



EUCAST

EUROPEAN COMMITTEE
ON ANTIMICROBIAL
SUSCEPTIBILITY TESTING

European Society of Clinical Microbiology and Infectious Diseases



CLINICAL AND
LABORATORY
STANDARDS
INSTITUTE®

www.EUCAST.org

www.CLSI.org

Breakpoints

Why EUCAST and not CLSI?

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EUCAST and CLSI

EUCAST	CLSI
<p>Established 1998 (National Committees formed in 1970s-80s)</p>	<p>Established 1970s Formerly NCCLS (National Committee for Clinical Laboratory Standards)</p>
<p>Susceptibility testing is sole remit</p>	<p>Remit covers all aspects of laboratory medicine.</p> <p style="text-align: center;">CLSI ↓ Area Committee Microbiology ↓ Subcommittee on Antimicrobial Susceptibility testing</p>

EUCAST and CLSI Organisation

EUCAST	CLSI
<p>Steering Committee (11) with representatives of European breakpoint committees and three representatives of other countries (plus two “visiting members”)</p> <p>5-6 meetings per year</p>	<p>Voting committee (12) with representatives of the profession and industry</p> <p>12 “advisors” (profession, industry, FDA, CDC)</p> <p>2 meetings per year</p>
<p>General committee with representatives of all European (and some non-European) countries, FESCI & ISO</p>	<p>Membership by subscription</p> <p>No national representation</p>
<p>Consultation with NACs and open consultation via website</p>	<p>Consultation at meetings</p>
<p>Industry consultative role</p>	<p>Industry part of decision process</p>

EUCAST and CLSI

Relationship to regulatory authorities

EUCAST	CLSI
EUCAST sets breakpoints for European Medicines Agency (EMA) Advises ECDC and EFSA	United States Food and Drug Administration (FDA) sets official breakpoints CLSI sets breakpoints for new agents if requested by the company.
EUCAST breakpoints in EMA Specifications of Product Characteristics (SmPCs)	FDA breakpoints in US SmPCs.
EMA Standard Operating Procedure defines relationship with EUCAST	

EUCAST and CLSI

Breakpoint setting for new agents

EUCAST	CLSI
In parallel with submission to EMA for marketing authorisation	In addition to FDA if requested by the company (cannot suggest anything different from FDA for 2 years)
Closed presentation to Steering Committee (SC) by company	Open presentation to CLSI by the company
Discussion process involving the SC, EMA, National Breakpoint Committees and the company over several weeks	Discussion following the presentation
Consensus decision on breakpoints by SC	Voting committee vote following discussion

EUCAST and CLSI

Review and harmonisation of breakpoints for existing agents

EUCAST	CLSI
Review of breakpoints ongoing	Few changes to breakpoints (official FDA breakpoints unchanged)
Harmonisation of breakpoints for all the most widely used agents in Europe completed	No involvement in harmonisation of breakpoints

EUCAST and CLSI breakpoint expression and intermediate category

EUCAST	CLSI
Susceptible $\leq x$ mg/L Resistant $> y$ mg/L	Susceptible $\leq x$ μ g/mL Resistant $\geq y$ μ g/mL
e.g. Enterobacteriaceae with cefotaxime Susceptible ≤ 1 mg/L Resistant > 2 mg/L	Susceptible ≤ 1 μ g/mL Intermediate 2 mg/L Resistant ≥ 4 μ g/mL
Intermediate inferred	Intermediate spelt out

EUCAST and CLSI breakpoints

Microorganisms	Number of Breakpoints	Same breakpoints for		
		S and R	S	R
Enterobacteriaceae	35	3	8	1
<i>Pseudomonas</i>	17	0	9	2
<i>Acinetobacter</i>	10	1	3	2
<i>Staphylococcus</i>	27	5	6	1
<i>Enterococcus</i>	8	0	2	3
Streptococcus A,B,C,G	12	2	2	2
<i>S. pneumoniae</i>	26	4	4	5
<i>H. influenzae</i>	24	0	3	0

