisk behandling. Men det har også blitt lagt vår sårbare antibiotikaberedskap.

Synergy testing ceftazidime-avibactam + aztreonam

Clinical Microbiology and Infection 28 (2022) 521–547



Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com



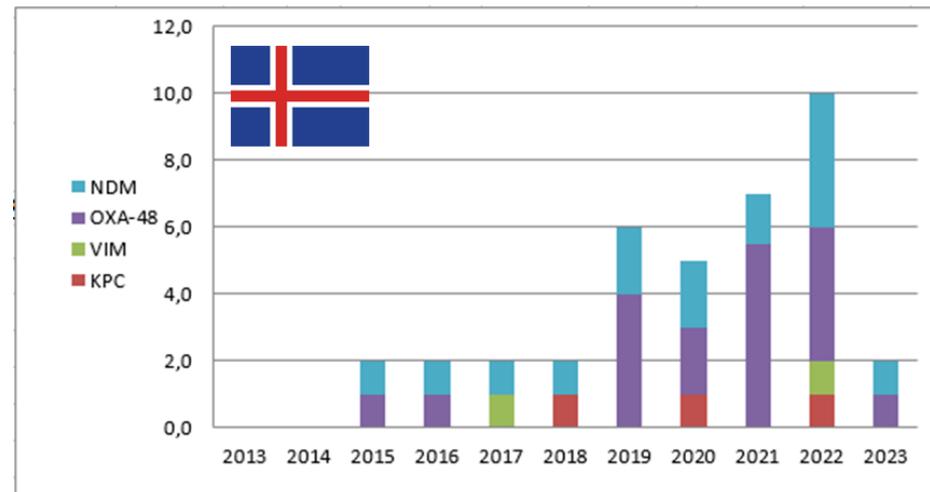
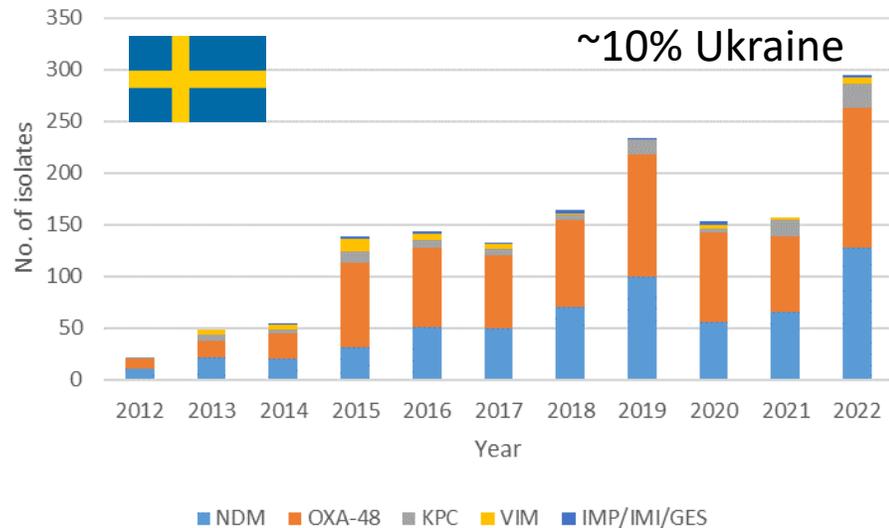
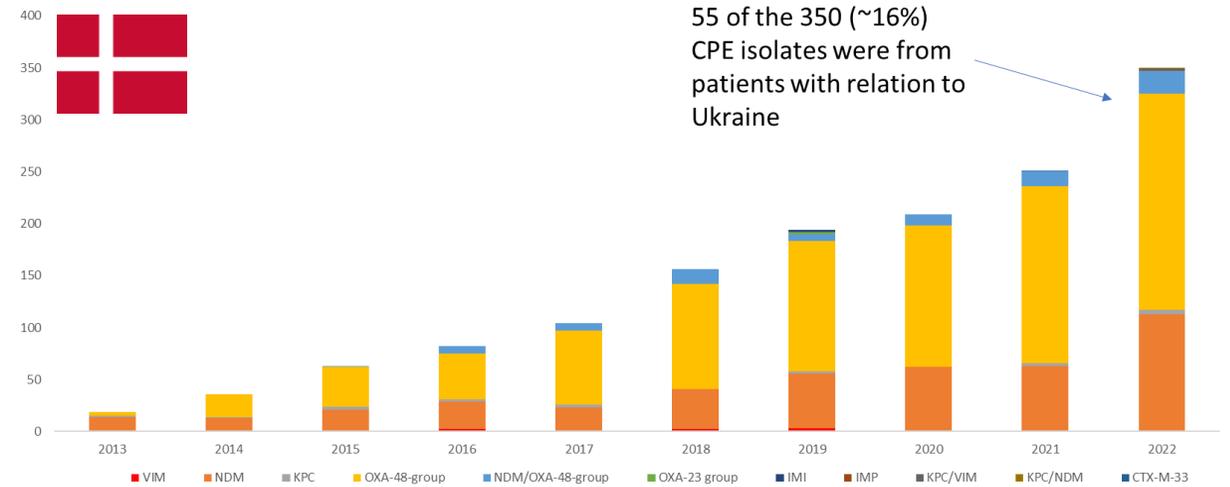
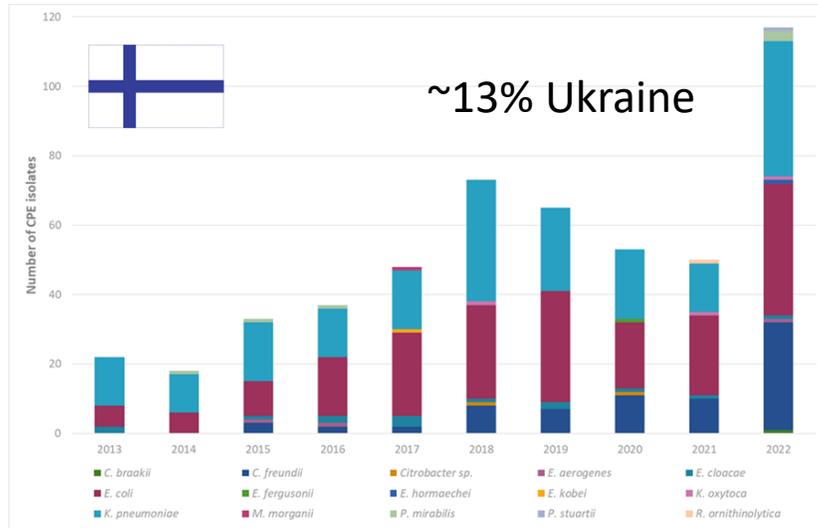
Guidelines

