National Food Institute

Technical University of Denmark

Recent developments in fluoroquinolone resistance

Community Reference Laboratory Antibiotic Resistance

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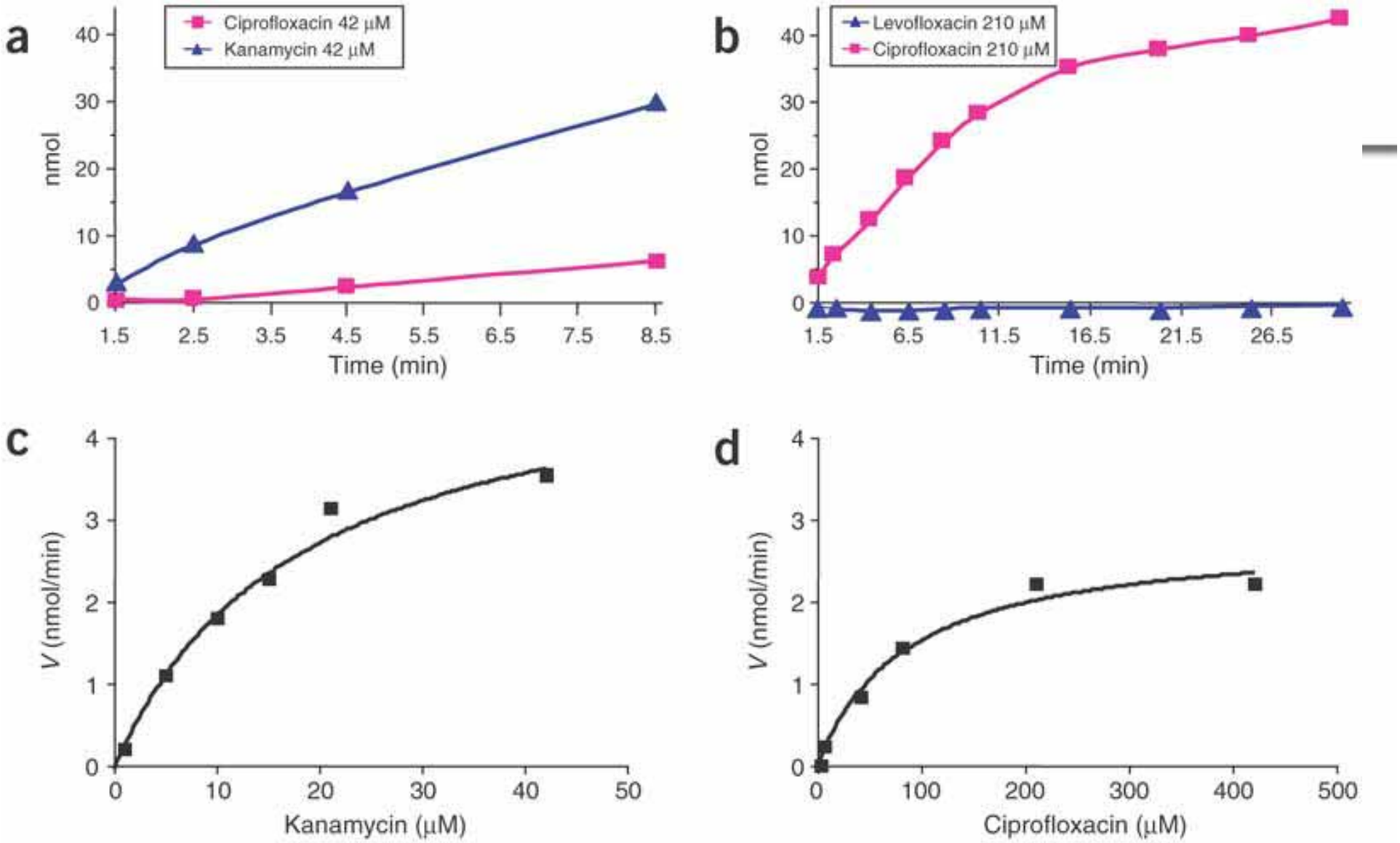
Resistance to quinolones – until 1998 (1994)

- Mutations in genes involved in DNA replication
  - gyrA, gyrB, pacC, parE
- Spread of resistance through spread of the clone

