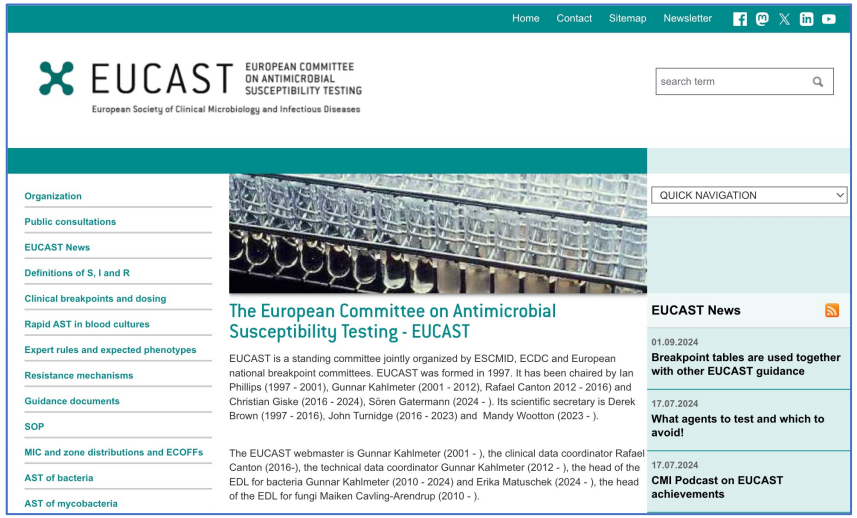
EUCAST breakpoint tables and website



Gunnar Kahlmeter

EUCAST Technical Data Coordinator

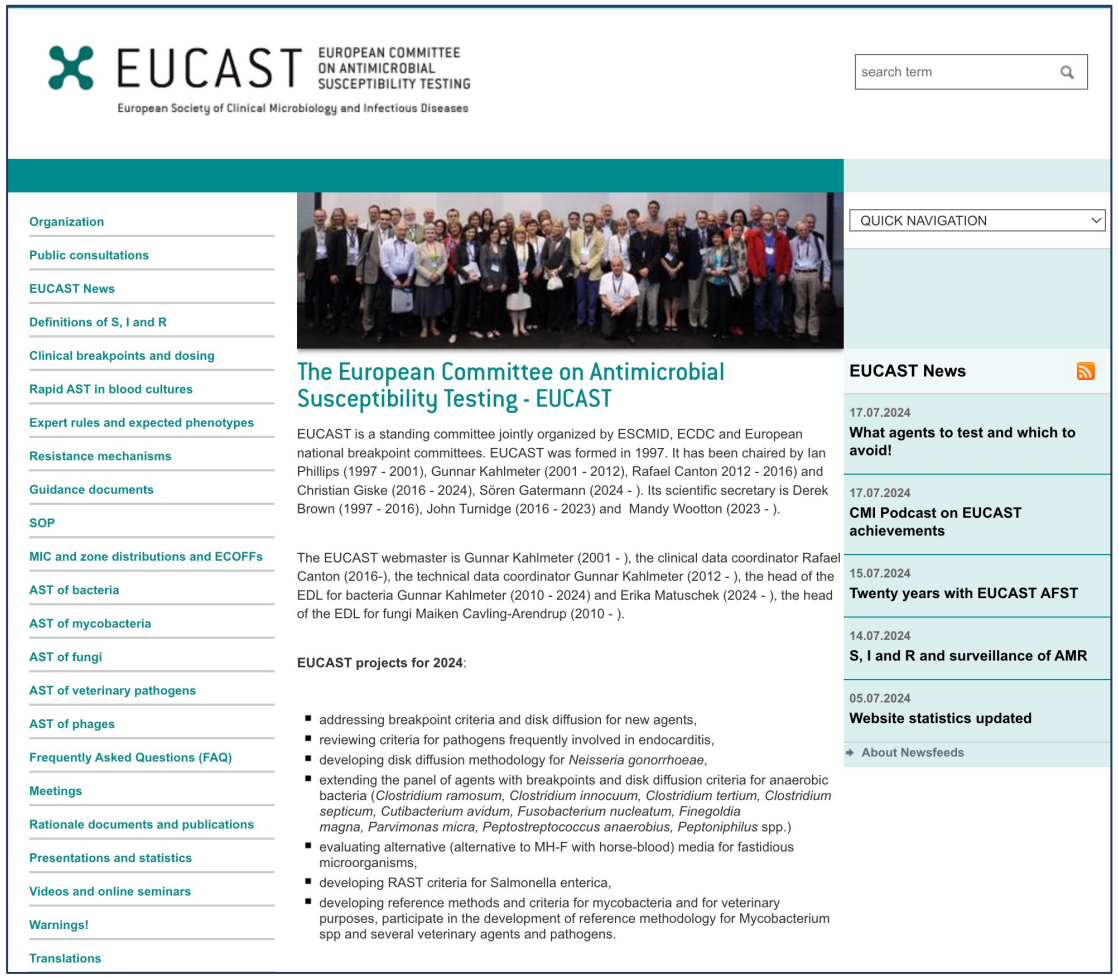
Växjö

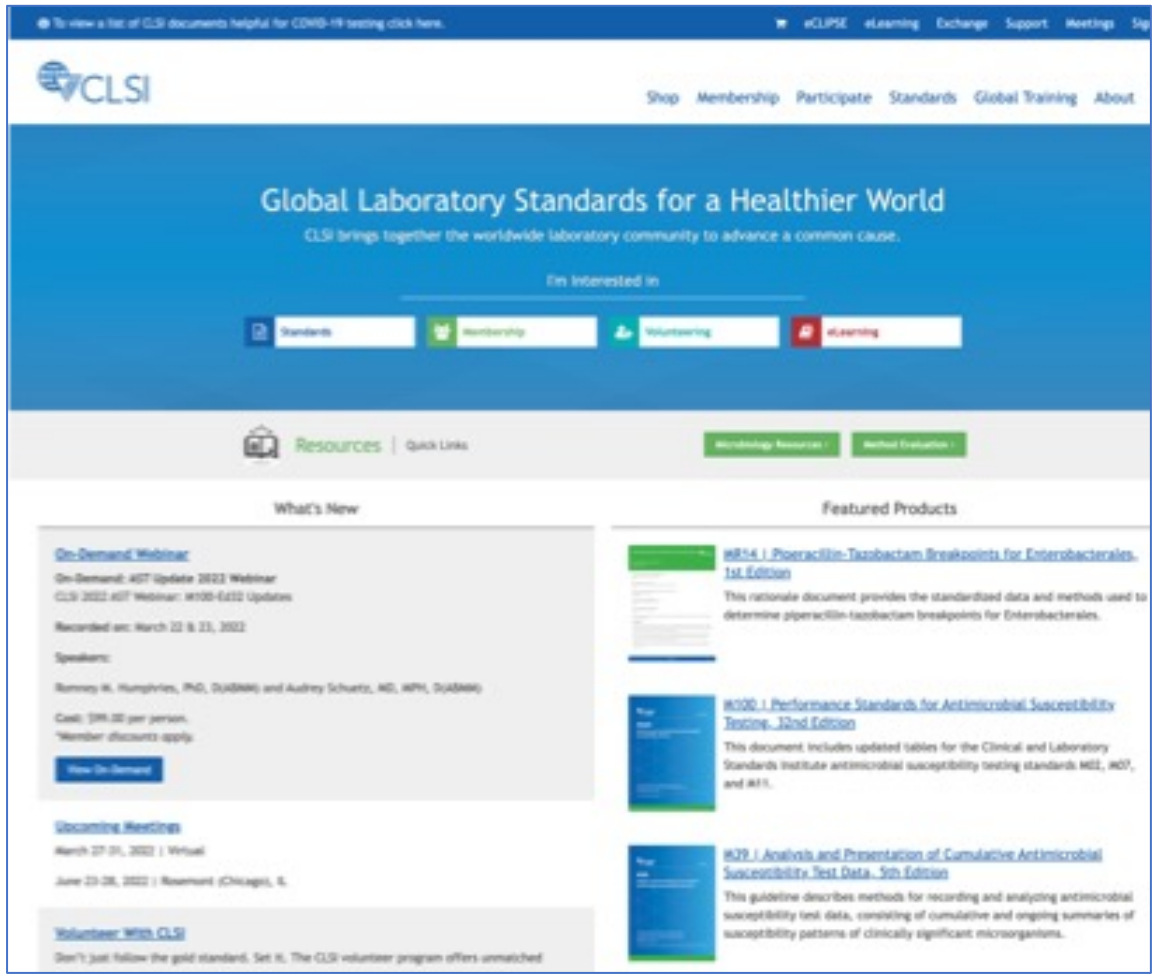
Sweden

Breakpoint tables from EUCAST and CLSI

- EUCAST (see www.eucast.org)
  - Available for free, both for viewing and printing
  - All adjunctive documents also freely available and often via links in tables

- CLSI (see www.clsi.org)
  - Principle: for sale allthough some overviews can now be obtained for free
  - Adjunctive documents for sale


EUCAST
EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING
European Society of Clinical Microbiology and Infectious Diseases
search term
Organization
Public consultations
EUCAST News
Definitions of S, I and R
Clinical breakpoints and dosing
Rapid AST in blood cultures
Expert rules and expected phenotypes
Resistance mechanisms
Guidance documents
SOP
MIC and zone distributions and ECOFFs
AST of bacteria
AST of mycobacteria
AST of fungi
AST of veterinary pathogens
AST of phages
Frequently Asked Questions (FAQ)
Meetings
Rationale documents and publications
Presentations and statistics
Videos and online seminars
Warnings!
Translations
QUICK NAVIGATION
The European Committee on Antimicrobial Susceptibility Testing - EUCAST
EUCAST is a standing committee jointly organized by ESCMID, ECDC and European national breakpoint committees. EUCAST was formed in 1997. It has been chaired by Ian Phillips (1997 - 2001), Gunnar Kahlmeter (2001 - 2012), Rafael Canton 2012 - 2016) and Christian Giske (2016 - 2024), Sören Gatermann (2024 -). Its scientific secretary is Derek Brown (1997 - 2016), John Turnidge (2016 - 2023) and Mandy Wootton (2023 -).
The EUCAST webmaster is Gunnar Kahlmeter (2001 -), the clinical data coordinator Rafael Canton (2016-), the technical data coordinator Gunnar Kahlmeter (2012 -), the head of the EDL for bacteria Gunnar Kahlmeter (2010 - 2024) and Erika Matuschek (2024 -), the head of the EDL for fungi Maiken Cavling-Arendrup (2010 -).
EUCAST projects for 2024:
addressing breakpoint criteria and disk diffusion for new agents,
reviewing criteria for pathogens frequently involved in endocarditis,
developing disk diffusion methodology for Neisseria gonorrhoeae,
extending the panel of agents with breakpoints and disk diffusion criteria for anaerobic bacteria (Clostridium ramosum, Clostridium innocuum, Clostridium tertium, Clostridium septicum, Cutibacterium avidum, Fusobacterium nucleatum, Finegoldia magna, Parvimonas micra, Peptostreptococcus anaerobius, Peptoniphilus spp.)
evaluating alternative (alternative to MH-F with horse-blood) media for fastidious microorganisms,
developing RAST criteria for Salmonella enterica,
developing reference methods and criteria for mycobacteria and for veterinary purposes, participate in the development of reference methodology for Mycobacterium spp and several veterinary agents and pathogens.
EUCAST News
17.07.2024
What agents to test and which to avoid!
17.07.2024
CMI Podcast on EUCAST achievements
15.07.2024
Twenty years with EUCAST AFST
14.07.2024
S, I and R and surveillance of AMR
05.07.2024
Website statistics updated
About Newsfeeds


CLSI
Shop
Membership
Participate
Standards
Global Training
About
Global Laboratory Standards for a Healthier World
CLSI brings together the worldwide laboratory community to advance a common cause.
I'm interested in
Resources
Quick Links
What's New
Featured Products

EUCAST EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING

European Society of Clinical Microbiology and Infectious Diseases

search term

- Organization
- Public consultations
- EUCAST News
- Definitions of S, I and R
- Clinical breakpoints and dosing
- Rapid AST in blood cultures
- Expert rules and expected phenotypes
- Videos and online seminars
- Warnings!
- Translations

QUICK NAVIGATION

The European Committee on Antimicrobial Susceptibility Testing - EUCAST

EUCAST is a standing committee jointly organized by ESCMID, ECDC and European

- developing RAST criteria for *Salmonella enterica*;
- developing reference methods and criteria for mycobacteria and for veterinary purposes, participate in the development of reference methodology for Mycobacterium spp and several veterinary agents and pathogens.

