Analysing Resistance Surveillance Data: The Importance of Inter-Centre Variation

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BACKGROUND
- Many programmes of antibiotic resistance surveillance rely on a panel of collecting centres to provide bacterial isolates.
- Since bacteria are infectious, it is predictable that isolates from one collecting centre will be related more closely to each other than to those from other centres i.e. there will be centre heterogeneity or inter-centre variation - contrary to the assumptions of many statistical analyses.
- Individual collecting centres may not contribute for the whole duration of a long-term study, creating the possibility of spurious trends produced by loss and replacement of centres.
- We used simulation to investigate the potential impact of inter-centre variation and centre turnover on the ability of a surveillance programme to detect trends in resistance.

METHODS
- Simulated datasets were designed to capture the main features of the BSAC Respiratory Resistance Surveillance Programme.
- Simulated data were created for a 5-year study with 20 centres collecting 50 isolates/year, uniformly distributed over the year.
- Turnover (the probability of a centre dropping out and being replaced at the end of each year) was 0, 5, 10 or 20%.
- Baseline probability of resistance was chosen to give 1, 5, 10, 25 or 50% mean resistance rate at the start of the study.
- Trends were either no trend (odds ratio 1) or doubling of odds over 5 years (odds ratio 2 per 5 years).
- Inter-centre variation was simulated by assigning to each centre a log odds ratio drawn from a Normal distribution with mean 0 and standard deviation 0, 0.5 or 1.
- The probability of resistance for each simulated isolate was calculated from the baseline probability, odds ratio for time and odds ratio for centre.
- For each combination of parameters, 1000 simulated datasets were analysed by logistic regression, with and without centre.
- P-values for trend were from likelihood ratio tests. Power (at 5% significance) is the percentage of analyses with p ≤ 0.05.

RESULTS
- See graphs and table.

CONCLUSION
- It is essential to account for inter-centre variation when analysing trends in resistance surveillance data to avoid unacceptably high error rates.

Type 1 error / false positive
If an analysis produces a significant result when there is no real trend to find, this is a false positive or type 1 error. By choosing a significance level of 5%, we expect and accept a 5% error rate of this type.

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Choice of simulation parameters
A variety of organism-resistance combinations from the BSAC Resistance Surveillance Programmes were analysed by logistic regression. The distribution of the estimated log-odds for centres was reasonably close to Normal in each case.

To match the observed variation in annual centre turnover was 6% in the Respiratory Programme after six seasons and 4% in the Bacteraemia Programme after five. We believe that higher values are plausible in other studies.

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