Resistance to quinolones - recent developments

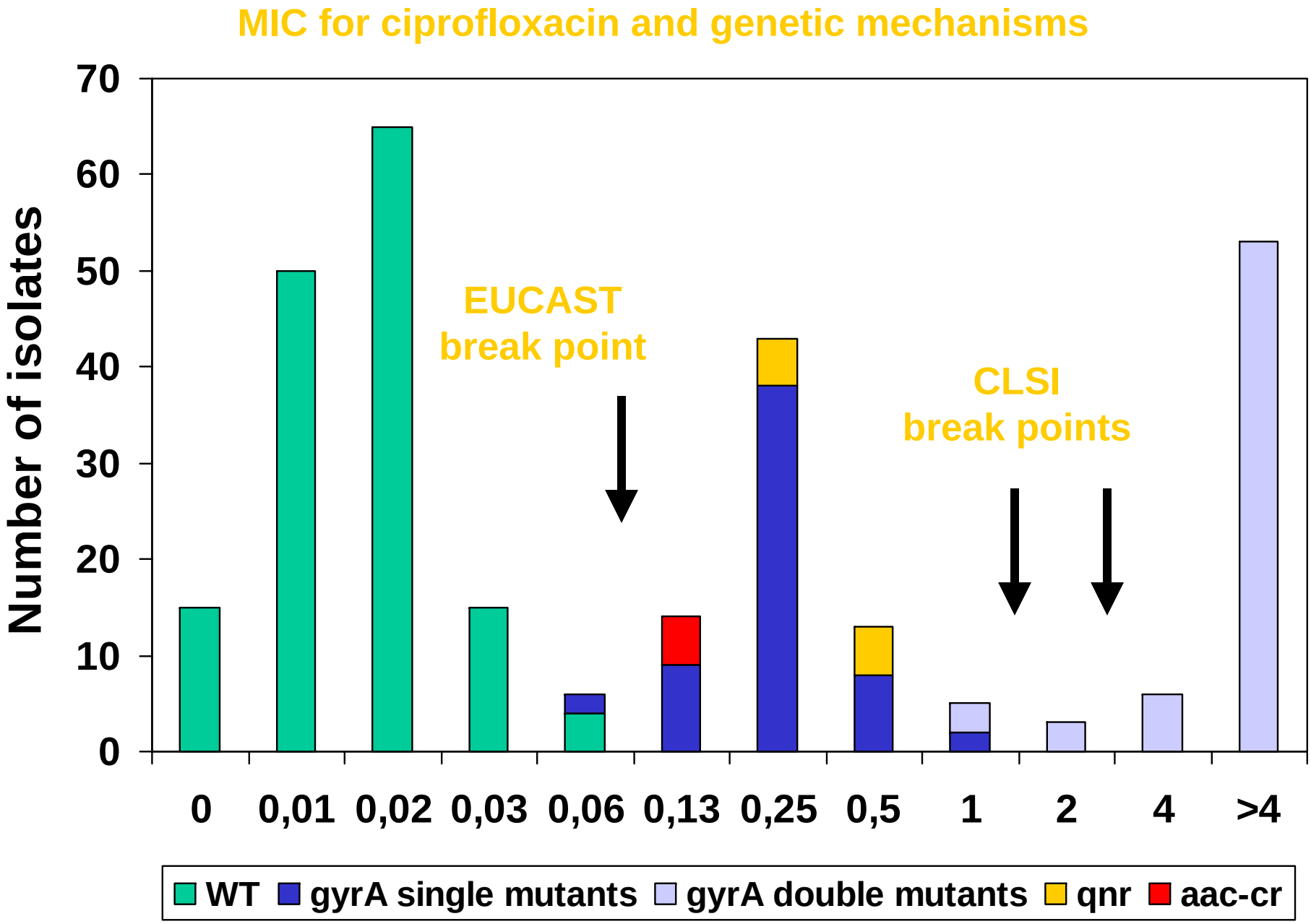
- 1998 - New transferable gene (qnr) in Klebsiella from USA
- 2003 – qnr in E. coli from Shanghai
- 2004-07
  - emergence of qnr genes on multiple resistance plasmids, new species, new genes (qnrA – six variants, qnrB-six variants, qnrS-two variants)
- 2006 – a new mechanism – variant of acc(6')-Ib-cr (found worldwide)

