



Forecasting carbapenem resistance from antimicrobial consumption surveillance: Lessons learnt from an OXA-48-producing *Klebsiella pneumoniae* outbreak in a West London renal unit



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ABSTRACT

This study aimed to forecast the incidence rate of carbapenem resistance and to assess the impact of an antimicrobial stewardship intervention using routine antimicrobial consumption surveillance data. Following an outbreak of OXA-48-producing *Klebsiella pneumoniae* (January 2008–April 2010) in a renal cohort in London, a forecasting ARIMA model was derived using meropenem consumption data [defined daily dose per 100 occupied bed-days (DDD/100 OBD)] from 2005–2014 as a predictor of the incidence rate of OXA-48-producing organisms (number of new cases/year/100,000 OBD). Interrupted times series assessed the impact of meropenem consumption restriction as part of the outbreak control. Meropenem consumption at lag –1 year (the preceding year), highly correlated with the incidence of OXA-48-producing organisms ($r=0.71$; $P=0.005$), was included as a predictor within the forecasting model. The number of cases/100,000 OBD for 2014–2015 was estimated to be 4.96 (95% CI 2.53–7.39). Analysis of meropenem consumption pre- and post-intervention demonstrated an increase of 7.12 DDD/100 OBD/year (95% CI 2.97–11.27; $P<0.001$) in the 4 years preceding the intervention, but a decrease thereafter. The change in slope was –9.11 DDD/100 OBD/year (95% CI –13.82 to –4.39). Analysis of alternative antimicrobials showed a significant increase in amikacin consumption post-intervention from 0.54 to 3.41 DDD/100 OBD/year (slope +0.72, 95% CI 0.29–1.15; $P=0.01$). Total antimicrobials significantly decreased from 176.21 to 126.24 DDD/100 OBD/year ($P=0.05$). Surveillance of routinely collected antimicrobial consumption data may provide a key warning indicator to anticipate increased incidence of carbapenem-resistant organisms. Further validation using real-time data is needed.

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1. Introduction

Antimicrobial resistance among common bacterial pathogens is increasing worldwide, with inappropriate and excessive use of antimicrobials attributed as a cause [1,2]. Enterobacteriaceae are among the most important causes of serious hospital-acquired and community-onset bacterial infections and have seen a particular rise in antimicrobial resistance [3,4]. The spread of one resistance mechanism in particular within Enterobacteriaceae, namely extended-spectrum β -lactamase (ESBL) production, has over the last decade contributed to a significant increase in carbapenem use [5]. Subsequently, carbapenemase-producing Enterobacteriaceae

have appeared and have threatened the efficacy of this antibiotic class.

Classically, antimicrobial resistance surveillance has been predominantly retrospective and based upon routinely collected microbiology data [6], with outbreaks of highly-resistant organisms rarely predicted. Calls for alternative surveillance techniques have been made, with an early detection system for falling drug effectiveness key to implementing rapid interventions in order to prevent the emergence or delay the spread of drug resistance. This has been advocated at the national level in the UK through the recent 'UK 5 year antimicrobial resistance strategy 2013 to 2018 [7] and at the international level through the 2013 G8 summit and various health organisations reports [3,8,9].

The link between overuse of a particular class of antimicrobials and selecting possible drug resistance is well established [10]. Therefore, one potential approach to improving surveillance

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for carbapenem resistance may be to use routinely collected hospital antimicrobial consumption data as a predictor for the potential occurrence of antimicrobial resistance. This approach has the potential to meet some of the public health objectives of a surveillance system, namely (i) the detection and/or prediction of epidemics, (ii) documentation of the spatiotemporal spread of the disease, (iii) quantitative estimation and characterisation of the disease burden and (iv) evaluation of control and prevention interventions [11].

