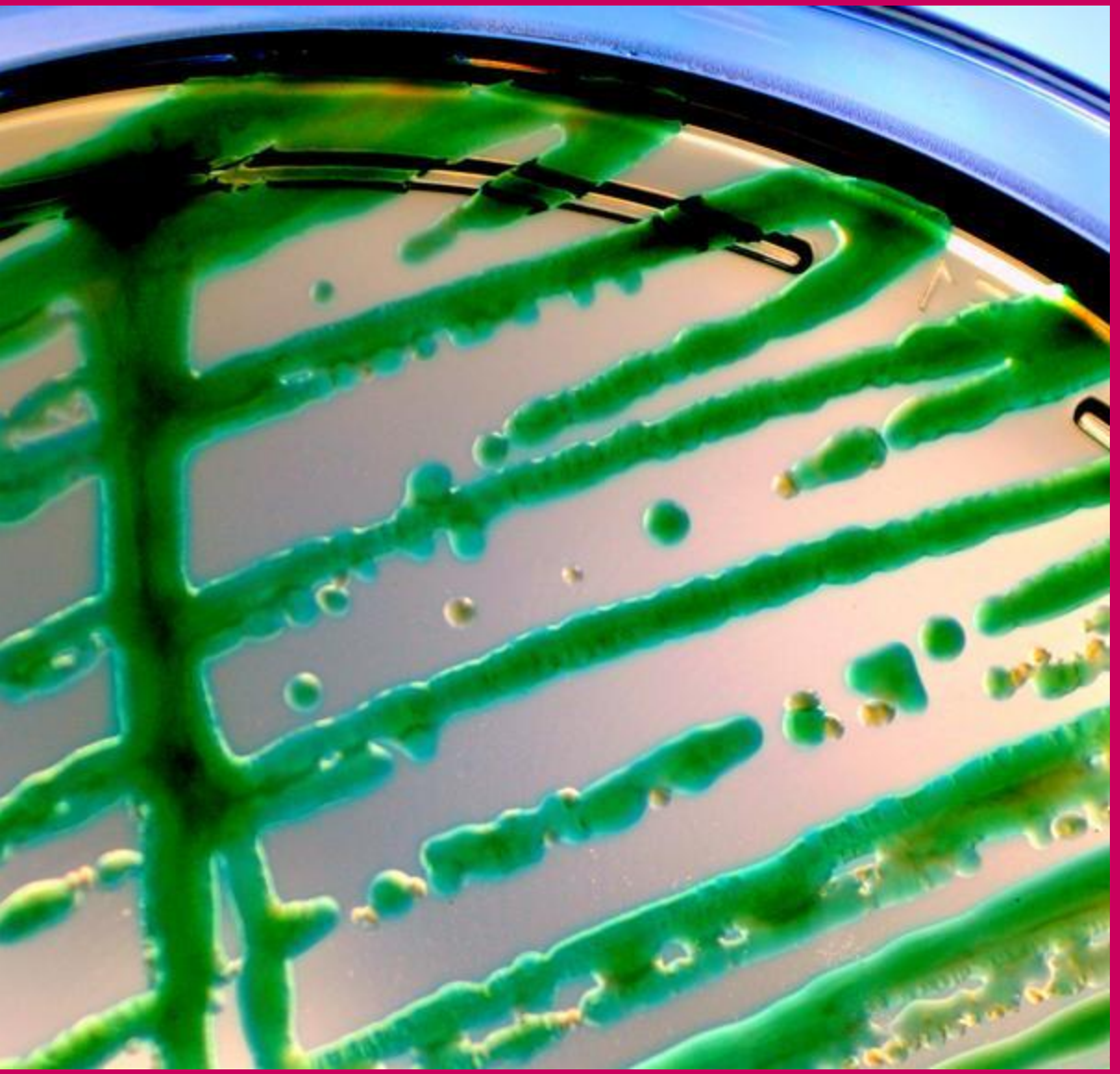


Rijksinstituut voor Volksgezondheid
en Milieu
*Ministerie van Volksgezondheid,
Welzijn en Sport*

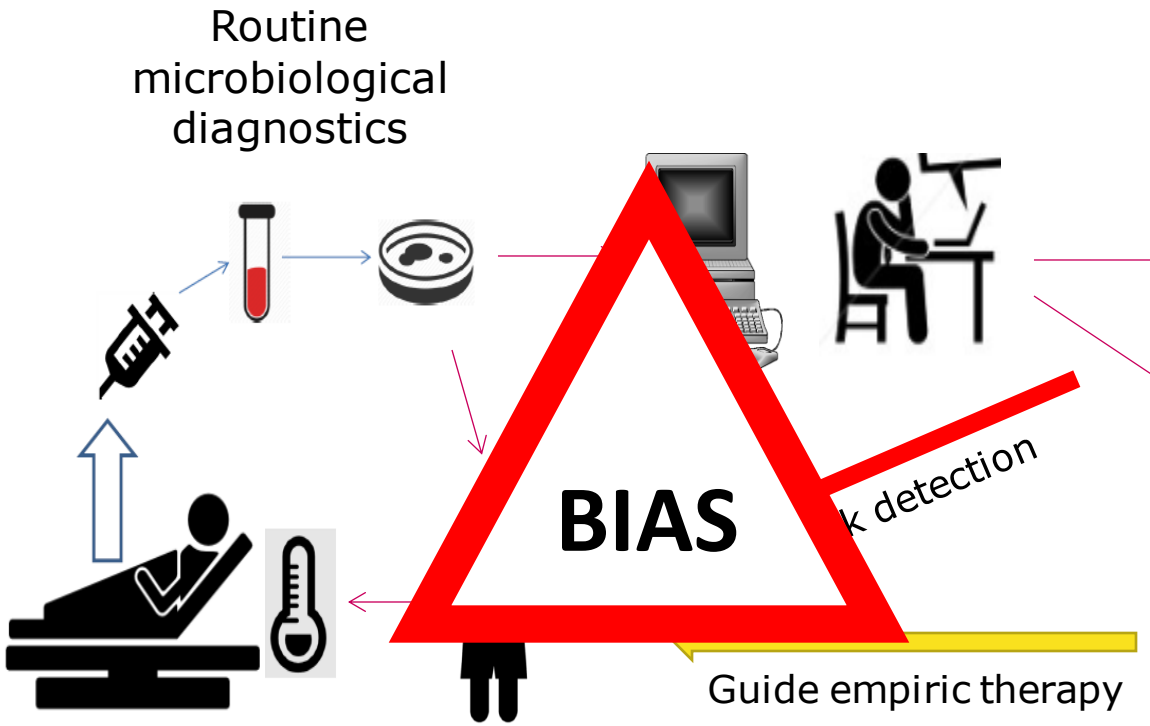
Interpretation of AMR surveillance data: sources of error and bias

Carolien Ruesen, PhD

Coordinator WHO Collaborating Centre for Antimicrobial Resistance Epidemiology and Surveillance

Centre for Infectious Disease Control, RIVM

AMR surveillance based on *routine diagnostics*



	#Pat	#Iso
Escherichia coli	639	732
Klebsiella pneumoniae	88	104
Klebsiella oxytoca	33	41
Enterobacter cloacae groep	20	31
Citrobacter freundii groep	14	21
Serratia marcescens	22	31
Morganella morganii	0	0
Proteus mirabilis	76	86
Salmonella enteritidis	2	2
Salmonella paratyphi	0	0
Salmonella typhi	0	0
Salmonella typhimurium	1	1
Shigella spec	1	1
Yersinia spec	0	0
Acinetobacter spec	36	38
Pseudomonas aeruginosa	111	151

