ECDC EARS-Net External Quality Assessment (EQA) 2011

Christine Walton, Nita Patel
UK NEQAS for Microbiology, Colindale London (UK)

Derek Brown
EUCAST

UK NEQAS

Objectives of EARS-Net External Quality Assessment

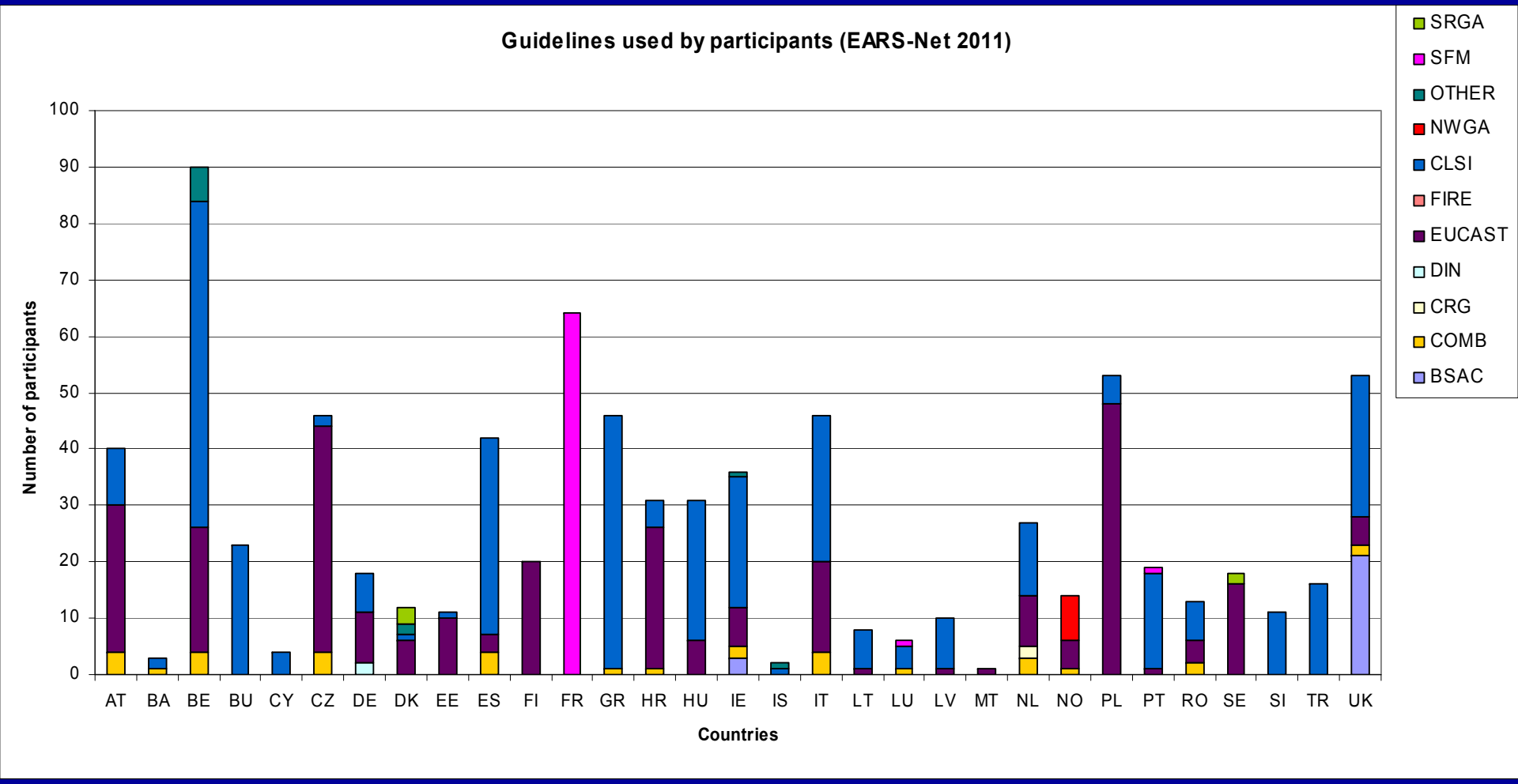
- To assess the accuracy of susceptibility test reporting by laboratories
- To assess the comparability of routine susceptibility test results between laboratories and countries
- Education

Participation in EARS-Net EQA 2011 (2010)

- 31 (31) countries
- 911 (871) laboratories
- 90% (88%) laboratories responded

Only possible to return results via the UK NEQAS website

Guidelines followed in EARS-Net EQA 2011



	2010		2011
CLSI	66%	→	47%
EUCAST	14%	→	35%
EUCAST-based national guidelines	18%	→	13%

Methods use in EARS-Net EQA 2011 (2010)

