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Original article

Counting the cost of an outbreak of carbapenemase-producing *Enterobacteriaceae*: an economic evaluation from a hospital perspective

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ABSTRACT

Objective: To perform an economic evaluation on the cost associated with an outbreak of carbapenemase-producing *Enterobacteriaceae* (CPE).
Methods: We performed an observational economic evaluation of an outbreak of CPE (NDM-producing *Klebsiella pneumoniae*) affecting 40 patients in a group of five hospitals across three sites in West London. Costs were split into actual expenditure (including anti-infective costs, enhanced CPE screening, contact precautions, temporary ward-based monitors of hand and environmental practice, and environmental decontamination), and 'opportunity cost' (staff time, bed closures and elective surgical missed revenue). Costs are estimated from the hospital perspective over the 10-month duration of the outbreak.
Results: The outbreak cost €1.1m over 10 months (range €0.9–1.4m), comprising €312 000 actual expenditure, and €822 000 (range €631 000–€1.1m) in opportunity cost. An additional €153 000 was spent on Estates renovations prompted by the outbreak. Actual expenditure comprised: €54 000 on anti-infectives for 18 patients treated, €94 000 on laboratory costs for screening, €73 000 on contact precautions for 1831 contact precautions patient-days, €42 000 for hydrogen peroxide vapour decontamination of 24 single rooms, €43 000 on 2592 hours of ward-based monitors, and €6000 of expenditure related to ward and bay closures. Opportunity costs comprised: €244 000 related to 1206 lost bed-days (range 366–2562 bed-days, €77 000–€512 000), €349 000 in missed revenue from 72 elective surgical procedures, and €228 000 in staff time (range €205 000–€251 000). Reduced capacity to perform elective surgical procedures related to bed closures (€349 000) represented the greatest cost.
Conclusions: The cost estimates that we present suggest that CPE outbreaks are highly costly. **J.A. Otter, CMI 2016;■:1**

Introduction

Carbapenemase-producing *Enterobacteriaceae* (CPE) have emerged globally over the last decade, resulting in antibiotic-resistant infections that are difficult to treat and costly to healthcare facilities [1,2]. Prevalence of CPE is high in some parts of the world (notably parts of southern Europe, Israel and increasingly parts of the USA), but relatively low in the UK [2–5]. Although there are some success stories in bringing CPE under control, notably in Israel and in some reports from the USA [3,6], there is a limited evidence base for the effectiveness and cost related to interventions to prevent the spread of CPE [7–9]. Therefore, a multimodal strategy is recommended including screening, contact precautions/patient isolation, hand and environmental hygiene, and antimicrobial stewardship [7–9]. A number of additional measures have also been advocated by some, including ward-based hand and environmental monitors, hydrogen peroxide vapour room decontamination, and ward and bay closures [6,8,10].

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Developing accurate data on the cost of healthcare-associated infections (HCAI) is difficult, and attempts to count the cost of HCAI need to account for actual expenditure and opportunity costs [11,12]. Costs commonly associated with HCAI include extended length of stay, missed revenue (which may be linked directly to extended length of stay), staff time, drug and diagnostic costs, and intervention-related costs such as through ward closure, additional contact precautions, and environment interventions [11,13]. Although some data on the cost associated with controlling hospital outbreaks of Gram-negative bacteria is available, we are not aware of any studies reporting the cost of controlling an outbreak of CPE [11,14–18]. CPE are likely to generate higher costs than other resistant Gram-negative bacteria such as extended-spectrum β-lactamase-producing *Enterobacteriaceae* because they are more difficult to treat clinically, and prompt more extensive prevention and control activities [6,7,19].

In addition to the requirement for consistent basic infection prevention and control practice [20], guidelines, such as the CPE Toolkits in England and the USA [21,22], advocate extensive additional infection prevention and control preparations and interventions in response to the threat of CPE. However, although there are cost-effectiveness evaluations of some aspects of the prevention and control of some resistant Gram-negative bacteria [13,23], there have been no formal evaluations of the cost and effectiveness of these Toolkits and other guidelines [7–9]. Data on costs related to the management of CPE are urgently needed to inform cost-effectiveness evaluations of prevention initiatives.

Methods

Between July 2014 and October 2015, 40 patients were identified with the same strain of CPE (a New Delhi metallo-β-lactamase (NDM)-producing *Klebsiella pneumoniae*) in a group of five hospitals (three acute and two specialist; an eye hospital and a women's and children's hospital) across three sites in West London with approximately 1500 beds and 190 000 admissions each year. Outbreak strains were initially defined as clonal by variable number of tandem repeats analysis and confirmed by whole genome sequencing. Thirty-two patients were first identified by a screening specimen and eight by a clinical specimen over two hospital sites. The outbreak was first recognized in March 2015 and declared over in December 2015. We evaluated the costs and impact associated with the outbreak during the active phase (March–December 2015). The outbreak was centred on renal wards at Hospital A, and vascular wards at Hospital B; there is frequent contact between the two specialties. Patients with the outbreak strain also spent time on other wards outside the renal and vascular services during the outbreak period, including at Hospital C. The renal patient group has frequent travel and treatment abroad, which is a risk factor for CPE [24,25].

