P1104

Routine susceptibility testing: selection bias, sensitivity, specificity and performance related to MIC

21st ECCMID / 27th ICC
7-10 May 2011
Milan, Italy

R. Reynolds[1], R. Hope[2] , K. Maher[3] and The BSAC Extended Working Party on Resistance Surveillance[1]

[1]British Society for Antimicrobial Chemotherapy, Birmingham, B1 3NJ [2]Health Protection Agency, London, NW9 5HT, [3]Quotient Bioresearch Limited, Fordham, CB7 5WW

rosy.reynolds@nbt.nhs.uk
Dept Medical Microbiology
Southmead Hospital
Bristol, BS10 5NB, UK

BACKGROUND

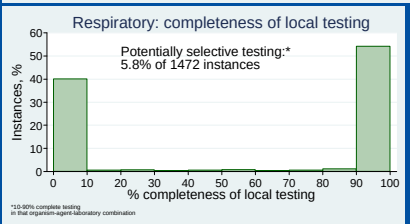
Routine susceptibility testing influences treatment choice and contributes to large-scale surveillance studies. It is important to understand its performance in comparison to highly-standardised reference methods.

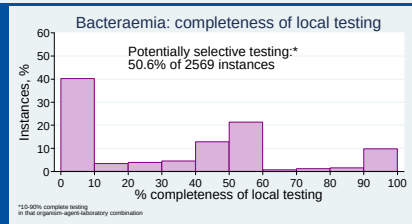
METHODS - BSAC Resistance Surveillance Project:†

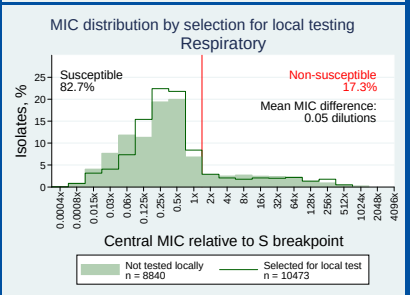
- 32 hospital laboratories contributed clinically significant isolates from blood (2008 & 2009) and respiratory infections (RTI, 2008/09), with their local results.
- Two central laboratories (one for RTI, one for blood) re-tested isolates by the BSAC agar dilution MIC method with BSAC/EUCAST breakpoints.
- Local and central results were compared separately for RTI and blood isolates.
- Excluded organism-agent combinations with fewer than 25 local test results.

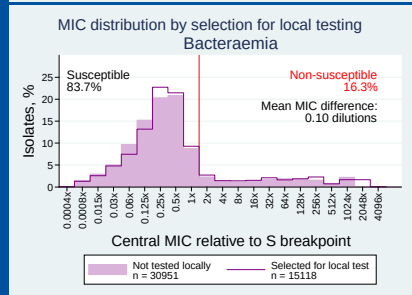
RESULTS - SELECTION BIAS

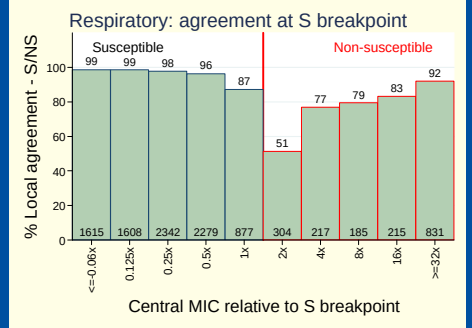
- Incomplete (potentially selective) testing was more widespread for blood isolates (51%) than for RTI (6%) but centrally-measured MICs differed by less than 0.1 dilutions overall between cases that were tested locally and those that were not.
- Overall differences in susceptibility (S) between locally tested and untested isolates were small: 16.7 *vs*. 18.0% were non-susceptible (NS) by central test in RTI, and 13.1 *vs*. 12.8% NS in blood infections.