European Society of Clinical Microbiology and Infectious Diseases (ESCMID) guidelines for the treatment of infections caused by multidrug-resistant Gram-negative bacilli (endorsed by European society of intensive care medicine)

For patients with severe infections caused by CRE carrying metallo- β -lactamases and/or resistant to new antibiotic monotherapies, we suggest aztreonam and ceftazidime-avibactam combination therapy.



Other Nordic countries



Onward transmission?

RAPID COMMUNICATION

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 Reichert¹, Martina Cremanns², Jessica Eisfeld², Yvonne Pfeifer³, Annika Heck¹, Tim Eckmanns¹, Guido Werner³, Sören Gatermann², Sebastian Haller^{1,***}, Niels Pfennigwerth^{2,***}

1. Department of Infectious Disease Epidemiology, Robert Koch Institute, Berlin, Germany
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3. Department of Infectious Diseases, Robert Koch Institute, Wernigerode, Germany

«...clusters corresponding to dissemination and suggesting onward transmission in Germany»

RAPID COMMUNICATION

Multidrug-resistant organisms in patients from Ukraine in the Netherlands, March to August 2022

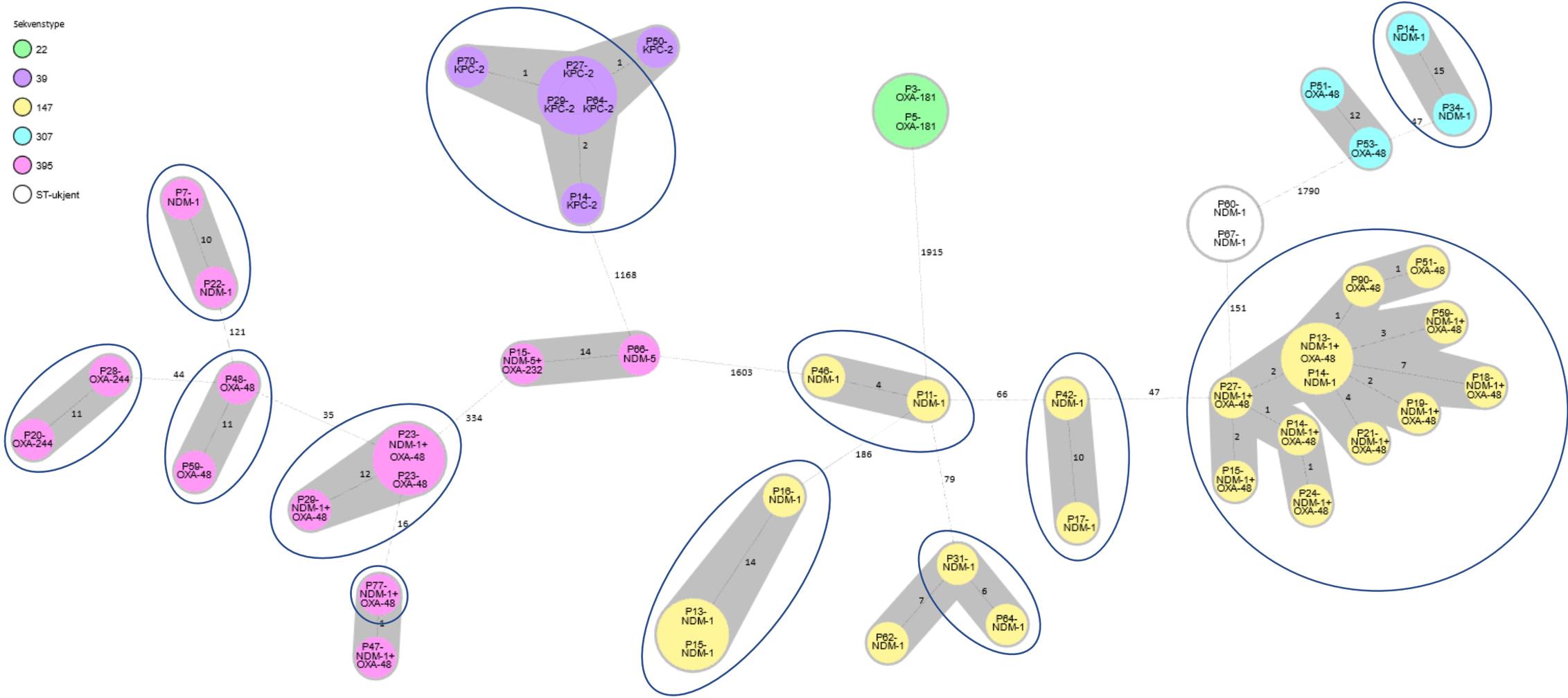
Romy D Zwittink^{1,*}, Cornelia CH Wielders^{1,*}, Daan W Notermans¹, Nelianne J Verkaik², Annelot F Schoffelen¹, Sandra Witteveen¹, Varisha A Ganesh¹, Angela de Haan¹, Jeroen Bos¹, Jacinta Bakker¹, Caroline Schneeberger-van der Linden¹, Ed J Kuijper^{1,***}, Sabine C de Greeff^{1,***}, Antoni PA Hendrickx^{1,***}, on behalf of the Dutch CPE and MRSA Surveillance Study Groups³

1. Centre for Infectious Disease Control (CIb), National Institute for Public Health and the Environment (RIVM), Bilthoven, the Netherlands
2. SWAB Working Group Surveillance of Antibiotic Resistance, Department of Medical Microbiology and Infectious Diseases, Erasmus University Medical Center, Rotterdam, the Netherlands
3. The members of the network are acknowledged at the end of the article

*«...four potential transmission events of *K. pneumoniae* between patients from Ukraine and the Netherlands»*

Transmission before transfer

UKR



Challenge - How to identify transmission between UKR-patients within Norway?