Surveillance using routine data

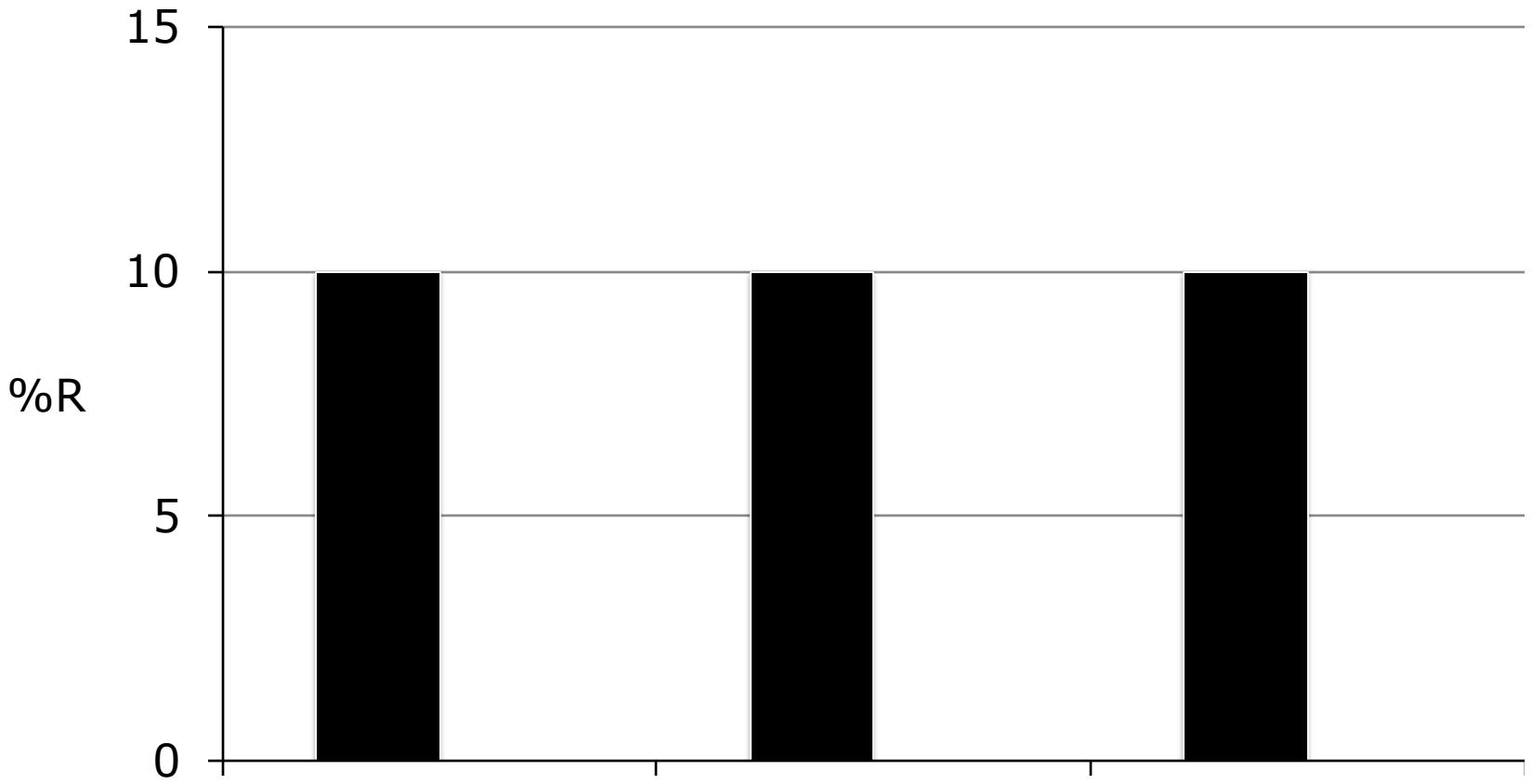
Advantages

- Large numbers for relatively little costs
- Relatively insensitive to outbreaks
- Gives a good overall picture of resistance
- Can be used to follow trends and emerging resistance
- Guide antibiotic therapy and support infection prevention (under certain conditions!)

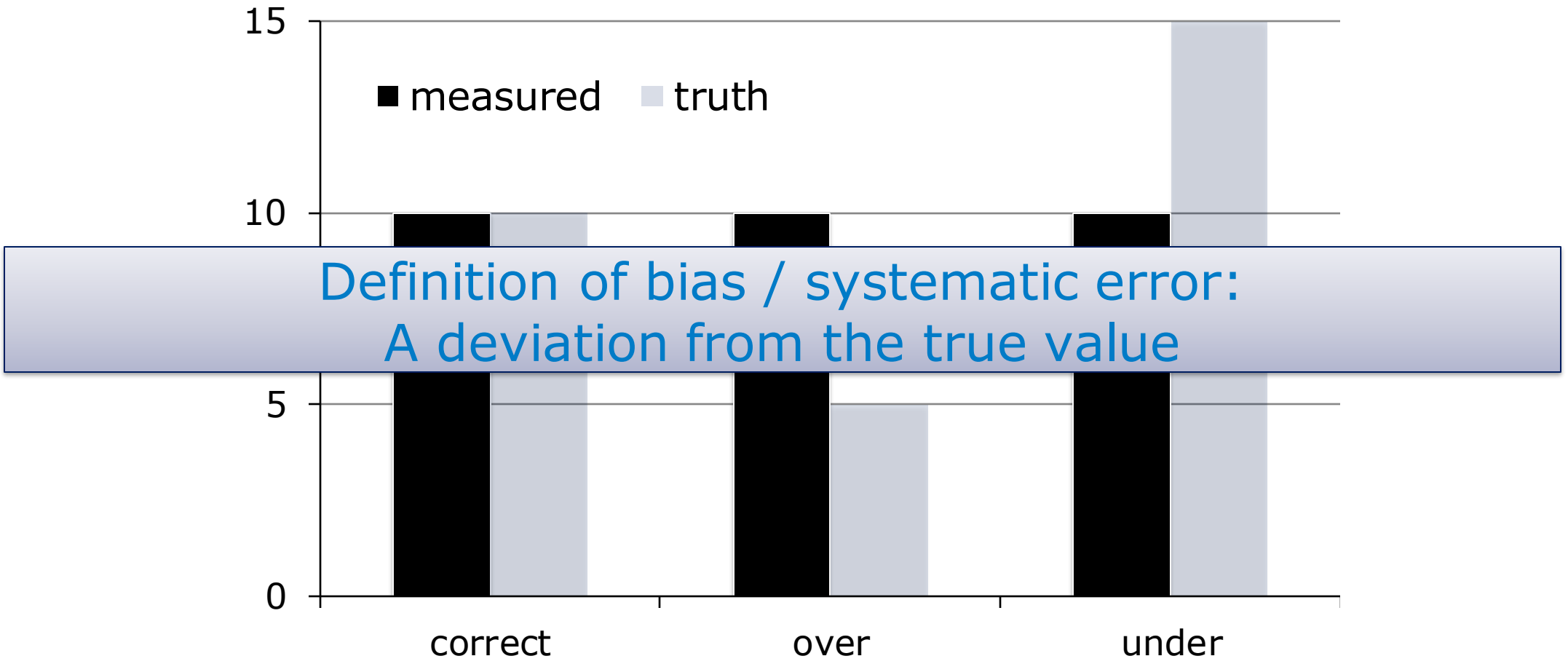
Disadvantages

- No data on colonisation
- Difficult to standardize
- Risk of error and bias

Is our estimate the truth?

