

Detection of carbapenemases in *Acinetobacter baumannii* (and *P. aeruginosa*)

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NordicAST WS 220524

Common features of these possibly carbapenemase-producing organisms (CPOs)

Causes hospital-acquired infections in patients with abnormal host defenses

Gram-negative rods
Strictly aerobic
Environment

Causes hospital outbreaks

Masters of adaptation

Can be multidrug-resistant and really difficult to treat

Reliable phenotypical tests for carbapenemases are lacking



Confusion about definitions and mixed use of them:
carbapenem-resistant or carbapenemase-producing ?
CPO Pa/Ab or ESBL-carba Pa/Ab?
Acinetobacter baumannii or Acinetobacter spp.?
Pseudomonas aeruginosa or Pseudomonas spp.?



But some things are different..

No flowchart for detection of carbapenemases in the NordicAST BP table

No Explanatory method document on NordicAST website

Isolates that are meropenem or imipenem I/R should be sent to ref lab for carbapenemase detection depending on national guidelines



NordicAST Nordic Committee on Antimicrobial Susceptibility Testing

NordicAST Organisation **Methods** Quality control Breakpoints and Dosages AST report panel

Workshops and Webinars Links RSS

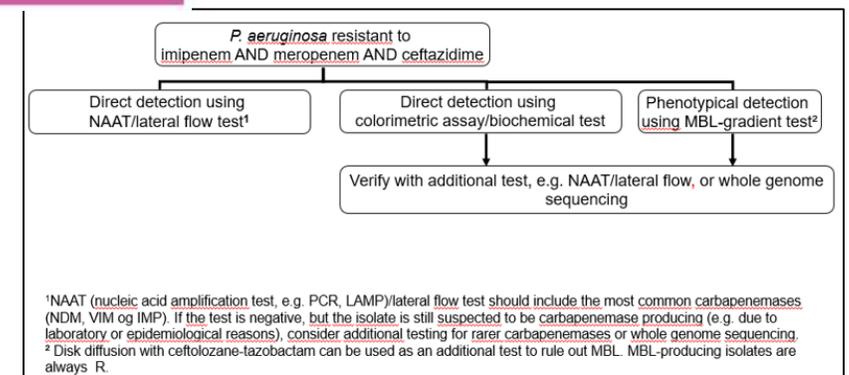
Method document in quality control

Method documents in quality control are available [here](#).

