



**How to use Quality control to increase AST quality in your lab?**

**EQA**

**External Quality Assessment**

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# EQA programs

- **EARS-Net (~900 labs, 29 countries)**
  - Now co-ordinated by ECDC
- UKNEQAS
  - Charitable consortium of EQA labs
- National EQAs (eg public health institutes)

# EARS-Net 2025 Strains

- *Klebsiella pneumoniae* (2025 EARS-Net 1)
- *Acinetobacter baumannii* (2025 EARS-Net 2)
- *Staphylococcus aureus* (2025 EARS-Net 3)
- *Acinetobacter baumannii* (2025 EARS-Net 4)
- *Escherichia coli* (2025 EARS-Net 5)
- *Streptococcus pneumoniae* (2025 EARS-Net 6)
  - Reduced viability, participation approved despite failure to revive this strain

# EARS-Net Scoring system

## Level of difficulty

### Difficult

- AST one-fold dilution from different S/I/R
- MIC value within ATU
- Recently changed or newly introduced breakpoint

### Easy

- AST away from different S/I/R
- No recent changes

## Error categories

### Very major error (VME)

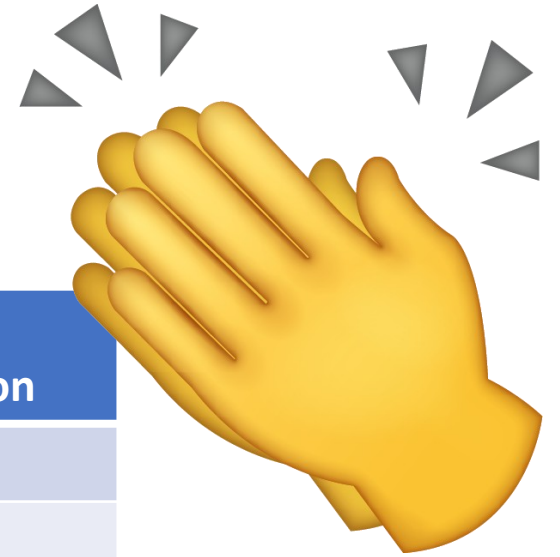
- R reported as S or I

### Major error (ME)

- S or I reported as R

### No error

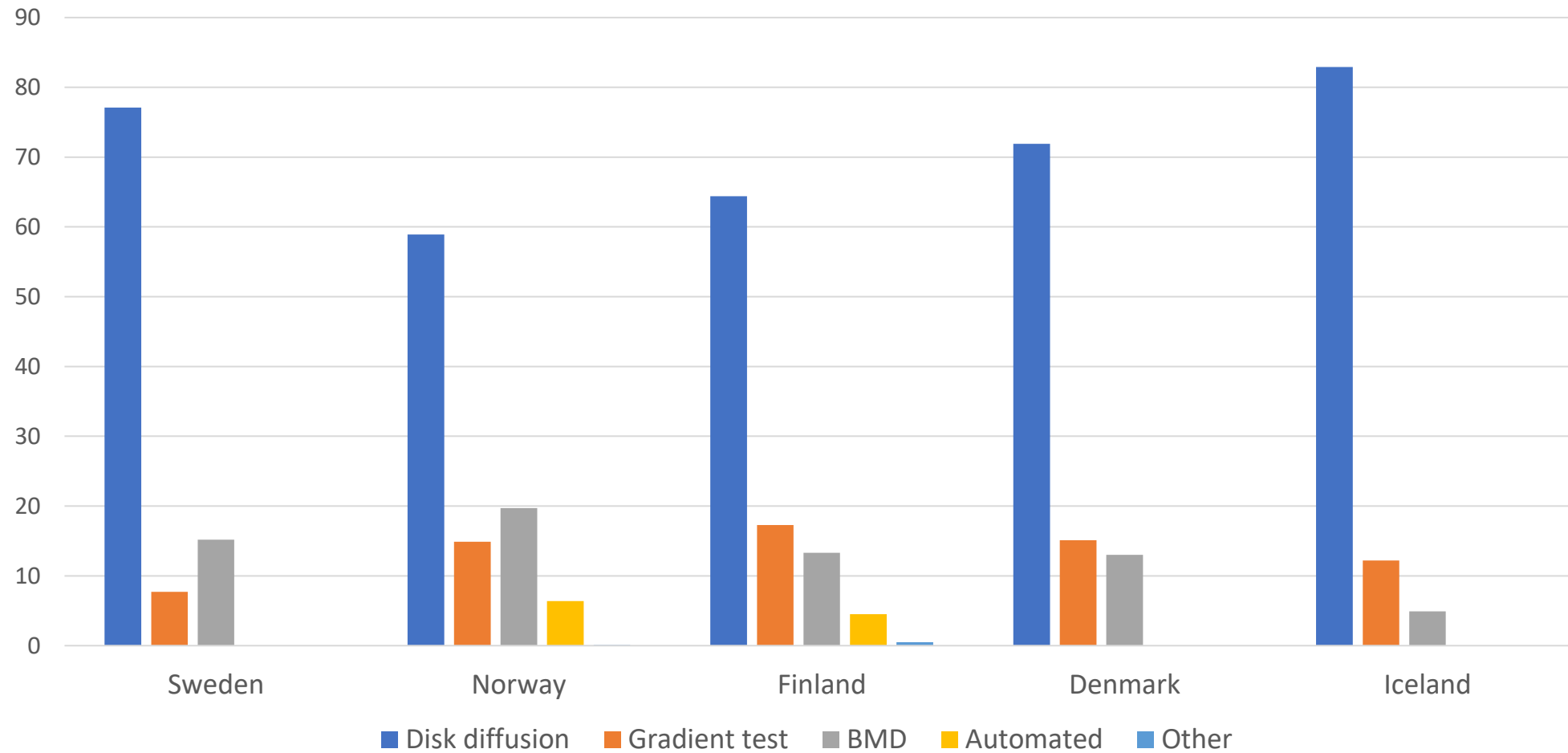
# EARS-Net Nordic countries



	Labs submitting results	Number of tests	Average no of tests per lab	Correct interpretation
Sweden	21	1326	63	<b>96.0%</b>
Norway	17	981	58	<b>94.8%</b>
Denmark	4	192	48	<b>97.4%</b>
Finland	13	663	51	<b>94.3%</b>
Iceland	1	82	82	<b>95.1%</b>