EUCAST News

17.07.2024

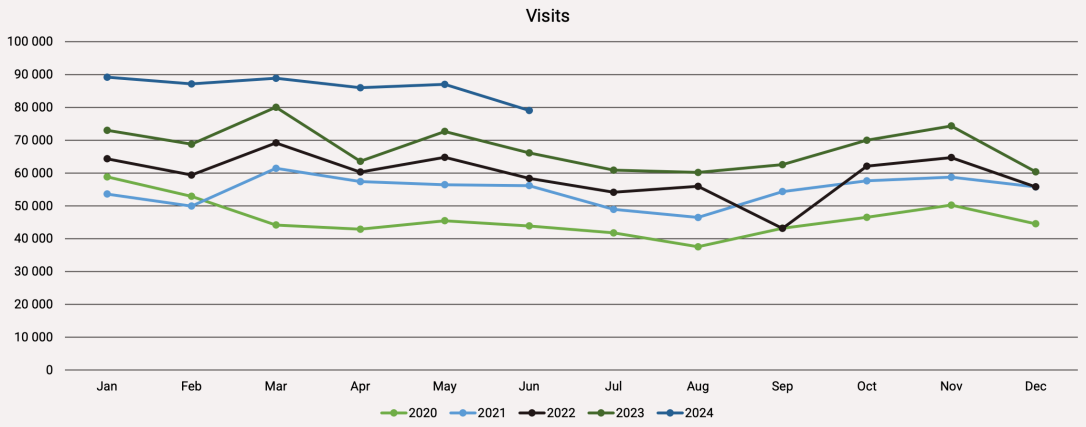
What agents to test and which to

VISITS

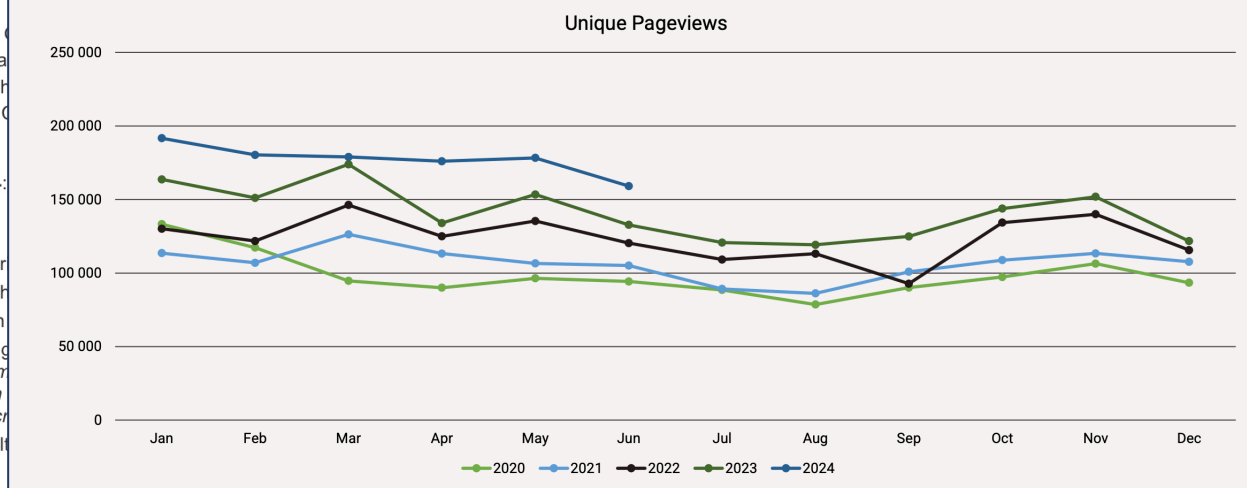
EUCAST EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING

European Society of Clinical Microbiology and Infectious Diseases

Visits for eucast.org 2020–2024



Unique Pageviews for eucast.org 2020–2024



EUCAST EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING
European Society of Clinical Microbiology and Infectious Diseases

search term

Clinical breakpoints and dosing of antibiotics

- Organization
- Public consultations
- EUCAST News
- Definitions of S, I and R
- Clinical breakpoints and dosing
  - About "Clinical breakpoints".
  - Rationale documents
  - Splitting MIC wild type distributions
  - When there are no breakpoints?
  - Breakpoints in brackets
  - EUCAST setting breakpoints.
- Rapid AST in blood cultures
- Expert rules and expected phenotypes
- Resistance mechanisms
- Guidance documents
- SOP
- MIC and zone distributions and ECOFFs
- AST of bacteria
- AST of mycobacteria
- AST of fungi
- AST of veterinary pathogens
- AST of phages
- Frequently Asked Questions (FAQ)
- Meetings
- Rationale documents and publications
- Presentations and statistics
- Videos and online seminars
- Warnings!

The European Committee on Antimicrobial Susceptibility Testing – EUCAST

Clinical breakpoints and dosing of anti

Clinical breakpoints - breakpoints and guidance

Breakpoints are part of a system for categorising microorganisms as susceptible (S and I) and resistant (R) to agents approved for use in the treatment of infectious diseases. Below are links to the yearly updated breakpoint tables, but other parts of the system are equally important. These are for example **"Expert Rules" and "Expected Phenotypes"**, **"What to do when there are no breakpoints"** (and other guidance documents), how to cope with "IE", "Dash", "Breakpoints in brackets" and disease specific breakpoints. All major changes have been subjected to **public consultation** and following these will facilitate understanding the EUCAST process.

Breakpoint tables

- Breakpoints bacteria (print)
- Breakpoints bacteria (screen)
- Breakpoints fungi
- Dosing table

Make sure the device you are using for the presentation of tables can correctly display footnotes ($Note_1$,$Note^2$) and other typographical tools.

- Clinical breakpoints (v 14.0) - file for printing (1 Jan, 2024)
- Clinical breakpoints (v 14.0) - file for screen (1 Jan, 2024)
- Aztreonam-avibactam – Addendum (22 May, 2024) Rationale Document available
- Cefepime-enme
- Clinical breakpo
- Dosages (v 14.0) - file for printing and screen (1 Jan, 2024)

Next slide for an enlarged view

The major changes between the 2023 and 2024 breakpoint tables are:

- Fosfomycin iv breakpoints revised
- Cefiderocol ATUs revised, and zone diameter breakpoint for Enterobacterales adjusted
- Ciprofloxacin breakpoints for staphylococci revised
- Breakpoint for C. difficile and fidaxomicin added
- Breakpoints for Bacillus anthracis added
- Breakpoints for Brucella melitensis added
- PK-PD breakpoints removed from the table (see explanation in the PK-PD tab) and **"When there are no breakpoints"**

For questions and comments on breakpoints, use the EUCAST **subject related contact form**.

Make sure the device you are using for the presentation of tables can correctly display footnotes ($Note_1$,$Note^2$) and other typographical tools.

Clinical breakpoints and dosing of antibiotics

The European Committee on Antimicrobial Susceptibility Testing – EUCAST

Clinical breakpoints and dosing of anti

Clinical breakpoints - breakpoints

Breakpoints are part of a system for categorising microorg
and resistant (R) to agents approved for use in the treatm
are links to the yearly updated breakpoint tables, but othe
important. These are for example **"Expert Rules" and "Exp**
"**What to do when there are no breakpoints**" (and other gui
with "IE", "Dash", "Breakpoints in brackets" and disease s
changes have been subjected to **public consultation** and f
understanding the EUCAST process.

- **Clinical breakpoints (v 14.0)** - file for printing (1 Jan, 20
- **Clinical breakpoints (v 14.0)** - file for screen (1 Jan, 20
- **Aztreonam-avibactam** - Addendum (22 May, 2024). **Ra**
- **Cefepime-enmetazobactam** - Addendum (22 May, 2024
- **Clinical breakpoints - fungi**
- **Dosages (v 14.0)** - file for printing and screen (1 Jan, 2

The major changes between the 2023 and 2024 breakpoint tables are:

- Fosfomycin iv breakpoints revised
- Cefiderocol ATUs revised, and zone diameter breakpoint for Enterobacterales adjusted
- Ciprofloxacin breakpoints for staphylococci revised
- Breakpoint for C. difficile and fidaxomicin added
- Breakpoints for Bacillus anthracis added

- Tab ”Notes” in breakpoint tables
- Expert Rules
- Expected Phenotypes
- What to do when there are no breakpoints
- Guidance Documents
- Definitions of S, I and R
- How to understand IE, dash and brackets
- How to understand arbitrary breakpoints
- How to understand and use the ”ATU”

- Rationale Documents
- MIC distributions and ECOFFs
- Warnings

About Clinical breakpoint tables.

Clinical breakpoints are for everyday use to advise on patient therapy. Breakpoint tables are updated on the 1st of January each year. Tentative new tables are published in early December - this is for consultation and to permit laboratories to prepare for changes. Between the yearly updates, errata may be published as a new version of the breakpoint table whereby the version number is increased from X.0 to X.1. Should there be a need to change or add to breakpoints between new versions of the tables, these are are published as addendums in separate documents.

In EUCAST tables, **the I category (Susceptible, increased exposure)** is not listed. It is implied and refer to the values between the S breakpoint and the R breakpoint. Thus, a breakpoint listed as S<=1 mg/L and R>8 mg/L the I category is 2 - 8 (technically >1 - 8) mg/L.

For a breakpoint listed as S>=22 mm and R<18 mm the I category is 18-21 mm. For species where no "susceptible" category (S) exists and for which isolates without resistance mechanisms are categorised as "susceptible, increased exposure" (I), an arbitrary breakpoint of S≤0.001 mg/L is used to signal that no isolates are expected to be categorised "S". For disk diffusion susceptibility testing the corresponding arbitrary breakpoint is S≥50

The I category is implied – it refers to what is left between S and R.

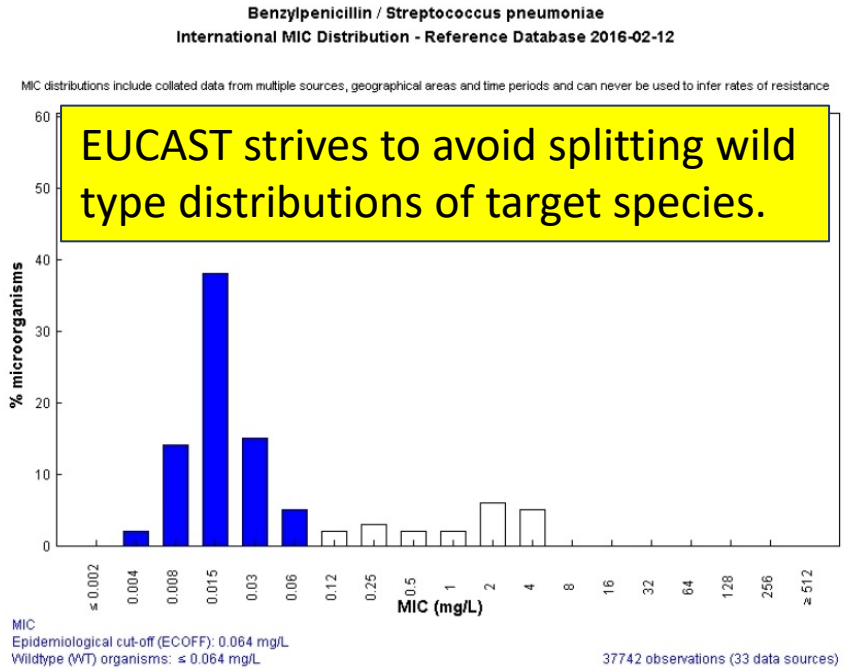
If the values are the same for S and R, there is no I category.