Denmark vs. The Netherlands

Species/MLST	Carbapenemase	Numbers of Danish isolates from patients with relation to Ukraine (n=77)	Cluster No.	Numbers of Danish isolates in the clusters from patients with relation to Ukraine	Numbers of Dutch isolates in the clusters from patients with relation to Ukraine
<i>K. pneumoniae</i> (n=38)					
ST16	NDM-5	1			
ST23	NDM-1, OXA-48	1			
ST39	NDM-1	1	KP1	1	1
	KPC-2	1			
ST147	NDM-1	1	KP2	1	1
	NDM-1, OXA-48 ¹	10	KP3	7	3
	NDM-1	1	KP4	1	1
	NDM-1	1	KP5	1	1
	NDM-1	1			
ST307	OXA-48	1			
	NDM-1	1	KP6	1	5
	NDM-1	3			
	NDM-9	1			
ST392	OXA-48	1			
ST395	OXA-48	3	KP7	3	1
	OXA-48	3			
	NDM-1 ²	3	KP8	3	1
	NDM-1	2	KP9	2	1
ST5859	NDM-1, OXA-232	2	KP10	2	2

Isolates from Ukrainian patients in Denmark is related to isolates from Ukrainian patients in The Netherlands

Onward transmission other Nordic countries?



- Feb. 24. 2022 – Jan. 23. 2023: 77 CPO from Ukrainian patients vs. 371 CPO National CPO surveillance
-> No further nosocomial spread

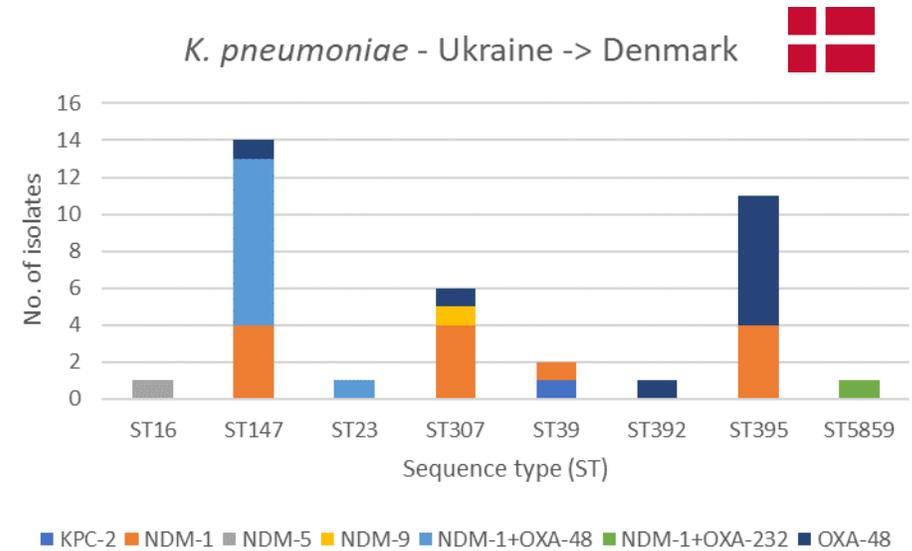
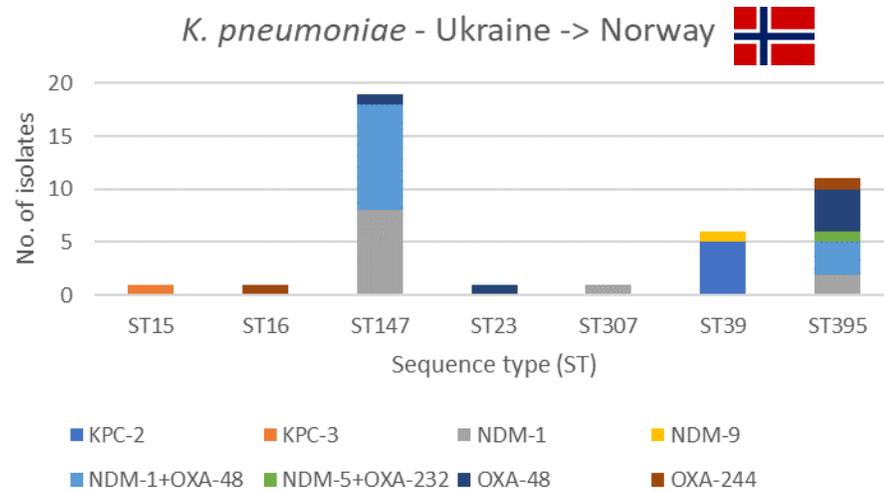


