Practical application of antibiotic use data

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No conflict of interest

Questions for the ACASEM Survey

Question 1. Antimicrobial stewardship activities in hospitals should be combined with infection control interventions

True False

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Question 2. Point prevalence surveys can be used to assess

- Prevalence of antibiotic use
- Appropriateness of antibiotic therapy by diagnosis
- Appropriateness of antibiotic prescriptions according to the class of antibiotic
- Appropriateness of antibiotic therapy by medical specialization
- Dose and administration route
- All mentioned above

Question 3. Dose and length of antibiotic treatment is dependent on

Localization of disease

Type of microorganism

Speed of response to treatment

All the factors

Sl.vēstures/Amb.kartes Nr.....2646..... Nosūtītājiestāde/nodaļa.....KAN.....

Novertējums SIR sistēmā: S-jūtīgs
I-mēreni jūtīgs
R-rezistents

Izmeklējamais materiāls ...ūs Putes.....

Mikroorganisms Antibiotikas nosaukums	1 Klebsiella pneumoniae	2 ESBL + karbapenemāzes	3
Penicillin			
Oxacillin			
Ampicillin	R		
Amoxicilli/Clavulanate	R		
Piperac./Tazobactam	R		
Aztreonam			
Imipenem	R		
Cephalothin	R		
Cefazolin	R		
Cefoxitin			
Cefuroxime			
Cefoperazone			
Ceftriaxone	R		
Ceftazidime	R		
Cefotaxime	R		
Amikacin			
Gentamicin	R		
Tobramycin	R		
Erythromycin			
Ciprofloxacin	R		
Ofloxacin			
Norfloxacin			
Chlorampfenicol	R		
Clindamycin			
Rifampin			
Doxycycline			
Tetracycline			
Trimethoprim/Sulfamethoxazole	R		
Vancomycin			
Nitrofurantion			
Linezolid			
Meropenem			
Cefepime			
Ampicillin/Sulbactam			

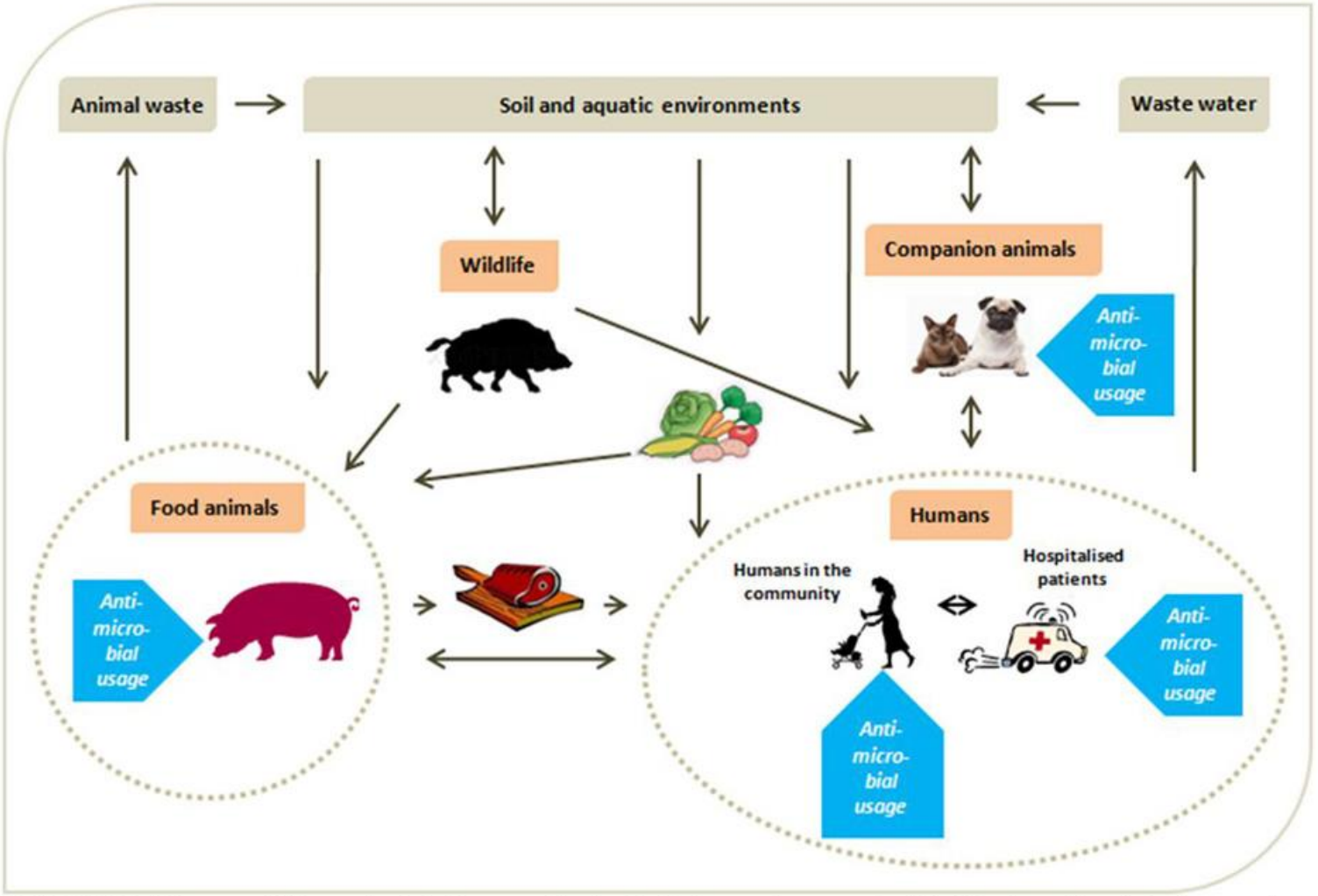
Testēšanas pārskata izsniegšanas datums.....10. 03. 2011

Ārsta paraksts (zīmogs).....

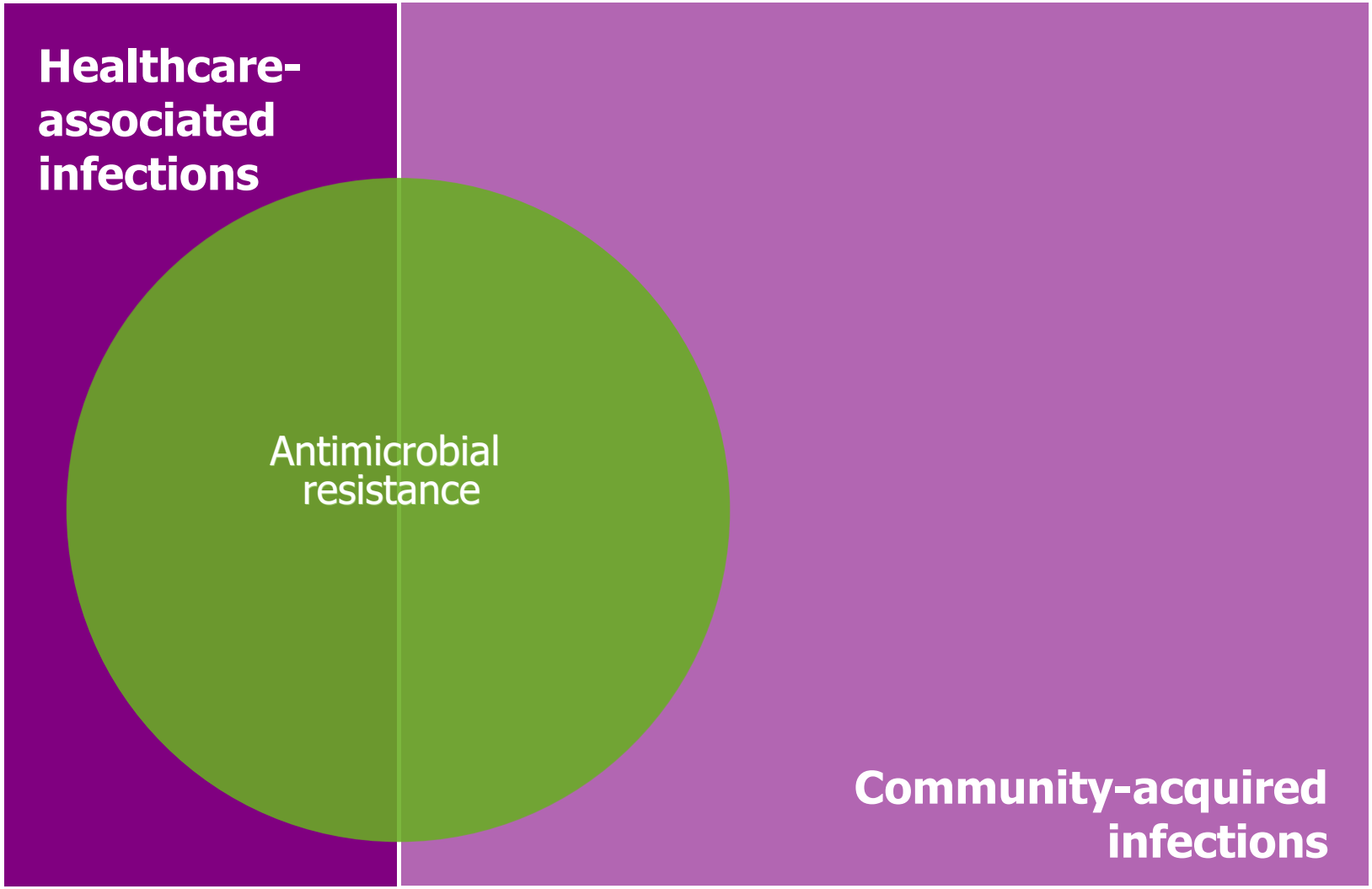
Laboratorijas ārste
TATJĀNA OBIDENOVA

Testēšanas rezultāti attiecās tikai uz noteiktu testēšanas objektu. Bez VSIA P.Stradiņa KUS CL mikrobioloģijas un serologijas nodaļas rakstiskas atļaujas nav atļauta testēšanas pārskata reproducēšana pilnā apjomā.

