Infection Prevention in Practice 3 (2021) 100164

Available online at www.sciencedirect.com

Infection Prevention in Practice

journal homepage: www.elsevier.com/locate/ipip

Short Report

# Carbapenemase-producing organism (CPO) colonisation at a district general hospital: universal screening may help reduce transmission

Lynette Phee [a,c,*], Stephanie Paget [a], Judy Jacques [b], Binutha Bharathan [a], Husam El-Mugamar [a], Anand Sivaramakrishnan [a]

[a] Department of Microbiology, Barnet and Chase Farm Hospitals, Royal Free London NHS Foundation Trust, UK
[b] Infection Prevention and Control Team, Barnet Hospital, Royal Free London NHS Foundation Trust, UK
[c] Department of Pathology, Singapore Health Services, SKH, Singapore

ARTICLE INFO

*Article history:*
Received 28 February 2021
Accepted 23 July 2021
Available online 20 August 2021

*Keywords:*
Carbapenemase
Incidence
Screening
Surveillance
Colonisation

SUMMARY

***Objective:*** Assess the potential of hospital-wide routine screening by determining the prevalence and incidence of carbapenemase-producing organisms (CPOs) isolated from rectal screens at Barnet and Chase Farm Hospitals.

***Methods:*** 3,553 samples were collected between 01/12/2018 and 31/08/2019: from adult critical care wards (universal screening - admission, discharge and weekly), from medical wards with risk-factor based screening according to the prevailing Public Health England (PHE) carbapenemase-producing Enterobacteriaceae (CPE) screening guidelines, or on an ad hoc basis. Prevalence was defined as previously documented positive CPO colonisation, or new positive status, as a proportion of all eligible samples. Incidence was defined as all newly positive patients per 1,000 patient-days.

***Results:*** Overall CPO prevalence was 2.1% (95% CI: 1.61—2.58%). Inpatient prevalence was significantly higher at 2.6% vs outpatient at 0.5% ($p < 0.001$). Incidence was 0.44 per 1,000 patient-days (95% CI: 0.33—0.57), with a rate ratio between Barnet and Chase Farm of 4.9 ($p = 0.013$). Incidence was highest where universal screening strategy was applied (3.9 per 1000 patient-days, 95% CI: 2.4—5.91). This was 2.5 times higher than risk-factor based screening ($p = 0.005$) and 23.5 times that of wards without routine surveillance implemented ($p < 0.001$).

***Conclusion:*** Surveillance remains a cornerstone in controlling CPO transmission. Our local incidence, lacking hospital-wide screening, significantly exceeded the reported UK average. Universal screening could help to uncover the true prevalence and incidence of CPO, thereby providing the necessary information to properly control transmission, reducing nosocomial outbreaks and ultimately reducing the overall cost to healthcare.



* Corresponding author.
*E-mail address:* lynette.phee@nhs.net (L. Phee).

https://doi.org/10.1016/j.infpip.2021.100164

## Introduction

Antimicrobial resistance (AMR) threatens the foundation of modern medicine. The situation is particularly grave in the case of multi-drug resistant Gram-negative infections, notably carbapenemase-producing organisms (CPOs) which render agents of last resort (carbapenems) useless [1—3]. Carbapenemase genes, often found on mobile genetic elements (e.g. plasmids), spread from host cell to donor cells efficiently by way of horizontal transfer. This property is key to the continued success of CPOs, compounding fears of a new "Post-antibiotic Era" [1,2].

Concerted efforts have been made by healthcare professionals, policymakers and industry to slow its progression, whilst novel treatment strategies are being developed [3]. A robust CPO surveillance and screening programme is a cornerstone of any healthcare institution's plan to combat AMR. It provides both an epidemiological marker of AMR and informs infection prevention and control teams of potential clusters and outbreaks. In the UK, implementation of CPO screening programmes is decided locally by individual institutions, with wide-ranging heterogeneity of practice.