This study sought to assess the reliability and accuracy of an automated and systematic approach to antimicrobial resistance surveillance using pharmacy-derived antimicrobial consumption data. More specifically, we sought to determine the ability of this process to satisfy two of the main objectives of a surveillance system: (i) prediction of potential outbreaks; and (ii) evaluation of the impact of antimicrobial stewardship interventions. This is validated in the context of the previously described outbreak of OXA-48-producing *Klebsiella pneumoniae*, the first described in the UK, which occurred in the multi-site tertiary referral renal cohort of a West London teaching hospital between January 2008 and April 2010 [12].

2. Materials and methods

2.1. Data collection and data processing

2.1.1. Design and setting

This was a retrospective ecological study of antimicrobial usage and resistance conducted in the multi-site (renal medicine, renal transplant and haemodialysis satellites) renal cohort of a West London teaching hospital between May 2005 and April 2014. The teaching hospital has 28 renal inpatient beds and 23 dialysis beds and the satellite unit implicated in the outbreak had a further 26 dialysis beds, with a total renal patient cohort approximating 3100 dialysis and transplant outpatients. It is the largest facility in Europe for nephrology, dialysis and transplantation, treating a large ethnically and demographically diverse population.

2.1.2. Drug consumption data

Drug consumption data were collected using the hospital pharmacy system. This system was interrogated for information on antimicrobial agents, including antimicrobial name, dose, formulation, route of administration, pack quantity, number of packs issued, specialty, ward and hospital site. Renal inpatient and haemodialysis day-case consumption data were examined at yearly time points between May 2005 and April 2014. This captured data for 4 years before and 5 years after the intervention to contain the outbreak of OXA-48-producing *K. pneumoniae*. Antimicrobial agents used against Gram-negative infections were analysed. Antimicrobial consumption in grams was converted into defined daily doses (DDD) using the 2013 release of the DDD by the WHO Collaborating Centre for Drug Statistics Methodology [13]. The DDD was adjusted for bed occupancy and presented as DDD per 100 occupied bed-days per year (DDD/100 OBD/year). For the purpose of this study, a renal dialysis visit was considered as 1 OBD.

2.1.3. Microbiology data

Between January 2008 and April 2010, an outbreak of 13 patients (11 clinical cases) with OXA-48-producing *K. pneumoniae* occurred in the multi-site renal cohort of a West London teaching hospital; cohort screening of 1146 patients, contemporaneous to the outbreak, identified 2 more cases [12]. This outbreak was limited to the renal cohort. Subsequent to the outbreak, routine screening was conducted in the renal unit; four other cases were identified (three

clinical cases). Between May 2005 and April 2014, a total of 17 cases of acquisition of OXA-48-producing *K. pneumoniae* were identified in the renal cohort. The incidence rate (number of new cases per year per 100,000 OBD) was plotted over time to describe the trend in relation to antimicrobial consumption.

In addition to OXA-48-producing *K. pneumoniae*, two further Enterobacteriaceae (*Escherichia coli* and *Citrobacter freundii*) encoding this carbapenemase were identified from the renal cohort [14]. It was not possible to identify whether this represented plasmid transmission of the resistance element from *K. pneumoniae* to these other Enterobacteriaceae within the context of the outbreak; they were therefore not included in the analysis.

2.1.4. Intervention to contain the outbreak

Epidemiological investigation of the outbreak was undertaken to identify potential contributory factors and was previously described by Thomas et al. [12]. Conclusions derived from that investigation were that antimicrobial consumption was one of the main drivers of the OXA-48-producing *K. pneumoniae* outbreak. Therefore, the main component of the multilevel intervention focused on reinforcing antimicrobial stewardship through various strategies, in addition to immediate infection control measures (case isolation, screening of contacts, barrier nursing and other infection control precautions) [12]. A programme to improve antimicrobial prescribing had been established within the renal unit to promote a restriction in carbapenem prescribing, which started sharply in order to contain the outbreak. Local renal antimicrobial prescribing policies were reviewed and updated to advocate use of meropenem only in the presence of aminoglycoside-resistant micro-organisms.

2.2. Data analysis

2.2.1. Prediction of potential outbreaks

Time series analysis methods were applied to develop a forecasting model of the incidence of OXA-48-positive *K. pneumoniae* with current or past values (lags) of meropenem consumption used as explanatory variables.

