Revised EUCAST Breakpoints: The Impact on Antimicrobial Prescribing in *Pseudomonas* spp. Infections

Contributors: Robert Armstrong[1], Matthew Christie[2], Dr Joanne Malkin[1] and Dr Robert Usher[1]

[1] Microbiology department. University Hospital of North Durham (UHND), County Durham and Darlington Foundation Trust; [2] Pharmacy Department. University Hospital of North Durham (UHND), County Durham and Darlington Foundation Trust. Correspondence can be made to rob.usher@nhs.net or joanne.malkin@nhs.net

ACKNOWLEDGEMENTS: Sharon Campbell (Microbiology Manager, UHND), Rachel Turnbull (University of Sunderland), Vicky Blakey (Microbiology, UHND), Gemma Muzzioli (Microbiology, UHND), Alex Ralston (Microbiology, UHND).
KEYWORDS: Pseudomonas; EUCAST; antimicrobial susceptibility; stewardship

University of Sunderland

NHS County Durham and Darlington NHS Foundation Trust

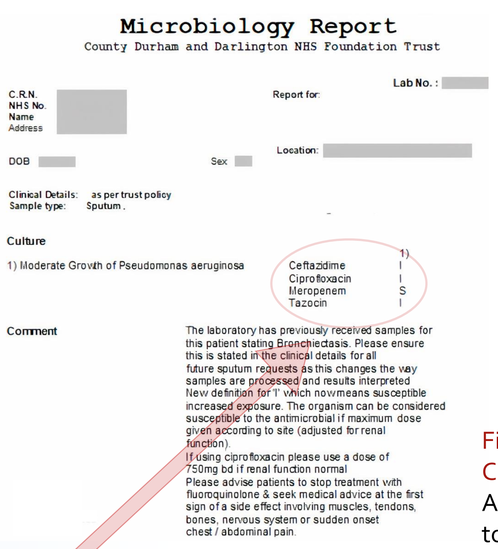
Background

Pseudomonas spp. is a multi-drug resistant (MDR) gram-negative, rod shaped bacteria. It is an opportunistic pathogen which can colonise patients and lead to potentially fatal bloodstream, lung and urinary tract infections. For phenotypically resistant isolates there is often few treatment option available (1).

The European Committee on Antimicrobial Susceptibility Testing (EUCAST) recently updated the clinical breakpoints for antimicrobial agents to advise on patient therapy (2). Therefore, for organisms such as wild-type *P. aeruginosa*, antimicrobials such as ceftazidime, piperacillin-tazobactam, and ciprofloxacin - previously reported as 'S' (susceptible) – were subsequently interpreted as 'I' (susceptible, increased exposure'), meaning that there is an increased likelihood of success if dosing regimen is adjusted accordingly.

In May 2022, the microbiology department at University Hospital of North Durham (UHND), County Durham and Darlington Foundation Trust (CDDFT) implemented these EUCAST revisions. It became clear that laboratory reports would contain majorly 'I' results, and the only 'S' being reported were for the 'last resort' antimicrobials, such as meropenem (see circled example report, right), raising some antimicrobial stewardship (AMS) concerns if there was a reluctance to use 'I' reported antibiotics by prescribing clinicians (2). Adding to these concerns, a recent study showed meropenem usage may go up 10-fold as a result of these revised breakpoint changes (3).

The primary aim of this study was to assess and compare any changes in reporting and prescribing pre and post implementing EUCAST's revised breakpoints at CDDFT.



Microbiology Report
County Durham and Darlington NHS Foundation Trust

Lab No. :

C.R.N.
NHS No.
Name
Address

Report for:

Location:

DOB

Sex

Clinical Details: as per trust policy
Sample type: Sputum.

Culture

1) Moderate Growth of Pseudomonas aeruginosa

	1)
Ceftazidime	I
Ciprofloxacin	I
Meropenem	S
Tazocin	I

Comment

The laboratory has previously received samples for this patient stating Bronchiectasis. Please ensure this is stated in the clinical details for all future sputum requests as this changes the way samples are processed and results interpreted
New definition for 'I' which nowmeans susceptible increased exposure. The organism can be considered susceptible to the antimicrobial if maximum dose given according to site (adjusted for renal function).
If using ciprofloxacin please use a dose of 750mg bd if renal function normal
Please advise patients to stop treatment with fluoroquinolone & seek medical advice at the first sign of a side effect involving muscles, tendons, bones, nervous system or sudden onset chest / abdominal pain.

