NEQAS – How it works and what it tells us

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BSAC user day London: 11 Oct 2012

United Kingdom National External Quality Assessment Scheme for antimicrobial susceptibility testing

Participants in UK NEQAS antimicrobial susceptibility testing May 2012

641 participants,38 countries	
Austria	44
Belgium	6
Boznia & Herzegovina	11
Croatia	3
Cyprus	1
Denmark	14
Finland	21
Germany	1
Greece	6
Hong Kong	1
Ireland	40
Israel	12
Iceland	2
Italy	98
Kenya	4
Kuwait	12
Latvia	1
Malawi	1
Malta	1
Netherlands	18
Nigeria	1
Norway	13
Oman	1
Philipines	1
Poland	1
Portugal	41
Qatar	1
Romania	1
Saudia Arabia	1
South Africa	9
Sweden	23
Switzerland	23
Slovenia	9
Thailand	1
Turkey	2
United Arab Emirates	2
Uganda	1
United Kingdom	216
UK non-clinical	3

UKNEQAS

UKNEQAS organism selection

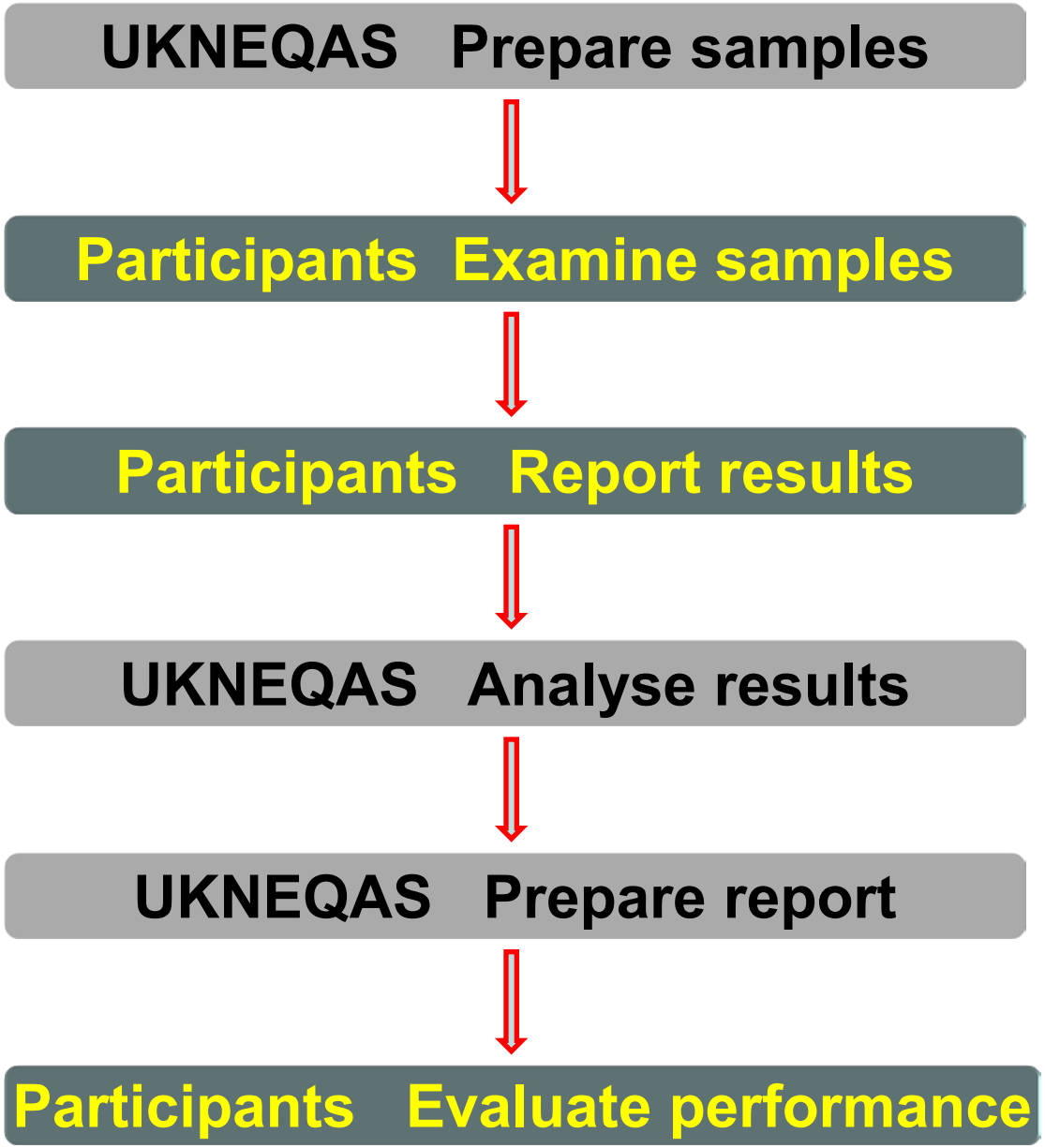
- General policy for strain selection suggested by the UKNEQAS Antimicrobial Susceptibility Testing Specialist Advisory Group (ASTSAG)
- Discussion in UKNEQAS Microbiology Steering Committee

- Organisms
  - Typical routine isolates
  - Isolates with particular resistance mechanisms
  - Difficult organisms
  - Isolates from various sources