Costs associated with the outbreak were split into actual expenditure, and 'opportunity cost'. Opportunity cost was sub-divided into increased staffing time (which did not accrue actual expenditure for the hospital group but would have otherwise been spent meeting other duties), missed revenue (due to reduced capacity to perform revenue-generating procedures), and the cost of extended length of stay. Costs are estimated from the hospital perspective over the duration of the outbreak. Costs were converted from £ to € using an exchange rate of €1.18 to £1.00, correct as of 12 July 2016.

Outbreak costs included additional length of stay for case patients and anti-infective costs, and infection control intervention-related costs such as: enhanced CPE screening, infection team staff time, contact precautions (isolation), ward/ bay/ bed closures, elective surgical missed revenue, temporary ward-based monitors of hand and environmental practice, environmental decontamination and estates improvements.

Additional length of stay for case patients

Additional length of stay associated with patients involved in the outbreak created 'blocked beds' and prevented admissions and treatment of other patients. Additional length of stay associated with CPE was calculated by comparing the length of stay of the 40 case patients with the mean length of stay for patients admitted to the same specialty with the same primary diagnosis code during the outbreak period. To adjust for time-dependent bias, the length of stay for case patients was calculated from date of 'event' (first infection or colonization with CPE) rather than the date of admission, and control patients with a length of stay shorter than the mean time to event in the case patient group for each specialty–diagnosis code combination were removed from the analysis [26–28]. Using this approach, the mean and range (calculated using 95% CI of the mean) of bed-days accrued and associated costs for each specialty were calculated. The costs of additional bed-days were extracted from hospital records for level 1 (regular), level 2 (high-dependency unit; HDU) and level 3 (intensive care unit; ICU).

Anti-infective costs

Eighteen patients were treated with colistimethate sodium (colistin) and / or tigecycline during the study. The cost of treating these patients, including an average of two colistin levels for each patient treated with colistin, was determined from pharmacy records.

Infection control intervention-related costs

Enhanced screening for CPE

Universal admission and weekly screening were implemented across the vascular and renal specialties when the outbreak was first recognized in March 2015. In addition, weekly screening was performed during the stay of known case patients on wards outside the renal and vascular specialties, which continued for 4 weeks after the transfer or discharge of these patients. Finally, due to concern that silent transmission had occurred on the renal wards and possibly in haemodialysis centres before the identification of the outbreak, a point prevalence survey of CPE carriage was performed in the ten outpatient haemodialysis units managed by the hospital group. The cost of screens was determined locally as €9 per screen, which was actual expenditure to the hospital group. This was an average cost of processing both positive and negative screens at the prevalence level encountered during the outbreak, including both laboratory reagents and additional staff employed to manage the increase in screening specimens sent to the laboratory as a result of the outbreak. The additional staffing opportunity cost associated with explaining the need for a rectal screen to patients, collecting the screen, and completing the necessary documentation was estimated through discussions with ward staff.

Staff time

Separate estimates were made for the number of hours spent managing the outbreak aside from regular duties for the infection prevention and control (IPC) nursing team (a senior and junior IPC nurse for both sites affected by the outbreak), data and epidemiology team (a hospital epidemiologist and data analyst), and management team (three senior medical consultants (director of infection prevention and control, infection control doctor and senior microbiologist), a consultant pharmacist, lead IPC nurse (IPCN), non-clinical service manager and an administrator). Staff time in other clinical teams was also included: a multidisciplinary team to manage the therapy of patients who were treated (a consultant pharmacist, two infection medical consultants, a senior IPCN,

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patient's consultant and ward manager), a panel to review cases where the patient died (a senior medical consultant not directly involved in the care of the patient, infection control doctor, and administrative co-ordinator), facilities site leads, and communications representative from the hospital group for regular teleconferences with external agencies. In all cases, staff were asked to provide a conservative estimate of the amount of time taken directly managing the outbreak. Staff time for nursing and allied healthcare professional bands was taken from the 15/16 Financial Year Agenda for Change costs, and staff time for medical staff was estimated based on mid-grade costings from finance records. A ± 10% was applied to staffing costs to reflect the uncertainty of the estimates.

Contact precautions (isolation)

The cost for gloves and aprons required to deliver contact precautions was estimated from the MRSA Pathfinder project as €22 per day in 2011, inflated to €24 per day in 2015 [29]. This estimate did not include the cost of switching to an infectious waste stream, which was calculated by multiplying the estimated mass of waste generated per isolation day by the difference in disposal costs of infectious versus non-infectious waste. Also, an individual stock of packaged supply items was held at the bedside and discarded each time a case patient was transferred or discharged. To calculate the costs associated with this, bedside stock lists were costed for regular and level 3 (ICU/HDU) beds.

Bed closures

Eight bay closures and four ward closures were associated with the outbreak. The number of individual bed-days lost was counted by retrospectively reviewing daily ward patient lists during the closure periods. These lost bed-days were costed according to the ward they occurred on, with costs of a bed-day at level 1 (regular ward), level 2 (HDU) and level 3 (ICU) extracted from hospital records. The cost of switching to the infectious waste stream was calculated by multiplying the estimated mass of waste generated per isolation day by the difference in disposal costs of infectious versus non-infectious waste. The cost of curtain changes and mattresses was extracted from hospital records.