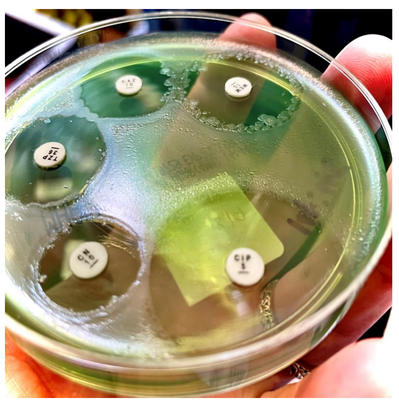


Figure 1: Example of culture and sensitivity reporting of Pseduomonas spp at CDDFT. *Pseudomonas* spp. is first isolated from clinical specimens (middle). Antibiotic sensitivities are performed by disk diffusion (right) before being reported to requesting clinicians (left).

Results

A total of 1695 clinically significant *Pseudomonas* spp. isolates were from reported from Jan 22-Sept 22. Of these, 144 isolates from in-patient settings were included in this study.

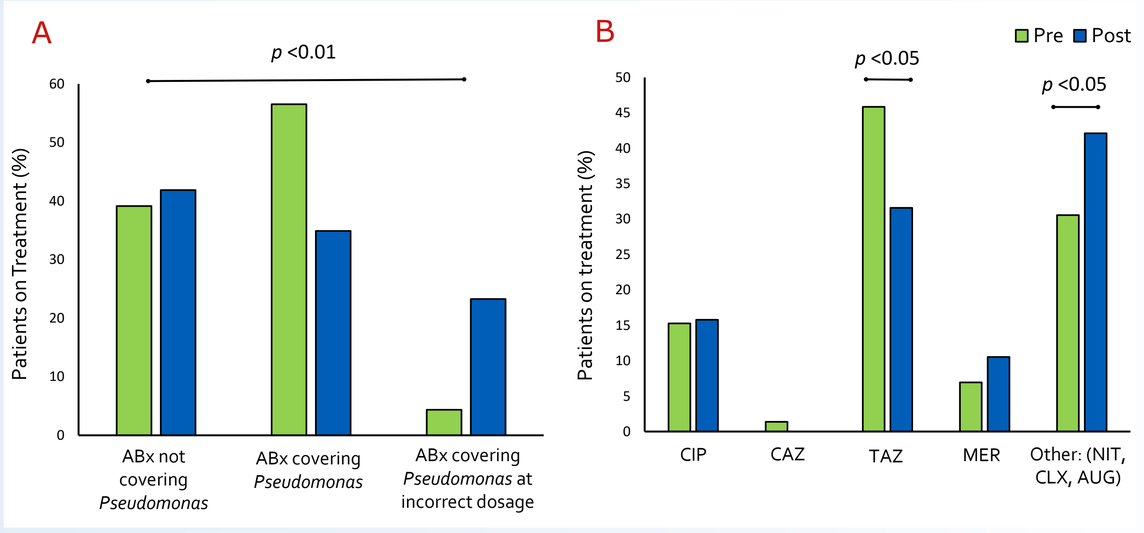


Figure 2: Antibiotics prescribed for *Pseudomonas* infections at CDDFT. The prescribed ABx not having anti-Pseudomonal activity did not change post implementation. However, worryingly, the anti-Pseudomonal ABx prescribed reduced after the EUCAST implementation, despite the organism (and sensitivity) being on the laboratory reports (p= <0.01). Moreover, the frequency of ABx being prescribed at the incorrect dose also increased (p= <0.01) (Fig 2A). When deep-diving into which ABx were being prescribed, there was a significant reduction in the use of piperacillin-tazobactam, and an increase of urinary ABx that are not effective treatment options for *Pseudomonas* spp., including nitrofurantoin, cephalexin and co-amoxiclav (p= <0.05) (Fig 2B). There was no significant increase in the use of 'last resort' antibiotic, meropenem.

Key: ABx = antibiotics, CIP = ciprofloxacin, CAZ, = ceftazidime, TAZ = pipercillin-tazobactam, MER = meropenem, NIT = nitrofurantoin, CLX – cephalexin, AUG = co-amoxiclav.