# Methodology



# Results by method

	DD (n)	DD correct%	Gradient test (n)	Gradient test correct%	BMD (n)	BMD correct%
Sweden	1 023	<b>96.8</b>	102	<b>92.2</b>	201	<b>94.0</b>
Norway	578	<b>96.5</b>	146	<b>92.5</b>	193	<b>90.2</b>
Denmark	138	<b>99.3</b>	29	<b>96.6</b>	25	<b>88.0</b>
Finland	427	<b>97.0</b>	115	<b>82.6</b>	88	<b>94.3</b>
Iceland	68	<b>98.5</b>	10	<b>80.0</b>	4	<b>75.0</b>

# What to learn from EARS-Net 2025?

## Strain 1: *Klebsiella pneumoniae* (blaNDM-1)



Figure 4. Reported interpretation of AST results for strain '2025 EARS-Net 1' (*Klebsiella pneumoniae*) by antimicrobial agent and anticipated difficulty of identification

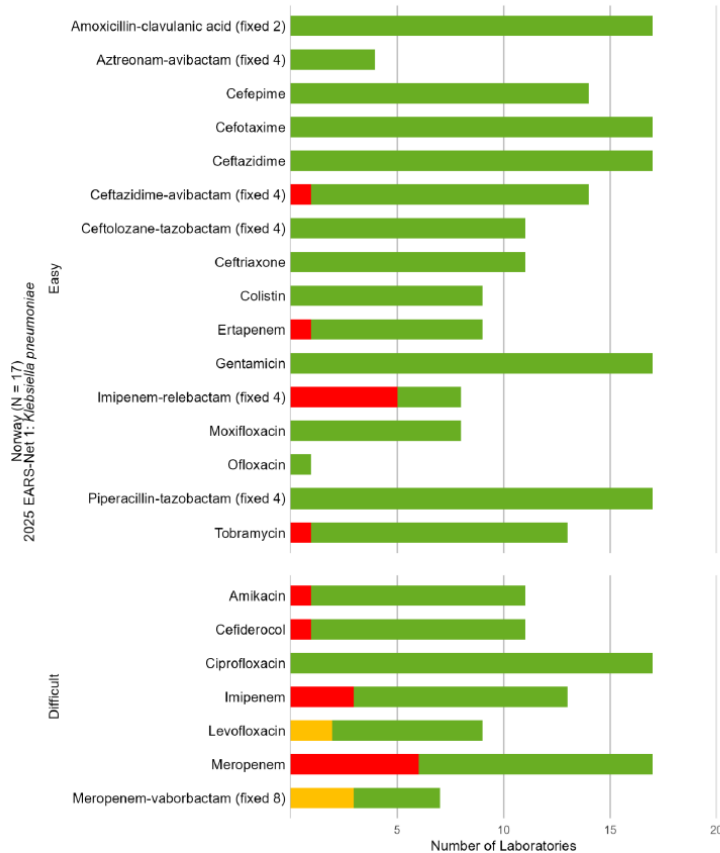
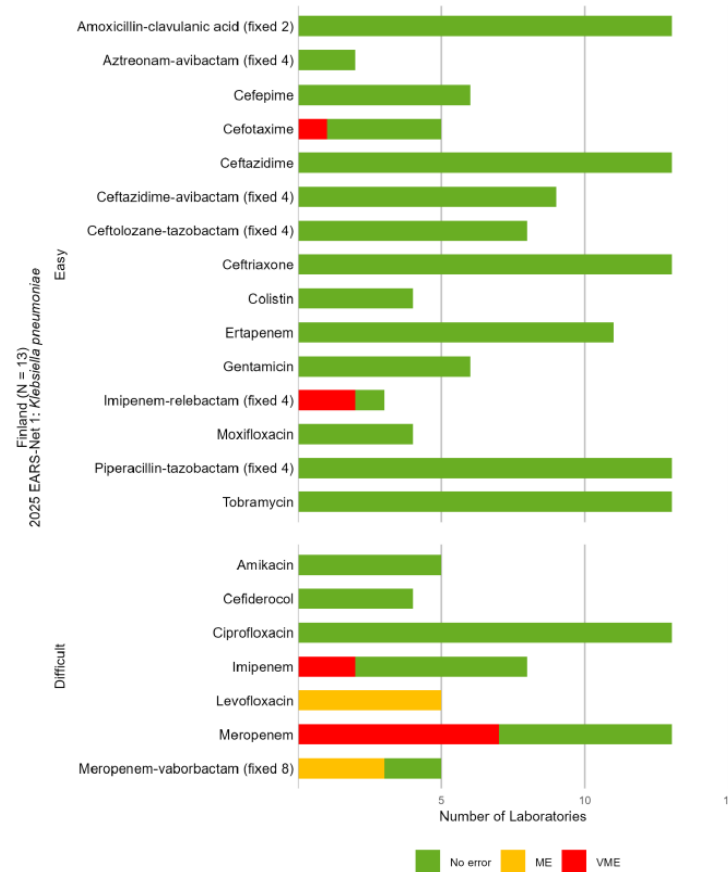


Figure 4. Reported interpretation of AST results for strain '2025 EARS-Net 1' (*Klebsiella pneumoniae*) by antimicrobial agent and anticipated difficulty of identification



Common problems	Target MIC mg/L	Bps	Error	Method(s)
Meropenem	16 (R)	2/8	VME	BMD,DD, GrT
Imipenem	8 (R)	2/4	VME	
Imipenem-relebactem	8 (R)	2/2	VME	GrT
Meropenem-vaborbactam	8 (S)	8/8	ME	DD, GrT
Levofloxacin	1 (I)	0.5/1	ME	DD, GrT