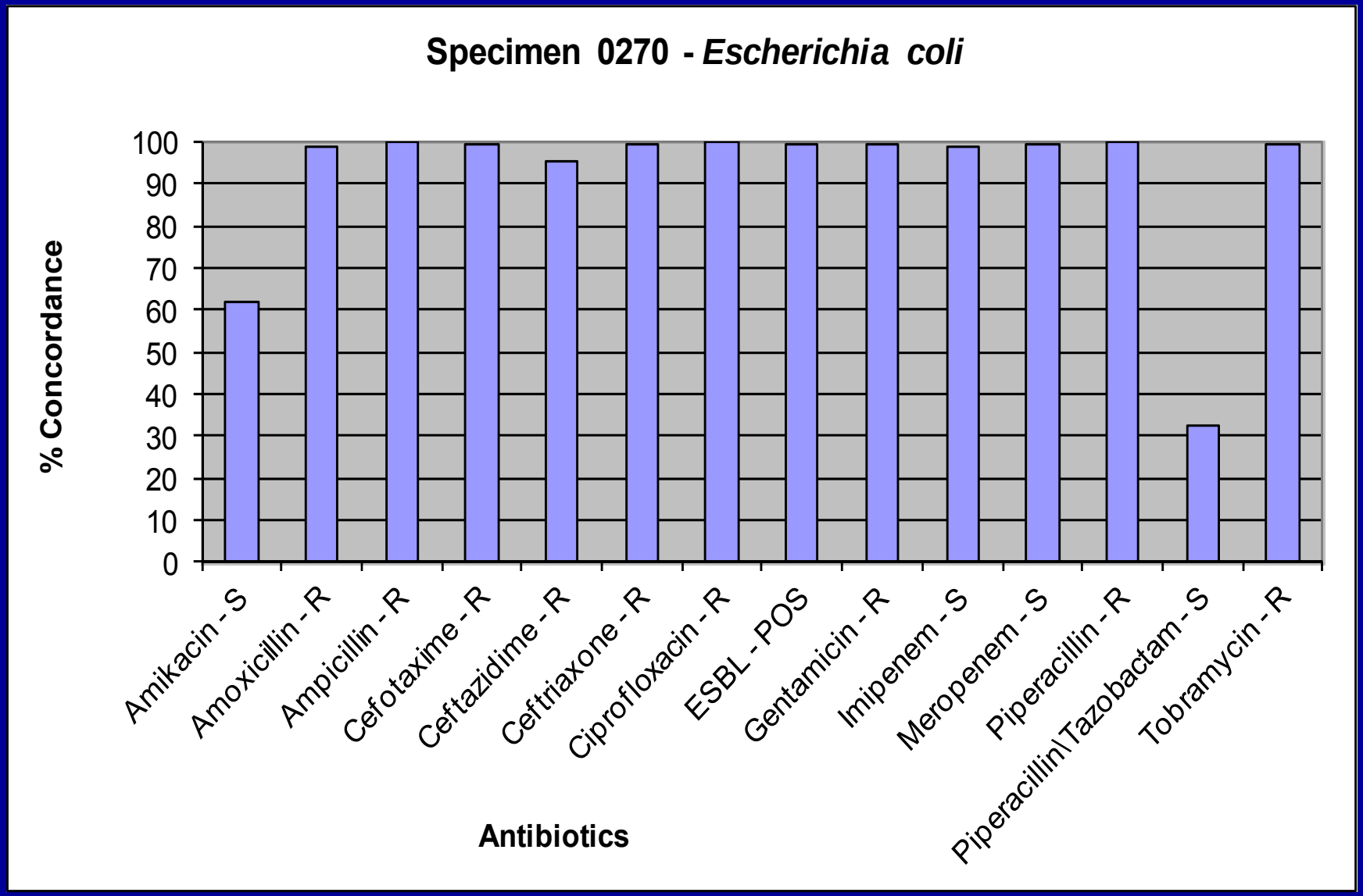
Antimicrobial susceptibility testing

- Automated 42% (35%)
- Disk diffusion 34% (33%)
- Multiple 16% (23%)

Escherichia coli (specimen 0270)

Antimicrobial agent	Reference MIC (mg/L)	EUCAST	CLSI
Amikacin	4 - 8	S	S
Amoxicillin	Infer from amp	R	R
Ampicillin	≥128 - ≥128	R	R
Cefotaxime	≥128 - ≥128	R	R
Ceftazidime	16 - 64	R	R
Ceftriaxone	≥128- ≥128	R	R
Ciprofloxacin	64 - ≥128	R	R
Gentamicin	32 - ≥128	R	R
Imipenem	0.06 - 0.12	S	S
Meropenem	0.016 - 0.03	S	S
Piperacillin		R	R
Piperacillin-tazobactam	8 - 16	S/I	S
Tobramycin	32 – 64	R	R
ESBL (CTX-M-15)		Pos	Pos

Escherichia coli (specimen 0270)



Escherichia coli (specimen 0270)

Piperacillin-tazobactam borderline susceptible/ intermediate (reference MICs 8-16 mg/L)

- Reporting variable (32.7% S, 23.7% I, 43.6% R)
- Not related to guideline used
  - EUCAST 43.0% reported resistant
  - CLSI 40.8% reported resistant
- Differences between methods
  - Automated 63.1% of 225 reported R
  - MIC 55.3% of 103 reported R
  - Disk diffusion 24.5% of 310 reported R
- Many laboratories not reporting “as found”
  - Automated 9% edited to a more resistant category
  - MIC 24% edited to a more resistant category
  - Disk diffusion 34% edited to a more resistant category

Escherichia coli (specimen 0270)

Amikacin borderline susceptible (ref MICs 4-8 mg/L)

- Reporting variable (61.8% S, 31.6% I, 6.6% R)

- Differences in guideline used
  - Susceptible reports EUCAST 58% CLSI 65%

- Differences between methods

	S (%)	I (%)	R (%)
– Automated (n=333)	44	45	4
– MIC (n=71)	65	20	15
– Disk diffusion (n=262)	76	18	6