- No further nosocomial spread



- No further nosocomial spread

K. pneumoniae - High-risk clones & a diversity of carbapenemases



- Globally disseminated high-risk clones: ST147, ST307, ST395
- ST23: hypervirulent *K. pneumoniae*!

MICROBIAL GENOMICS RESEARCH ARTICLE
Rodrigues et al., *Microbial Genomics* 2022;8:000737
DOI: 10.1099/mgen.0.000737

Genomic evolution of the globally disseminated multidrug-resistant *Klebsiella pneumoniae* clonal group 147

Carla Rodrigues¹, Siddhi Desai², Virginie Passet¹, Devarshi Gajjar² and Sylvain Brisse^{1*}

J Antimicrob Chemother 2019; **74**: 577–581
doi:10.1093/jac/dky492 Advance Access publication 4 December 2018

Journal of Antimicrobial Chemotherapy

Emergence and rapid global dissemination of CTX-M-15-associated *Klebsiella pneumoniae* strain ST307

Kelly L. Wyres^{1*†}, Jane Hawkey^{1†}, Marit A. K. Hetland², Aasmund Fostervold^{3,2}, Ryan R. Wick¹, Louise M. Judd¹, Mohammad Hamidian¹, Benjamin P. Howden³, Iren H. Löhr^{2†} and Kathryn E. Holt^{1,2‡}

Shaikhullina et al. *Genome Medicine* (2023) 15:9
https://doi.org/10.1186/s13073-023-01159-6

