Intensive Care Unit Wastewater Interventions to Prevent Transmission of Multispecies *Klebsiella pneumoniae* Carbapenemase–Producing Organisms

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**Background.** The increasing prevalence of nosocomial carbapenemase-producing *Enterobacteriaceae* is a concern. However, the role of the environment in multispecies outbreaks remains poorly understood. There is increasing recognition that hospital wastewater plumbing may play a role.

**Methods.** Covers were installed on all hoppers (a "toilet-like" waste disposal system) in adult intensive care units (ICUs) of a university hospital; additionally in the surgical ICU, sink trap heating and vibration devices were also installed. Patient acquisitions of *Klebsiella pneumoniae* carbapenemase–producing organisms (KPCOs) for patients who were admitted to an intervention unit were compared for 18-month preintervention and intervention periods.

**Results.** Sixty hopper covers and 23 sink trap devices were installed. Fifty-six new multispecies KPCO acquisitions occurred preintervention compared to 30 during the intervention. Decreases for all KPCO acquisitions (odds ratio [OR], 0.51; 95% confidence interval [CI], 0.31–0.81; *P* = .003) and KPCO-positive clinical cultures (OR, 0.29; 95% CI, 0.17–0.48; *P* < .001) per admission in patients exposed to an intervention unit were observed. The incidence rate ratio was 0.51-fold (95% CI, 0.43–0.61) lower for all KPCO acquisitions during the intervention. The effect of the sink trap devices alone could not be determined, although the proportion of sink drain cultures positive for KPCO decreased (12/15 [80%] sites sampled preintervention vs 40/840 [5%] sampled during the intervention; *P* = .001).

**Conclusions.** An intervention targeting wastewater plumbing fixtures, by installation of hopper covers, demonstrated a decrease in patient KPCO acquisitions. Considering wastewater reservoirs in nosocomial transmission of multispecies carbapenemase–producing *Enterobacteriaceae* may be critical.

**Keywords.** carbapenem-resistant *Enterobacteriaceae*; *Klebsiella pneumoniae* carbapenemase; sink; toilet.

Carbapenem-resistant *Enterobacteriaceae* are among the most concerning emerging resistant organisms [1] in part because carbapenemase genes often reside on mobile genetic elements such as plasmids, which can be exchanged between pathogenic and environmental bacteria [2]. Although hospital wastewater was identified as a potential nosocomial source for antibiotic-resistant gram-negative bacteria in the 1970s [3], it has been increasingly implicated in outbreaks with carbapenem-resistant organisms (CROs) and may act as a reservoir that amplifies resistance [4, 5]. Traditional models of patient–patient transmission may not be appropriate for nonclonal, plasmid-mediated outbreaks of carbapenemase or other β-lactamase resistance genes, where adherence to standard precautions (eg, promotion of hand hygiene, implementation of contact precautions) does not seem to have a significant effect [6]. Transmission networks that involve wastewater reservoirs and the efficacy of intervention efforts have not been rigorously studied, except to describe outbreaks in single medical units [7].

Many recent reports have focused on sink traps and drains as potential CRO transmission reservoirs [5]. Recently, we demonstrated a mechanism for dissemination in a sink laboratory model where biofilm spread from the sink trap to the sink drain; organisms were then dispersed when impacted by water from the sink faucet [8]. Particles and organisms have been shown to disperse to the wider environment from toilet flushing [9], albeit this work has been performed largely in relation to *Clostridium difficile* [10–12]. Gram-negative organisms, including CROs, could plausibly be similarly dispersed by hopper/toilet flushing.

Received 28 September 2017; editorial decision 9 January 2018; accepted 1 February 2018; published online February 2, 2018.

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Nosocomial acquisition of Klebsiella pneumoniae carbapenemase–producing organisms (KPCOs) occurs in our institution despite a robust screening and isolation program and early adoption of the Centers for Disease Control and Prevention's (CDC) toolkit to prevent CRO transmission [13, 14]. Previously, we used genomics to characterize transmission networks and found that the majority of transmissions could not be explained by patient-to-patient events [15, 16]. These findings suggest that there was a nonpatient nosocomial reservoir that contributed to transmission of multispecies KPCOs. Here, we investigate the presence of KPCOs in the wastewater environment and the impact of environmental interventions on patient KPCO acquisition.