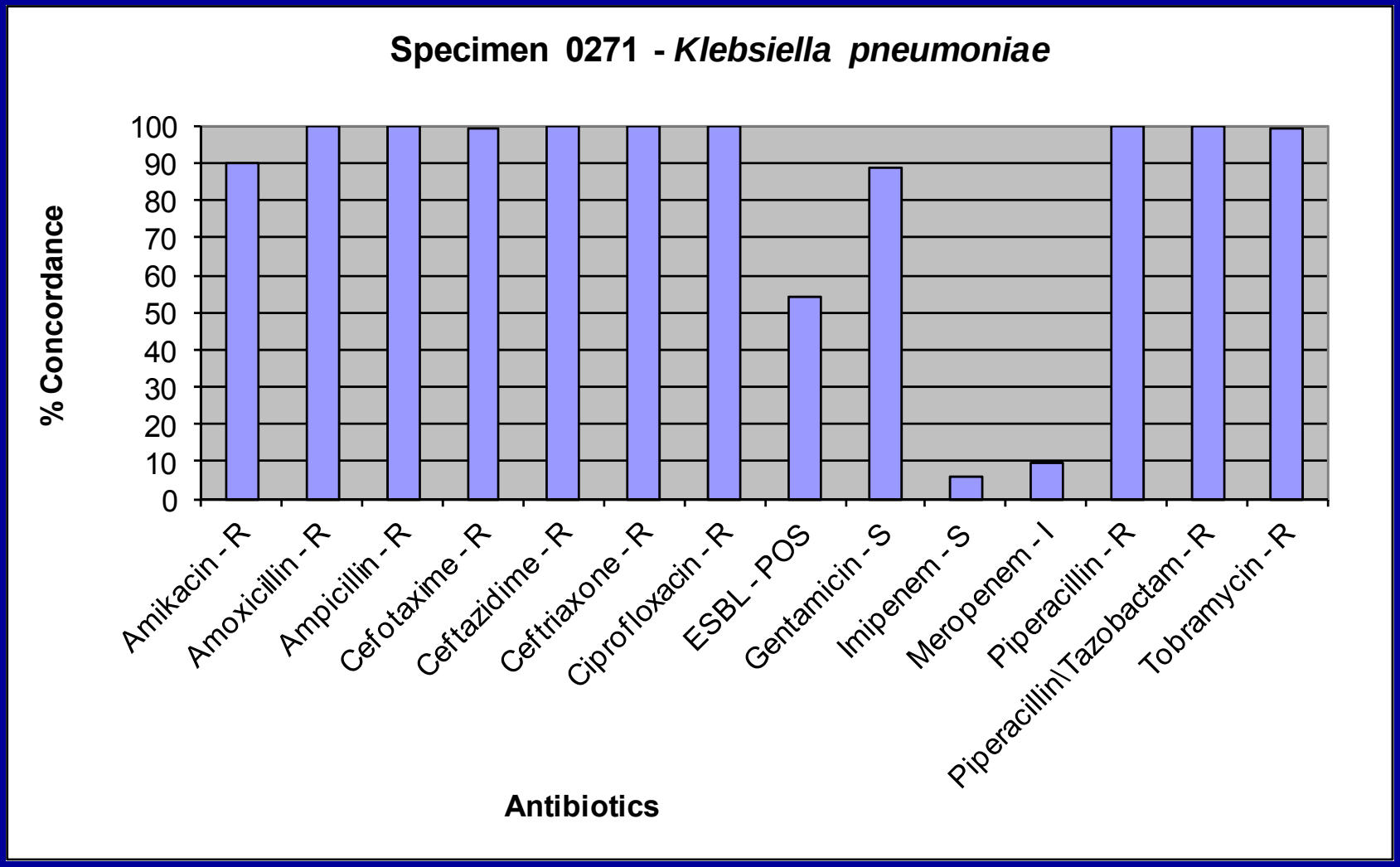
Klebsiella pneumoniae (specimen 0271)

[KPC carbapenemase]

Antimicrobial agent	Reference MIC (mg/L)	EUCAST	CLSI
Amikacin	16 - 16	I	S
Amoxicillin	≥128 - ≥128	R	R
Ampicillin	≥128 - ≥128	R	R
Cefotaxime	≥128 - ≥128	R	R
Ceftazidime	≥128 - ≥128	R	R
Ceftriaxone	≥128 - ≥128	R	R
Ciprofloxacin	≥128 - ≥128	R	R
Gentamicin	1 – 1	S	S
Imipenem	1 – 1 (16*)	S (R)	S (R)
Meropenem	4 – 4 (32*)	I (R)	R (R)
Piperacillin		R	R
Piperacillin-tazobactam	≥128 - ≥128	R	R
Tobramycin	≥128 - ≥128	R	R
ESBL (SHV-12)		Pos	Pos

*MIC repeated in reference laboratory after distribution

Klebsiella pneumoniae (specimen 0271)



Klebsiella pneumoniae (specimen 0271)