A national survey of carbapenemase prevalence and incidence carried out in 2014 as part of the wider European survey of carbapenemase-producing Enterobacteriaceae (EuSCAPE) project, estimated CPE prevalence in the UK (from clinical samples submitted by 21 sentinel laboratories across the country) to be 0.02%, and CPE incidence was 0.007 per 1000 patient-days nationwide, with the incidence in London almost double at 0.012 per 1000 patient-days [4]. A cost effectiveness study of CPO screening conducted by Lapointe-Shaw *et al.* [5] concluded that screening was not cost effective when CPO prevalence was below 0.015%, conversely, savings were predicted with universal screening when prevalence rates exceeded 0.3% [5].

Barnet and Chase Farm Hospitals are located in north London, serving a population of approximately 700,000. The Barnet site (BH) is a district general hospital offering acute medical care, whilst the Chase Farm site (CFH) mainly caters for elective surgical patients. CPO prevalence at the time was estimated to be low (sporadic cases only), as was the majority of the rest of England, and whilst a plan for CPO surveillance was recommended by Public Health England (PHE), universal screening for CPO was not mandatory [6]. At our institutions, only 5 wards had any form of active surveillance in place at the time of the study, and we sought to assess the impact of active surveillance programmes on CPO incidence and transmission.

## Methods

All rectal swabs sent to the laboratory for CPO screen from Barnet and Chase Farm Hospitals between 01/12/18 and 31/08/19 were included in this retrospective observational study. CPO screening was performed by first inoculating a selective and differential chromogenic agar (Colorex™ mSuperCarba™, E & O Laboratories Ltd, Bonnybridge, UK), which was incubated aerobically for 18—24h at 37C. Isolated Enterobacteriaceae, *Acinetobacter spp.* and *P. aeruginosa* were screened for the presence of OXA-48-like, NDM and KPC carbapenemase enzymes with RESIST3-O.K.N. K-SeT lateral flow assay (Coris BioConcept, Gembloux, Belgium) in Enterobacteriaceae, or ROSCO KPC, MBL and Oxacillinase detection kit assay in *Acinetobacter spp.* or *P. aeruginosa* (Rosco Diagnostica, Taastrup, Denmark). If carbapenemase tests were negative, and the antibiogram alluded to the presence of a possible carbapenemase (i.e. isolates with a meropenem MIC $>$ 0.125 mg/L), the isolate was sent to the reference laboratory for further confirmatory tests by molecular methods.

Universal screening was performed for all critical care patients (Barnet site only) — on admission, weekly on Mondays during their inpatient stay, and on discharge to other inpatient wards or care facilities.

Risk-factor based screening was performed on admission to two medical wards at the Barnet site and one at the Chase Farm site, as per the prevailing Public Health England (PHE) carbapenemase acute care toolkit guidelines in 2018—2019 [6]. Briefly, any patient fulfilling the following criteria within the preceding 12 months were screened — hospital stay abroad (regardless of CPO acquisition risk profile), or in a UK hospital with known nosocomial transmission of CPOs; previous history of CPO colonisation and/or infection; close contact of an individual with a history of CPO colonisation and/or infection.

All other inpatient wards did not have a specific routine CPO screening programme in place during the study period. All wards were subjected to ad-hoc contact screening (patients with epidemiologically defined exposure to a confirmed case of CPO were identified for CPO screening by the infection control team) when a single CPO positive case was identified. An outbreak was defined as having at least one contact colonised and/or infected with a CPO harbouring a similar resistance determinant.

Contact precautions were taken upon confirmation of CPO-positive status, in single-patient isolation rooms where possible, and at the time of the study, there was no hospital policy for pre-emptive isolation unless they were a previously known case, or a contact of a patient with, CPO colonisation or infection.

Statistical analyses were performed in R (version 3.6.3). Fisher's exact test was used to compare relative prevalence of CPO colonisation, and poisson regression for pairwise comparison of incidence rates. For analysis of prevalence and incidence, samples from patients colonised with CPOs were only included once (i.e. deduplicated).