Implications of differences between EUCAST and CLSI breakpoints

Resistance rates may be different despite no difference in MIC distribution

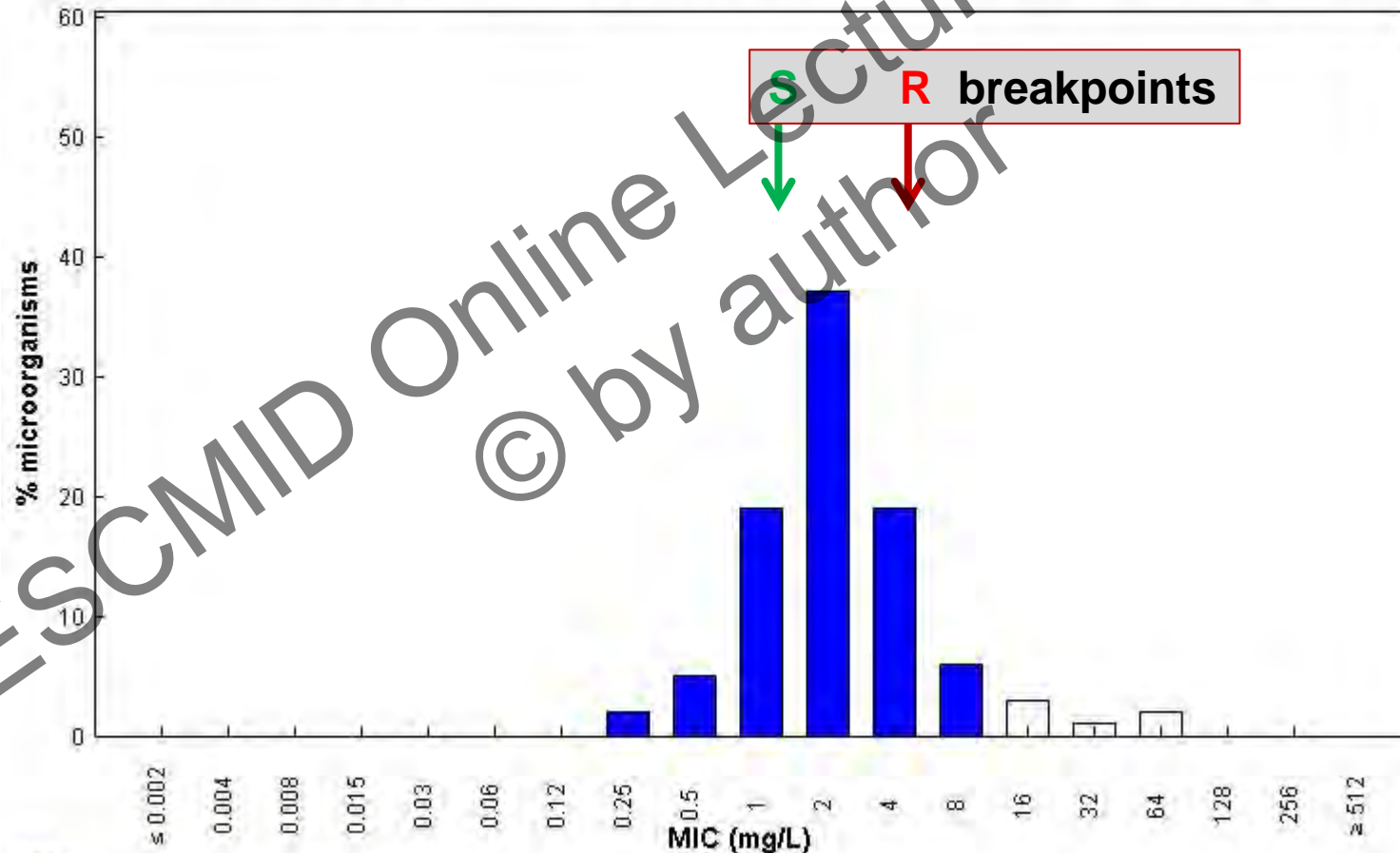
Implications for:

- Guidance on appropriate therapy
- Comparing surveillance data from different studies
- Laboratories changing guidelines used