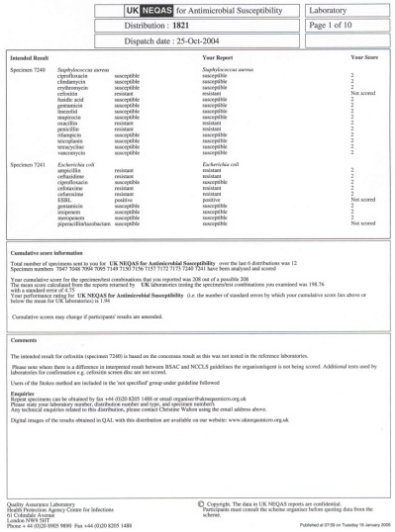
UKNEQAS reference testing

- Reference MICs by ISO method in two independent laboratories
- Molecular confirmation for particular resistance genes if required
- Transfer of selected isolates to QAL
- Check by Etest and/or disk diffusion before freeze drying
- Post freeze drying check in independent laboratory by Etest and disk diffusion.

The EQA process (UKNEQAS)



EQA Report


UK NEQAS for Antimicrobial Susceptibility | Laboratory
Distribution : 1821 | Page 1 of 10
Dispatch date : 25-Oct-2004

Intended Result | Your Report | Your Score

Specimen 7240 *Staphylococcus aureus*
ciprofloxacin susceptible
clindamycin susceptible
erythromycin susceptible
fusidic acid susceptible
gentamicin susceptible
linezolid susceptible
mupirocin susceptible
oxacillin resistant
penicillin resistant
rifampicin susceptible
teicoplanin susceptible
tetracycline susceptible
vancomycin susceptible

Specimen 7241 *Escherichia coli*
ampicillin resistant
ceftazidime resistant
ciprofloxacin susceptible
cefotaxime resistant
cefuroxime resistant
ESBL positive
gentamicin susceptible
imipenem susceptible
meropenem susceptible
piperacillin/tazobactam susceptible

Cumulative score information

Total number of specimens sent to you for **UK NEQAS for Antimicrobial Susceptibility** over the last 6 distributions was 12
Specimen numbers: 7047 7048 7004 7005 7149 7150 7151 7152 7153 7240 7241 have been analysed and scored

Your cumulative score for the specimen/test combinations that you reported was 208 out of a possible 208
The mean score calculated from the reports returned by UK laboratories testing the specimen/test combinations you examined was 198.76
Your ranking was 1 out of 1
Your performance rating for **UK NEQAS for Antimicrobial Susceptibility** (i.e. the number of standard errors by which your cumulative score lies above or below the mean for UK laboratories) is 1.94

Cumulative scores may change if participants' results are amended.

Comments

The intended result for cefoxitin (specimen 7240) is based on the consensus result as this was not tested in the reference laboratories.

Please note where there is a difference in interpreted result between BSAC and NCCLS guidelines the organism/agent is not being scored. Additional tests used by laboratories for confirmation e.g. cefoxitin screen disc are not scored.

Users of the Stokes method are included in the 'not specified' group under guideline followed

Enquiries
Repeat specimens can be obtained by fax +44 (0)20 8205 1488 or email organism@ukneqasmicro.org.uk
Please state your laboratory number, distribution number and type, and specimen number/s
Any technical enquiries related to this distribution, please contact Christine Walton using the email address above.

Digital images of the results obtained in Q.4/1 with this distribution are available on our website: www.ukneqasmicro.org.uk

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Published at 07:00 on Tuesday 18 January 2005

- Reference MIC results
- Your results
- Scores highlighting your performance
- Cumulative score over time and mean for all laboratories
- Detailed results for laboratories using the same method as you
- Details of results with different guidelines
- Comments on particular problems

UK NEQAS

Scoring of UKNEQAS antimicrobial susceptibility testing

- Standard scoring for most specimens
- Variations to scoring scheme proposed by ASTSAG
- Reviewed and approved by UKNEQAS Microbiology Advisory Panel
- Reviewed and approved by UKNEQAS Microbiology Steering Committee

Scoring of antimicrobial susceptibility testing

Intended reported result	Score for results reported		
	S	I	R
Susceptible	2	1	0
Intermediate	1	2	1
Resistant	-1	1	2

E. coli specimen 0847 (April 2012) Ampicillin susceptible (MIC 4-8 mg/L)

Guideline	Percent reporting		
	S	I	R
All (n=530)	90.9	4.7	4.6
BSAC (79)	93.7	0	6.3

Score 2 | Score 1 | Score 0

S. haemolyticus specimen 0737 (Feb 2012) Gentamicin resistant (MIC 16 mg/L)

Guideline	Percent reporting		
	S	I	R
All (n=610)	3.4	3.6	93.0
BSAC (79)	0	0	100

Score -1 | Score 1 | Score 2

Results are not scored if….

