The Illusion of MIC Creep in MRSA

C2-145

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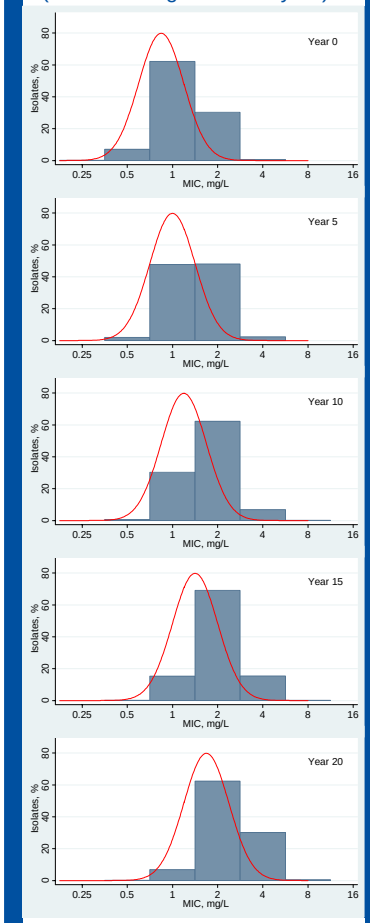
1 MODEL OF MIC CREEP
(0.05 doubling dilutions / year)



BACKGROUND

Upward creep of vancomycin MICs for MRSA has been claimed in studies in some countries, but experimental variation over time could produce artefacts in historical data.

METHODS

- The BSAC Bacteraemia Resistance Surveillance Programme receives blood isolates from 25 centres in the UK and Ireland each year.
- MICs are measured centrally by the BSAC agar doubling-dilution method.
- 19 centres contributed in every year from 2001 to 2007.
- 271 MRSA were randomly selected from these 19 sites and re-tested in a single week using 1.4-fold (√2-fold) dilutions; results were compared with the historical data.
- Analysis was by interval regression* of $\log_2$(MIC) for trend over time.
- Prior power calculation showed that the re-test study would have >90% power† to detect creep at a rate of 0.05 doublings/year, illustrated in figure 1.

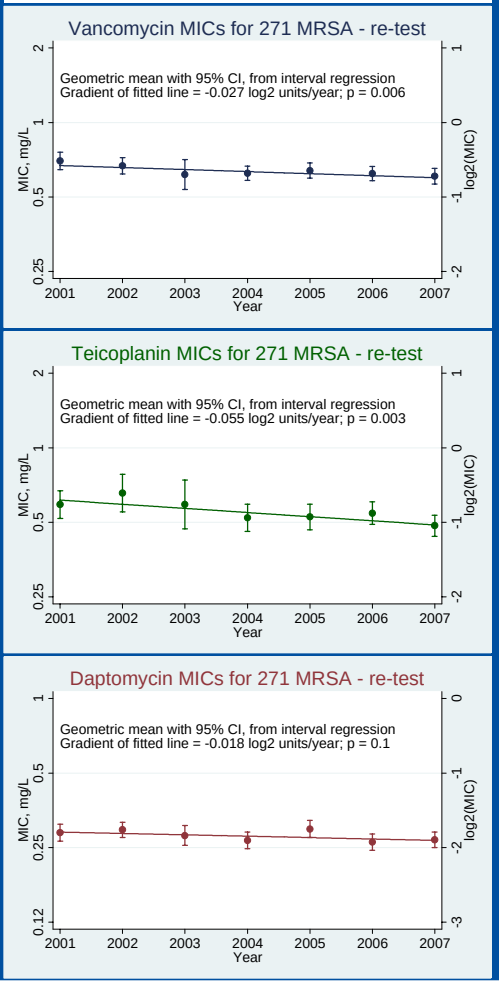
RESULTS

- Historical data suggested significant trends in MICs, upwards for vancomycin (0.07 doublings/year) and downwards for teicoplanin (0.07 halvings/year).
- **Re-test results showed that there were no significant upward trends in MICs for vancomycin, teicoplanin or daptomycin.** All identified trends were downwards and very slow:
  - vancomycin 0.03 halvings/year (p=0.006)
  - teicoplanin 0.06 halvings/year (p=0.003)
  - daptomycin 0.02 halvings/year (p=0.1, NS)

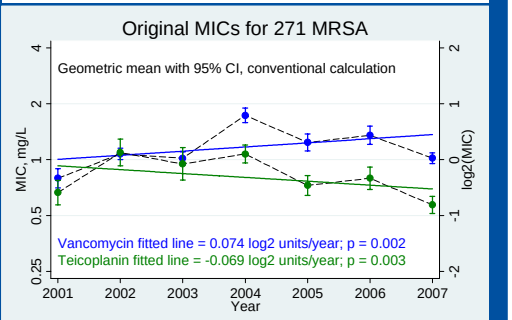
* Interval regression recognises that MICs are not known exactly but are in the interval between the tested concentrations, and assumes that MICs have a normal distribution on a log scale.

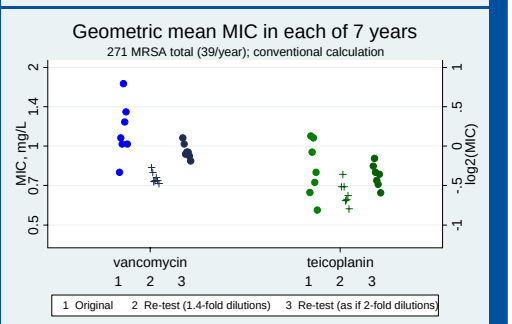
† Actual power was higher, as re-test MICs were less variable than the historical MICs used in the calculation.

2 RE-TEST RESULTS
no upward creep



3 YEAR-TO-YEAR VARIATION
can give the spurious appearance of creep





Historical MICs varied between years much more than re-test MICs on the same isolates. This year-to-year experimental variation gave a misleading impression of trend in MICs.

CONCLUSIONS

- **The use of historical data to detect subtle MIC creep can mislead.**
- **There is clear evidence against upward creep in glycopeptide MICs for MRSA in the UK and Ireland from 2001 to 2007.**

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Organism ID and Susceptibility Testing: R. Hope[7], M. Warner[7] and staff at HPA[7].
Collecting Laboratories: *See* www.bsac.org.uk *or* White 2008, JAC 62 (Suppl 2) ii3 - ii14
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