Reference MICs before and after distribution suggest strain variation

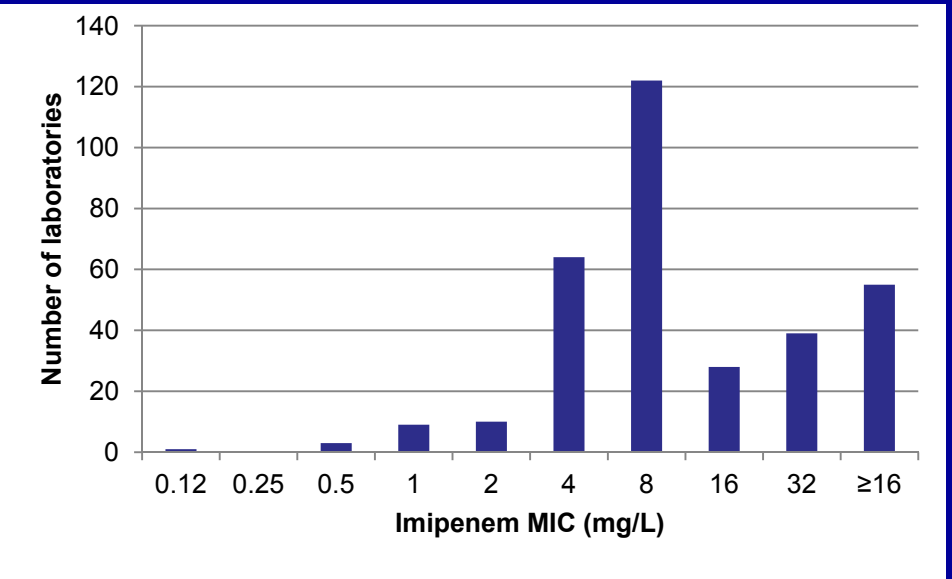
imipenem 1 mg/L (S); 16 mg/L (R) on post-distribution repeat

meropenem 4 mg/L (I/R); 32 mg/L (R) on post-distribution repeat

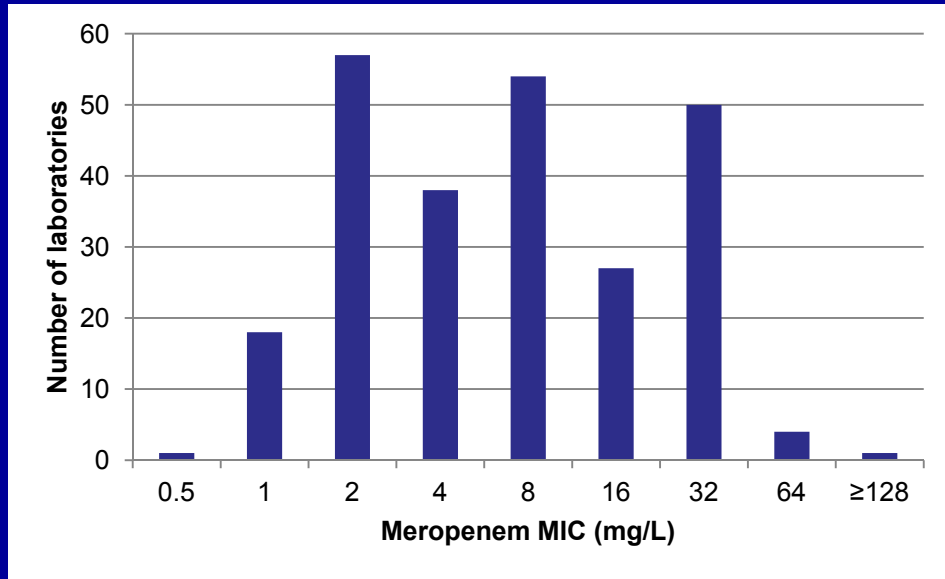
ertapenem 16 mg/L (R); 64 mg/L (R) on post-distribution repeat

- MIC reports from participants

imipenem



meropenem



Klebsiella pneumoniae (specimen 0271)

Results from participants

- Imipenem 6.3% S, 19.3% I, 74.4 R
- Meropenem 6.4% S, 9.5% I, 84.1% R

- Differences between guidelines used
  - Imipenem EUCAST 6.3%, CLSI 6.7% reported S
  - Meropenem EUCAST 7.6%, CLSI 5.2% reported S
- Differences between methods (imipenem)
  - Automated 3.8% of 263 reported S
  - Disk diffusion 12.2% of 229 reported S
- Differences between methods (meropenem)
  - Automated 7.6% of 304 reported S
  - Disk diffusion 5.2% of 248 reported S

Klebsiella pneumoniae (specimen 0271)

Aminoglycoside modifying enzyme, probably AAC(6')

- Tobramycin resistant (MIC ≥128 mg/L)
- Amikacin borderline intermediate /susceptible (MIC 16 mg/L)
- Gentamicin susceptible (MIC 1 mg/L)

- Reports from participants

	S (%)	I (%)	R (%)
– Tobramycin (n=647)	0.5	0.3	99.2
– Amikacin (n=734)	1.2	9.0	89.8
– Gentamicin (n=779)	88.7	8.1	3.2

