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# The novel application and effect of an ultraviolet light decontamination strategy on the healthcare acquisition of carbapenem-resistant Enterobacterales in a hospital setting

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SUMMARY

***Background:*** The role of the hospital environment as contributory to healthcare acquisition of multidrug-resistant organisms (MDROs) is increasingly recognized. Ultraviolet light decontamination can minimize the environmental bioburden, thereby potentially reducing healthcare acquisition. This effect has been demonstrated for typical environmental MDROs, e.g. meticillin-resistant *Staphylococcus aureus*, vancomycin-resistant enterococci, and *Clostridioides difficile*; however, its role in reducing carbapenem-resistant Enterobacterales (CRE) incidence rates is unclear.

***Aim:*** To evaluate the impact of continuous ultraviolet light (C-UV) on healthcare acquisition rates of CRE.

***Methods:*** A 26-month pragmatic, prospective interventional study with addition of C-UV decontamination to standard cleaning was conducted in units at high risk for CRE acquisition. Introduction of C-UV followed a 12 month baseline period, with a two-month wash-in period. Implementation included terminal decontamination at discharge and a novel in-use protocol, whereby rooms occupied for $\geq$48 h were decontaminated during the course of the patients' in-hospital stay. Incidence density rates of CRE during the intervention period were compared to the baseline period using interrupted time series regression. Rates were adjusted for ward/admission prevalence and analysed according to C-UV protocol.

***Findings:*** The in-use C-UV protocol demonstrated a significant negative association with the incidence density rate of CRE when adjusting for CRE admission rate ($P = 0.0069$). CRE incidence density rates decreased significantly during the intervention period ($P = 0.042$). Non-intervention units demonstrated no change in incidence density rates when adjusting for ward and/or admission prevalence.

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***Conclusion:*** C-UV decontamination can potentially reduce healthcare acquisition of CRE when implemented with an in-use protocol.


## Introduction

Current infection prevention and control (IPC) efforts place emphasis on the role of the hospital environment in contributing to the transmission of micro-organisms. The transmission of multidrug-resistant organisms (MDROs) is facilitated by contaminated surfaces and the suboptimal cleaning and decontamination of the environment. *Clostridioides difficile*, meticillin-resistant *Staphylococcus aureus* (MRSA), and vancomycin-resistant enterococci (VRE) have all been shown to contaminate the environment through prolonged shedding and persistence on inanimate objects [1]. This increased bioburden creates opportunities for dissemination via contaminated hands and equipment. Thus cleaning of the hospital environment is considered a critical component of the IPC strategy in reducing the risk of horizontal transmission [2].

Currently multidrug-resistant Gram-negative bacilli (MDR-GNB), including extended-spectrum β-lactamase-producing Enterobacterales (ESBL-E) and carbapenem-resistant Enterobacterales (CRE), pose a significant challenge in terms of treatment and control. Evidence suggests that contamination of the environment plays an important role in the transmission of enteric MDR-GNB such as ESBL-E and CRE [3]. Strategies to prevent acquisition of these MDR-GNB are multifaceted with environmental decontamination considered an important intervention alongside hand hygiene, contact precautions, isolation, and antimicrobial stewardship [4,5].

Touchless technologies for environmental decontamination have gained prominence and there is a growing body of evidence that these technologies provide incremental benefit to traditional cleaning methods [6]. However, the evidence considered in context of a hierarchical schema from laboratory to bedside has not demonstrated robust evidence for reductions in hospital-acquired infections (HAIs) [2,7,8].

Ultraviolet (UV) light has been evaluated in numerous clinical studies and many of these have demonstrated a reduction in HAI rates. The majority of these have focused on Gram-positive MDROs, specifically *C. difficile* infection (CDI), with many studies demonstrating a statistically significant reduction in CDI rates [2]. By contrast, the BETR study, a multicentre randomized control trial, did not demonstrate a reduction in CDI infection rates when UV light was added to bleach-based cleaning [7]. With respect to MDR-GNB, a study by Rock *et al.* evaluated the efficacy of continuous UV (C-UV) light on CRE. They demonstrated a $>5$ $\log_{10}$ reduction in CRE isolates on high-touch surfaces when exposed to 15 min of C-UV [9]. There is scant evidence that C-UV can reduce HAI rates due to CRE. Haas *et al.* evaluated the impact of pulsed-UV on multiple MDROs, including MDR-GNB. They demonstrated a statistically significant reduction in MDRO rates from 0.52 to 0.42 per 1000 patient days [10]. The study did not specify organism types and likely included *Pseudomonas aeruginosa* and *Acinetobacter baumannii*.