Exchange of resistance mechanisms and bacteria between different reservoirs

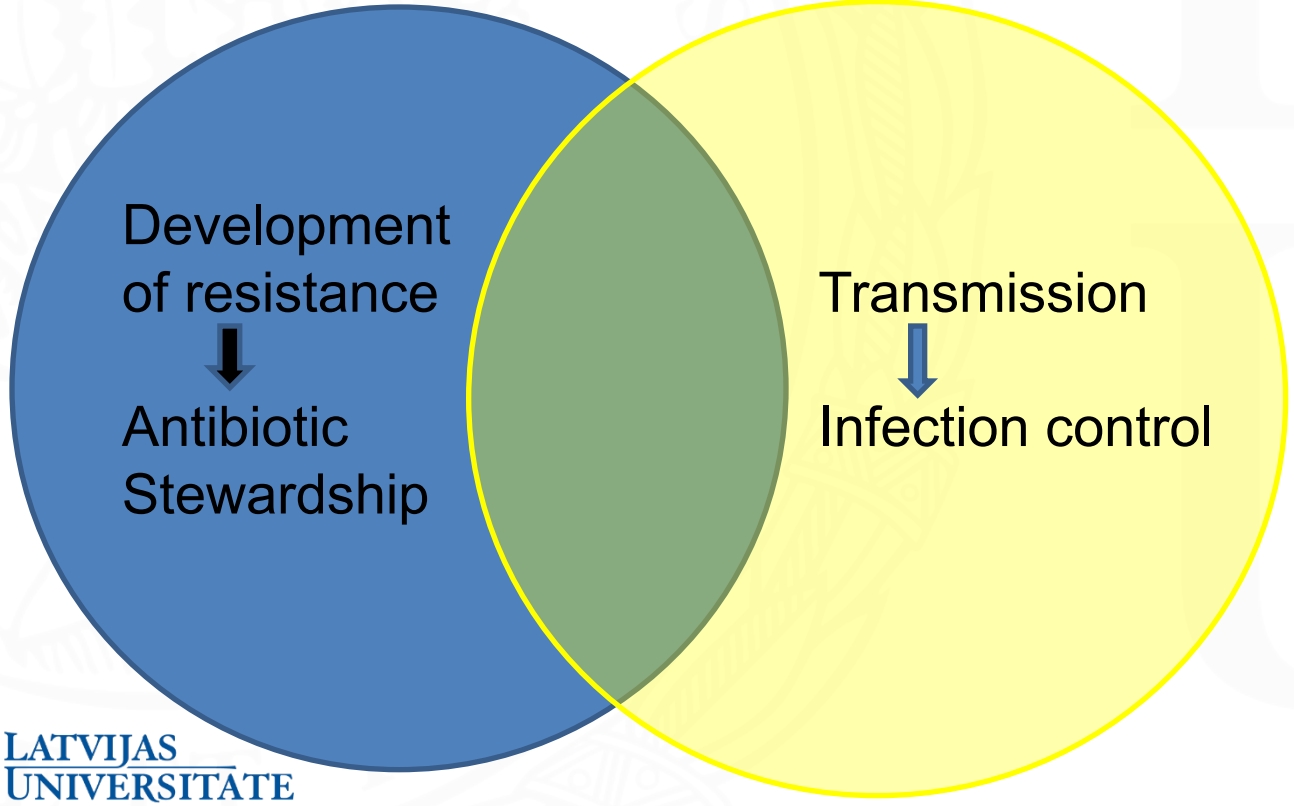


ECDC/EFSA/EMA first joint report on the integrated analysis of the consumption of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from humans and food-producing animals