- There is a major discrepancy between EUCAST and CLSI reports in reference laboratories
- There is a problem with the specimen affecting results
- Low proportion of participants fail to get the expected result

Scoring of antimicrobial susceptibility testing when concordance is low

Reference	Concordance	Score when reported		
		S	I	R
S/S	S + I < 80%	-	-	-
R/R	R + I < 80%	-	-	-
S/S	S + I ≥ 80%	2	1	0
R/R	R + I ≥ 80%	-1	1	2

K. pneumoniae specimen 0318 (May 2011) Cefuroxime susceptible (MIC 4-8 mg/L)

Guideline	Percent reporting		
	S	I	R
All (n=508)	78.5	4.5	17.0
BSAC (113)	72.6	0.9	26.5

Score 2 | Score 1 | Score 0

Scoring of antimicrobial susceptibility testing when reference result varies

Reference	Concordance	Score when reported		
		S	I	R
S/I	S + I < 80%	-	-	-
R/I	R + I < 80%	-	-	-
S/I	S + I ≥ 80%	2	2	1
R/I	R + I ≥ 80%	0	2	2

M. morganii specimen 0447 (Aug 2011) Imipenem susceptible/intermediate (MIC 1-2 mg/L)

Guideline	Percent reporting		
	S	I	R
All (n=341)	78.3	12.6	9.1
BSAC (64)	85.9	7.8	6.3
	Score 2	Score 2	Score 1

Performance may be affected by breakpoint guidelines used

Guideline (April 2012)	All participants (%)	UK participants (%)
BSAC	132 (20.6)	128 (59.3)
EUCAST	308 (48.0)	51 (23.6)
CLSI	202 (31.4)	37 (17.1)

E. faecalis specimen 0138 (Jan 2011) vancomycin MIC 8-16 mg/L (vanB)

Guideline	Breakpoints (mg/L)		Percent reporting		
	S≤	R>	S	I	R
EUCAST* (n=316)	4	4	5.1	1.9	93.0
BSAC (154)	4	4	3.2	2.6	94.2
CLSI (n=314)	4	16	10.2	35.0	54.8

*Including EUCAST-based guidelines

P. aeruginosa specimen 0489 (Aug 2011) piperacillin-tazobactam MIC 32-64 mg/L

Guideline	Breakpoints (mg/L)		Percent reporting		
	S≤	R>	S	I	R
EUCAST* (n=340)	16	16	14.1	0.9	85.0
BSAC (n=160)	16	16	22.5	1.9	75.6
CLSI (n=210)	64	64	55.2	2.4	42.4

*Including EUCAST-based guidelines

Guidelines are not always followed

S. aureus specimen 0185 (Feb 2011) mupirocin MIC 4-16 mg/L

Guideline	Breakpoints (mg/L)		Percent reporting		
	S≤	R>	S	I	R
EUCAST* (n=248)	1	256	13.3	34.3	52.4
BSAC (n=146)	1	256	11.7	30.8	57.5
CLSI (n=208)	256	256	19.2	11.1	69.7

*Including EUCAST-based guidelines

75% of 93 labs reporting R and using CLSI breakpoints with automated systems reported MICs >8 or ≥8 mg/L and therefore cannot distinguish high and low-level resistance

CLSI disk diffusion method requires 200µg disk

21/21 using 200µg disk reported S or I, 20/22 using 5µg disk reported R

BSAC disk diffusion method requires MIC if resistant with 5µg disk

56/69 using 5µg disk reported R, suggesting MIC was not tested

S. aureus specimen 9889 (Aug 2010) fusidic acid MIC 4-8 mg/L

Guideline	Breakpoints (mg/L)		Percent reporting		
	S≤	R>	S	I	R
EUCAST* (n=240)	1	1	0	2.1	97.9
CLSI (n=297)	-	-	1.0	40.1	58.9

*Including EUCAST-based guidelines

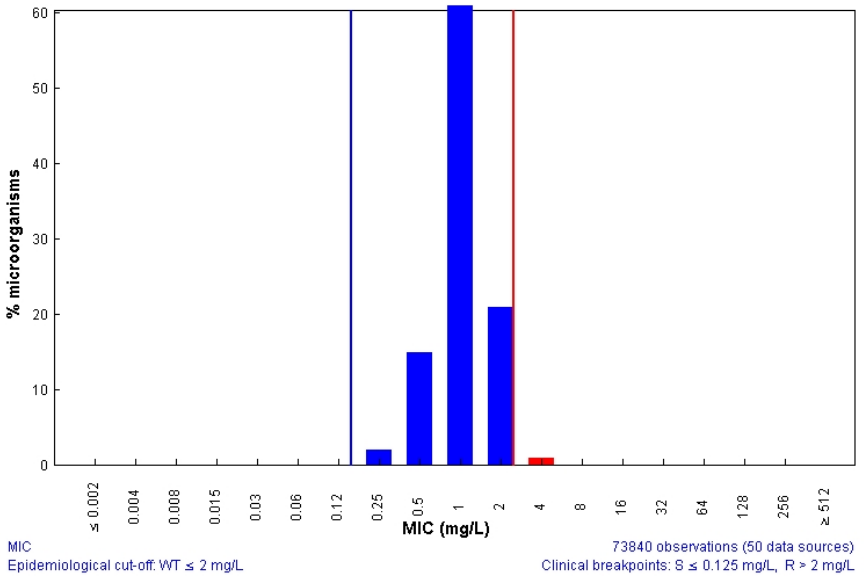
S. pneumoniae specimen 0272 (EARS-Net 2011) ciprofloxacin MIC 0.5-1 mg/L

Guideline	Breakpoints (mg/L)		Percent reporting		
	S≤	R>	S	I	R
EUCAST* (n=202)	0.12	2	30.2	67.8	2.0
CLSI (n=181)	-	-	92.9	14.9	2.2

*Including EUCAST-based guidelines

EUCAST wild type is intermediate – susceptible very rare

CLSI no breakpoints for ciprofloxacin



UKNEQAS

Performance is affected by method used

Method (April 2012)	All participants (%)	UK participants (%)
Automated	319 (49.7)	82 (38.0)
Disc diffusion	254 (39.5)	118 (54.6)
MIC	21 (3.3)	1 (0.5)
Breakpoint	3 (0.5)	3 (1.4)
Other	7 (1.1)	1 (0.5)
Multiple	38 (5.9)	11 (5.0)

E. faecalis specimen 0138 (Jan 2011) vancomycin MIC 8-16 mg/L (vanB)

EUCAST resistant, CLSI intermediate

Method	Percent reporting		
	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

Enterococci and vancomycin

- Examine with transmitted light (plate held up to light).
  - Fuzzy zone edges and colonies within zone indicate vancomycin resistance and should be investigated further.