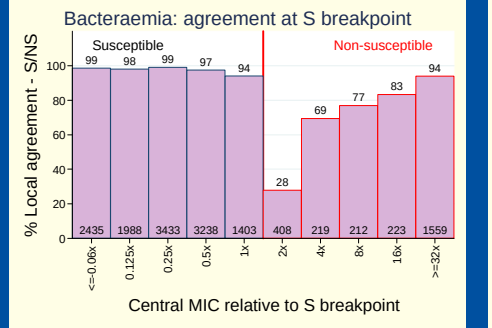








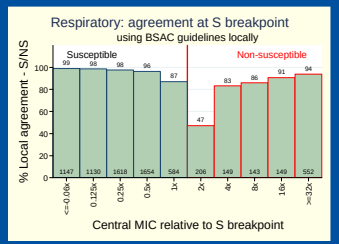


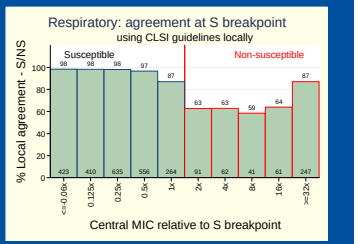


N in analysis	Blood	RTI
Centres	28	22
Isolates	5,628	2,472
Organisms x agents	94	72
Central MIC results	46,069	19,313
Local SIR results	15,118	10,473

CONCLUSIONS - SELECTION

- There was no evidence of widespread impact of selection bias on local results.
- However, these results cannot rule out the possibility of selection bias in some specific organism-agent combinations.





RESULTS - LOCAL TEST PERFORMANCE

- Central MIC testing detected non-susceptibility in 16% of tests on RTI isolates and 17% on blood.
- Local and central S/NS classification agreed in 94% (RTI) and 95% (blood) of cases. In RTI and blood, respectively, 2.8 and 1.8% of local results were false NS, and 3.2 and 3.6% false S.
- Agreement was much higher for S isolates (specificity 97-98%) than for NS (sensitivity 79-81%).
- Agreement was lower for borderline cases i.e. MICs near the S breakpoint, and remarkably so (28-51%) for MICs just above the breakpoint. Even at MICs as high as 8x breakpoint, local tests wrongly reported >20% as susceptible.
- In RTI, local test sensitivity using BSAC guidelines (83%) was higher than with CLSI guidelines (75%); CLSI sensitivity was below 65% even for MICs up to 16x breakpoint.

Source & local method	Sensitivity %	Specificity %	Agreement %
RTI - all	80.7	96.6	94.0
RTI - CLSI guidelines	74.5	96.5	92.5
RTI - BSAC guidelines	83.2	96.7	94.5
Blood - all	79.3	97.8	94.6

CONCLUSIONS - PERFORMANCE

- Approximately 20% of all non-susceptible isolates were wrongly reported as susceptible in local tests, with potential clinical implications.
- Nonetheless, used for surveillance, local test results somewhat overestimate the extent of non-susceptibility since it is uncommon and so false NS results outnumber false S.

Working Party Members (April 2011): A. MacGowan[1] (Chair), M. Allen[2], D. Brown[3], H. Grundmann[4], M. Heginbothom[5], R. Hope[6], E. Lee[7], D. Livermore[5], K. Maher[8], I. Morrissey[8], J. Porter[9], R. Reynolds[1], A. Shah[10], J. Steenbergen[11], C. Thomson[11], A. White[12].
Organism ID and Susceptibility Testing: R. Hope[6] and K. Maher[8].
Collecting Laboratories: *See* www.bsacsurv.org *or* White 2008, JAC 62 (Suppl 2) ii3–ii14.

[1]North Bristol NHS Trust ; [2]Novartis; [3]EUCAST Scientific Secretary; [4]RIVM, Netherlands; [5]Public Health Wales; [6]Health Protection Agency, London; [7]Johnson&Johnson; [8]Quotient Bioresearch Ltd., Microbiology; [9]Pfizer; [10]Astellas; [11]Cubist; [12]Tony White Ltd.

Central Laboratories: Health Protection Agency, London; Quotient Bioresearch Ltd.

Sponsors 2008–2009: Astellas, AstraZeneca, Cerexa, Johnson&Johnson, Novartis, Pfizer, Wyeth.
Support: BSAC.

†Reynolds 2008, JAC 62 (Suppl 2) ii15–ii18.

QUOTIENT BIORESEARCH MICROBIOLOGY

Health Protection Agency

BSAC british society for antimicrobial chemotherapy

www.bsac.org.uk