Arbitrary breakpoints
S≤0.001, R>2 mg/L
S≥50 mm, R<20 mm

A breakpoint may be valid for a family (Micrococcaceae), a genus (*Staphylococcus* spp) or a species (*S. aureus*).

Clinical breakpoints and dos

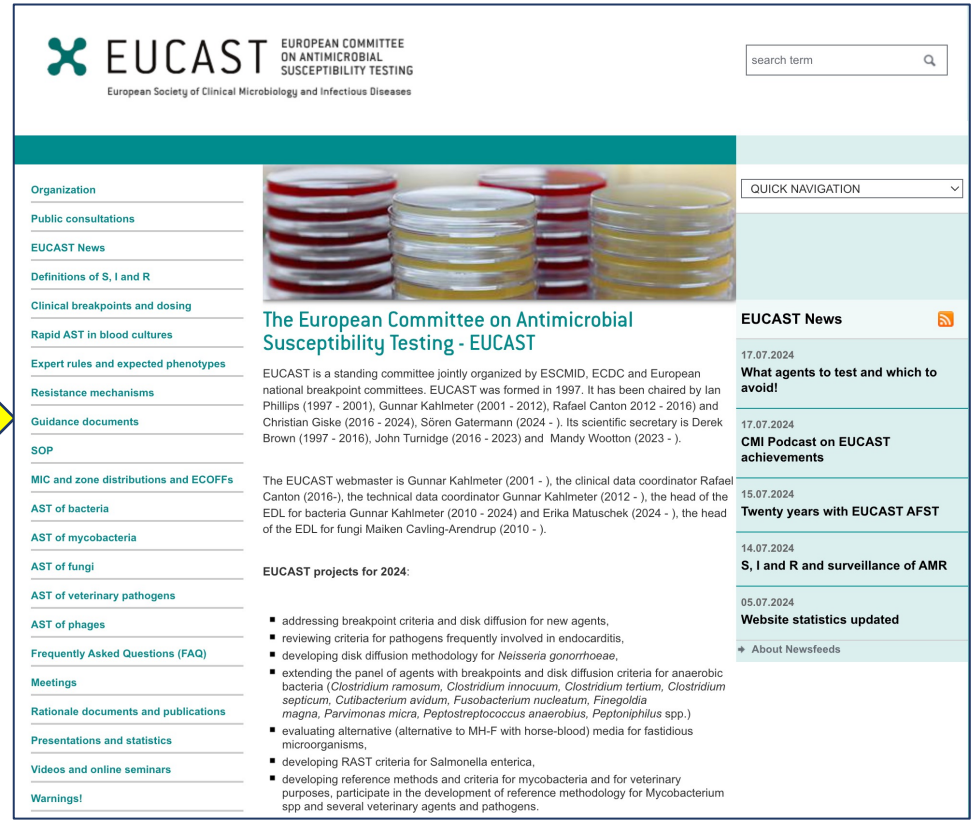
Figure 1: Benzylpenicillin MIC distributions for *Streptococcus pneumoniae.*



The range of MICs within the wild type is largely a consequence of technical variation within and between laboratories, with biological differences in susceptibility among isolates playing a lesser part. It is normal for the wild type MIC distribution to span 3-5 two-fold dilution steps.

Whenever possible, EUCAST avoids splitting the wild type when setting breakpoints because the technical variation within the wild type would result in susceptibility testing results being inherently non-reproducible. The closer the breakpoint is to the wild type median MIC, the greater the detrimental effect on reproducibility.

Also, the biological variation inside the wild type distribution, where there organisms are devoid of resistance genes and mechanisms, is of little importance compared to robustly differentiating between organisms with and without resistance genes/mechanisms.



EUCAST Guidance Documents

- **Cefiderocol MIC broth microdilution guide** (1 January, 2024). See also the **Warning on cefiderocol susceptibility testing**.
- **When there are no breakpoints!** (29 February, 2024). **Previous version** (30 June, 2023), **Previous version** (1 December 2021 - 30 June, 2023), **Previous version** (5 July, 2016 - 1 December 2021).
- **Guidance on the use of fosfomycin intravenously** (28 May, 2024); **Previous version** (5 December, 2023).
- **ATU - the Area of Technical Uncertainty - Guidance to laboratories on how to deal with the** antimicrobial susceptibility testing (originally published 2018; updated 2019, 2020, 2022, and 8 February 2024).
  Graphs to illustrate ATUs (Updated 5 February, 2024).
- **Guidance on the use of ceftriaxone and cefotaxime in Staphylococcus aureus** (8 February, 2023)
- **Aminopenicillin breakpoints Enterobacterales following revision 2023 - guidance on implementation** (14 January, 2023; an error in the flowchart was corrected on Sept 15, 2023).
- **Setting breakpoints for agent-inhibitor combinations** (14 December, 2021). Previous version of **Setting breakpoints for agent-inhibitor combinations** (2 October, 2017).
- **Breakpoints in brackets in breakpoint tables** (2 December 2021)
- **Phenotypic screening tests to detect and exclude resistance of clinical relevance** (update 22 August, 2022). **Previous version** (13 June, 2022). **Previous version** (2 Febr, 2022). **Previous version** (1 Dec 2021)
- **Implementation and use of the 2022 revised colistin breakpoints** (January, 2022; minor edits on **previous version** from Nov, 2021)
- **Legionella pneumophila susceptibility testing** (30 May, 2021); previous version **Legionella pneumophila susceptibility testing** (11 Dec, 2017)
- **Implementation and use of the 2020 revised aminoglycoside breakpoints** (first published 21 Jan, 2020; updated April 2020)
- **Daptomycin in endocarditis and bloodstream infections caused by enterococci** (also available in CMI as a **EUCAST position paper; 2020)**
- **Breakpoints for topical use of antimicrobial agents** (revised 12 April 2022, 21 Nov, 2019; 22 Dec, 2016)
- **Guidance for industry on the working order between pharmaceutical industry, EMA and El** (5 May, 2019)
- **Cefotaxime and ceftazidime disks with and without clavulanic acid for ESBL confirmation** (12 February, 2019)
- **Guidance on tigecycline dosing**, 21 July, 2022. **Previous version** (23 December, 2018)
- **The 2019 modifications of susceptibility categories S, I and R categories** (22 October, 2018).
  This presentation also informs laboratories on how to implement the Area of Technical Uncertainty.
- **EUCAST system for antimicrobial name abbreviations** (January 2022). **Previous version** (13 July, 2018)
- **Recommendations for colistin (polymyxin E) MIC testing** - joint EUCAST and CLSI recommendation (22 March, 2016)
- **Burkholderia cepacia complex** (20 July, 2013)
- **Stenotrophomonas maltophilia** (1 Feb 2012)
- **Oral cephalosporins and Enterobacterales breakpoints** (14 July, 2020). **Previous version** (16 Feb 2012)
- **Direct susceptibility testing** (16 Feb 2012), See also **"EUCAST Rapid AST directly from positive blood culture bottles"**

Breakpoint tables for interpretation of MICs and zone diameters

Version 14.0, valid from 2024-01-01

This document should be cited as "The European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters. Version 14.0, 2024. http://www.eucast.org."

A light yellow background (and underlined text) is used throughout to announce one or more changes since the previous table.

European Committee on Antimicrobial Susceptibility Testing

Breakpoint tables for interpretation of MICs and zone diameters

Version 14.0, valid from 2024-01-01

Notes

1. The EUCAST clinical breakpoint tables contain clinical MIC breakpoints (determined or revised during 2002-2023) and their inhibition zone diameter correlates. The EUCAST breakpoint tables version 14.0 includes corrected typographical errors, clarifications, breakpoints for new agents and/or organisms, revised MIC breakpoints and revised and new zone diameter breakpoints. Changes are best seen on screen or on a colour printout since cells containing a change are yellow. New or revised comments are underlined. Removed comments are shown in strikethrough font style.

2. PK-PD (Non-species related) breakpoints are listed separately.

3. Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.

4. Antimicrobial agent names in blue are linked to EUCAST rationale documents. MIC and zone diameter breakpoints in blue are linked to the search page of the EUCAST MIC and zone diameter distribution database.

5. The document is released as an Excel file suitable for viewing on screen and as an Acrobat pdf file suitable for printing. To utilize all functions in the Excel file, use Microsoft original programs only. The Excel file enables users to alter the list of agents to suit the local range of agents tested. The content of single cells cannot be changed. Hide lines by right-clicking on the line number and choose "hide". Hide columns by right-clicking on the column letter and choose "hide".

6. EUCAST breakpoints are used to categorise results into three susceptibility categories:
S - Susceptible, standard dosing regimen: A microorganism is categorised as *Susceptible, standard dosing regimen,* when there is a high likelihood of therapeutic success using a standard dosing regimen of the agent.
I - Susceptible, increased exposure: A microorganism is categorised as *Susceptible, increased exposure** when there is a high likelihood of therapeutic success because exposure to the agent is increased by adjusting the dosing regimen or by its concentration at the site of infection.
R - Resistant: A microorganism is categorised as *Resistant* when there is a high likelihood of therapeutic failure even when there is increased exposure.
*Exposure is a function of how the mode of administration, dose, dosing interval, infusion time, as well as distribution and excretion of the antimicrobial agent will influence the infecting organism at the site of infection.

7. Dash in breakpoint tables indicates that the agent is unsuitable for treatment of infections caused by the organism or group of organisms and that testing and clinical use should be avoided. If included, report resistant without prior testing.

8. "IE" indicates that there is insufficient evidence that the organism or group is a good target for therapy with the agent. An MIC with a comment but without an accompanying S, I or R categorisation may be reported.

9. A screening test uses one agent to predict resistance or susceptibility to one or more antimicrobial agents in the same class. The screening test is often more sensitive and/or robust than testing individual agents. Using a screening test will often reduce the number of tests needed in primary susceptibility testing since it will predict susceptibility and/or resistance to several agents. Guidance on how to act on the screening test result is described in the Note related to each specific screening test.
Negative screening test: MIC below or equal to or zone diameter above or equal to the susceptible breakpoint for the screening agent. No resistance mechanisms to the antimicrobial class detected.
Positive screening test: MIC above or zone diameter below the resistant breakpoint for the screening agent. Resistance mechanisms to the antimicrobial class detected.

10. For an agent and a species, the ECOFF (epidemiological cut-off) value is the highest MIC (or the smallest inhibition zone diameter) for organisms devoid of phenotypically detectable acquired resistance mechanisms. Breakpoints in brackets are based on ECOFF values for relevant species. They are used to distinguish between organisms with and without acquired resistance mechanisms. ECOFFs do not predict clinical susceptibility but in some situations and/or when the agent is combined with another active agent, therapy may be considered.

11. Breakpoints in brackets distinguish between isolates without and with phenotypically detectable resistance mechanisms. They are based on ECOFFs but since they may serve more than one species, the value may represent a best fit. For these agents, clinical evidence as monotherapy is usually lacking but for a specific indication or in combination with another active agent or measure they may still be used. Isolates with resistance can be reported R (resistant). Reporting S or I should be avoided and if considered necessary, there should be a comment to explain the need for adjunctive measures as mentioned above.

12. An MIC breakpoint of S ≤ 0.001 mg/L is an arbitrary, "off scale" breakpoint (corresponding to a zone diameter breakpoint of "S ≥ 50 mm") which categorises wild-type organisms (organisms without phenotypically detectable resistance mechanisms to the agent) as "Susceptible, increased exposure" (I). For these organism-agent combinations, never report “Susceptible, standard dosing regimen” (S).