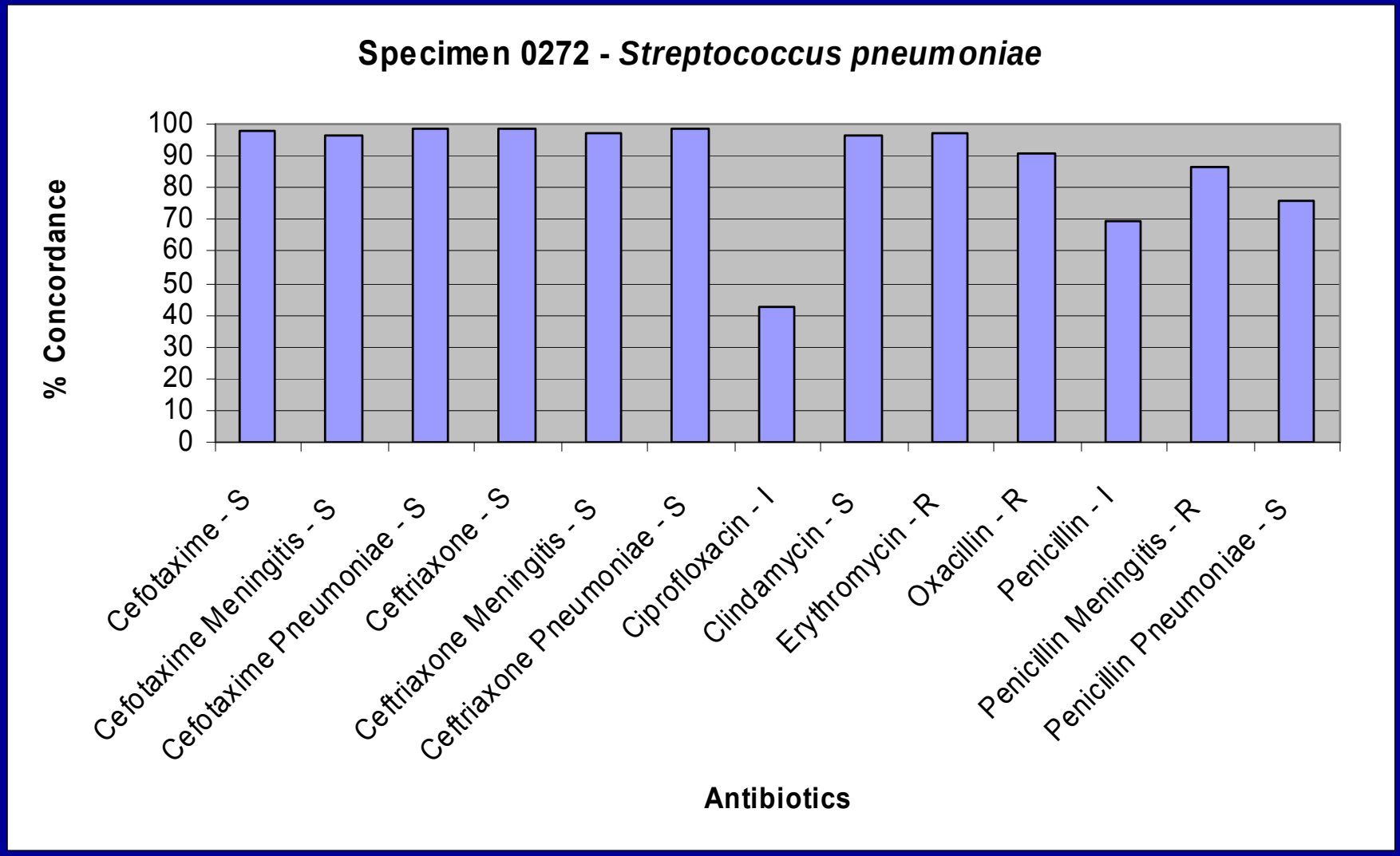
- EUCAST expert rule advises reporting amikacin intermediate if the organism appears susceptible

Streptococcus pneumoniae (specimen 0272)

Penicillin "intermediate"

Antimicrobial agent	Reference MIC (mg/L)	EUCAST	CLSI
Cefotaxime	**0.25 - 0.5**		
meningitis		**S**	**S**
pneumonia		**S**	**S**
Ceftriaxone	**0.25 - 0.5**		
meningitis		**S**	**S**
pneumonia		**S**	**S**
Ciprofloxacin	**0.5 - 1**	**I**	**No interpretation**
Clindamycin	**0.12 – 0.12**	**S**	**S**
Erythromycin	**32 - ≥128**	**R**	**R**
Penicillin:	**0.5 - 0.5**	**I**	**I**
meningitis		**R**	**R**
pneumonia		**S**	**S**

Streptococcus pneumoniae (specimen 0272)



Streptococcus pneumoniae (specimen 0272)

Penicillin intermediate (MIC 0.5 mg/L)

- If pneumonia report susceptible
- If meningitis report resistant

- Reports from participants

	S (%)	I (%)	R (%)
– Oxacillin (n=523)	4.6	4.6	90.8
– Penicillin (n=615)	23.6	69.8	6.6
– Penicillin pneumonia (n=740)	76.1	20.8	3.1
– Penicillin meningitis (n=741)	5.5	8.1	86.4

Streptococcus pneumoniae (specimen 0272)

Ciprofloxacin (MIC 0.5-1 mg/L)