ECDC official slide

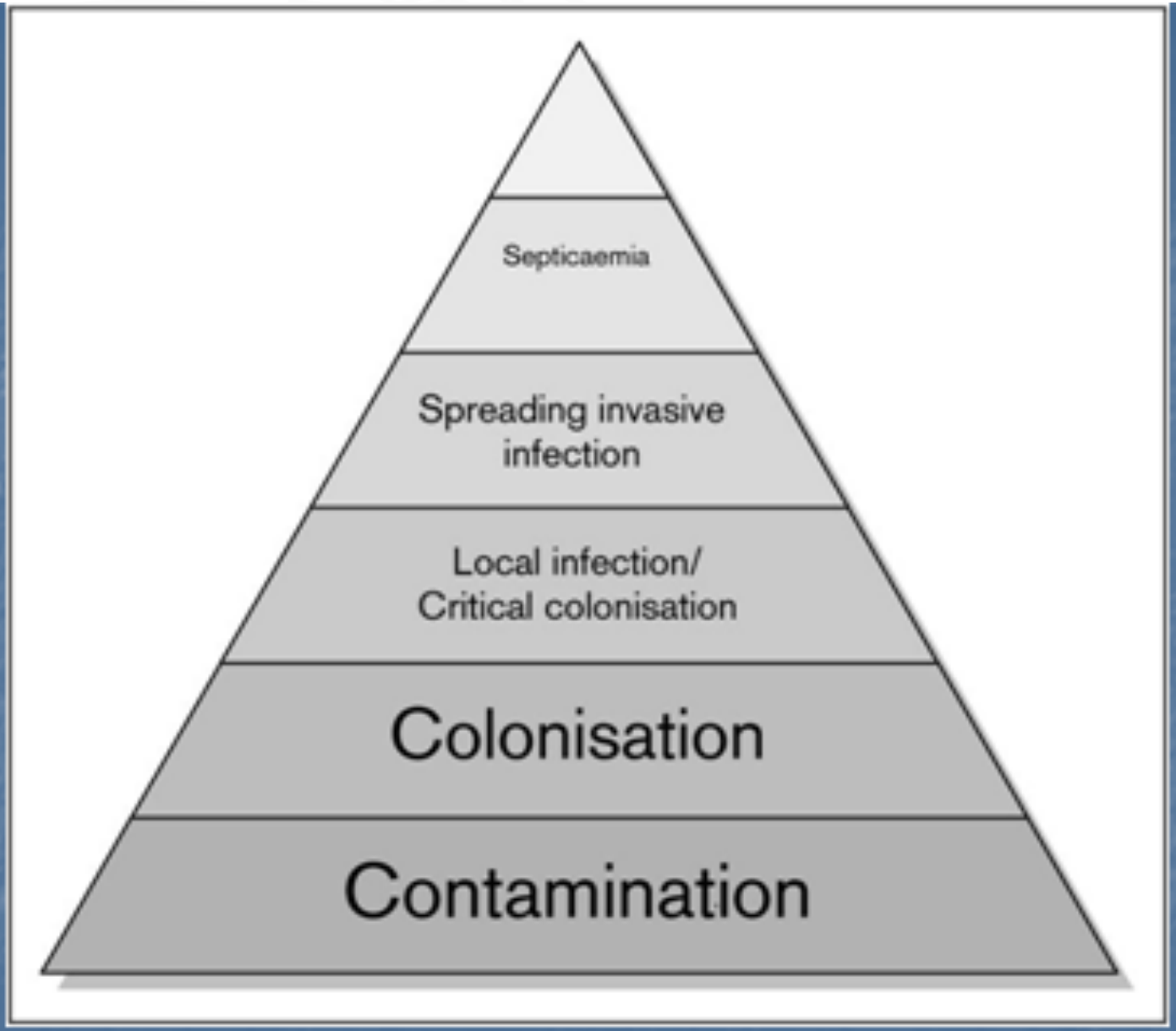
Containment of spread of MDR pathogens



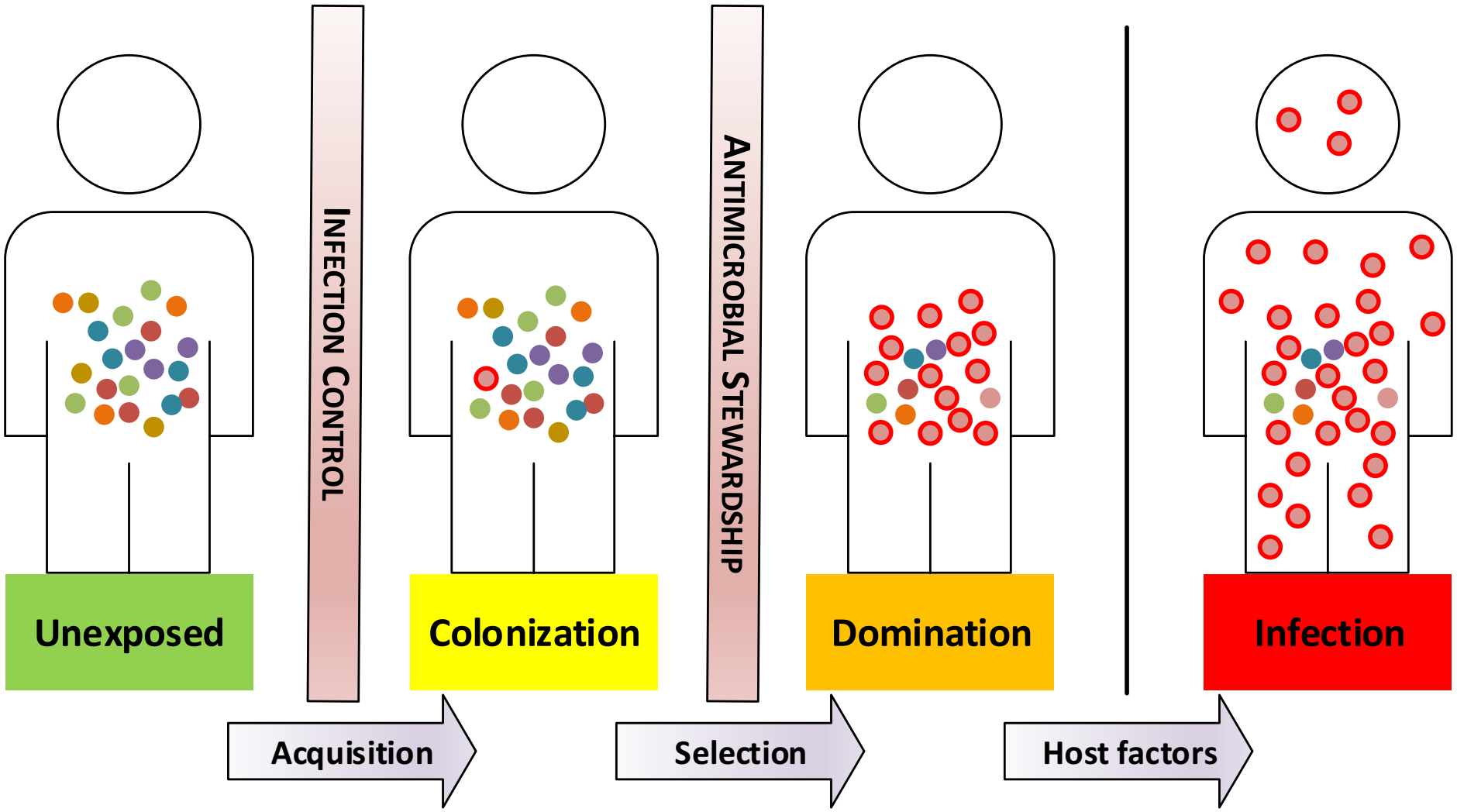
Antimicrobial stewardship (AMS)

- Definition of AMS: a strategy aiming at promoting responsible antibiotic use

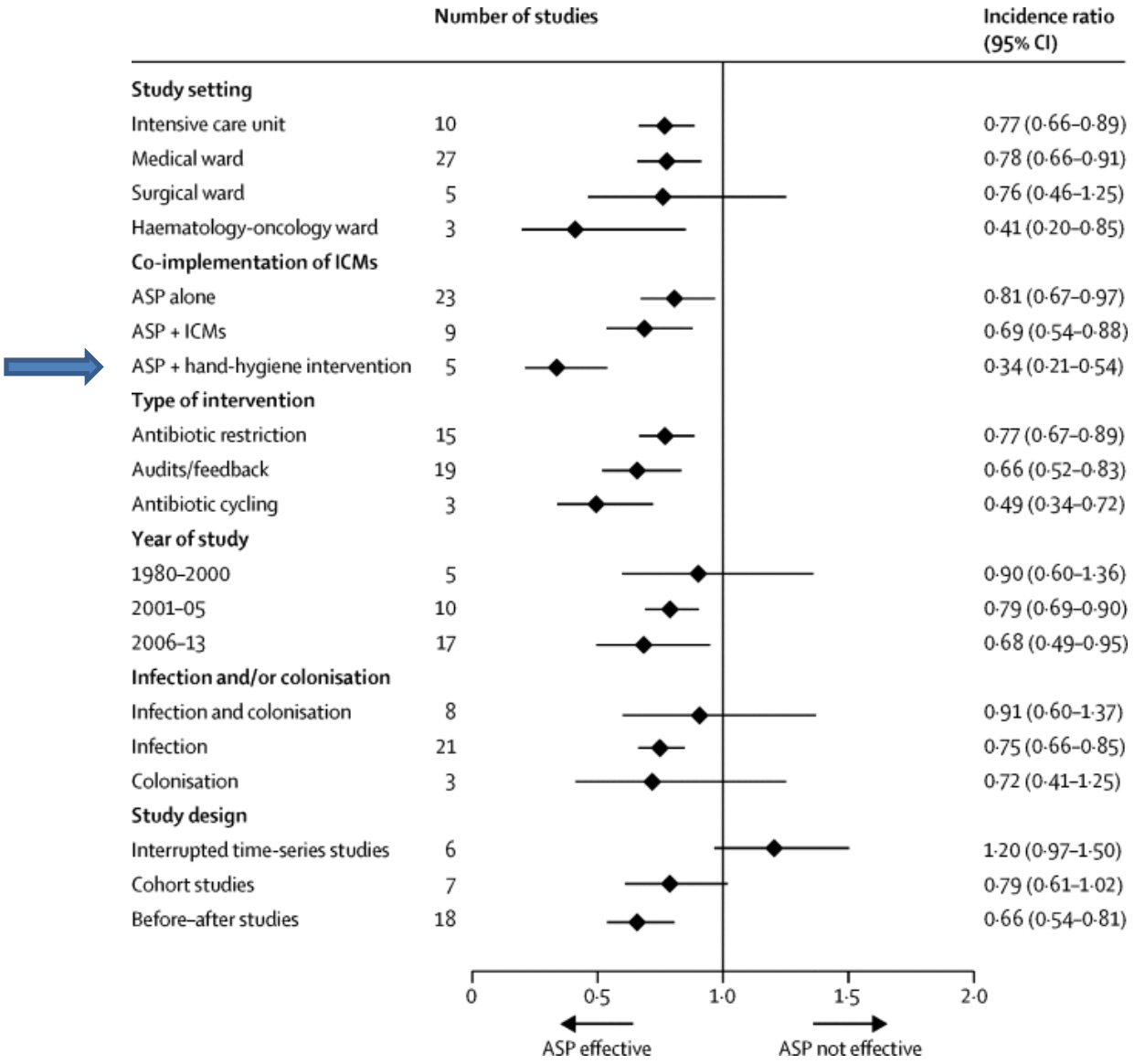
- AMS programme in hospitals= a set of interventions to fine tune antibiotic use in regards to
  - Efficacy
  - Toxicity
  - Resistance-induction
  - *Clostridium difficile* induction
  - IV to PO switch
  - Cost
  - Discontinuation