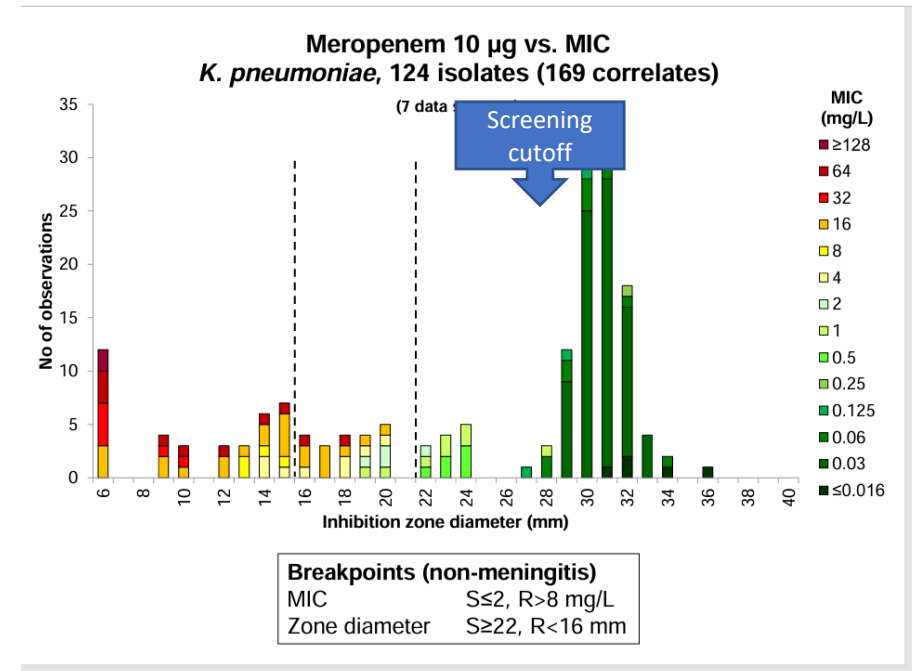
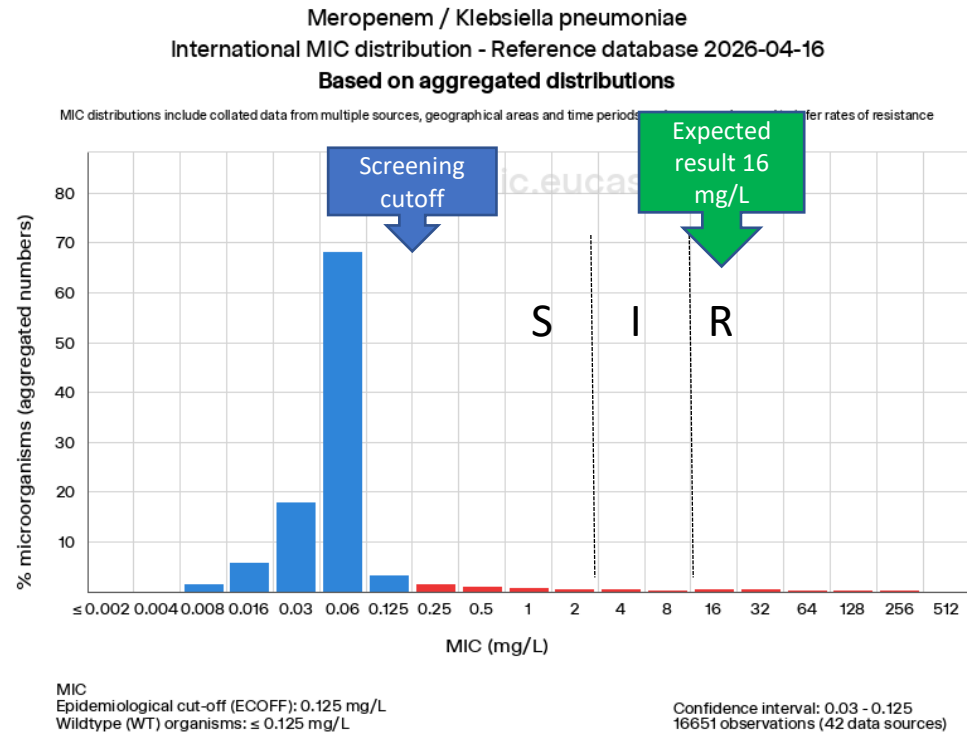
VME: very major error (false S/I)

ME: major error (false R)

Methods: BMD broth micro dilution, DD disk diffusion, GrT gradient test



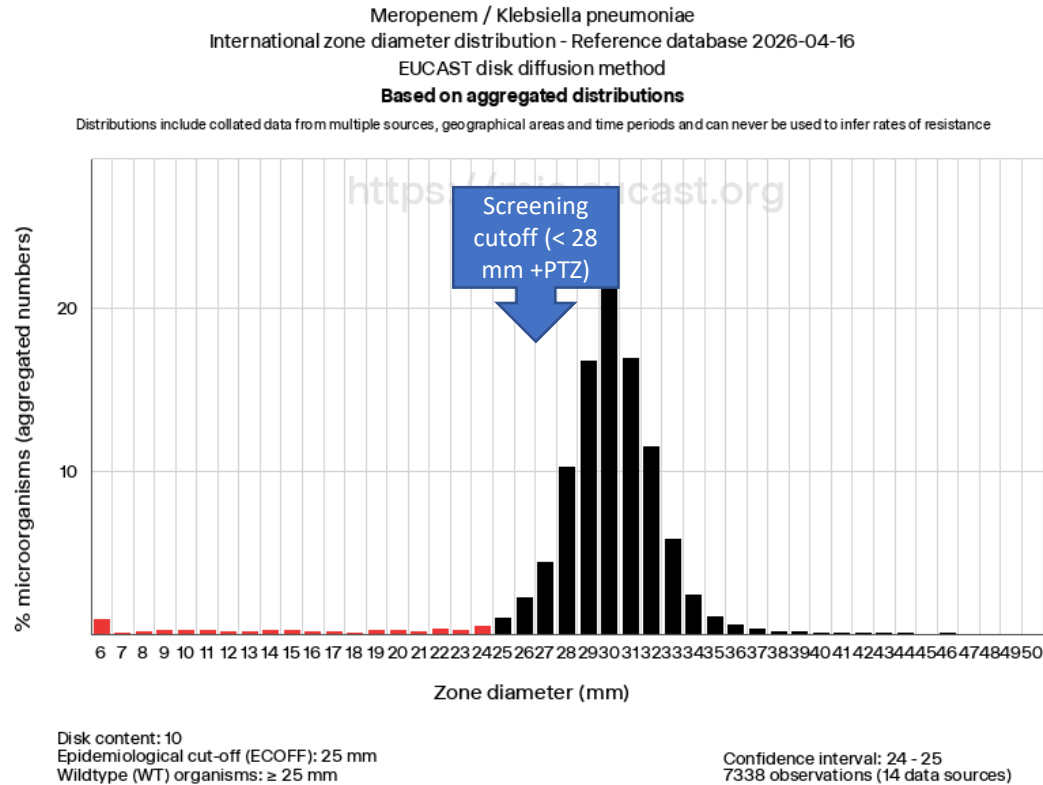
# The importance of screening cutoffs in finding CPE (carbapenemase-producing Enterobacterales)