13. For some organism-agent combinations, results may be in an area where the interpretation is uncertain. EUCAST has designated this an Area of Technical Uncertainty (ATU). It corresponds to an MIC value and/or zone diameter interval where the categorisation is doubtful. See separate page for more information on ATU and how to deal with results in the ATU.

14. In order to simplify the EUCAST tables, the "Susceptible, increased exposure" (I category) is not listed. It is interpreted as values between the S and the R breakpoints. For example, for MIC breakpoints listed as S ≤ 1 mg/L and R > 8 mg/L, the I category is 2-8 (technically >1-8) mg/L, and for zone diameter breakpoints listed as S ≥ 22 mm and R < 18 mm, the I category is 18-21 mm.

15. For *Escherichia coli* with fosfomycin, *Staphylococcus aureus* with benzylpenicillin, enterococci with vancomycin, *Haemophilus influenzae* with beta-lactam agents, *Stenotrophomonas maltophilia*, *Aeromonas* spp., *Achromobacter xylosoxidans* and *Burkholderia pseudomallei* with trimethoprim-sulfamethoxazole, and for anaerobic bacteria in general, it is crucial to follow specific reading instructions for correct interpretation of the disk diffusion test. For these, pictures with reading examples are included at the end of the corresponding breakpoint table. For general and other specific reading instructions, please refer to the EUCAST Reading Guide.

16. With a few exceptions, EUCAST recommends the use of the broth microdilution reference method as described by the International Standards Organisation for MIC determination of non-fastidious organisms. For fastidious organisms, EUCAST recommends the use of the same methodology but with the use of MH-F broth (Mueller-Hinton broth with lysed horse blood and beta-NAD), see EUCAST media preparation file at www.eucast.org. There are a number of commercially available surrogate methods, for which it is the responsibility of the manufacturer to guarantee the accuracy of the system and the responsibility of the user to quality control the results.

17. By international convention, MIC dilution series are based on twofold dilutions up and down from 1 mg/L. At dilutions below 0.25 mg/L, this leads to concentrations with multiple decimal places. To avoid having to use these in tables and documents, EUCAST has decided to use the following format (in bold): 0.125→**0.125**, 0.0625→**0.06**, 0.03125→**0.03**, 0.015625→**0.016**, 0.0078125→**0.008**, 0.00390625→**0.004** and 0.001953125→**0.002** mg/L.

18. Definitions of "uncomplicated UTI" and “Infections originating from the urinary tract” used with EUCAST breakpoints:
Uncomplicated UTI: acute, sporadic or recurrent lower urinary tract infections (uncomplicated cystitis) in patients with no known relevant anatomical or functional abnormalities within the urinary tract or comorbidities.
Infections originating from the urinary tract: Infections originating from, but not confined to, the urinary tract, including acute pyelonephritis and bloodstream infections.

Abbeviations
NA = Not Applicable
IP = In Preparation

Guidance on reading EUCAST Breakpoint Tables

EUCAST Clinical Breakpoint Tables v. 14.0, valid from 2024-01-01

MIC determination (broth microdilution according to ISO standard 20776-1)
Medium:
Inoculum:
Incubation:
Reading:
Quality control:

EUCAST methodology and quality control for MIC determination

Disk diffusion (EUCAST standardised disk diffusion method)
Medium:
Inoculum:
Incubation:
Reading:
Quality control:

EUCAST methodology and quality control for disk diffusion

An arbitrary "off scale" breakpoint which categorises wild-type organisms as "Susceptible, increased exposure (I)".

Breakpoints with a species name apply only to that particular species (in this example *S. aureus*)

The I category is not listed but is interpreted as the values between the S and the R breakpoints. If the S and R breakpoints are the same value there is no I category.

Agent A: No I category
Agent B: I category: 4 mg/L, 23-25 mm
Agent H: I category: 1-2 mg/L, 24-29 mm

Area of Technical Uncertainty
See specific information on how to handle technical uncertainty in antimicrobial susceptibility testing.

Antimicrobial agent	MIC breakpoint (mg/L)			Disk content (µg)	Zone diameter breakpoint (mm)			Notes
	S ≤	R >	ATU		S ≥	R <	ATU	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.
Antimicrobial agent A	1[1]	1[1]		X	20[A]	20[A]		1. Notes that are general comments and/or relating to MIC breakpoints.
Antimicrobial agent B	2[2]	4		Y	26	23		2. New comment
Antimicrobial agent C	0.001	8		X	50	18		~~Removed comment~~
Antimicrobial agent D, *S. aureus*	IE	IE			IE	IE		
Antimicrobial agent E	-	-			-	-		A. Comment on disk diffusion
Antimicrobial agent F	IP	IP			IP	IP		
Antimicrobial agent G (screen only)	NA	NA		Y	25	25		
Antimicrobial agent H	0.5	2		Z	30	24		
Antimicrobial agent I	(8)[1]	(8)[1]		30	(18)[A]	(18)[A]		

A screening test that uses one agent to predict resistance or susceptibility to one or more antimicrobial agents in the same class

Not Applicable

Changes from previous version highlighted in yellow

The agent is unsuitable for treatment. Susceptibility testing is not recommended

In Preparation

MIC breakpoints in blue are linked to MIC distributions

Zone diameter breakpoints in blue are linked to zone diameter distributions

Antimicrobial agents in blue are linked to EUCAST rationale documents

Breakpoints in brackets are used to distinguish between organisms with and without acquired resistance mechanisms (see Notes)

Insufficient evidence that the organism or group is a good target for therapy with the agent

Pseudomonas aeruginosa

Fluoroquinolones	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)		
	S ≤	R >	ATU		S ≥	R <	ATU
Ciprofloxacin	0.001	0.5		5	50	26	
Delafloxacin	IE	IE			IE	IE	
Levofloxacin	0.001	2		5	50	18	
Moxifloxacin	-	-			-	-	
Nalidixic acid (screen only)	NA	NA			NA	NA	

"IE" in breakpoint tables indicate a lack of evidence for clinical efficacy on which to determine breakpoints - however, EUCAST has not disqualified the agent. Laboratories are recommended to consult guidance document on "What to do when there are no breakpoints".

Aminoglycosides[1]	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)		
	S ≤	R >	ATU		S ≥	R <	ATU
Amikacin (systemic infections)	(16)[1]	(16)[1]		30	(15)[A]	(15)[A]	
Amikacin (infections originating from the urinary tract)	16	16		30	15	15	
Gentamicin (systemic infections)	IE	IE			IE	IE	
Gentamicin (infections originating from the urinary tract)	IE	IE			IE	IE	
Netilmicin	IE	IE			IE	IE	
Tobramycin (systemic infections)	(2)[1]	(2)[1]		10	(18)[A]	(18)[A]	
Tobramycin (infections originating from the urinary tract)	2	2		10	18	18	

Pseudomonas aeruginosa

Fluoroquinolones	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)		
	S ≤	R >	ATU		S ≥	R <	ATU
Ciprofloxacin	0.001	0.5		5	50	26	
Delafloxacin	IE	IE			IE	IE	
Levofloxacin	0.001	2		5	50	18	
Moxifloxacin	-	-			-	-	
Nalidixic acid (screen only)	NA	NA			NA	NA	

Dash ("-") indicates that the agent is unsuitable for systemic infections caused by the species.
EUCAST refrained from determining breakpoints and recommend that the agent is not included in susceptibility test reports. If included, report **resistant** without prior testing.

Aminoglycosides[1]	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)		
	S ≤	R >	ATU		S ≥	R <	ATU
Amikacin (systemic infections)	(16)[1]	(16)[1]		30	(15)[A]	(15)[A]	
Amikacin (infections originating from the urinary tract)	16	16		30	15	15	
Gentamicin (systemic infections)	IE	IE			IE	IE	
Gentamicin (infections originating from the urinary tract)	IE	IE			IE	IE	
Netilmicin	IE	IE			IE	IE	
Tobramycin (systemic infections)	(2)[1]	(2)[1]		10	(18)[A]	(18)[A]	
Tobramycin (infections originating from the urinary tract)	2	2		10	18	18	

Pseudomonas aeruginosa

Fluoroquinolones	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)		
	S ≤	R >	ATU		S ≥	R <	ATU
Ciprofloxacin	0.001	0.5		5	50	26	
Delafloxacin	IE	IE			IE	IE	
Levofloxacin	0.001	2		5	50	18	
Moxifloxacin	-	-			-	-	
Nalidixic acid (screen only)	NA	NA			NA	NA	
Norfloxacin (uncomplicated UTI only)	-	-			-	-	
Ofloxacin	-	-			-	-	

Arbitrary breakpoints (S ≤0.001 mg/L; S≥50 mm) prevent the reporting of "S" (Susceptible at normal dosing).

Aminoglycosides[1]	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)		
	S ≤	R >	ATU		S ≥	R <	ATU
Amikacin (systemic infections)	(16)[1]	(16)[1]		30	(15)[A]	(15)[A]	
Amikacin (infections originating from the urinary tract)	16	16		30	15	15	
Gentamicin (systemic infections)	IE	IE			IE	IE	
Gentamicin (infections originating from the urinary tract)	IE	IE			IE	IE	
Netilmicin	IE	IE			IE	IE	
Tobramycin (systemic infections)	(2)[1]	(2)[1]		10	(18)[A]	(18)[A]	
Tobramycin (infections originating from the urinary tract)	2	2		10	18	18	

Pseudomonas aeruginosa

Fluoroquinolones	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)		
	S ≤	R >	ATU		S ≥	R <	ATU
Ciprofloxacin	0.001	0.5		5	50	26	
Delafloxacin	IE	IE			IE	IE	
Levofloxacin	0.001	2		5	50	18	
Moxifloxacin	-	-			-	-	
Nalidixic acid (screen only)	NA	NA			NA	NA	

Breakpoints in brackets – the agent should not be used without supplementary active therapy (another active agent or measure). The breakpoint in bracket will distingusih between organisms with and without resistance mechanisms. The caveat for use should be made clear in reports.

Aminoglycosides[1]	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)		
	S ≤	R >	ATU		S ≥	R <	ATU
Amikacin (systemic infections)	(16)[1]	(16)[1]		30	(15)[A]	(15)[A]	
Amikacin (infections originating from the urinary tract)	16	16		30	15	15	
Gentamicin (systemic infections)	IE	IE			IE	IE	
Gentamicin (infections originating from the urinary tract)	IE	IE			IE	IE	
Netilmicin	IE	IE			IE	IE	
Tobramycin (systemic infections)	(2)[1]	(2)[1]		10	(18)[A]	(18)[A]	
Tobramycin (infections originating from the urinary tract)	2	2		10	18	18	

”Screen only” in breakpoint tables

9. A screening test uses one agent to predict resistance or susceptibility to one or more antimicrobial agents in the same class. The screening test is often more sensitive and/or robust than testing individual agents. Using a screening test will often reduce the number of tests needed in primary susceptibility testing since it will predict susceptibility and/or resistance to several agents. Guidance on how to act on the screening test result is described in the Note related to each specific screening test.

Negative screening test: MIC below or equal to, or zone diameter above or equal to, the susceptible cut-off for the screening agent. No resistance mechanisms to the antimicrobial class detected.

Positive screening test: MIC above or zone diameter below the resistant cut-off for the screening agent. Resistance mechanisms to the antimicrobial class detected.