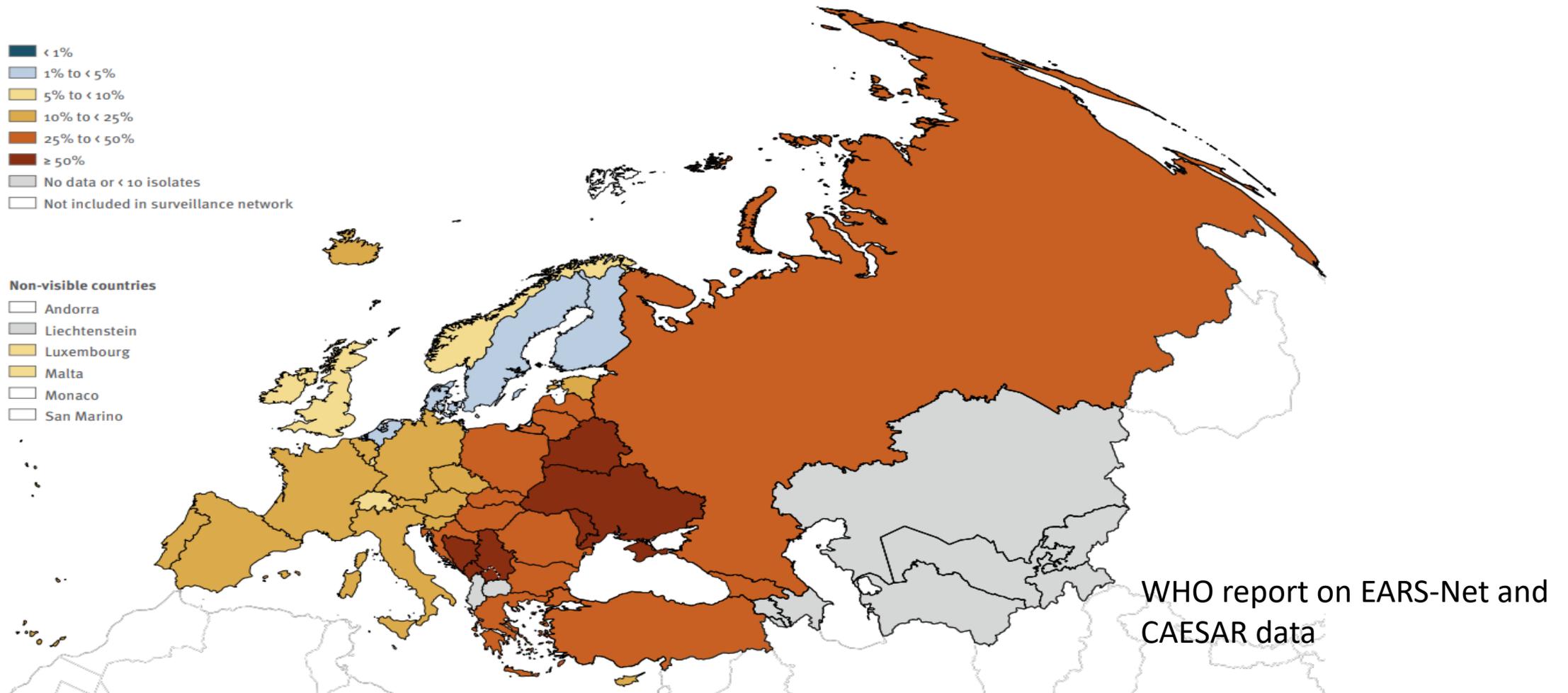
Explanatory methods documents

Visa 50 rader

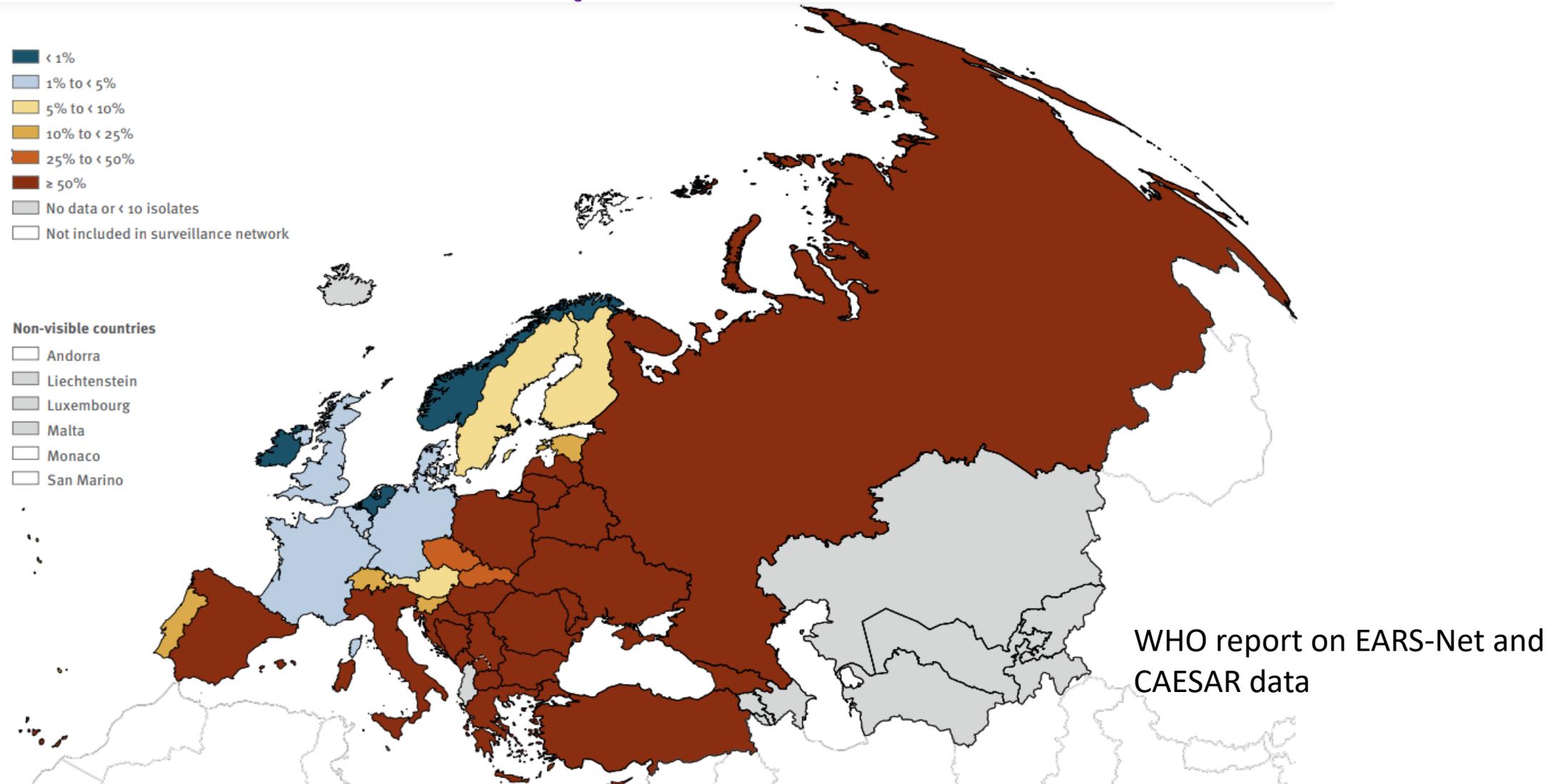
Kod	Titel
VRE	Screening for Vancomycin-resistant Enterococci (VRE) carriage
Streptococcus pneumoniae	Detection of reduced penicillin susceptibility in Streptococcus p
Staphylococcus spp.	Detection of methicillin resistance in staphylococci
Staphylococci and streptococci	Inducible clindamycin-resistance in staphylococci and streptoc
Pseudomonas	Pseudomonas aeruginosa og karbapenemaser (ESBLCARBA)