# Strain 5: *E. coli* (blaNDM, blaOXA-181)

- With this strain, the expected results for all antibiotics were at least two dilutions or 4 mm away from clinical bps
  - Inherent variation does not explain deviations
- Yet, VME:s (false S/I) were reported for
  - Meropenem; expected MIC>16; DD, GrT
  - Meropenem-vaborbactam; expected MIC>16; GrT
  - Imipenem; expected MIC >8; DD, BMD, GrT
  - Imipenem-relebactam; expected MIC >4; BMD, GrT
- Sweden had lower rates of above VMEs (as compared to Finland and Norway), however some ME's (false R) with aztreonam-avibactam were reported using DD

# How to improve with CPE and ensure safe patient treatment?



1. Confirm that your distribution is located correctly
2. Confirm that strains with inhibition zone  $<$  (or MIC  $>$ ) the cutoff are noticed, even if interpreted S/I
3. Check those strains for carbapenemase production (molecular or lateral flow test)
4. If a carbapenemase is found, and meropenem/imipenem interpreted I/S, add the comment ( $\pm$  remove the interpretation)
5. Next slide

## 1. EXPECTED ACTIVITY OF BLBLIs AND CEFIDEROCOL ON $\beta$ -LACTAMASE-PRODUCING GRAM-NEGATIVE BACTERIA

Tables 1.1-1.3 describe the expected activity of BLBLIs and cefiderocol relevant for Enterobacterales, *Pseudomonas* spp., and *A. baumannii* complex, respectively, expressing clinically important  $\beta$ -lactamases. The activity must be examined by EUCAST recommended antimicrobial susceptibility testing methods.

**Table 1.1. Enterobacterales – expected activity of BLBLIs and cefiderocol**<sup>1</sup>

Antimicrobial	ESBL (CTX-M)	Chromosomal/plasmid-mediated AmpC (CMY, DHA)	Class A carbapenemases (KPC, IMI, GES)	Class B carbapenemases (NDM, VIM, IMP)	Class D carbapenemases (OXA-48-like)	Multiple carbapenemases (A/B+A/D+B/D)
Amoxicillin-clavulanic acid <sup>2</sup>	+	-	-	-	-	-
Ampicillin-sulbactam <sup>2</sup>	+	-	-	-	-	-
Aztreonam-avibactam	+	+	+	+ <sup>3</sup>	+	+
Cefepime-enmetazobactam	+	+ <sup>4</sup>	-	-	+ <sup>4</sup>	-
Cefepime-zidebactam	+	+	+	+ <sup>5</sup>	+ <sup>5</sup>	+/-
Cefiderocol	+	+	+	+/-	+	+/-
Ceftazidime-avibactam	+	+	+	-	+	-
Ceftolozane-tazobactam	+	-	-	-	-	-
Imipenem-relebactam <sup>6</sup>	+	+	+	-	-	-
Meropenem-vaborbactam	+	+	+	-	-	-
Piperacillin-tazobactam	+	-	-	-	-	-

<sup>1</sup> +: activity to be expected; -: no activity to be expected; +/-: variable activity to be expected.

<sup>2</sup> Relevant for *E. coli*, *Klebsiella* spp. (except *K. aerogenes*), *Raoultella* spp. and *P. mirabilis*. Not relevant for AmpC-producing Enterobacterales.

<sup>3</sup> The activity of the combination is due to the lack of class B carbapenemase (metallo- $\beta$ -lactamases – MBLs) hydrolytic activity against aztreonam and avibactam's inhibitory activity against ESBLs/AmpCs that are frequently found in class B carbapenemase-producing isolates. Avibactam has no inhibitory activity against class B carbapenemases.

<sup>4</sup> The activity of the combination is due to the limited OXA-48/AmpC-hydrolytic activity against cefepime and enmetazobactam's inhibitory activity against ESBLs that are frequently found in OXA-48-like-producing isolates (7, 10).

<sup>5</sup> The activity of the combination is mainly due to the synergistic bactericidal effect arising from complementary PBP inhibition by zidebactam and cefepime, rather than restoration of cefepime activity through  $\beta$ -lactamase inhibition. Direct inhibitory activity of zidebactam against class B/OXA-48-like carbapenemases is not expected.

<sup>6</sup> BLBLI relevant for Enterobacterales except *Morganellaceae* which has reduced susceptibility to imipenem.

## 5. For new BL-BLI combinations and cefiderocol, check the expected result from BL-BLI document to avoid VMEs:

- with NDM, relebactam or vaborbactam are not supposed to improve activity of imipenem or meropenem (even if the expected result of meropenem-vaborbactam for *Klebsiella* was S!). Aztreonam-avibactam and cefepime-zidebactam are likely effective, cefiderocol  $\pm$ .