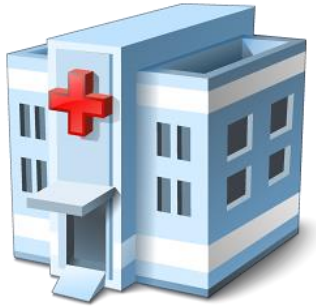


Is our estimate the truth?

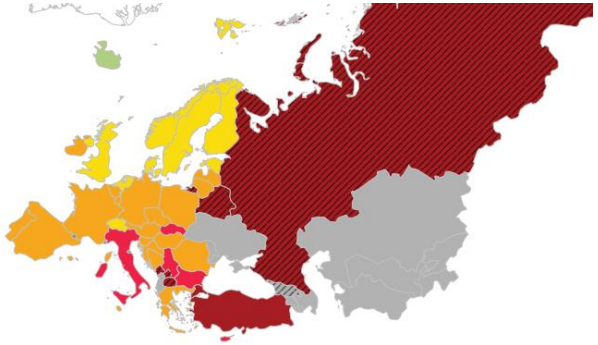


Definition of bias / systematic error:
A deviation from the true value

Representativeness



Type of hospital



Geographical region

Type of department

Season

Error and bias in national AMR surveillance

Surveillance system

1. Geographical region
