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Control of endemic multidrug-resistant Gram-negative bacteria after removal of sinks and implementing a new water-safe policy in an intensive care unit

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SUMMARY

Background: Contaminated handwashing sinks have been identified as reservoirs that can facilitate colonization/infection of patients with multidrug-resistant (MDR) Gram-negative bacteria (GNB) in intensive care units (ICUs).

Aim: To assess the impact of removing patients' sinks and implementing other water-safe strategies on the annual rates of ICU-acquired MDR-GNB.

Methods: This six-year quasi-experimental study was conducted from January 2011 to December 2016. The intervention was carried out in August 2014 in two adult ICU wards with 12 rooms each. To assess the changes in annual MDR-GNB rates before and after the intervention, we used segmented regression analysis of an interrupted time-series. Crude relative risk (RR) rates were also calculated.

Findings: The incidence rates of MDR-GNB were 9.15 and 2.20 per 1000 patient-days in the pre- and post-intervention periods, respectively. This yielded a crude RR of acquiring MDR-GNB of 0.24 (95% confidence interval: 0.17–0.34). A significant change in level was observed between the MDR-GNB rate at the first point of the post-intervention period and the rate predicted by the pre-intervention time trend.

Conclusion: The implementation of a new water-safe policy, which included the removal of sinks from all patient rooms, successfully improved the control of MDR-GNB spread in an ICU with endemic infection. Our results support the contribution of sink use with the incidence of MDR-GNB in endemic environments.

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Introduction

Multidrug-resistant (MDR) Gram-negative bacteria (GNB) are a major problem in healthcare settings worldwide [1–3]. These bacteria are often involved in hospital outbreaks, and occur in intensive care units (ICUs) [4–7]. The hands of healthcare workers are the most important facilitator of cross-transmission from colonized/infected patients or from contaminated environments where micro-organisms may persist [8]. Sinks have also been associated with ICU outbreaks caused by MDR-GNB, especially *Pseudomonas* spp. and *Klebsiella* spp. [9,10].

Accepted measures for controlling outbreaks caused by these bacteria are hand hygiene, contact precautions, active patient screening and environmental cleaning [11–13]. However, some researchers have reported that removing sinks was also necessary for successful resolution of outbreaks [14,15]. Indeed, it has been shown that sinks continue to be contaminated by MDR-GNB in non-outbreak settings, especially when used for handwashing by healthcare workers and the disposal of body fluids. Therefore, sinks might contribute to the persistent spread of these bacteria in endemic settings [16–18].

In our ICU, we have shown that enhancing infection control measures, according to guidelines, facilitated the successful control of endemic *Acinetobacter baumannii* [11,19]. Despite maintaining these control measures, we continued to observe progressive increases in the numbers of patients who acquired clonal MDR *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* during their ICU stays. Molecular typing of MDR *K. pneumoniae* clinical isolates showed sequence types (ST) ST326 and ST101 as the dominant clones causing infections in the ICU [4]. Among the infections caused by MDR *P. aeruginosa*, ST175 was the major clone, followed by the carbapenemase producers ST235 and ST253 strains [7]. Since these bacteria are associated with damp environments, our infection control team hypothesized that sinks could be reservoirs of infection and they proposed to hospital managers the removal of sinks from ICU rooms.

Herein, we evaluate the impact of removing sinks from patients' rooms as a part of a new water-safe policy on the number of new patients acquiring MDR-GNB in our ICU department.

Methods

Setting and study design

This was a six-year quasi-experimental study that comprised a pre-intervention period of 43 months from January 2011 to July 2014 and a post-intervention period of 29 months from August 2014 to December 2016. Sinks were removed in August 2014. All interventions were performed at Bellvitge University Hospital, a 700-bed teaching hospital located in the southern metropolitan area of Barcelona that accepts referrals for more than two million people requiring high-complexity procedures. The intervention was implemented in two mixed (medical and surgical) adult intensive care wards, each with 12 single rooms.

Outcomes

The primary outcome was the annual rate for all new cases of ICU-acquired MDR-GNB bacteria, including both *K. pneumoniae* and *P. aeruginosa*. The secondary outcomes were the separate annual rates of new cases for ICU-acquired MDR *K. pneumoniae* and *P. aeruginosa*.

Figure 1. A sink before the intervention.

Definitions

For analysis, only *K. pneumoniae* producing extended-spectrum β-lactamases (ESBLs) and/or carbapenemase and extensively drug-resistant (XDR) *P. aeruginosa* (producing Verona integron-encoded metallo-β-lactamase (VIM) carbapenemase or not) were considered MDR-GNB. A new case was defined as an MDR-GNB recovered from a clinical sample in a patient hospitalized in the ICU for >48 h. For surveillance, we considered the first isolation in a clinical sample of each of the MDR-GNB per patient (infection or colonization). Isolates obtained from screening rectal swabs were not included.