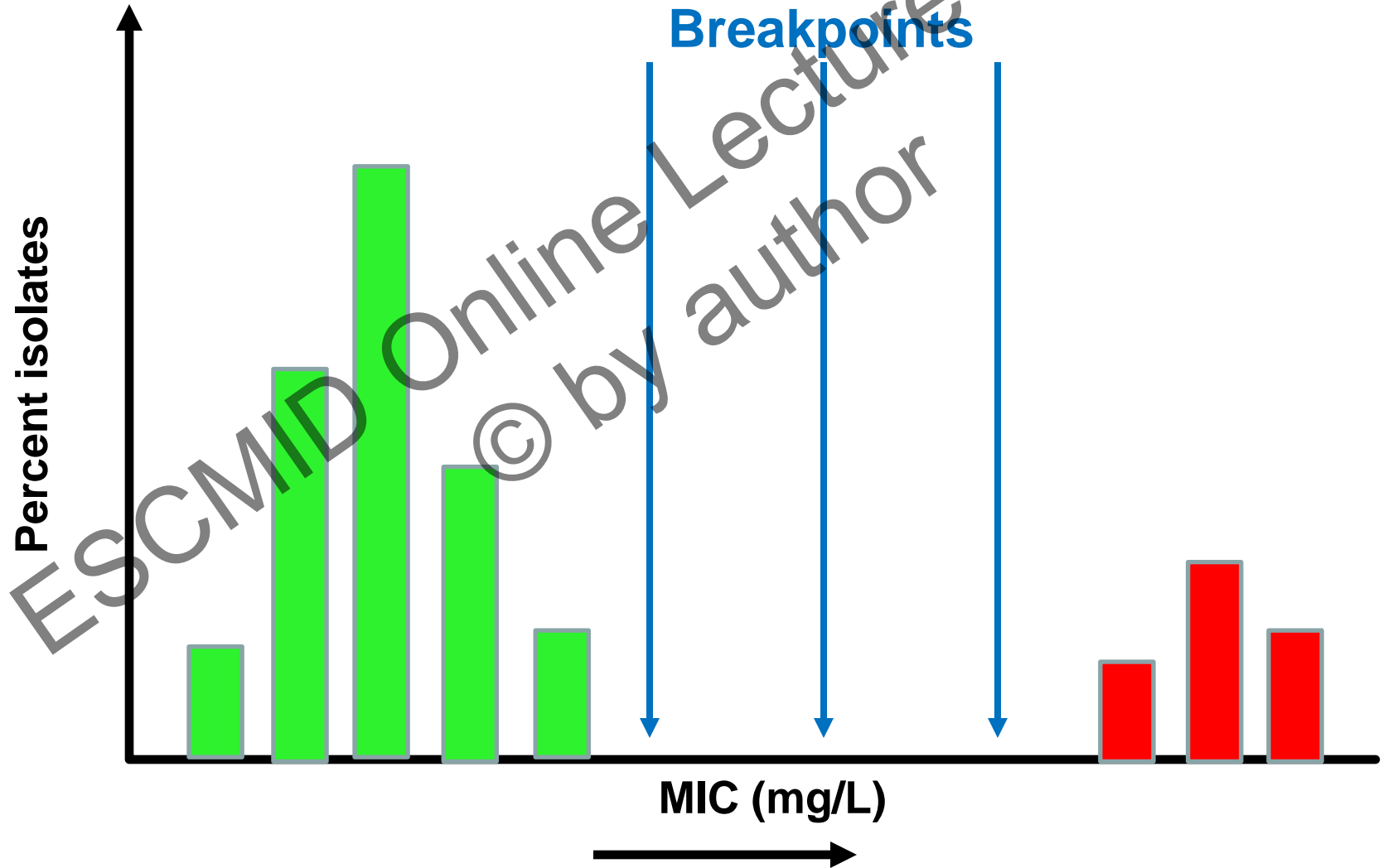
Practical effect of different breakpoints depends on the MIC distribution