# Strain 4: *A. baumannii* and cefiderocol

Figure 10. Reported interpretation of AST results for strain '2025 EARS-Net 4' (*Acinetobacter baumannii*) by antimicrobial agent and anticipated difficulty of identification

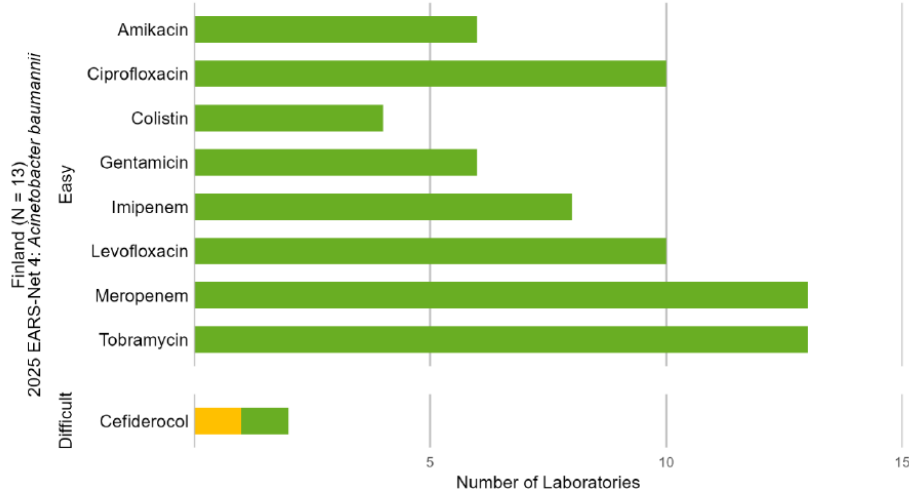


Figure 10. Reported interpretation of AST results for strain '2025 EARS-Net 4' (*Acinetobacter baumannii*) by antimicrobial agent and anticipated difficulty of identification

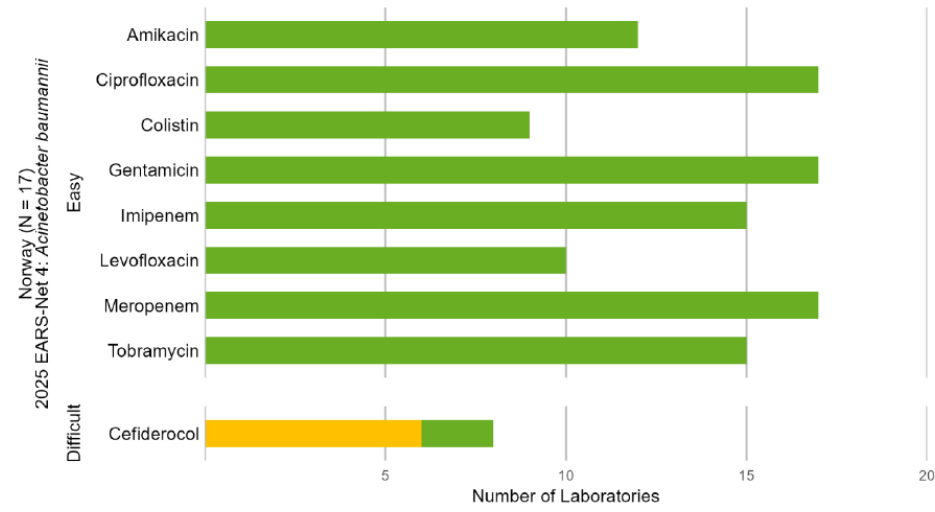


Figure 10. Reported interpretation of AST results for strain '2025 EARS-Net 4' (*Acinetobacter baumannii*) by antimicrobial agent and anticipated difficulty of identification

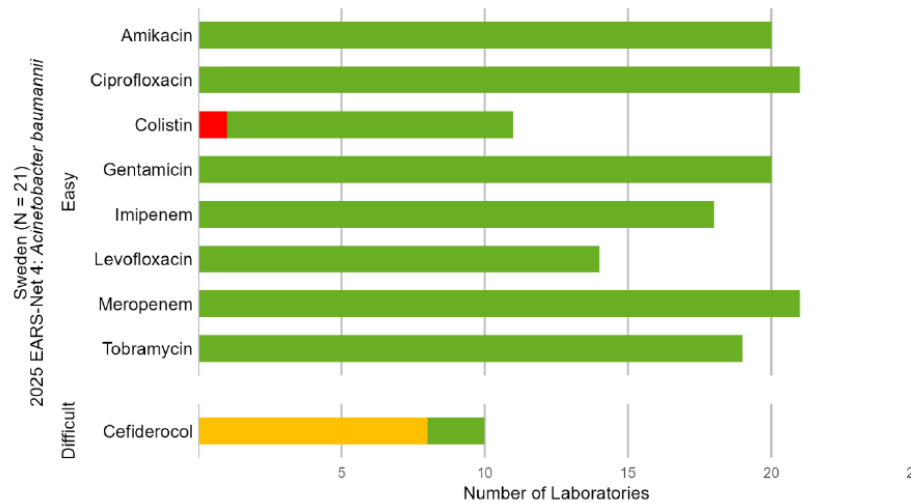
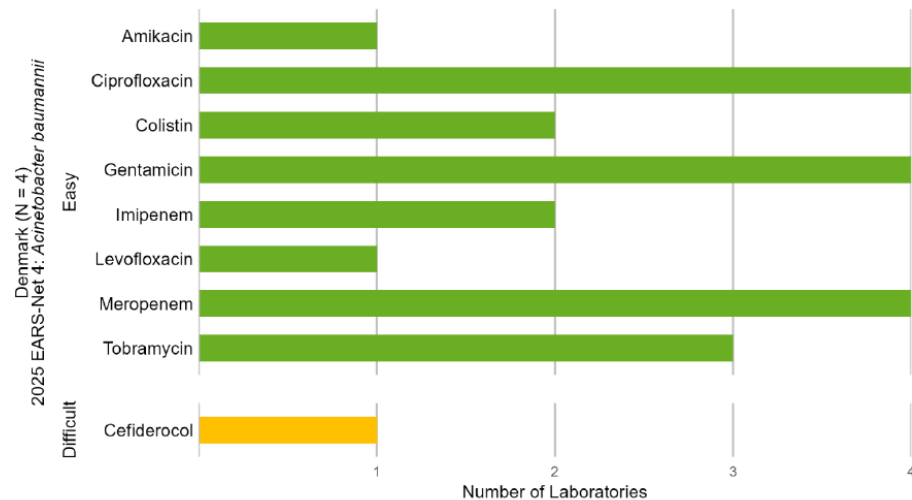
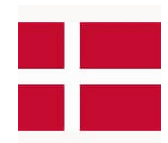
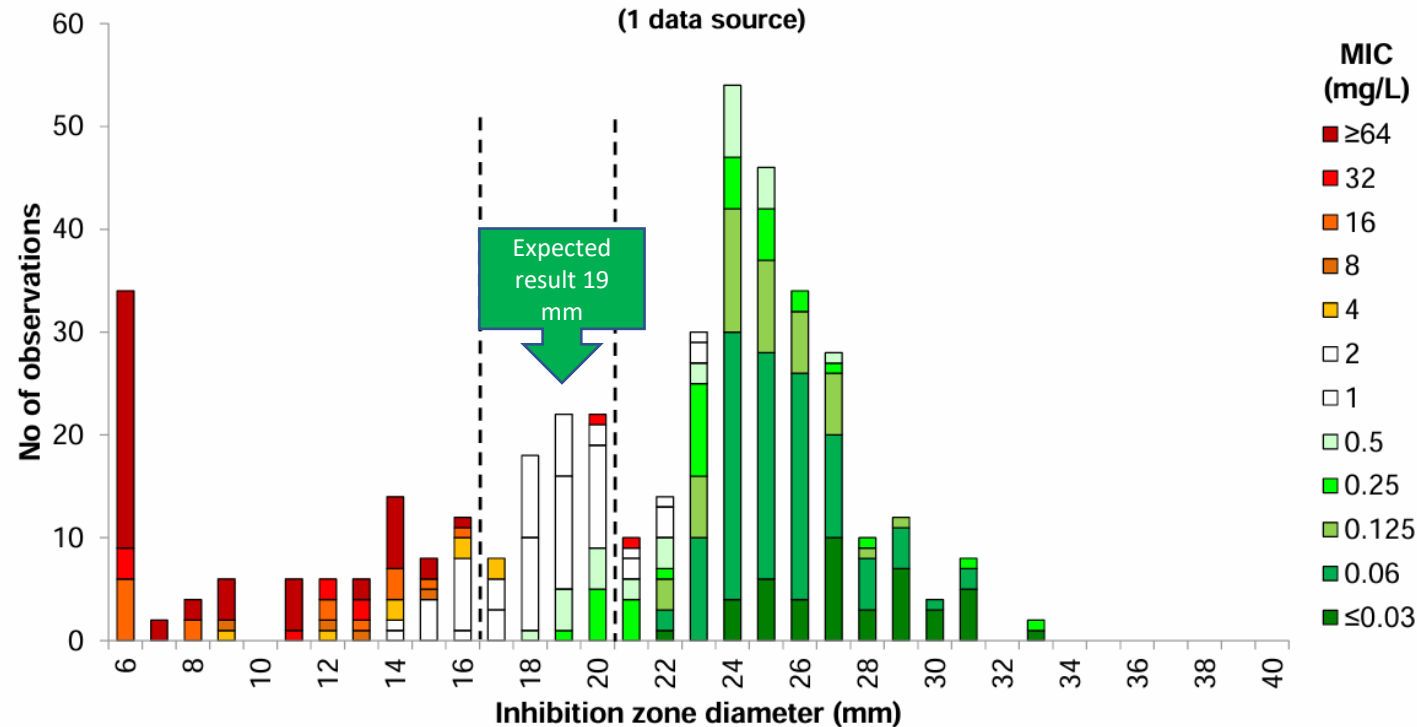