Invasive isolates of *Pseudomonas* spp. with resistance to carbapenems 2020



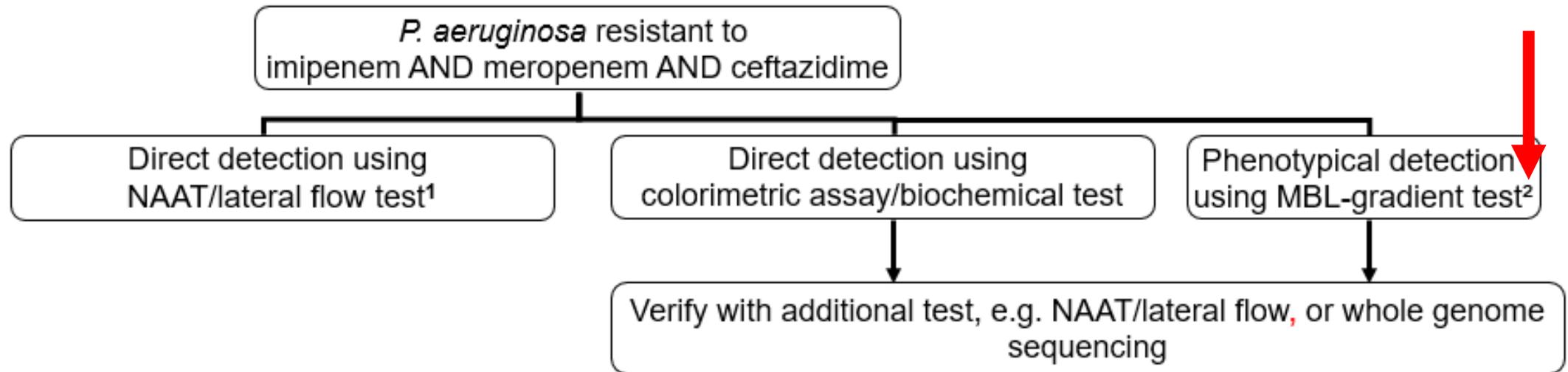
Invasive isolates of *Acinetobacter* spp. with resistance to carbapenems 2020



