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Background

- The BSAC Bacteraemia Resistance Surveillance Programme offers an ideal multi-centre setting to test for subtle trends ('creep') in MIC.
- The programme has measured the MICs of blood isolates from 25 centres in the UK and Ireland each year since 2001 using the BSAC agar doubling-dilutions method.
- Re-testing the stored isolates avoids the weaknesses of studies that involve a single institution or use historical MIC data.

Methods

- 271 MRSA were randomly selected from 19 centres that contributed isolates every year from 2001 to 2007 (39 per year).
- Their vancomycin and teicoplanin MICs were re-measured in a single week, using the BSAC method but with 1.4-fold dilutions instead of doubling dilutions for greater precision.

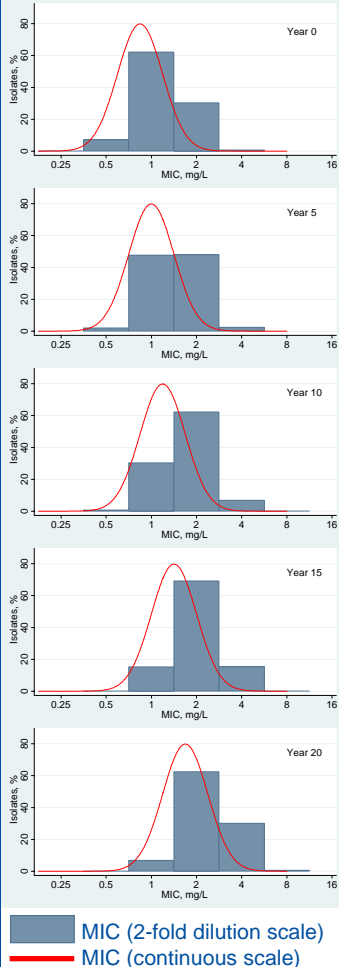
Analysis

- Analysis by interval regression for trend in \log_2 MIC over time used robust standard errors to account for clustering by centre.
- The study had >90% power to detect a gradual increase or decrease in MIC of 0.05 doubling-dilutions/year (see **Model**).

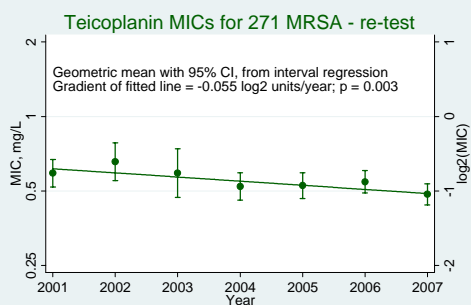
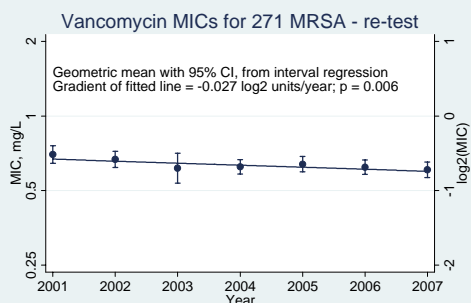
Results

- Compared with the historical data for the same isolates, re-test MICs showed much less year-to-year variation.
- Historical MICs suggested upward creep for vancomycin and downward creep for teicoplanin, but this was not borne out on re-testing.
- The re-test results, avoiding experimental variation across time, showed a significant but very slow trend downwards in MICs of both vancomycin and teicoplanin, at a rate of 0.03 and 0.06 doubling dilutions/year, respectively.

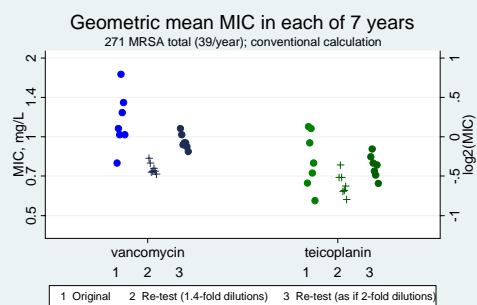
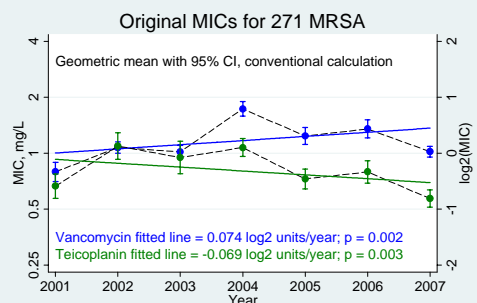
Hypothesised MODEL of MIC creep (0.05 doubling dilutions/year)



RE-TEST RESULTS no upward creep



ORIGINAL RESULTS variation gives the impression of creep



Summary

- Experimental variation exists between MICs measured at different times, and this can give the misleading impression of subtle MIC creep over time.
- Simultaneous re-testing of isolates is required to avoid this problem.
- The re-test study of 271 BSAC bacteraemia isolates had sufficient power to detect very gradual trends.
- There is clear evidence against any upward creep in glycopeptide MICs for MRSA from blood in the UK and Ireland between 2001 and 2007.**
- The source of variation between MICs measured in different years is not known. It might be related to different batches of media, or the reading of plates by different staff or machines.

BSAC Bacteraemia Resistance Surveillance Project. Sponsors (2001 -2009): Astellas, AstraZeneca, Cerexa, Cubist, Johnson&Johnson, MSD, Novartis, Pfizer, Theravance, Wyeth. **Support:** BSAC.

Collecting laboratories: please see www.bsacsurv.org **Central Laboratory:** HPA Centre for Infections, London. **Organism ID and Susceptibility Testing:** R. Hope, M. Warner, staff at HPA Centre for Infections