Figure 10. Reported interpretation of AST results for strain '2025 EARS-Net 4' (*Acinetobacter baumannii*) by antimicrobial agent and anticipated difficulty of identification



## Cefiderocol 30 µg vs. MIC *Acinetobacter baumannii*, 105 isolates (420 correlates)



EUCAST recommends disc diffusion, because MIC testing is tricky and all commercial systems have problems.

Note: no clinical bps because of lacking clinical evidence. The expected result is in the area where strains may have some acquired resistance mechanisms.

“The expected AST result was less than four millimeters away from the clinical breakpoint; thus these deviations can be due to inherent method variation. However, they might also be attributable to systematic or random errors in the laboratories’ procedures”

No clinical breakpoints. Isolates with MIC values  $\leq 0.5$  mg/L (zone diameter  $\geq 21$  mm) are mostly devoid of resistance mechanisms. Isolates with MICs 1-2 mg/L (white bars) have some acquired resistance mechanisms. Isolates with MIC values  $> 2$  mg/L (zone diameter  $< 17$  mm) have acquired resistance mechanisms and will likely be resistant.

# Adhere to EUCAST methodology

Run QC on:

*Escherichia coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 27853

Incubate 16-20 hours – no more no less

Training (hazy zones, trailing, microcolonies, edge reading)

Storage (according to manufacturer's instructions)

Check your distributions vs. those available at EUCAST website

[Cefiderocol disk diffusion training.pdf](#)

# EARS-Net strain 6: *S. pneumoniae*



Figure 14. Reported interpretation of AST results for strain '2025 EARS-Net 6' (*Streptococcus pneumoniae*) by antimicrobial agent and anticipated difficulty of identification

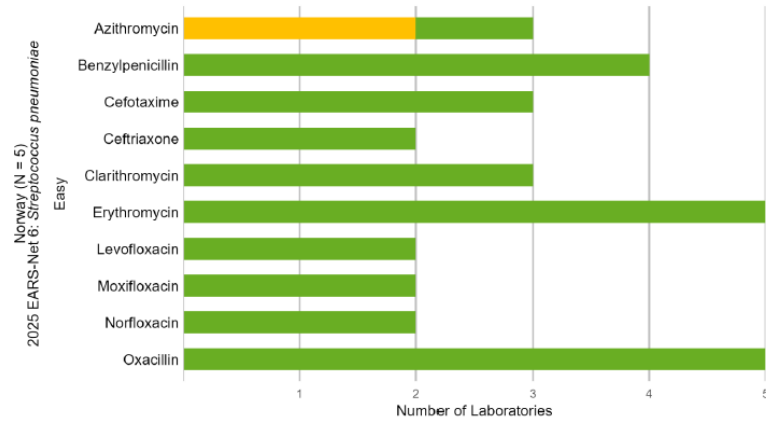


Figure 14. Reported interpretation of AST results for strain '2025 EARS-Net 6' (*Streptococcus pneumoniae*) by antimicrobial agent and anticipated difficulty of identification