- EUCAST intermediate, CLSI no interpretation

- Reports from participants

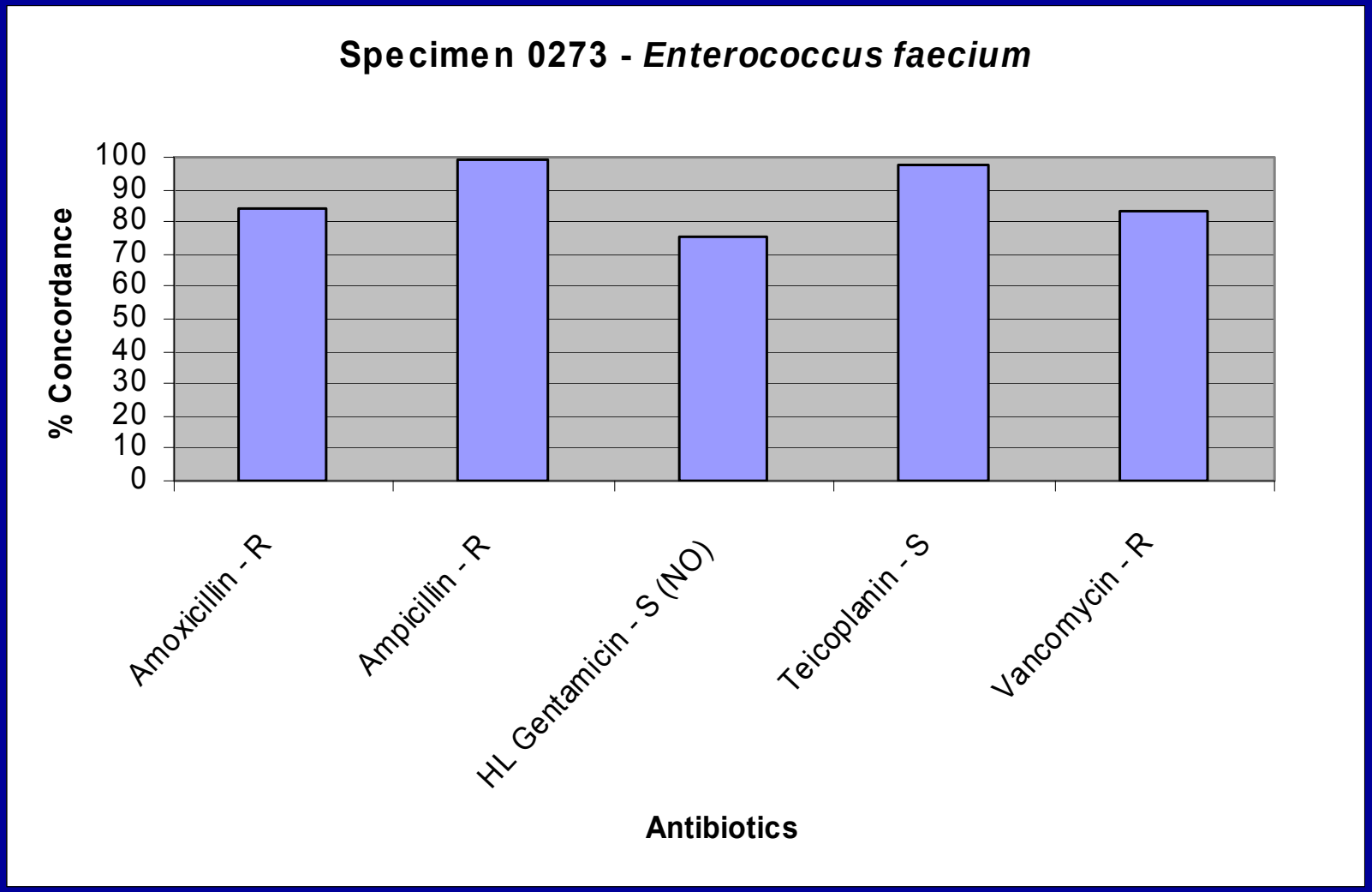
	S (%)	I (%)	R (%)
– EUCAST (n=202)	30.2	67.8	2.0
– CLSI (n=181)	82.9	14.9	2.2

Enterococcus faecium (specimen 0273)

VanB glycopeptide resistance

Antimicrobial agent	Reference MIC (mg/L)	EUCAST	CLSI
Amoxicillin	**Infer from amp**	**R**	**R**
Ampicillin	**16 - 32**	**R**	**R**
Gentamicin (HLGR)	**4 - 4**	**S (not HLR)**	**S (not HLR)**
Teicoplanin	**0.5 - 1**	**S**	**S**
Vancomycin	**8 - 16**	**R**	**I**

Enterococcus faecium (specimen 0273)



Enterococcus faecium (specimen 0273)

Vancomycin (MIC 8-16 mg/L, VanB)

- EUCAST resistant, CLSI intermediate

- Reports from participants

  8.0% susceptible, 8.7% intermediate, 83.3% resistant

- Differences between guidelines

	S (%)	I (%)	R (%)
– EUCAST (n=395)	7.9	4.8	87.3
– CLSI (n=378)	8.7	14.8	76.5

- Differences between methods

	S (%)	I (%)	R (%)
– Automated (n=333)	3.9	6.2	89.9
– MIC (n=71)	2.8	13.9	83.3
– Disk diffusion (n=262)	15.5	11.6	72.9

Enterococcus faecium (specimen 0273)

Test for Gentamicin high-level resistance

- EUCAST and CLSI not high level gentamicin resistant (MIC 8-16 mg/L)

- Results from participants
  - 24.7% reported high-level gentamicin resistance
  - 75.3 reported not high-level gentamicin resistant

  - Failure to distinguish high- and low-level resistance?
  - Unlikely to be related to use of low content disks as reporting of HLGR was as common with automated or MIC methods as with disk diffusion, and reported MICs were mostly 4-8 mg/L

Enterococcus faecium (specimen 0273)

Ampicillin (MIC 16-32 mg/L) and amoxicillin (inferred from ampicillin)