METHODS

Setting
A single-center, prospective, observational intervention study was performed at the University of Virginia, a 619-bed tertiary care hospital, and at a 44-bed associated long-term acute care facility from August 2014 through October 2017. A robust KPCO prevention program existed throughout the study period, as previously described [16], and included perirectal screening on admission to the medical intensive care unit (MICU) and surgical intensive care unit (SICU) and weekly screening of all patients in the MICU and SICU as well as in units where any known KPCO-colonized patient was present [14]. During the intervention period, additional discharge screening was performed in the MICU and SICU. Screening was performed as previously described [14] until February 2017 when the indirect carbapenemase test was replaced by the modified carbapenemase inactivation method [17]. Clinical Enterobacteriaceae and Aeromonadaceae with an elevated ertapenem or meropenem minimum inhibitory concentration by VITEK2 (Biomerieux, Durham, North Carolina) immediately underwent CarbaR (Cepheid Sunnyvale, California) carbapenemase polymerase chain reaction (PCR) testing.

Definitions
The study was divided into 3 time periods: an 18-month preintervention period (1 August 2014 to 31 January 2016), a 3-month installation period (1 February 2016 to 30 April 2016) during which hopper (a toilet-like solid waste disposal system) covers and sink trap heater devices were installed, and an 18-month intervention period (1 May 2016 to 31 October 2017) following cover/device installation.

Patients were included in the study if they had a positive KPCO culture obtained >48 hours after their first admission, had spent time in an adult ICU unit with an in-room hopper (hereafter designated a “hopper unit”) within the prior 90 days, and were first identified during the preintervention or intervention study periods. Patients were excluded from the study if the hopper unit stay was within the 90-day look-back window but outside of the designated study time periods.

Patients with KPCO cultured only from perirectal surveillance screens were classified as “colonized.” Patients with KPCO from a nonperirectal culture site were classified as having a “clinical culture.” The number of patient-days for hopper units only, patient admissions to a hopper unit, and perirectal screens on patients who stayed in a hopper unit in the last 90 days during the study period were used as denominators.

Interventions
Each patient room in the following ICUs had a hopper (Figure 1A): MICU (n = 16 rooms), cardiothoracic (12), cardiac (10), SICU (12), and neurological (10). Sixty hopper covers (Figure 1B) were installed on all patient care room hoppers during the installation period. Staff education accompanied hopper cover installation, including instructions to close prior
to flushing and to not place patient care items on the covers. As the SICU historically had the highest rates of KPCO acquisition in addition to the hopper covers, 23 sink trap heaters—vibration units (Moveosiphon ST24; MoveoMed, Dresden, Germany) were installed on all sinks (15 patient rooms, 2 staff bathrooms, 1 staff lounge, 2 nursing station/medication preparation areas, 1 anteroom, 1 procedure room, and 1 soiled utility room sink; Figure 1C). The devices were set to be highly sensitive to a temperature decrease and therefore were heated almost continuously between 75°C and 85°C. Our standard ICU room layout has a hopper in one corner and a sink in the other corner, with the bed in between (Figure 2). During the intervention period, weekly independent hopper use audits were performed to assess compliance, and sink trap heater devices were checked for problems (eg, malfunction, leakage).