The aim of the present study was to evaluate the impact of C-UV decontamination on the hospital epidemiology of MDRO, with particular focus on CRE, in a single-centre hospital. The hypothesis for the study was that introduction of C-UV, as a component of the environmental decontamination strategy, would reduce healthcare acquisition of CRE by reducing the environmental bioburden of organisms. To test the hypothesis, a prospective, pre/post intervention trial design was used in five units with a high-risk for acquisition of these organisms.

## Methods

### *Setting*

The Wits Donald Gordon Medical Centre (WDGMC) is a 210-bed quaternary referral hospital specializing in the care of complex medical and surgical patients including oncology and transplant. Baseline prevalence and incidence data from the hospital's MDRO surveillance system were used to identify and target five high-risk units for intervention. These high-risk units were critical care, oncology, transplant and gastrointestinal surgery units, where the incidence density rates of CRE are high. The three remaining units in the hospital (paediatric oncology, medical, geriatrics and non-gastrointestinal surgery) with low incidence density rates of CRE were utilized as controls. The units are comprised of mixed single, double, and multiple occupancy rooms. MDRO patients are isolated in single rooms where possible, or cohorted if harbouring same MDRO.

### *Standard practices*

#### *Cleaning*

Standard cleaning of units takes place according to the Mediclinic corporate hospital policy. Daily cleaning of all surfaces in units is done with detergent (quaternary ammonium compound) and water, with bathrooms and toilets disinfected with a 1:1000 hypochlorite solution. In critical care units, surfaces are disinfected twice daily with 1:1000 hypochlorite solution. Terminal cleaning of units occupied by patients harbouring an MDRO involves disinfection of all surfaces with a 1:1000 hypochlorite solution following standard cleaning with detergent and water.

#### *MDRO surveillance system*

Denominator data is captured from the existing IPC hospital surveillance system and includes patient bed-days (inpatient days) per unit and entire facility, and number of admissions for the entire facility [11]. Laboratory-identified MDRO events are categorized according to the SHEA/HICPAC recommendations, as outlined in the NHSN MDRO/CDI module protocol [12,13]. Briefly, a healthcare facility onset (HO) event includes all clinical specimens collected after three days (i.e. on day 4 or after) in hospital, and a community onset (CO) event includes all clinical specimens submitted within three days of admission. Measures for exposure burden and healthcare acquisition are as per the current CDC definitions and include admission prevalence rate, overall patient prevalence rate and overall

infection/colonization incidence density rate [12]. The definition of a CRE is as per the CDC MDRO protocol with the exception that it includes any Enterobacterales isolate and is not limited to *E. coli*, *Klebsiella pneumoniae*, *Klebsiella oxytoca*, and *Enterobacter* species. Patients are routinely screened for MRSA (nasal swab) and CRE (rectal swab) upon admission to the hospital. Patients identified from these screening cultures are isolated and placed on contact precautions. Being a referral hospital with many patients admitted frequently for follow-up, known MDRO patients are automatically placed in isolation and on contact precautions upon admission.

### Study design

The baseline period was January 1st to December 31st, 2018. The intervention period was January 1st, 2019 to February 28th, 2020, including a two-month wash-in period (January to February 2019). The intervention was the addition of C-UV environmental decontamination to standard cleaning/disinfection for rooms during and after occupation by patients with a CRE isolated from a clinical specimen.

A pragmatic design was used to incorporate C-UV decontamination into the standard practice of cleaning and disinfection. Cleaning personnel within the designated service provider's staff complement were trained on how and when to use the UVDI-360 room sanitizer (UltraViolet devices, Inc., Santa Clarita, CA, USA). The single instrument was operational daily between 07:00 and 19:00. Cycles were preset at 5 min per cycle with number of cycles per room determined by size of room (maximum of 2.5 m radius from centred position of instrument per cycle). Number of cycles and average cycle time were captured using data directly downloaded from the instrument. The research team was not operationally involved in the management and use of the C-UV instrument. The research team coordinated the implementation phase, provided training and technical support, and collected the data. This was considered a pragmatic approach as we were interested in observing the impact of the C-UV decontamination in a real-world setting, where resource limitation and compliance to IPC protocols are a constant challenge.