E. faecalis
non-VRE

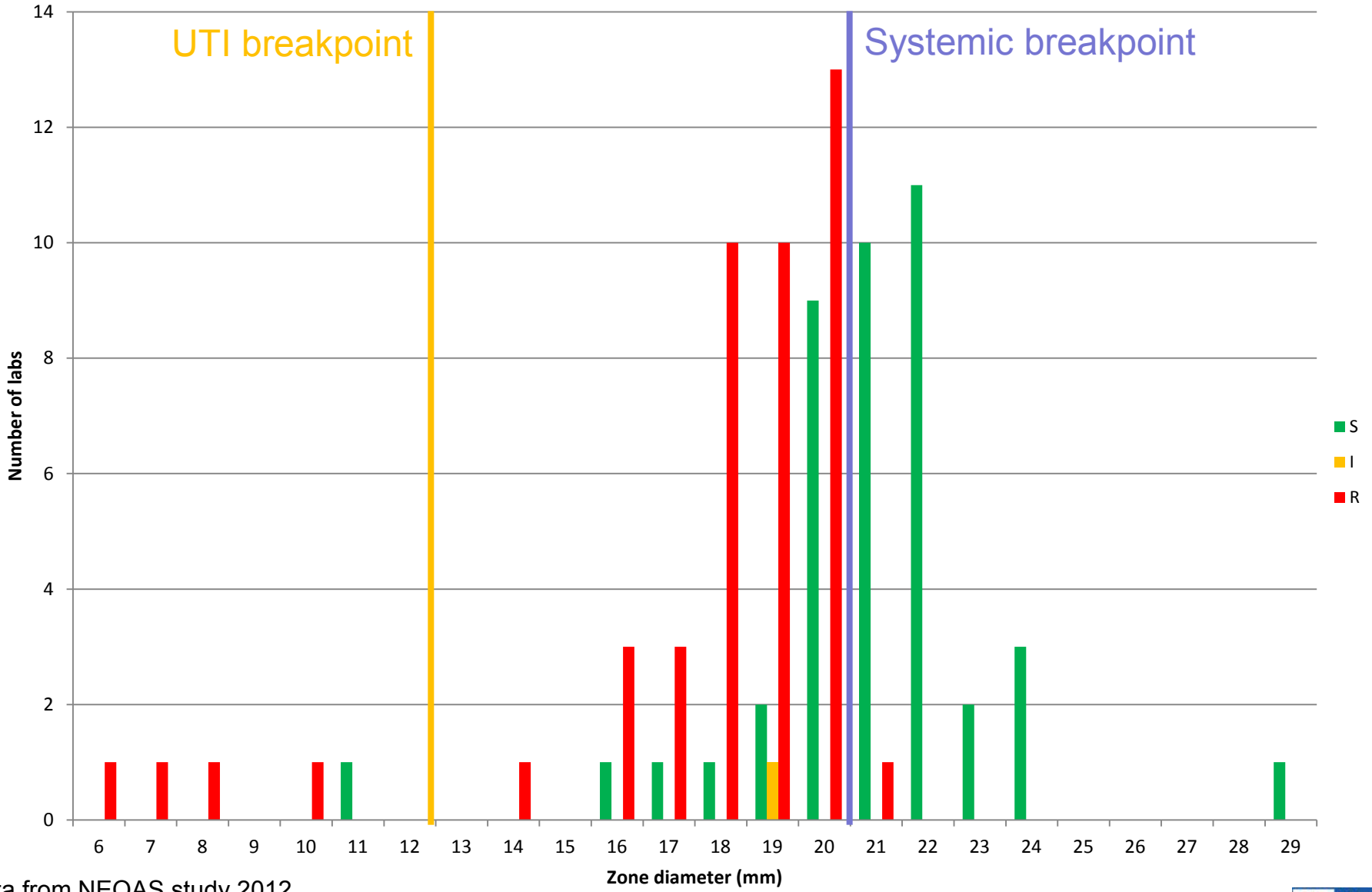
E. faecium
VRE

Borderline susceptibility reduces the reliability of results

E. coli specimen 0927 (May 2012) amoxicillin-clavulanic acid MIC 8 mg/L

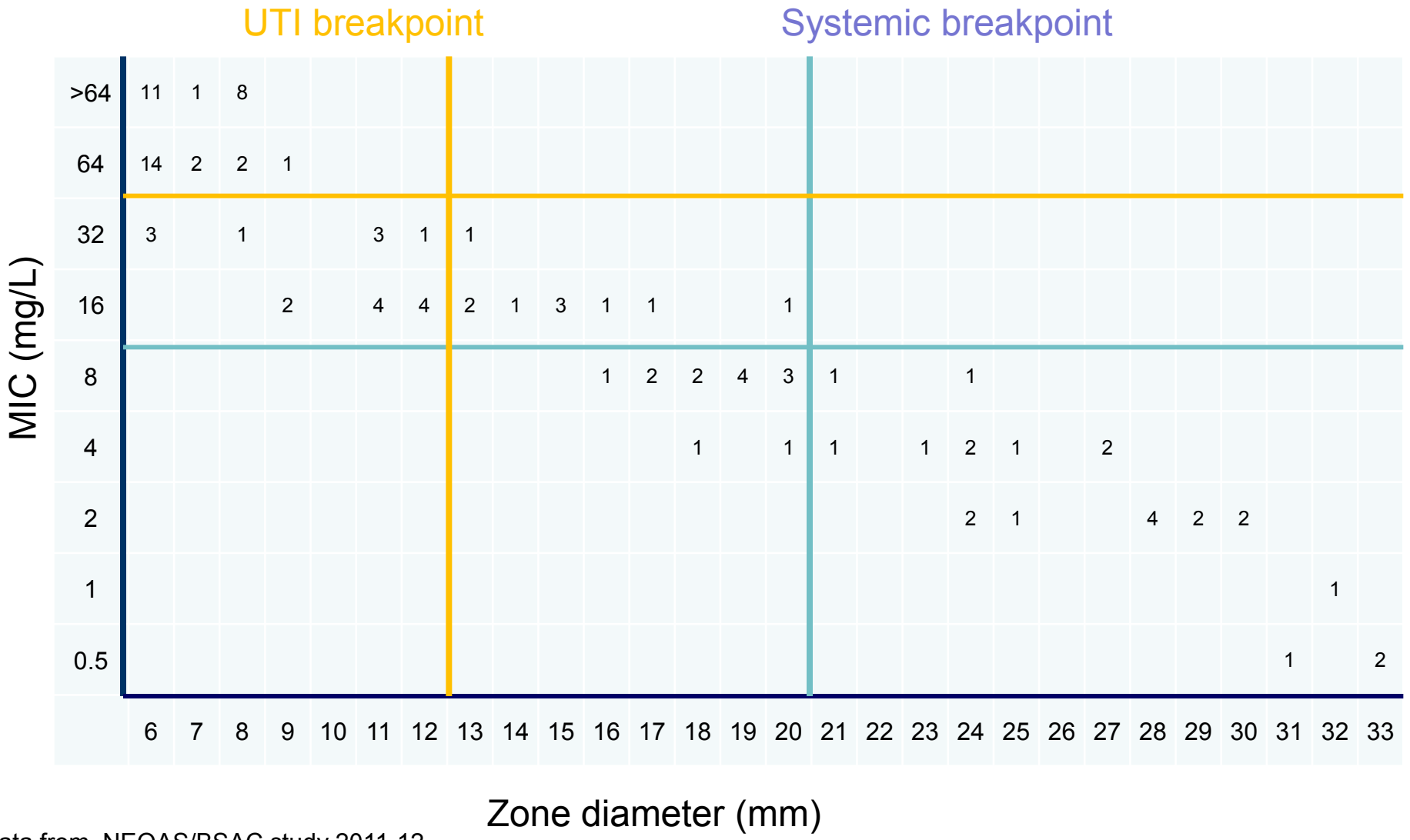
Guideline	Breakpoints (mg/L)		Percent reporting		
	S≤	R>	S	I	R
BSAC (n=120)	8	8	58.7	0.8	40.5
EUCAST ex. BSAC (n=256)	8	8	94.9	1.6	3.5
CLSI (n=193)	8	16	94.3	1.0	4.7

Amoxicillin-clavulanic acid zone diameters for BSAC method for NEQAS *E. coli* 0927