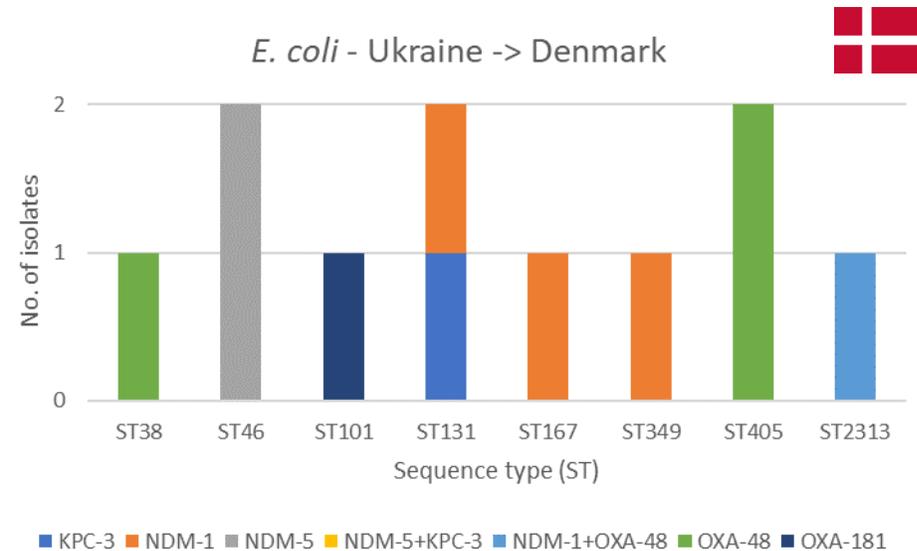
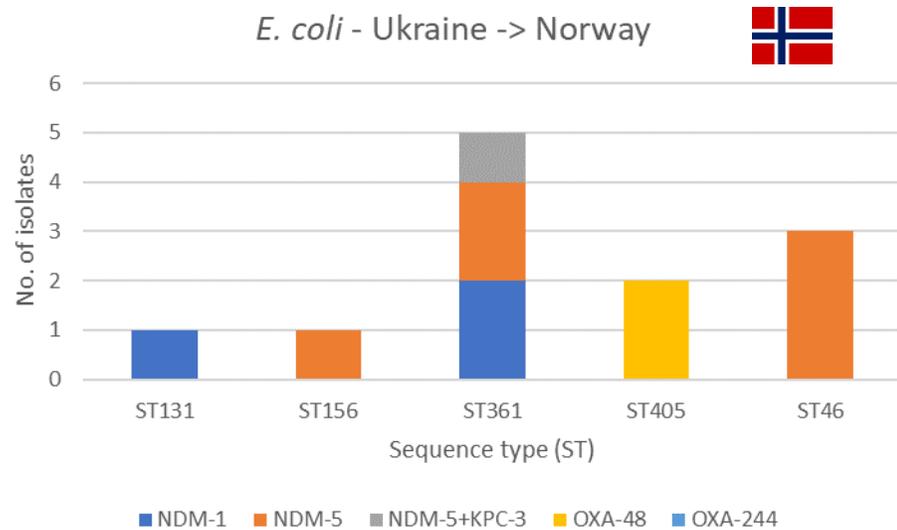
Genome Medicine

RESEARCH Open Access

Genomic analysis of the international high-risk clonal lineage *Klebsiella pneumoniae* sequence type 395

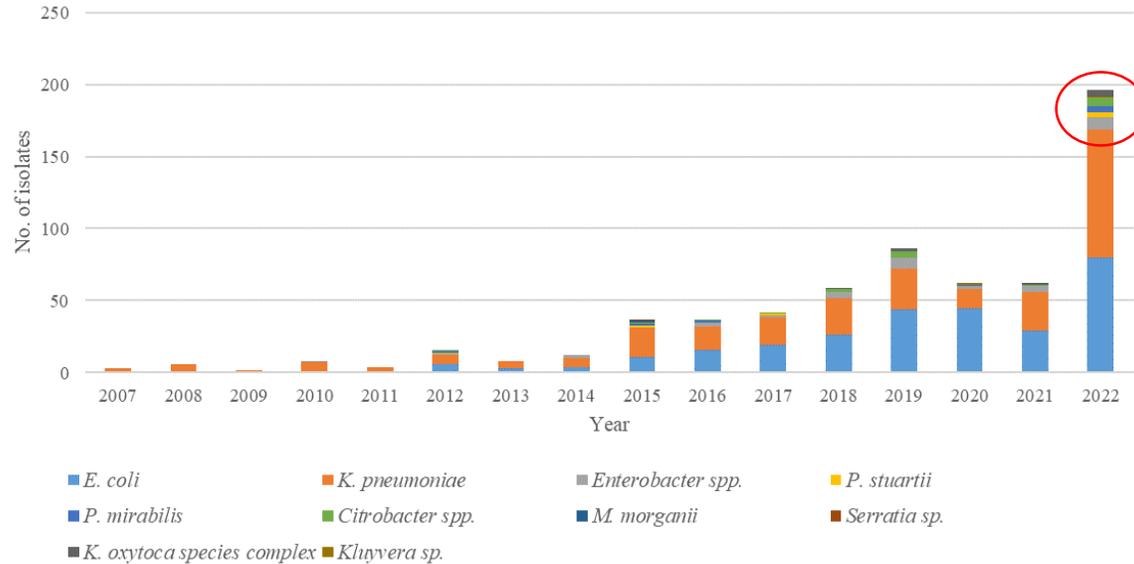
Elvira R. Shaikhullina^{1†}, Michael Schwabe^{2†}, Thomas Rohde², Valeria V. Shapovalova³, Marina S. Dyachkova⁴, Alina D. Matsvay⁵, Yuliya A. Savochkina³, Andrey A. Shelenkov³, Yulia V. Mikhaylova³, Katharina Sydow², François Lebreton⁶, Evgeny A. Idelevich^{6,7}, Stefan E. Heiden⁸, Karsten Becker⁹, Roman S. Kozlov¹⁰, German A. Shipulin¹¹, Vasily G. Akimkin⁴, Michael Laik⁴, Sebastian Guenther⁴, Andreas E. Zautner¹⁰, Jürgen A. Böhrner¹², Aysla M. Mardanova¹³, Ruth Bouganim¹⁴, Dor Marichaim¹⁵, Katharina J. Hoff¹⁶, Katharina Schaeffler^{17,18} and Mikhail V. Edelstein¹⁴