Mangram et al 1999 Infect Contr Hosp Epid

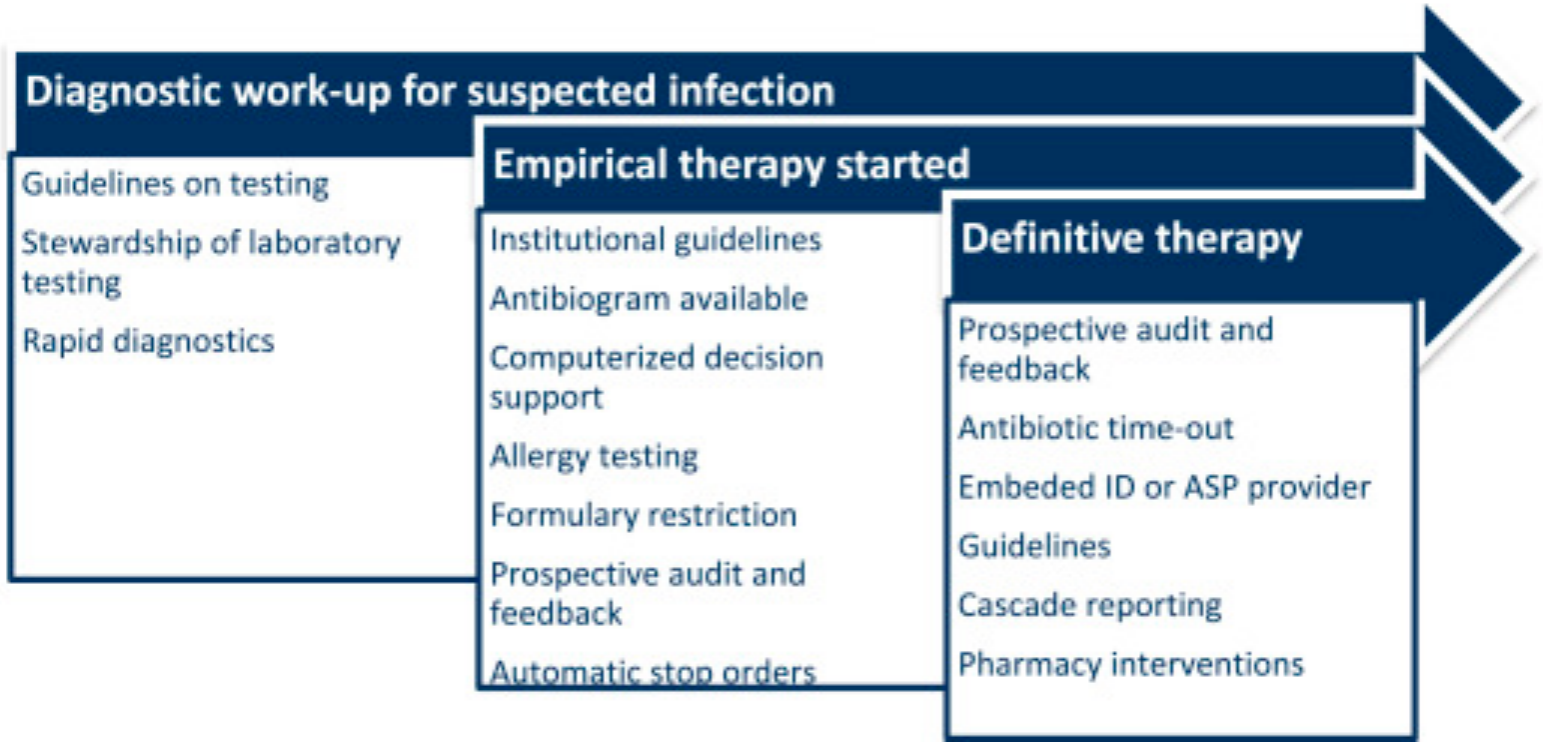


Prof. Dr. Jörg Vehreschild Personal communication



Baur D. Systematic review 2017 Lancet infectious Diseases

Opportunities antibiotic stewardship policies



Doemberg SB et al, 2017 Infectious Disease Clinics of Northern America

Where to start AMS activity?

- Clear opportunity to improve
  - PPS data
  - Laboratory surveillance reports
  - Healthcare associated infection surveillance
- Potential high impact on use and spread of resistance
  - Intensive care units
  - Transplantation
  - Nephrology

How to start?

- Start with friendly collegues
- Frequent personal presence
- Start small
- Build on success
- Monitor your impact and adapt
- Avoid multiplicity of advisers for the same patient/department
- Feedback to collegues
  - Short and easy to understand
  - Real time involvement

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Planning stage

- Administrative support
- Creation of the team
- Choose monitoring system
- List of indicators
- Information for the department

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How to measure and assess antibiotic use?

- Electronic records RDD or PDD
- Point prevalence surveys PDD
- Pharmacy
  - DDD/stays,
  - Packages
  - Grams
  - Euros

DDD usefullness

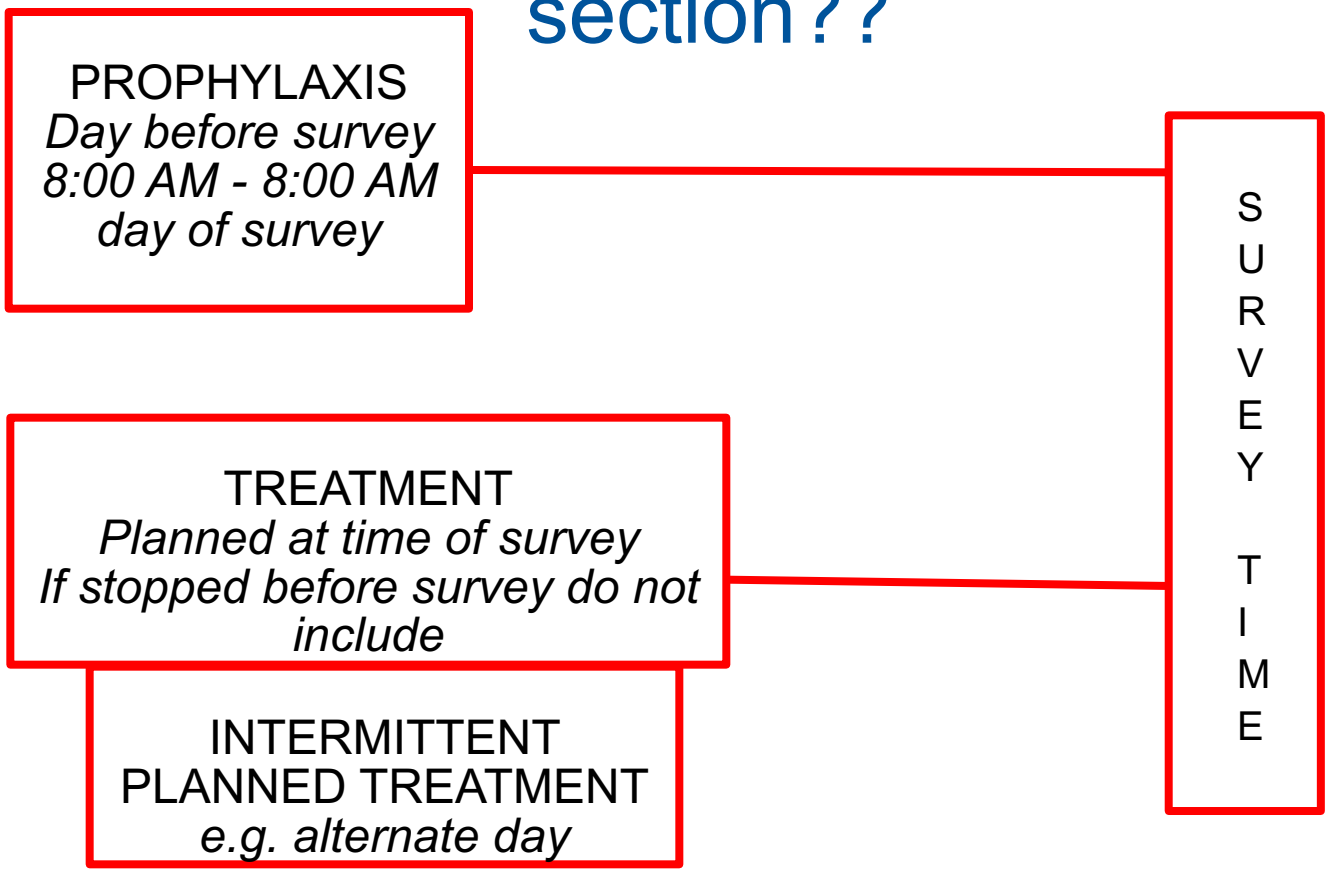
- Reduction in general consumption DDD/stays
- Reduction in consumption of selected antibiotics DDD/stays
- Replacement by different antibiotic DDD/stays

- Difficult due to patient mix

Point prevalence approach

- One day, one clinical unit
- All patients on antibiotics/all patients
  - Patient demographics
  - Reason for antibiotics
  - Antibiotic
  - Dose

What to include on antimicrobial section??



Carl Suetens. Personal communication

European Prevalence Survey of Healthcare-Associated Infections and Antimicrobial Use
Form A. Patient-based data (standard protocol)

Patient data (to collect for all patients)

Hospital code ____

Ward name (abbr.)/Unit Id ____ Ward specialty ____

Survey date: ___ / ___ / _____ (*dd/mm/yyyy*)

Patient Counter: _____

Age in years: ____ yrs; Age if < 2 year old: _____ months

Sex: M F **Date of hospital admission:** ___ / ___ / _____ *dd / mm / yyyy*

Consultant/Patient Specialty: ____

Surgery since admission:

O No surgery O Minimal invasive/non-NHSN surgery

O NHSN surgery O Unknown

McCabe score: O Non-fatal disease

O Ultimately fatal disease

O Rapidly fatal disease

O Unknown

Central vascular catheter:	O No	O Yes	O Unk
Peripheral vascular catheter:	O No	O Yes	O Unk
Urinary catheter:	O No	O Yes	O Unk
Intubation:	O No	O Yes	O Unk
Patient receives **antimicrobial(s)**(1):	O No	O Yes	
Patient has **active HAI**(2):	O No	O Yes	

IF YES

(1) At the time of the survey, except for surgical prophylaxis 24h before 8:00 AM on the day of the survey; if yes, fill antimicrobial use data; (2) [infection with onset ≥ Day 3, OR SSI criteria met (surgery in previous 30d/1yr), OR discharged from acute care hospital <48h ago, OR CDI and discharged from acute care hospital < 28 days ago OR onset < Day 3 after invasive device/procedure on D1 or D2] AND [HAI case criteria met on survey day OR patient is receiving (any) treatment for HAI AND case criteria are met between D1 of treatment and survey day]; if yes, fill HAI data

Antimicrobial (generic or brand name)	Route	Indication	Diagnosis (site)	Reason in notes

Route: P: parenteral, O: oral, R: rectal, I: inhalation; **Indication**: CI - LI - HI: treatment intention for community-acquired (CI), long/intermediate-term care-acquired (LI) or acute hospital-acquired infection (HI); surgical prophylaxis: SP1: single dose, SP2: one day, SP3: >1day; MP: medical prophylaxis; O: other; UI: Unknown indication; **Diagnosis**: see site list, only for treatment intention **Reason in notes**: Y/N