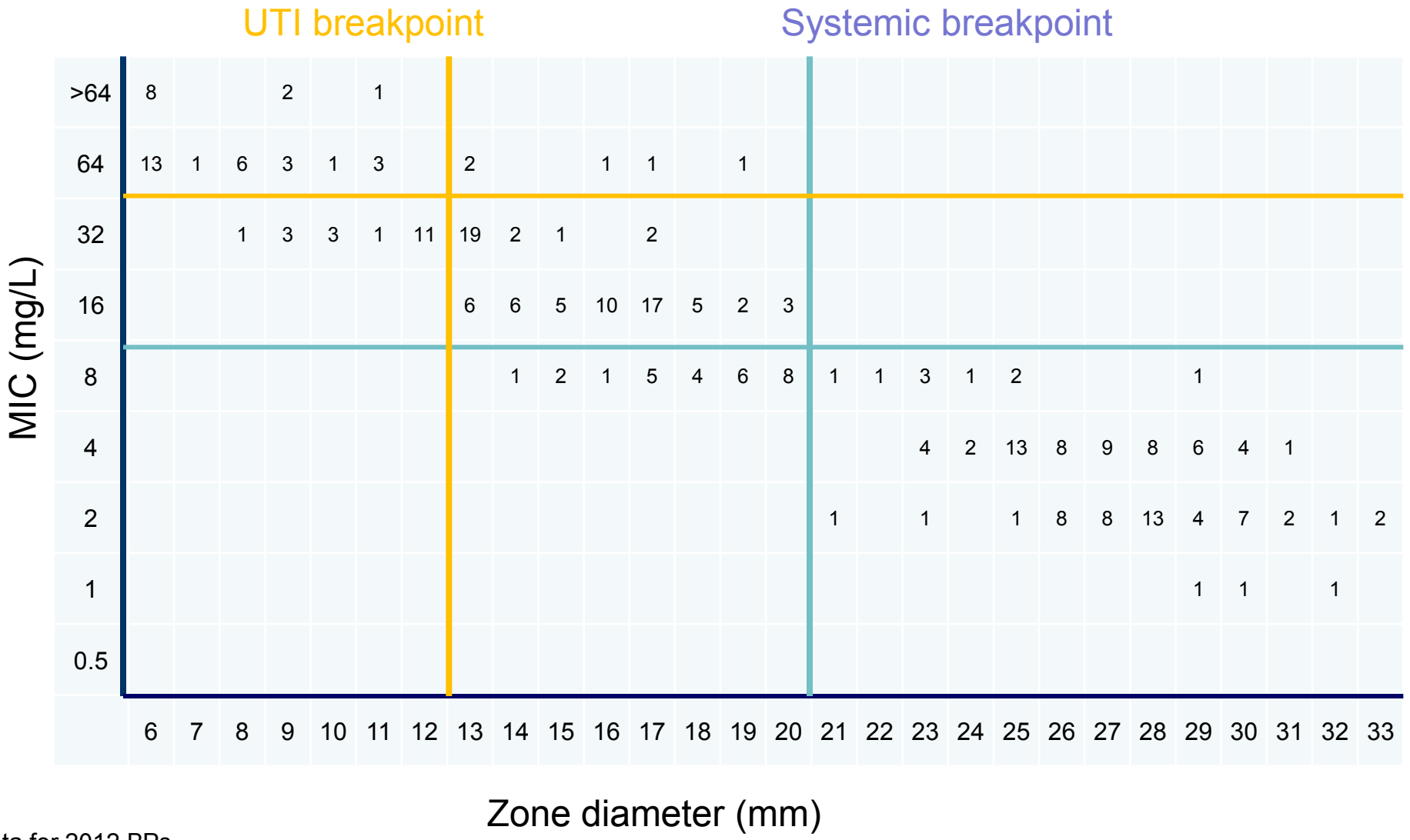
Data from NEQAS study 2012

Amoxicillin-clavulanic acid MIC (2:1 ratio) v. zone diameter for Enterobacteriaceae by BSAC method



Data from NEQAS/BSAC study 2011-12

Amoxicillin-clavulanic acid MIC (2:1 ratio) v. zone diameter for Enterobacteriaceae by BSAC method



Data for 2012 BPs

Uncertainty in reporting penicillin susceptibility in *S. pneumoniae*

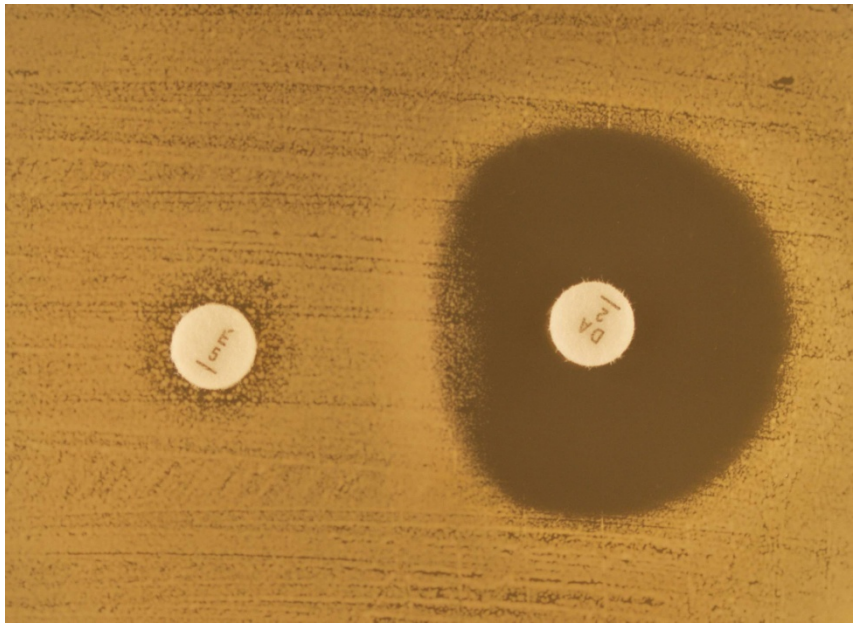
- Screen with oxacillin disk
- If resistant, determine the MIC and interpret susceptibility depending on the site of infection

S. pneumoniae specimen 0272 (EARS-Net 2011) penicillin MIC 0.5 mg/L

"Intermediate" to penicillin
Susceptible if from pneumonia
Resistant if from meningitis

Reporting	Interpretation		Percent reporting		
	EUCAST	CLSI	S	I	R
Oxacillin (n=523)	R	R	4.6	4.6	90.8
Penicillin					
Test result (n=615)			23.6	69.8	6.6
Pneumonia (n=740)	S	S	76.1	20.8	3.1
Meningitis (n=741)	R	R	5.5	8.1	86.4

Uncertainty in reporting dissociated (MLSB-inducible) resistance to clindamycin in *S. aureus*



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S. aureus specimen 0364 (June 2011)
Clindamycin MIC 0.06-0.25 mg/L but resistance induced by erythromycin

Guideline	Percent reporting		
	S	I	R
EUCAST* (n=198)	48.5	0.5	51.0
BSAC (n=50)	48.0	0	52.0
CLSI (n=219)	58.4	0	41.6

*Including EUCAST-based guidelines

- 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

Uncertainty in reporting cephalosporin susceptibility for Enterobacteriaceae with inducible AmpC

E. cloacae specimen 9581 (Jan 2010) Inducible AmpC

Agent	MIC (mg/L)	% reporting		
		S	I	R
Cefotaxime (n=550)	0.12-0.5	91.2	0.5	8.3
Ceftazidime (n=630)	0.25-0.5	90.6	0.4	9.0

Inducible AmpC typical for *Enterobacter* spp. (also *C. freundii, Serratia* spp., *M. morganii* and *Providencia* spp.)