Environmental Sampling
Drain sampling was performed by inserting BBL CultureSwab EZ (Becton, Dickinson, Franklin Lakes, New Jersey) into drain holes 2.5 cm below the drain. Wastewater sampling was performed by collecting 50 mL of water from the sink trap and hopper. Weekly sampling of the sinks with the sink trap heating devices took place during the intervention period. Drain swabs were placed in 4.5 mL tryptic soy broth (TSB) with a 10-µg ertapenem disk. Sink trap or hopper water was spun at 3000 rpm for 15 minutes followed by removal of the supernatant, with the remaining 1 mL of pelleted water and debris inoculated into 4.5 mL of TSB with a 10-µg ertapenem disk. These cultures were incubated overnight at 34°C, then 10 µL was plated to Colorex KPC agar (North East Laboratories, Waterville, Maine) and again incubated overnight at 34°C. Pigmented colonies suggestive of Enterobacteriaceae or Aeromonadaceae were subcultured to blood agar followed by the indirect carbapenemase test. If positive, blaKPC PCR [18] and species identification with matrix-assisted laser desorption/ionization time-of-flight or VITEK2 (BioMerieux, Durham, North Carolina) were performed.

Data and Statistical Analyses
Patient data were collected from electronic medical records in a data warehouse. Data analysis was performed in R using the Stats and survival packages (R, version 3.3.2; 31 October 2016). Fisher exact test was performed to compare rates of acquisition (per patient days and patient admissions) for the preintervention to intervention periods, clinical cultures per patient admissions, and new perirectal colonizations per surveillance screens in patients exposed to a hopper unit within the preceding 90 days.

We performed Poisson regression to model the number of new acquisitions per month using the study period as a categorical variable and the monthly patient days for hopper units as an offset.

Survival analysis techniques modeled time to KPCO acquisition in the preintervention and intervention periods, where patients who acquired KPCO were compared to patients who were exposed to a hopper unit, had ≥1 perirectal screen, and remained negative during the period of analysis for a 60-day period after admission [19].

We used Cox regression to model hazard rates for acquisition [19]. Hours spent in hopper and nonhopper units were

![Figure 2](https://example.com/figure2.png)  
**Figure 2.** Adult intensive care unit layout of hopper and sink with general proximity to patient.
used as covariates, and the study period was used as a categorical variable [19]. Population groups included patients who acquired KPCO and patients with ≥1 perirectal screen who remained negative. Patients were right censored upon discharge from the hospital without KPCO acquisition.

Interventions were put in place for quality improvement purposes. Patient data review was performed under the University of Virginia Institutional Review Board Protocol (18393 and 18776).

RESULTS

Intervention Analysis

Of the patients who were exposed to a hopper unit, there were 56 new KPCO acquisitions in the preintervention period compared to 30 during the intervention period, representing a decrease using both patient admissions to a hopper unit and hopper unit patient-days as denominators. Significant reductions were observed for both clinical cultures and perirectal colonizations during the intervention period despite an increase in perirectal screening (Table 1).

Poisson analysis showed a decrease in the monthly incidence rates in the intervention period, with the incidence rate ratio for KPCO acquisition 0.51-fold (95% confidence interval [CI], 0.39–0.61) lower during the intervention compared to the preintervention period.

The 60-day time to acquisition curves for each period are shown in Figure 3. The log-rank test of time to acquisition demonstrated that the observed number of acquisitions for the intervention period was significantly lower than expected ($z = 10.42; P = .001$).

Cox regression analysis showed that hours spent in a room with a hopper had a significant contribution to risk of acquisition during the preintervention period (hazard ratio [HR], 1.013: 1.004–1.028; $P = .003$) but not during the intervention period (HR, 0.996–1.022; $P = .14$) when modeled separately. However, there were no significant interactions between intervention period and hours spent in hopper units when modeled together (HR, 0.9824–1.008; $P = .43$). Interestingly, there were 40 and 19 patients not exposed to a hopper unit in the previous 90 days who acquired KPCO during the preintervention and intervention periods, respectively, which represented a decrease in total acquisition per 10,000 nonhopper unit patient-days (odds ratio, 0.46; 95% CI, 0.25–0.81; $P = .005$), suggesting a broader institutional-wide effect (see Supplementary Tables 1 and 2 and Supplementary Figure 1).

Evaluating patients who acquired KPCO after exposure to the SICU alone where both sink trap device and hopper covers were installed, there were nonsignificant reductions in KPCO acquisition between the study periods per patient admission (26/1713 patients preintervention vs 14/1703 patients during the intervention; $P = .08$).