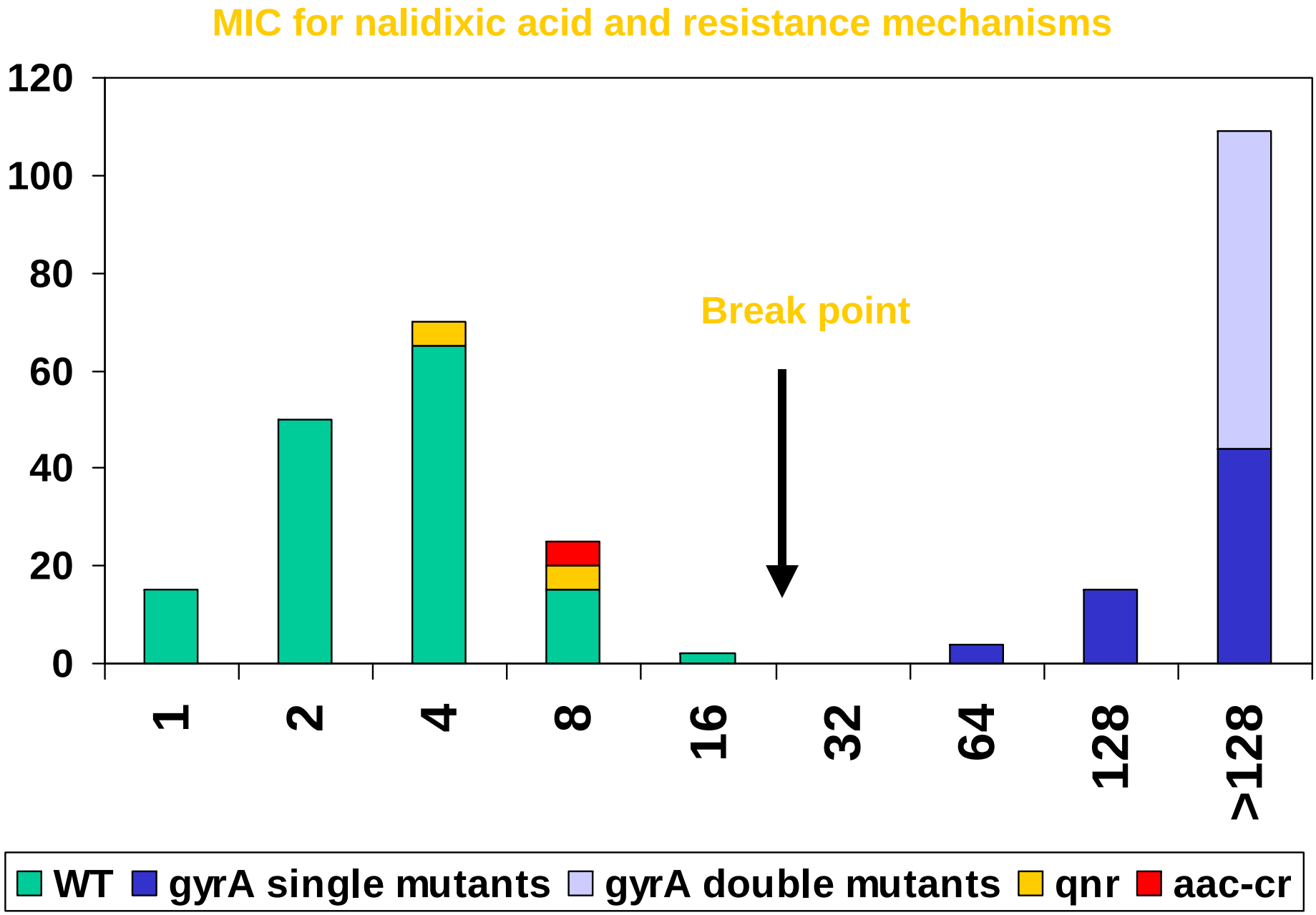


Robicsek et al. 2006

Break points

- CLSI
  - MIC <=1, 2, >=4
  - Zone >=21, 16-20, <=15
- EUCAST <=0,06


MIC for ciprofloxacin and genetic mechanisms
Number of isolates
70
60
50
40
30
20
10
0
EUCAST
break point
CLSI
break points
0
0,01
0,02
0,03
0,06
0,13
0,25
0,5
1
2
4
>4
WT
gyrA single mutants
gyrA double mutants
qnr
aac-cr


MIC for nalidixic acid and resistance mechanisms
120
100
80
60
40
20
0
Break point
1
2
4
8
16
32
64
128
>128
WT
gyrA single mutants
gyrA double mutants
qnr
aac-cr