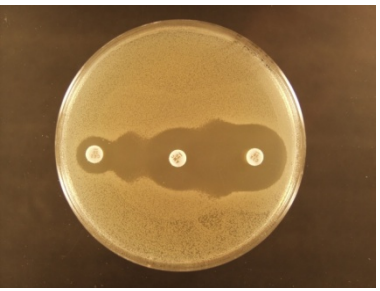
May mutate to stably derepressed state during treatment.

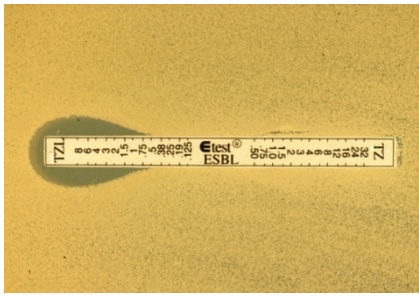
Reporting inducible AmpC in Enterobacteriaceae

EUCAST Expert rule 9.2. *Enterobacter* spp., *C. freundii, Serratia* spp., *M. morganii*. If susceptible in vitro to cefotaxime, ceftriaxone or ceftazidime in monotherapy then note that the use in monotherapy of cefotaxime, ceftriaxone or ceftazidime *(or in combination with an aminoglycoside)* should be discouraged owing to the risk of selecting resistance, or suppress the susceptibility testing results for these agents.

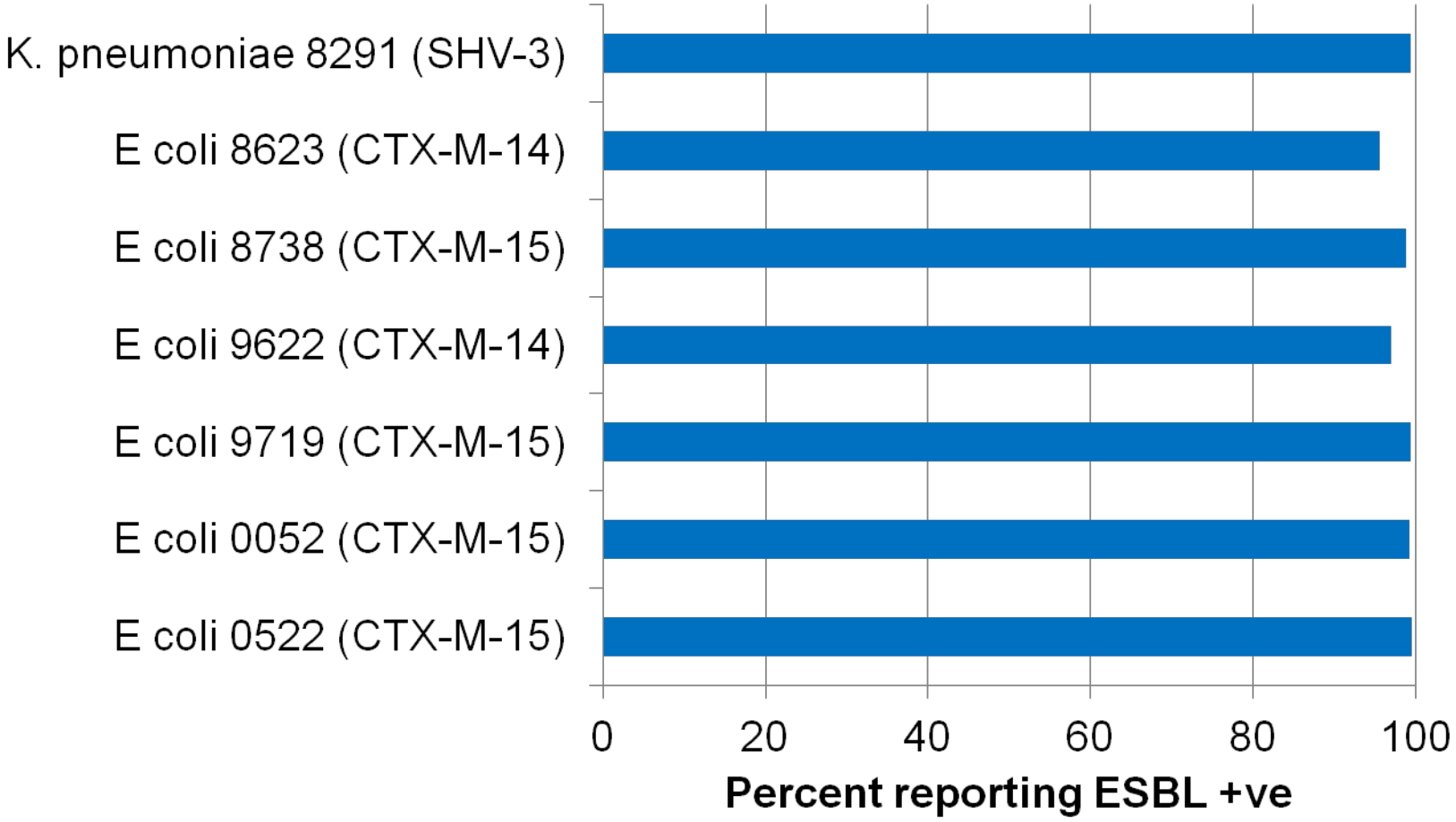
CLSI *Enterobacter*, *Citrobacter, Serratia*
May develop resistance during prolonged therapy with third-generation cephalosporins as a result of derepression of AmpC β-lactamase. Therefore isolates that are initially susceptible may become resistant within three to four days after initiation of therapy. Testing of repeat isolates may be warranted.