## Results

A total of 3,553 CPO screening samples were included in this study. Overall prevalence of CPO across both sites was 2.1% (95% confidence interval: 1.61%—2.58%; n = 73). Inpatient prevalence was 2.6%, which was significantly higher than prevalence in outpatient settings (0.5%) with a rate ratio of 5.1 and two-tailed $p < 0.001$ (95% confidence interval: 2.1—16.47).

CPO incidence rate across both sites was 0.44 per 1,000 patient-days (95% confidence interval: 0.33—0.57). The incidence rate was higher at the Barnet site (0.5 per 1000 patient-days; 95% confidence interval: 0.37—0.66), compared with the Chase Farm site (0.1 per 1000 patient-days; 95% confidence interval: 0.01—0.37), with a rate ratio of 4.9 ($p = 0.013$). CPO incidence rate at the Barnet site was highest amongst inpatients in wards where a universal screening strategy was in place, with a rate of 3.9 per 1,000 patient-days (95% confidence interval: 2.4—5.91; n = 21). The incidence rate in universal

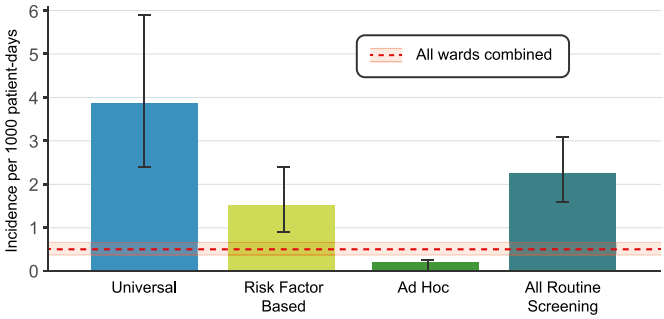


**Figure 1.** CPO incidence rates at BH by screening programme.

screening wards was significantly higher compared with risk-factor based (n = 18) screening wards (rate ratio of 2.5; $p = 0.005$) and with wards without any routine CPO surveillance programme (rate ratio of 23.5; $p < 0.001$). See Figure 1 for details of differential CPO incidence rates by prevailing routine surveillance strategy. Of note, all pairwise comparisons of incidence rates were statistically significant ($p < 0.01$).

The mean age of patients with CPO colonisation was 72.4 ± 16.2 years, compared to those without at 68.6 ± 18.1 years. There was no significant difference between mean age of newly identified OXA-48 colonised patients (71.4 ± 16.8 years) compared with the next most common carbapenemase, NDM (76.7 ± 13.9 years). Colonised patients were older, regardless of the type of CPO determinant, with only a few patients being under the age of 50. Although the age differences were not statistically significant ($p > 0.05$) between OXA-48 and NDM colonised patients, OXA-48-like carbapenemase were the only type of CPO determinant identified amongst younger patients (age < 50), whilst NDM colonisation tended to be observed in the older patients, perhaps signifying the colonisation potential of OXA-48-like carbapenemases in the wider local community. See Figure 2 for details.

## Discussion

The dual crises of rapid global expansion of CPOs and the dearth of novel effective therapeutic agents, has led to concerted efforts by both policymakers and healthcare professionals. The inaugural U.K. guidance for managing CPOs [6], including advice on detection and surveillance, was published as part of the government's broader 5-year plan to tackle antimicrobial resistance [7]. Surveillance remains a key strategic focus in the latest report (AMR plan for 2019–2024) and active monitoring of CPOs was specifically mentioned [8]. PHE has consequently revised its recommendations on CPO surveillance strategies, casting a far wider net for admission screening, and acknowledging the increased risk of CPO colonisation with prolonged hospital stay and antibiotic therapy [9].

