

The background of the slide is a photograph of several laboratory test tubes. The tubes are arranged in a row, and each contains a liquid that has turned a distinct orange or reddish-brown color. The tubes are held in a white rack. The text is overlaid on this image.

Carbapenemase-producerende *Enterobacteriaceae* (CPE)

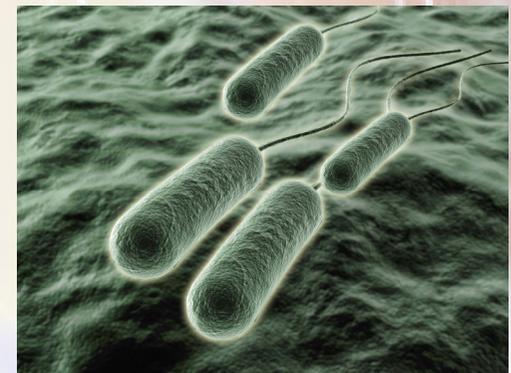
NordicAST Workshop 2015

Mikala Wang

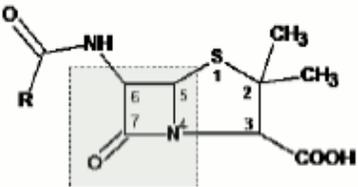
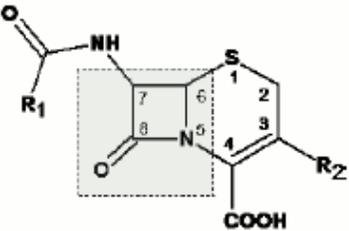
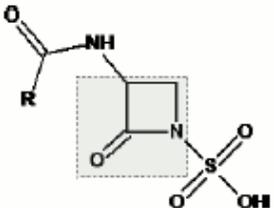
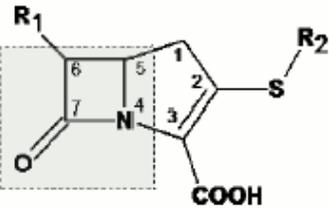
Aarhus Universitetshospital

Carbapenemaser

- Enzymer der spalter næsten alle penicilliner, cephalosporiner og carbapenemer (meropenem, ertapenem, doripenem, imipenem)
- Ses hos *Enterobacteriaceae*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*



Betalaktam-antibiotika

Group	Structure
Penicillins	
Cephalosporins	
Monobactams	
Carbapenems	



Benzylpenicillin, dicloxacillin,
ampicilin, mecillinam,
piperacillin-tazobactam



Cefuroxim, ceftriaxon,
ceftazidim, cefepime



Aztreonam



Meropenem, imipenem,
doripenem, ertapenem

Infektion med CPE

- Risikofaktorer:
 - Dårlig almentilstand, antibiotikabehandling, intensivophold
- Estimerede 10-30% af koloniserede får en infektion
- Studier indikerer mortalitet ved CPE infektion er 3-6 x mortaliteten ved infektion med carbapemfølsomme *Enterobacteriaceae*

Hyppigste carbapenemase-enzymmer hos *Enterobacteriaceae*

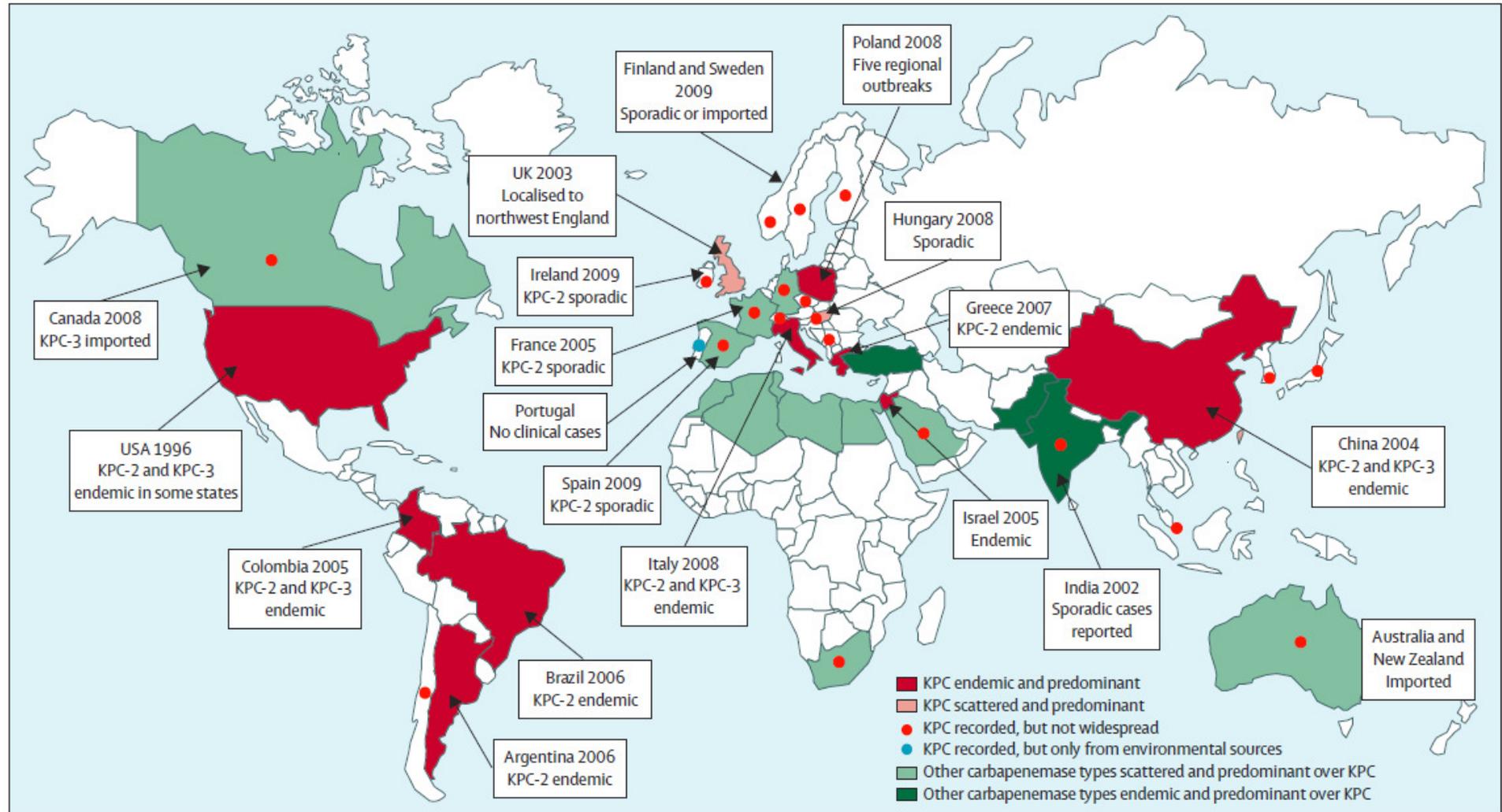
Ambler klasse	Viktigste enzymer	Typiske species	Spredning
A	KPC	<i>K. pneumoniae</i>	Nosokomial
B	NDM	<i>K. pneumoniae, E. coli</i>	Nosokomial, samfundservervet
D	OXA-48-like	<i>K. pneumoniae, E. coli</i>	Nosokomial, samfundservervet

