The Illusion of MIC Creep in MRSA

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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 log2(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.

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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Collecting Laboratories: See www.bsac.org.uk or White 2008, JAC 62 (Suppl 2) i-14
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