Fluoroquinolones *Streptococcus pneumoniae*	**MIC breakpoints (mg/L)**			**Disk content (µg)**	**Zone diameter breakpoints (mm)**			**Notes** Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.
	S ≤	**R >**	**ATU**		**S ≥**	**R <**	**ATU**	
Ciprofloxacin	-	-			-	-		**A.** The norfloxacin disk diffusion test can be used to screen for fluoroquinolone resistance. **See Note B.**
Delafloxacin	IE	IE			IE	IE		**B.** Isolates categorised as screen negative can be reported susceptible to moxifloxacin and as "susceptible increased exposure" (I) to levofloxacin. Isolates categorised as screen positive should be tested for susceptibility to individual agents or reported resistant.
Levofloxacin	0.001	2		5	50[A]	16[A]		
Moxifloxacin	0.5	0.5		5	22[A]	22[A]		
Nalidixic acid (screen only)	NA	NA			NA	NA		
Norfloxacin (screen only)	NA	NA		10	10[B]	10[B]		
Ofloxacin	-	-			-	-		

EUCAST 2024

Streptococcus pneumoniae

Expert Rules and Intrinsic Resistance Tables

An MIC breakpoint of S ≤ 0.001 mg/L is an arbitrary, "off scale" breakpoint (corresponding to a zone diameter breakpoint of "S ≥ 50 mm") which categorises wild-type organisms (organisms without phenotypically detectable resistance mechanisms to the agent) as "Susceptible, increased exposure" (I). For these organism-agent combinations, never report "Susceptible, standard dosing regimen" (S).

MIC determination (broth microdilution according to ISO standard 20776-1)
Medium: Mueller-Hinton broth + 5% lysed horse blood and 20 mg/L β-NAD (MH-F broth)
Inoculum: $5x10^5$ CFU/mL
Incubation: Sealed panels, air, 35±1°C, 18±2h
Reading: Unless otherwise stated, read MICs at the lowest concentration of the agent that completely inhibits visible growth. See "EUCAST Reading Guide for broth microdilution" for further information.
Quality control: *Streptococcus pneumoniae* ATCC 49619. For agents not covered by this strain, see EUCAST QC Tables.

Disk diffusion (EUCAST standardised disk diffusion method)
Medium: Mueller-Hinton agar + 5% defibrinated horse blood and 20 mg/L β-NAD (MH-F)
Inoculum: McFarland 0.5 from blood agar or McFarland 1.0 from chocolate agar
Incubation: 5% CO_2, 35±1°C, 18±2h
Reading: Unless otherwise stated, read zone edges as the point showing no growth viewed from the front of the plate with the lid removed and with reflected light. See "EUCAST Reading Guide for disk diffusion" for further information.
Quality control: *Streptococcus pneumoniae* ATCC 49619. For agents not covered by this strain, see EUCAST QC Tables.

Penicillins[1]	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)		
	S ≤	R >	ATU		S ≥	R <	ATU
Benzylpenicillin (indications other than meningitis)[2]	0.06	2			Note[A]	Note[A]	
Benzylpenicillin (meningitis)	0.06	0.06			Note[A]	Note[A]	
Ampicillin (indications other than meningitis)	0.5	1		2	22	19	
Ampicillin (meningitis)	0.5	0.5			Note[A,B]	Note[A,B]	
Ampicillin-sulbactam[3]	Note[1,4]	Note[1,4]			Note[A,C]	Note[A,C]	
Amoxicillin iv (indications other than meningitis)	Note[1,4]	Note[1,4]			Note[A,C]	Note[A,C]	
Amoxicillin iv (meningitis)	0,5	0,5			Note[A,B]	Note[A,B]	
Amoxicillin oral	0,5	1			Note[A,C]	Note[A,C]	
Amoxicillin-clavulanic acid iv[3]	Note[1,4]	Note[1,4]			Note[A,C]	Note[A,C]	
Amoxicillin-clavulanic acid oral[3]	0.5[5]	1[5]			Note[A,C]	Note[A,C]	
Piperacillin	Note[1,4]	Note[1,4]			Note[A,C]	Note[A,C]	
Piperacillin-tazobactam[3]	Note[1,4]	Note[1,4]			Note[A,C]	Note[A,C]	
Ticarcillin	-	-			-	-	
Ticarcillin-clavulanic acid	-	-			-	-	
Temocillin	-	-			-	-	
Phenoxymethylpenicillin	Note[1]	Note[1]			Note[A]	Note[A]	
Oxacillin (screen only)[1]	NA	NA		1	20[D]	Note[D]	
Cloxacillin	-	-			-	-	
Dicloxacillin	-	-			-	-	
Flucloxacillin	-	-			-	-	
Mecillinam oral (pivmecillinam) (uncomplicated UTI only)	-	-			-	-	

Notes
Numbered notes relate to general comments and/or MIC breakpoints.
Lettered notes relate to the disk diffusion method.

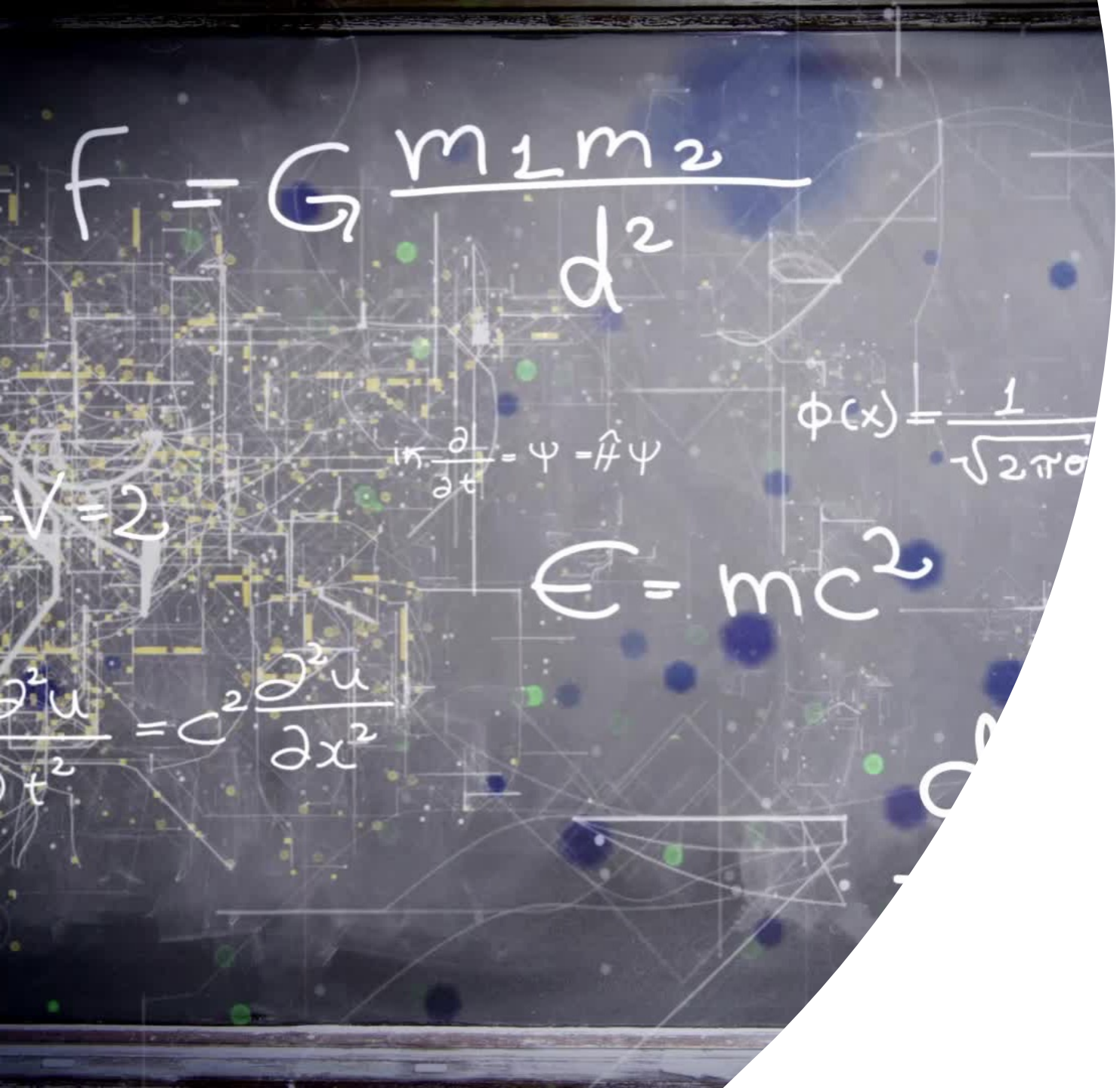
1/A. The oxacillin 1 µg disk diffusion screening test or a benzylpenicillin MIC test shall be used to exclude beta-lactam resistance mechanisms. When the screen is negative (oxacillin inhibition zone ≥20 mm, or benzylpenicillin MIC ≤0.06 mg/L) all beta-lactam agents for which clinical breakpoints are available, including those with "Note" can be reported susceptible without further testing, except for cefaclor, which if reported, should be reported as "susceptible, increased exposure" (I). When the screen is positive (oxacillin zone <20 mm, or benzylpenicillin MIC >0.06 mg/L), **see flow chart below**.
2. For breakpoints and dosing in pneumonia, see table of dosages.
3. The addition of a beta-lactamase inhibitor does not add clinical benefit.
4/C. Susceptibility inferred from ampicillin (indications other than meningitis).
5. For susceptibility testing purposes, the concentration of clavulanic acid is fixed at 2 mg/L.

B. For isolates with an oxacillin 1 µg zone <9 mm, determine the MIC. For isolates with an oxacillin zone ≥9 mm, report susceptible without further testing.
~~**D. Perform an MIC or infer susceptibility from the ampicillin 2 µg disk diffusion test with ampicillin breakpoints S≥22, R<19 mm.**~~
D. For interpretation of the oxacillin disk screen, see flow chart below.

Oxacillin (screen only)[1]
"Screen only tests" exclude resistance to one or several agents. Screen tests prioritise sensitivity over specificity. If positive, report resistant or test individual agent.

Task: familiarise yourself with the EUCAST breakpoint tables and some of the linked guidance documents

- http://www.eucast.org
- https://www.eucast.org/clinical_breakpoints
- https://www.eucast.org/expert_rules_and_expected_phenotypes
- https://www.eucast.org/eucastguidancedocuments
  - Breakpoints in brackets
  - When there are no breakpoints
  - Screening to detect or exclude resistance to a class of agents