First, a cross-correlation analysis (Pearson test) at different time lags between both series of data, namely incidence rate of OXA-48-positive *K. pneumoniae* and meropenem consumption, was performed to identify the point in time where the series are best aligned. Meropenem consumption with the most associated time lag to OXA-48-positive *K. pneumoniae* incidence was then included and tested as an external predictor in an autoregressive integrated moving average (ARIMA) model for multiple time series. Box and Jenkins approach was used to identify the parameters of the model [15,16]. ARIMA models were used as they fit appropriately to time series data to predict future points in the series, and can include other time series as predictors. The Portmanteau test (Q test) was used to identify whether the residuals of the ARIMA model deviated from white noise.

The accuracy of the univariate model (without external predictors, i.e. lagged meropenem consumption) and the model of multiple time series were estimated and compared using the root mean square error (RMSE) and the coefficient of determination [stationary R -squared (R^2)]. A significant decrease of RMSE, which is a measure of the differences between values predicted by a model and the values actually observed, using Wilcoxon signed-rank test denotes an improvement of the model. The R^2 characterises the goodness of fit of a model. Data points fit particularly well a statistical model when R^2 is close to 1. One-step-ahead forecast (year 2014–2015) for OXA-48-positive *K. pneumoniae* incidence was performed using the model with the best goodness of fit.

2.2.2. Evaluation of the impact of the antimicrobial stewardship intervention

The impact of the intervention on meropenem consumption was first evaluated using a segmented regression analysis of interrupted time series (ITS) [17,18]. Data were plotted yearly using fiscal years. This quasi-experimental design was appropriate given the availability of at least three data points before and three data points after the intervention, with a clearly defined intervention period [19]. The analysis enabled estimation of the intervention effect whilst taking account of time trend and autocorrelation among the observations. The ITS allowed an estimation of the change in level immediately after the intervention, which is defined as the difference between the observed level at the first intervention time point and that predicted by the pre-intervention time trend, the estimation of the difference between pre- and post-intervention slopes, and the estimation of yearly average intervention effect after the intervention phase [20]. After testing the absence of first-order autocorrelations with the Durbin–Watson statistic, a time series regression model without adjustment for autocorrelation was fitted to the data of meropenem consumption.

The change in alternative (non-meropenem) antimicrobial consumption was analysed post-intervention between 2008–2009 and 2013–2014. The change rate and trend (slope) for each antimicrobial active against Gram-negative infections were estimated. Total antimicrobials included all of the drugs in the therapeutic subgroup ‘ATC code J01 Antibacterials for systemic use’ from the Anatomical Therapeutic Chemical (ATC) classification system [13].

As an indirect control, meropenem consumption in the renal cohort post-intervention from 2009–2013 was compared with the overall consumption of meropenem over the same period in two other sites of the West London teaching hospital network (who share overarching antimicrobial and infection control policies; identified as hospital 1 and hospital 2) previously described [14]. We also looked at other resistance indicators in the renal cohort post-intervention, i.e. the proportion of *Pseudomonas* spp. displaying meropenem non-susceptibility and the proportion of Enterobacteriaceae with an ESBL/AmpC phenotype [14].

Statistical analysis was performed using Stata v.12 (StataCorp LP, College Station, TX).

3. Results

3.1. Forecasting the incidence of OXA-48-producing *Klebsiella pneumoniae*

The interrelationship among both times series, meropenem drug consumption and incidence of resistant isolates was identified using cross-correlations at different time lags (in increments of 1 year). After ensuring stationarity, absence of residual autocorrelation and a normal distribution of disturbances, meropenem consumption at lag –1 (i.e. meropenem consumption the preceding year) was the most positively correlated with the incidence of OXA-48-producing *K. pneumoniae* (Fig. 1) (Pearson correlation $r=0.71$; $P=0.005$). The ARIMA model including meropenem consumption at lag –1 as a predictor was fitted to the incidence of OXA-48-producing *K. pneumoniae* [meropenem coefficient in the model = 1.07, 95% confidence interval (CI) 0.10–2.05; $P=0.03$]. This increased the model’s accuracy in estimating the incidence of OXA-48-producing *K. pneumoniae* compared with the univariate ARIMA model without any predictors (RMSE = 1.41 and $R^2 = 79\%$ for the multivariate model versus RMSE = 2.92 and $R^2 = 15\%$ for the univariate model). The difference between the two RMSE were statistically different with Wilcoxon signed-rank test ($P<0.001$). One-step (year)-ahead forecasting for 2014–2015 was then applied to the incidence rate of resistant cases using the multiple time series