Effect of different breakpoints shown with MIC distributions

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



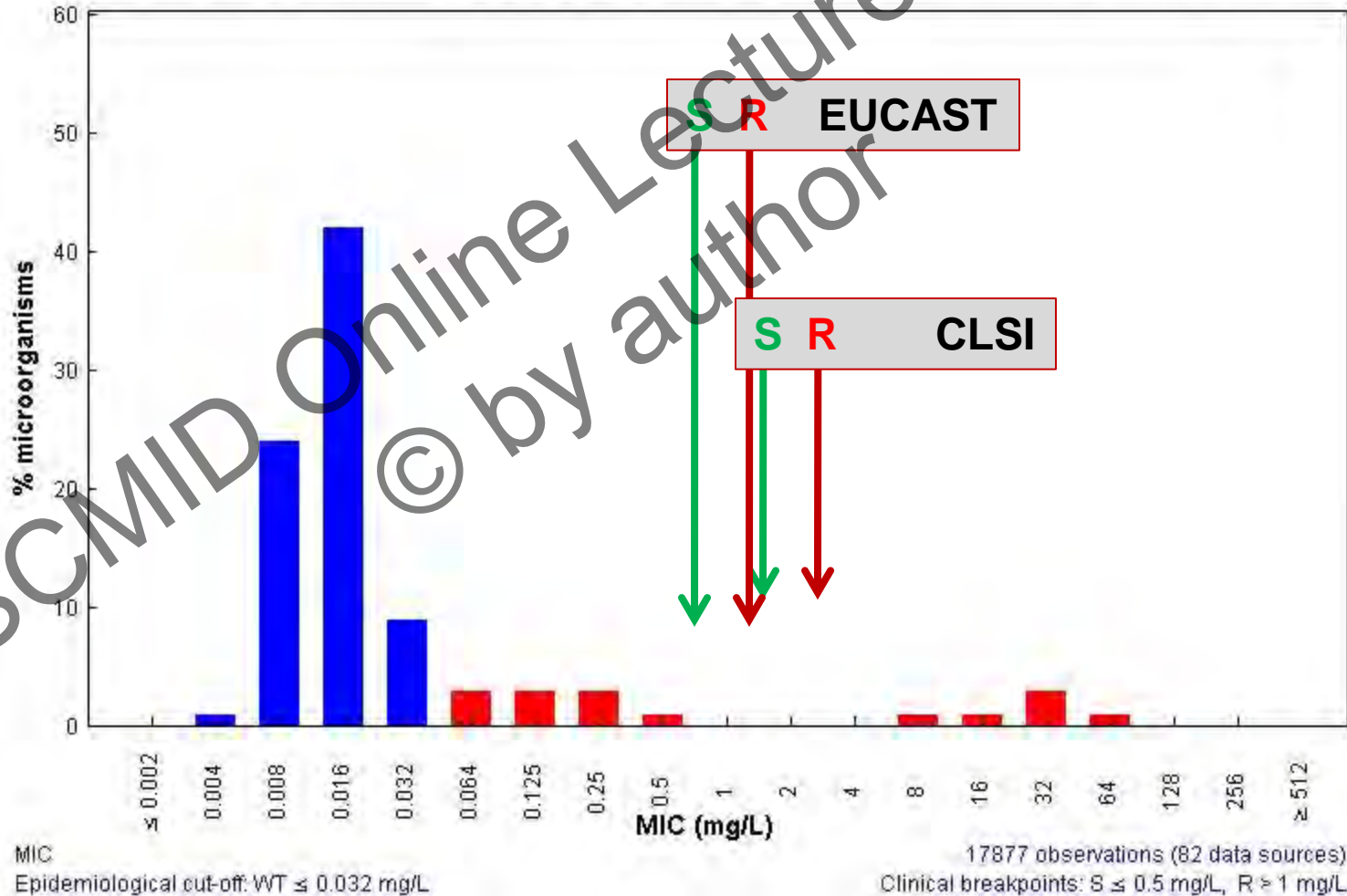
Differences in breakpoints but no effect on resistance rates