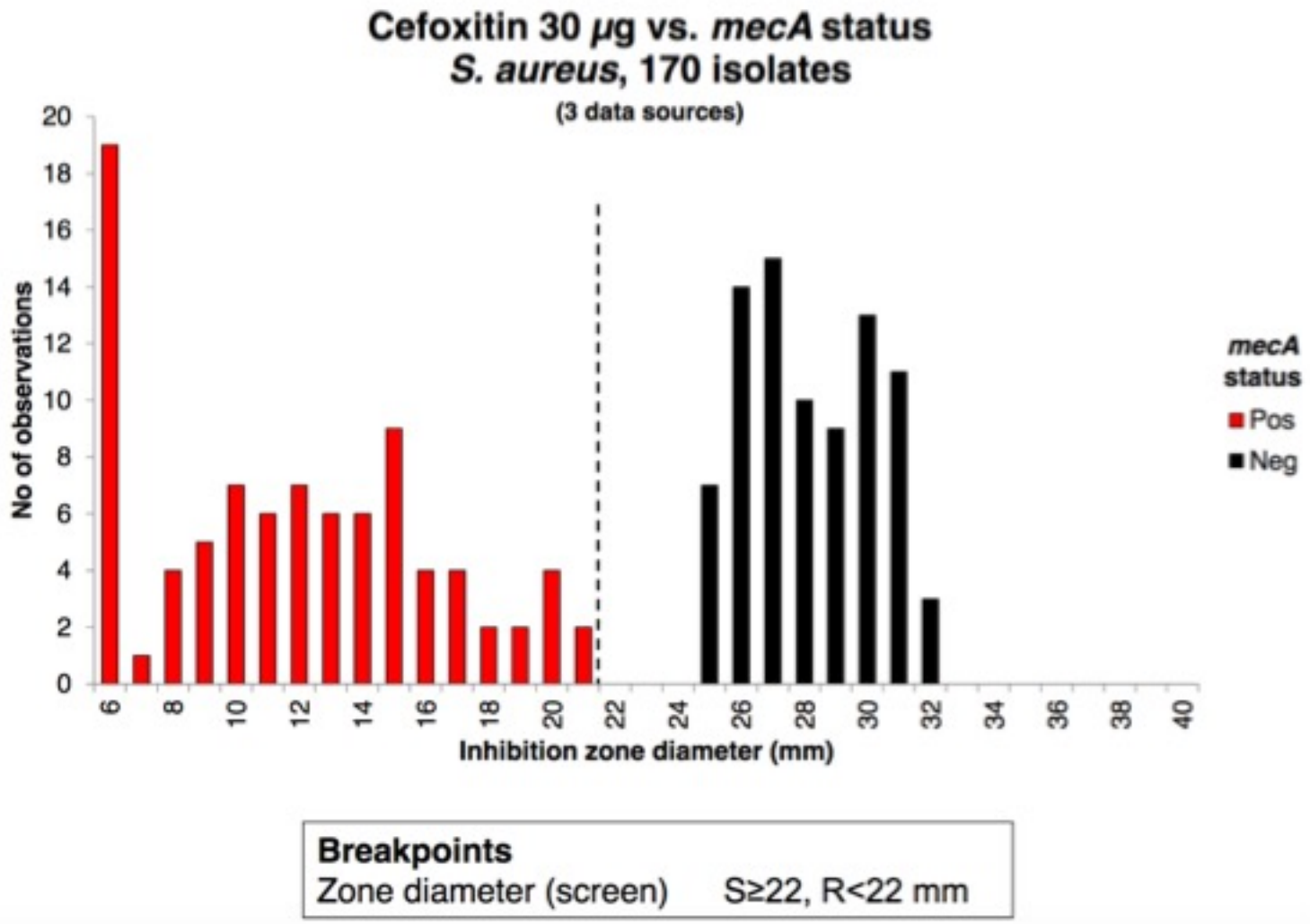


ATU

The Area of Technical Uncertainty

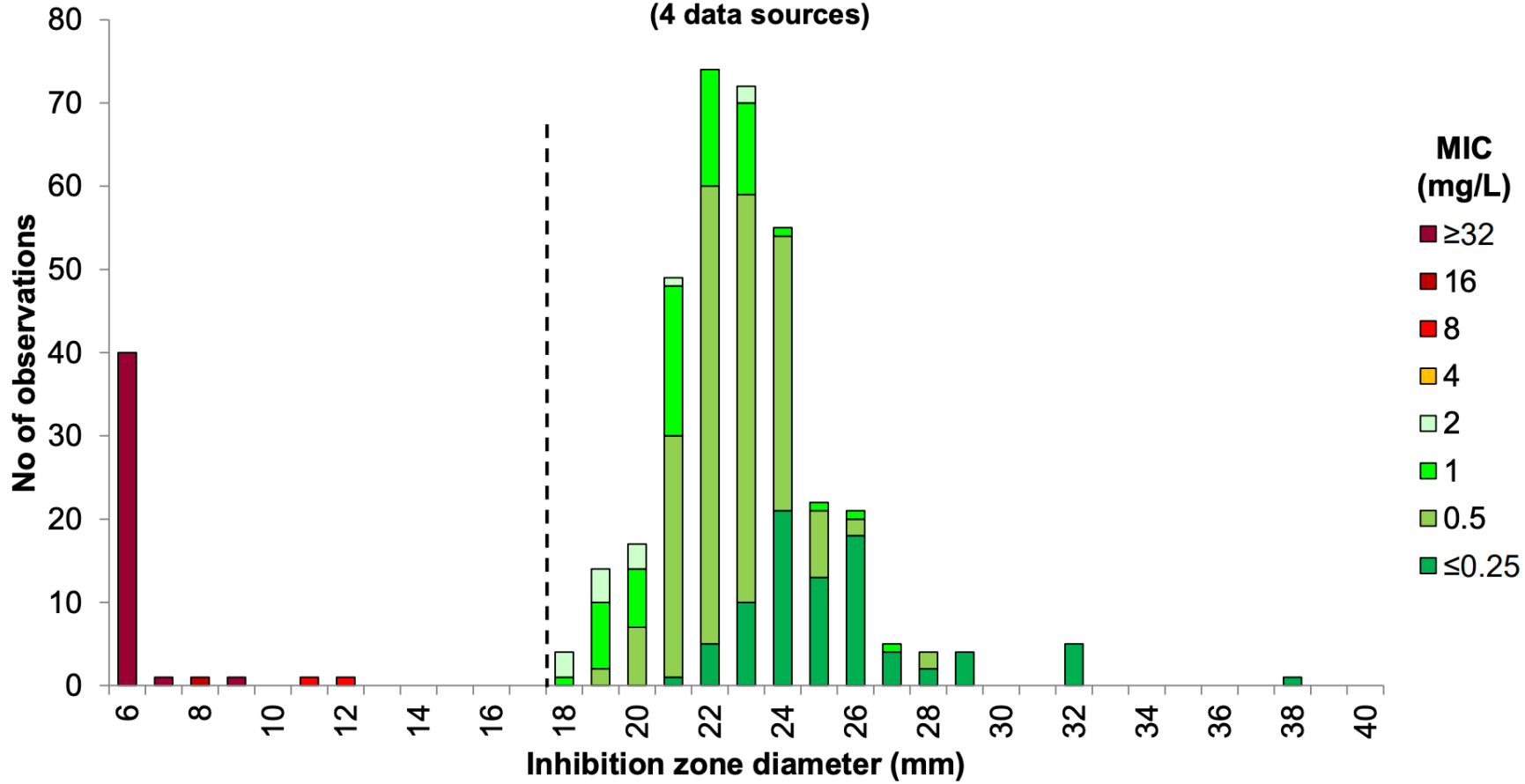
Gunnar Kahlmeter 2022

Most AST is unproblematic



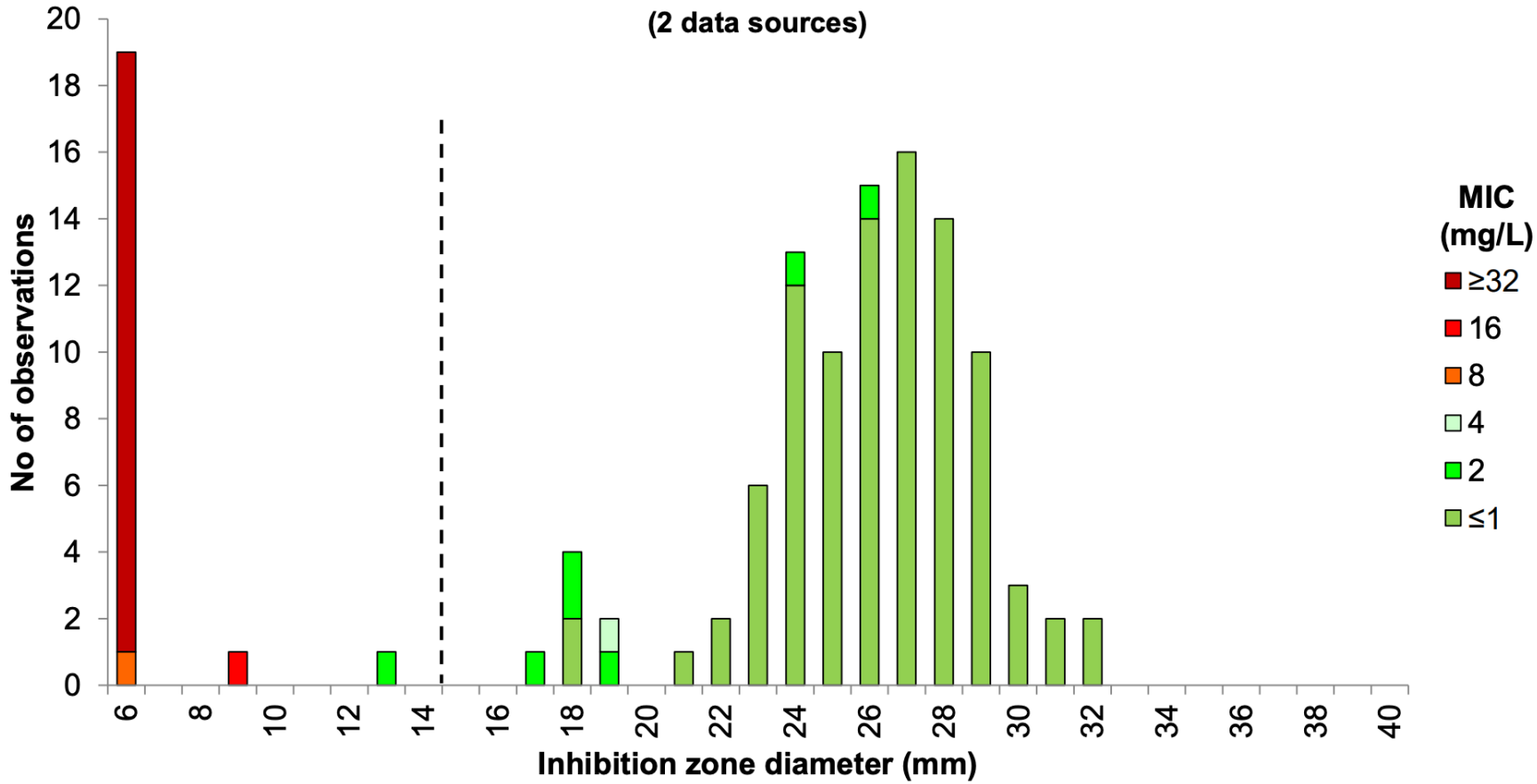
Tobramycin 10 µg vs. MIC
P. aeruginosa, 285 isolates (392 correlates)

(4 data sources)



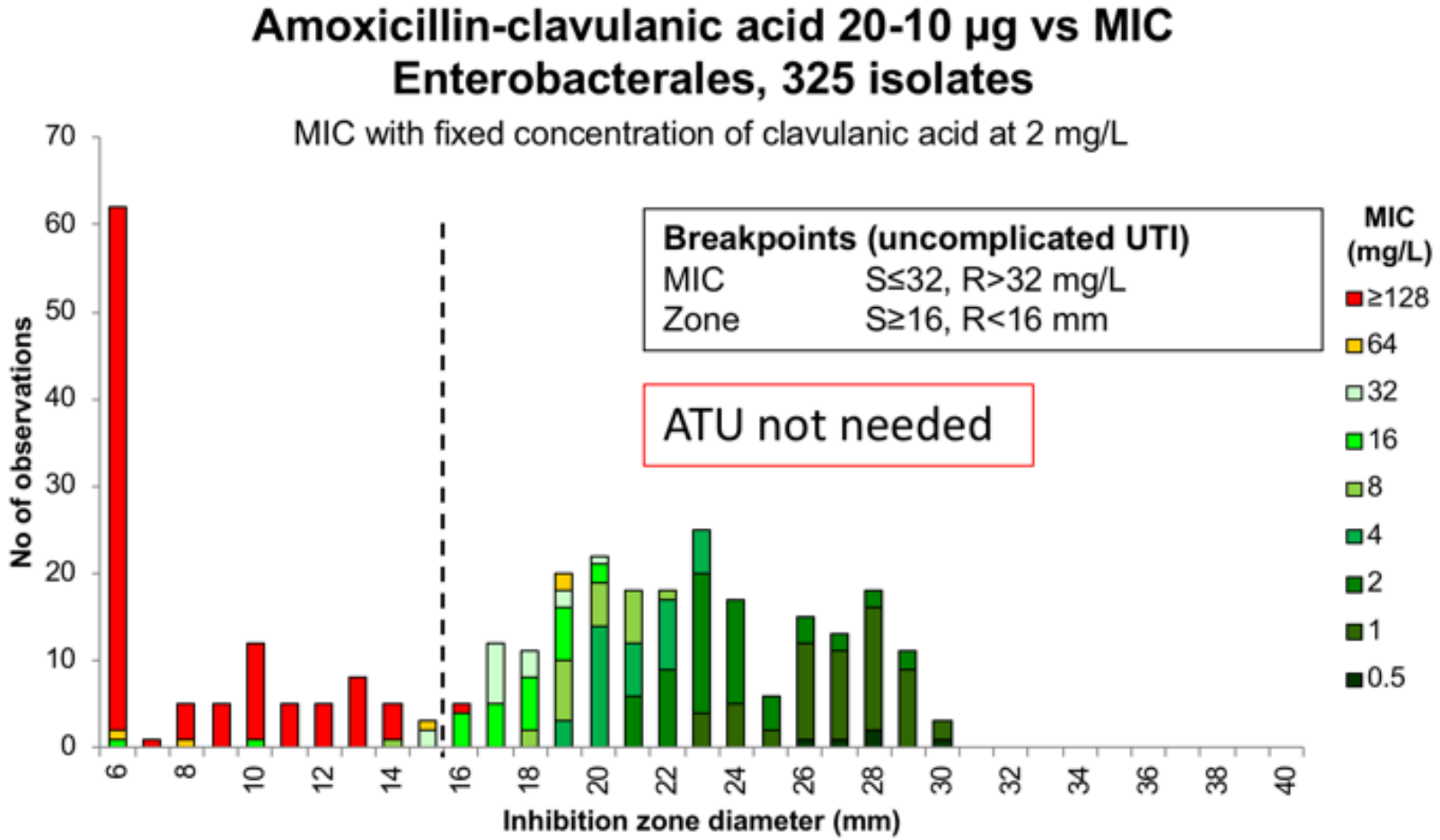
Breakpoints	
MIC	S≤2, R>2 mg/L
Zone diameter	S≥18, R<18 mm