2. Hospital types

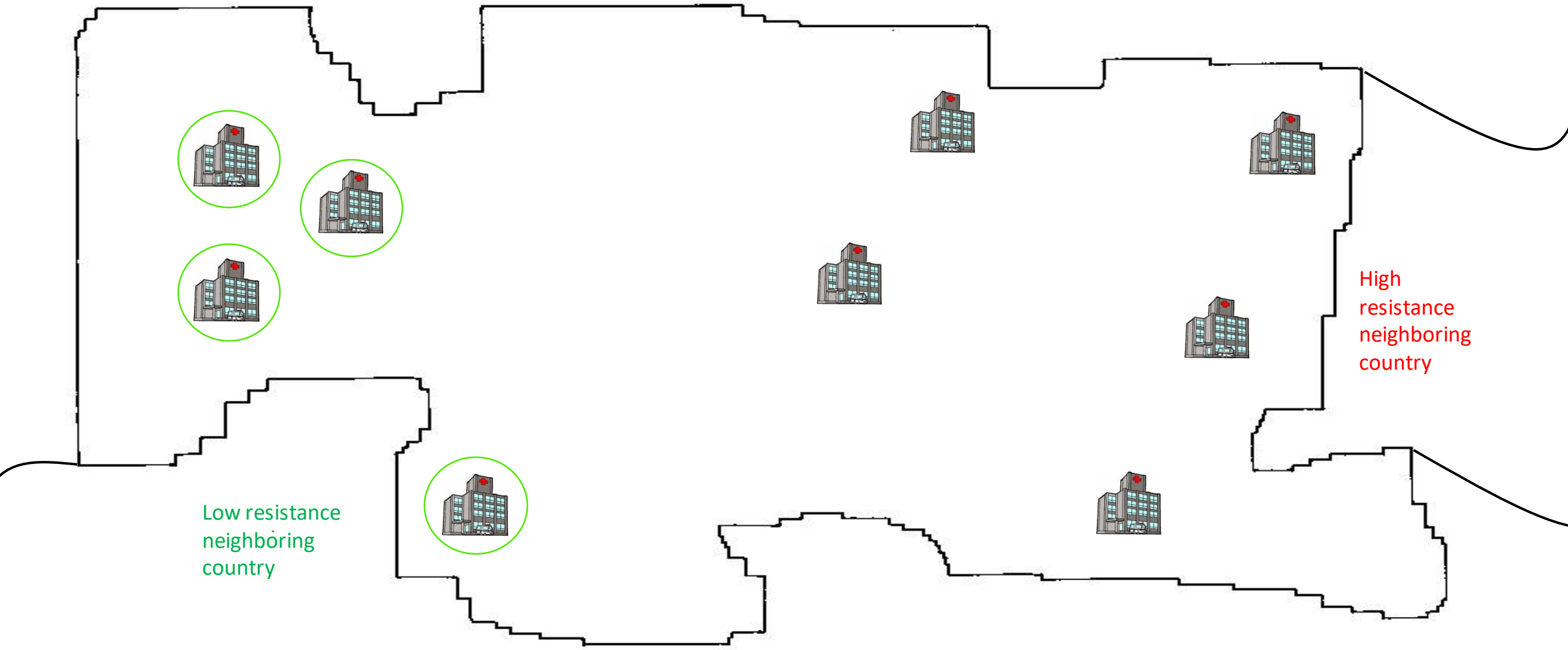
Sampling procedures

1. Selection of patients
2. Sampling after treatment
3. Follow-up samples
4. Sample size

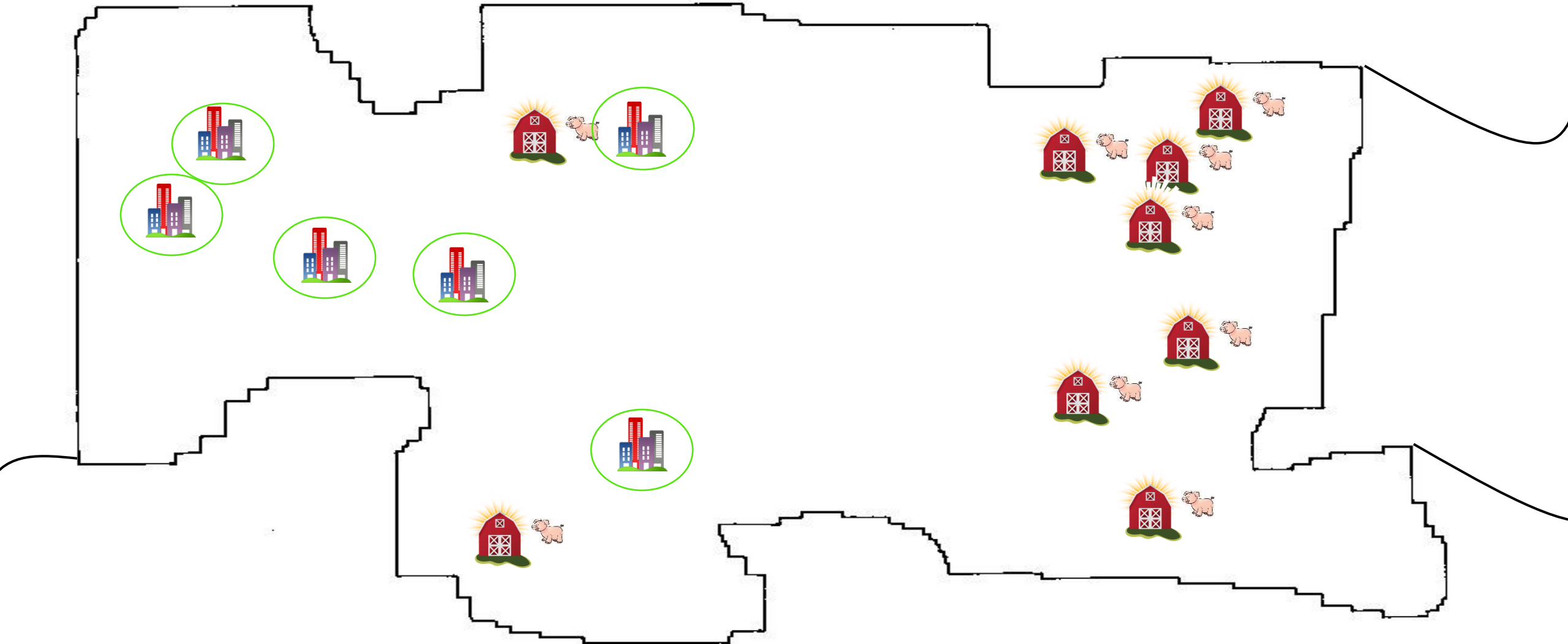
Laboratory procedures

1. AST guidelines
2. Measurement error
3. Selective testing

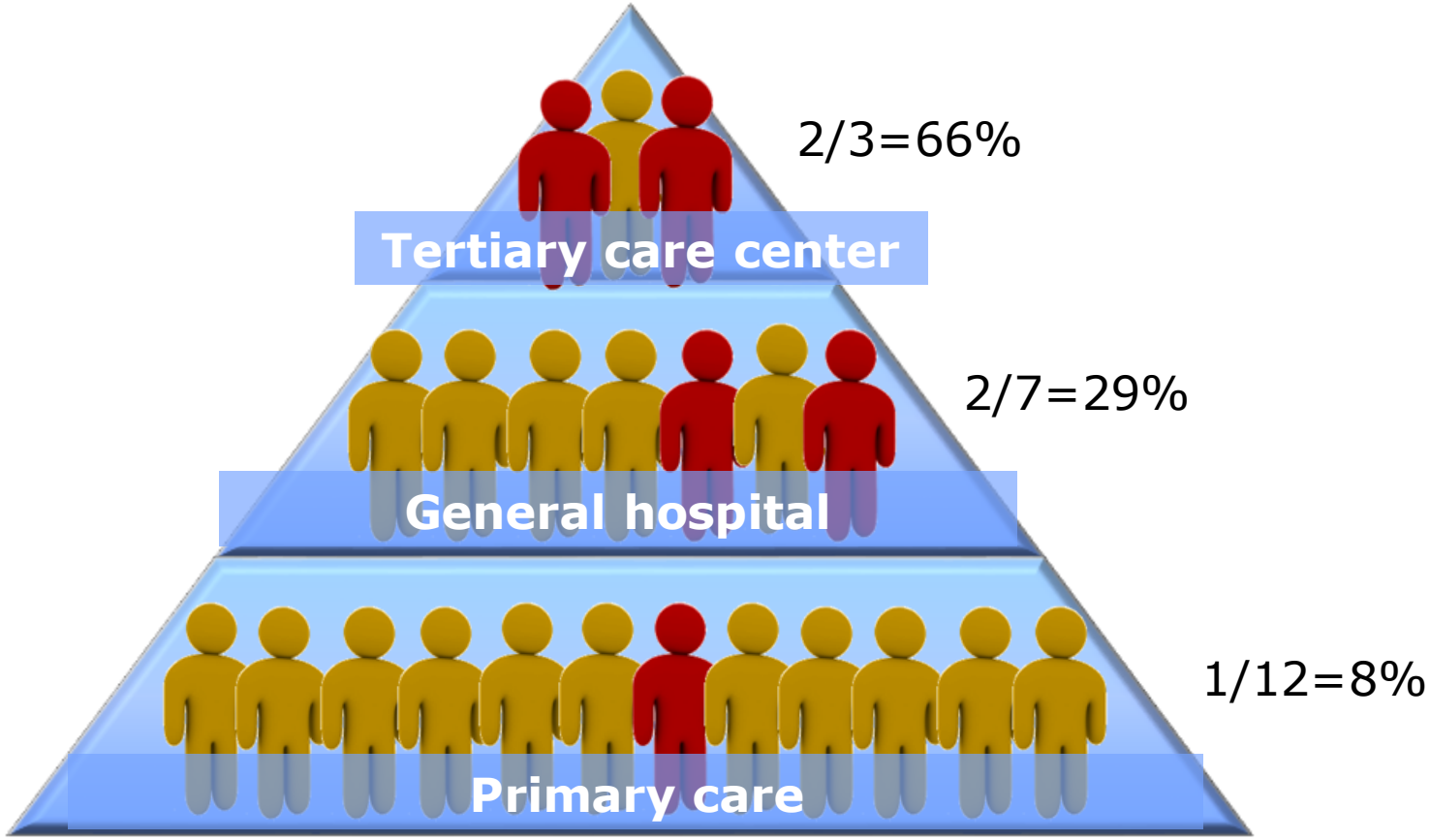
Surveillance system – 1. geographical region