Any room, including multi-occupancy rooms, in the designated units was eligible for C-UV decontamination according to the following three protocols: after being vacated by a patient due to (i) discharge (D); (ii) transfer to another unit (T); (iii) in-use room (I), where the room was occupied by patients with an MDRO for a period $\geq$48 h. In these instances patients were either encouraged to vacate the room (under IPC guidance for contact precautions), or decontamination was undertaken when rooms were vacated for medical/surgical management reasons, e.g. theatre, radiology, physiotherapy. The rationale for the I-protocol was that environmental contamination during a patient stay is extensive and the increasing bioburden of organisms in occupied rooms may contribute significantly to horizontal transmission.

No other targeted IPC interventions were implemented for the entire study duration. The same temporal and spatial surveillance definitions that were followed in the baseline period were applied throughout the study period. Given the pragmatic nature of the study and the intention to assess the compliance with study protocol, the number of qualifying decontamination opportunities and number of actual rooms decontaminated was also recorded. Additional IPC measures that were monitored during the baseline and study period included the following: data on hand hygiene compliance, environmental cleaning quality, overall prevalence of MDROs and antimicrobial consumption.

The study was designed and conducted in accordance with the ORION statement [14]. The study was approved by the University of the Witwatersrand Human Research Ethics Committee (clearance number: M160657).

### Data analysis

Surveillance denominator data is captured and stored on the REDCap system [15]. Clinical specimen MDRO data is collated by the ICNET™ clinical surveillance software and then imported into an Excel database. Facility-wide and unit-specific overall patient prevalence and colonization/infection incidence density rates per 1000 patient-days are calculated on a monthly basis. Facility-wide and unit-specific admission prevalence rates per 100 admissions are also calculated on a monthly basis.

The rate of C-UV decontaminations for protocols I, and D + T combined, per 1000 patient-days was calculated for each ward for each month.

The primary outcome was the unit-specific colonization/infection incidence density rate for CRE, comparing the intervention and baseline periods. Overall patient prevalence rate and admission prevalence rate per unit were also assessed to account for colonization pressure and its impact on incident cases of hospital-onset infection, during the two periods.

The following analyses to assess the primary outcomes were done for intervention units as well as non-intervention units:

Rate ratios with corresponding 95% confidence intervals and tests for trends in rates within each study period (baseline and C-UV) were estimated using Poisson regression according to four different models:

- A: unadjusted;
- B: controlling for ward;
- C: controlling for ward and admission rate of the organism;
- D: controlling for admission rate of the organism.

The change in incidence rate between the two study periods was compared using an interrupted time series (ITS) regression model.

The effect of the number of I-protocol decontaminations and the number of (D + T) C-UV decontaminations per 1000 patient-days on the incidence density rate during the C-UV period in the intervention wards was determined by Poisson regression, using the four model specifications (A–D) listed above.

Data analysis was carried out using SAS version 9.4 for Windows. $P < 0.05$ was considered significant.

## Results

### C-UV decontamination use

During the intervention period in the targeted units, there were 6081 discharges and 312 terminal cleaning opportunities as defined by patients placed under contact isolation

precautions. There were 304 patients that occupied a room for ≥48 h and were thus eligible for the I-protocol. The median stay of these 304 patients was 2.6 days (range: 2.4–123) with a cumulative stay of 2746.2 days. Overall, C-UV was performed 4861 times with D-protocol decontamination comprising the majority (64%, $N = 3134$), and I-protocol decontamination the minority (9%, $N = 460$). There was a decline in the total number of decontaminations over the course of the intervention period, reflected in the I and (D + T) rates per 1000 patient-days (Figure 1).

### *Overall impact of C-UV decontamination on healthcare acquisition of CRE*

The overall CRE incidence density rates were stable for the 12 months before use of C-UV (baseline) ($P_{trend} = 0.79$) and for the 12 months during C-UV ($P_{trend} = 0.20$) (Figure 2). The incidence density rate in the C-UV period did not differ significantly from that in the baseline period (2.59 vs 3.38 cases per 1000 patient-days ($P = 0.072$), respectively) (Table I). Adjusting for ward and/or admission rates did not change this finding although the effect was marginally non-significant ($P = 0.065$ and 0.053). The effect of admission rate was significant in models C ($P = 0.020$) and D ($P < 0.0001$) with a positive association between CRE admission rates and incidence density rate (the incidence density rate increases by ~0.1 cases per 1000 patient-days for every one-unit increase in CRE admission rate).

The ITS regression demonstrated a significant decrease in the incidence density rate during the C-UV intervention period ($P = 0.042$).