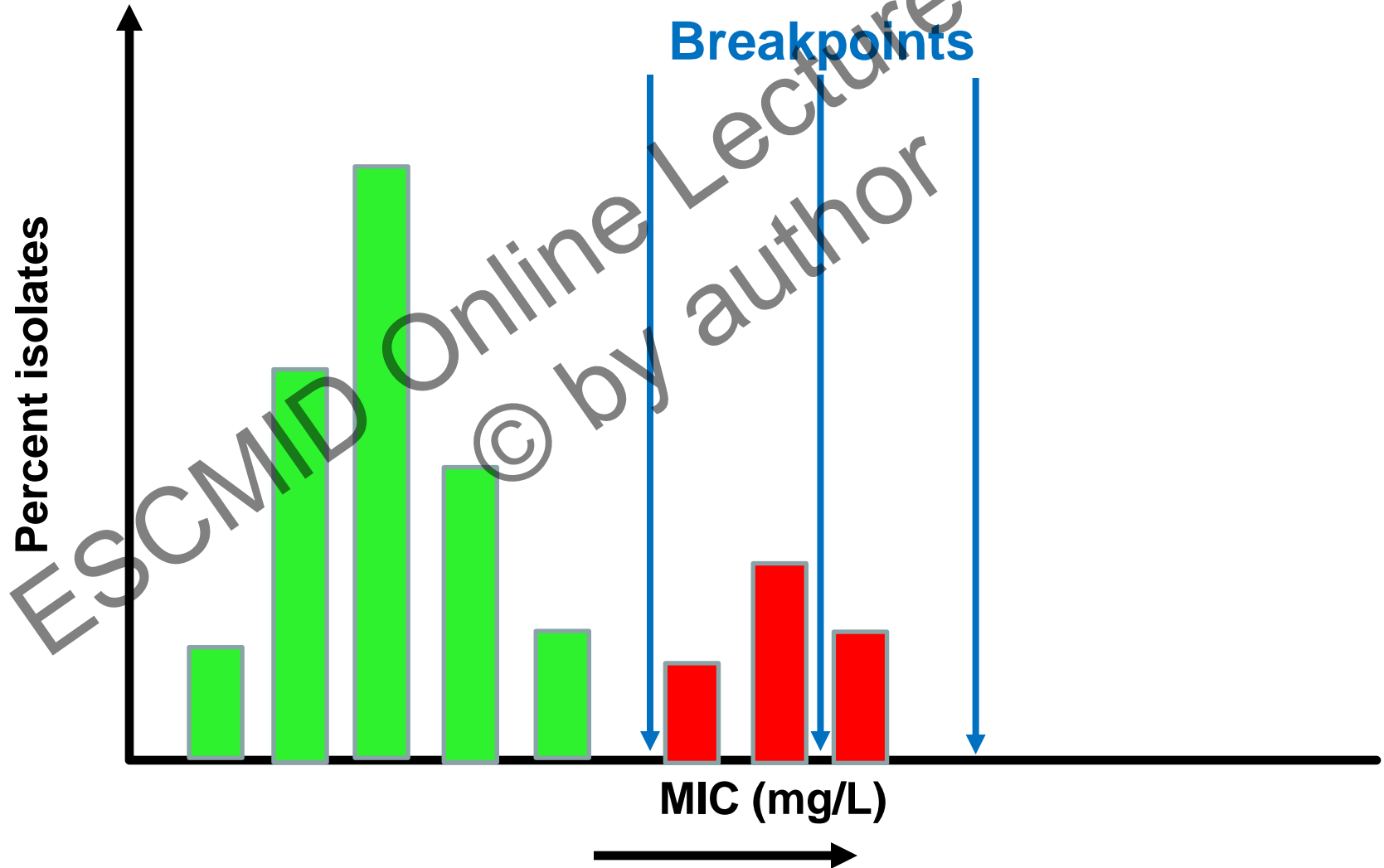
Ciprofloxacin breakpoints for *E. coli*

Ciprofloxacin / Escherichia coli
EUCAST MIC Distribution - Reference Database 2010-05-10