Surveillance system – 1. geographical region



Surveillance system – 2. hospital types



Overall resistance: 5/22 = 23%

Error and bias in national AMR surveillance

Surveillance system

1. Geographical region
2. Hospital types

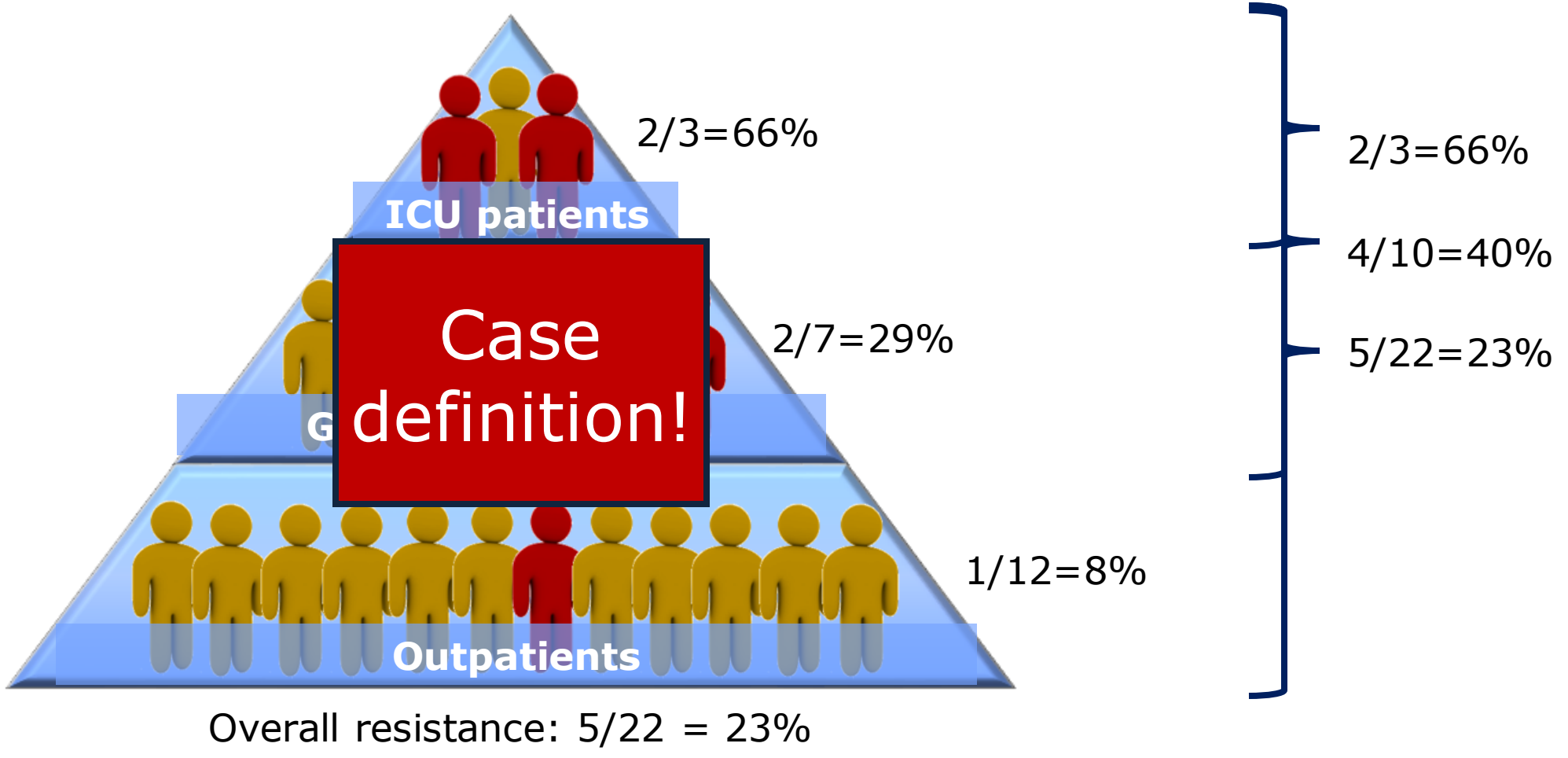
Sampling procedures

1. Selection of patients
2. Sampling after treatment
3. Follow-up samples
4. Sample size

Laboratory procedures

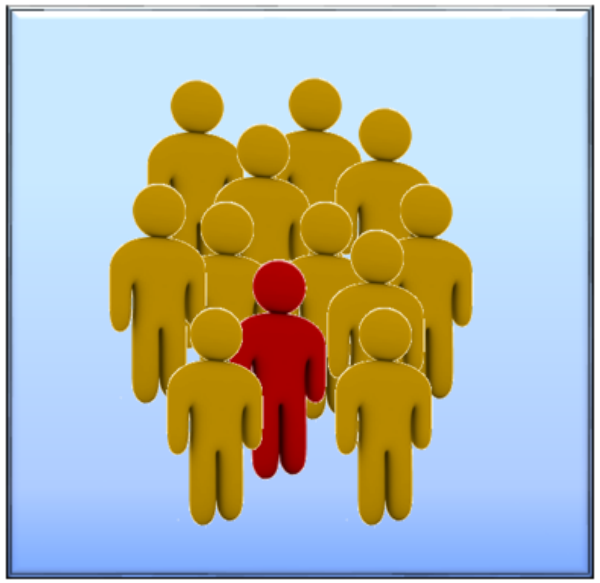
1. AST guidelines
2. Measurement error
3. Selective testing