Detection of carbapenemases in *P. aeruginosa*

Detection of carbapenemases in *P. aeruginosa*

NordicAST v 12.0

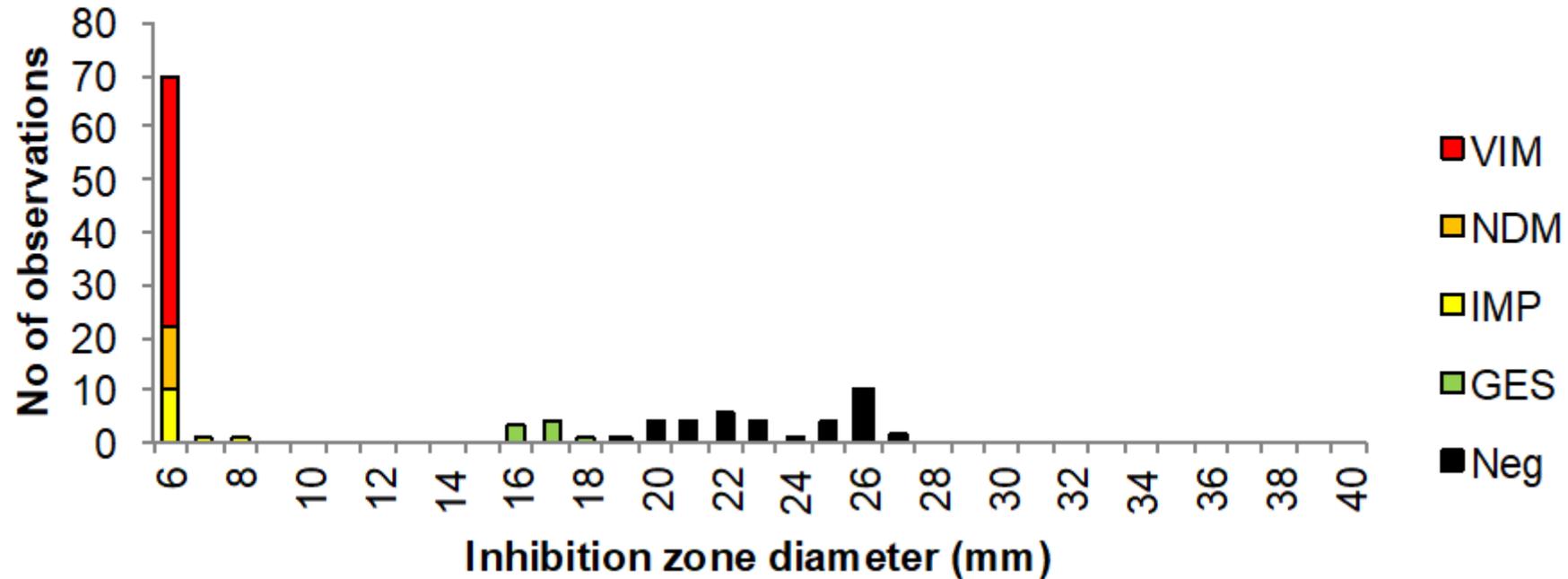


¹NAAT (nucleic acid amplification test, e.g. PCR, LAMP)/lateral flow test should include the most common carbapenemases (NDM, VIM og IMP). If the test is negative, but the isolate is still suspected to be carbapenemase producing (e.g. due to laboratory or epidemiological reasons), consider additional testing for rarer carbapenemases or whole genome sequencing.

² Disk diffusion with ceftolozane-tazobactam can be used as an additional test to rule out MBL. MBL-producing isolates are always R.

Ceftolozane-tazobactam as a marker for MBL-production in *P. aeruginosa*?

**Ceftolozane-tazobactam 30-10 µg vs. MBL
P. aeruginosa, 29 isolates (116 correlates)**



S ≥ 23 mm R < 23 mm

Data from EDL and C. Giske-group

Detection of carbapenemases in *A. baumannii*

Acinetobacter spp.



Approximately 50 species named

- **Most species are not considered human pathogens. Often named *Acinetobacter non-baumannii*-group. They exist in nature and have been isolated from:**
 - Water, plants and soil for example *A. calcoaceticus* and *A. johnsonii*
 - Food and healthy humans skin for example *A. johnsonii*, *A. lwoffii*, *A. radioresistens*
- **Clinically important and the cause of serious infections and hospital outbreaks: members of the *Acinetobacter baumannii*-group**

A. baumannii-group

Includes:

A. baumannii

A. nosocomialis

A. pittii

A. dijkshoornii

A. seifertii

Big differences within the group regarding mortality and prevalence as well as the ability to cause hospital outbreaks

A. baumannii- clinical relevance?

Often just causes colonisation of wounds and airways in healthy individuals
BUT can cause serious infections/mortality in ICU patients and other critically ill patients like:

- Ventilator-associated pneumonia (VAP), mortality 40%
- Bacteremia (often catheter-related infections), mortality 40%
- Wound infections (especially burn wounds)
- SSTI (incl necrotising fasciitis)
- UTI (catheter-related)
- Neurosurgical meningitis
- Community-acquired pneumonia (tropical parts of Australia, Taiwan, Singapore, Hong Kong)
- Even cases with endocarditis and eye-infection are described

A baumannii- development

- **The 1970s:** Usually treatable with ampicillin, gentamicin, fluoroquinolones. Reports on outbreak in burn units.
- **The 1980s:** Resistance towards several antibiotic classes more and more common. The first report on a carbapenem-resistant *A. baumannii* comes in 1985 from Edinburgh.
- **The 1990s:** Outbreaks with *A. baumannii* in burn units and ICUs increases all over the world.
- **The 2000s and onwards:** Outbreak! Many countries report more than 50% of the *A.baumannii* isolates to be carbapenem-resistant.
2006: First report on colistin-resistant isolates.
- Media breakthrough x2:
 - IDSA-one of the ESKAPE pathogens in 2004
 - Iraqibacter in US 2003-2006
- Recent years: Reports of multidrug-resistant and pandrug-resistant isolates of *A. baumannii* increases due to combinations of different carbapenemases