In the non-intervention wards, overall rates of infection were stable for the 12 months before use of C-UV (baseline; $P_{trend} = 0.99$) and for the 12 months during C-UV in other wards ($P_{trend} = 0.89$) (Figure 3). The rate of infection in the C-UV period did not differ significantly from that in the baseline period (0.99 vs 1.16 cases per 1000 patient-days ($P = 0.62$), respectively) (Table I). Adjusting for ward and/or admission rates did not change this finding. In the ITS regression the incidence density rate of CRE in the C-UV period did not differ significantly from that in the baseline period ($P = 0.75$) (Table I). Adjustment according to the models demonstrated no significant effect and no significant association between CRE admission rates and incidence density rates were seen.

### *Per-decontamination protocol impact of C-UV decontamination on healthcare acquisition of CRE*

Unadjusted, the rate of I-protocol decontaminations had a negative relationship with the incidence density rate of CRE, while the rate of (D + T)-protocol decontaminations had a positive relationship with the incidence density rate of CRE. These relationships were not significant after controlling for ward with and without the CRE admission rate (models B and C). Controlling only for CRE admission rate (model D) indicated that the rate of I-protocol decontaminations had a negative relationship with the incidence density rate of CRE ($P = 0.0069$; incidence density rate decreases by ~0.02 cases per 1000 patient-days for every one-unit increase in decontamination rate), while the incidence density rate of CRE was positively associated with the CRE admission rate ($P = 0.0013$; incidence