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



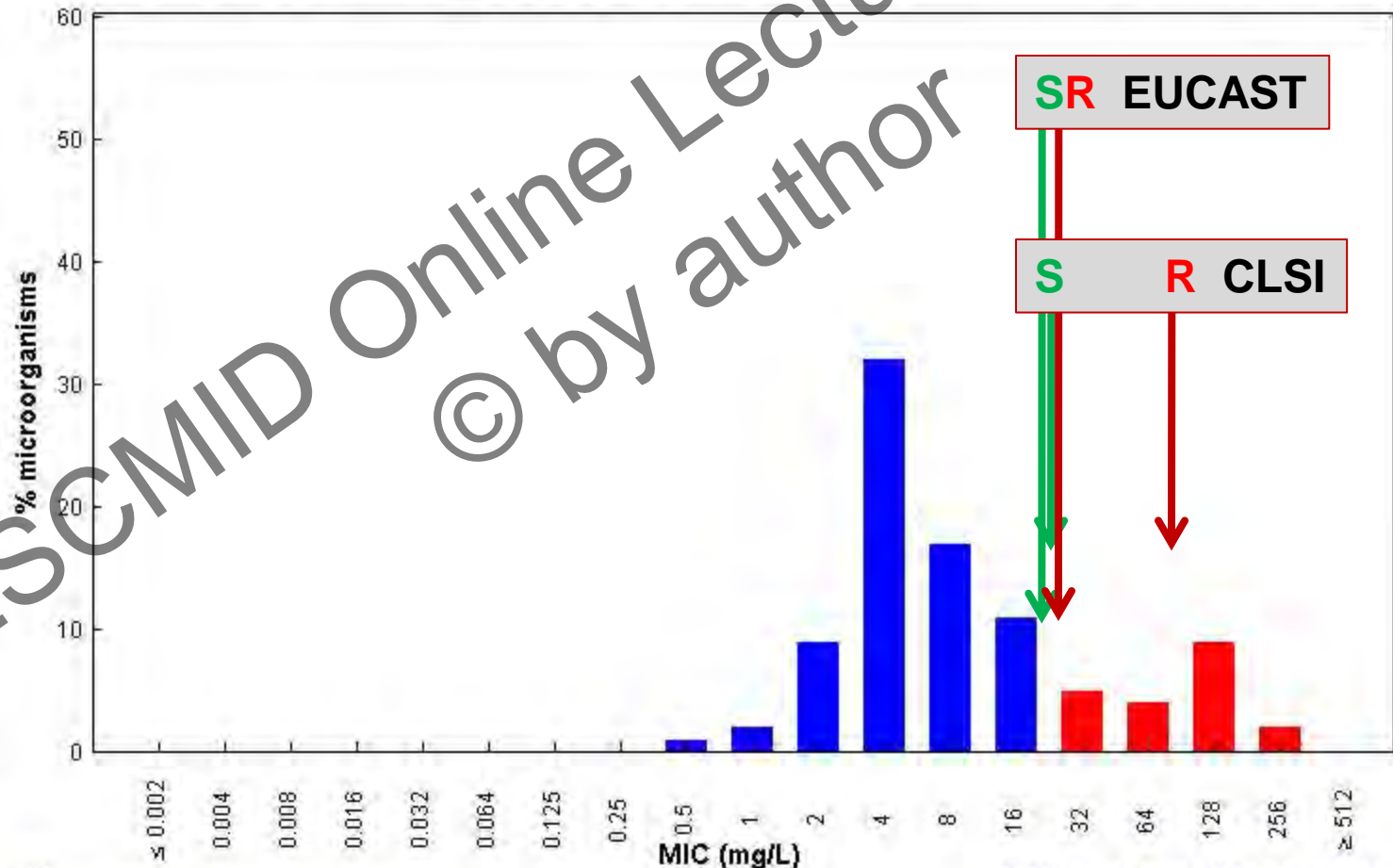
Differences in breakpoints affecting resistance rates



Piperacillin-tazobactam breakpoints for *P. aeruginosa*

Piperacillin-tazobactam / *Pseudomonas aeruginosa*
EUCAST MIC Distribution - Reference Database