Iraqibacter



**The Invisible
Enemy of Iraq**

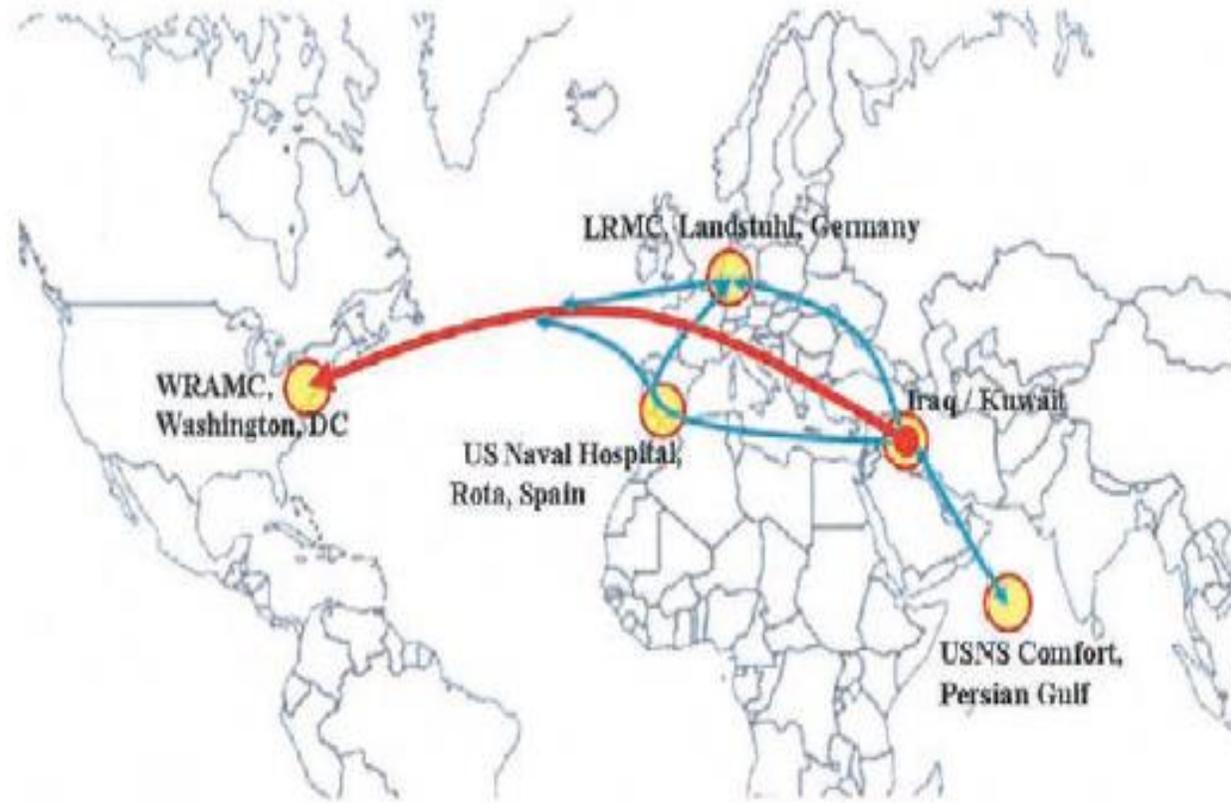