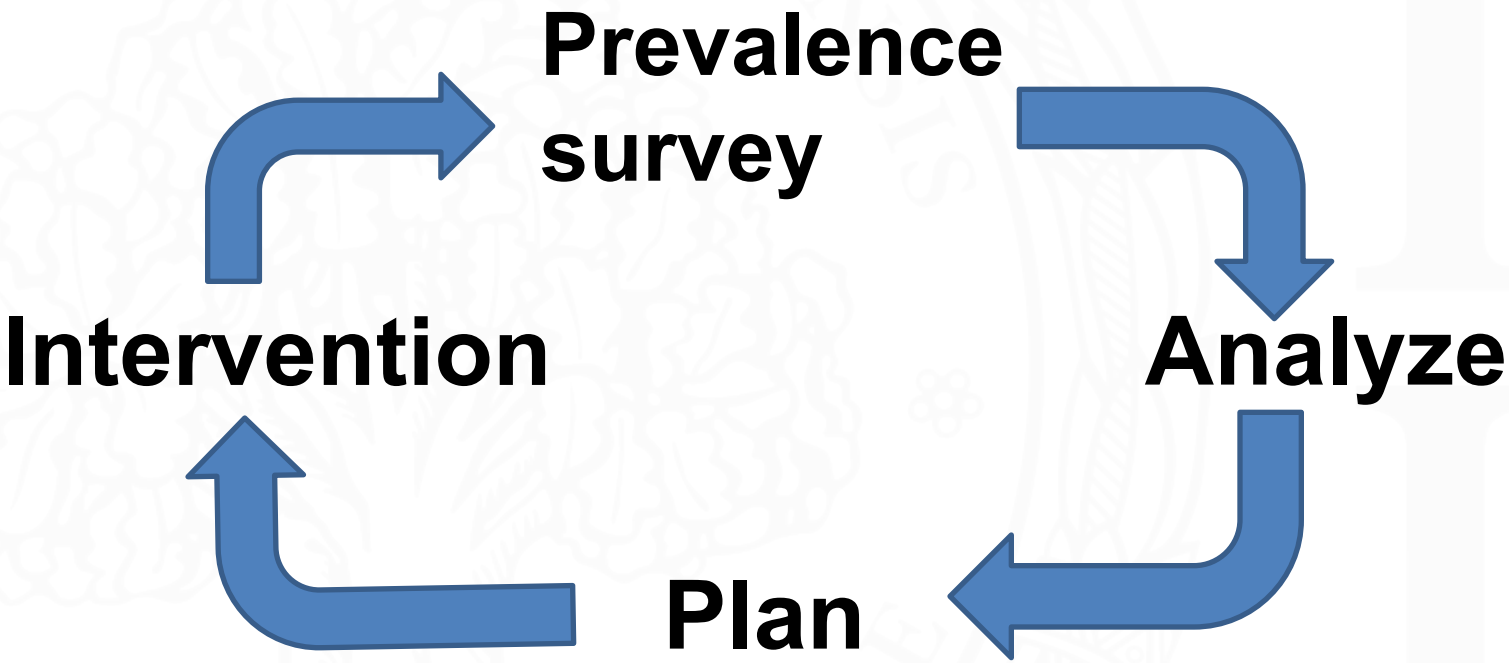
	HAI 1		HAI 2		HAI 3	
Case definition code						
Relevant device in situ before onset(3)	O Yes O No O Unknown		O Yes O No O Unknown		O Yes O No O Unknown	
Present at admission	O Yes O No		O Yes O No		O Yes O No	
Date of onset(4)	___ / ___ / _____		___ / ___ / _____		___ / ___ / _____	
Origin of infection	O current hospital O other hospital O other origin/ unk		O current hospital O other hospital O other origin/ unk		O current hospital O other hospital O other origin/ unk	
If BSI: source(5)						
	MO-code	R(6)	MO-code	R(6)	MO-code	R(6)
Microorganism 1						
Microorganism 2						
Microorganism 3						

(3) relevant device use (intubation for PN, CVC for BSI, urinary catheter for UTI) in 48 hours before onset of infection (even intermittent use), 7 days for UTI; (4) Only for infections not present/active at admission (dd/mm/yyyy); (5) C-CVC, C-PVC, S-PUL, S-UTI, S-DIG, S-SSI, S-SST, S-OTH, UO, UNK; (6) AMR marker 0,1,2 or 9, see table

GLOBAL-PPS PATIENT Form (Please fill in one form per patient on antimicrobial treatment/prophylaxis)

Ward Name/code	Activity [i] (M, S, IC)	Patient Identifier [ii]	Survey Number [iii]	Patient Age [iv]			Gender M or F
				Years (if ≥ 2 years)	**Months** (1-23 month)	**Days** (if <1 month)	

Antimicrobial Name [v]		1.		2.		3.		4.		5.	
Single Unit Dose [vi]	**Unit** (g, mg, or IU) [vii]										
Doses/ day [viii]	**Route** (P, O, R, I) [ix]										
Diagnosis [x] (see appendix II)											
Type of indication [xi] (see appendix III)											
Reason in Notes (Yes or No) [xii]											
Guideline Compliance (Y, N, NA, NI) [xiii]											
Is a stop/review date documented? (Yes or No)											
Treatment (E: Empirical; T: Targeted)											
Treatment based on biomarker data (Yes or No) [xiva]											
If yes, on which biomarker [xivb] (fill in: CRP, PCT or other)											
Targeted treatment choice based on microbiology data (Yes, No) [xv]											
IF YES: (This section is to be filled in only if the treatment choice is based on microbiology data AND the organism is one of the following)											
MRSA (Yes or No) [xvi]											
MRCoNS (Yes or No) [xvii]											
VRE (Yes or No) [xviii]											
ESBL-producing Enterobacteriaceae (Yes or No) [xix]											
3rd generation cephalosporin resistant Enterobacteriaceae non-ESBL producing											



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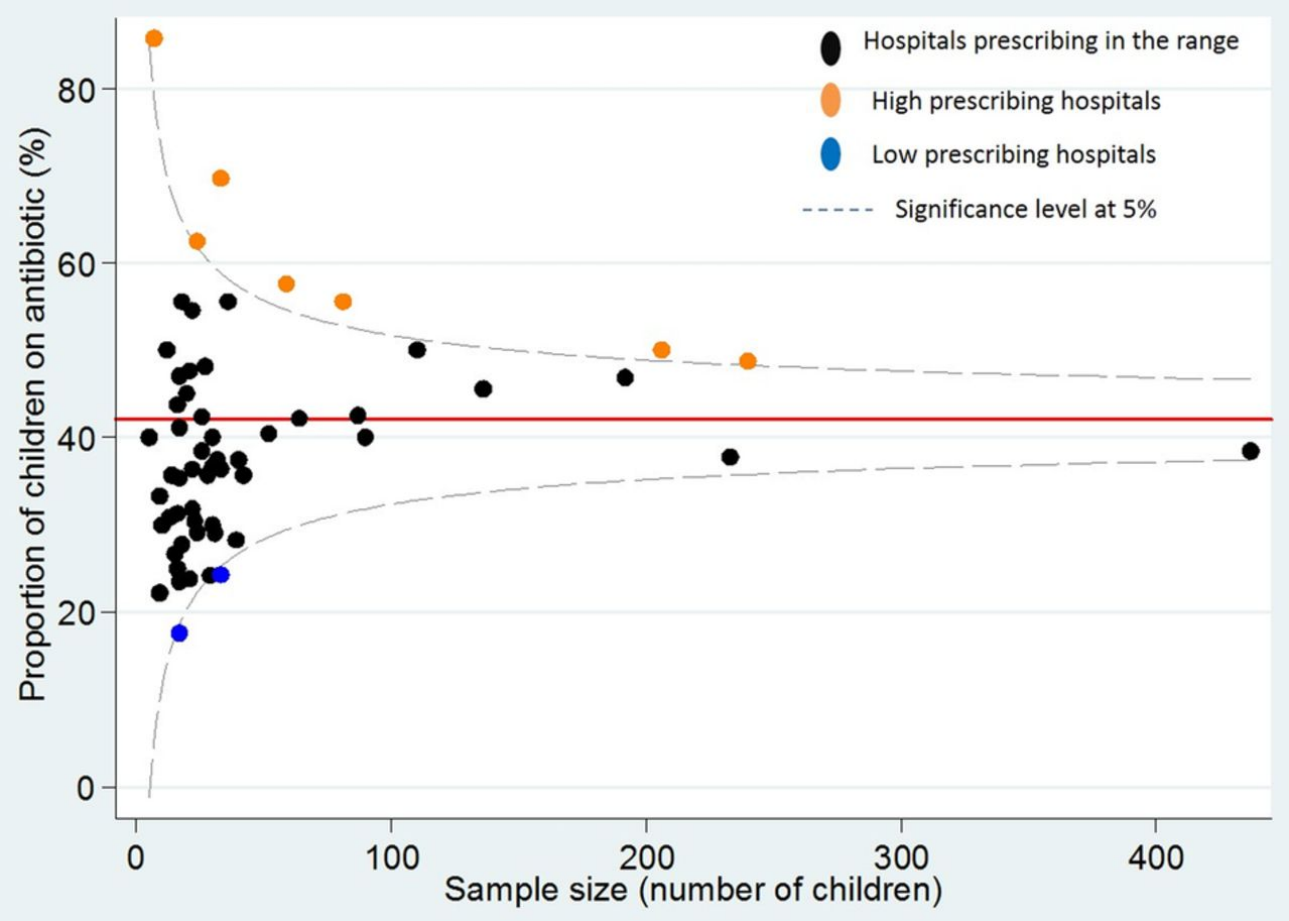
Interventions measured by point prevalence (Process measures)