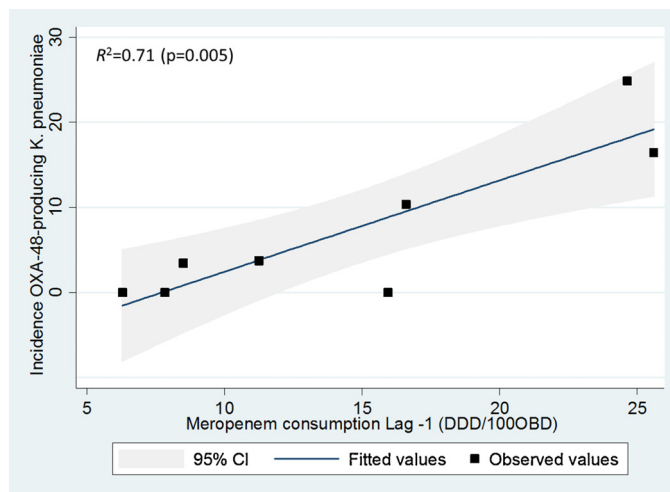


Fig. 1. Cross-correlation between meropenem consumption lag –1 (the preceding year) and the incidence rate of OXA-48-producing *Klebsiella pneumoniae* in a West London renal unit from 2008–2009 to 2013–2014.

model identified previously. The number of cases/100,000 OBD for 2014–2015 was estimated to be 4.96 (95% CI 2.53–7.39) (Fig. 2).

3.2. Evaluation of the impact of the antimicrobial stewardship intervention

The impact of the antimicrobial stewardship intervention following the outbreak of OXA-48-producing *K. pneumoniae* on meropenem consumption is depicted in Fig. 3.

Pre-intervention, meropenem consumption showed a year-on-year increase from 6.30 to 25.65 DDD/100 OBD/year between 2005–2006 and 2008–2009 (slope = +7.12 DDD/100 OBD/year, 95% CI 2.97–11.27; $P<0.001$). After the intervention, meropenem decreased year-on-year from 25.65 to 10.00 DDD/100 OBD/year between 2008–2009 and 2013–2014. The difference between the slope pre- and post-intervention was –9.11 (95% CI –13.82 to –4.39; $P<0.001$). A significant decrease between the predicted values derive from the pre-intervention model and the observed values post-intervention, of –18.99 DDD/100 OBD/year (95% CI –29.66 to –8.32; $P<0.001$) (relative effect = –54.64%), –28.10 (95% CI –41.68

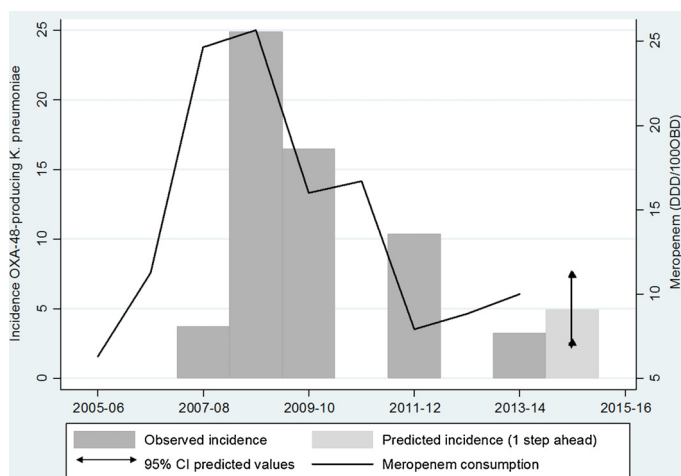


Fig. 2. Multiple time series analysis for forecasting one-step (year)-ahead incidence rate of OXA-48-producing *Klebsiella pneumoniae* (cases/100,000 OBD) using meropenem consumption (in DDD/100 OBD) lag –1 as an external predictor in a West London renal unit from 2008–2009 to 2013–2014. DDD, defined daily doses; OBD, occupied bed-days.