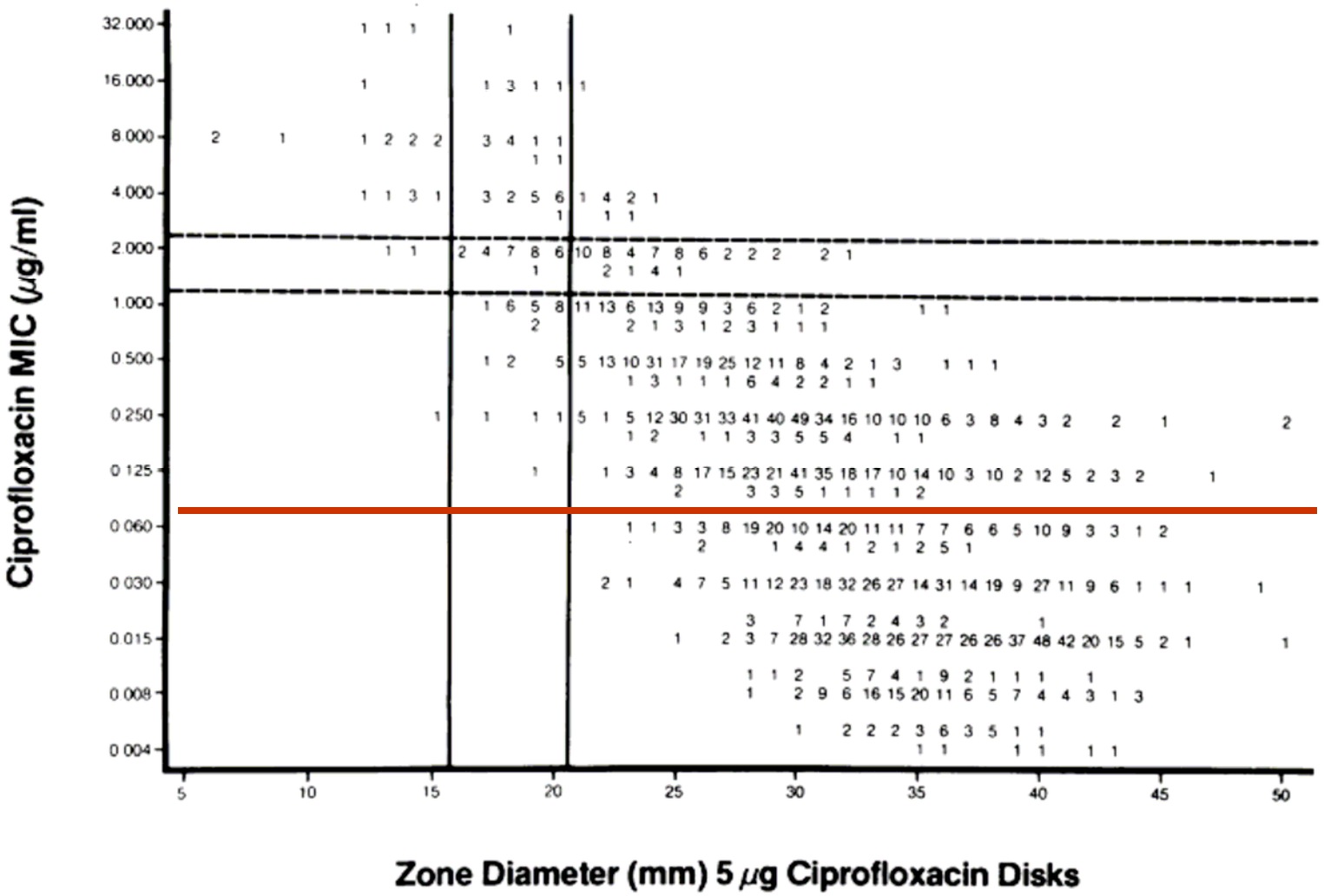
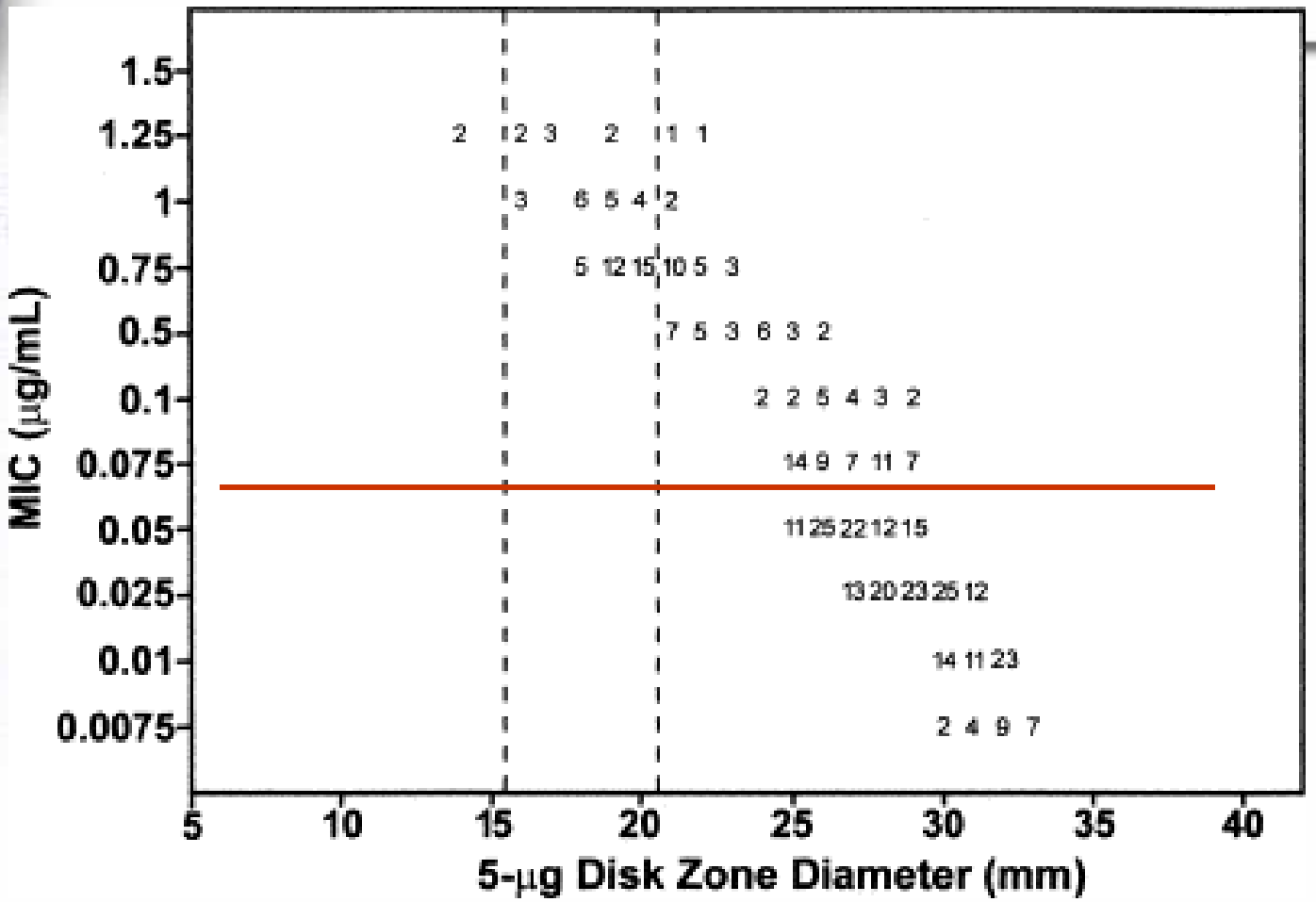


FIG. 1. Evaluation of 5-μg ciprofloxacin disks for testing the susceptibility of 1,959 gram-negative bacilli and 360 staphylococci. Data were accumulated from seven independent laboratories.

Barry et al. 1985



Scattergram for 421 *S.* Typhi isolates comparing MICs of ciprofloxacin with zone diameters (5 µg disk). The broken vertical lines represent the interpretive breakpoint suggested for Enterobacteriaceae (susceptible at ≥21 mm, resistant at ≤15 mm). Numbers indicate numbers of *S.* Typhi isolates. Pal et al. 2004. Int J Antimicrob Agents. 24(3):297-9.

Conclusions

- Worldwide emergence of new transferable FQ-resistance mechanisms
- Nalidixic acid is not useful for detection of new mechanisms
- EUCAST break point fits with resistance mechanisms
- Currently no break point for 5 mcg disc
- Please contact a reference laboratory if in doubt

Thank you!

National Food Institute

Technical University of Denmark

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Please note!
The Danish Institute for Food and Veterinary Research, DFVF has merged with five other institutes why Rene, Danilo, Michael, Susanne and I now works in the National Food Institute, FOOD-DTU. Our e-mail addresses have changed.

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