- New formulary and education
- New guidelines and education
- Shortened laboratory reports
- Switch from IV to oral

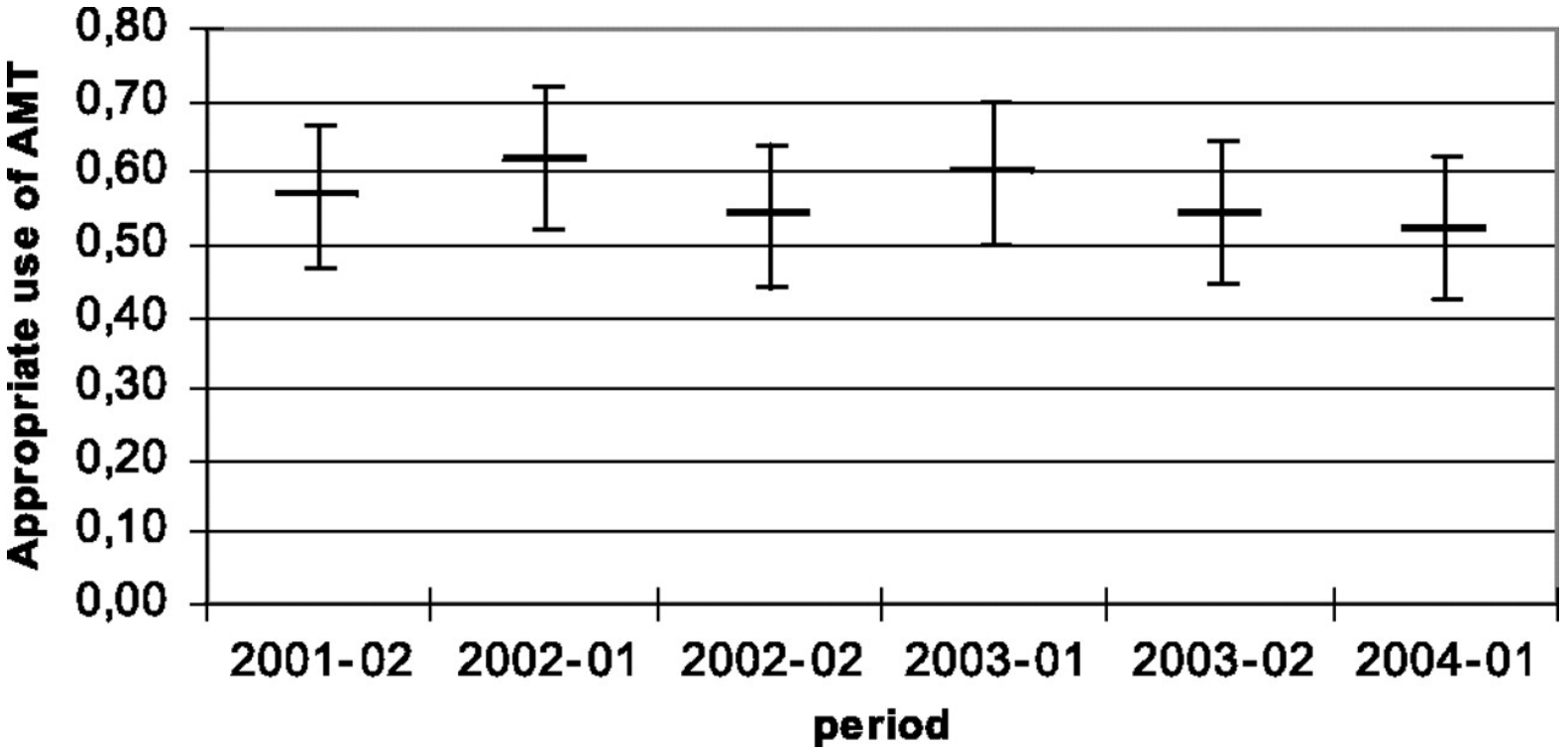
Funnel plot comparing hospital prescribing in the UK using proportion of children on antibiotics.



Myriam Gharbi et al. BMJ Open 2016;6:e012675

BMJ Open

Appropriateness of use of AMT (95% confidence interval) in six surveys between 2001 and 2004.



Ina Willemsen et al. Antimicrob. Agents Chemother. 2007;51:864-867

Antimicrobial Agents and Chemotherapy

Appropriateness of antibiotic prescriptions assesed with point prevance survey

- Appropriateness of antibiotic prescriptions according to the class of antibiotic
- Appropriateness of antibiotic therapy by diagnosis
- Appropriateness of antibiotic therapy by medical specialization

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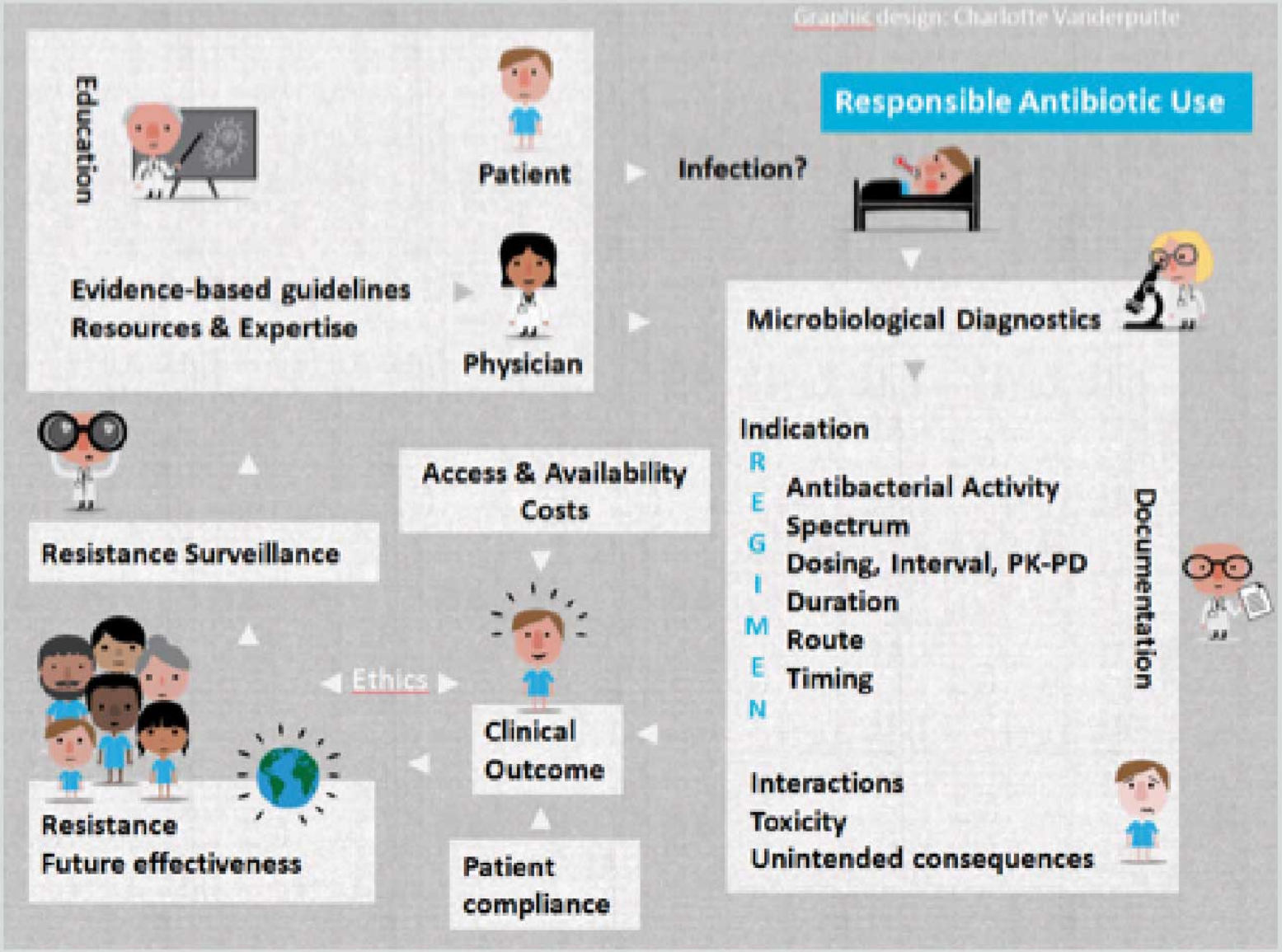
Willemsen I et al Eurosurveillance 2010

High quality of each prescription: ultimate goal of all AMS programmes.