- Resistant by EUCAST and CLSI

- Reports from participants

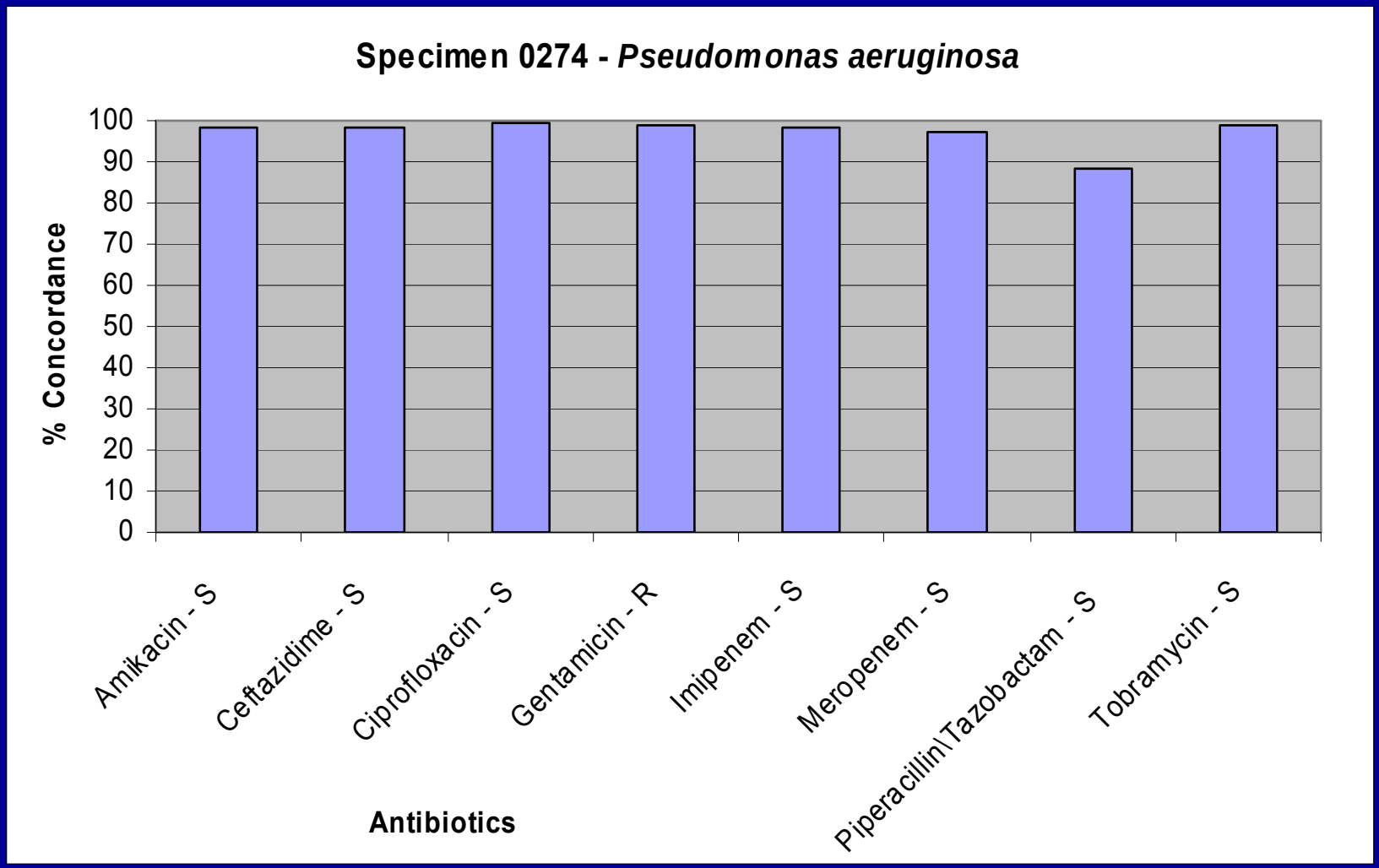
	S (%)	I (%)	R (%)
– Ampicillin (n=769)	0.8	0.4	98.8
– Amoxicillin (n=202)	7.9	7.9	84.2

  – 8/16 reporting amoxicillin S reported ampicillin R

Pseudomonas aeruginosa (specimen 0274)

Antimicrobial agent	Reference MIC (mg/L)	EUCAST	CLSI
Amikacin	1- 4	S	S
Ceftazidime	1- 2	S	S
Ciprofloxacin	0.12 - 0.5	S	S
Gentamicin	16 - ≥128	R	R
Imipenem	1 - 2	S	S
Meropenem	0.5 - 2	S	S
Piperacillin-tazobactam	4 - 8	S	S
Tobramycin	0.5 - 1	S	S

Pseudomonas aeruginosa (specimen 0274)



Pseudomonas aeruginosa (specimen 0274)

Piperacillin-tazobactam (MIC 4-8 mg/L)

- Susceptible by EUCAST and CLSI
- Reports from participants (n=258)