Elective surgical missed revenue

The cost of missed revenue due to reduced elective vascular surgical throughput was calculated by counting the number of cancelled procedures related to closures, and estimating the additional lost activity from procedures that were not booked during periods of closure based on average daily throughput for the previous 12 months. The number of procedures cancelled or not booked was then multiplied by the average tariff for elective vascular surgery (€4846) to calculate the missed revenue.

Ward-based monitors

Ward-based monitors of adherence to hand hygiene and environmental and equipment cleaning were introduced in response to evidence of ongoing transmission despite enhanced infection control measures [6]. The hourly cost of these additional staff members was calculated based on the band of staff used. Unlike other staff costs, the cost of monitors was actual expenditure for the hospital group, because the monitors were introduced specifically in response to the outbreak and would not otherwise have been employed by the hospital group. Monitors were given training by senior staff on the wards.

Environmental decontamination

Enhanced disinfection using sodium hypochlorite was introduced in response to the outbreak. Wards in the renal and vascular specialties increased the frequency of cleaning from once to three times daily, and switched from using detergent to using sodium hypochlorite. However, since the hospital group's cleaning service is contracted to a third party, these changes in cleaning and disinfection did not incur any additional actual expenditure or opportunity cost. In the later stages of the outbreak, due to evidence of environmentally associated transmission of CPE, hydrogen peroxide vapour was implemented [8,10]. The cost of hydrogen peroxide vapour was extracted from hospital finance records.

Estates improvements

Estates work performed in response to the outbreak included the creation of a waste storage room and improved segregation of clean and dirty in the sluice on two vascular wards, and the creation of a new en-suite facility for an existing single room on a vascular ward. The cost of the Estates improvements was extracted from hospital finance records, and considered separately to the other actual expenditure because, although prompted by the outbreak, they were not performed solely for the management of CPE.

This analysis followed the CHEERS guidelines for reporting economic evaluations and included all applicable items as recommended [30]. Ethics approval was not required for this service evaluation. Costs are reported to the nearest €1 in the tables (or cent for unit costs), and summary costs to the nearest €1000 in the text.

Results

The outbreak cost a total of €1 133 000 (range €943 000–€1 424 000) over 10 months, comprising €312 000 of actual expenditure and €822 000 (range €631 000–€1 112 000) in opportunity cost (Table 1). An additional €153 000 was spent on Estates renovations prompted by the outbreak. The hierarchy of cost areas is summarized in Fig. 1. Reduced capacity to perform 72 elective surgical procedures related to bed closures represented the greatest cost (€349 000), followed by €228 000 in staff time (range €205 000–€251 000). The opportunity costs were notably greater than the actual expenditure.

The cost of bed-days was extracted from hospital records as €198 for a regular ward, €276 for an HDU, and €1133 for an ICU. When accounting for time to event, 840 bed-days attributable to CPE were associated with outbreak-case patients costing €244 000 (range 0–2196 bed-days, €0–€435 000) (Table 2). The number of bed-days associated with outbreak-case patients was considerably higher when not accounting for time to event: 2279 bed-days, range 847–3769 (see Supplementary material, Table S1). The actual expenditure on tigecycline and colistin, and the colistin levels for patients who were treated was €54 000 (Table 3).

A total of 9927 rectal screens were taken in response to the outbreak, comprising 69.9% weekly, 17.1% admission and 13.0% renal outpatient dialysis screens (Table 4). The additional staffing opportunity cost associated with explaining the need for a rectal screen to patients, collecting the screen, and completing the necessary documentation was estimated to be 15 minutes per screen. The screening had an actual expenditure of €94 000 and an opportunity cost related to staff time of €61 000.

The IPC staff time opportunity cost totalled €152 000, which included 3 days per week of IPCN site team staff time at Hospital A and 2 days per week at Hospital B, 1 day per week of data and epidemiology team time, and 1 hour per week of management team time for internal outbreak management plus 2 hours for each of the 26 teleconferences with external agencies (Table 5). Staff time opportunity cost outside of IPC totalled €15 000, including 18 hours for the multidisciplinary clinical team advising on treatment, 42 hours of facilities site lead time, 52 hours of communications time, and 65 hours of mortality review time for the 13 patients who

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Table 1
Actual expenditure and opportunity costs associated with an outbreak of CPE