Sampling procedures – 1. patient population

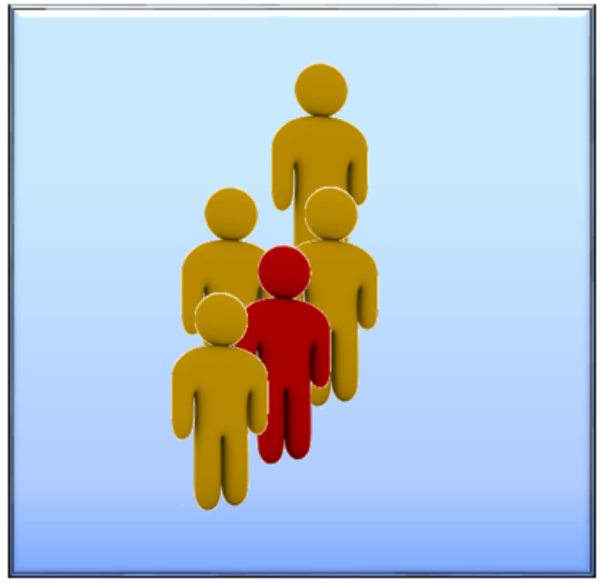


Overall resistance: 5/22 = 23%

Sampling procedures – 2. sampling after treatment



1/12=8%



1/5=20%

Sampling procedures – 3. follow-up samples

Patient	Number of isolates in dataset
1	5
2	2
3	2
4	1
5	6
6	1
Total	**17**

S

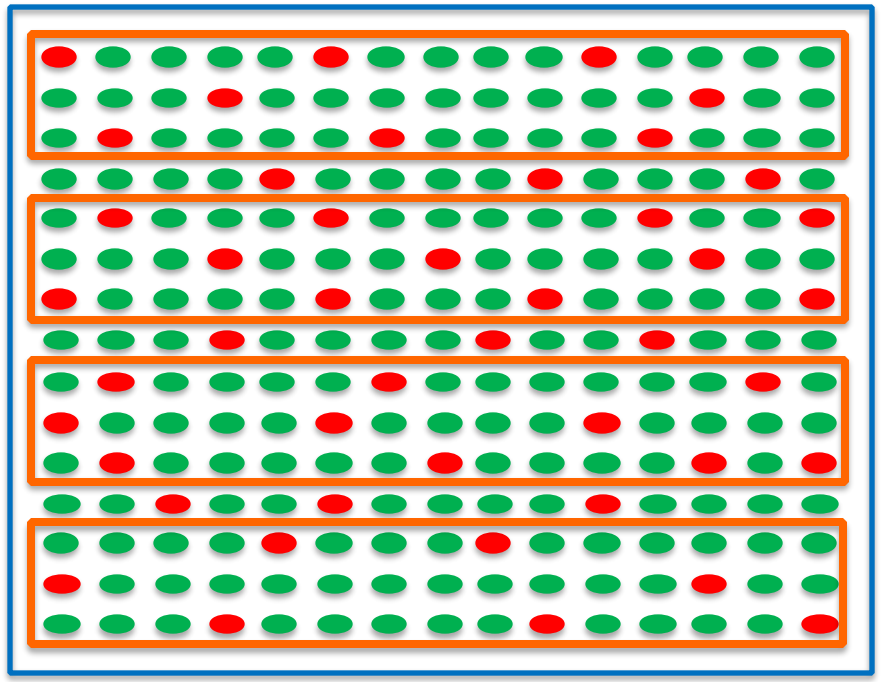
R

All isolates => %R= 11/17=65%

One isolate per patient => %R= 2/6=33%

De-duplication

Sampling procedures – 4. sample size



Overall resistance: 45/225 = 20.0%

8/45 = 17.8% -/+ : 15.6/20.0%

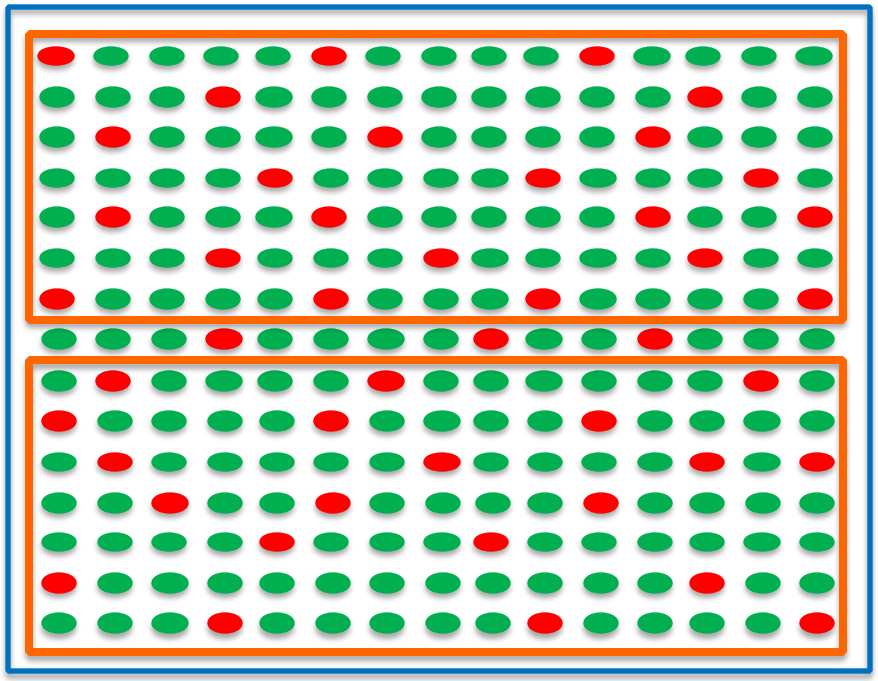
11/45 = 24.4% -/+ : 22.2/26.7%

10/45 = 22.2% -/+ : 20.0/24.4%

7/45 = 15.6% -/+ : 13.3/17.8%

Random sampling error / natural statistical variation

Sampling procedures – 4. sample size



22/105 = 21.0% -/+ : 20.0/21.9%

20/105 = 19.0% -/+ : 18.1/20.0%

Overall resistance: 45/225 = 20.0%

Error and bias in national AMR surveillance

Surveillance system

1. Geographical region
2. Hospital types

Sampling procedures

1. Selection of patients
2. Sampling after treatment
3. Follow-up samples
4. Sample size

Laboratory procedures

1. AST guidelines
2. Measurement error
3. Selective testing

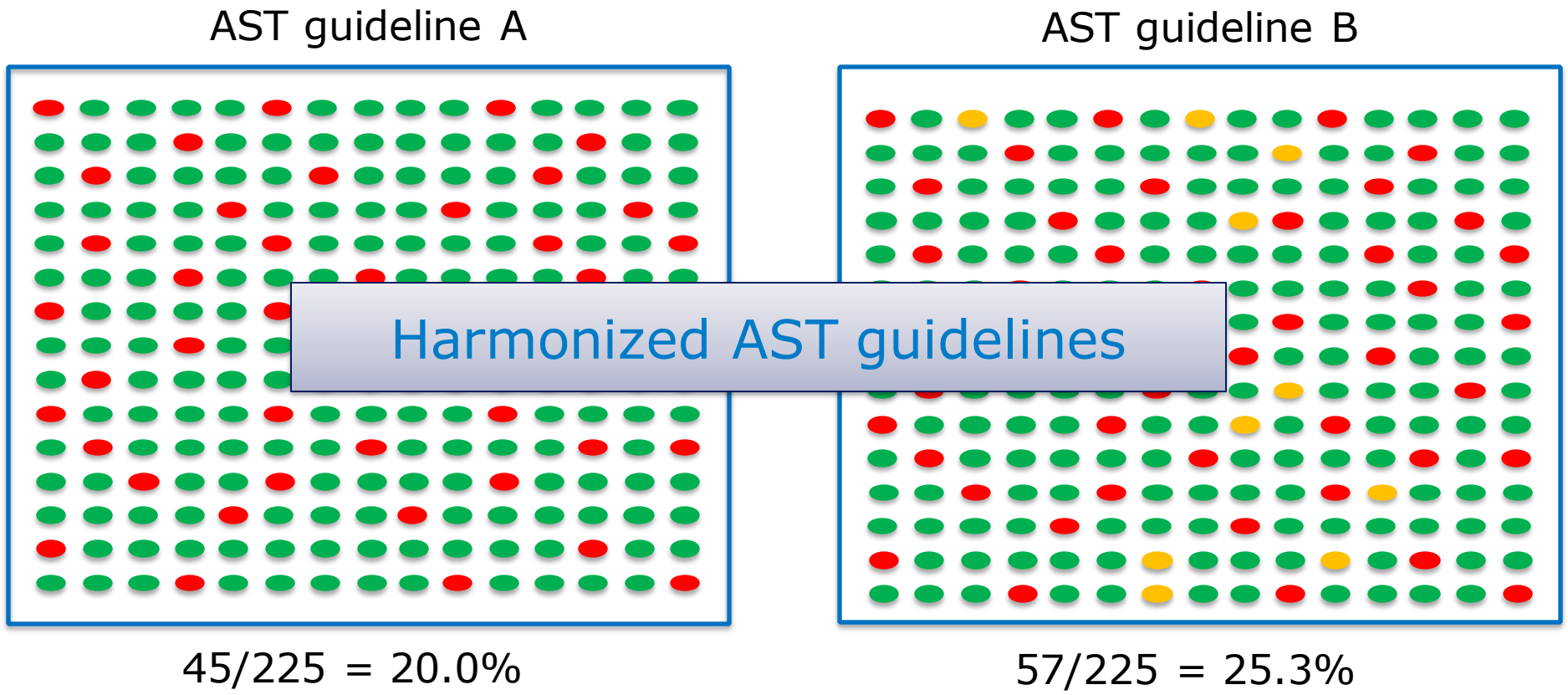
Laboratory procedures – 1. AST guidelines

- EUCAST / CLSI / other guidelines
  - Breakpoints
  - Expert rules

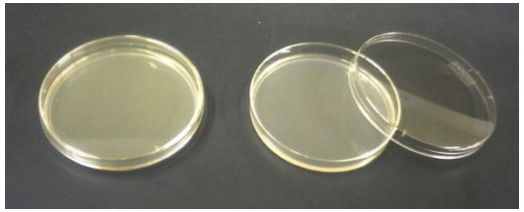
E. coli - Ceftazidime		
Guideline	**MIC Breakpoint**	
CLSI	S	≤4
	I	8
	R	≥16
EUCAST	S	≤1
	R	>4

→ different % SIR

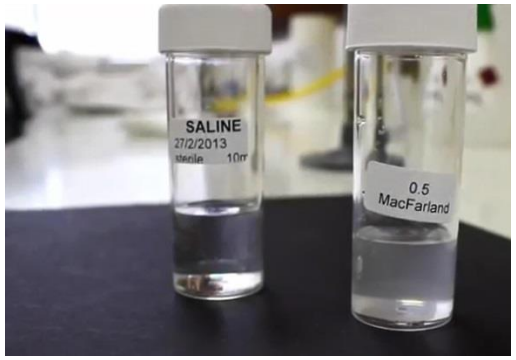
Laboratory procedures – 1. AST guidelines