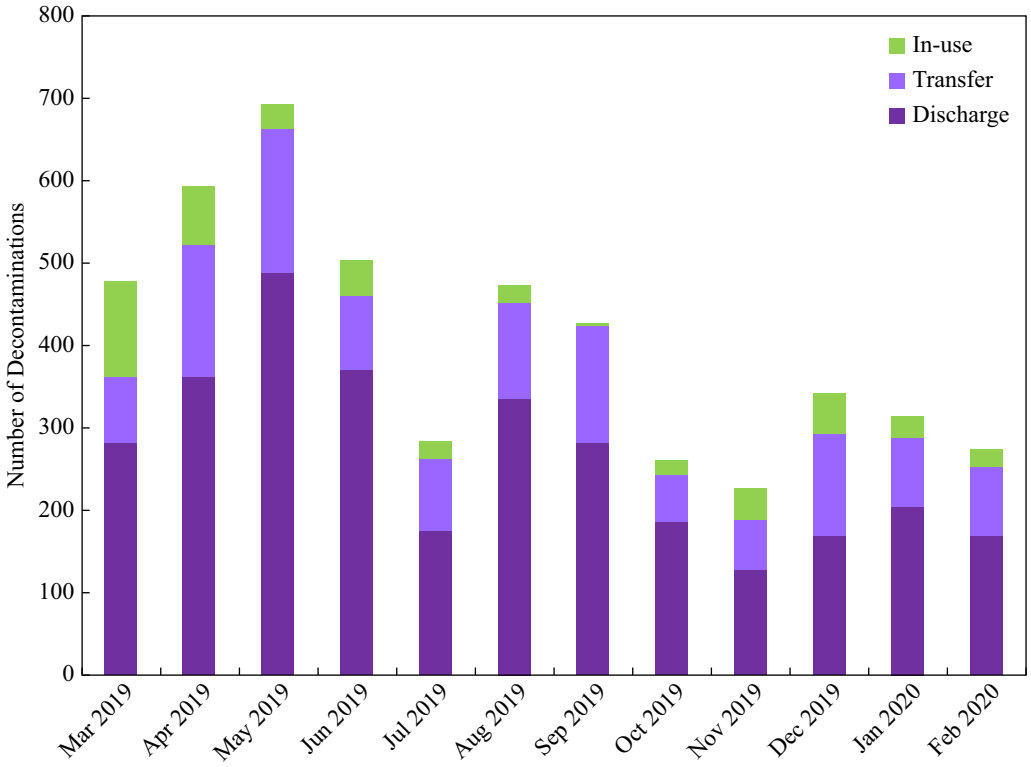


**Figure 1.** Number of decontaminations per protocol during the intervention period.

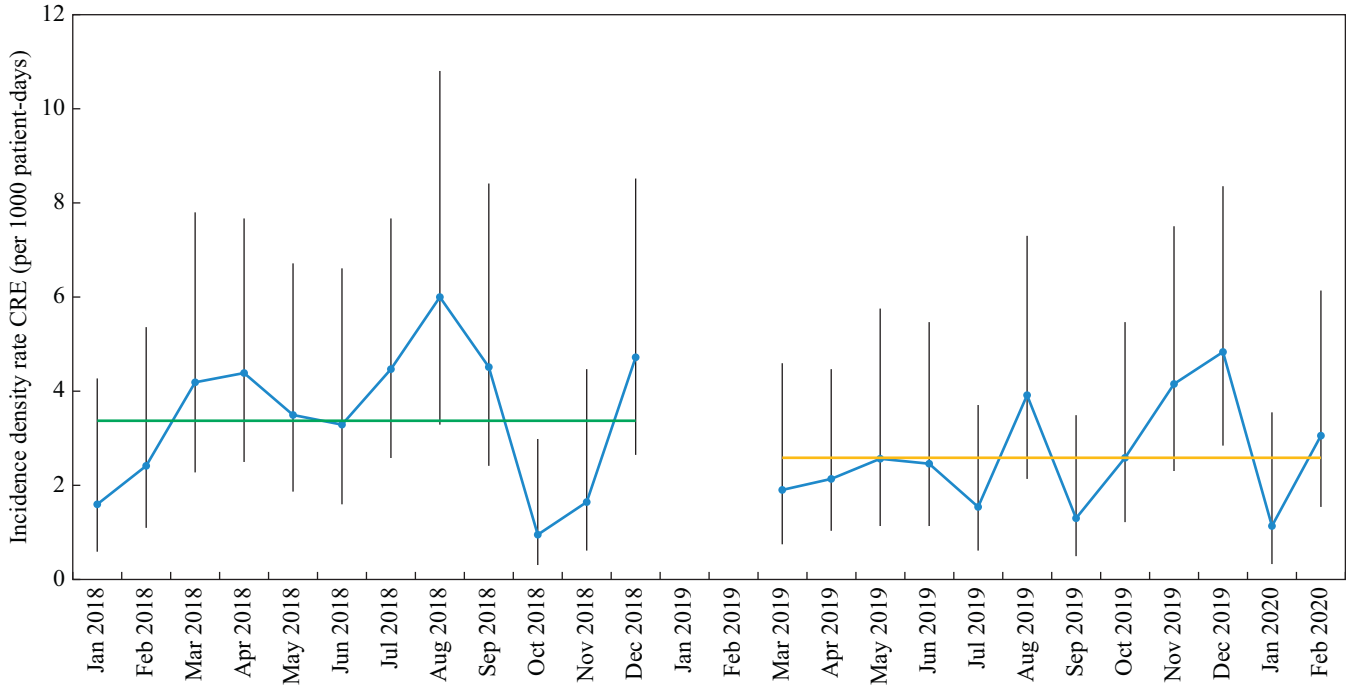


**Figure 2.** Incidence density rate of carbapenem resistant Enterobacterales (CRE) in baseline and intervention periods for intervention wards (95% confidence intervals). Green line: mean baseline incidence density rate of CRE per 1000 patient-days. Orange line: mean continuous ultraviolet light intervention incidence density rate of CRE per 1000 patient-days.

density rate increases by ~0.1 cases per 1000 patient-days for every one-unit increase in CRE admission rate) (Figure 4).

## Discussion

This was a pragmatic, pre/post-intervention study aimed at assessing the effectiveness of C-UV in reducing healthcare acquisition of CRE. The addition of C-UV to standard cleaning was found to reduce the incidence density rate of CRE when C-UV is implemented concurrently in rooms occupied by CRE-colonized patients. The pragmatic nature of the study, with no direct involvement of the research team, was aimed to evaluate the use of this technology in a real-world setting.

**Table I**
Incidence density rates of hospital-acquired carbapenem-resistant Enterobacterales before and during ultraviolet decontamination

