Healthcare-associated infections

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Focus on

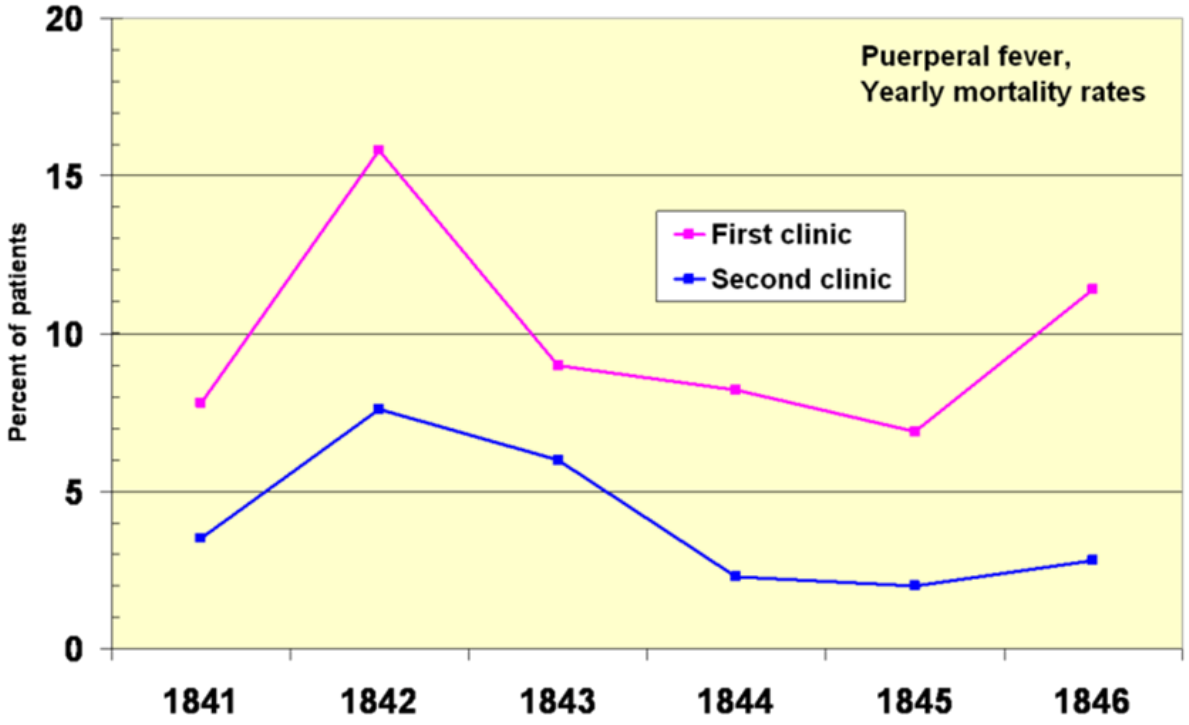
- **Epidemiological typing of hospital-associated bacterial pathogens**
- **Genetics, epidemiology and antibiotic resistance of *Acinetobacter baumannii***

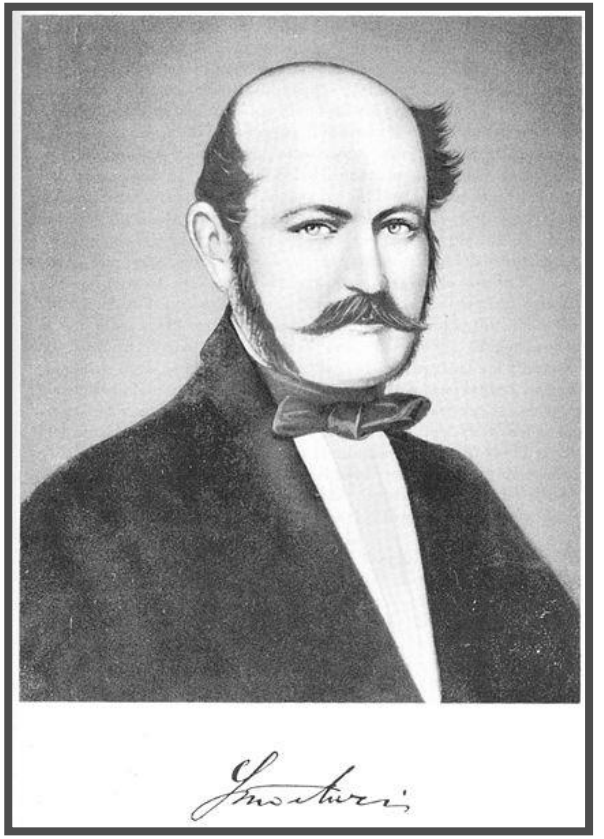
Lecture outline

- **Legacy of Ignaz Semmelweis**
- **Health care-associated infections (HAIs)**
- **Multidrug-resistant HAI bacterial pathogens**
  with *Acinetobacter baumannii* as a model organism

Ignaz Semmelweis (1818–1865)

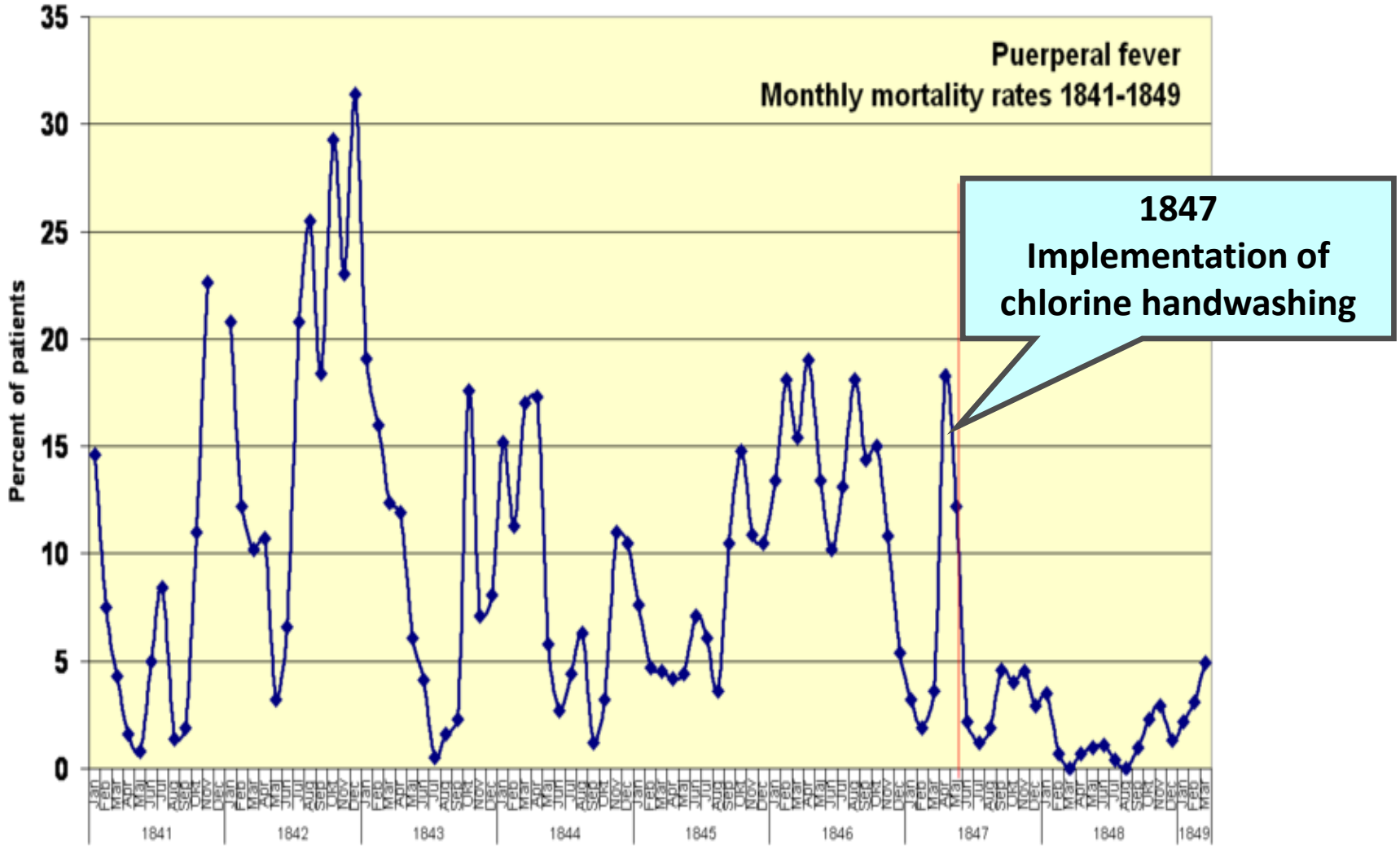
- **1846, The first maternity clinic at the Vienna general hospital**
- **„Puerperal fever“ (*Febris puerperalis*)**





https://en.wikipedia.org/wiki/Ignaz_Semmelweis

Ignaz Semmelweis

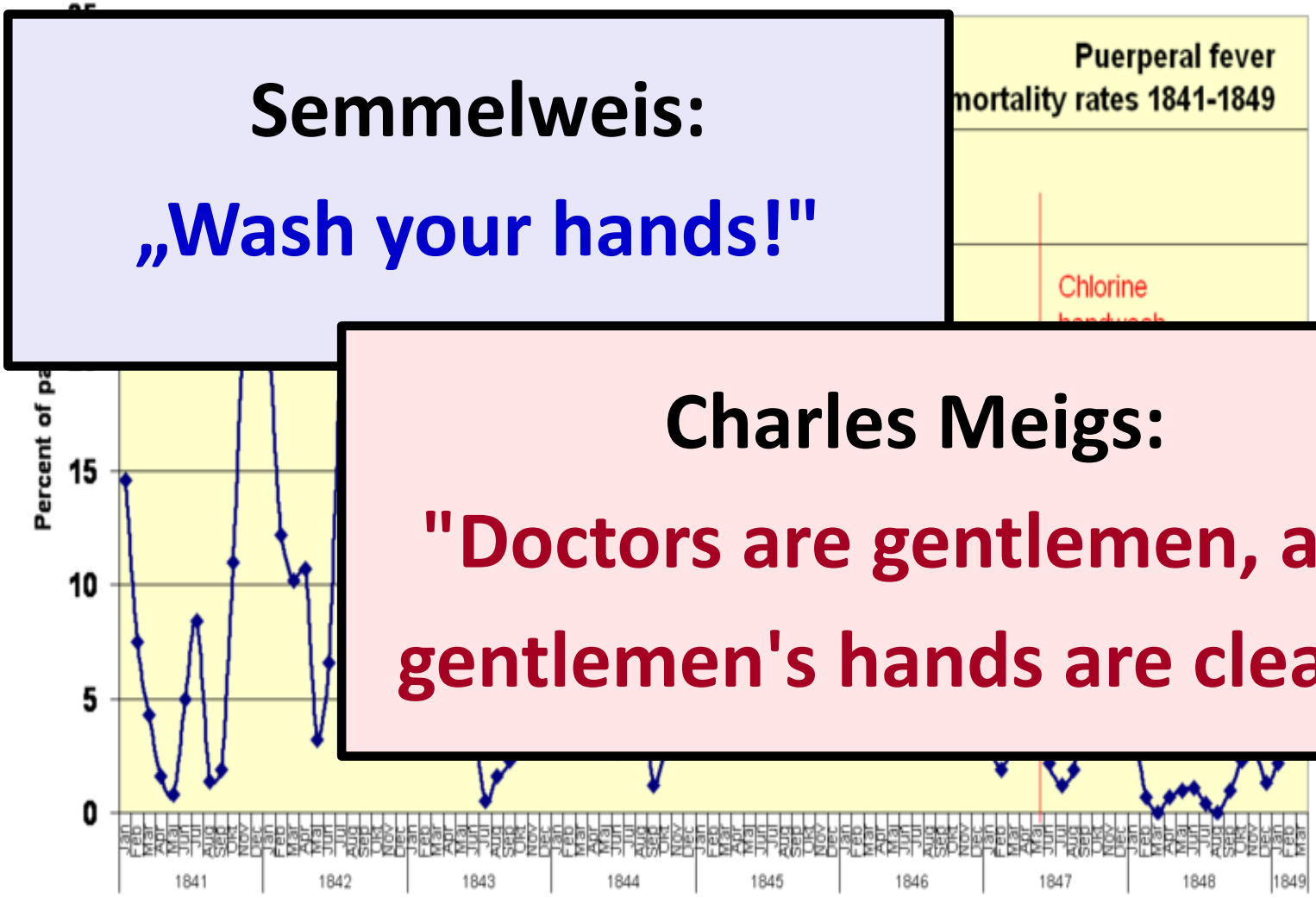


Ignaz Semmelweis

Semmelweis:

„Wash your hands!"