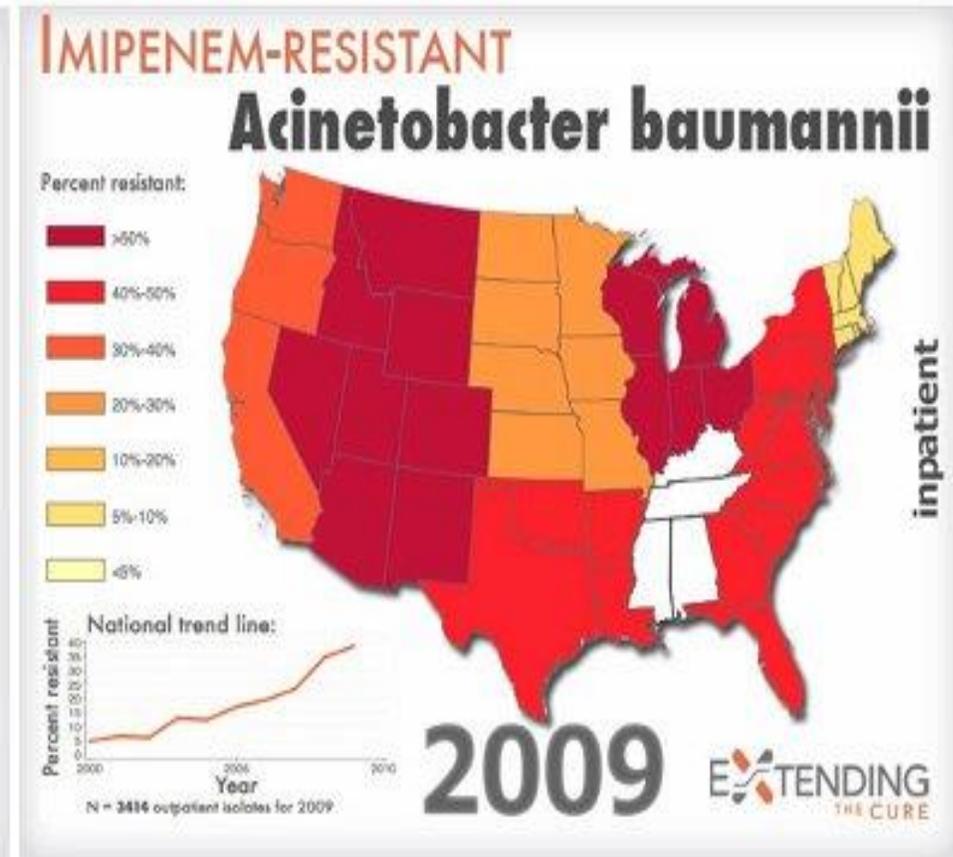
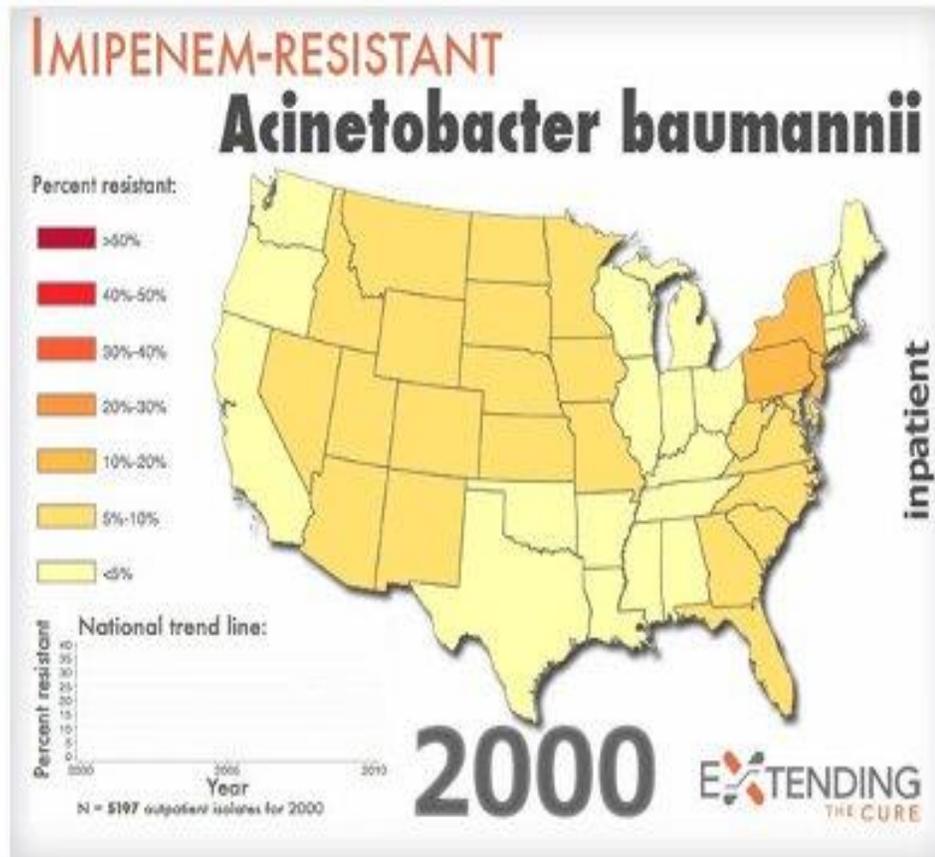