| Model | Before ultraviolet decontamination January 2018 to December 2018 | | During ultraviolet decontamination March 2019 to February 2020 | | Rate ratio (95% CI), *P*-value | Coefficient for admission rate (*P*-value) in incidence density rate regression | ITS regression: *P*-value for comparison between periods |
|---|---|---|---|---|---|---|---|
| | No. | Rate (/1000 patient-days) | No. | Rate (/1000 patient-days) | | | |
| Intervention wards | | | | | | | |
| Model A[a] | 101 | 3.38 | 85 | 2.59 | 0.77 (0.58–1.02), 0.072 | – | 0.042 |
| Model B[b] | | | | | 0.77 (0.57–1.02), 0.065 | – | |
| Model C[c] | | | | | 0.76 (0.57–1.02), 0.065 | 0.052 ($P = 0.020$) | |
| Model D[d] | | | | | 0.75 (0.56–1.00), 0.053 | 0.10 ($P < 0.0001$) | |
| Non-intervention wards | | | | | | | |
| Model A[a] | 22 | 1.16 | 18 | 0.99 | 0.85 (0.46–1.59), 0.62 | – | 0.75 |
| Model B[b] | | | | | 0.85 (0.46–1.59), 0.62 | – | |
| Model C[c] | | | | | 0.84 (0.45–1.57), 0.59 | 0.050 ($P = 0.51$) | |
| Model D[d] | | | | | 0.84 (0.45–1.57), 0.59 | 0.048 ($P = 0.51$) | |

CI, confidence interval; ITS, interrupted time series.
[a] Unadjusted.
[b] Controlling for ward.
[c] Controlling for ward and admission rate of the organism.
[d] Controlling for admission rate of the organism.

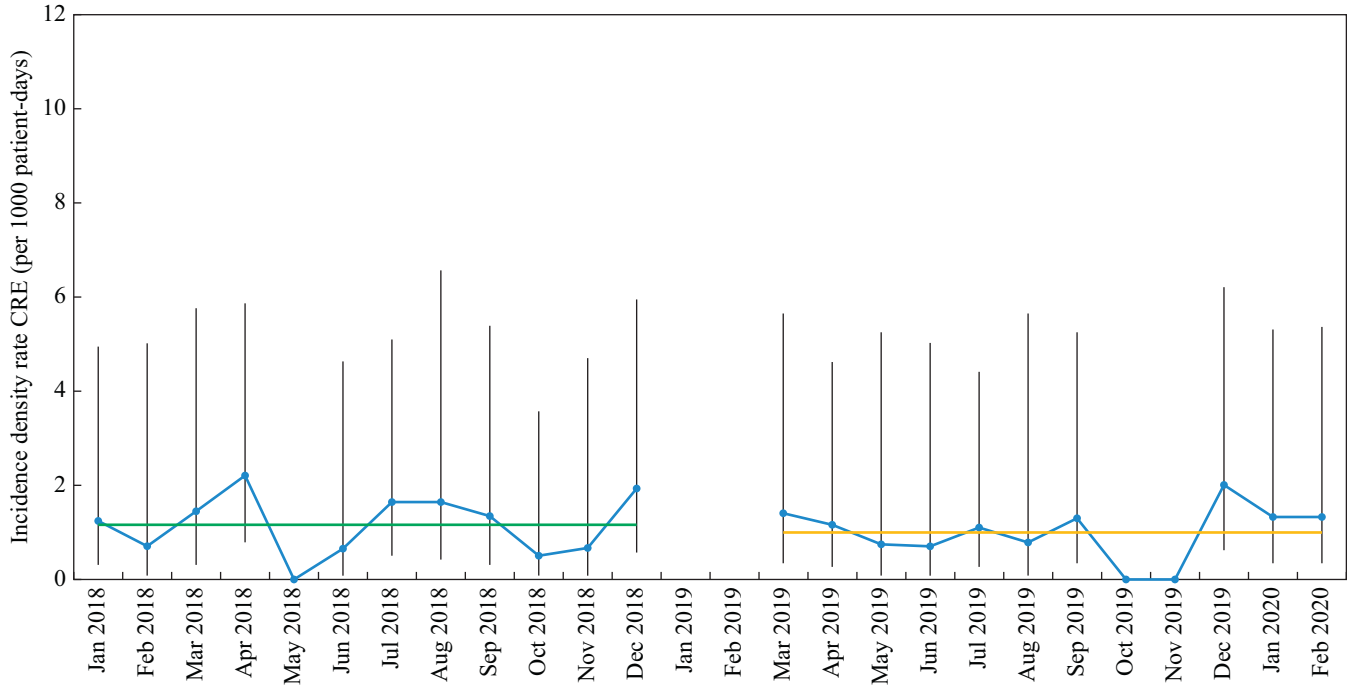


**Figure 3.** Incidence density rate of carbapenem-resistant Enterobacterales (CRE) in baseline and intervention periods for non-intervention wards (95% confidence intervals). Green line: mean baseline incidence density rate of CRE per 1000 patient-days. Orange line: mean continuous ultraviolet light intervention incidence density rate of CRE per 1000 patient-days.