S (%)	I (%)	R (%)
88.1	6.2	5.7

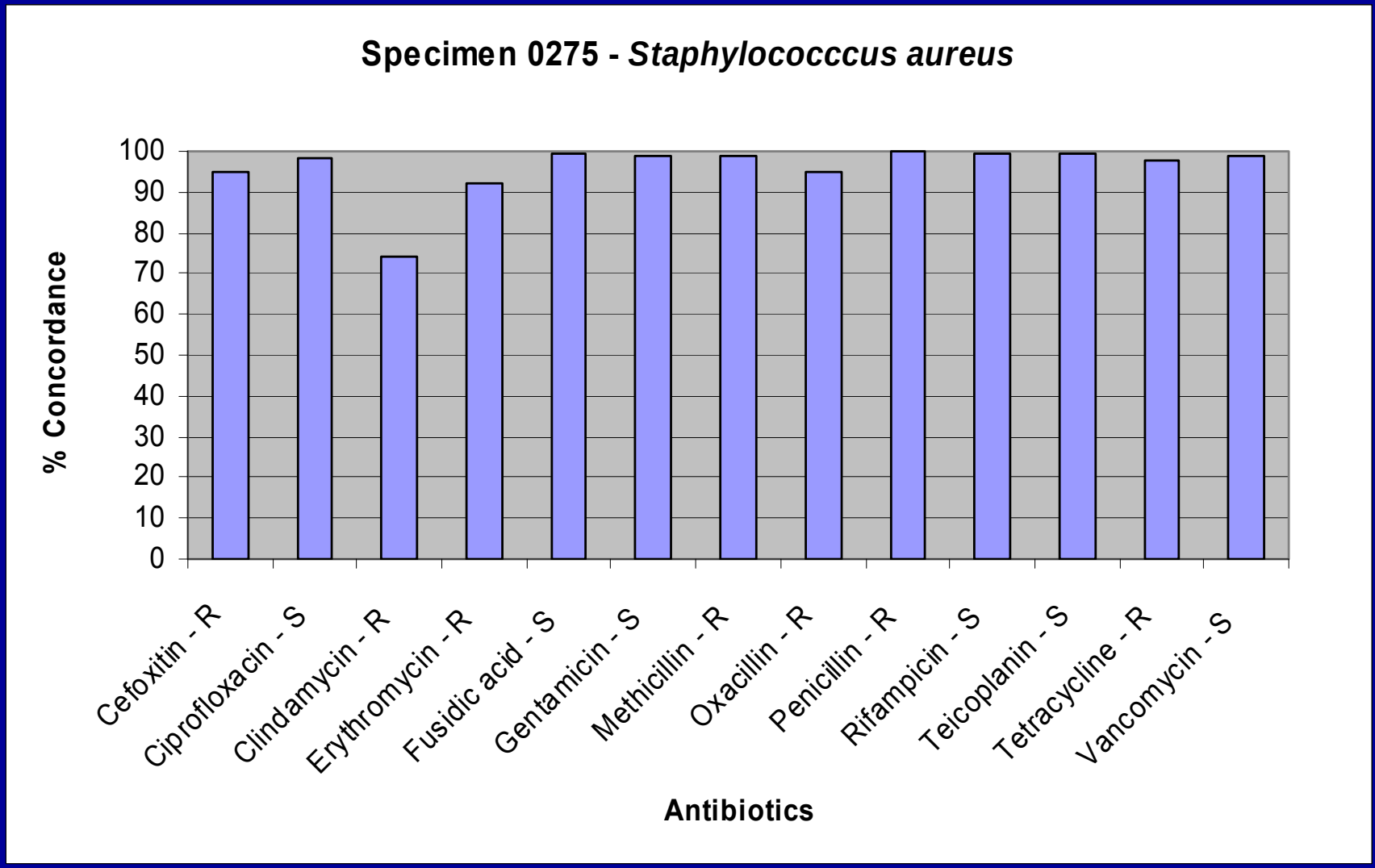
- No association with methods or guidelines

Staphylococcus aureus (specimen 0275)

MRSA multiple resistant

Antimicrobial agent	Reference MIC (mg/L)	EUCAST	CLSI
Cefoxitin	8 - 16	R	R
Ciprofloxacin	0.5 – 0.5	S	S
Clindamycin	0.12 – 0.12	Dissociated resistance	Dissociated resistance
Erythromycin	8 - 64	R	R
Fusidic acid	0.06 - 0.12	S	S
Gentamicin	0.25 – 0.5	S	S
Methicillin	Infer from cefox/ox	R	R
Oxacillin	8 - 32	R	R
Penicillin	1 - 4	R	R
Rifampicin	0.004 - 0.008	S	S
Teicoplanin	1 - 1	S	S
Tetracycline	64 - 64	R	R
Vancomycin	1 - 2	S	S

Staphylococcus aureus (specimen 0275)



Staphylococcus aureus (specimen 0275)

Cefoxitin (MIC 8-16 mg/L), oxacillin (MIC 8-32 mg/L)

- Resistant by EUCAST and CLSI

- Reports from participants

	S (%)	I (%)	R (%)
– Cefoxitin (n=671)	4.2	0.6	95.2
– Oxacillin (n=658)	5.0	0	95.0

  - Failure to detect resistance not related to method or guideline
  - 5 reported oxacillin susceptible, cefoxitin resistant
  - 6 reported cefoxitin susceptible, oxacillin resistant

Staphylococcus aureus (specimen 0275)

Clindamycin dissociated resistance (MIC 0.12-0.5 mg/L, but resistance induced by erythromycin)

- Reports from participants (n=775)

  24.0% susceptible 1.8% intermediate 74.2% resistant

- Reports of susceptible not related to guideline or method

- EUCAST expert rules recommend reporting resistant, or susceptible with warning of possible failure due to selection of resistant mutants. Avoid use in serious infections

- CLSI – report resistant with note that some may respond

Conclusions 2011

- Participation and performance was comparable with previous years
- Performance good for most organism-agent combinations
- Discrepancies more common when:
  - Susceptibility borderline
  - Critical differences between guidelines
  - Failure to follow guidelines

And finally....

Many thanks to all laboratories and national distributors

Country specific data will be provided by UK-NEQAS

UK NEQAS