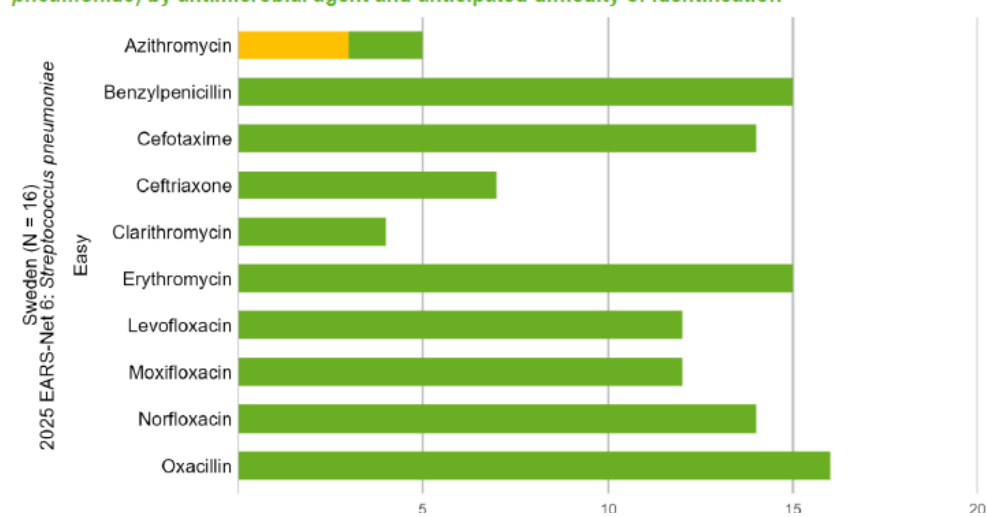


Figure 14. Reported interpretation of AST results for strain '2025 EARS-Net 6' (*Streptococcus pneumoniae*) by antimicrobial agent and anticipated difficulty of identification

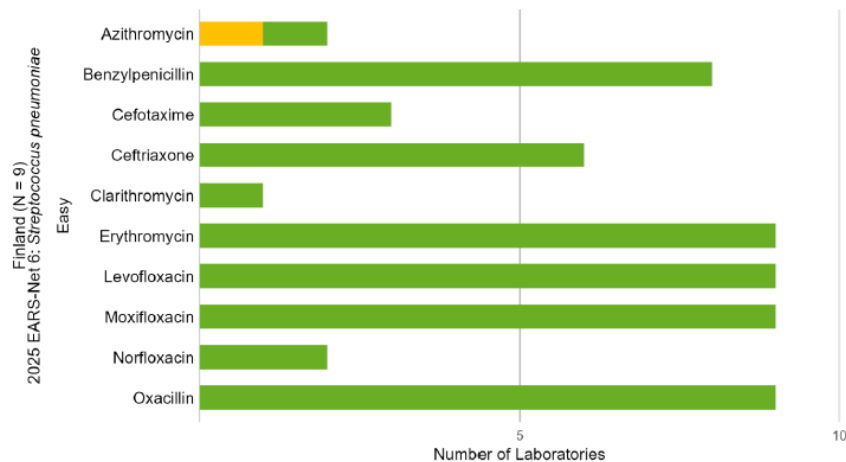
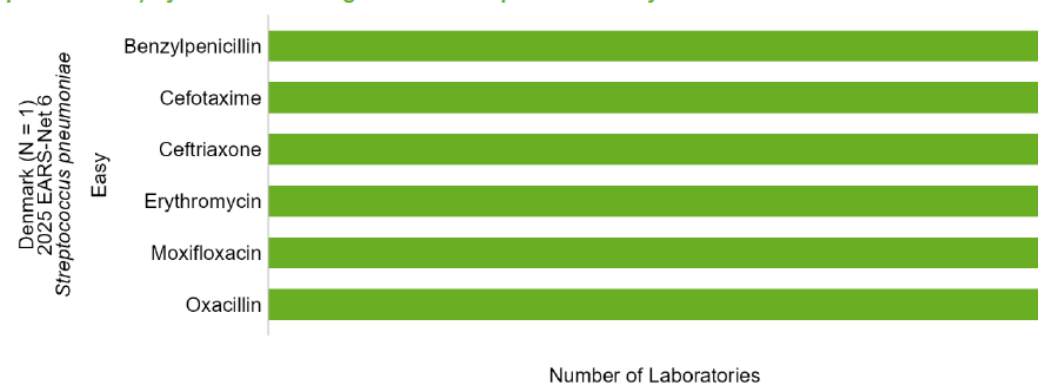
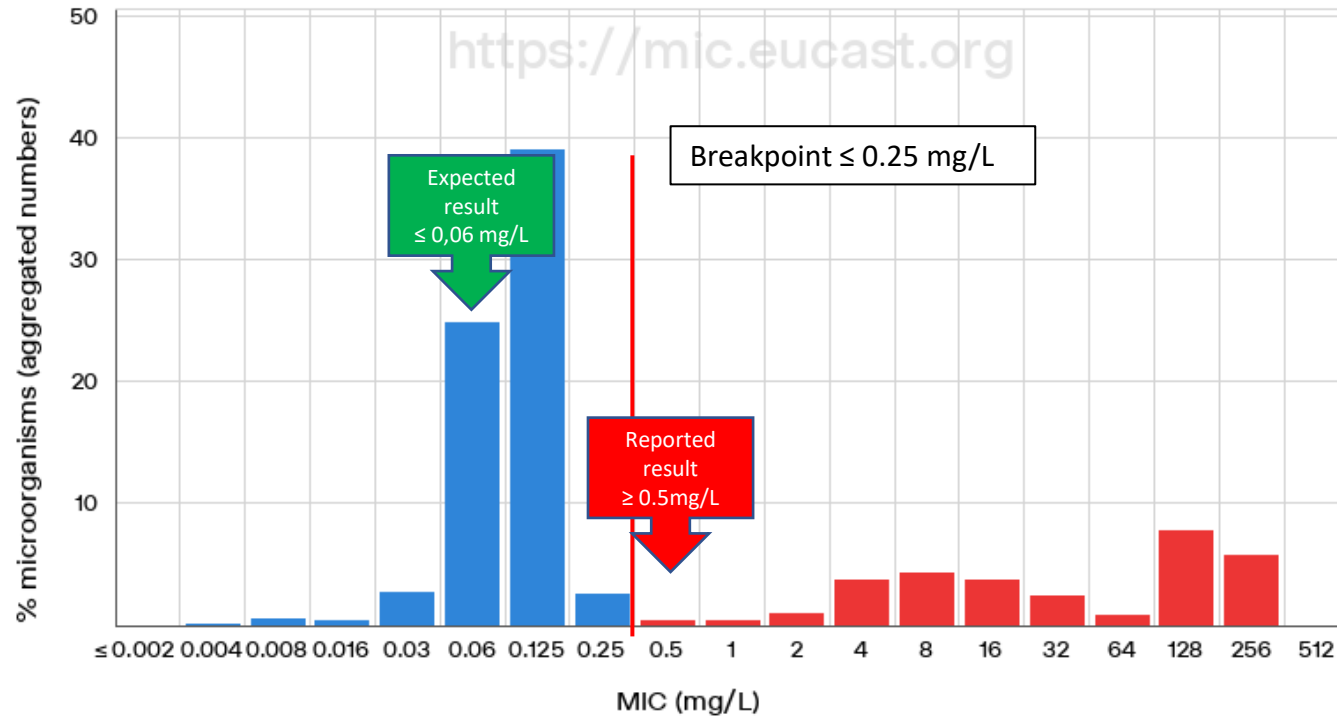