Trimethoprim 5 µg vs. MIC
Enterobacterales, 122 isolates



Breakpoints	
MIC	S≤4, R>4 mg/L
Zone diameter	S≥15, R<15 mm

Amoxicillin-clavulanic acid vs. Enterobacterales with breakpoints for uncomplicated UTI

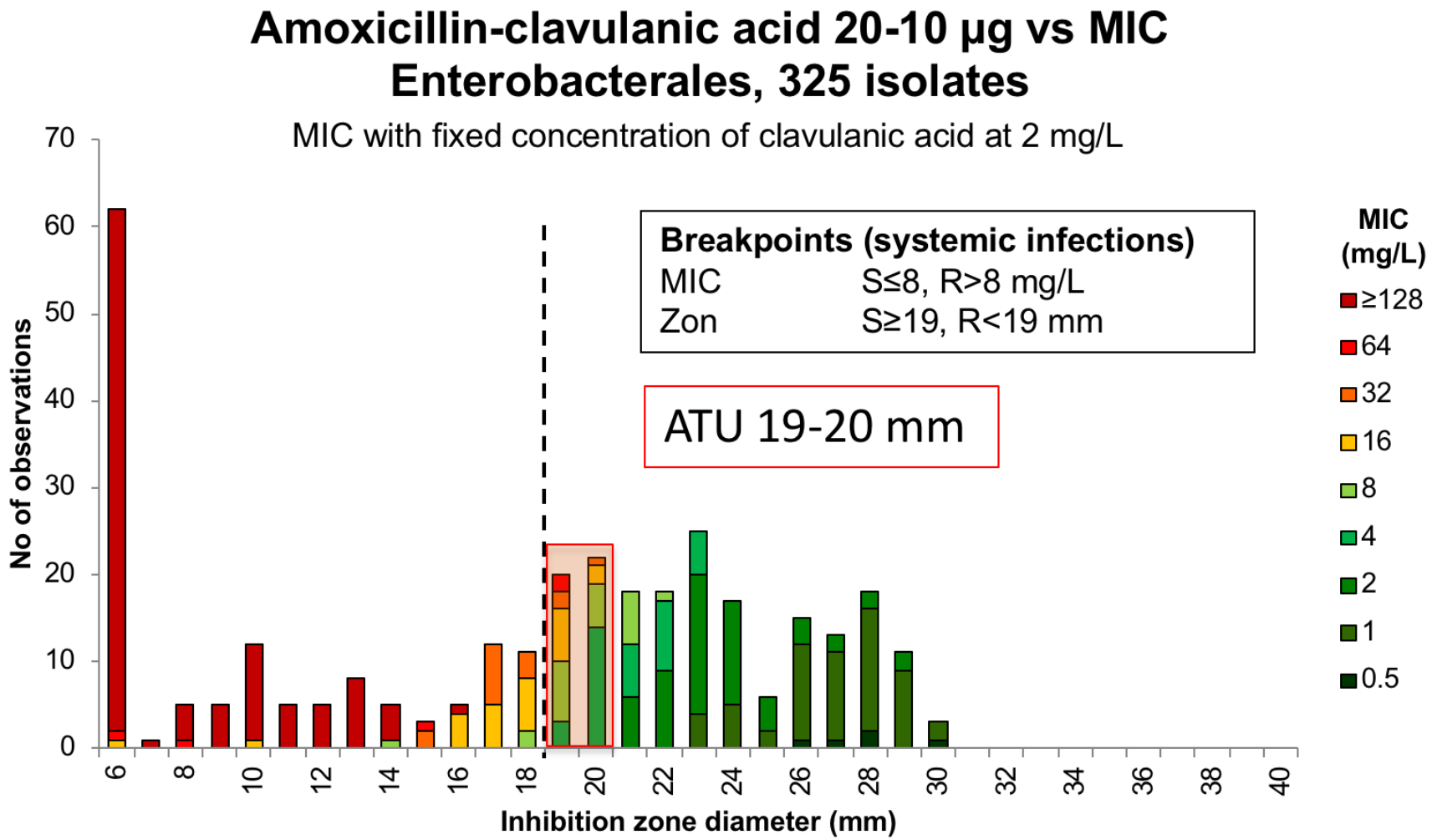


BUT, sometimes there is a need to “warn” laboratory staff

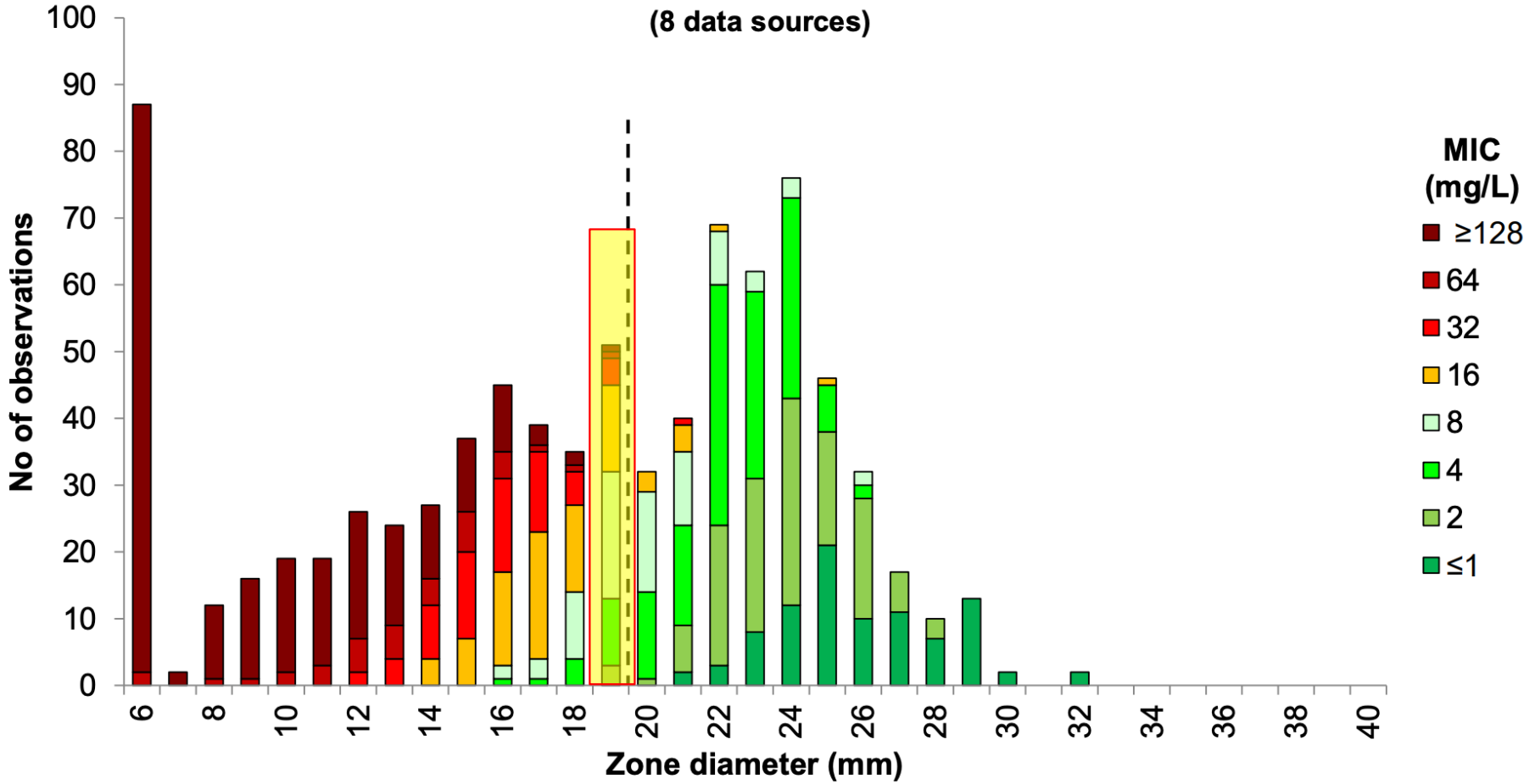
- variation in the method
- variation in the interpretation
  - Breakpoint splits wild type (mostly avoided by EUCAST)
  - Poor separation between susceptible and resistant population
  - Breakpoint splits an important resistant population
  - Incomplete correlation between disk diffusion and MIC results

ATUs are to warn staff about problems which are not due to poor quality of AST material.