E. coli - High-risk clones & a diversity of carbapenemases



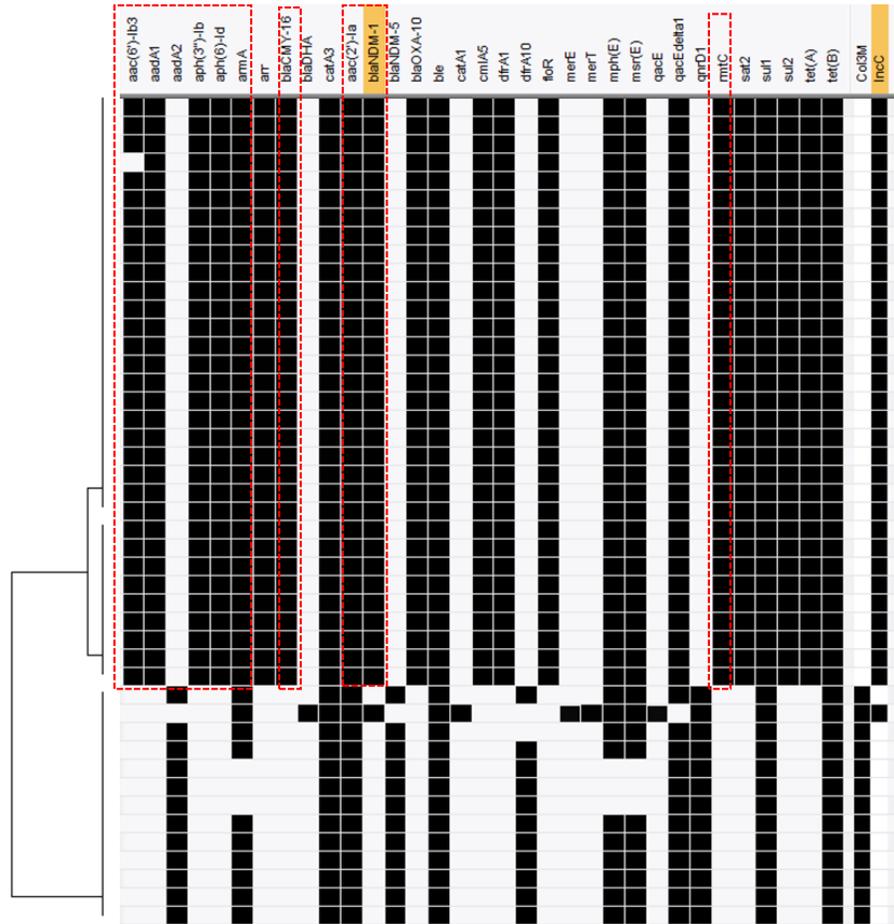
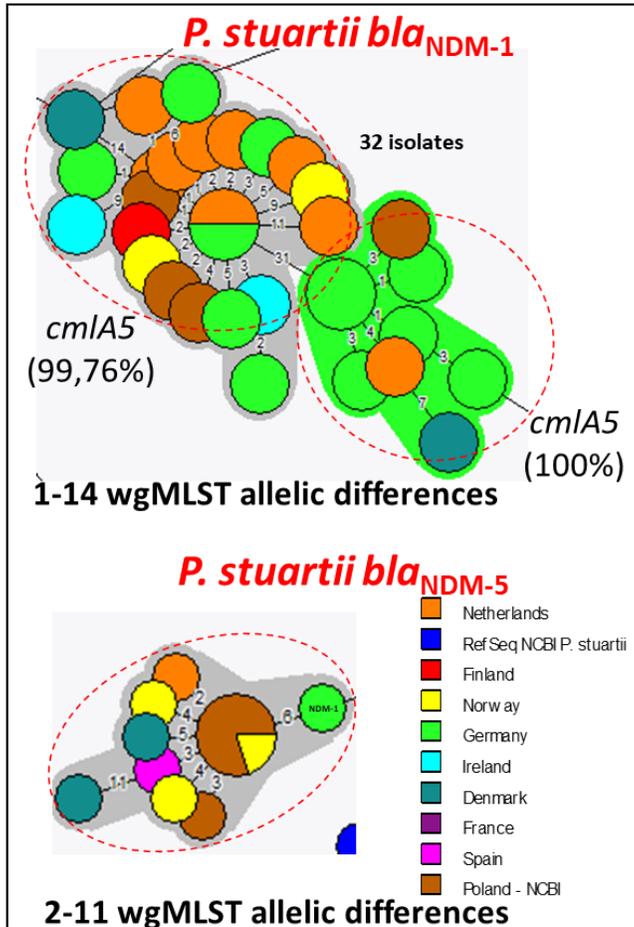
- Known high-risk clones: **ST131, ST167, ST38, ST405**