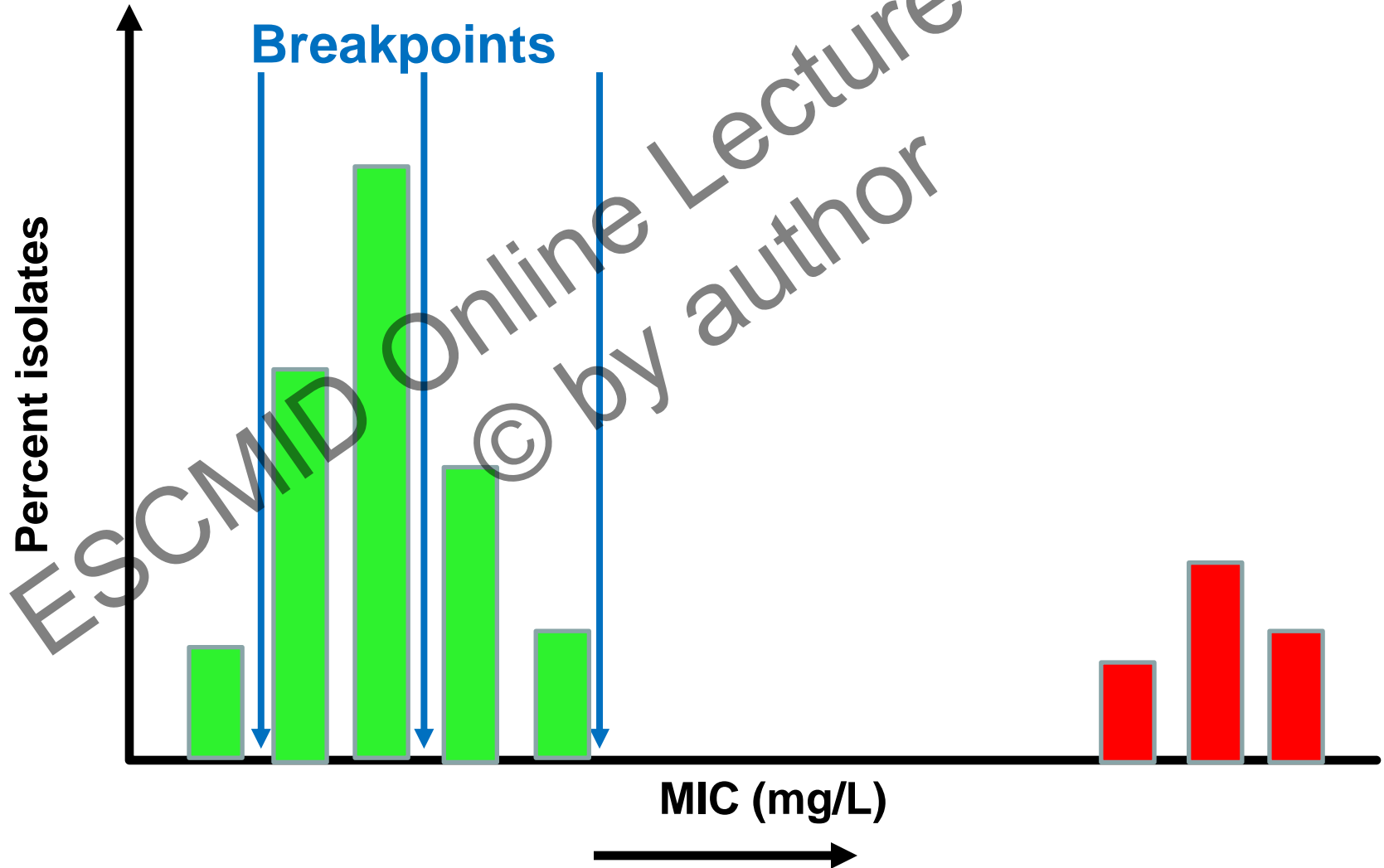
MIC distributions include collated data from multiple sources, geographical areas and time periods and can never be used to infer rates of resistance



MIC
Epidemiological cut-off: WT ≤ 16 mg/L

31500 observations (68 data sources)
Clinical breakpoints: S ≤ 16 mg/L, R > 16 mg/L