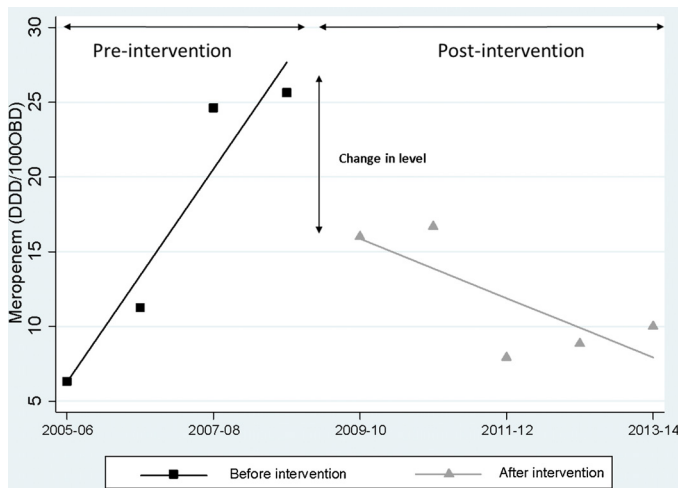


Fig. 3. Interrupted time series of meropenem consumption (in DDD/100OBD) before and after a targeted antimicrobial stewardship intervention in a renal cohort in West London, 2005–2014. DDD, defined daily doses; OBD, occupied bed-days.

to -14.51 ; $P < 0.001$) (relative effect = -67.09% , -37.20 (95% CI -54.52 to -19.89 ; $P < 0.001$) (relative effect = -75.92% , -46.31 (95% CI -67.74 to -24.88 ; $P < 0.001$) (relative effect = -82.51%) and -55.42 (95% CI -81.18 to -29.66 ; $P < 0.001$) (relative effect = -87.62%) were respectively observed 1, 2, 3, 4 and 5 years after the intervention.

Consumption of alternative antimicrobials post-intervention is described Table 1 and Fig. 4. In the post-intervention phase, the two alternative Gram-negative antimicrobial classes showed a significant increase in consumption from 2008–2009 to 2013–2014; amikacin increased from 0.54 to 3.41 DDD/100 OBD/year (slope = $+0.72$, 95% CI 0.29–1.15; $P = 0.01$) and cephalosporins from 0.98 to 1.88 DDD/100 OBD/year (slope = $+0.19$, 95% CI 0.12–0.27; $P < 0.01$). Use of ertapenem and imipenem demonstrated a non-significant increase over the post-intervention period, although usage of the latter was in general particularly low. The commonly encountered inhibitor/penicillin combinations, i.e. amoxicillin/clavulanic acid and piperacillin/tazobactam (TZP), did not change significantly over time (respectively, slope = -0.09 , 95% CI -1.31 to 1.12, $P = 0.85$; and slope = $+0.65$, 95% CI -0.96 to 2.27, $P = 0.33$). Quinolones significantly decreased from 24.82 to 18.57 DDD/100 OBD/year (slope = -1.42 , 95% CI -2.05 to -0.78 ; $P < 0.01$). The overall amount of antimicrobials consumed significantly decreased from 176.21 to 126.24 DDD/100 OBD/year (slope = -7.21 , 95% CI -14.85 to -0.01 ; $P = 0.05$).