The role of no-touch environmental decontamination remains controversial despite mounting evidence of its effectiveness. In our institution the environmental cleaning service is outsourced with the service provider held accountable to a defined standard according to hospital policy. The service is periodically audited but operationally the service provider is independent and we aimed to establish the feasibility of adding C-UV to environmental decontamination. The implementation thereof proved challenging as seen by a progressive decline in usage over time and low adherence to the I-protocol.

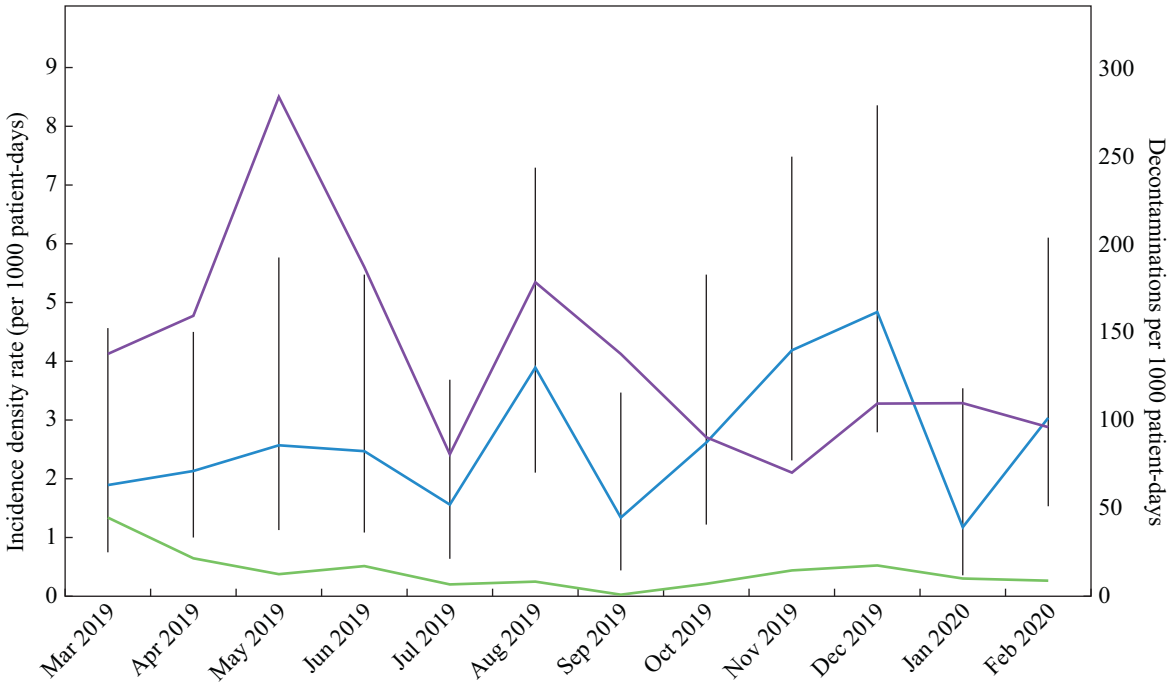


**Figure 4.** Incidence density rate of carbapenem-resistant Enterobacterales (CRE) relative to the per-protocol decontamination rates (95% confidence intervals). Green line: in-use protocol continuous ultraviolet light rate per 1000 patient-days. Purple line: discharge/transfer protocol continuous ultraviolet light rate per 1000 patient-days. Blue line: incidence density rate of CRE per 1000 patient-days.

The I-protocol was a novel and important component of our study as it was our hypothesis that use of C-UV, while patients were occupying a room, would reduce the bioburden of organisms leading to a reduction in the potential for horizontal transmission events. The well-described risk of increased acquisition of MDRO from rooms previously occupied by patients harbouring these same organisms supports the rationale [16]. Furthermore, a post-hoc analysis of the BETR study demonstrated an increased risk of target organism acquisition following admission to a room previously occupied by a patient harbouring that organism, with the addition of C-UV in a targeted manner mitigating this effect [17]. However, this is typically seen for established hospital-associated environmental organisms such as VRE, *C. difficile*, and *A. baumannii* where no-touch decontamination as a means to reduce infection rates is supported by a growing literature [2,18]. The Enterobacterales are a very different proposition in terms of epidemiology and the current evidence for non-touch technologies in reducing infection rates associated with these organisms is limited.