Hyppigste carbapenemaser

- **KPC** (Klebsiella pneumoniae carbapenemase)
- **OXA-48**-like
- **MBL** (metallobetalactamaser)
 - **NDM**
 - **VIM**
 - **IMP**



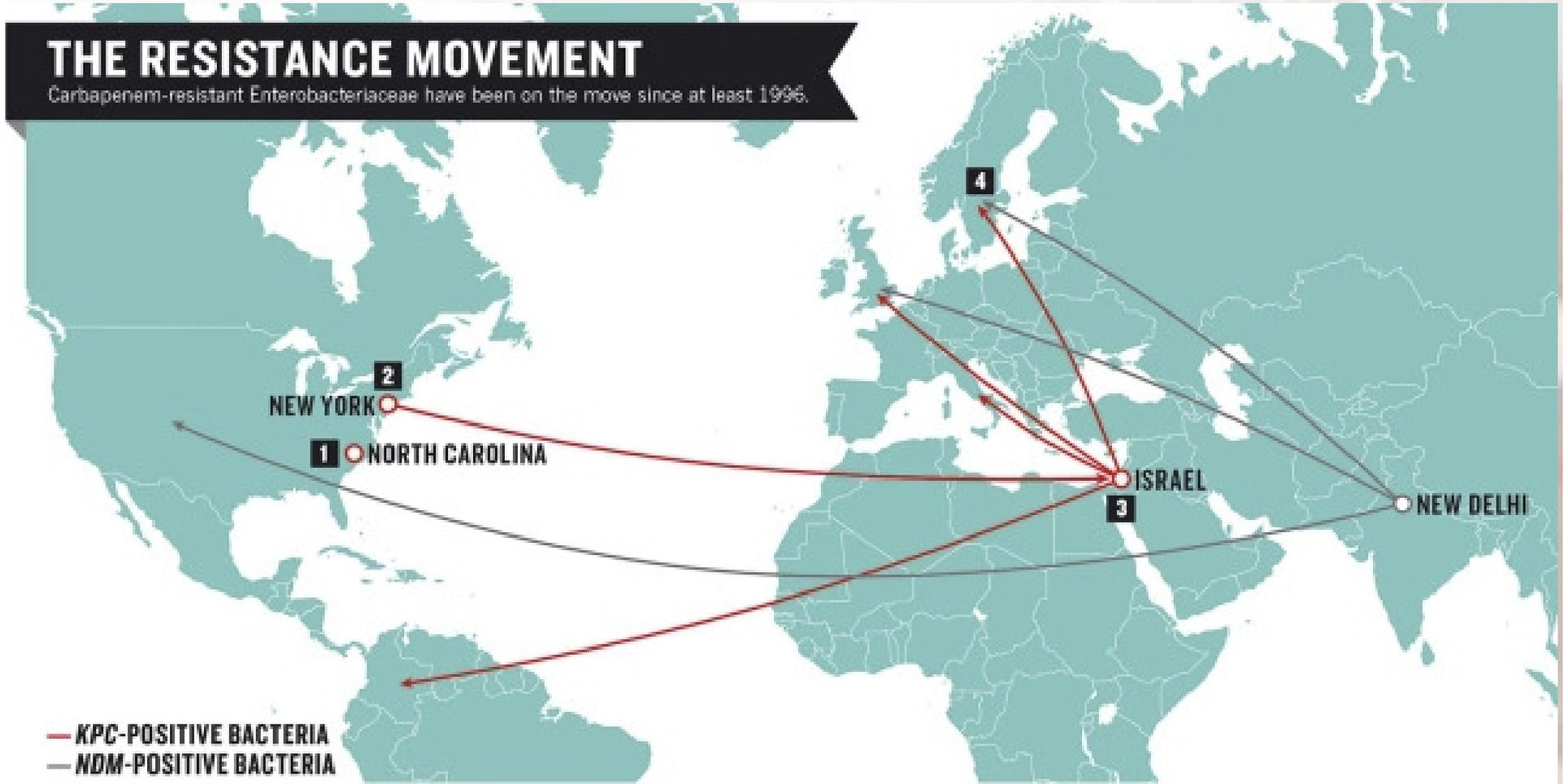
KPC epidemiologi



KPC

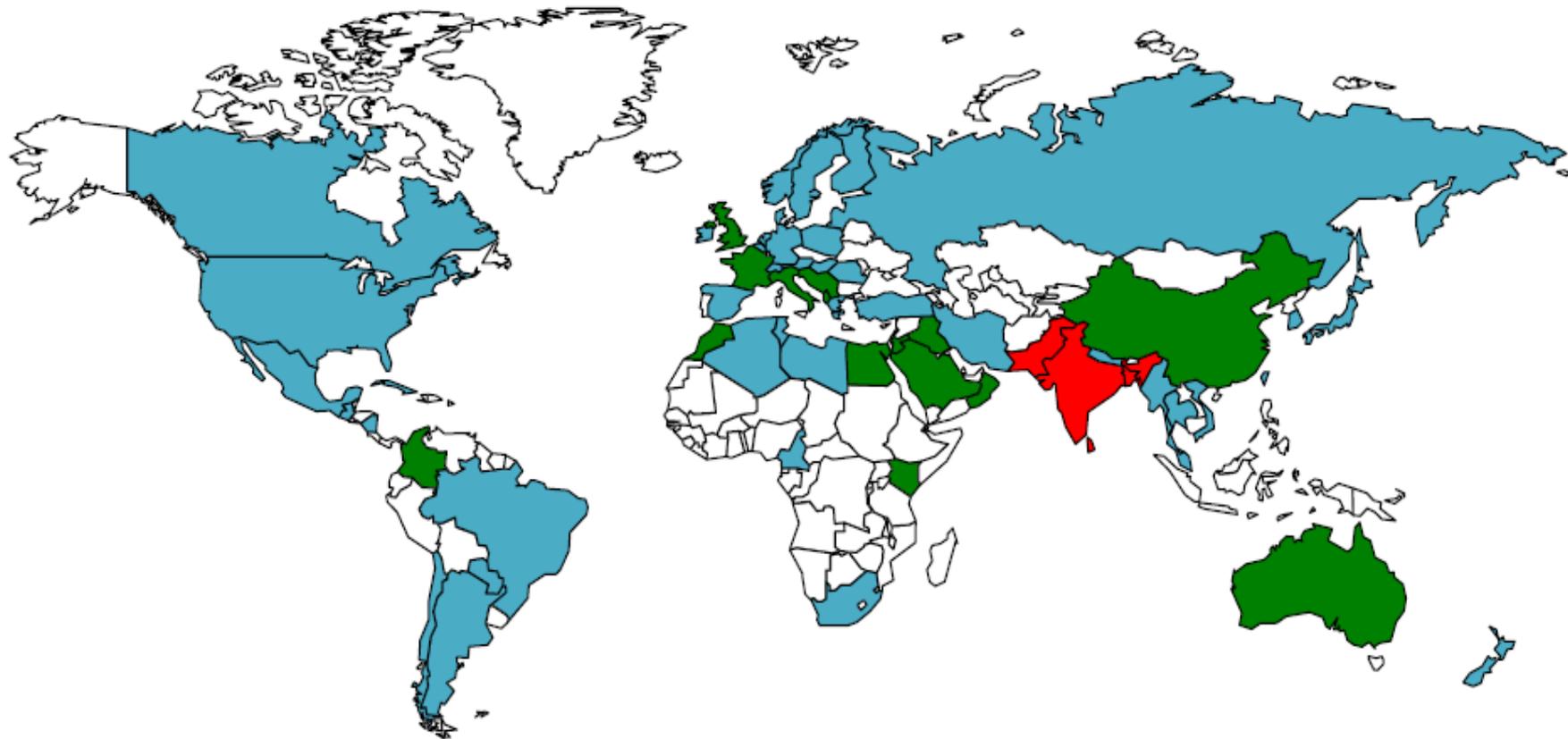
- KPC-2 identificeret i 1996 på USA's østkyst
- USA, Israel, Grækenland, Italien, Colombia, Argentina (Kina, Polen?)
- Hovedsageligt i *K. pneumoniae*
- Nosokomial
- 19 varianter
- Især domineret af en succesfuld klon, ST258 (og ST512), KPC- 2 & KPC-3