Figure 1: **The 22 domains of responsible antibiotic use identified through a systematic review. On the right side of the figure are the domains affecting the individual patient and on the left of the figure are the societal domains**



Impact of diagnostic testing

- Accurate identification of bacterial infection and rapid identification and susceptibility testing can improve antibiotic use and clinical outcomes
- Negative test results can assist providers with stopping antibiotics
- Cascade reporting of antibiotics may improve appropriate selection of antibiotics

Resistance testing

- Strains are sorted according to level of Minimal Inhibitory Concentration (MIC) versus reference breakpoints
- c and C are the minor and major breakpoints

Susceptible		Intermediate		Resistant
MIC <	c	≤ MIC <	C	≤ MIC

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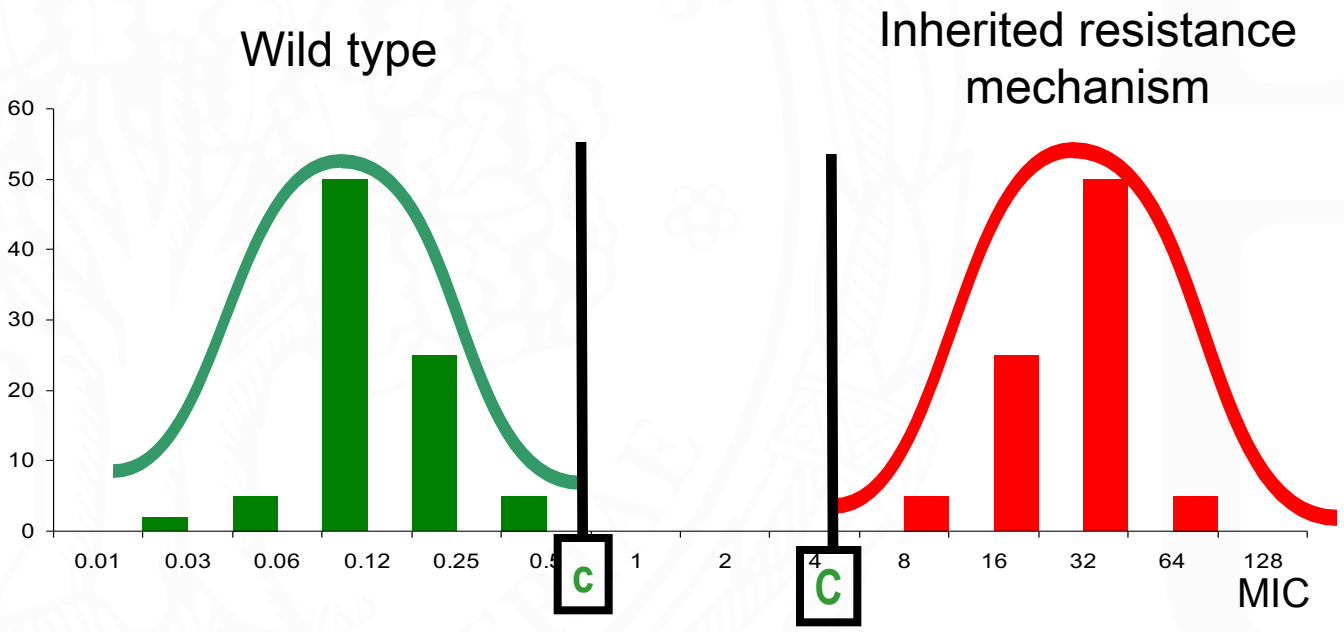
Breakpoints

Breakpoints are determined using two approaches

- Pharmacological concept
- Clinical and epidemiological concept

- Breakpoints are the expression of a consensus among the scientific community at a given time in a country or region

The epidemiological concept for breakpoints



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Dosages

EUCAST Clinical Breakpoint Tables v. 7.1, valid from 2017-0

EUCAST breakpoints are based on the following dosages (see section 8 in Rationale Documents).

Penicillins	Standard dose	High dose
Benzylpenicillin	0.6 g x 4 iv	2.4 g x 6 iv
Ampicillin	0.5 -1 g x 3-4 iv	1-2 g x 4-6 iv
Ampicillin-sulbactam	3 g x 3 iv	4 g x 3 iv
Amoxicillin	0.5 g x 3 iv Oral dosage under discussion	2 g x 6 iv Oral dosage under discussion
Amoxicillin-clavulanic acid	(1 g amoxicillin + 0.2 g clavulanic acid) x 3 iv Oral dosage under discussion	(2 g amoxicillin + 0.2 g clavulanic acid) x 3 iv Oral dosage under discussion
Piperacillin	4 g x 3 iv	4 g x 4 iv
Piperacillin-tazobactam	(4 g piperacillin + 0.5 g tazobactam) x 3 iv	(4 g piperacillin + 0.5 g tazobactam) x 4 iv
Ticarcillin	3 g x 4 iv	3 g x 6 iv
Ticarcillin-clavulanic acid	(3 g ticarcillin + 0.1 g clavulanic acid) x 4 iv	(3 g ticarcillin + 0.1 g clavulanic acid) x 6 iv
Temocillin		
Phenoxymethylpenicillin	0.5-2 g x 3-4	None
Oxacillin	Clinical breakpoints not available	Clinical breakpoints not available
Cloxacillin	0.5 g x 4 oral or 1 g x 4 iv	1 g x 4 oral or 2 g x 6 iv
Dicloxacillin	0.5-1 g x 4 oral or 1 g x 4 iv	2 g x 4 oral or 2 g x 6 iv
Flucloxacillin	1 g x 3 oral or 2 g x 4 iv	1 g x 4 oral or 2 g x 6 iv
Mecillinam	0.2-0.4 g x 3 oral	None

Microorganism	Antibiotic	MIC_{50} (mg L^{-1})	MPC_{50} (mg L^{-1})
Pseudomonas aeruginosa	Imipenem	2	32
	Meropenem	0.5	8
	Doripenem	0.5	4
Escherichia coli	Imipenem	0.25	0.5
	Meropenem	0.03	0.06
	Doripenem	0.03	0.125

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Modified from Credito et al. (2010)