Ignaz Semmelweis



Semmelweis:

„Wash your hands!"

Charles Meigs:

"Doctors are gentlemen, and gentlemen's hands are clean."

Health care-associated infections (HAIs)

- Definitions
- Impact
- Endogenous vs. exogenous HAIs
- Clinical types
- Prevention and control
- Pathogens: overview and prevalence

HAI definitions

- **Healthcare Associated Infections (HAIs)**

  ≈ hospital acquired infections/nosocomial infections

- **Diseases/pathologies related to the presence of an infectious agent or its products in association with exposure to healthcare (HC) facilities, procedures or treatments**
- **Infections acquired in a hospital or a HC facility**
  - the infection not present or incubating at the time of contact with the HC environment
  - typically, symptom onset >48 h after contact with a HC facility provides evidence of HAI

General impact of HAIs (WHO)

- **Prevalence:** ≈1 in 10 (10%) patients globally (7% high-income; 15% low/middle-income countries; up to 30% in ICUs)
- **Mortality:** Of >5M deaths globally linked to antibiotic resistant, 63.5% were linked to of HAIs in 2019
- **Burden:** Prolonged stays, long-term disability, massive health system costs, antibiotic resistance rise; higher in low/middle-income countries

Impact of HAIs in Europe (2009)
mortality, extra costs and hospital stay

• No. of inhabitants (EU 27)	498,000,000
• No. of hospital admissions	81,000,000
• Admissions per 100,000	16,247
• No. of HAI cases	4,131,000
• **Incidence of HAI**	**5.1%**
• **No. of deaths (directly related)**	**37,179**
• No. of deaths (indirect)	111,537
• Extra hospital stay (days)	16,000,000
• **Extra costs**	**4,480,000,000 €**

Council recommendation on patient safety incl. prevention and control of healthcare associated infections 2009, Impact assessment report

Endogenous HAIs

- **≈ 70% of HAIs**
- **Arising from patient's own microbiota**
- **Triggered** usually **by a therapeutic or diagnostic intervention**
- **Associated with the patient's condition and comorbidities**, which reduce their immunity to infection
- **Limited preventability**
- **Can be reduced by optimal clinical care** (appropriate and sparing use of therapeutic and diagnostic interventions)
- **Example:** antibiotic treatment resulting in the selection of a pre-existing organism that is naturally resistant to the antibiotic used (e.g., pseudomembranous colitis caused by *Clostridioides difficile*)

Exogenous HAIs

- **≈ 30% of HAIs**
- **Originating from external sources** including healthcare staff, contaminated environment, or medical devices.
- **Transmission of pathogens mainly by contact - staff hands, contaminated medical devices**, less commonly by droplets or air
- **High preventability** - its level is proportional to compliance with measures to prevent transmission of infectious agents
- **Example:** epidemics of infections caused by multidrug-resistant bacteria that are transmitted between patients in hospitals, between hospitals or on a broader geographical scale
- **Agents:** MRSA, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Acinetobacter baumannii* etc.

European point prevalence survey (EPPS) 2011–2012

- **The first Europe-wide point prevalence survey on HAIs and antimicrobial use**
- **Data from a total of 273,753 patients in 1,149 hospitals in 30 European countries** submitted to ECDC in order to estimate the prevalence of HAIs in Europe
- **It estimates that on any given day, about 80,000 patients (5.6%) have at least one HAI**

www.ecdc.europa.eu/en/publications-data/point-prevalence-survey-healthcare-associated-infections-and-antimicrobial-use-0

HAIs: type distribution (EPPS 2011–2)

Table 11. Prevalence of HAI by HAI type and relative frequency of HAI types, ECDC PPS 2011–2012

	N of patients with HAI	HAI%	N of HAIs	Rel%
All HAI types	**13829**	**6.0**	**15000**	**100**
Pneumonia	2902	1.3	2907	19.4
Other lower respiratory tract infections	607	0.3	609	4.1
Surgical site infections	2933	1.3	2941	19.6
Urinary tract infections	2848	1.2	2848	19.0
Bloodstream infections	1576	0.7	1585	10.6
Catheter-related infections without bloodstream infection	233	0.1	233	1.6
Cardiovascular system infections	203	0.1	204	1.4
Gastro-intestinal system infections[a]	1130	0.5	1134	7.6
Skin and soft tissue infections	598	0.3	599	4.0
Bone and joint infections	243	0.1	245	1.6
Central nervous system infections	97	0.0	97	0.6
Eye, ear, nose or mouth infection	454	0.2	454	3.0
Reproductive tract infections	87	0.0	87	0.6
Systemic infections[b]	933	0.4	934	6.2
Other/unknown	123	0.1	123	0.8

72.7%

7.6%

6.2%

- ***C. difficile* infections (3.6 %) – in contrast, 15% if HAIs in the U.S.**

Bloodstream infections (BSI)
(EPPS 2011–2)

	Number of HAIs	Percentage
Origin of bloodstream infections (BSI)[a]		
Total BSI	1585	100.0
Catheter-related (C) BSI[e]	626	39.5
C-CVC	527	33.2
Of which CRI3-CVC	345	65.5
C-PVC	99	6.2
Of which CRI3-PVC	52	52.5
Secondary (S) BSI[f]	456	28.8
S-Pulmonary infection	65	4.1
S-Urinary tract infection	127	8.0
S-Surgical site infection	79	5.0
S-Digestive tract infection	78	4.9
S-Skin/soft tissue infection	35	2.2
S-Other infection sites	72	4.5
BSI of unknown origin & missing	503	31.7
BSI of unknown origin[g]	310	19.6
Missing BSI origin	193	12.2

Device-associated HAIs

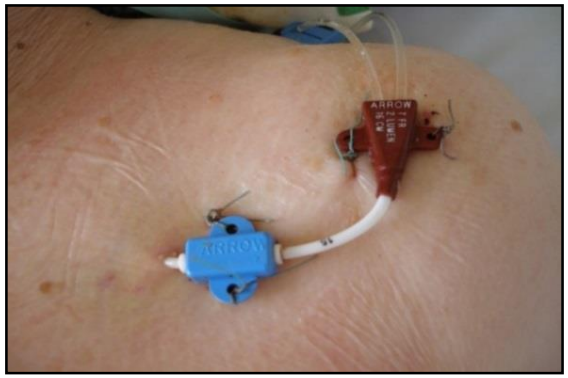
- Central Line-Associated BloodStream Infection (CLA BSI)
- Ventilator-Associated Pneumonia (VAP)
- Surgical Site Infection (SSI)
- Catheter-associated Urinary Tract Infections (CA UTI)

are principal contributors to healthcare hazard and threat to patient safety as they can cause prolonged hospital stay, sepsis, and mortality in the ICU

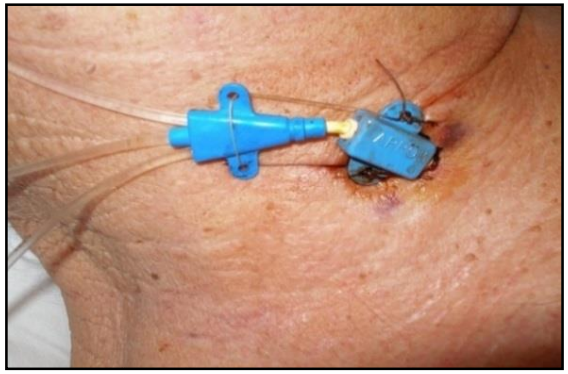
Catheter-related infections

central venous catheters – different risks of BSI

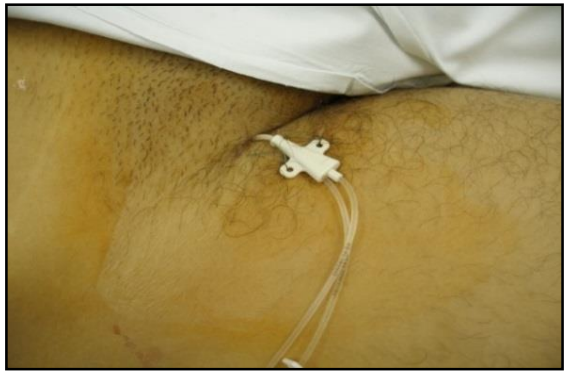
Subclavian vein



Jugular vein



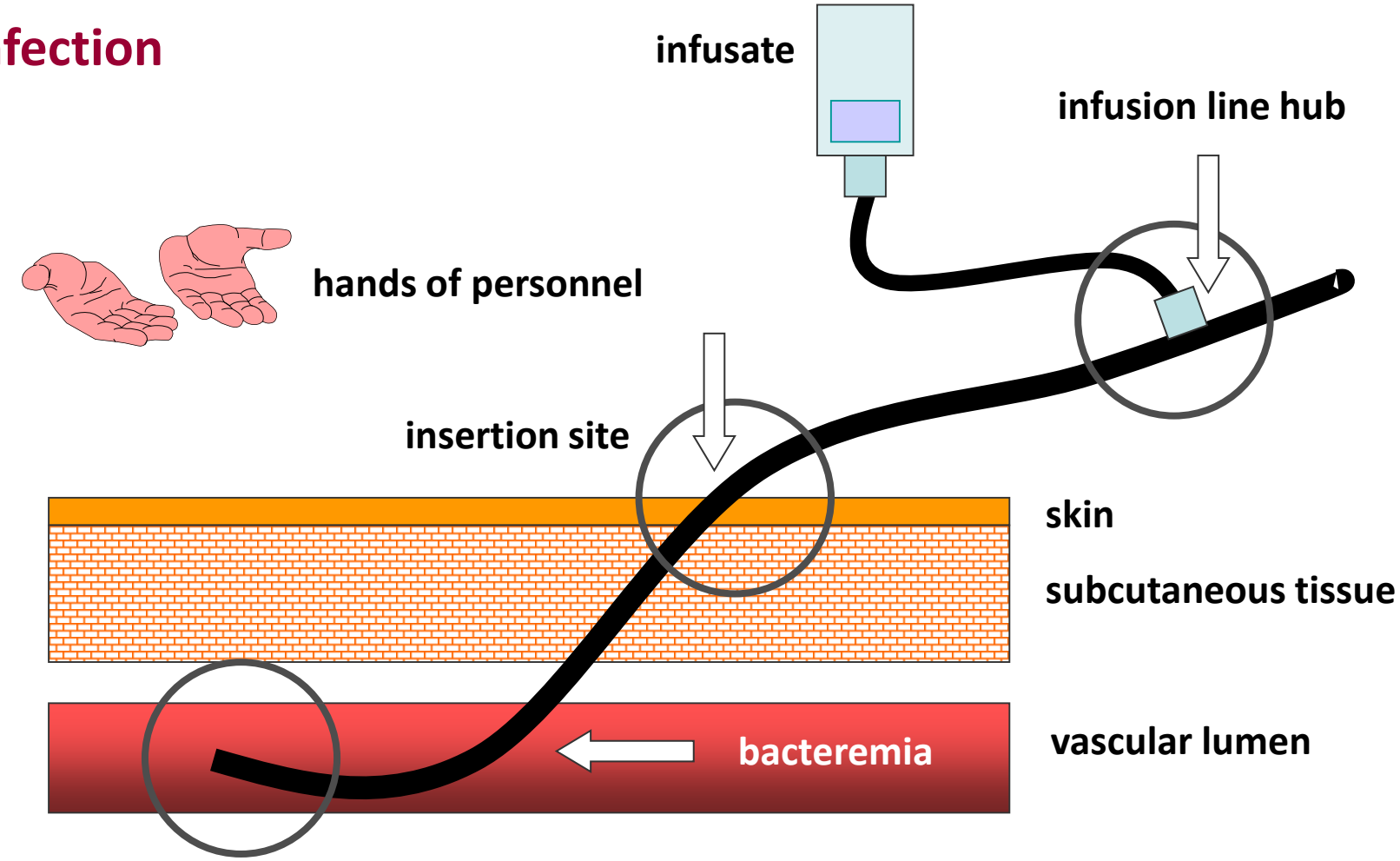
Femoral vein



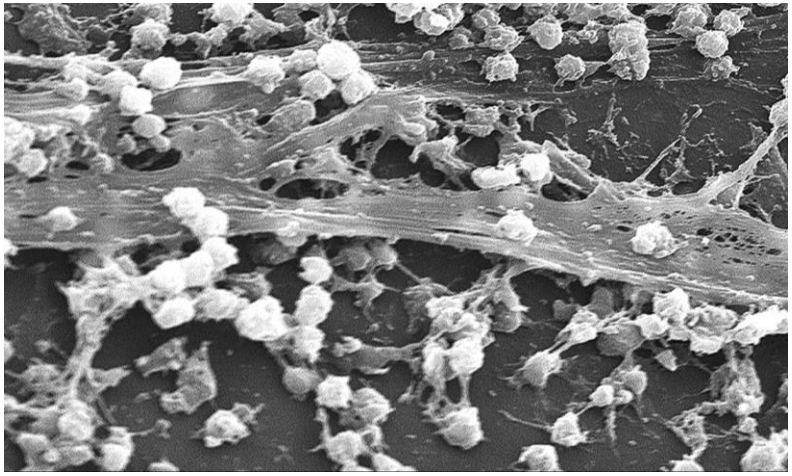
Risk of HAI

Catheter-related infections
colonization and infection

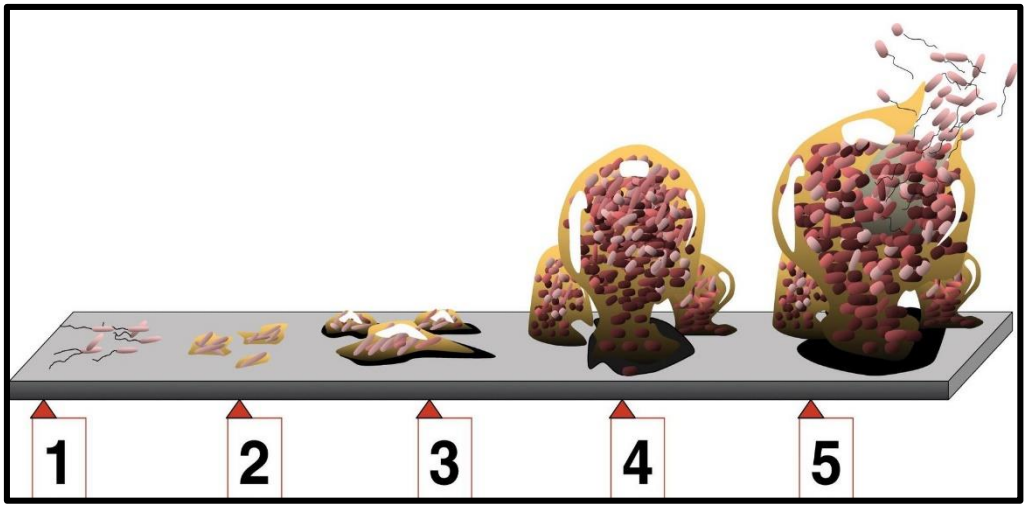
Potential sources of infection

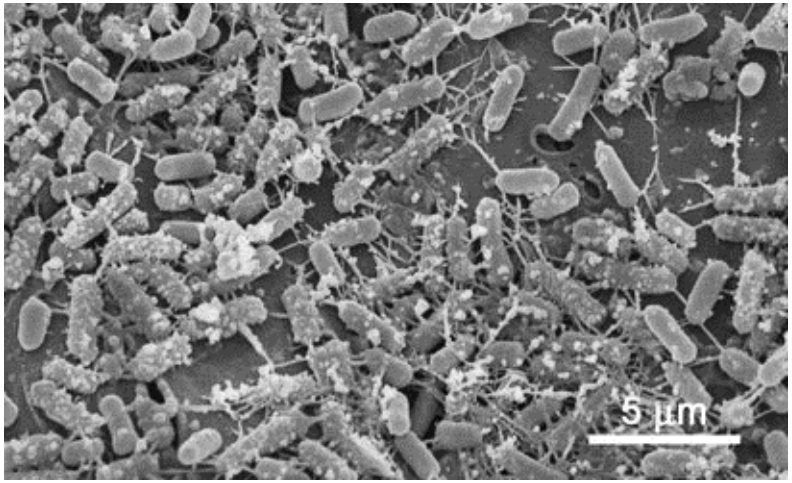


Catheter-related infections
bacterial biofilm



S. aureus **biofilm on a catheter**





E. coli **biofilm**

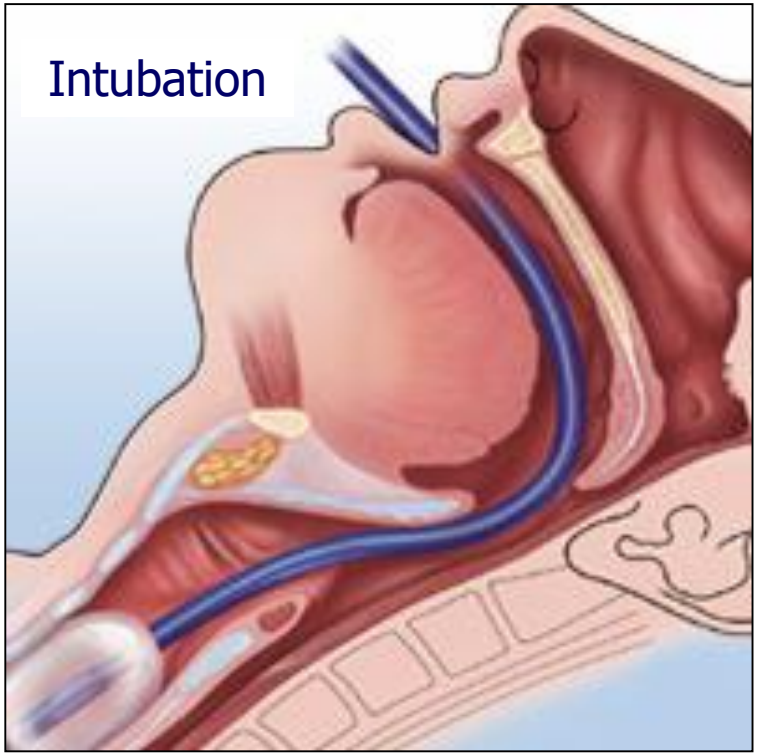
Biofilm development

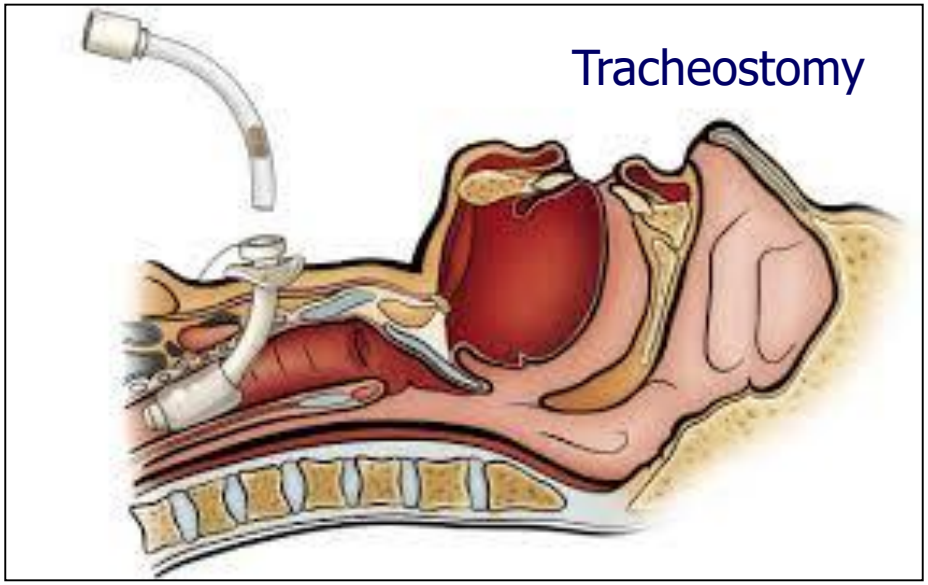
1. Initial attachment
2. Irreversible attachment
3. Maturation I
4. Maturation II
5. **Dispersion**

https://en.wikipedia.org/wiki/Biofilm

Nosocomial pneumonia

- **Intubation-associated pneumonia**
- **Ventilator-associated pneumonia (VAP)**





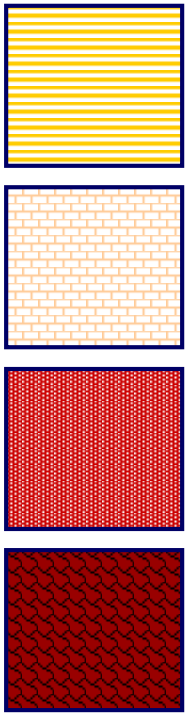
Ventilator-associated pneumonia (VAP)
classification and etiology

- **VAP early onset** (day 3–5 of hospitalization; good ATB susceptibility)
  - *Staphylococcus aureus*
  - *Streptococcus pneumoniae*
  - *Haemophilus influenzae*
  - Enterobacteria (*Escherichia coli*, *Klebsiella pneumoniae*)

- **VAP late onset** (≥ day 6, MDR, worse prognosis; contamination via e.g. suction of aspirate, intestinal source via a nasogastric tube).
  - *Pseudomonas aeruginosa* (incl. MDR)
  - *Staphylococcus aureus* (risk of MRSA)
  - Enterobacteria (incl. MDR)
  - *Acinetobacter* (incl. MDR)

- **Rare/unusual agents**
  - *Candida* spp. (common in immunocompromised individuals)
  - Enterococci

Surgical site infections
classification



Skin

Subcutaneous

Fascia, muscles

Organs, body spaces

Superficial incisional infection

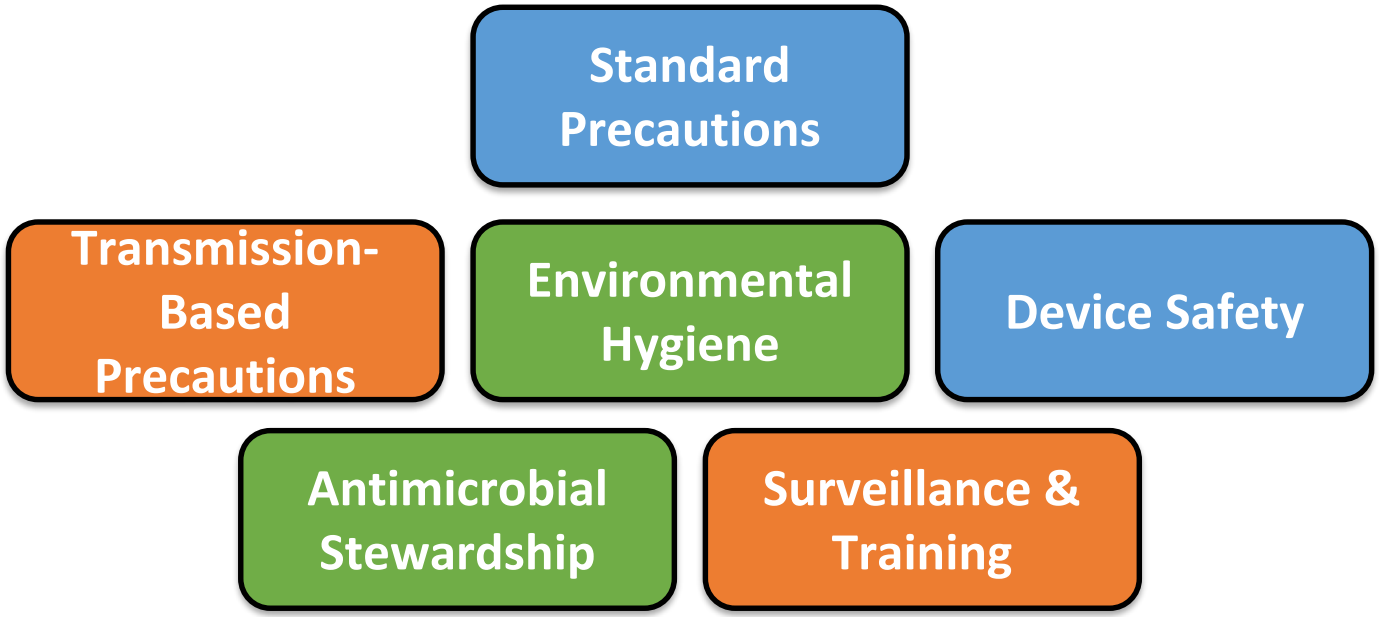
Deep incisional infection

Organ-space infections

Surgical site infections
etiology

Surgical discipline	*S. aureus*	CN staph.	Strepto-cocci	G- rods	Anaerobes
Cardiothoracic surgery	XX	XX			
Vascular surgery	XX	XX			
Neurosurgery	XX	XX	X		X
Orthopaedics	XX	XX		X	
Thoracic surgery	XX	XX	X	X	X
Head and neck surgery	XX		XX		XX
Abdominal surgery			X	XX	XX
Gynaecology			XX	XX	XX
Urology			XX	XX	

Infection prevention and control (IPC)



- **IPC measures** (incl. hand hygiene) can reduce HAIs and antibiotic resistance by 35–70% across all income levels.
- **Large gaps remain:** only 3.8% of countries meet national IPC minimums; only 15.2% of facilities meet required standards.
- **Needed:** stronger surveillance, better staff training, and adequate resources.

Preventability of HAI

Targeted infection control based on surveillance

SENIC study (USA 1975, ≈ 400 hospitals):

- **Surveillance + infection control** — **32 % decrease**
- Infection control without surveillance — 6 % decrease
- No precautions — 18 % increase

Space for improvement (with current evidence-based strategies)

Umscheid et al. Infect Control Hosp Epidemiol 2011

- Catheter-related bloodstream infection — **65–70% (100%)**
- Surgical site infections — 55%
- Ventilator associated pneumonia — 55%
- Urinary tract infections (catheter assoc.) — **65–70%**

HAIs are solvable to a great extent by rigorous adherence to GUIDELINES ON IPC

Etiological agents of HAIs

Bacteria

Gram-positive cocci

- Coagulase-negative staphylococci
- *Staphylococcus aureus*
- *Streptococcus* spp.
- *Enterococcus* spp.

Clostridioides difficile

Nontuberculous mycobacteria

Enterobacterales

- *Klebsiella* spp.
- *Escherichia coli*
- *Proteus mirabilis*
- *Enterobacter* spp.

Non-fermenters

- *Pseudomonas aeruginosa*
- *Acinetobacter* spp.
- *Burkholderia cepacia*

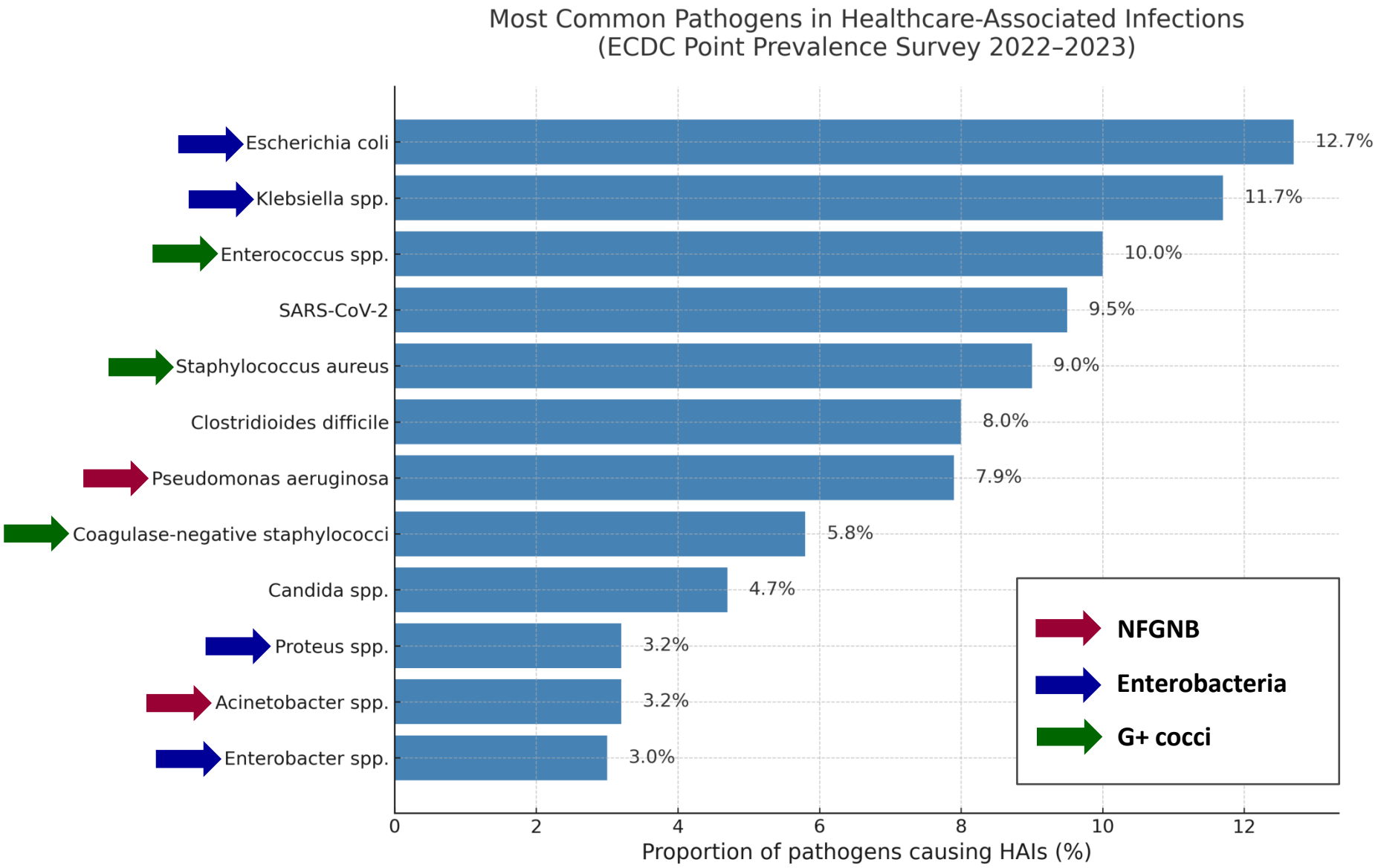
Fungi

- *Candida* spp.
- *Aspergillus fumigatus*

Viruses

- Hepatitis B and C viruses
- HIV virus
- Influenza virus
- Norovirus
- Rhinovirus
- Cytomegalovirus
- Herpes simplex virus

Etiological agents of HAIs (EPPS 2022–2023)



Multidrug-resistant HAI bacterial pathogens

- Hospital ecosystem vs. HAI agents
- High-priority (ESKAPE) pathogens
- Epidemic clones
- European Antimicrobial Resistance Surveillance Network
- *Acinetobacter baumannii*
  - Country-wide epidemiology
  - Example of a hospital outbreak

Hospital ecosystem × HAI pathogens

- Extensive use of disinfection, biocides and antibiotics
- Patients with severe underlying diseases and impaired defensiveness
- Invasive therapeutic and diagnostic procedures
- High-risk departments (intensive care, neonatal, burn)

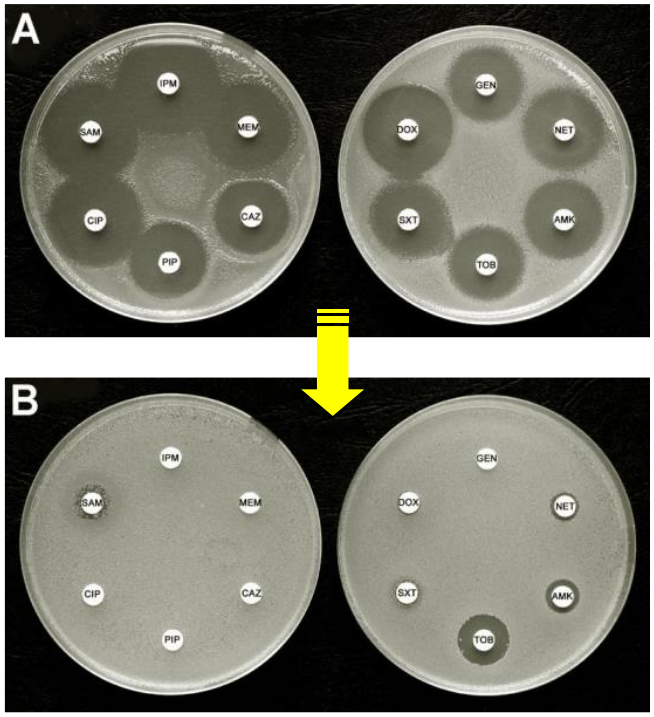
- Ubiquitous organisms capable of surviving in hostile external environments
- Primarily resistant to many biocides and antibiotics and further development of resistance
- Low pathogenicity

Multidrug-resistant HAI agents - ESKAPE

Clinical Infectious Diseases 2009; 48:1–12

Bad Bugs, No Drugs: No ESKAPE! An Update from the Infectious Diseases Society of America

Helen W. Boucher,[1] George H. Talbot,[2] John S. Bradley,[3,4] John [illegible]wards, Jr,[5,6,7] David Gilbert,[8] Louis B. Rice,[9,10] Michael Scheld,[11] Brad Spellberg,[5,6,7] and John Bartlett[12]



Pathogens that cause the majority of US hospital infections and effectively "escape" the effects of antibacterial drugs

Multidrug-resistant HAI agents - ESKAPE

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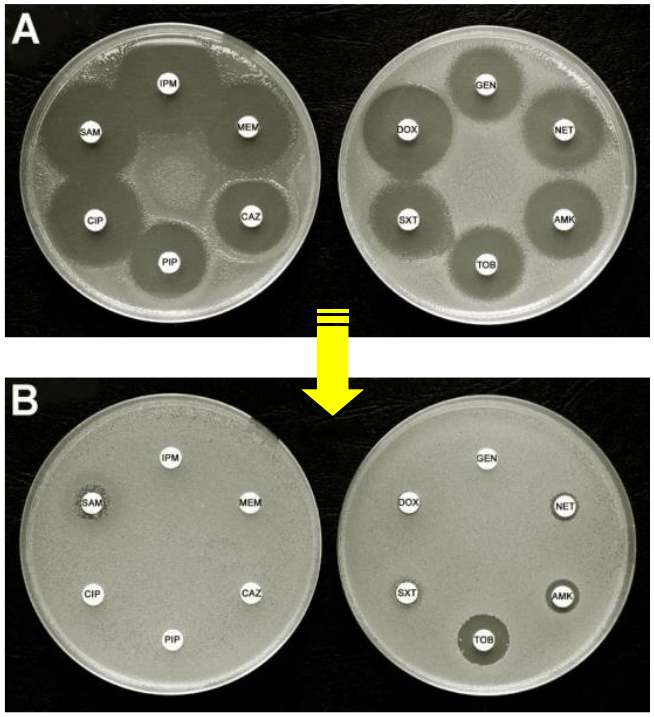


Enterococcus faecium
Staphylococcus aureus
Klebsiella pneumoniae
Acinetobacter baumannii
Pseudomonas aeruginosa
***Enterobacter* spp.**

WHO 2017 Priority Pathogens List

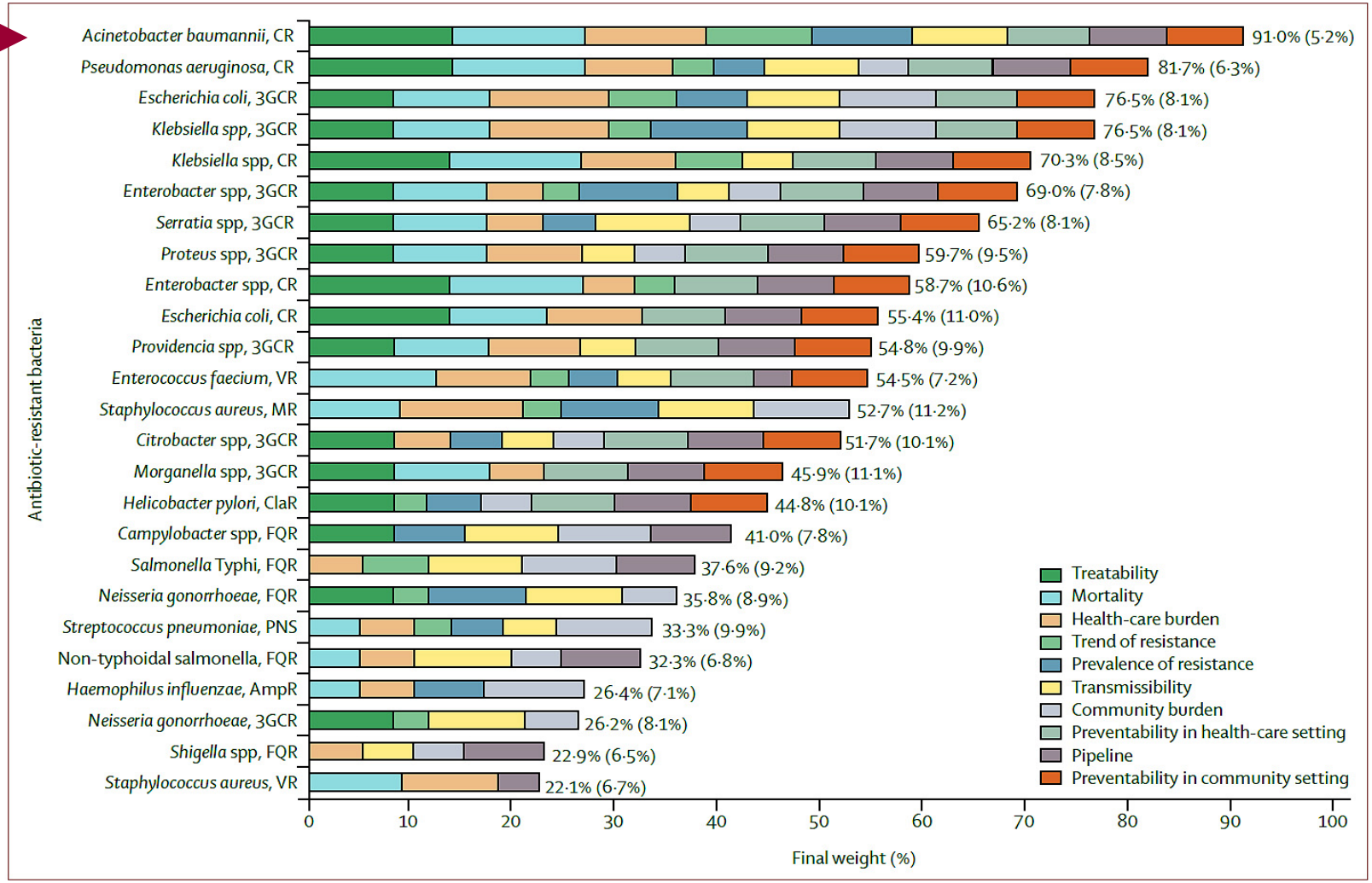


***Figure 2*: Final ranking of antibiotic-resistant bacteria**

Mean (SD) pathogen weights were derived by the software from the survey participants' preferences. The segments represent the contribution of each criterion to each pathogen's final weight. CR=carbapenem resistant. 3GCR=third-generation cephalosporin resistant. VR=vancomycin resistant. MR=meticillin resistant. ClaR=clarithromycin resistant. FQR=fluoroquinolone resistant. PNS=penicillin non-susceptible. AmpR=ampicillin resistant.

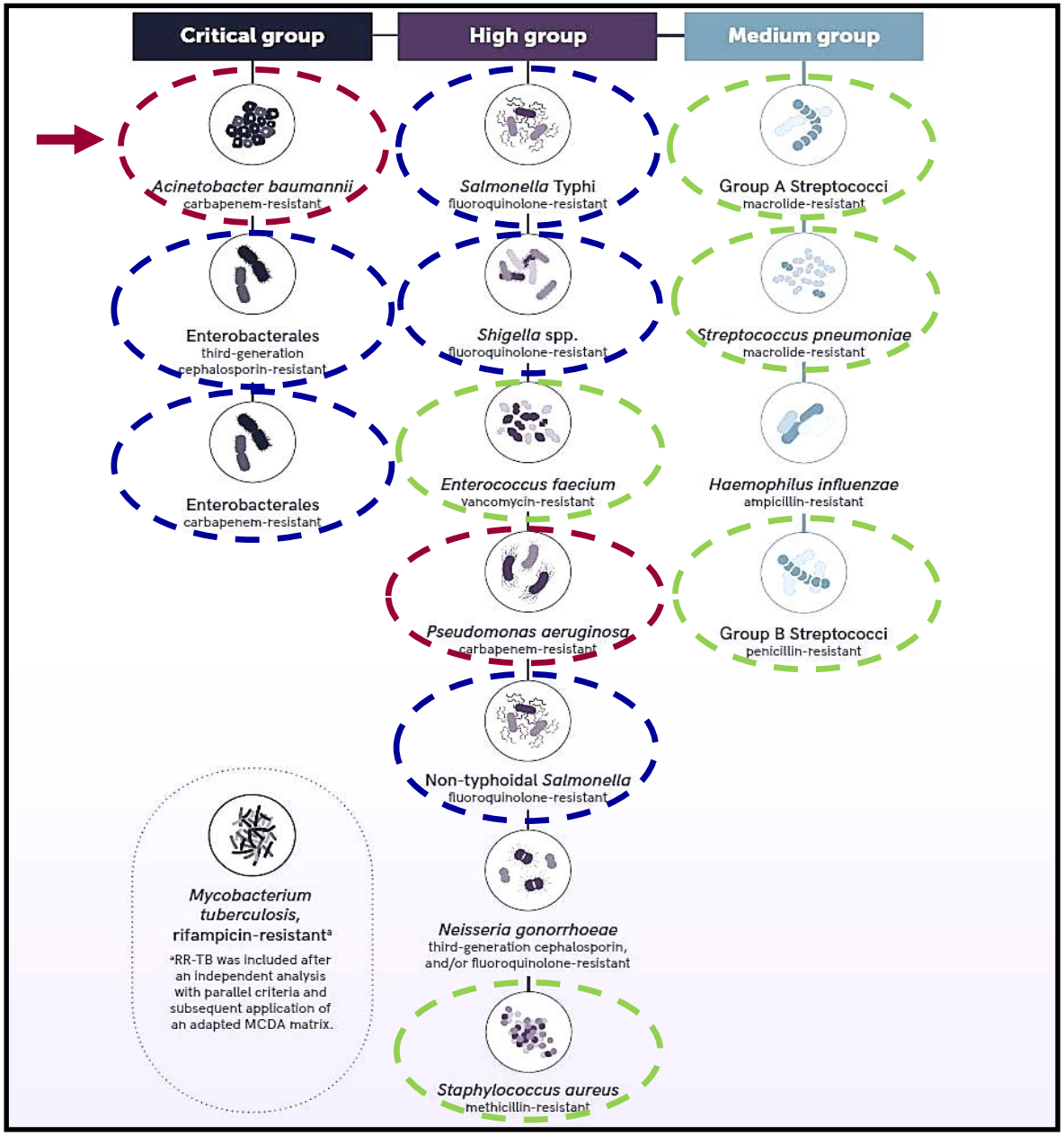
Lancet Infect Dis 2018; 18: 318

WHO bacterial priority pathogens list (2024)

NFGB

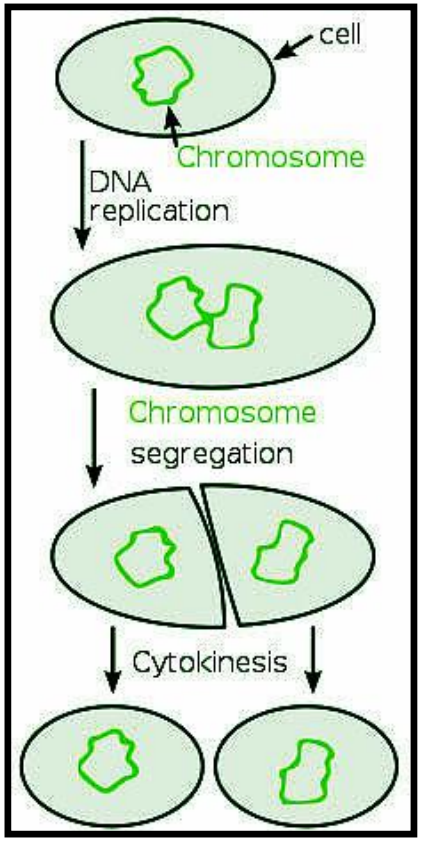
Enterobacteria

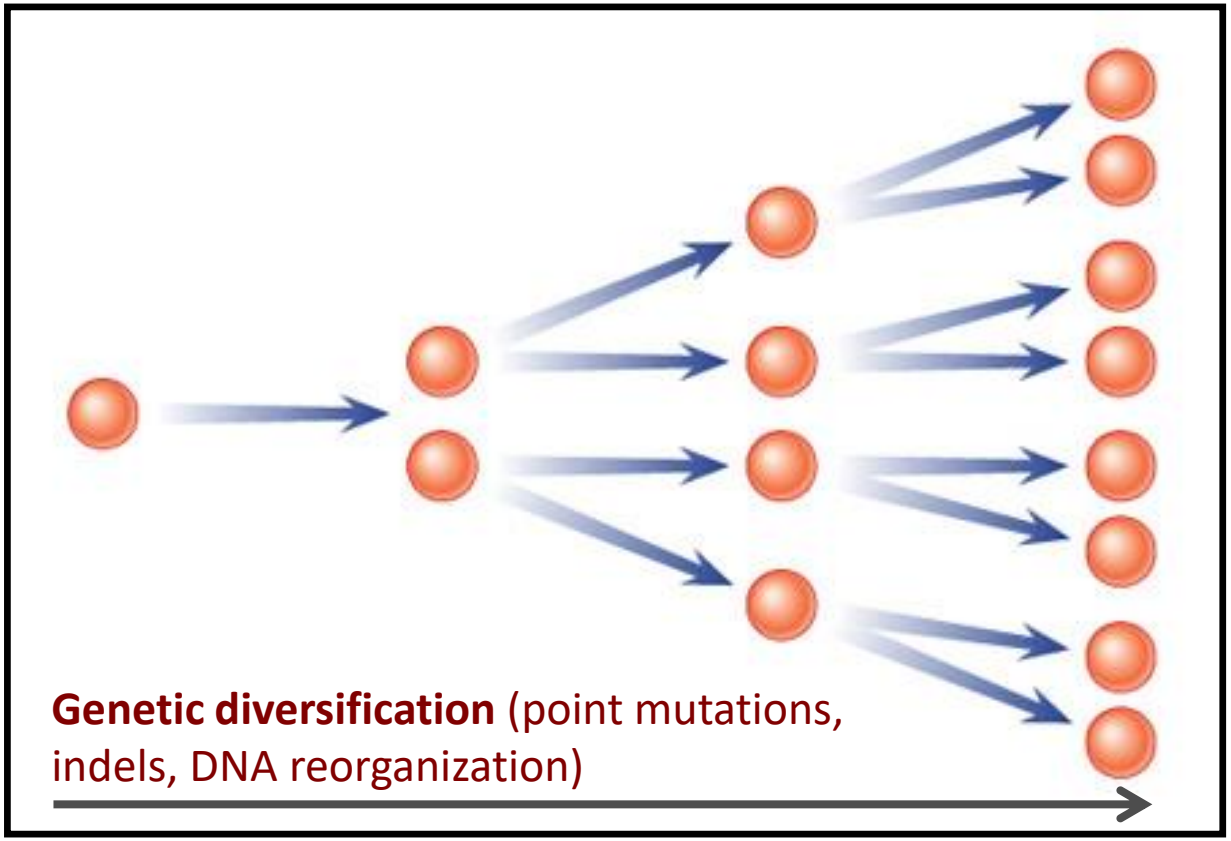
G+ cocci



Bacteria are haploid & clonal

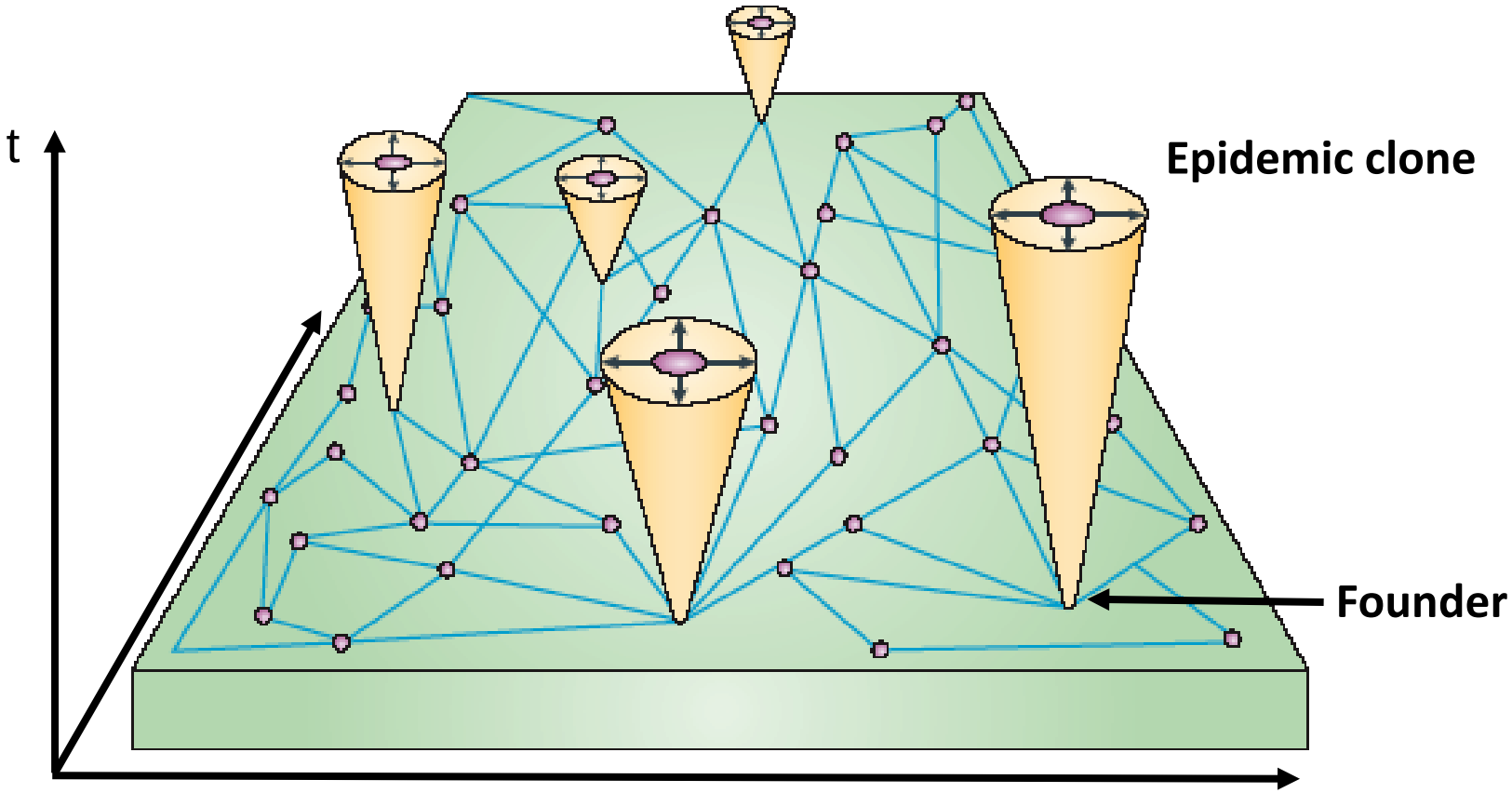
- **Bacteria are haploid and reproduce asexually by binary fission**
- **"Clonal propagation": multiplication of genetically "identical" organisms**





Epidemic clone

- **A group of organisms having the same ancestor, which is in terms of epidemic spread more successful compared with other lineages (strains) of a given species**



Maynard Smith et al. Bioassays 2000; 22: 1115

European Antimicrobial Resistance Surveillance Network (EARS-Net)

- **European Centre for Disease Prevention and Control (ECDC)**
- **The largest publicly funded system for antimicrobial resistance (AMR) surveillance in Europe**
- **EARS-Net is based on routine clinical antimicrobial susceptibility data from local and clinical laboratories reported to ECDC by appointed representatives from the member states**
- **Only data from invasive isolates (i.e. from blood and cerebrospinal fluid) are included in EARS-Net**

www.ecdc.europa.eu/en/about-us/partnerships-and-networks/disease-and-laboratory-networks/ears-net

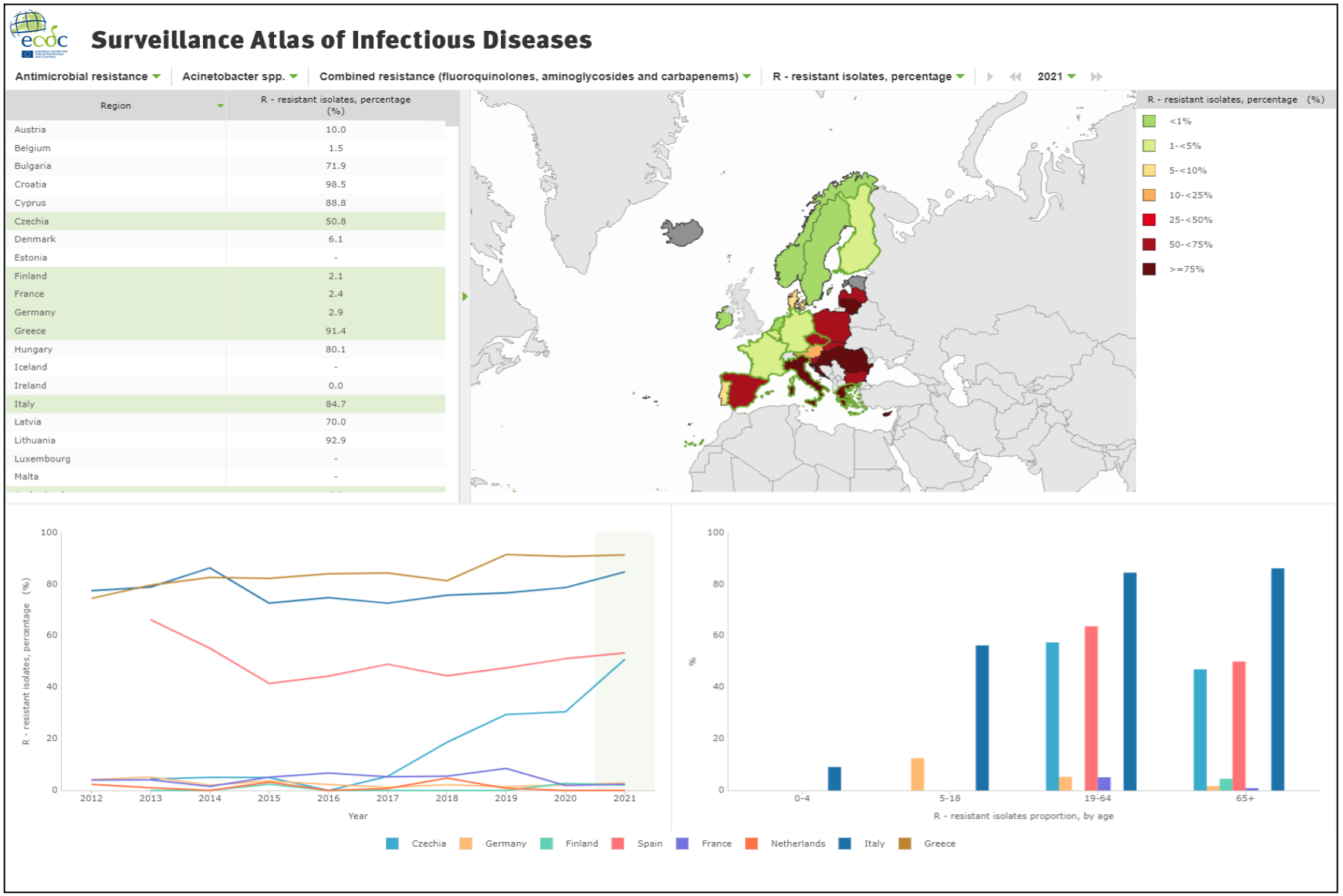
European Antimicrobial Resistance Surveillance Network (EARS-Net)

Surveillance of antimicrobial susceptibility of eight bacterial pathogens commonly causing infections in humans:

- ***Escherichia coli***
- ***Klebsiella pneumoniae***
- ***Pseudomonas aeruginosa***
- ***Acinetobacter***
- ***Streptococcus pneumoniae***
- ***Staphylococcus aureus***
- ***Enterococcus faecalis***
- ***Enterococcus faecium***

EARS-Net *Acinetobacter* 2021

Combined resistance to carbapenems, fluoroquinolones and aminoglycosides



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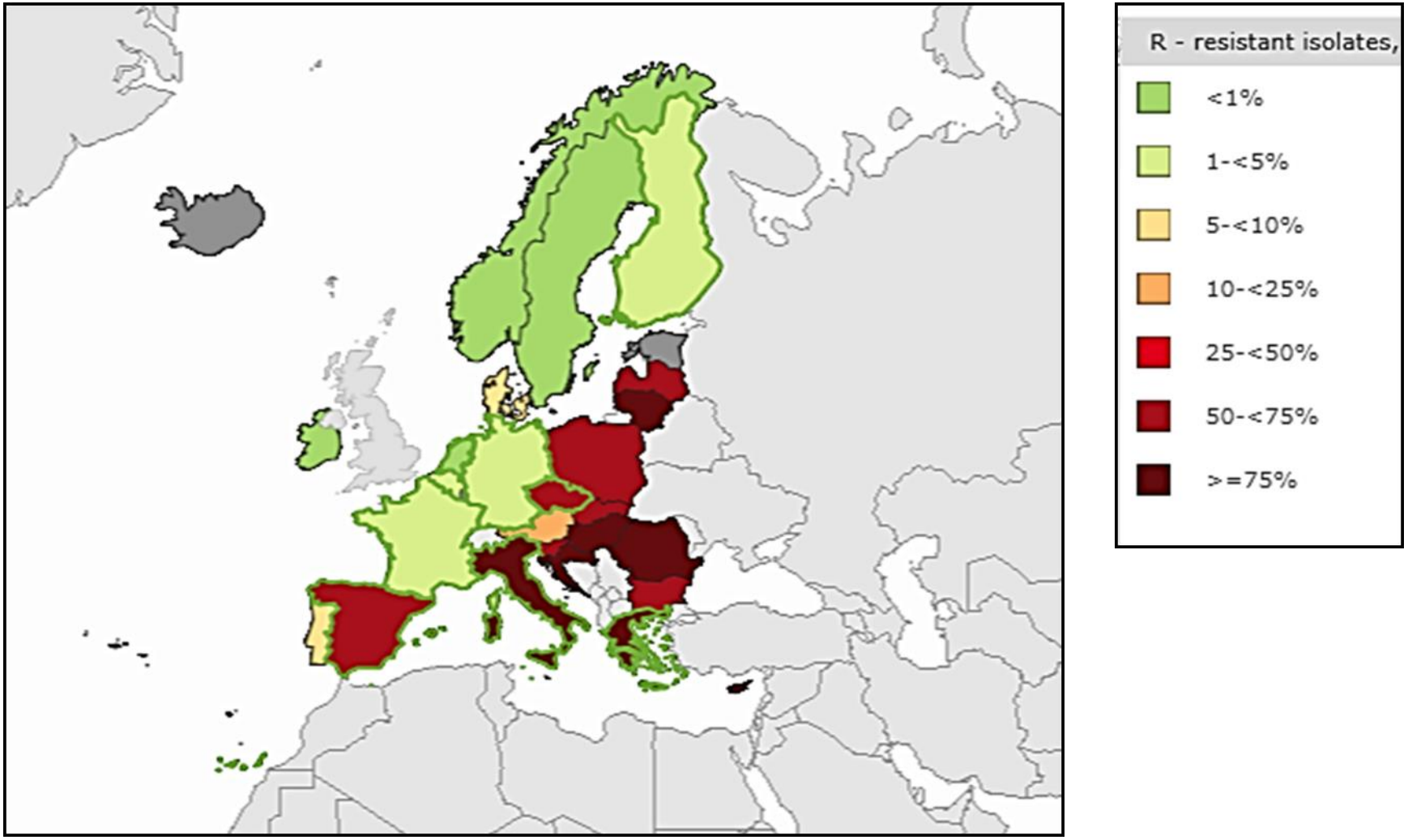
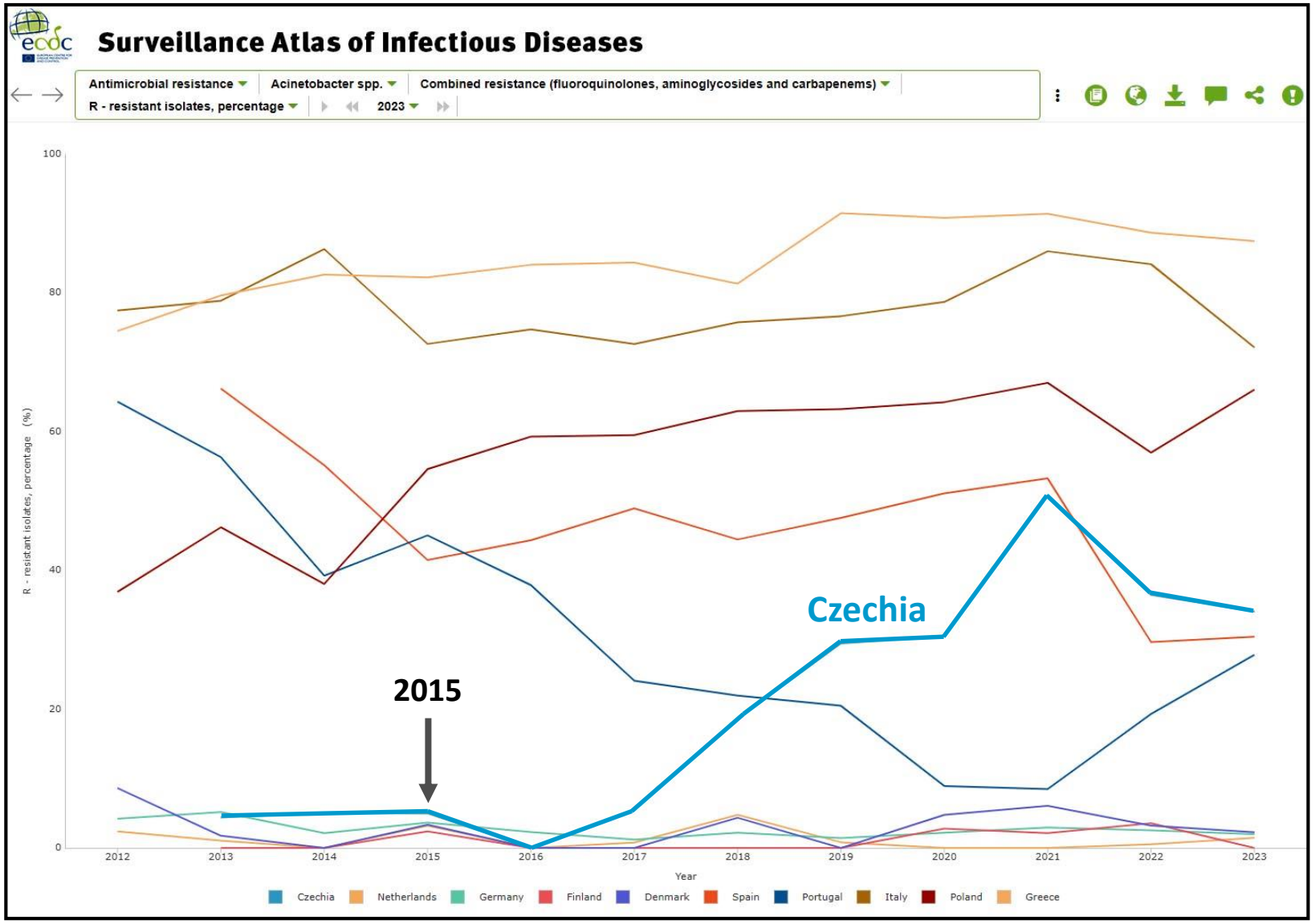


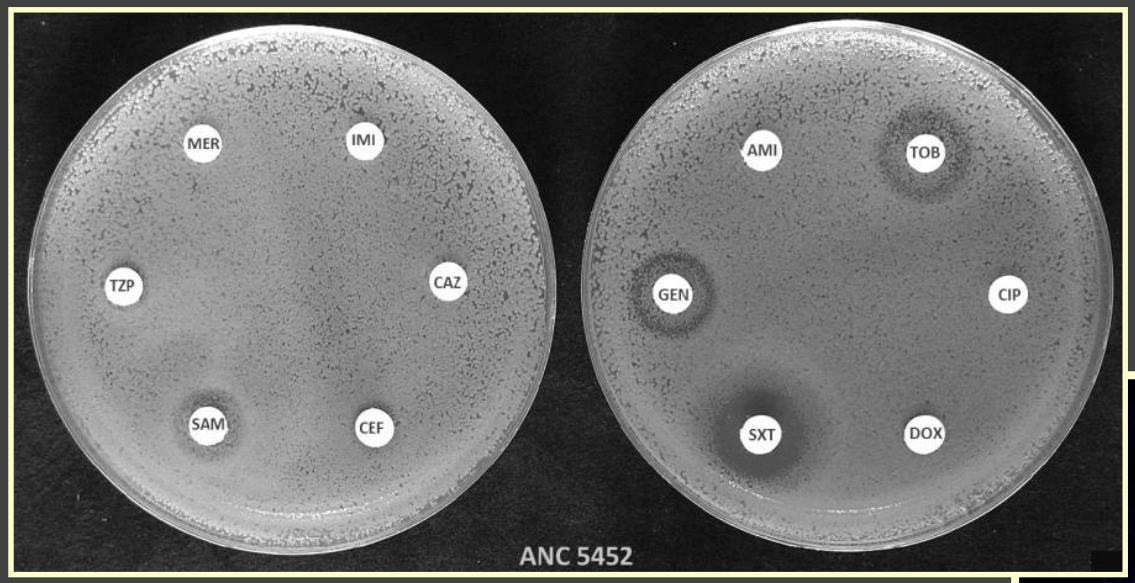
EARS-Net *Acinetobacter* 2023

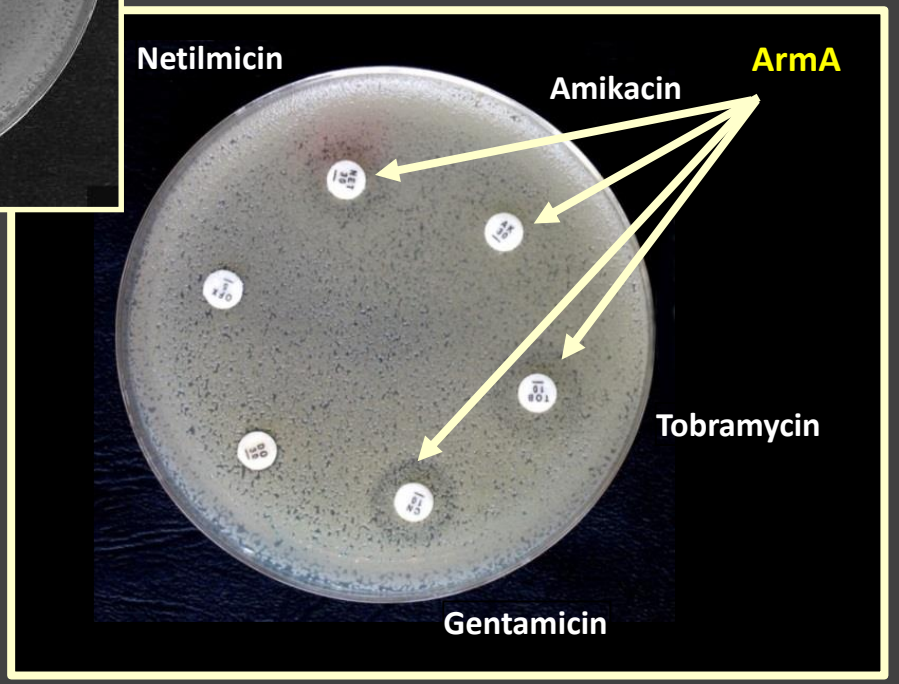
Combined carbapenem/fluoroquinolone/aminoglycoside resistance



MDR *A. baumannii* in Czechia since 2015

IC2 subclone carrying the carbapenemase **OXA-23** and methylase **ArmA**, susceptible only to colistin



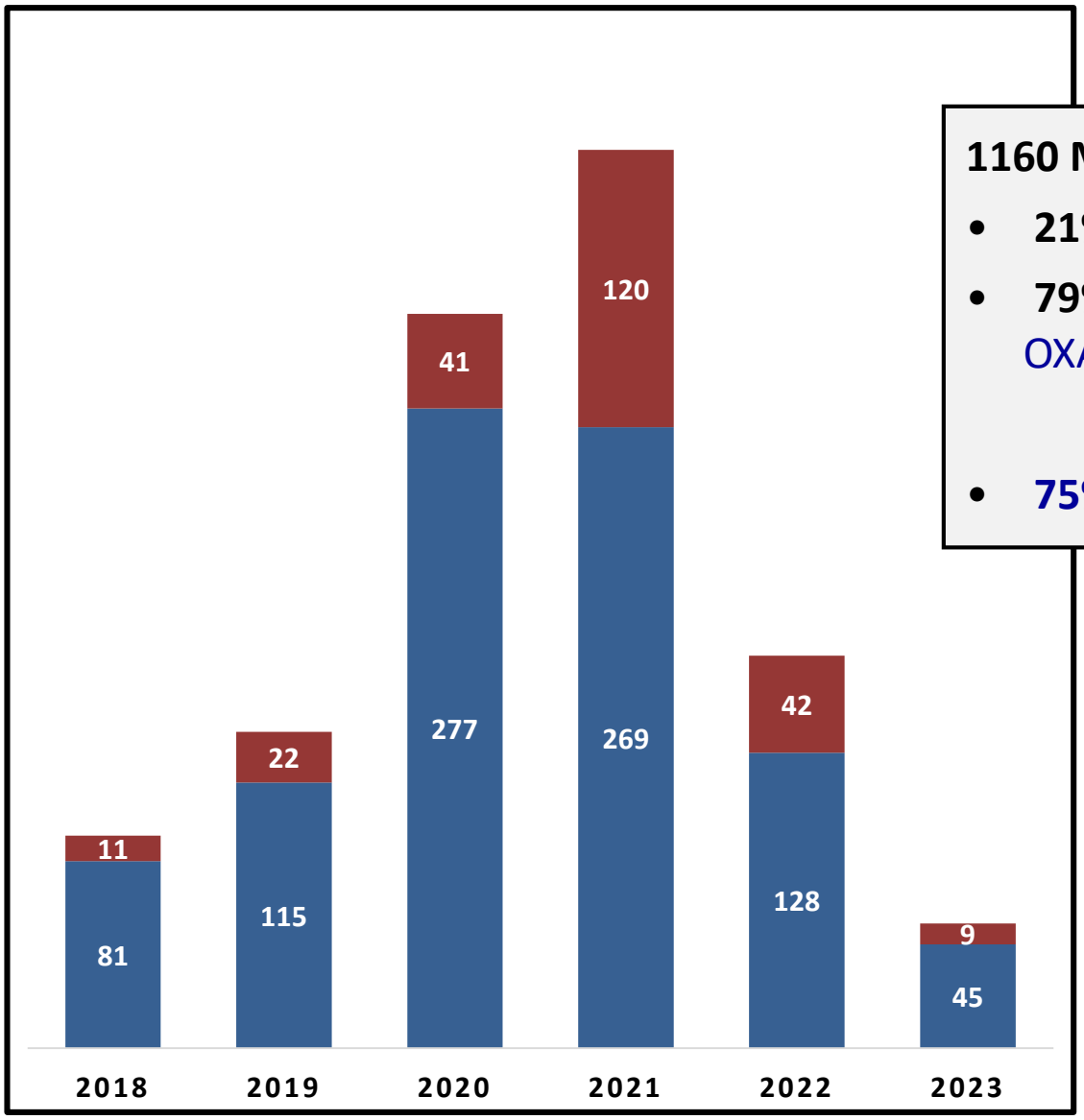


Extenzivně rezistentní kmeny *Acinetobacter baumannii* nesoucí geny pro karbapenemázu OXA-23 a metylázu ArmA v nemocnicích České republiky

Extensively drug-resistant Acinetobacter baumannii strains carrying genes encoding carbapenemase OXA-23 and methylase ArmA in hospitals of the Czech Republic

Lenka Radolfová-Křížová, Martina Maixnerová, Vladislav Jakubů, Alexandr Nemec

MDR/XDR *A. baumannii* in Czechia: 2018–23



1160 MDR/XDR isolates

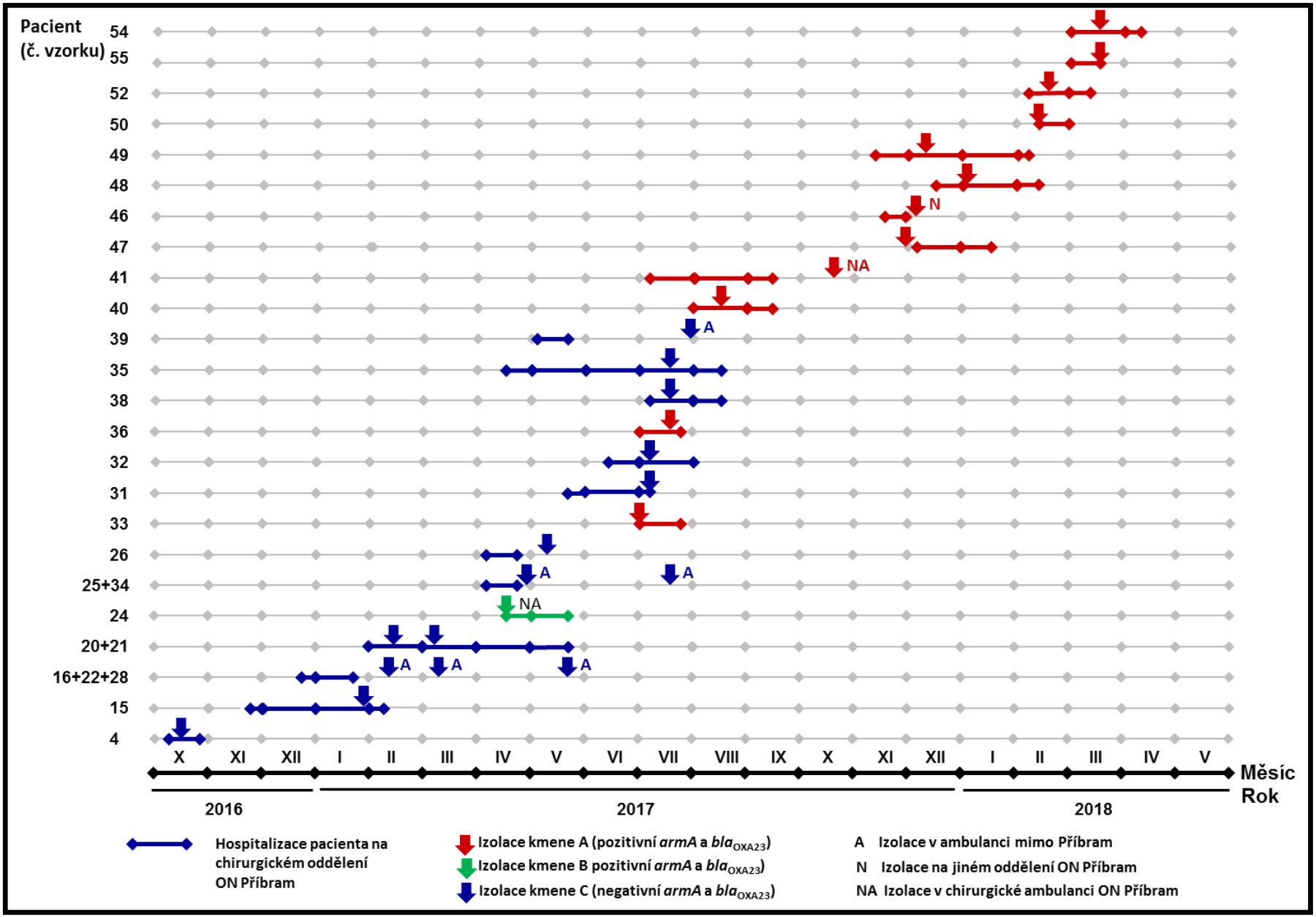
- **21% MDR**
- **79% XDR** (93 % IC2-OXA23-ArmA)

- **75% IC2-OXA23-ArmA**

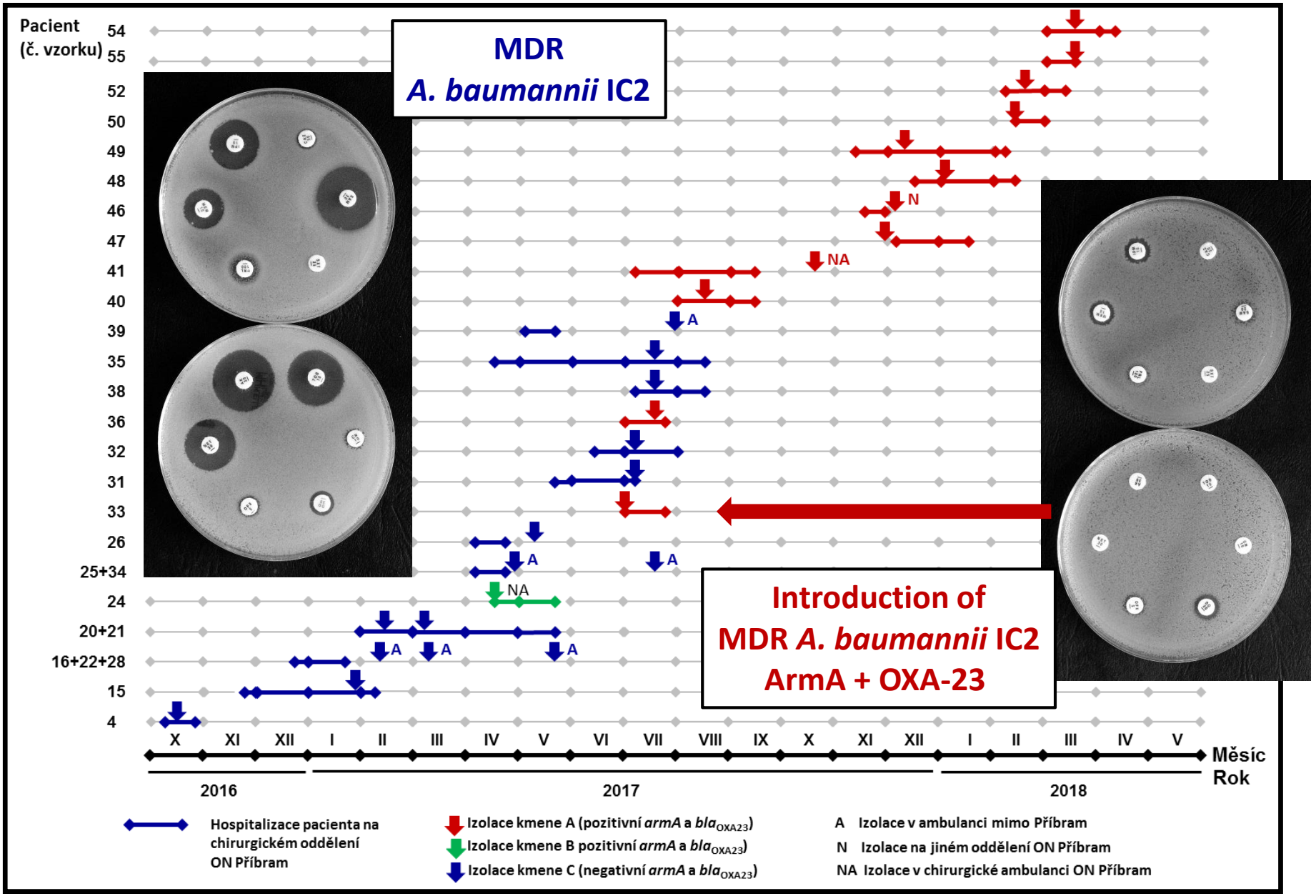
Investigation of an *A. baumannii* outbreak

- **In 2016–2018, MDR *A. baumannii* isolates were found in patients (mostly in wound specimens) treated in the surgical unit of a regional hospital.**
- **These isolates, showing different resistance patterns, were collected either during hospitalization or later during follow-up visits in outpatient clinics.**
- **Aim: To understand the epidemiological background of this issue.**

Colonized/infected patients



Colonized/infected patients



Hospital outbreak - conclusions

- **The large number of MDR *A. baumannii* isolates came from two overlapping monoclonal outbreaks, each caused by a different MDR strain.**
- **The second strain (OXA-23/ArmA) entered the surgical unit through a patient transferred from another hospital.**
- **Both MDR strains stayed in patients for several months even after they were discharged from hospital care.**

Example of:

- **(i) population replacement of an original outbreak strain with a more resistant one**
- **(ii) dissemination of MDR strains owing to long-term colonization of patients**

HAIs - final remarks

- **Millions of people worldwide get HAIs each year, with an estimated average prevalence of 10% among hospitalized patients.**
- **Every healthcare facility should run an effective infection-prevention program to monitor, prevent, and control how infections spread in the hospital environment.**
- **Since infection prevention depends on detecting both infections and colonization by potential pathogens, the clinical microbiology laboratory plays a critical role in the infection prevention program.**

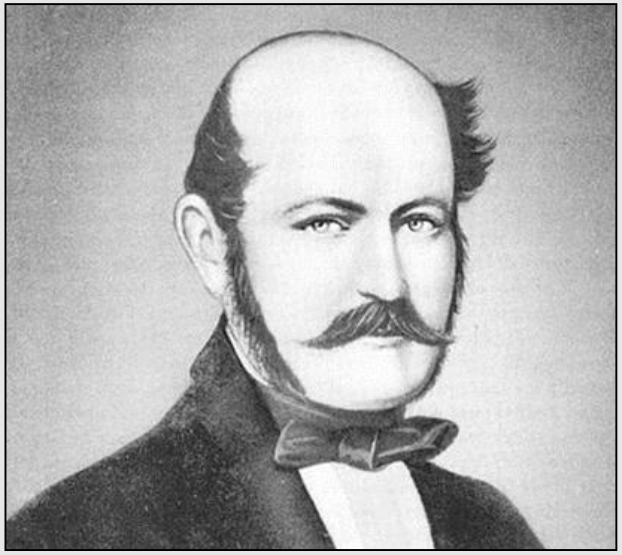
A call to action for each of you:

As a physician, you should do your best to ensure

strict adherence to the principles of infection prevention and control.

Doing so will

save lives, shorten healthcare stays and conserve resources.



Wash your hands!

www.cdc.gov/handwashing/when-how-handwashing.html