Risk-factor based admission screening is still recommended by the updated PHE CPO guidance and includes host factors (multiple hospital treatments e.g. haemodialysis), admission to high-risk units (e.g. critical care, transplant wards, burns units) and recognition of possible CPO acquisition during inpatient stay at any hospital anywhere in the world [9]. This should augment recording of accurate surveillance information, thereby enhancing pre-emptive infection control measures. This guidance also advises each healthcare institution to understand their own local epidemiology, and step up screening efforts in patients or wards where there may be additional risk factors (e.g. exposure to broad-spectrum antibiotics, host immunosuppression, admission from non-acute settings with higher-than-background population risk of CPO colonisation) [9]. The risk-factor based screening wards at Barnet were medical wards where patients were mostly elderly, with multiple comorbid factors. Risk-factor based screening has since been extended to all wards, apart from critical care where universal screening remains.

The higher CPO incidence observed at the Barnet site compared to the Chase Farm site, may be due in part to the lack of universal CPO screening at Chase Farm during the study period, however, there were also differences inherent to the patient population served by each site. During the study period, Barnet was an acute care district general hospital, whilst Chase Farm largely served as a hub for elective surgical patients, with fewer CPO risk factors (e.g. exposure to broad-spectrum antibiotics, prolonged stay on high-risk units). Moreover, the main inpatient ward at Chase Farm comprised largely of single-occupancy rooms, further reducing the risk of patient-to-patient transmission.

The application of the revised and more inclusive PHE guidance could perhaps enable earlier and more comprehensive

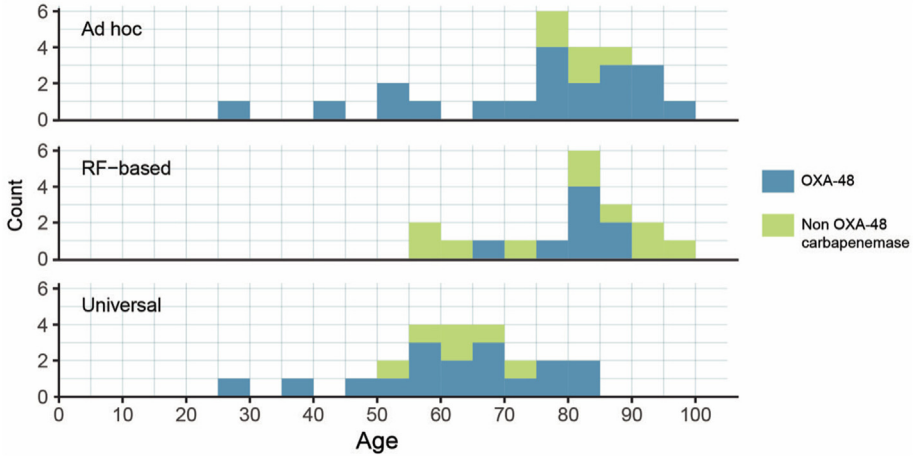


**Figure 2.** OXA-48 incidence rate by age groups.

detection of new cases of CPO, and hopefully curtail nosocomial spread. Even though 5 times more screens were being performed on universal screening wards (0.3 screens/patient-day) versus risk-factor based screening wards (0.06 screens/patient-day), the CPO incidence were similar (21 versus 18 cases respectively). Routine surveillance identified 19 out of the 21 new CPO cases in universal screening wards, compared with just 6 out of 18 in risk-factor based screening wards. The rest of the new cases were identified during active screening of exposed contacts. The difference in proportion of new CPO cases identified by active surveillance compared with contact screening was statistically significant, $p < 0.001$. The period prevalence (for the duration of the study) of CPO in universal screening wards was 1.7%. All patients were screened on a weekly basis for the duration of their stay in the universal screening wards in addition to admission screens, whereas risk-factor based screening was only performed at the point of admission.

The prevailing surveillance programme in our universal screening wards, whilst more inclusive than the earlier PHE guidance, has been validated by the updated 2020 version. The expansion of active CPO surveillance programmes in acute trusts, could garner more accurate information regarding our CPO epidemiology, and help to understand the nature of CPO carriage (acquisition versus unmasking of long-term carriage). Most importantly it may reduce time to detection, enabling effective infection prevention and control measures to be instituted, optimising resources and reducing potential harm.