Laboratory procedures – 2. measurement error



Preparation and storage of agar plates

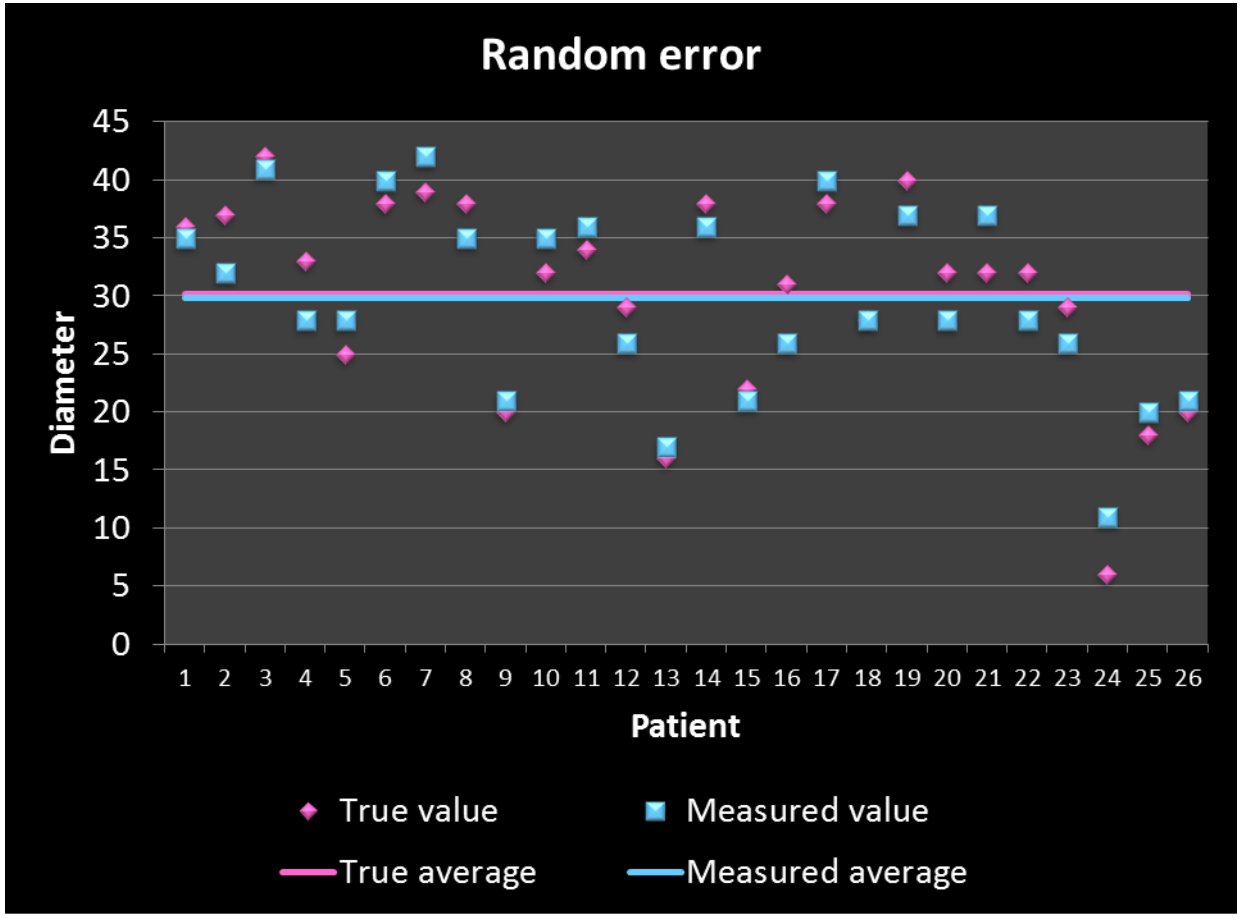


Inoculum

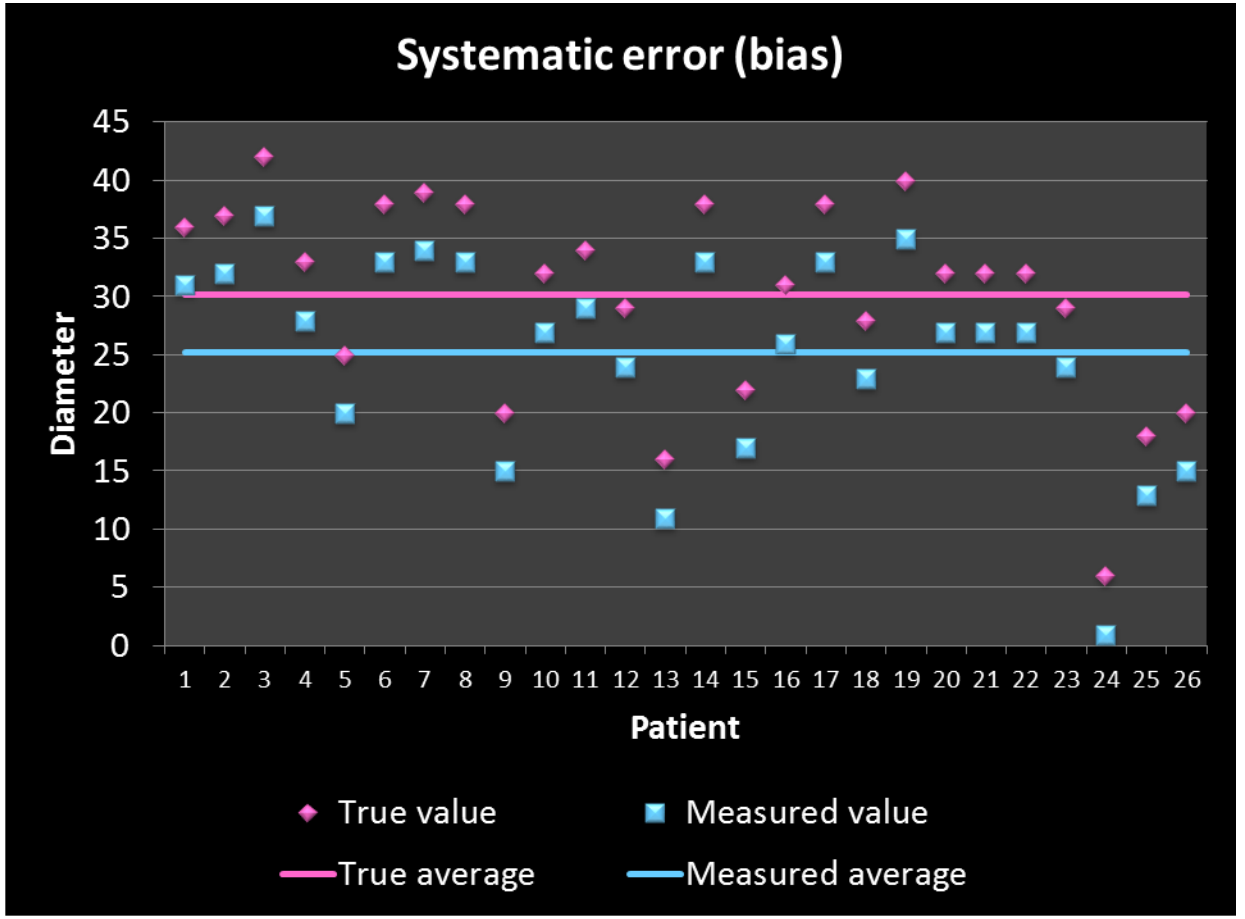
Uncalibrated automated system

Random vs. systematic measurement error

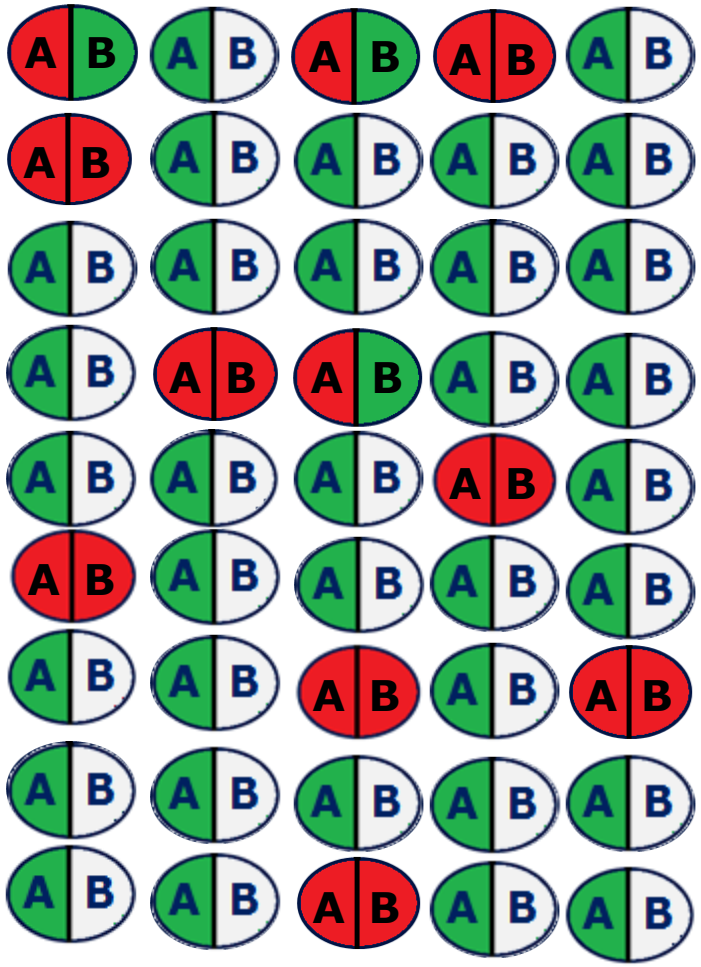
Laboratory procedures – 2. measurement error



Laboratory procedures – 2. measurement error



Laboratory procedures – 3. selective testing



Testing all isolates against both drugs
A: 11/45=24%
B: 10/45=22%

Sequential testing:
A: 11/45=24%
B: 8/11=**73%**

- Check for and report on differences in numbers of isolates
- Exclude data for pathogen-antibiotic combination in lab, when tested for <50% of isolates of the pathogen

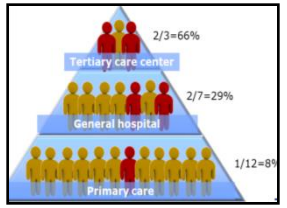
Most error and bias can not be corrected afterwards!

1. Prevent error and bias during data collection
   - Design of surveillance system
   - Case definitions for sampling
   - Standardize! Make **consistent**, **uniform**, **comparable**

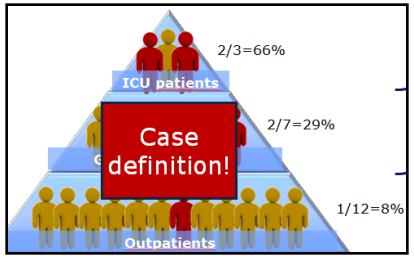
2. Interpret results carefully
   - Understand how error and bias influence your data

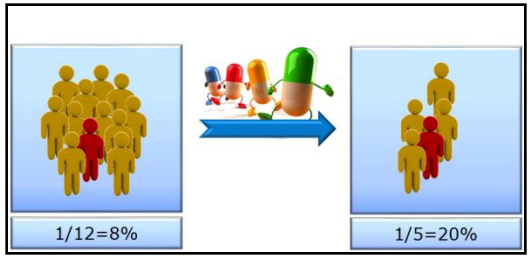
Interpretation and reporting of results – questions to ask yourself

- How is the surveillance system designed?
  - Geographical representativeness
  - Selection of hospitals in surveillance

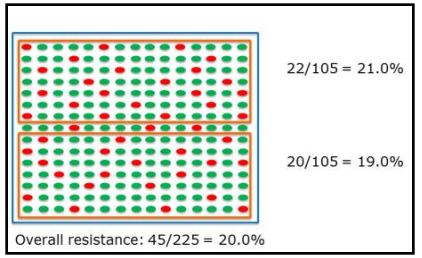