KPC & NDM: directions of travel



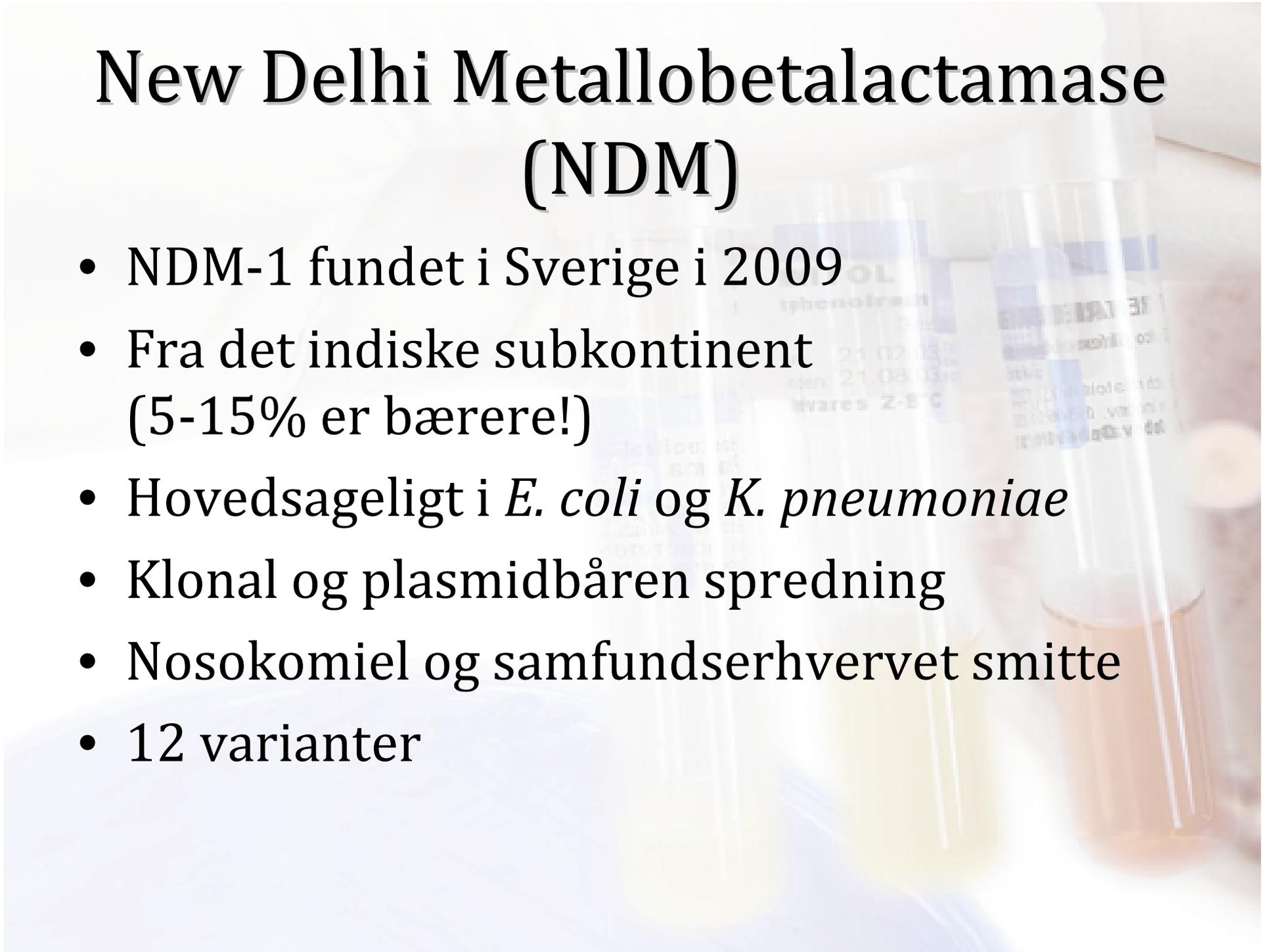
NDM producers

- Unknown distribution of NDM producers
- Sporadic spread of NDM producers
- Outbreaks caused by NDM producers
- Endemicity of NDM producers

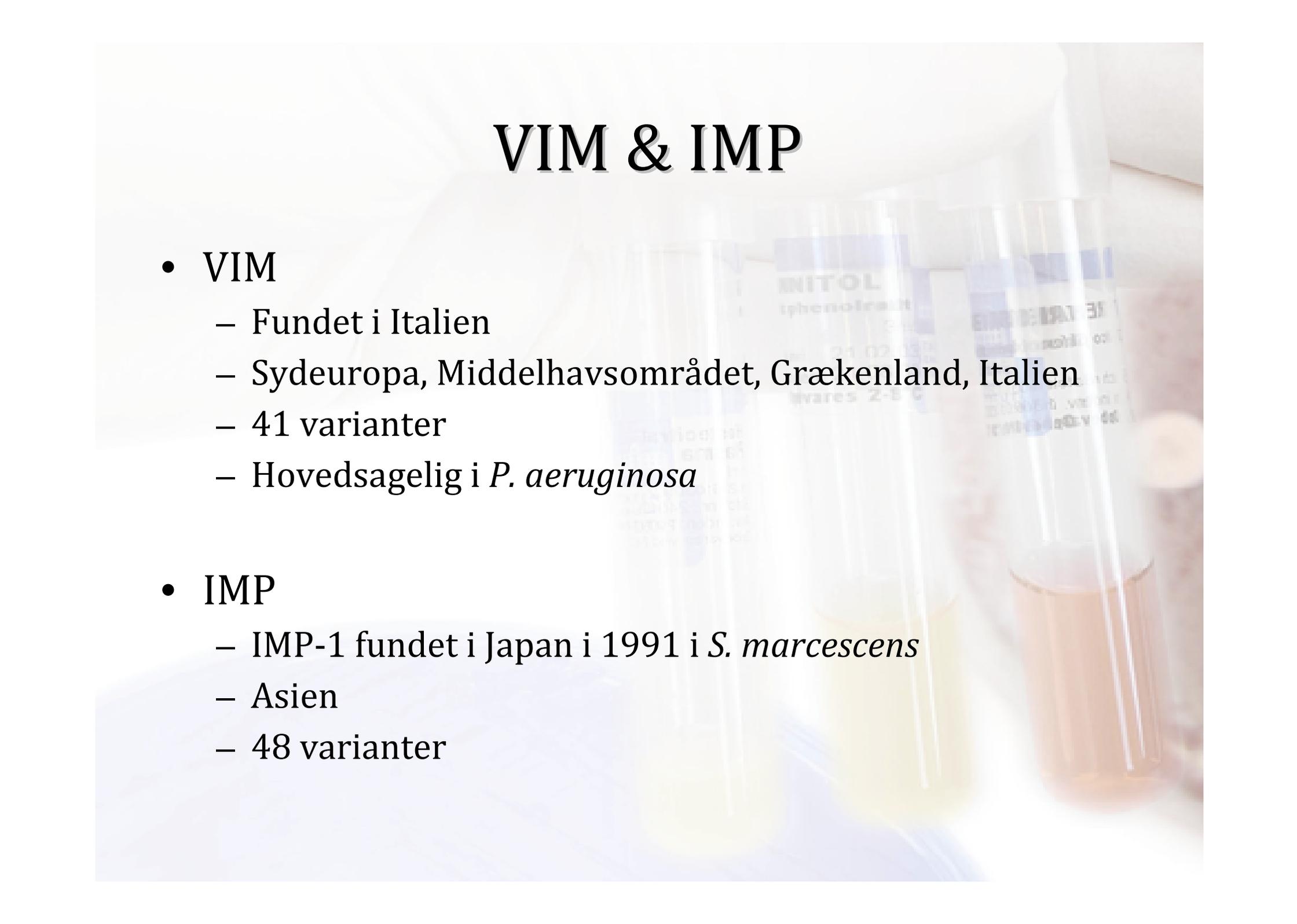


New Delhi Metallobetalactamase (NDM)

- NDM-1 fundet i Sverige i 2009
- Fra det indiske subkontinent
(5-15% er bærere!)
- Hovedsageligt i *E. coli* og *K. pneumoniae*
- Klonal og plasmidbåren spredning
- Nosokomial og samfundserhvervet smitte
- 12 varianter



VIM & IMP

The background of the slide is a photograph of several laboratory test tubes in a rack. The tubes contain liquids of various colors: one is clear, one is yellow, one is orange, and one is reddish-brown. The labels on the tubes are partially visible and include the word 'INITOL' and 'phenol'.