A complex protocol, including screening questions for CPO risk factors, reduces the likelihood that staff will understand or adhere to the guidelines. Consideration of a universal screening programme may result in better compliance.

This was an observational study with the main purpose of consolidation of the CPO colonisation rates encountered at our institution with the then prevailing practice for both surveillance and infection control measures. As routine surveillance (universal admission and weekly screening, risk-factor based screening) was only performed in a limited number of wards during the study period, prevalence and incidence rates presented here may only serve as a estimate. A hospital-wide prospective period prevalence study would be required to obtain a more accurate picture comparing the CPO detection rates using different strategies.

## Conclusion

The importance of a robust active surveillance programme to effectively control the spread of CPO cannot be understated. It must be the cornerstone of any successful CPO management strategy.

The local CPO incidence rate, despite the lack of a hospital-wide screening policy, was significantly higher than the national average (which itself is likely to be an underestimation). It would be reasonable to suspect that the true incidence rate is higher still. Universal admission screening could help to better understand our local epidemiology. The application of targeted ongoing screening of inpatients may additionally enable pre-emptive infection control measures to be instituted. This will reduce nosocomial outbreaks and ultimately reduce the overall cost to healthcare whilst minimising risk to patients.

## CRediT author statement

**Lynette Phee**: Conceptualisation, Methodology, Formal analysis, Investigation, Data curation, Writing — Original Draft, Writing — Review & Editing, Visualisation, Project administration. **Stephanie Paget**: Conceptualisation, Investigation, Resources, Writing — Review & Editing. **Judy Jacques**: Conceptualisation, Project administration. **Binutha Bharathan**: Investigation, Data curation, Validation. **Husam El-Mugamar**: Conceptualisation, Supervision. **Anand Sivaramakrishnan**: Conceptualisation, Methodology, Resources, Writing — Review & Editing, Supervision, Project administration.

## Conflict of interest statement

None declared.

## Funding sources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.infpip.2021.100164.

## References

[1] Bonomo RA, Burd EM, Conly J, Limbago BM, Poirel L, Segre JA, et al. Carbapenemase-Producing Organisms: A Global Scourge. Clin Infect Dis 2018;66:1290—7. https://doi.org/10.1093/cid/cix893.
[2] Watkins RR, Bonomo RA. Overview: Global and Local Impact of Antibiotic Resistance. Infect Dis Clin North Am 2016;30:313—22. https://doi.org/10.1016/j.idc.2016.02.001.
[3] Jackson N, Czaplewski L, Piddock LJV. Discovery and development of new antibacterial drugs: learning from experience? J Antimicrobial Chemotherapy 2018;73:1452—9. https://doi.org/10.1093/jac/dky019.
[4] Trepanier P, Mallard K, Meunier D, Pike R, Brown D, Ashby JP, et al. Carbapenemase-producing Enterobacteriaceae in the UK: a national study (EuSCAPE-UK) on prevalence, incidence, laboratory detection methods and infection control measures. J Antimicrob Chemother 2017;72:596—603. https://doi.org/10.1093/jac/dkw414.
[5] Lapointe-Shaw L, Voruganti T, Kohler P, Thein H-H, Sander B, McGeer A. Cost-effectiveness analysis of universal screening for carbapenemase-producing Enterobacteriaceae in hospital inpatients. Eur J Clin Microbiol Infect Dis 2017;36:1047—55. https://doi.org/10.1007/s10096-016-2890-7.
[6] Public Health England. Acute trust toolkit for the early detection, management and control of carbapenemase-producing Enterobacteriaceae. 2013.
[7] Department of Health. UK five year antimicrobial resistance strategy: 2013 to 2018. 2013.
[8] Her Majesty's Government. Tackling antimicrobial resistance 2019-2024: the UK's five-year national action plan. 2019.
[9] Public Health England. Framework of actions to contain carbapenemase-producing Enterobacterales. 2020.