		Number	Actual expenditure (€)	Opportunity cost (€)		
				Staffing	Missed revenue	Bed days
Additional bed-days due to extended length of stay for case patients (days)[a]		840				167 463
Anti-infective costs	Anti-infective costs[b]		54 317			
Laboratory/screening	Screening (no. of screens)[c]	9927	93 711			
	Staff time to collect screens (hours)[d]	2482		60 868		
IPC[e] team time	IPC nurse site team (hours)[f]	1440		98 927		
	Data and epidemiology team (hours)[g]	288		17 084		
	Management team (hours)[h]	88		36 427		
Staff time outside of IPC	MDT meetings re treatment (hours)[i]	18		6550		
	Mortality review panel (hours)[j]	65		3911		
	Facilities (hours)[k]	42		1827		
	Communications representative (hours)[l]	52		2668		
Isolation	Cost of gloves and aprons (n of isolation days)[m]	1831	44 119			
	Stock disposal[n]		27 834			
	Cost of infectious waste stream (n isolation days)[o]	1831	706			
Ward-based monitors	Hours of HCA time (hours)[p]	2592	41 902			
Environment/equipment	Cost of hydrogen peroxide vapour decontamination[q]	24 rooms	42 848			
Elective surgical missed revenue[r]					348 931	
Closed beds	Closed bed-days due to bay and ward closures[s]					76 995
	Cost of infectious waste stream[t]		789			
	Curtain changes[u]		1931			
	Mattress disposal[v]		3599			
Totals	Grand total €1 133 407 (range €943 117–1 424 144)		311 756	228 262[w]	348 931	244 458[x]

Abbreviations: CPE, carbapenemase-producing *Enterobacteriaceae*; HCA, healthcare assistant; ICU, intensive care unit; IPC, infection prevention and control; IPCN, infection prevention and control nurse; MDT, multidisciplinary team.

[a] See Table 2 and Supplementary material, Table S1. Additional length of stay for the case patients compared with controls matched by specialty and diagnosis code after adjusting for time to event ranged from 0 to 2196 bed-days, costing €0–€435 375.

[b] See Table 3. Cost of tigecycline and colistin (€51,249), and colistin levels (colistin levels assumed 2 per patient treated with colistin ($n = 13$) at €118 each = €3068).

[c] See Table 4. Number of screens multiplied by cost per screen (€9). Total number of screens = admission ($n = 1696$) and weekly ($n = 4536$) screens on renal and vascular wards, weekly screens when a CPE patient was an outlier on other wards ($n = 2402$), and the point prevalence survey in the outpatient haemodialysis units ($n = 1293$).

[d] Fifteen minutes per patient of band 5/6 nursing time at €24.53 per hour.

[e] Infection prevention and control.

[f] See Table 5. Two days per week (16 hours) at Hospital B for 36 weeks (576 hours) plus 3 days per week (24 hours) at Hospital A for 36 weeks (864 hours) = 1440, at €68.70 per hour per site-based nursing team (each including a band 8a site lead, and a band 7 senior nurse).

[g] One day (8 hours) per week for 36 weeks (288 hours) at €59.32 per hour (including an 8a hospital epidemiologist, and a band 5 analyst).

[h] One hour per week for internal outbreak meetings (36 weeks = 36 hours), 2 hours per external teleconferences (26 teleconferences = 52 hours) at €413.94 per hour (including three senior medical consultants (director of infection prevention and control, infection control doctor, and senior microbiologist), a consultant pharmacist, lead IPCN, non-clinical service manager, and an administrator.

[i] Eighteen hours required, one for each patient that was treated using antibiotics, at €363.88per hour (including a consultant pharmacist, two infection consultants, a senior IPCN, patient's consultant, and ward manager).

[j] Cost of 13 reviews. Each review required 2 hours of senior medical consultant time, 1 hour of infection doctor time, 2 hours of co-ordinator time; a total of 65 hours at €60.17 per hour.

[k] Nine hours of 8b management time for 2 sites (18 hours) plus 1 hour for each hydrogen peroxide vapour (24 hours), at €43.51 per hour.

[l] Twenty-six teleconferences = 52 hours of 8c communications representative time, at €51.31 per hour.

[m] €21.92 per day in the MRSA Pathfinder study, inflated to €24.10 in 2015.

[n] See Table 6. 97 regular discharges or transfers, and 31 Level 3 (ICU) discharges or transfers. The cost of discarded stock was €139.56 for regular discharges, and €461.18 for Level 3 discharges.

[o] See Table 7. A cost of infectious waste per isolation-room day was calculated as €0.39.

[p] Healthcare assistant, band 3. Were in place for a total of 108 days, 24/7 (2592 hours), at €16.17 per hour.

[q] Hydrogen peroxide vapour cost €1785.32 per room on average over the 24 single rooms.

[r] See Table 8. A total of 22 cancellations and 50 cases that were not performed due to closures related to the outbreak occurred during periods of closure, at a mean cost of €4846 per procedure.

[s] See Table 9. A total of 309 regular level care beds, and 57 Level 2 (HDU) bed-days were lost due to closures during the outbreak, at a cost of €198 per regular bed-day, and €276 per HDU bed-day.

[t] A cost per day of an infectious waste stream was calculated for cohort bays and partially occupied bays on closed wards, at €3.08 per bay-day.

[u] Curtains were changed each time a known case patient vacated a bay A total of four curtains were replaced at Hospital A (costing €109), 28 were laundered at Hospital A (costing €106), and 97 were laundered at Hospital B (costing €1717)

[v] A small number of mattresses were discarded when long-standing cohort bays were disbanded, comprising four dynamic mattresses at Hospital A (costing €2360) and five regular mattresses at Hospital B (costing €1239).

[w] Range €205 436–€251 088, based on a ± 10% uncertainty estimate around staffing costs.

[x] Range €76 995–€512 370 based on uncertainty around length of stay attributable to CPE cases.

died during the outbreak. The actual expenditure for ward-based monitors (2592 hours) was €42 000.

The actual expenditure incurred through isolation was €45 000 for the 1 831 isolation days during the outbreak, comprising €44 000 for gloves and aprons, and €1000 for the additional cost of the infectious waste stream (€24 per isolation day in total) (Tables 6 and 7). In addition, stock disposal cost €132 for regular and €454 for ICU/HDU transfers or discharges, amounting to €28 000 in actual expenditure from the 97 regular and 31 level 2/3 transfers and discharges (Table 6). The cost of decontaminating 24 single rooms using hydrogen peroxide vapour was €43 000.

Ward and bay closures accrued 309 regular bed-days lost, and 57 HDU bed-days lost, which resulted in a €77 000 bed-day opportunity cost (Tables 8 and 9). In addition, the cost of switching to the infectious waste stream (€1000), curtain changes (€2000), and mattress disposal (€4000) added €7000 of actual expenditure to the cost of ward and bay closures. Related to this, 22 elective vascular procedures were cancelled and a further 50 procedures

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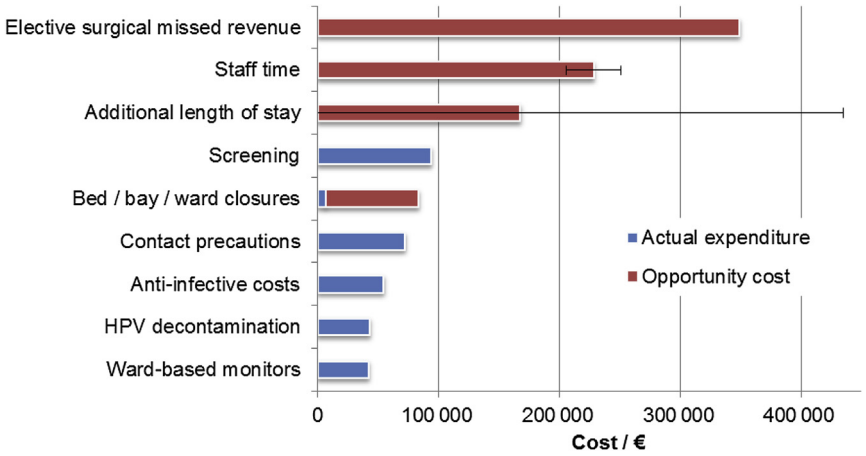

Fig. 1. Hierarchy of costs. Error bars represent the range in cost estimates.

Table 2
Additional bed-days due to extended length of stay for case patients, adjusted for time to event

Specialty	Mean LOS case patients	CI lower	CI upper	Mean LOS control patients	CI lower	CI upper	ΔLOS mean	ΔLOS min.	ΔLOS max.	No. of case patient spells	Bed-days mean	Bed-days min.	Bed-days max.	Cost/€	Cost min/€	Cost max/€
Elderly medicine	10.8	—	—	19.0	—	—	0.0	0.0	0.0	1	0	0	0	0	0	0
General medicine	12.1	0.0	31.4	1.5	0.8	2.2	10.6	0.0	30.6	5	53	0	153	10 540	0	30 321
Renal	20.0	7.0	33.0	11.1	5.3	16.9	8.9	0.0	27.8	30	268	0	833	53 136	0	165 213
Vascular	31.6	17.7	45.5	14.9	7.0	22.8	16.7	0.0	38.5	31	518	0	1192	102 618	0	236 292
Neonatal ICU	1.7	—	—	23.5	—	—	0.0	0.0	0.0	1	0	0	0	0	0	0
Adult ICU	11.0	4.0	17.9	9.9	0.0	25.7	1.0	0.0	17.9	1	1	0	18	1169	0	3548
										Total	840	0	2196	167 463	0	435 375

Abbreviations: ICU, intensive care unit; LOS, length of stay.

Table 3
Anti-infective costs

	Colistin	Colistin levels	Tigecycline	Total per patient
Patient 1	2	236		238
Patient 2	22	236		258
Patient 3			92	92
Patient 4			458	458
Patient 5			641	641
Patient 6			641	641
Patient 7	221	236	458	915
Patient 8			915	915
Patient 9	65	236	1235	1537
Patient 10	393	236	1830	2459
Patient 11	65	236	2745	3046
Patient 12	65	236	3660	3961
Patient 13	155	236	4255	4646
Patient 14	430	236	5536	6201
Patient 15	307	236	5765	6308
Patient 16	724	236	5399	6359
Patient 17	283	236	6405	6925
Patient 18	340	236	8144	8720
Total	3073	3068	48 176	54 317

Table 4
Number of patients screened for carbapenemase-producing *Enterobacteriaceae*

Outpatient screens	
Renal outpatient screening	1293
Admission screens	
Admission screens—vascular wards[a]	518
Admission screens—renal wards[b]	1178
Total admission screens	1696
Weekly screens—vascular and renal wards	
No. of inpatient beds—vascular wards	47
No. of inpatient beds—renal wards	79
Total weekly screens (36 weeks)	4536
Outlier[c] weekly screens	
Weekly screening outliers in non-renal/vascular wards	2402
Total	9927

[a] In all, 518 (76.8%) of 674 admissions to vascular wards were screened.
[b] In all, 1178 (90.9%) of 1296 admissions to renal wards were screened.
[c] 'Outlier' = patient with a carbapenemase-producing *Enterobacteriaceae* outbreak strain who was an inpatient on a non-renal/vascular ward. In this scenario, weekly screening of all patients on the ward occurred during their stay and for four weeks after their discharge from the ward.

were not booked because of periods of closure, resulting in missed revenue of €349 000.

Costs as a result of the outbreak continued to be incurred outside the outbreak period. Universal admission and weekly screening have continued beyond the outbreak management period in the affected specialties. Of 27 patients alive at the end of December 2015, three patients subsequently died, five patients have been discharged with end-of-life care plans, four regularly attend outpatient haemodialysis, 12 are regular attendees of outpatient clinics, and three have been discharged completely from the hospital system.

Discussion

We identified a total cost of €1.1m associated with an outbreak of CPE, which was accrued over a 10-month period. Around €0.3m was actual expenditure, and €0.8m was opportunity cost. Opportunity cost is more difficult to account for. Staff time spent managing the outbreak did not cost the hospital more money (apart from a small number of staff employed specifically for managing the outbreak). However, the time spent managing the outbreak meant that there was less time for other duties. While increased focus on IPC in the renal and vascular specialties would most likely have helped to prevent the transmission of other

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Table 5
Staff costs

	Grade[a]	Hourly cost (€)	Hourly cost GBP
IPC management team			
Director of IPC	Senior medical consultant	79.33	67
Consultant microbiologist	Senior medical consultant	79.33	67
Infection control doctor	Senior medical consultant	79.33	67
Hospital group lead nurse	8c	51.31	43
Consultant pharmacist	8c	51.31	43
Non-clinical service manager	8c	51.31	43
Administrator	5	22.03	19
Total cost per hour		413.94	351
IPC nursing site team			
Site lead	8a	37.29	32
Senior IPCN	7	31.41	27
Total cost per hour		68.70	58
IPC data and epidemiology team			
Hospital epidemiologist	8a	37.29	32
Data analyst	5	22.03	19
Total cost per hour		59.32	50
Treatment multidisciplinary team			
Consultant pharmacist	8c	51.31	43
Infection consultant	Senior medical consultant	79.33	67
Infection consultant	Senior medical consultant	79.33	67
IPC site lead	8a	37.29	32
Patient's consultant	Senior medical consultant	79.33	67
Ward manager	8a	37.29	32
Total cost per hour		363.88	308
Other			
Communications rep	8c	51.31	43
Facilities manager	8b	43.51	37
Band 6 nurse	6	27.02	23
Band 5/6 midpoint	5/6	24.53	21
Band 5 nurse	5	22.03	19
HCA band 3	3	16.17	14

		no. of hours per review	Unit cost (€)	Total cost (€)
Patient safety and effectiveness team				
Medical consultant reviewer	Senior medical consultant	2	79.33	158.66
Infection control doctor	Senior medical consultant	1	79.33	79.33
Co-ordinator	7	2	31.41	62.82
Total per patient			190.07	300.82
Total			2470.97	3910.63
Hours per patient		5		
Total hours ($n = 13$ patients)		65		
Cost per hour		60.16		

Abbreviation: HCA, healthcare assistant; IPC, infection prevention and control; IPCN, infection prevention and control nurse.
[a] Grade = NHS Agenda for Change salary costs from the 2015/16 financial year.

Table 6
Stock disposal

	n
Number of level 1 transfers and discharges	97
Number of level 2/3 transfers and discharges	31
	Cost (€)
Cost of discarded supplies per level 1 discharge	140
Cost of discarded supplies per level 3 discharge	461
Cost of level 1 discharges	13 537
Cost of level 2/3 discharges	14 297
Total	27 834

Table 7
Waste disposal

Difference in cost of infectious versus non-infectious waste stream, per tonne, €	128.54
Cost per person per isolation day	
Waste per day, kg (estimate from Facilities)	3
Waste per day, tonnes	0.003
Cost of waste per day, €	0.39
Cost per isolation bay per isolation day	
Staff change bins four times per day	4
Waste per bag, kg (estimate from Facilities)	6
Waste per day, kg	24
Waste per day, tonnes	0.024
Cost of waste per day, €	3.08

pathogens too, it is also likely that the time spent by the IPC team in managing the outbreak in two specialties had a negative impact on the delivery of other IPC activity across the rest of the organization; this should be the subject of future studies. The outbreak period persisted over 10 months, but a number of important cost pressures remain, including the ongoing cost of universal and weekly CPE screening on the affected wards plus more extensive hospital group-wide screening, and the continued management of patients who were affected during the outbreak and who still have regular inpatient and outpatient contact. Furthermore, enhanced screening introduced in response to the outbreak has resulted in a sharp increase in the number of sporadic and clustered cases of CPE identified in the hospital group, which should serve to help prevent future outbreaks.

The strengths of the evaluation include that most of the costs were derived from hospital finance records, including locally derived estimates of bed-day costs; these are likely to be more

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Table 8
Cancelled surgery

	Cancellations	Lost activity	Cost (€)
Apr 2015	3	21	116 310
May 2015	3	15	87 233
Jun 2015	9	0	43 616
Aug 2015	7	14	101 771
Total	22	50	348 931

accurate than estimates obtained from the literature. The analysis included both actual expenditure and opportunity costs, with comprehensive coverage of potential areas of cost. The evaluation provides a UK-based cost estimate using the experience of an NHS Trust (hospital group). Limitations include the use of published estimates for some costs, which may not reflect accurately the costs actually incurred. Furthermore, the cost estimates that are accurate locally may not be generalizable to other hospitals and healthcare systems. Other factors will also influence the generalizability of our findings, including the size of the hospital, and the cost of labour. The cost of environmental interventions aside from the costs of hydrogen peroxide vapour decontamination is not included because of the structure of the agreement with our cleaning contractor, who absorbed additional actual expenditure and opportunity cost without any additional charge to the hospital. This will serve to underestimate the substantial costs that would be associated with the environmental interventions in hospitals who have an in-house cleaning service, or a differently structured contracted cleaning service. Socio-economic costs of the outbreak were not included, nor were long-term CPE-related costs related to persistent carriage of the organism. We are unaware of any legal costs associated with the outbreak, but these may occur in future or in other settings. Reputational costs are not considered, which may be particularly important for some revenue-generating specialties including private patients and elective surgery. Also not considered are costs associated with changes to the antimicrobial programme stemming from the outbreak, including a review of surgical prophylaxis regimens in renal transplant and vascular graft procedures to account for colonized patients. Additional length of stay associated with CPE was calculated by comparing the length of stay of the 40 case patients with the mean length of stay for patients admitted to the same specialty with the same primary diagnosis code. We identified a large range in length of stay attributable to CPE from 0 to 2196 days after adjusting for time to event. There are several

Table 9
Ward and bay closures

	Bay days	Ward days	Bed days lost – level 1	Bed days lost – level 2 (HDU)	Curtain changes
Ward and bay closures					
Hospital A Ward A M bay: Apr 14–15, 20–27 and May 4 2015	11		23		6
Hospital A Ward A K bay: Apr 14–15, Apr 20–May 5 2015	16		31		5
Hospital A Ward A HDU: Apr 14–May 5 2015	22			48	5
Hospital A Ward A: Aug 5–12 2015		8	25	9	16
Hospital A Ward B H bay: Apr 20–27 2015	8		11		6
Hospital A Ward B A bay: May 20–22 2015	3		4		5
Hospital A Ward B G bay: Aug 17–24 2015	8		8		5
Hospital A Ward B May 23–June 8 2015		17	181		21
Hospital A Ward C: Aug 20–26 2015		7	17		12
Hospital A Ward D: Sept 19–20 2015		2	1		16
Hospital B Ward E B bay June 24–July 08 2015	15			0	28
Hospital B Ward F C bay July 8–August 10 2015	34		8		4
Total	117	34	309	57	
Bed-day costs	Cost (€)				
Level 1 bed-day cost	198				
Level 2 (HDU) bed-day cost	276				
Level 3 (ICU) bed-day cost	1133				
Level 1 bed-days lost cost	61 256				
Level 2 bed-days lost cost	15 739				
Bed-days lost cost total	76 995				
Cost of infectious waste stream[a]	Cost (€)	*n*			
Cost of bay closure infectious waste stream	361	117			
Hospital A Ward A closure	86				
Hospital A Ward B closure	236				
Hospital A Ward C closure	86				
Hospital A Ward D closure	19				
Cost of infectious waste stream total	789				
Curtain change/laundering costs	Cost (€)				
Hospital A curtain change cost	18				
Hospital B curtain change cost	27				
Hospital B curtain laundering cost	4				
	Cost (€)	*n*			
Hospital A curtain changes	1717	97			
Hospital B curtain changes	109	4			
Hospital B curtains laundered	106	28			
Curtain total	1931				
Mattress costs	Cost (€)				
Normal mattress cost	248				
Dynamic mattress cost	590				
Five mattresses at Hospital A	1239				
Four dynamic mattresses at Hospital B	2360				
Mattress total	3599				

[a] Cost of infectious waste stream for each ward closure was calculated by multiplying the number of bays and single rooms on the ward by the cost of infectious waste stream per bay (€3.08) and room (€0.39).

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reasons why CPE may have increased length of stay during the outbreak. First, even though 32 of the 40 case patients were first identified by screening cultures, 22 patients had a positive clinical specimen at some point during the outbreak period, and 18 were treated using anti-infectives. Second, in a number of cases where the patient was colonized only, a 'downstream' healthcare facility was unwilling to accept the patient due to their CPE colonization status, resulting in delays for patients who were medically fit for discharge. Our adjustment for time-dependent bias substantially reduced the cost associated with additional length of stay. However, this is a rather crude method to calculate attributable length of stay; crucial confounders, such as the fact that patients included in the outbreak had a high degree of acuity, were not included and therefore attributable length of stay may be overestimated [26–28]. Cost estimates such as these would benefit from further statistical studies into attributable length of stay accounting for confounders such as age, illness score or co-morbidities [26,27].

Several other studies have evaluated the costs of containing outbreaks of Gram-negative bacteria. For example, Dik *et al.* calculated the mean cost per patient outbreak day for three separate Gram-negative outbreaks in the Netherlands (two extended-spectrum β-lactamase-producing *K. pneumoniae*, one affecting nine patients over 17 days in a rehabilitation ward and one affecting five patients over 24 days in a nursing ward, and one *Serratia marcescens* outbreak affecting eight patients over 86 days in the ICU) to be €956 [11]. Using this cost multiplied by the 1831 inpatient bed-days for the 40 patients in our outbreak equals €1.7m, compared with our estimated cost of €1.4m. However, it is of note that fixed personnel costs were not included in the study by Dik *et al.* [11], in contrast to our evaluation. Other studies have identified considerably smaller costs, due to evaluating the cost of smaller and more localized outbreaks of different organisms [14–18]. For example, Spearing *et al.* calculated the cost of an outbreak of *Salmonella* sp. affecting 52 patients and staff over 4 weeks hospital-wide in an Australian hospital to be US $95 000 (€85 000) [14]. Jiang *et al.* calculated the cost of an outbreak of *Acinetobacter baumannii* affecting nine patients over 9 weeks in a US ICU to be US $371 079 (€333 971) [15]. Garlantézec *et al.* calculated the cost of an outbreak of *A. baumannii* affecting five patients over 2 months in the ICU to be €264 553 [16], and Bou *et al.* calculated the cost of an outbreak of *P. aeruginosa* affecting 67 patients over 3 months in the ICU to be €312 936 [17]. In line with other studies [11], the largest cost was associated with lost bed-days—including related to extended length of stay of case patients, and lost bed-days associated with ward closures. We also included the cost of Estates improvements associated with the outbreak. A significant portion of the Estates improvements cost was building a new en-suite single room on a vascular ward, illustrating the high cost of generating new isolation rooms suitable for IPC.

The perspective of the analysis assumes that the hospital's fixed costs are relevant to the decision maker. Fixed costs, unlike variable costs, will not change with CPE burden. For example an extended length of patient stay will not alter fixed bed-day costs, as they will still have to be paid regardless of the patient occupying the bed. However, a higher-level decision maker will include a value for fixed costs as they will incur an opportunity cost for fixed costs used, i.e. the capacity that could have been released for other healthcare uses. Although data on the effectiveness of interventions to prevent the transmission of CPE is lacking [7,8], the sizeable costs associated with the outbreak itself (mainly due to additional length of stay) and interventions to contain the outbreak (mainly due to bed closures and related missed revenue from elective surgery, and staff time) would have been averted if in-hospital transmission had been prevented. Therefore, CPE prevention activities are likely to be cost-effective. There are no studies evaluating the cost-effectiveness of the various prevention Toolkits and guidelines that are available for CPE [21,22]. A number of studies have suggested alternative strategies to those outlined in CPE Toolkits, for example employing universal screening of high-risk specialties, rather than risk-factor-based screening of all admissions [31,32]. During this outbreak, universal admission and weekly screening were performed in the affected specialties, combined with weekly screening when patients with known CPE were cared for outside the affected specialties. This, combined with a point-prevalence screen in the outpatient dialysis units, resulted in a total of almost 10 000 screens with an actual expenditure of around €94 000 and staff costs of over €60 000. Although the comprehensive screening programme introduced in response to the outbreak was over and above the recommendations of national guidelines [22], these costs illustrate the likely cost of widespread admission screening for CPE, which must be balanced against the risk of silent transmission of CPE. Further work is required to establish effective interventions to prevent the spread of CPE, and determine the relative cost-effectiveness of various approaches to IPC. The large cost associated with containing the outbreak accrued over a relatively short period of time (10 months) supports the case for the relatively small investment required for proactive comprehensive universal and targeted infection prevention activities (e.g. screening and isolation) and minimizing antibiotic exposure and selection pressure [33,34]. With rising levels of antimicrobial resistance worldwide, investment in IPC is an increasing priority. CPE are highly resistant and present a growing threat in the UK and abroad. The cost estimates that we present suggest that CPE outbreaks are highly costly, highlighting the serious nature and high cost of antimicrobial resistance and prompting an urgent focus on preventive measures.

Transparency declaration

JAO was previously employed part-time by Bioquell (ceased April 2015) and is now a consultant to Gama Healthcare outside the submitted work; MG has attended a Pfizer advisory board outside the submitted work. All other authors have no conflicts of interest to declare.

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Contributorship

JAO led the collection of data, analysis and drafted the manuscript. FD, SM, JS, MG, DP, Merlyn Marsden, Tracey Galletly, Tom Addey and Diane Gates collected the data. PB, DP and JR analysed the data. AHH conceived the study and co-ordinated the study development. All authors contributed to the development of the manuscript.

Appendix A. Supplementary data

Additional Supporting Information may be found in the online version of this article can be found at http://dx.doi.org/10.1016/j.cmi.2016.10.005.

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