The data published by Moore et al. [14] and used as an indirect control for the purpose of this study demonstrated that the decrease in meropenem consumption (14.2 to 8.5 DDD/100 OBD from 2009 to 2013) in the renal unit (excluding haemodialysis day-case consumption) was not seen elsewhere. The overall consumption of meropenem in hospital 1 and 2 increased, respectively, from 7.7 to 10.6 DDD/100 OBD and from 3.9 to 6.1 DDD/100 OBD. Furthermore, when other resistant organism prevalence in the renal cohort was analysed, an increase of ESBL/AmpC-producing Enterobacteriaceae increasing year-on-year post-intervention (from 35.6% to 51.5%) but a decrease in meropenem non-susceptible *Pseudomonas* spp. (from 32.9% to 18.6%) was observed [14].

4. Discussion

We demonstrated that monitoring antimicrobial consumption is a valid surveillance tool for forecasting potential emergence and

outbreaks of carbapenem-resistant organisms as well as for monitoring the impact of an antimicrobial stewardship intervention. Such surveillance of hospital antimicrobial consumption, and evaluation of antimicrobial stewardship programmes, is considered to be of key importance in controlling bacterial resistance and healthcare-associated infections if implemented in real time [7].

This study assessed the reliability of a predictive model using antimicrobial consumption data as a surveillance system for monitoring antimicrobial resistance. The historical example of an outbreak of OXA-48-producing *K. pneumoniae* in a renal cohort in West London between 2008 and 2010 was used to validate this as a proof of concept.

We demonstrated that monitoring antimicrobial consumption can be an accurate tool to forecast potential outbreaks. We stressed a temporal association between meropenem consumption and OXA-48-producing *K. pneumoniae* incidence. Moreover, we developed an ARIMA model using meropenem consumption the preceding year as an external predictor to forecast the incidence rate of OXA-48-producing *K. pneumoniae*; 71% ($R^2 = 0.71$) of the total variation in OXA-48-producing *K. pneumoniae* incidence could be explained by the model. Using this outbreak of carbapenem-resistant organisms in exemplar, a prediction model can be devised for future routine surveillance including real-time data.

The results also demonstrated that monitoring antimicrobial consumption enabled the evaluation of an antimicrobial stewardship intervention to contain the outbreak of OXA-48-producing *K. pneumoniae*. The results, which derived from ITS analysis, confirmed that the intervention was effective in reducing meropenem consumption in the renal cohort, consequently reducing the antimicrobial selective pressure towards carbapenem resistance. The ITS analysis demonstrated a significant increase in meropenem consumption pre-intervention that may be explained by some of the local and specialty drivers of antimicrobial prescribing in the renal services: (i) fear over increasing prevalence of antimicrobial resistance to the cephalosporin, fluoroquinolone and aminoglycoside antimicrobials among *E. coli* and other Enterobacteriaceae [4]; (ii) preference for the pharmacokinetic/pharmacodynamic profile of meropenem over that of TZP for haemodialysis patients [21,22]; (iii) a disinclination towards use of aminoglycosides owing to associated toxicity; and (iv) an avoidance for ciprofloxacin in treatment regimens owing to its impact on *Clostridium difficile*-associated infections [23,24]. An investigation into the drivers behind meropenem usage in renal services needs to be undertaken, including multifactorial motivators that may include self-reported prescriber drivers but also contextual organisational and external factors. The success of the intervention, which was demonstrated in our analyses by a significant decrease in both meropenem usage and total consumption of antimicrobials post-implementation, was reached through a common effort of a multidisciplinary antimicrobial team, i.e. clinical microbiologists, renal clinicians, pharmacists and infectious diseases physicians. The impact of the intervention was still significant and sustainable 5 years after deployment of the first measures for containing the outbreak, although a small but non-significant increase in meropenem consumption was observed in the most recent fiscal year analysed. Such longevity of impact was facilitated both by the amendment of antimicrobial policy to reflect the new practice and by the regular ongoing multidisciplinary antimicrobial review rounds, but the need to be mindful of any decrease in the intensity of the antimicrobial stewardship intervention is constant.