Figure 1. Aeromedical evacuation route from Iraq and Kuwait to US Military hospitals in Europe and the United States. LRMC, Landstuhl Regional Medical Center; USNS, US Naval Ship; WRAMC, Walter Reed Army Medical Center.

Scott et al. Clin Inf Dis
2007;44 1577-84

Carbapenem resistance in *Acinetobacter baumannii* in the US after the war in Iraq



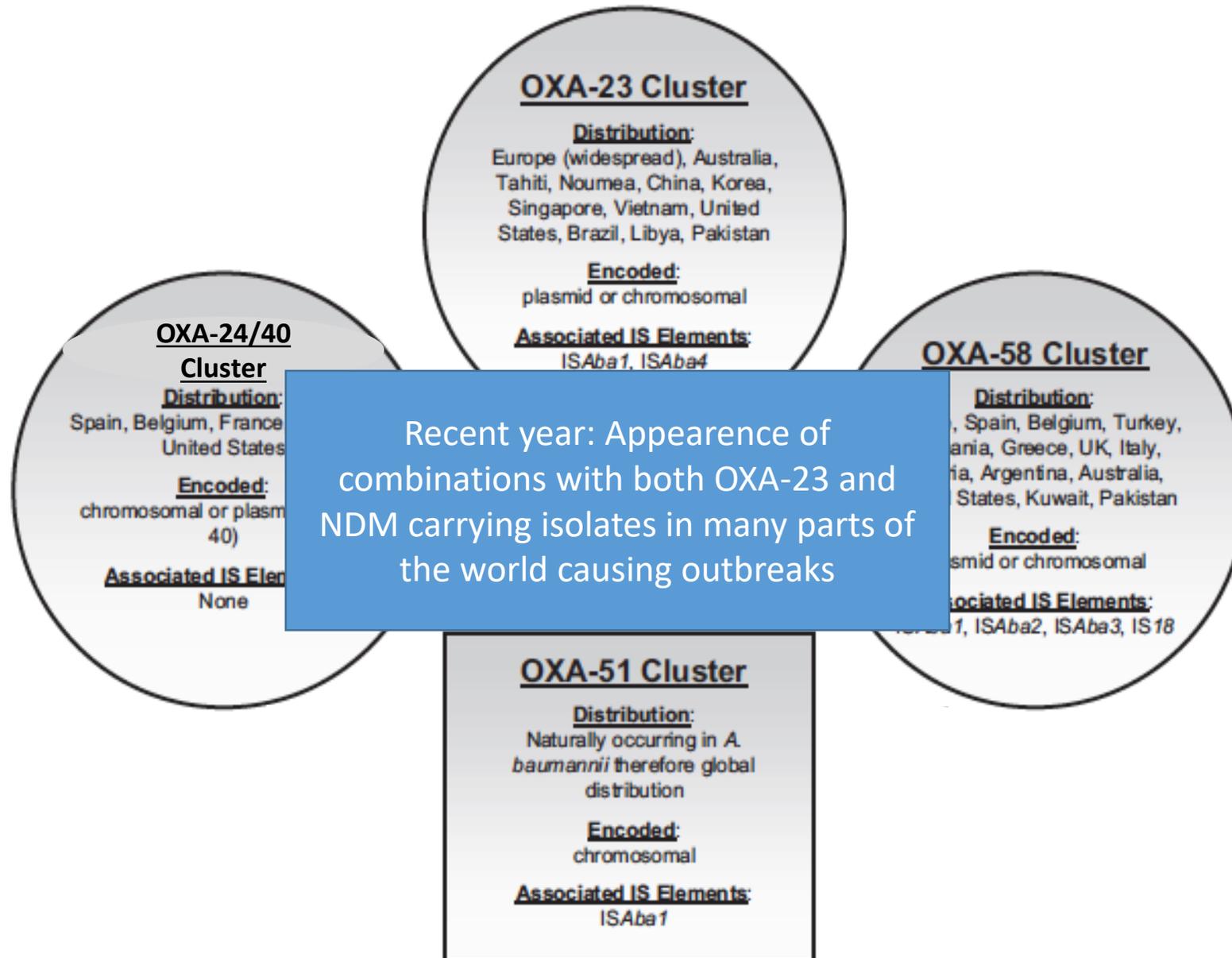
From: Center for disease dynamics, economics and policy (CDDEP)

A. baumannii and carbapenem resistance mechanisms

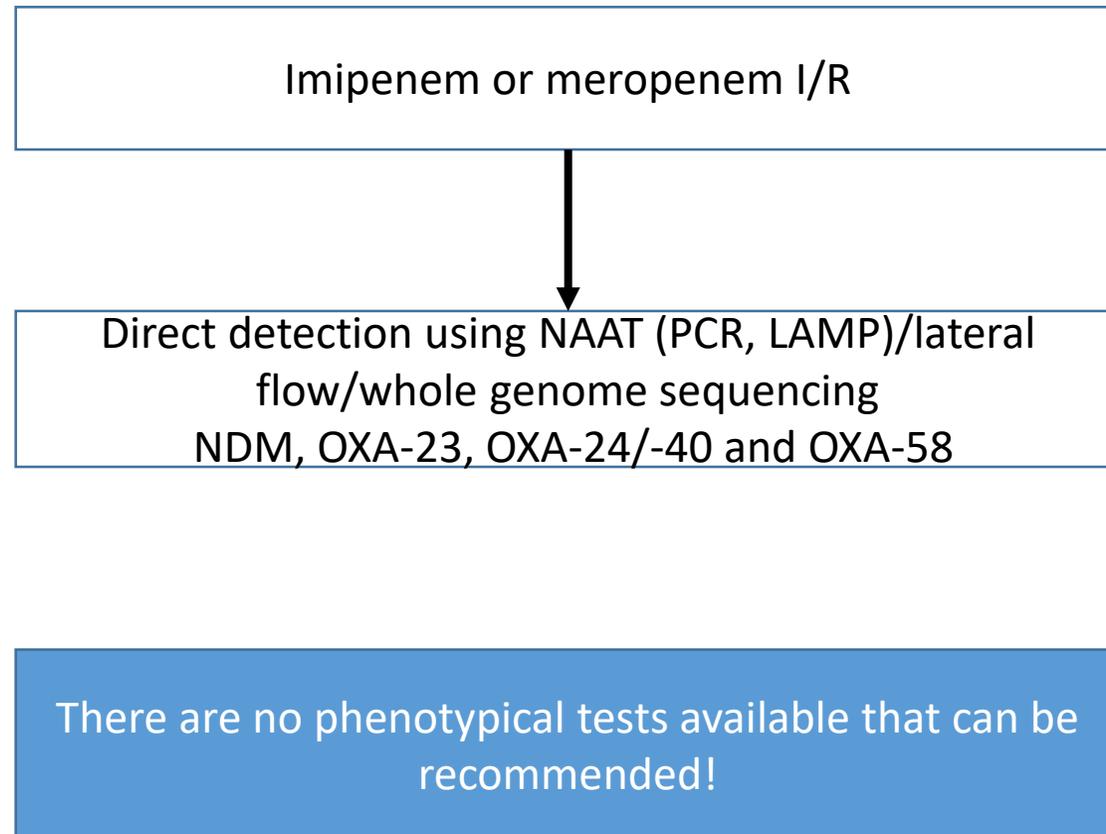
- Porin loss or alteration (change in OMP, outer membrane proteins)
- Modified penicillin-binding proteins (PBP)
- Multidrug efflux-pumps (mainly AdeABC efflux system)
- **Chromosomal carbapenemase OXA-51**, insertion of ISAba1 upstream of the gene is needed for gene expression
- **Acquired carbapenemases**