- What sampling procedures were used?
  - Was a clear case definition formulated and adhered to?
  - Did sampling occur before treatment?
  - Are follow-up samples included? (exclude them from analyses!)
  - Is the sample size large enough for robust estimates?



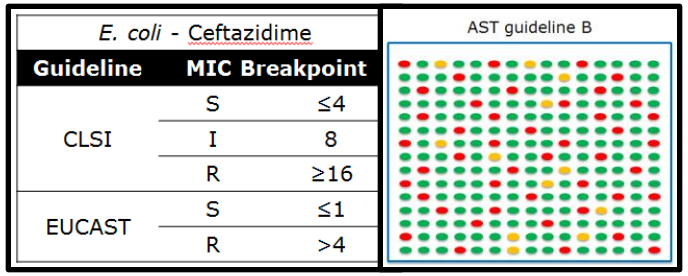


Patient	Number of isolates in dataset
1	5
2	2
3	2
4	1
5	6
6	1
Total	17



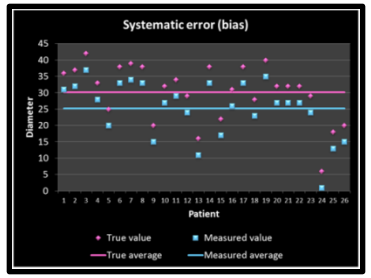
Interpretation and reporting of results – questions to ask yourself

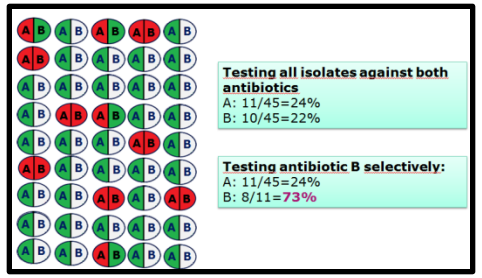
- Could laboratory procedures have caused bias / incomparable results?
  - Are harmonized AST guidelines and clinical breakpoints used?
  - Are exceptional phenotypes confirmed? (plausibility of laboratory results, i.e. indications for measurement error)
  - Are there indications for selective testing (are all isolates tested for all relevant antibiotics)?



E. coli - Ceftazidime

Guideline	MIC Breakpoint	
CLSI	S	≤4
	I	8
	R	≥16
EUCAST	S	≤1
	R	>4





Conclusion

- AMR surveillance data are extremely valuable in taking measures to prevent and control the spread of AMR
  - Awareness & advocacy
  - Infection prevention and control

- AMR surveillance data are subject to different types of error and bias
  - Magnitude unclear
  - Use of results for empiric therapy guidelines: with great caution!!!!!!
  - Interpret data carefully and report on how potential bias influenced the data

Thank you