We also demonstrated that the intervention had an impact on increasing alternative antimicrobial consumption. Whilst the overall antimicrobial consumption and quinolone usage did decrease significantly, a significant increase in amikacin and cephalosporin consumption post-intervention and a small rise in TZP consumption was observed. Use of TZP with amikacin as first-line treatment

Table 1
Impact of a targeted antimicrobial stewardship intervention on antimicrobial drug consumption (DDD/100 OBD) in a West London renal unit from 2008–2009 to 2013–2014.

	2008–2009	2009–2010	2010–2011	2011–2012	2012–2013	2013–2014	Change rate (%) ^a	Slope ^b	Standard error	P-value
Amikacin	0.54	0.67	1.17	1.91	4.06	3.41	526.81	0.72	0.16	0.01
Amoxicillin/clavulanic acid	15.35	12.68	13.77	17.15	14.29	13.08	–14.83	–0.09	0.44	0.85
Cephalosporins ^c	0.98	0.99	1.09	1.50	1.62	1.88	91.98	0.19	0.03	<0.01
Ertapenem	1.44	0.99	1.42	0.67	1.85	1.53	6.10	0.06	0.11	0.58
Gentamicin	0.61	0.60	0.22	1.99	0.31	0.60	–2.90	0.02	0.17	0.90
Imipenem	0.03	0.02	0.00	0.00	0.10	0.09	186.66	0.02	0.01	0.16
Meropenem	25.65	16.00	16.68	7.92	8.83	10.00	–61.02	–3.10	0.91	0.03
Piperacillin/tazobactam	8.41	11.45	13.47	15.80	13.30	11.41	35.64	0.65	0.58	0.33
Quinolones	24.82	22.96	22.47	20.45	17.53	18.57	–25.20	–1.42	0.23	<0.01
Total ^d	176.21	137.49	145.27	143.76	137.14	126.24	–28.36	–7.21	2.76	0.05

DDD, defined daily doses; OBD, occupied bed-days.

^a Change rate between 2008–2009 and 2013–2014.

^b Trend in antimicrobial consumption from 2008–2009 to 2013–2014.

^c Cephalosporins used in renal unit includes cefalexin, cefazolin, cefotaxime, ceftazidime, ceftriaxone and cefuroxime.

^d Total includes antibacterials for systemic use [Anatomical Therapeutic Chemical (ATC) code J01] [13].

for sepsis was then associated with additional precautions, particularly in the presence of impairment of renal function and renal replacement therapy. Use of amikacin instead of gentamicin could be explained by local epidemiology data, which showed high rates of gentamicin resistance in Gram-negative organisms but preserved amikacin susceptibility (data not shown), possibly attributable to clonal expansion of a specific aminoglycoside resistance mechanism among Enterobacteriaceae in the local cohorts. The data reported by Moore et al. [14] suggest that consumption of meropenem in two control groups increased slightly over the post-intervention period while decreasing in the renal cohort. These results emphasise the efficacy of the intervention in reducing meropenem consumption in the renal cohort. Although the rates of ESBL/AmpC-producing Enterobacteriaceae in the renal cohort were noted to increase during the post-implementation period, there was no contemporaneous increase in β -lactam or cephalosporin prescribing to account for this. The variation in ESBL/AmpC-producing Enterobacteriaceae prevalence may therefore reflect other driving factors, possibly that of more widespread clonal expansion of resistant strains [25].

In this study, we advocate measurement of hospital antimicrobial consumption at the cohort-specific level as a monitoring and prediction tool to inform antimicrobial resistance surveillance. However, this approach presents some limitations. First, this system would be more robust using patient-level antimicrobial prescribing data supported by recording of clinical indications and linked to patient-level microbiology data. Furthermore, whilst the electronic and accurate nature of this data set enables ease of extraction and facilitates a move towards the goal of automated real-time analyses, the yearly aggregated data available for this study have the potential to limit the accuracy of the estimated forecast values. As an interim, a monthly surveillance system is being validated and will be used for future prospective surveillance. A further limitation of this study reflects uncertainty over the optimal metric to quantify antimicrobial consumption. Use of DDD/100 OBD is not an optimal measure, especially among renal impairment patients or paediatric populations as it is weight- and dosage-independent [26]. Recent evidence suggests ‘days of therapy’ as an index could present advantages over DDD measures by limiting the impact of dosage variability among patients [26,27].