CRE are the predominant MDRO in our institution and we consistently see a positive correlation between the incidence density rate and overall prevalence rate. This is largely impacted by the patient population served by the hospital, where patients have chronic conditions requiring multiple admissions. These same patients are colonized with CRE, hence the admission prevalence contributes significantly to overall prevalence rate. We found a significant inverse relationship between the rate of I-protocol decontamination and the incidence density rate of CRE, when adjusted for CRE admission. To our knowledge this is the first study to demonstrate this finding and it provides evidence for a novel application of C-UV. Addition of C-UV to environmental decontamination should include a targeted I-protocol, whereby rooms are disinfected while occupied by patients harbouring a CRE. Waiting for patients to be discharged before adding C-UV to the decontamination protocol results in an increased bioburden with potential for horizontal transmission. Our ITS model demonstrated a significant reduction in the incidence density rate of CRE during the intervention period. Given that the I-protocol was only used 460 times out of a possible 1373 (34% compliance), the effect could possibly be even more significant as the difference in overall incidence density rates comparing baseline to intervention was marginally non-significant.

These results also suggest that the admission prevalence rate could be used as a proxy for establishing the intensity of C-UV decontamination required, as the effect of the I-protocol appears more pronounced with increasing admission prevalence. It thus seems prudent to utilize UV-C technology in a more targeted manner, directed by the hospital epidemiology.

Although not a primary outcome of our study, we did monitor (using the same methodology) the effect of the addition of C-UV to standard cleaning and disinfection on the incidence density rate of *C. difficile* — which is the second most problematic organism in our institution and thus we were interested in any potential effects. No significant effect on incidence density rate of *C. difficile* was found, irrespective of method of analysis. This was not unexpected as we used one standard protocol, irrespective of organism type, and thus *C. difficile* rooms were not treated differently. The 5 min protocol was probably insufficient exposure time for *C. difficile*, where a cycle time of $\geq$10 min is required to achieve a $>$3 $\log_{10}$ reduction in spores on direct surfaces [19]. By contrast, a 5 min cycle for CRE has demonstrated a $>$5 $\log_{10}$ reduction for direct surfaces and $>$4 $\log_{10}$ reduction for indirect surfaces [20]. The effect of an I-protocol with a longer cycle time on the incidence density rate of *C. difficile* may show benefit and requires further investigation.

There are several limitations of this single-centre study. Our predominant CRE type is the carbapenemase OXA-48$_{like}$ genotype and there are possibly different transmission determinants for different CRE types, hence our results may not be generalizable across different settings with different MDR-GNB profiles. We did not assess the impact of C-UV on other MDROs (VRE, MRSA) due to the low prevalence and incidence of these MDROs in our institution. At an operational level our pragmatic design highlighted a number of implementation challenges. The C-UV instrument was sponsored for the duration of the study and we had access to only one instrument. Therefore we had to select carefully where and how to use the instrument. We selected those units with the highest prevalence and incidence of CRE. This targeted adoption of the technology meant that there were often competing interventions due to the high occupancy rate of the hospital. This selective use may have limited the true impact of the intervention as patients are frequently transferred between units, evident from the 27% T-protocol usage. Conversely, a targeted implementation plan dictated by admission prevalence may prove to be of greater value than the typical shotgun approach. Practically the implementation of an I-protocol was challenging, as patients require education around the benefits thereof and coordination between ward and cleaning staff is necessary. Further use of the instrument will now focus on improved compliance with the I-protocol and correlation with admission prevalence to ensure sustainability and determine whether a further reduction in incidence density rates is possible.

One strength of our study is that no additional targeted IPC interventions were introduced during the study period and our surveillance data support these findings. We monitored antimicrobial use, hand hygiene and environmental cleaning for all units throughout the study period, with no significant changes implemented or differences noted between the two periods. The non-intervention wards were used as a control group to assess for external influences and found no significant effect on incidence density rates, suggesting that the observed effect was directly attributable to introduction of C-UV light. We acknowledge that the control group of units comprises a different set of patients who are possibly at lower risk of CRE colonization/infection; however, these units do not have an insignificant number of CRE patients (incidence density rate of $\sim$1 per 1000 inpatient days) and these patients are managed according to the same IPC principles applied elsewhere in the hospital. Future application of the I-protocol in these lower density settings is warranted to determine whether a similar reduction can be achieved.

In summary, C-UV is potentially an important component of an enhanced decontamination protocol for the control of CRE in a hospital setting. This benefit is not dependent on a terminal decontamination strategy but requires targeted implementation based on admission prevalence and adoption of an I-protocol.

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**Conflict of interest statement**
None declared.

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