Amoxicillin-clavulanic acid vs. Enterobacterales with breakpoints for systemic infections

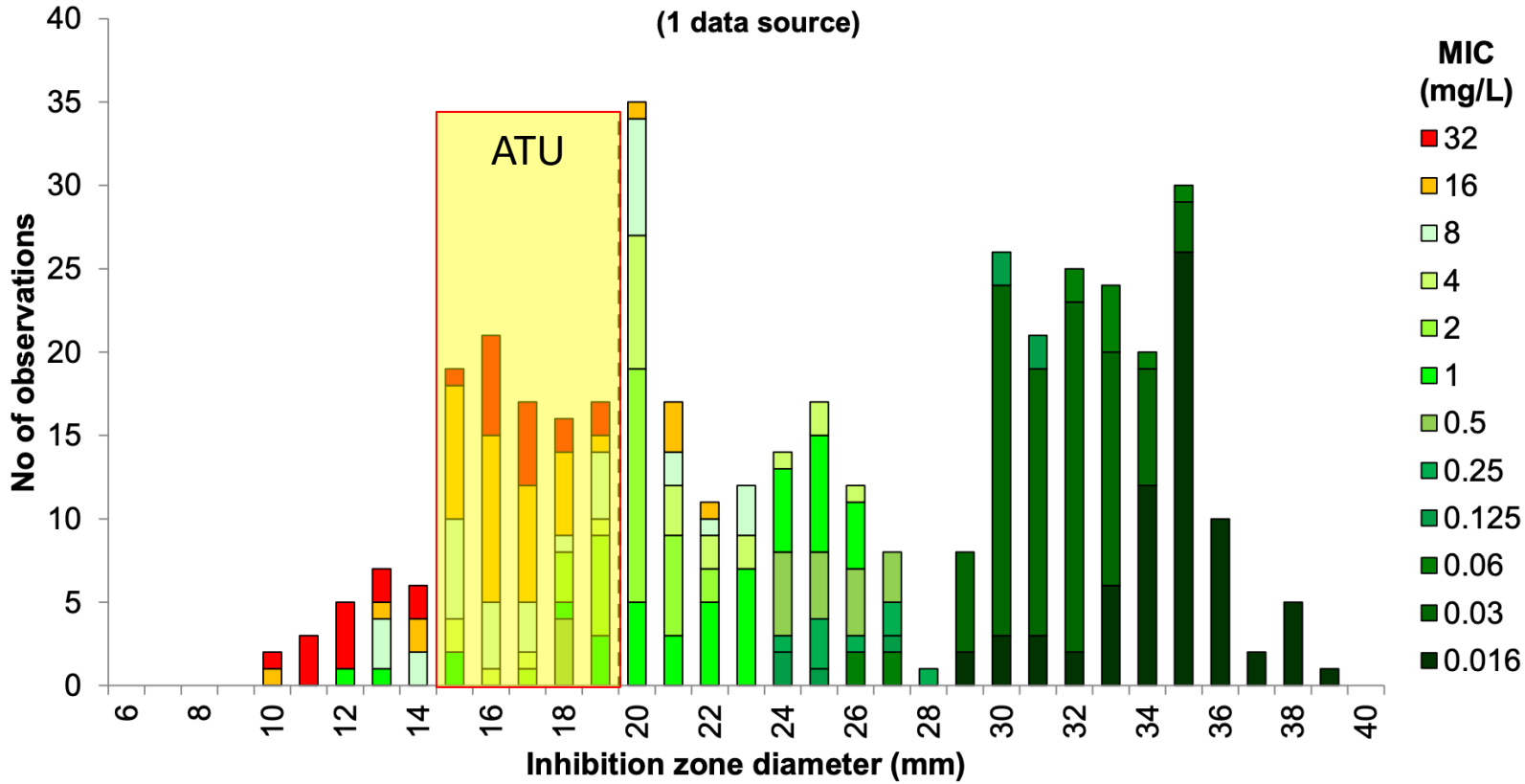


Piperacillin-tazobactam 30-6 µg vs. MIC
Enterobacterales, 531 isolates (840 correlates)



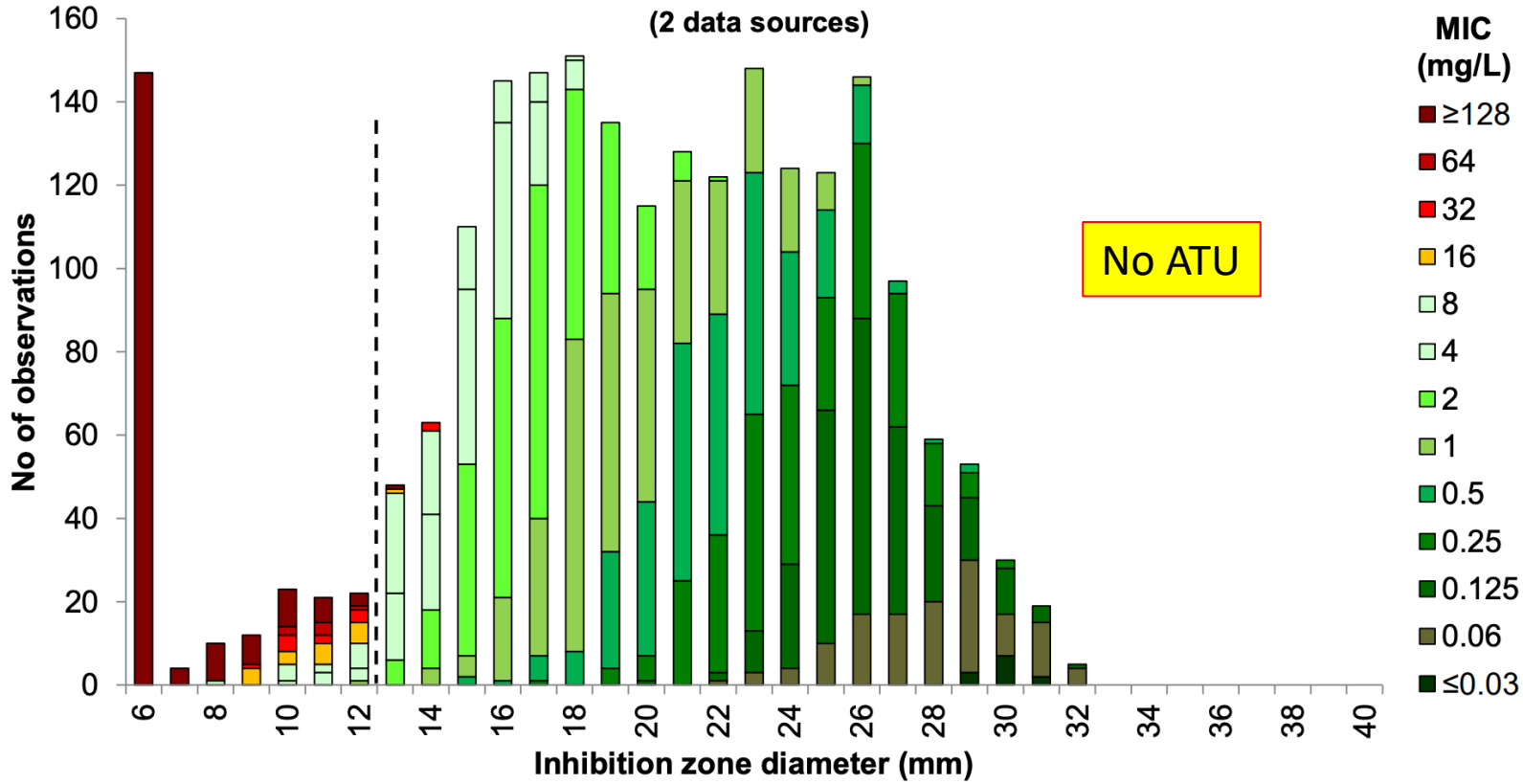
Breakpoints	
MIC	S≤8, R>8 mg/L
Zone diameter	S≥20, R<20 mm

Meropenem-vaborbactam 20-10 µg vs. MIC
Enterobacterales, 104 isolates (412 correlates)



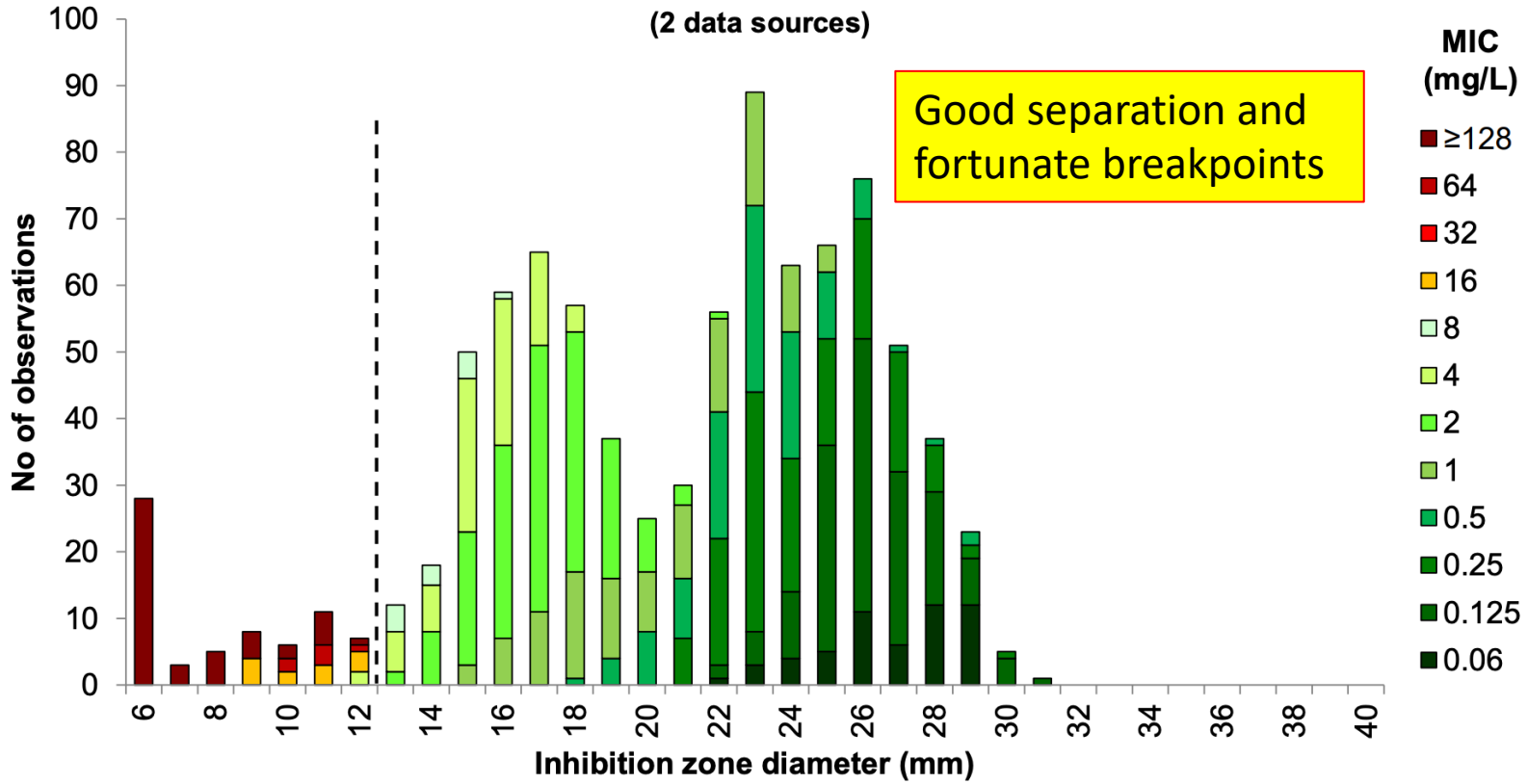
Breakpoints	
MIC	S≤8, R>8 mg/L
Zone diameter	S≥20, R<20 mm

Ceftazidime-avibactam 10-4 µg vs. MIC
Enterobacterales, 293 isolates (2207 correlates)



Breakpoints	
MIC	S≤8, R>8 mg/L
Zone diameter	S≥13, R<13 mm

Ceftazidime-avibactam 10-4 µg vs. MIC
E. coli, 124 isolates (888 correlates)



Breakpoints	
MIC	S≤8, R>8 mg/L
Zone diameter	S≥13, R<13 mm

ATU:

A warning or reminder in the laboratory

ATU in Kronoberg/Blekinge

Art	Piperacillintazobactam (ATU)*	Ciprofloxacin (ATU)*
E. coli	2.9 %	2.9 %
K.pneumoniae	6 %	6.6 %
Citrobacter freundi	4 %	2.3 %
Proteus mirabilis	<1 %	3.2 %
Morganella morganii	<1 %	5 %

*The per centage of routine isolates which were in the ATU.

Warning (ATU) – alternative actions

1. **Repeat the test** – if a technical problem is suspected (inoculum, disk, etc).
2. **Repeat test and confirm with alternative test** (MIC, PCR, PBP-agglutination…). Another test offering the same interpretation supports the initial interpretation.
3. **Report a "blank" with a comment:**
   "Ambiguous AST result which could not be interpreted".
4. **Report R if the conundrum cannot be solved.**
   "For Piperacillin 19 mm report "R" (or solve the problem).
5. **Explain and discuss with colleagues, over phone or lunch or via written guidelines.**

Try hard to solve IF.....

- easy to solve.
- in serious infections (blood culture results).
- if frequently recurring
- only few alternative antibiotics for therapy.