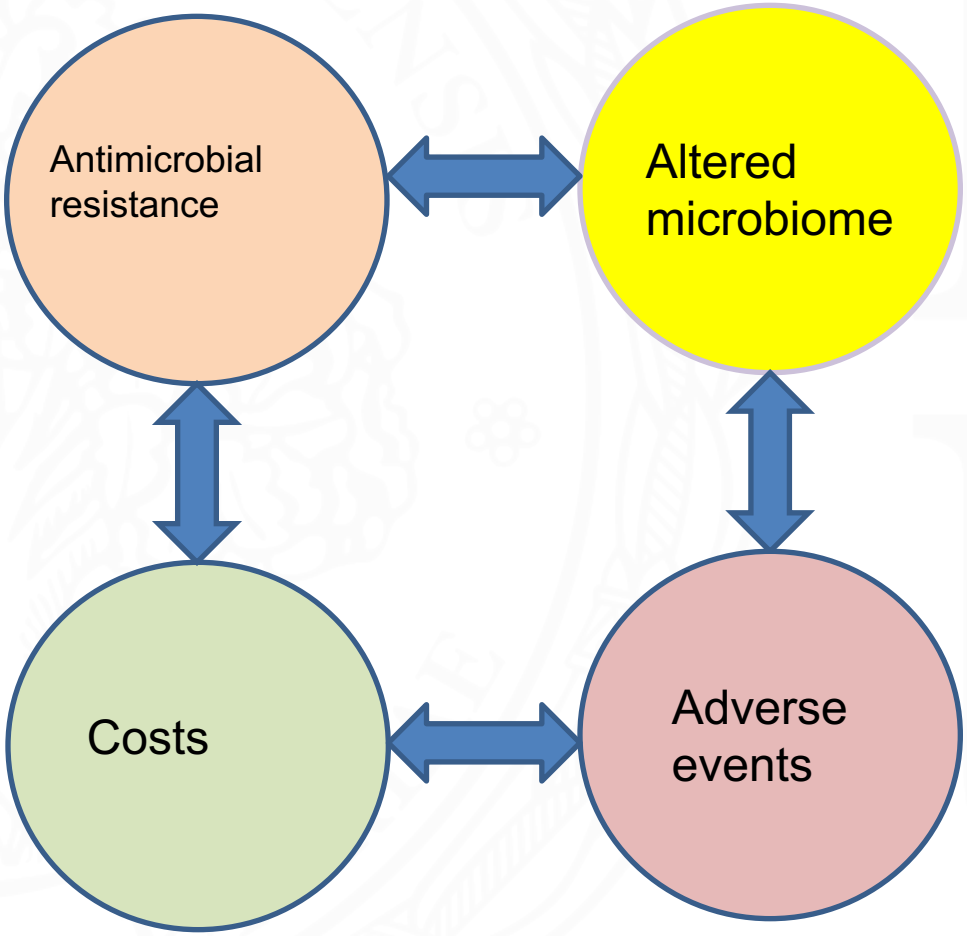
THE GLOBAL DEFINITION OF RESPONSIBLE ANTIBIOTIC USE: THREE HIGHLIGHTS

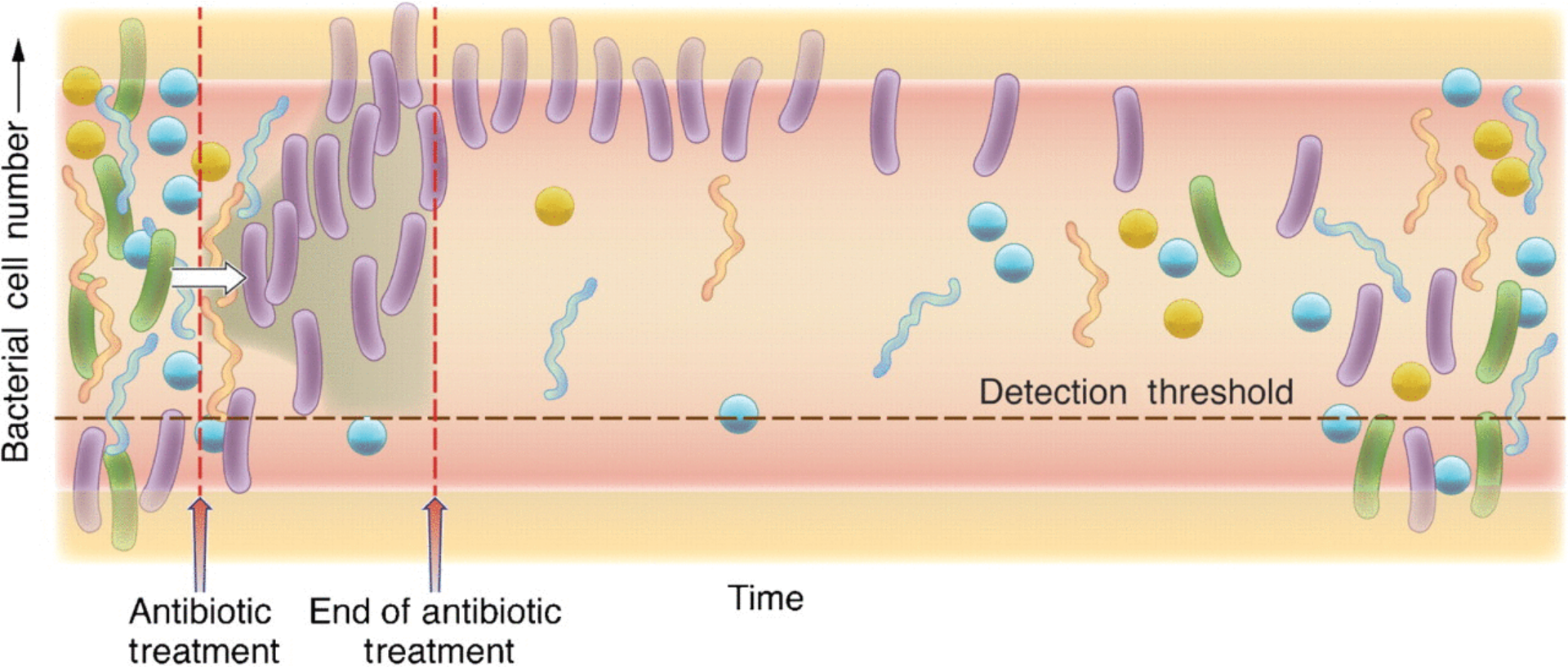
- Education
- Duration
- Access and availability

When the antibiotic treatment should be stopped

- When the benefit to the patient (but also for society) no longer outweights the potential harm

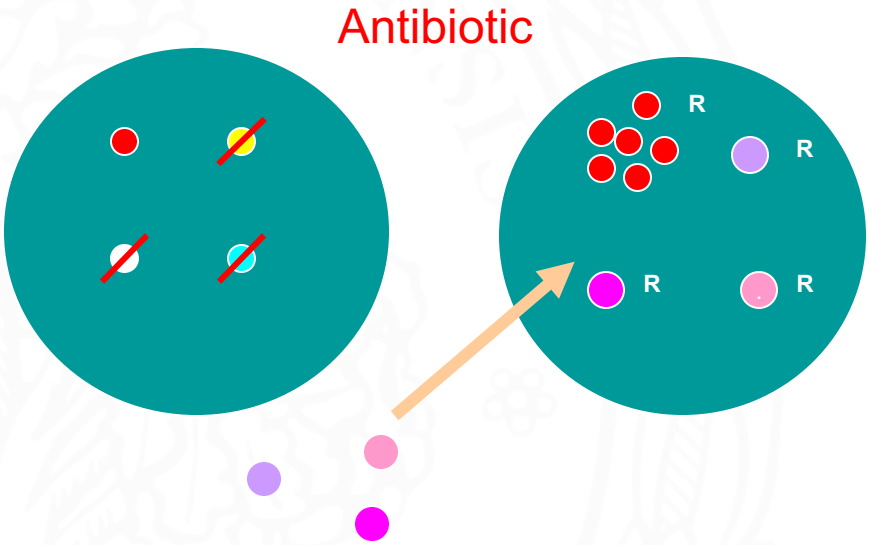
What are the harms of inappropriately prolonged antibiotic therapy?





Jernberg C et al Microbiology 2010 156: 3216-3223, doi: 10.1099/mic.0.040618-0

Antibiotic resistance selection pressure



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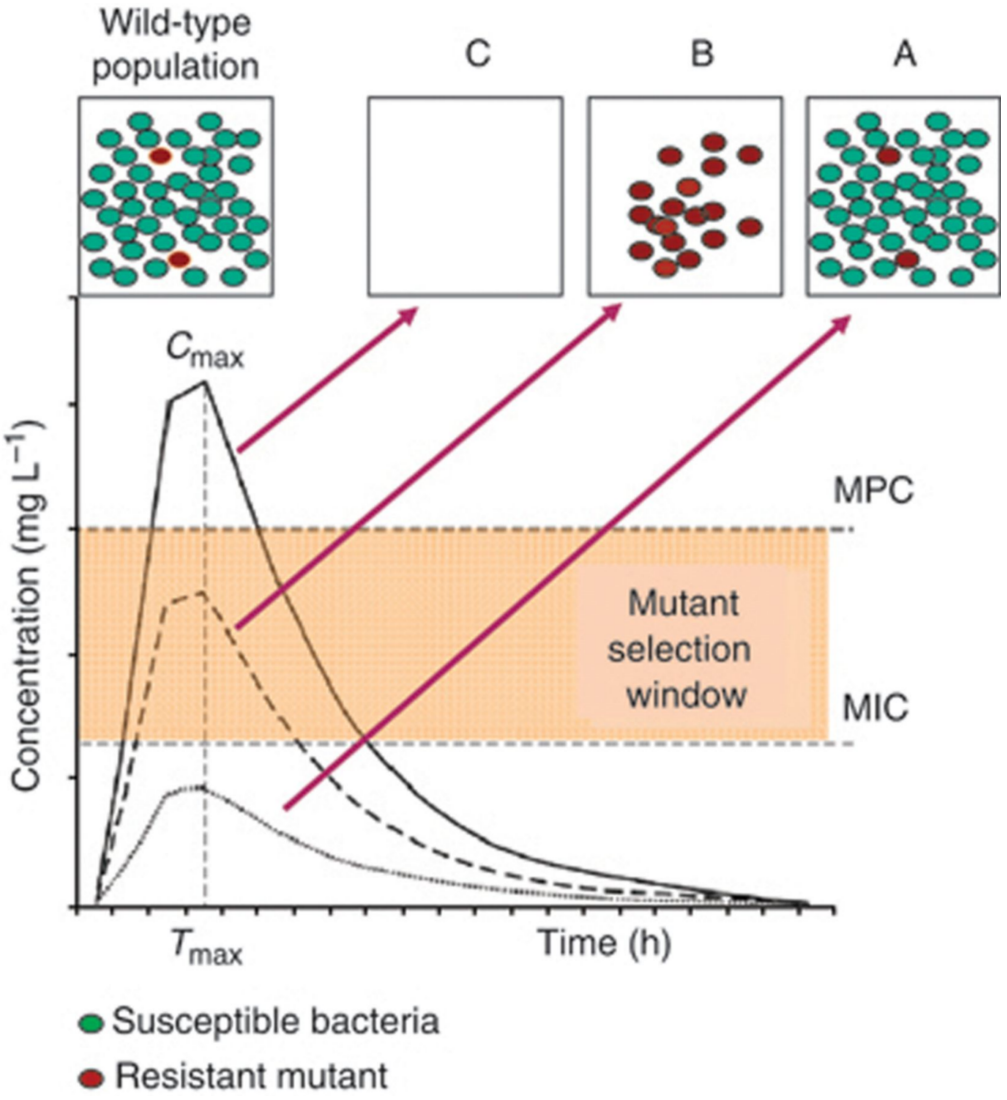
Macroepidemiological considerations

- Penicillins
- Aminoglycosides
- Nitrofurantoin, trimetroprim
- First generation cephalosporins
- Second generation cephalosporins
- Tetracyclines
- Macrolides
- 3rd generation cephalosporins
- Fluoroquinolones
- Carbapenems



From: Emergence and spread of antibiotic resistance following exposure to antibiotics
FEMS Microbiol Rev. 2011;35(5):977-991. doi:10.1111/j.1574-6976.2011.00295.x

How to stop antibiotics earlier?

- Reduction in procalcitonin and CRP
- No fever for 2-3 days
- Feeling well, eating well

Conclusions

- AMS interventions should be targeted and well planned
- Different methods can be used to asses the impact of AMS activities
- Microbiology laboratory support is essential to assure quality of AMS
- Selection of optimal treatment regimen for each patient is essential for credibility of AMS programmes

Questions for the ACASEM Survey

Question1. Antimicrobial stewardship activities in hospitals should be combined with infection control interventions

True

Point prevalence surveys can be used to assess impact of AMS interventions

- Prevalence of antibiotic use
- Appropriateness of antibiotic prescriptions according to the class of antibiotic
- Appropriateness of antibiotic therapy by diagnosis
- Appropriateness of antibiotic therapy by medical specialization
- All mentioned above

Dose and length of antibiotic treatment is dependent on

Type of disease

Type of microorganism

Speed of response to treatment

All of the factors