- VIM

- Fundet i Italien
- Sydeuropa, Middelhavsområdet, Grækenland, Italien
- 41 varianter
- Hovedsagelig i *P. aeruginosa*

- IMP

- IMP-1 fundet i Japan i 1991 i *S. marcescens*
- Asien
- 48 varianter

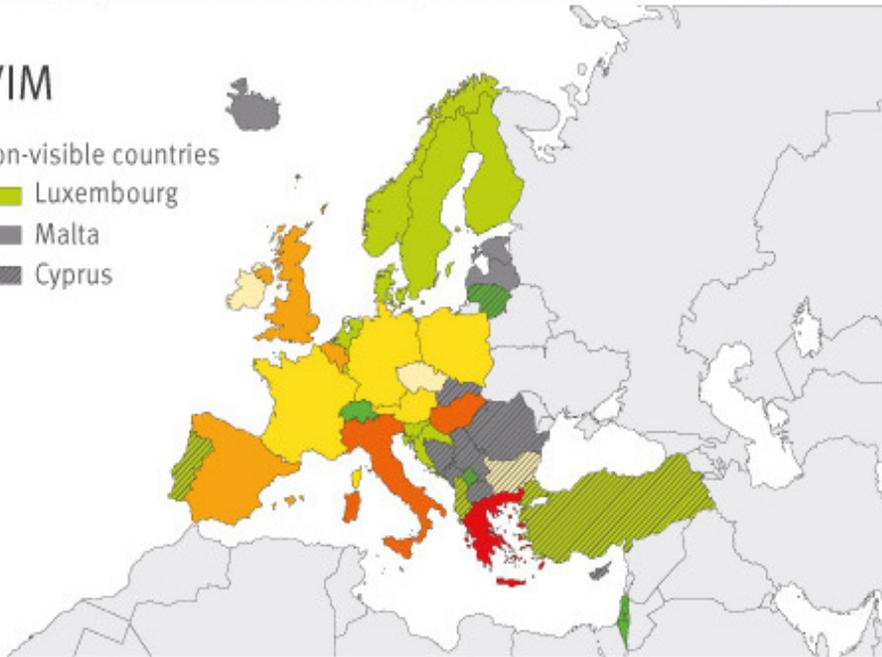
OXA-48-like

- Først fundet i Tyrkiet i 2001
- Nordafrika, Tyrkiet, Middelhavsområdet
- Hovedsageligt i *E. coli* og *K. pneumoniae*
- Nosokomial og samfundserhvervet smitte
- Self-conjugative plasmid, plasmidbåren spredning
- OXA-181, OXA-163, OXA-203

VIM

Non-visible countries

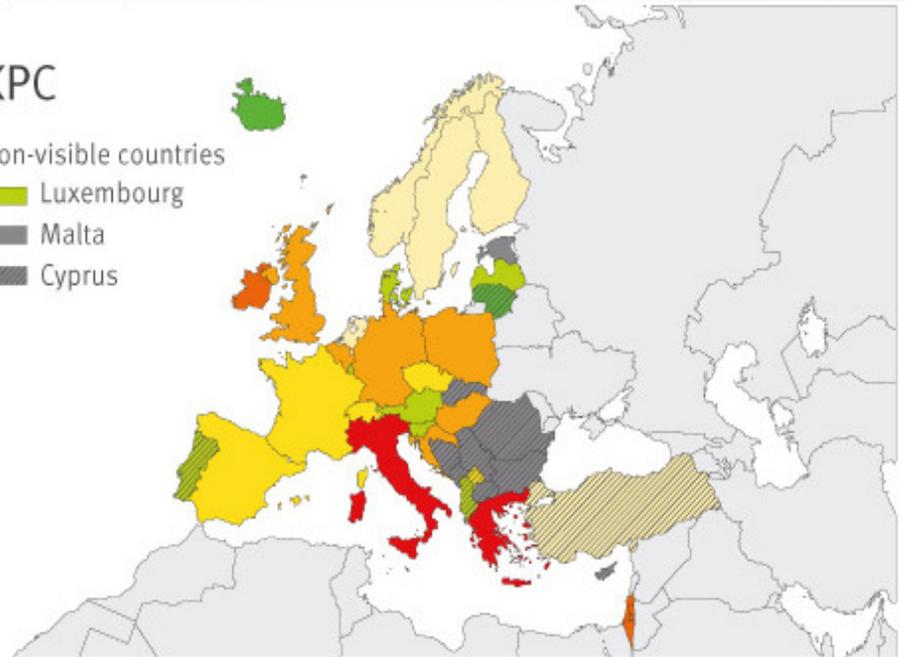
- Luxembourg
- Malta
- Cyprus



KPC

Non-visible countries

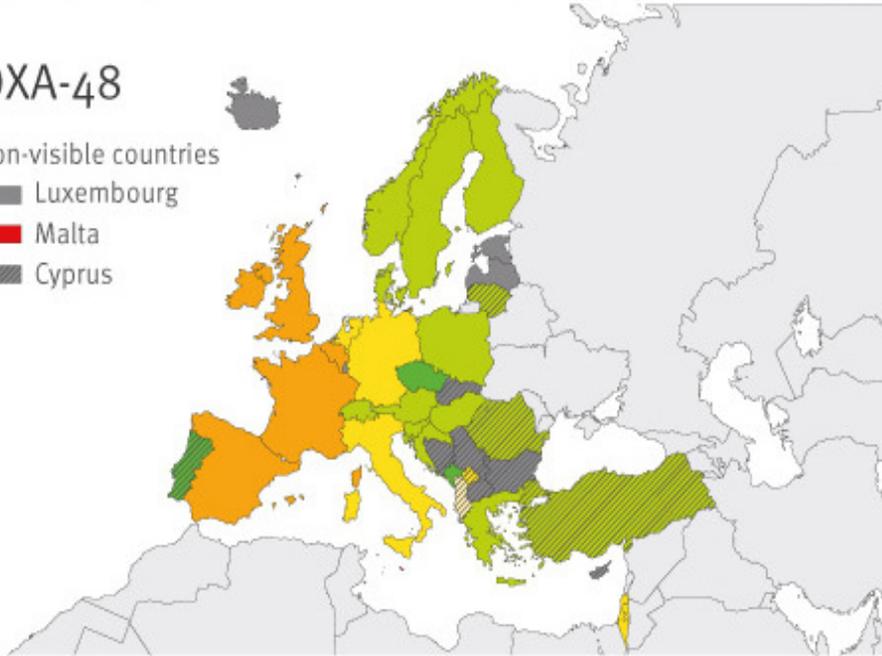
- Luxembourg
- Malta
- Cyprus



OXA-48

Non-visible countries

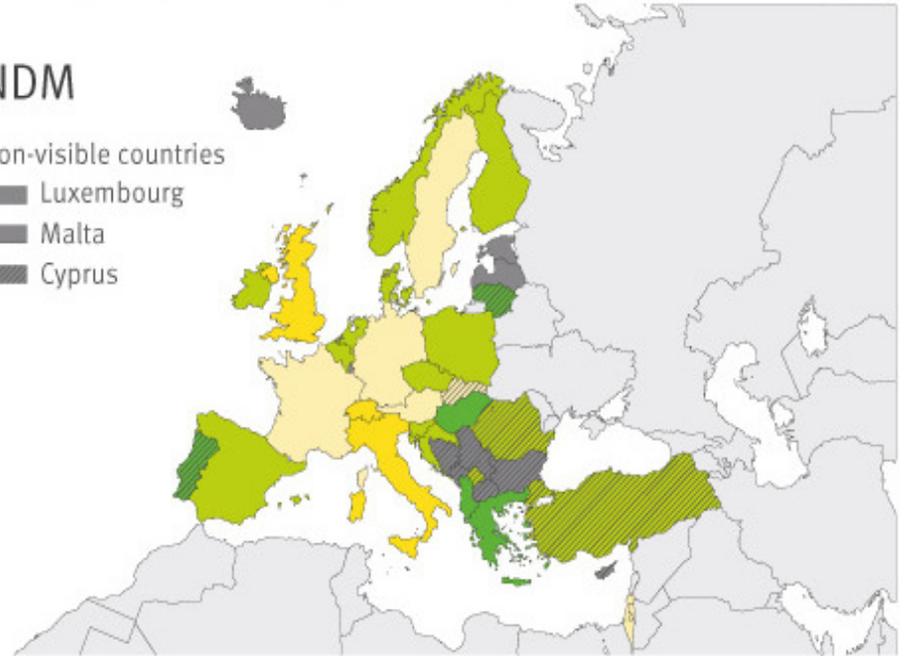
- Luxembourg
- Malta
- Cyprus



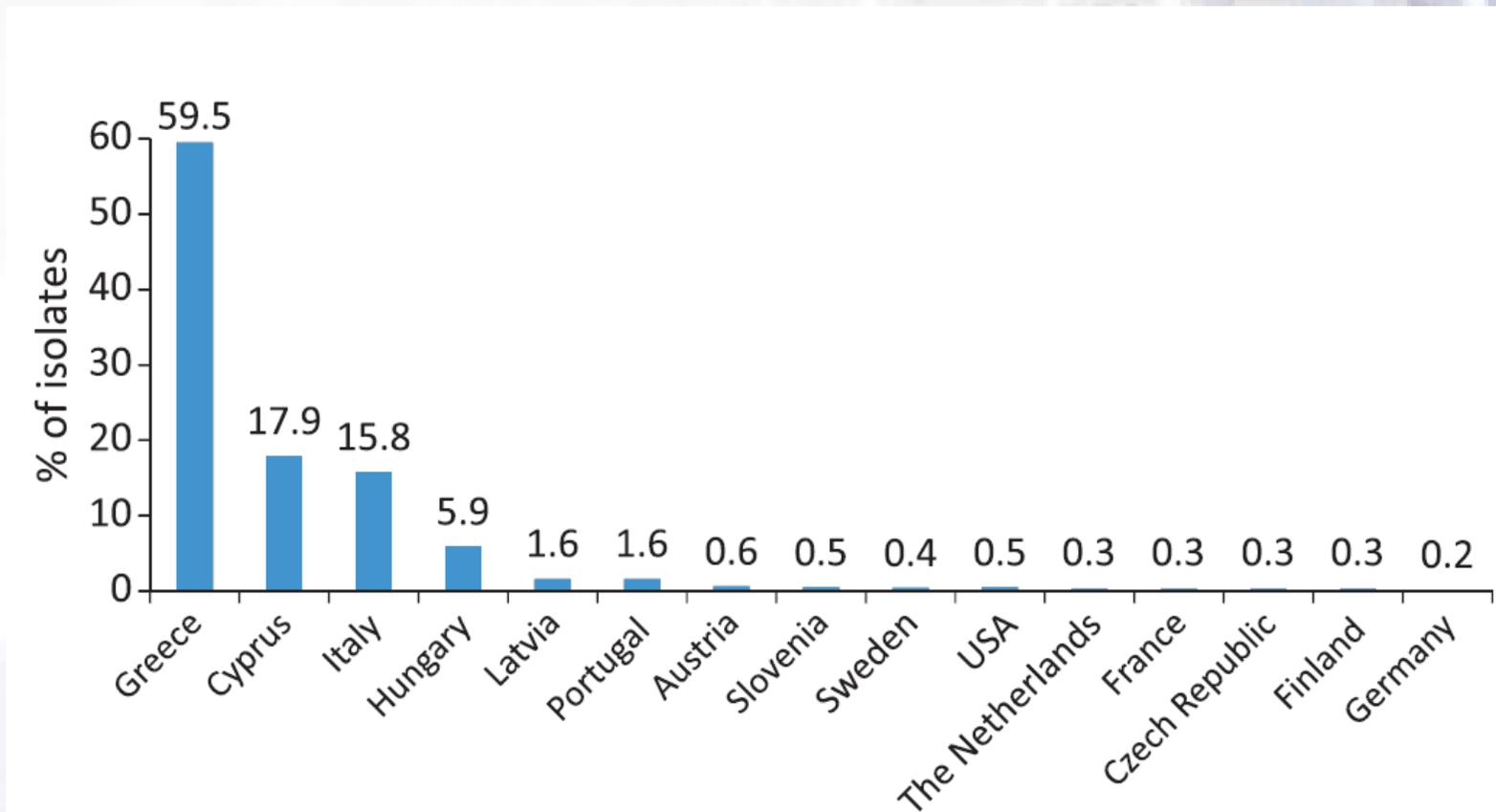
NDM

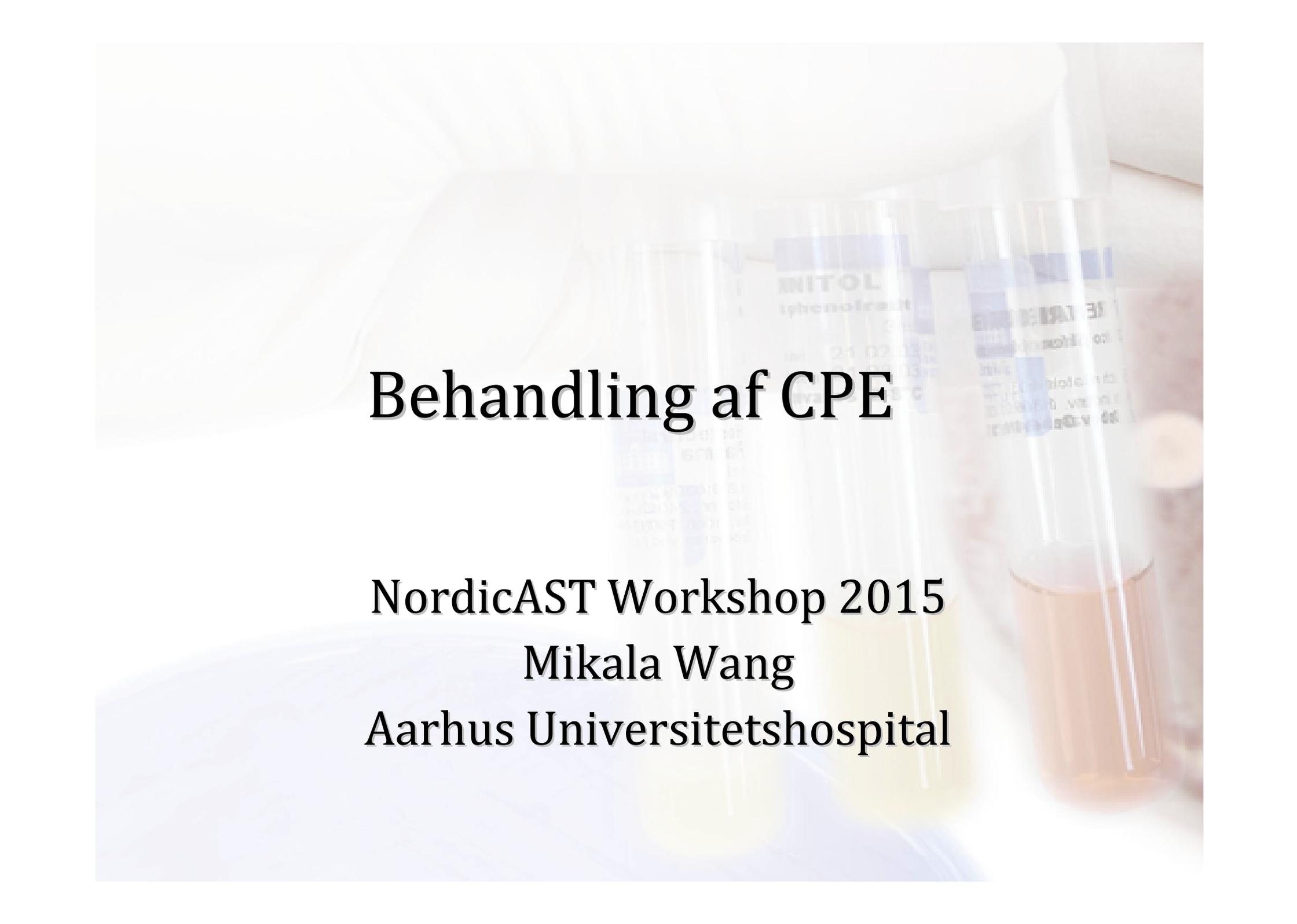
Non-visible countries

- Luxembourg
- Malta
- Cyprus



Nedsat meropenem-følsomhed hos *K. pneumoniae* i Europa



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Behandling af CPE

NordicAST Workshop 2015

Mikala Wang

Aarhus Universitetshospital

"Gamle" antibiotika

- Colistin
 - Suboptimal dosering
 - Lavere totaldosis colistin associeret med øget mortalitet
 - Toxicitetsovervejelser, nephro- og neurotoksik
- Fosfomycin
 - Meget begrænsede data
 - Risiko for resistensudvikling ved monoterapi
- Tigecyklin
 - Bacteriostatisk effekt på Gram negative
 - Lave serumkoncentrationer ved vanlig dosering (50 mg x 2)
 - Lavere mortalitet ved højdosis (100 mg x 2), men toxicitetshensyn

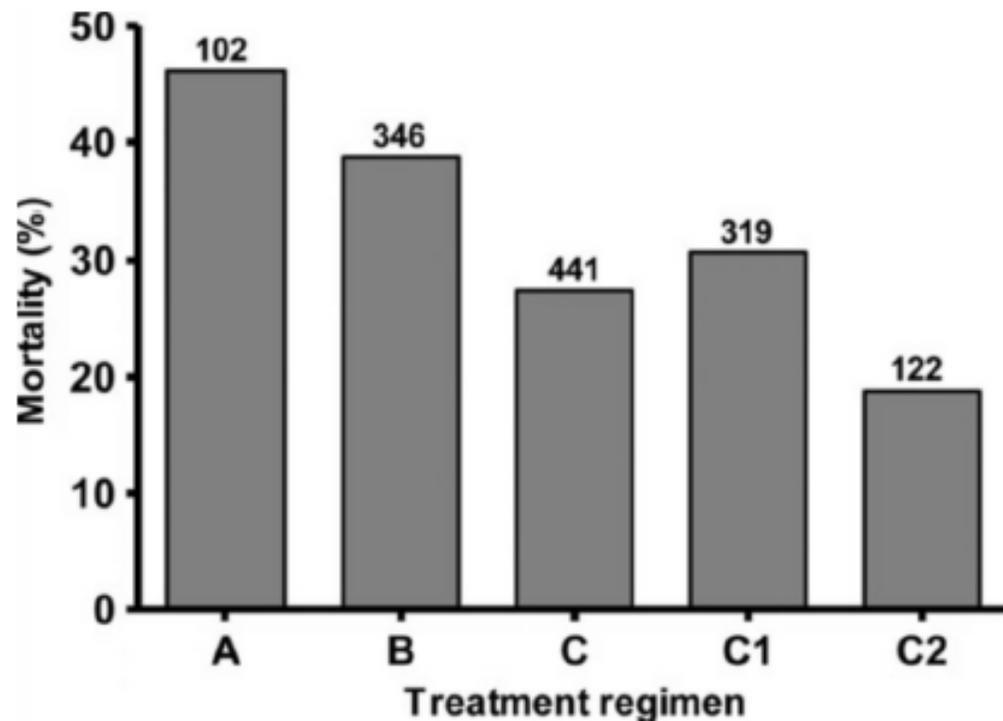
Carbapenem monoterapi

TABLE 5 Results of carbapenem monotherapy in 50 CPE-infected patients from 15 studies^a

MIC of carbapenem (μg/ml)	No. of patients	No. of successes	No. of failures	% Failure
≤1	17	12	5	29.4
2	12	9	3	25.0
4	7	5	2	28.6
8	6	4	2	33.3
Subtotal	42	30	12	28.6 ^b
>8	8	2	6	75.0 ^b
Total	50	32	18	36

Behandling af CPE

- retrospektiv analyse af data fra 889 patienter

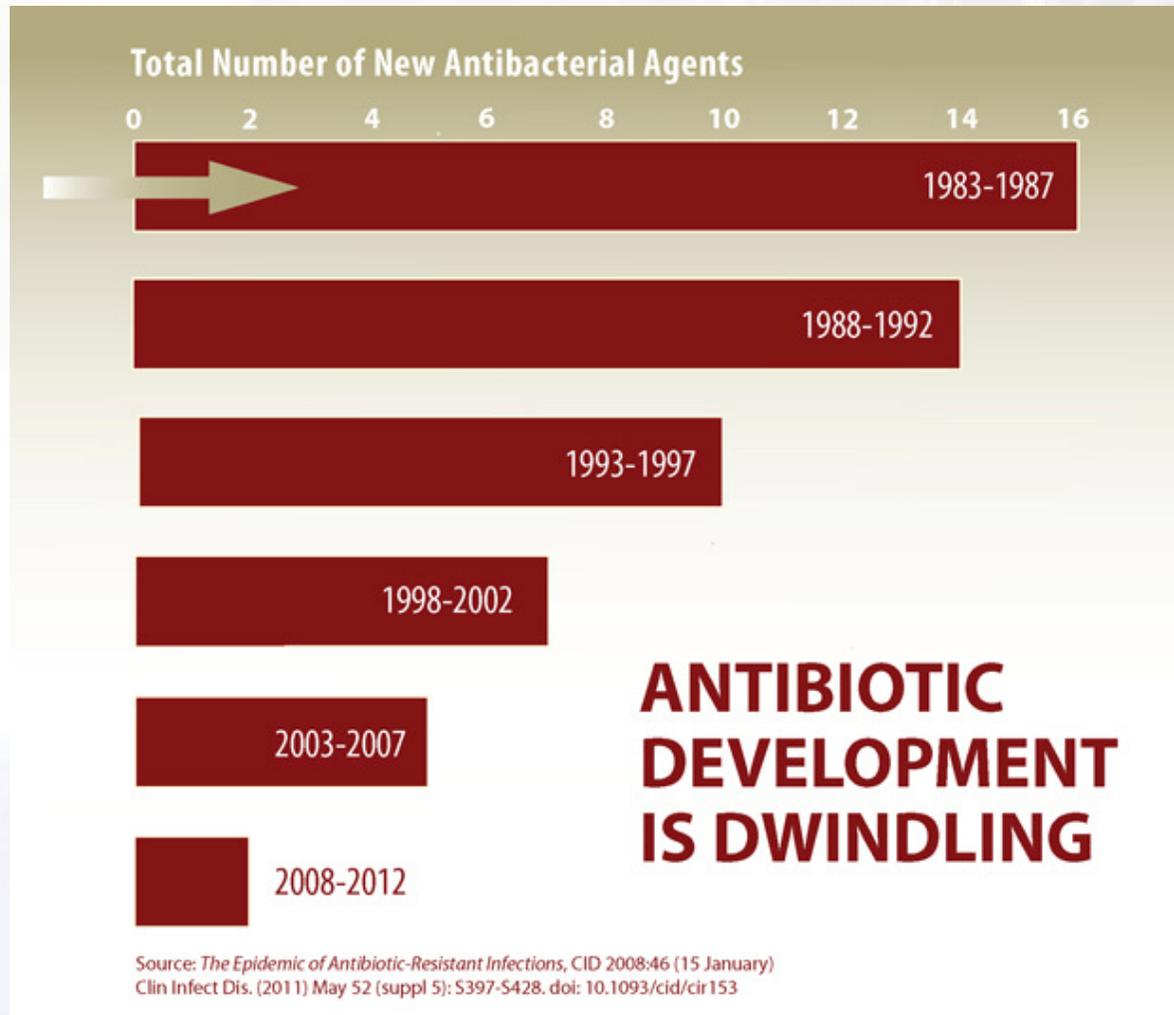


- A: Ingen aktiv behandling
- B: Monoterapi
- C: Kombinationsterapi (≥ 2 aktive stoffer)
- C1: Kombinationsterapi (≥ 2 aktive stoffer, excl. carbapenem)
- C2: Kombinationsterapi (≥ 2 aktive stoffer, incl. carbapenem)
- Regime C, C1, C2 vs. B:
p 0.001, p 0.034, p<0.0001

Konklusioner fra analysen

- Behandling med enkelt in vitro aktivt antibiotika
 - mortalitet ikke signifikant forskellig fra mortalitet hos patienter der ikke fik aktiv terapi
- Kombinationsterapi med ≥ 2 in vitro active antibiotika førte til bedre overlevelse end monoterapi
(mortalitet 27.4% vs. 38.7%; $p < 0.001$).
- Laveste mortalitet (18.8%) ved behandling med carbapenem-indeholdende kombinationer

Bad bugs, no drugs



Nye antibiotika på vej

- Carbavance
 - Aktiv mod KPC, men ikke OXA-48 og MBLs
- Ceftazidime-avibactam
 - Aktiv mod KPC og OXA-48, men ikke MBLs
- Plazomycin
 - Aminoglykosid
 - Aktiv mod de fleste CPE, fraset NDM-1