During both study periods, approximately 25% of patients (n = 12 in the preintervention period and 8 in the intervention period) acquired more than 1 species with bla_{KPC}. Species analysis of newly acquired KPCO demonstrated that colonizing/infecting organisms continued to be multispecies, with *Serratia marcescens*, *K. pneumoniae*, *Citrobacter freundii*, and *Enterobacter cloacae* complex as the most prominent species in both periods (Table 2).

Intervention Audits

SICU sink trap heaters were monitored weekly for 50 weeks, and 749 observations were made. A sink trap was noted to be dry on 4 occasions, to be leaking water on 3 occasions, to be unplugged on 2 occasions, and to be malfunctioning on 1 occasion.

**Table 1. Patients Who Were in a Hopper Unit Before Acquisition of *Klebsiella pneumoniae* Carbapenemase–Producing Organism**

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Preintervention</th>
<th>Intervention</th>
<th>Odds Ratio$^1$</th>
<th>95% Confidence Interval</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>KPCO acquisition</td>
<td>56</td>
<td>30</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Clinical culture</td>
<td>20</td>
<td>9</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Colonization</td>
<td>36</td>
<td>21</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Total patient days$^4$</td>
<td>25,332</td>
<td>26,417</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Total patient admissions$^5$</td>
<td>7427</td>
<td>7783</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Total perirectal cultures$^6$</td>
<td>5783</td>
<td>7088</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Acquisitions per 10,000 patient-days</td>
<td>22.10</td>
<td>11.36</td>
<td>0.51</td>
<td>0.31–0.81</td>
<td>.003</td>
</tr>
<tr>
<td>Acquisitions per 1000 patient admissions</td>
<td>754</td>
<td>3.85</td>
<td>0.51</td>
<td>0.31–0.81</td>
<td>.003</td>
</tr>
<tr>
<td>Clinical cultures per 1000 patient admissions</td>
<td>9.15</td>
<td>2.69</td>
<td>0.29</td>
<td>0.17–0.48</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>New perirectal colonizations per 1000 surveillance screens</td>
<td>8.4</td>
<td>3.52</td>
<td>0.41</td>
<td>0.24–0.68</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>


$^1$Patient admission to a hopper unit.

$^2$Perirectal screening culture for KPCO on patients exposed to a hopper unit.

$^3$Fisher’s Exact test.
occasion, requiring device exchange. Seven leakage events were observed (3 during weekly audits and 4 noted by hospital staff), which all took place more than 8 months after initial installation. Gasket rings were replaced over a 3-week period during month 12 of the 18-month intervention; no additional leaks were noted following gasket replacement.

Hopper cover use was also audited weekly in the SICU over 36 weeks, beginning roughly 3 months into the intervention period, with 431 observations. The following were noted as noncompliance events: 21 cases where an item was placed on the hopper lid (most commonly a urinal [n = 8] or bedpan [n = 6]), 14 where dialysate was running into the hopper from continuous venous hemodialysis, and 6 where the hopper cover was ajar with a patient in the room. Outside of the audit process, but early in the intervention period, a practice of placing a reusable canister for biliary refeeding on the hopper cover was noted [21]. This practice was modified following education of nursing staff 4 months into the intervention period to use a new canister with each biliary collection; there were no additional events with biliary collection noted in subsequent audits.

Environmental Analysis
All hoppers were sampled in a point-prevalence survey prior to the installation period; during this survey, 74% (53/72) were positive for KPCO (Enterobacteriaceae or Aeromonas spp). Thirty-one percent (22/72) of hoppers had multiple species (Table 2). Sink traps and drains were sampled in the SICU prior to installation of the sink trap devices, with 80% (12/15) of patient sinks positive for KPCO (by drain swab, sink trap water, or both), with a similar variety of species (Table 2). For nonpatient sinks located in common areas, the 2 staff bathroom sinks were positive for KPCO and the other 6 nonpatient sinks were negative. During the intervention period, SICU sink drains and sink traps were sampled nearly weekly, with 56 complete sampling events. KPCOs were identified in 40/840 (4.8%) sink samples, representing a significant decrease compared to baseline (12/15 [80%]; P = .0001). During the intervention, positive sinks were distributed across the unit, often positive when a colonized patient was in the room.