Figure 14. Reported interpretation of AST results for strain '2025 EARS-Net 6' (*Streptococcus pneumoniae*) by antimicrobial agent and anticipated difficulty of identification



Azithromycin / Streptococcus pneumoniae  
International MIC distribution - Reference database 2026-04-14  
Based on aggregated distributions

MIC distributions include collated data from multiple sources, geographical areas and time periods and can never be used to infer rates of resistance



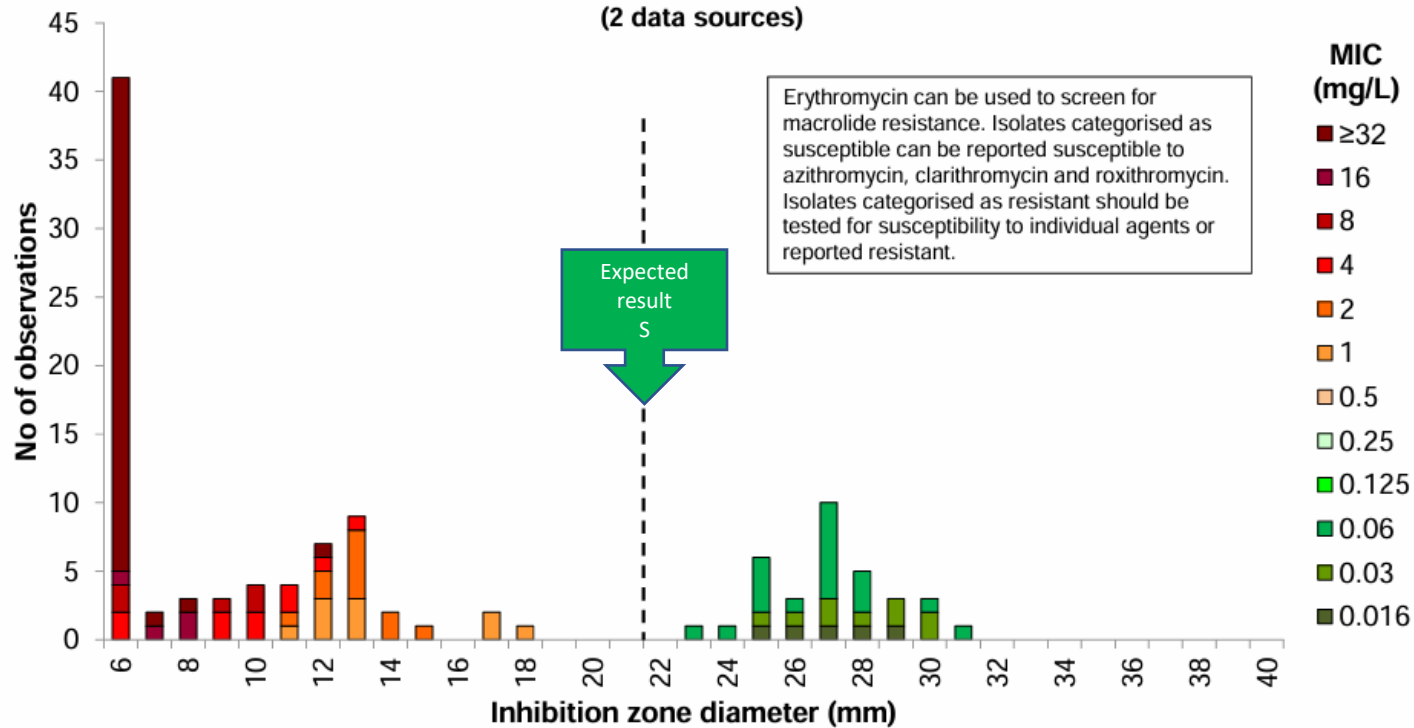
MIC  
Epidemiological cut-off (ECOFF): 0.25 mg/L  
Wildtype (WT) organisms: ≤ 0.25 mg/L

Confidence interval: 0.03 - 0.25  
71068 observations (7 data sources)

ME was reported if the result missclassified a susceptible result as resistant.

## Erythromycin 15 µg vs. Azithromycin MIC *S. pneumoniae*, 104 isolates (112 correlates)

(2 data sources)



### Breakpoints

Azithromycin MIC

$S \leq 0.25$ ,  $R > 0.25$  mg/L

Erythromycin zone diameter

$S \geq 22$ ,  $R < 22$  mm

# In conclusion

Adhere stictly to EUCAST methodology when testing

Make use of EUCAST guidance documents

Check your distributions vs. those at the Eucast website

If DD screening breakpoints are supplied for screening for antimicrobial classes use those primarily as they are often more robust and reproducible

## Most AST is unproblematic

- ...if your method is robust and QC:ed
- ...if your device is QC:ed, at both ends of the scale
- ...if your disks and gradient test are high quality
- ...if your MH medium is dependable
- ...if your staff properly trained

NordicAST WS 2019