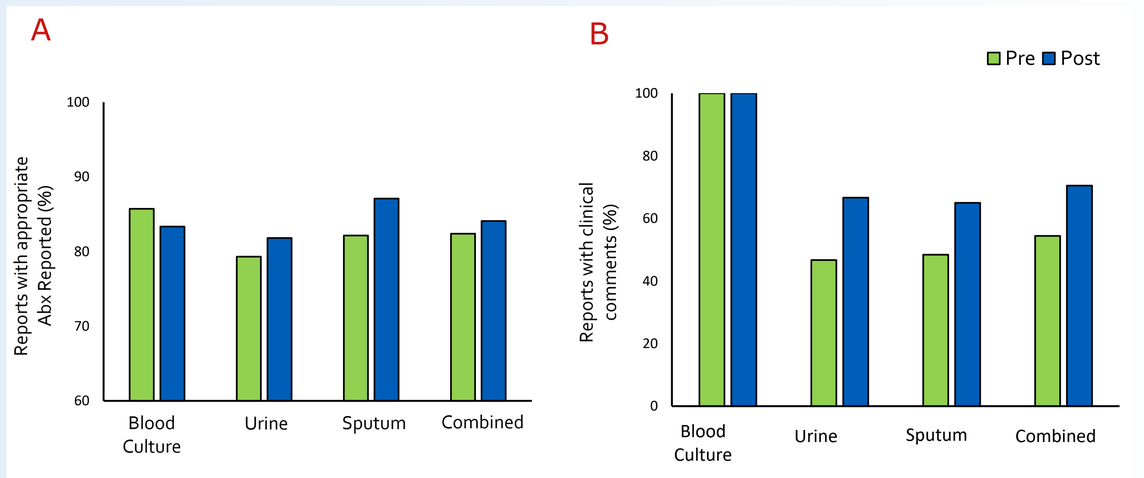
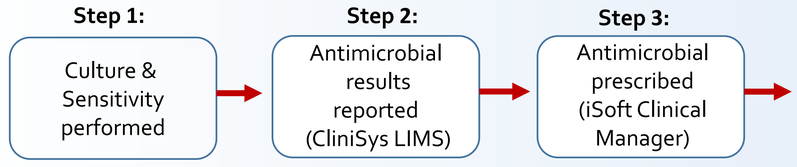


Figure 3: Quality of the laboratory reports and the information contained. The frequency of reports containing the appropriate ABx on laboratory reports increased after implementing EUCAST changes (Fig 3A). This was attributed to the increase in the release of ciprofloxacin and piperacillin-tazobactam on the reports, notably from infections of the respiratory and urinary tract. The frequency of reports containing appropriate dosing and advisory comments on reports also increased after EUCAST (Fig 3B). This was a result of the use of dosing and advisory ciprofloxacin comments. Predictably, all blood culture results contained appropriate clinical comments, but it was noted that there was no comments regarding the use of pipercillin-tazobactam.

Methods

In this retrospective study, we investigated in-patient *Pseudomonas* spp. isolated from infections from blood culture, sputum and urine specimens processed at microbiology (UHND), CDDFT, from Jan 2022-Sept 2022. GP patient data was excluded due to access of prescribing data.

Following routine reporting of culture and sensitivity (by disk diffusion method), all antimicrobial therapies prescribed by requesting clinicians was audited (data held on iSoft Clinical Manager). The issued susceptibility results and any consultant microbiologist comments going out on the laboratory reports was also investigated (reports obtained from ClinSys LIMS). Comparisons above was made pre and post-implementation of the revised EUCAST breakpoints. CHI squared (x^2) analysis was used to compare pre and post EUCAST revision-implementation data.



Discussion & Service Improvement Opportunities

The inappropriate use of ABx is problematic both in terms of patient management and for antimicrobial resistance concerns. Whilst 'last resort' and broad spectrum antibiotic use should rightly be conserved, they are sometimes the only options available for difficult to treat organisms such as *Pseudomonas spp*. (4).

Here, this study raises some concerns regarding patient management and AMS. The inappropriate use of ABx - regardless of EUCAST recommendations - represents an area for improvement, whether it be through education or better promotion of AMS to prescribing clinicians.

The reduction in the use of piperacillin-tazobactam and the increase in the use of non anti-pseudomonal ABx is a concern. A reason for this could be the confusion or a reluctance to prescribe ABx reported as 'I'. Historically, this has been an issue. Perhaps, a targeted 'use-of-piperacillin-tazobactam' comment could promote when it is needed. Interestingly, the use of ciprofloxacin was not affected post EUCAST change, despite it also being reported as 'I'. This could be due to the use of clinical comments promoting the correct use of it.

There was also inconsistencies in the reporting of the correct ABx which could lead to confusion when prescribing. As a result, Microbiology (UHND) is currently reviewing all reporting procedures ensuring standardisation when results are being authorised.

This study did not take into consideration of the complexity of some cases: some patient needs (e.g. allergy) or complications with infection (e.g. polymicrobial infections, resistance phenotype organisms) which may have meant alternative treatment (4).

Selected References

1. Sharma G, *et al*. *Biologicals*. 2014 Jan;42(1):1–7. 2. EUCAST. Available from: https://www.eucast.org/. 3. Munting A, *et al*. *Antimicrob Resist Infect Control*. 2022 Dec 30;11(1):165. 4. Dima L, et al. *Curr Opin Infect Diseases.* 2020 Dec;33(6):464-473