DISCUSSION
Here, we demonstrate that environmental interventions that targeted wastewater in ICUs decreased nosocomial acquisition of multispecies KPCOs for patients exposed to those units and across an entire hospital. While the bundled intervention included both hopper covers in all adult ICUs as well as sink trap devices in a single surgical ICU, the impact on transmission appears to have been driven by the use of hopper covers.

Hospital wastewater is an ideal environment for the development of drug resistance [21], as antimicrobials excreted in urine and stool collect in wastewater and result in significant selective pressure [22]. In addition, systems are continuously "seeded" with antibiotic-resistant bacteria from colonized patients. This environment can facilitate the exchange of resistance genes and mobile genetic elements among multiple species [4, 23]. Enhanced infection control practices recommended by the CDC...
focus on patient-to-patient transmission CRO, which may be insufficient for nosocomial acquisition during multispecies outbreaks [13, 24, 25]. Indeed, data demonstrating efficacy of the toolkit interventions have been derived largely from clonal outbreaks such as those with KPC-ST-258 K. pneumoniae [26, 27]. Our results suggest that KPCO acquisition is multifactorial where an intervention in hopper units had an impact hospital wide. We speculate that this reflects a decrease in new patient reservoirs that then get transferred to nonhopper units where acquisition may be driven by patient-to-patient transmission [13]. This effect may be seen within our institution because of the high level of KPCO awareness and years of experience in adhering to the CDC toolkit throughout the study periods [13, 16].

Most studies of CRO-associated environmental transmission have focused on sink drains [5]. Similar sink trap devices were successful at controlling an outbreak of Pseudomonas aeruginosa in a neonatal unit and an extended-spectrum β-lactamases–Klebsiella oxytoca outbreak in an adult ICU [28, 29]. The low number of events and bundled nature of our intervention limited our ability to assess the efficacy of the sink trap intervention alone. We demonstrate that the sink trap device considerably decreased, but did not eliminate, KPCO culture positivity of drain and sink trap samples, with 40 KPCO-positive sink drains/sink trap cultures following installation. Additional work is needed to fully evaluate the impact of sink trap devices in reducing transmission of KPCO from the environment to patients and in preventing the seeding of drains with patient-derived KPCO. The elimination of entrenched KPCO may require the removal of water and drainage systems from the ICU patient rooms, as recently demonstrated with other gram-negative organisms [7].

The cost for 60 hopper covers was $48,000 (including installation costs) and $50,000 for 23 sink trap heaters ($3000 per unit without installation or maintenance costs). Hopper covers are not required by the current US environmental hospital standards [30]; however, hoppers are required to be in an enclosed room separated from patient rooms. This standard was not in place when the hospital was built more than 30 years ago, but the hoppers were behind a lateral barrier (Figure 1). Even in an enclosed room, contamination of the environment in close proximity to the patient could potentially occur following flushing of an uncovered hopper or toilet [12].

Although CROs have been identified in hospital effluent [21, 31], there has been limited recognition of highly resistant organisms in toilet/hopper water, as was shown in our point prevalence survey. There was no intervention to alter the presence of KPCO in hopper water, although we did not perform longitudinal surveillance to assess this. The species profile of KPCO seen in the wastewater was consistent with that observed in our patient population, suggestive of exchange between the two. The principle behind hopper flushing is similar to that of a high-energy pressure-flushed toilet (rather than a gravity-flushed toilet), which generates

### Table 2. Species Breakdown of Patient and Environmental *Klebsiella pneumoniae* Carbapenemase–Producing Organisms from Different Time Points