Detection of ESBL-mediated resistance in Enterobacteriaceae

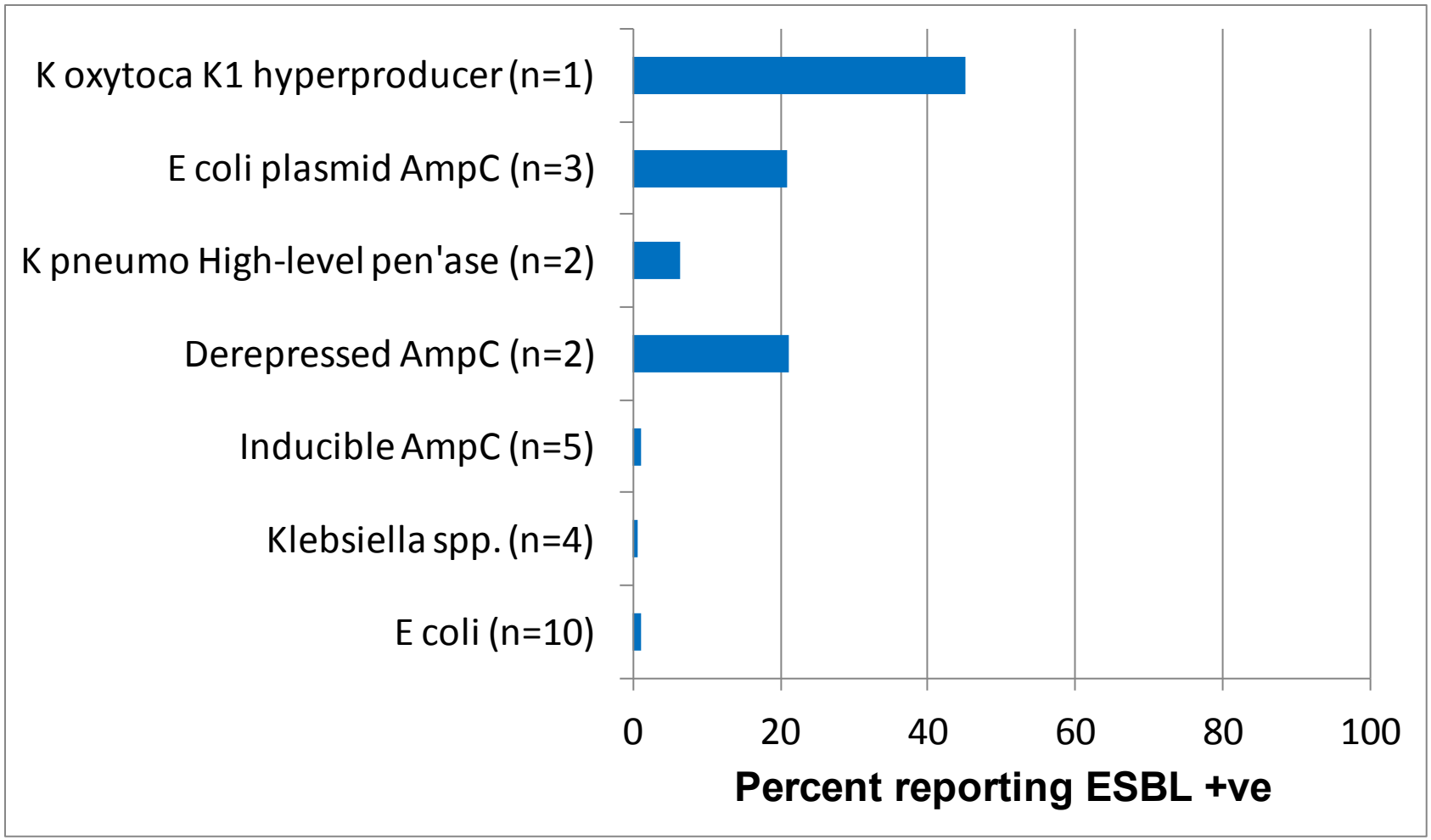




Detection of ESBLs in Enterobacteriaceae



Reports of ESBLs in Enterobacteriaceae without ESBLs



Summary: What does EQA provide?

- Independent assessment of performance
- Assessment of performance over time
- Comparison with other laboratories
- Highlights problem areas
- Performance related to guidelines and methods
- Gives practical experience of difficult tests (especially if resistance is uncommon)
- Provides background information and discussion of problem tests
- Performance indicator for accreditation

Summary: What are the limitations of EQA?

- Number of specimens distributed is small
- May be considered inappropriate to send some organisms
- Laboratories may not treat specimens as routine

Summary: What does EQA tell us?

- Scoring is not always straightforward
- Performance can be linked to guidelines and methods used for some tests
- Discrepancies more common when:
  - Differences between guidelines or methods
  - Failure to follow guidelines
  - Confusion over reporting
  - Susceptibility borderline
- Performance good for most organism-agent combinations