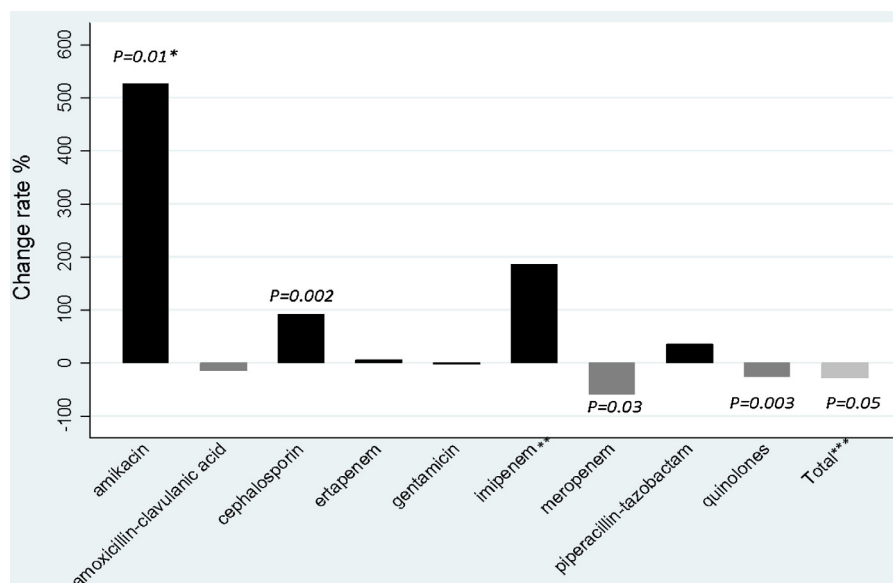


Fig. 4. Change rate of the consumption of antimicrobials active against Gram-negative bacteria (in DDD/100 OBD) between 2008–2009 and 2013–2014 in a West London renal cohort. DDD, defined daily doses; OBD, occupied bed-days.

Only an electronic-based system recording patients' medication administration data would enable routine use of this indicator to assess stewardship efforts. The usage of 'days of presence' instead of occupied bed-days as a denominator would be more specific in taking into account every location that patients occupied for any time on a given day, but again it requires electronic prescribing [27]. Finally, as the intervention had been implemented rapidly in response to a specific outbreak, no contemporaneous control group was available for the analysis. The ITS analysis was chosen for this reason, using the pre-intervention period as a control for the post-intervention period.

This study suggests that a surveillance system using antimicrobial consumption data may be able to be used as an early warning system to predict the potential emergence of resistant organisms, if a prospective validation was performed and the timeframe of data collection became monthly [28]. Monitoring antimicrobial consumption can also provide guidance on antimicrobial stewardship programmes and assess their impact within the hospital.

In conclusion, antimicrobial consumption data provide a key tool not only for the evaluation of antimicrobial stewardship interventions, but also for forecasting emergence and future potential outbreaks and trends in the prevalence of antimicrobial resistance. Monitoring antimicrobial consumption data should be considered in real time as an early warning system devised as part of healthcare organisations' antimicrobial stewardship programmes. Using this method, local practices can be compared nationally or internationally to aid control of unnecessary antimicrobial exposure. Various efforts have already started worldwide to control transmission of carbapenem resistance among Enterobacteriaceae [3,7,29,30]. A local real-time surveillance system for monitoring antimicrobial consumption across acute-care settings would complement national and international toolkits developed for containing the spread of resistance.

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Competing interests

MGi has consulted for The Medicines Company and AstraZeneca and has received travel sponsorship from Eumedica Ltd.; CPT has received travel sponsorship from Novartis and Pfizer; KB has consulted/received support for travel from Bayer, Pfizer, Astellas, Gilead, Novartis and Baxter; AHH and LSPM have consulted for bioMérieux. MGH and ETB declare no competing interests.

Ethical approval

Not required.

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