Rare carbapenemase-producing *Enterobacterales*



Species	ST-carbapenemase
<i>E. hormaechei</i> (n=2)	ST231-NDM-1 (n=2)
<i>K. oxytoca</i> (n=2)	ST2-NDM-1 (n=1); ST19-NDM-1 (n=1)
<i>P. mirabilis</i> (n=4)	NDM-1 (n=4)
<i>P. stuartii</i> (n=4)	NDM-1 (n=2); NDM-5 (n=2)
<i>Serratia</i> sp. (n=1)	OXA-48

Clusters of NDM-producing *P. stuartii* – UKR -> Europe



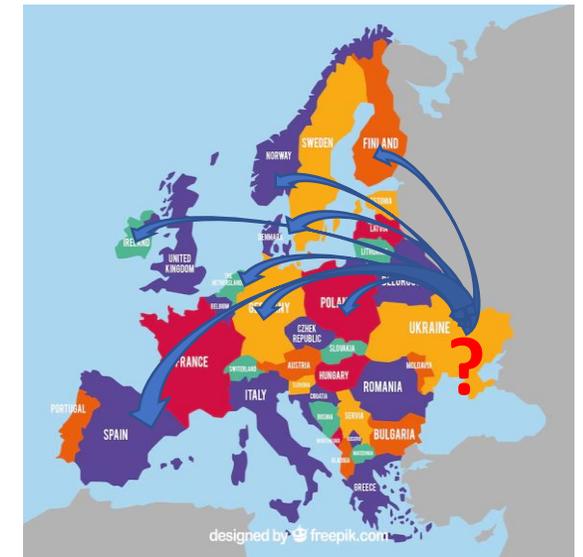
*bla*_{NDM-1}

*bla*_{NDM-5}

Conjugative NDM-1 plasmid



Spread to other *Enterobacterales*



Conclusions

- **High risk of CPE associated with Ukrainian patients**
- **Import of CPE from Ukraine only partially explain increase in CPE in the Nordic countries**
- **«Ukrainian» CPE population – high-risk clones and a diversity of carbapenemases**
- **Frequent transmission of clones before transfer to the Nordic countries - Onward transmission within Nordic countries has occurred**

Acknowledgements

- Anette Hammerum/Frank Hansen, Kati Räisänen, Barbro Mäkitalo/Karin Westmo, Kristján Orri Helgason for country specific data
- Antoni Hendrickx for *P. stuartii* data

- K-res staff:

