seven (25.9%) patients, there was no registry of previous exposure to healthcare facilities.

Among patients who recovered a microbiological isolate, a lower rate of in-vitro susceptible empiric therapy was administered to those with infections by ESBL (50%) and carbapenemase-producing Gram-negatives (26.9%) compared to other patients (77.4%) ($P < 0.01$). Patients with carbapenem-resistant isolates had significantly higher 30-day mortality in univariate analysis: 13 (48.1%) of 27 versus 166 (25.7%) of 646 ($P = 0.02$). Older age ($P = 0.04$), cancer ($P = 0.04$), HIV infection ($P = 0.02$), cirrhosis ($P = 0.04$), septic shock ($P < 0.01$), and higher quick-SOFA ($P = 0.04$) were associated with 30-day mortality in the final Cox regression model.

In our study, Gram-negative bacteria were the leading cause of infections in septic patients. There was a growing prevalence of carbapenem-resistant Gram-negatives over time, associated with worse outcomes. As expected, most of these patients had exposure to healthcare facilities, but only a minority of them had previously received carbapenem or had yielded isolates of these bacteria. These data raise the concern about the spread of multi-resistant organisms in healthcare facilities even without previous carbapenem exposure. Delays in adequate treatment plus scarce and/or suboptimal antibiotic options for the management of these infections may explain their higher mortality rate [6,7]. The factors that remained in our final multivariate model underline that severity status at diagnosis and comorbidities play a key role in clinical response.

This study warns us about the growing prevalence of multi-resistant infections in patients arriving at the hospital. Rapid tests for detection of carbapenemases could be a valuable tool for guiding therapy. Meanwhile, we need strict vigilance of Gram-negative resistance and adjustment of empiric treatment accordingly.

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Value of a hospital-wide point prevalence survey of carbapenemase-producing Enterobacterales — low-level prevalence confirmed

Sir,

Carbapenemase-producing Enterobacterales (CPE) are associated with limited treatment options, and increased morbidity and mortality [1,2]. Beaumont Hospital (BH) is an 820-bed tertiary hospital and is the Irish national referral centre for neurosurgery, renal transplantation and cochlear implantation. BH operates a risk-based CPE surveillance programme including admission and weekly rectal screening in high-risk ward areas (critical care, haematology and renal transplant), screening of inpatient contacts of new cases, non-domestic hospital transfers and interhospital transfers to selected specialty wards: transplant, urology, nephrology and neurosurgery. Isolates of Enterobacterale from clinical samples are screened routinely for carbapenemase production.

In October 2017, an upsurge of eight new cases of CPE occurred within a two-week period (Table I). As several ward areas not included in the existing CPE screening programme posed a potential reservoir, a hospital-wide point prevalence survey (PPS) for rectal CPE carriage was undertaken with the objective of determining the hospital CPE burden at that time.

Rectal swabs were collected from consenting inpatients from 6th to 19th November 2017. Swabs were inoculated on to chromID CARBA SMART chromogenic media (bioMérieux, Marcy L'Etoile, France); plates were incubated at 35°C for 18–24 h. Positive cultures were considered as Enterobacterales and speciated by the BD Bruker MALDI-TOF Biotyper (BD Diagnostics, Franklin Lakes, NJ, USA). Confirmation and characterization were performed using Xpert Carba-R (Cepheid, Sunnyvale, CA, USA) and RESIST-3 O.K.N. (CORIS BioConcept, Gembloux, Belgium).

In total, 837 rectal screens were performed. Duplicates and non-hospitalized patient screens were excluded; 722 patient screens (88% of total beds) across five directorates and 27 ward areas were included. The median patient age was 67 years (range 14–100 years), and 51% were male ($n = 369$). In total,

Table I

Demographic details of patients colonized with carbapenemase-producing Enterobacterales (CPE) detected during the point prevalence survey (PPS)

Patient	Sex	Age (years)	Directorate	CPE isolate	Patient origin	Admission history[a]	Time to CPE positive[b]	Detection history	CPE surveillance in that directorate or ward area
A	F	74	Medical	*Klebsiella pneumoniae*	OHCF	No previous BH admission. Transferred from a foreign acute hospital	0	Surveillance (rectal)	No screening[c]
B	M	64	Neurosciences	*Citrobacter freundii*	Community	Single BH admission	30	Surveillance (rectal)	Admission screening
C	F	45	Medical	*Citrobacter freundii*	Community	No previous BH admission. Recent discharge from a foreign acute hospital	18	PPS only	No screening
D	F	82	Medical	*Escherichia coli*	Community	None	57	PPS only	No screening
E	M	73	Medical	*Escherichia coli*	Community	Multiple BH admissions	27	PPS only	No screening
F	M	44	Neurosciences	*Escherichia coli*	OHCF	Single transfer from an Irish acute hospital	32	Surveillance (rectal) and PPS	Admission screening
G	F	87	Surgical	*Escherichia coli* and *Klebsiella pneumoniae*	Community	Multiple BH admissions	43	Clinical isolate (sputum) and PPS	No screening
H	F	66	Critical care	*Escherichia coli* and *Klebsiella pneumoniae*	OHCF	Single BH admission	12	Surveillance (rectal) and PPS	Admission and weekly screening
I	F	52	Neurosciences	*Enterobacter cloacae* and *Klebsiella oxytoca*	OHCF	Multiple transfers from an Irish acute hospital	18	Surveillance (rectal) and PPS	Admission screening
J	M	66	Medical	*Klebsiella pneumoniae* and *Enterobacter cloacae*	OHCF	Multiple transfers from an oncology clinic	55	Surveillance (rectal) and PPS	No screening
K	M	41	Medical	*Klebsiella pneumoniae* and *Klebsiella oxytoca*	Community	None	35	Surveillance (rectal) and PPS	Admission and weekly screening[d]
L	M	53	Medical	*Escherichia coli*	Community	Long-term inpatient	318	PPS only	No screening

OHCF, other healthcare facility; BH, Beaumont Hospital.

[a] Admission history to BH in 2017.

[b] Interval in days from admission to CPE positive.

[c] Admission screen performed due to transfer from foreign healthcare facility.

[d] Patient in a haematology ward area where admission screening is performed routinely.

16% of patients ($N = 115$) were admitted from another healthcare facility, 80% ($N = 574$) were admitted from the community, 3% ($N = 23$) were haemodialysis admissions and 1.5% were unknown ($N = 10$). The median interval from admission to CPE screen was five days (range 0–355 days).

Rectal carriage of CPE was detected in 10 inpatients on eight wards across four directorates, resulting in a carriage rate of 1.38% in November 2017 (Table I). All carbapenemases were characterized as OXA-48, and all patients were colonized and not infected at the time of detection. Six patients had a history of CPE, and four new colonized patients were identified.

The median age of patients colonized with CPE was 59.5 years (range 41–87 years), with a male:female ratio of 1:1, and the median interval from admission to screening was 33.5 days (range 12–318 days). Four patients (40%) were transferred from another healthcare facility. Eight patients (80%) had a history of admission to an Irish or foreign healthcare facility during 2017. Four patients colonized with CPE, admitted from the community, had not been identified previously.

The detected CPE carriage rate of 1.38% compares favourably with previous studies. In 2014, Poole *et al.* [3] reported a CPE carriage rate of 11% following screening of 618 inpatients over a three-day study in a large acute teaching hospital trust in central Manchester, England during a *Klebsiella pneumoniae* carbapenemase (KPC) outbreak. In 2012, a three-month prospective multi-centre acute hospital survey of faecal CPE carriage was conducted by Pantel *et al.* in Southern France [4]. A carriage rate of 0.26% was reported in this non-outbreak setting.

The fact that previously unidentified CPE-colonized patients were not uncovered in ward areas where active surveillance is established indicates the efficacy of the existing programme. An expanded programme might have a positive impact on control. Active surveillance of CPE rectal carriage has been demonstrated to result in transmission restriction [5]. Universal hospital admission CPE screening was assessed in a low-prevalence setting in a London NHS foundation trust in 2015 [6]. Due to lack of cost-effectiveness, the study did not support universal admission screening in settings where CPE is not endemic. However, poor compliance with risk-factor-based admission screening was highlighted.

This study had several limitations. Screening for CPE was undertaken over a 14-day study period, in contrast to sampling on a single day, due to ward level and laboratory service constraints. Patient admissions, discharges and ward transfers during this period were not controlled for, so the PPS only provides an overall representation of CPE carriage in the BH patient cohort. A culture-based screening methodology was employed. However, several studies have demonstrated the increased analytical sensitivity of molecular methodology; patients colonized with low numbers of CPE may not have been detected [1,7]. Additionally, as a single sample was taken from each patient, no allowance was made for the variability of CPE shedding, which may have impacted on detection [1].

This survey demonstrated that a hidden CPE reservoir was not present in the inpatient population in November 2017. This finding also indicates that the CPE burden has not become insurmountable. Control of CPE transmission through early detection and timely implementation of infection prevention and control measures is therefore of paramount importance.

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Opportunities lost may be the greatest cost of CPE outbreaks

Sir,

Carbapenemase-producing Enterobacteriaceae (CPE) outbreaks are reported internationally with increasing frequency, often associated with antimicrobial-resistant infections that are challenging to treat [1,2]. It is unsurprising, therefore, that considerable efforts are being made to understand both the sources and epidemiology of these incidences [3—5]. Further focus has been placed on calculating the economic costs of these outbreaks. Notably, Bartsch *et al.* found that the financial burden of CPE in the USA was higher than that attributable to many chronic and acute diseases [6]. Otter *et al.* performed a comprehensive audit of costs arising from a 40-patient CPE outbreak across five hospitals in the UK, reporting both actual and opportunity costs that accrued in 2015 [7].

Using an approach analogous to Otter *et al.*'s, we completed a retrospective review of accrued costs relating to a comparable 2015 CPE outbreak involving 27 patients in Limerick, Ireland. Although less comprehensive than the UK study, and focused somewhat more on patient experiences of CPE diagnosis [8], the direct economic comparison on an almost like-for-like basis (similar patient numbers) was insightful. Across shared parameters (e.g. anti-infective costs, screening, contact precautions, ward monitors and hydrogen peroxide vapour decontamination), the Irish costs amounted to €1,375,000, representing €835,000 more than the UK costs, despite 33% less Irish patient involvement. Forensic accounting may determine where the greatest disparities in cost are, although it is apparent that pricing of drugs, consumables and decontamination are reasonably similar.

Otter *et al.* described reduced capacity to perform elective surgical procedures and 840 bed-day closures as the largest contributors to loss of hospital income subsequent to their CPE outbreak, reflecting losses of €349,000 and €244,000, respectively [7]. In Limerick, 473 lost bed-days were recorded. Unlike UK hospitals, we are unable to attribute loss of income specifically. However, the impact of such reduced capacity is evident, with official statistics from the Irish Government reporting hospital in-patient and day-case waiting lists in excess of 80,000 in March 2018. With CPE now endemic in many Irish hospitals [2], it seems reasonable to predict ongoing budgetary requirements, dedicated isolation facilities and loss of bed-days. It is the latter that concerns us most, as delayed access to hospitalization increases time to treatment, and reduces those critical windows of opportunity in which elective or acute care can be most effective.

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