<table>
<thead>
<tr>
<th>Species</th>
<th>Patient Clinical and Surveillance Isolates</th>
<th>Environmental Samples</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Species per Unique Patient</td>
<td>Environmental Samples</td>
</tr>
<tr>
<td></td>
<td>Species per Unique Hopper (Adult ICUs)</td>
<td>Species per Unique Sink Drain and Sink Trap (Surgical ICU Only)</td>
</tr>
<tr>
<td>Total</td>
<td>Preintervention</td>
<td>Intervention</td>
</tr>
<tr>
<td></td>
<td>56 patients</td>
<td>30 patients</td>
</tr>
<tr>
<td></td>
<td>Baseline Positive Hopper (1 Sampling)</td>
<td>Baseline Positive Sink (1 Sampling)</td>
</tr>
<tr>
<td></td>
<td>12/15 (80%)</td>
<td>40/840 (5%)</td>
</tr>
<tr>
<td><em>Serratia marcescens</em></td>
<td>32</td>
<td>39</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em></td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td><em>Enterobacter cloacae complex</em></td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td><em>Citrobacter freundii</em></td>
<td>8</td>
<td>7</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td><em>Klebsiella oxytoca</em></td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td><em>Aeromonas spp.</em></td>
<td>4</td>
<td>22</td>
</tr>
<tr>
<td><em>Enterobacter aerogenes</em></td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td><em>Kluyvera intermedia</em></td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><em>Morganella morganii</em></td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td><em>Pantoea spp.</em></td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td><em>Raoultella sp.</em></td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td><em>Citrobacter spp. (non-C. freundii)</em></td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Other <em>Enterobacteriaceae</em></td>
<td>0</td>
<td>5</td>
</tr>
</tbody>
</table>

Abbreviation: ICU, intensive care unit.
the maximum number of droplets during flushing compared to other mechanisms [9] and represents a plausible explanation for dispersal of organisms in rooms that contain open hoppers or toilets.

There are several limitations to our study. Because our interventions were implemented as part of a quality effort to decrease transmission of KPCO, it was felt that both hopper covers and sink trap devices should be implemented simultaneously on the highest-risk unit (the SICU), which limited our ability to demonstrate independent effects of each intervention. As with any observational study, other events may have had an impact on reduced KPCO acquisition. Of note, hand-hygiene rates were relatively constant throughout the study period [16]. In month 13 of the intervention period (22 May 2017), the primary cleaning product used in the hospital was changed from a quaternary ammonium to a peracetic acid-based disinfectant. While the incident rate of KPCO acquisition dropped before the change in cleaning product, this does represent a third of the intervention period. With respect to laboratory testing methods, we changed to a more sensitive phenotypic carbapenemase detection method during the intervention (February 2017), which may have also had an impact on culture positivity. However, this intervention is likely to have led to an underestimation of the effect of our intervention (i.e., increased ascertainment of KPCO) [14, 17]. Last, we did not use molecular typing of isolates from patients or the environment that could provide additional resolution around transmission events.

In conclusion, hospitals must understand and assess the role of hospital wastewater plumbing in multispecies CRO transmission to facilitate appropriate interventions. The modes of CRO transmission are likely multimodal (i.e., environment-person, person-to-person, person-environment) and may be different in different contexts. Assessing the relative contribution of each mode of transmission is key to implementing appropriate interventions. Awareness of possible hopper/toilet-associated transmission of resistant gram-negatives contributes to mitigating these reservoirs. Installation and use of hopper and toilet covers represents a low-cost, acceptable, and effective intervention in these contexts.

Supplementary Data
Supplementary materials are available at Clinical Infectious Diseases online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Financial support. This work was supported by a contract from the Centers for Disease Control and Prevention (CDC) Broad Agency Announcement (BAA 2016-N-17812). D. W. C. and N. S. were supported by National Institute of Health Research (NIHR) NIHR Biomedical Research Centre, NIHR Oxford Health Protection Research Units on Healthcare Associated Infection and Antimicrobial Resistance, at University of Oxford in partnership with Public Health England (grant HPRU-2012-10041).

Potential conflicts of interest. All authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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