A. baumannii and acquired carbapenemases

- Ambler class D carbapenemases
 - **OXA-23-like.** Most common in Europe
 - OXA-24/40-like
 - OXA-58-like
- Ambler class B metallo-beta-lactamases
 - **NDM:** Regional hospital outbreak in France in 2013, Middle East, Africa
 - IMP, VIM, SIM: Very rare findings



What a flowchart for detection of carbapenemases in *A. baumannii* might look like



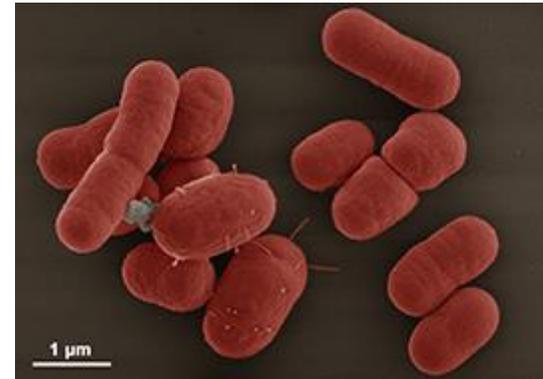
Key success factors of *Acinetobacter baumannii*

- Biofilm production and survival on inanimate surfaces up to 5 months
- Genomic plasticity: unique properties regarding acquiring antimicrobial resistance
- OXA-51, intrinsic enzyme which can confer carbapenem-resistance

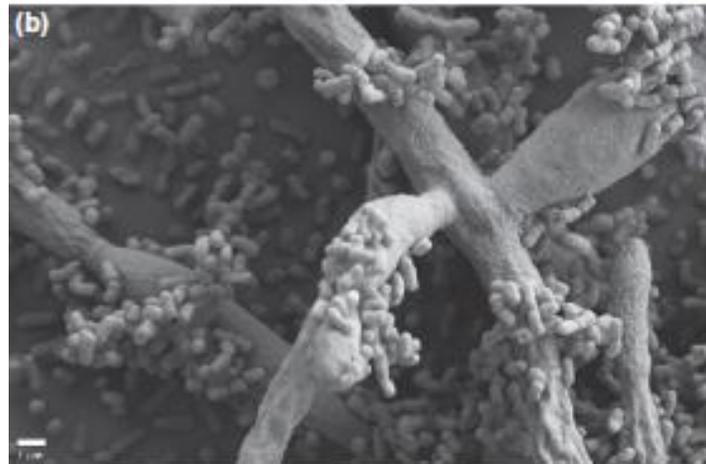
Carbapenem overusage selects A. baumannii and poor infection control are the key drivers of the resistance development in the world

A. baumannii is ...

- **NOT** commonly occurring in nature
- **NOT** part of the intestinal microbiome
- **BUT RATHER**
- A hospital pathogen!
- Resembling a gram-negative MRSA
- Coloniser of wounds and the respiratory tract
- Screening from other sample types than feces is needed!



Thank You!



McConnell MJ. FEMS Microbiol Rev 2013 Mar;37(2)

Detection of carbapenemases in *P. aeruginosa*

How can Ceftolozane-tazobactam help?