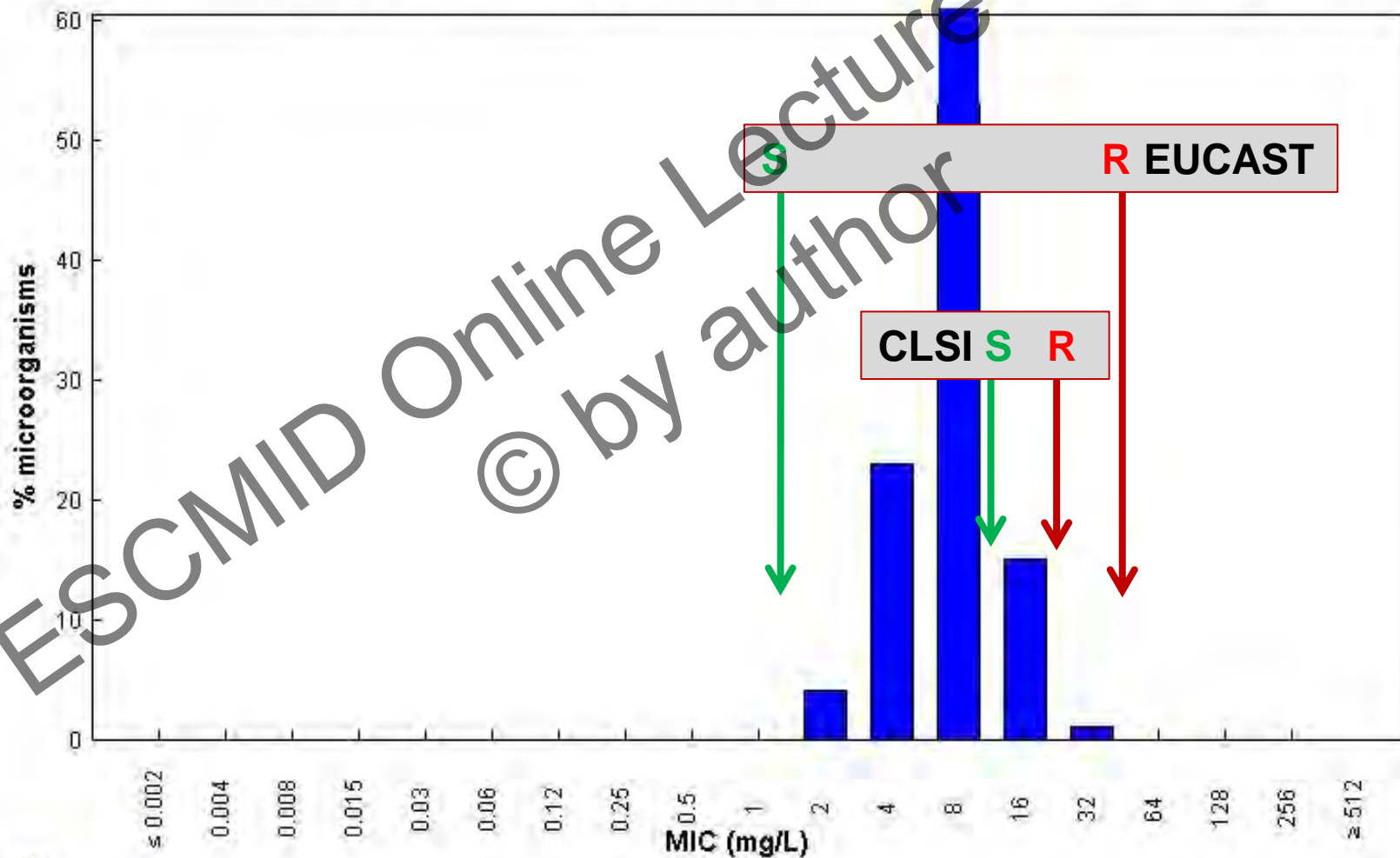
Differences in breakpoints affecting resistance rates



Clarithromycin breakpoints for *H. influenzae*

Clarithromycin / *Haemophilus influenzae*
International MIC Distribution - Reference Database 2014-09-16

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): 32 mg/L

Wildtype (WT) organisms: ≤ 32 mg/L

27846 observations (11 data sources)

EUCAST and CLSI Documents

EUCAST	CLSI
Clinical breakpoints	Clinical breakpoints
Rationale documents (RDs) giving breakpoint background	
Method guidelines	Method guidelines
Comprehensive expert rules with supporting explanations and references	Some expert rules included in breakpoint tables
Documents freely available	Documents for sale

EUCAST and CLSI Website resources

EUCAST

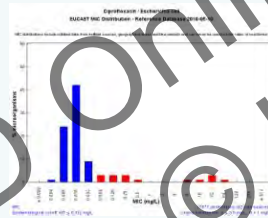
<http://www.EUCAST.org>

All EUCAST documents free

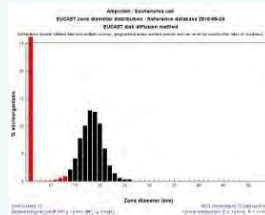
<http://mic.eucast.org/Eucast2>

MIC and zone diameter distributions

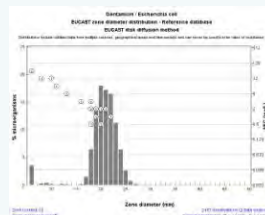
MIC distributions



Zone diameter distributions



MIC-zone diameter correlations



CLSI

<http://www.CLSI.org>

All CLSI documents for sale

EUCAST and CLSI Funding

EUCAST	CLSI
Contract with ECDC	Subscriptions of members
ESCMID	Sale of documents
National Breakpoint Committees	Government grant to support distribution of documents to developing countries

Conclusions

- There are significant differences between EUCAST and CLSI in organisation, funding, relationship to regulatory authorities and decision making
- Differences in breakpoints between CLSI and EUCAST probably have small effects on resistance rates for most organism-agent combinations but some differences are more significant
- In recent years EUCAST has reviewed breakpoints for all commonly used agents
- All EUCAST breakpoints and documents are freely available