Strategies for controlling MDR-GNB spread during the study period

Sinks and water policy

Pre-intervention. Each room had a wall-mounted sink with a shallow, stainless steel bowl and a plastic P-trap (Figure 1). The water spout flowed directly into the sink drain, causing splashes of water trapped in the P-trap. The distance from the sinks to the patients' beds or to the medication preparation area was ~1 m. There were no routine sink cleaning and disinfection programmes nor any barriers to prevent splashing. Healthcare workers used the sink water for handwashing and for maintaining patients' daily hygiene (for this, water was

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mixed manually with 4% chlorhexidine soap). Water used for maintaining patients' daily hygiene was discarded in the room sink.

Intervention. In August 2014, the two wards were closed to remove the sinks from all ICU rooms, leaving only two sinks in the central nurse room. We performed deep cleaning and disinfection of drains and valves in these central sinks and installed antibacterial water filters in the taps. Deep cleaning entailed disassembling the sink valve and scrubbing with detergent and disinfectant products. The external surfaces of the sinks were cleaned using microfibre cloths and hypochlorite solution. After the intervention, sinks and faucet surfaces were cleaned with a unique mop (specific for this purpose). Filters were replaced monthly according to the manufacturer's recommendations, and siphons and tap aerators were replaced every three months. Using filtered water from central sinks became mandatory for patient daily hygiene. Dirty water was discarded in a disposal room outside of the hospitalization area. From April 2015 forward, 2% chlorhexidine-impregnated washcloths were introduced in the ICU for patient hygiene when water was not needed.

Additional strategies applied concomitantly during the study period

Hand hygiene and contact precautions. Educational rounds to reinforce compliance with hand hygiene and contact precautions were regularly performed. Both application of alcohol-based solutions and washing hands with soap were permitted for hand hygiene, although using alcohol-based solution was strongly promoted. Patients colonized or infected with MDR-GNB were placed under contact precautions and retained under this condition until ICU discharge. Use of gloves and aprons was mandatory for entering the isolation room. Rooms were supplied with exclusive thermometer, blood pressure cuff, and stethoscope. Nurse cohorting was applied when possible.

Audits for hand hygiene in the ICU were performed at least once per year since 2010. In the pre-intervention period, compliance rate was 65%, and in the post-intervention period 70%. We did not perform audits for contact precautions.

Environmental cleaning. The current cleaning policies were introduced in February 2012 in the ICU [19]. Cleaning was performed using a microfibre cleaning system (TTS bucketless system; TTS, Santa Giustina in Colle, Italy); cloths were soaked in a basin containing 0.1% chlorine solution. Routine cleaning of high-touch surfaces was performed using disinfectant wipes with cationic surfactant tensioactifs, quaternary ammonium compounds, and polymeric biguanide (Clinell Universal Wipes; GAMA Healthcare, London, UK). Cloths were never shared between different rooms.

In 2016, ultraviolet light disinfection technologies were introduced in the hospital for performing terminal cleaning of isolated rooms.

Active surveillance cultures. An active surveillance programme was introduced in ICU in 1992 [20]. Over the study period, rectal swabs were performed at admission and weekly thereafter during the patient stay in the ICU if patient persisted with negative rectal swab. Adherence to this strategy varied during the period. During pre-intervention, the monthly average of rectal swabs performed was 48; during post-intervention, the monthly average was 52.

Antimicrobial stewardship programme. In April 2012, an antimicrobial stewardship programme was initiated to reduce antimicrobial consumption, especially for carbapenems and cephalosporins. The programme was based on an 'audit and feedback' strategy and performed by an infectious diseases physician and a pharmacist. Antimicrobial use was similar before and after the intervention.

Microbiological study

Isolates were obtained from clinical samples using standard microbiological methods. Identification was performed by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (Bruker Daltonik GmbH, Bremen, Germany) and the antimicrobial susceptibility by microdilution (MicroScan®; Beckman Coulter, Brea, CA, USA) using the European Committee on Antimicrobial Susceptibility Testing (EUCAST) recommendations and criteria [21]. Carbapenemase activity was tested by the modified Hodge test (with imipenem) and confirmed by polymerase chain reaction (Xpert® Carba-R Kit; Cepheid, Sunnyvale, USA).

Statistical analysis

The annual incidence rates were calculated by dividing the number of new positive clinical samples for MDR-GNB during the year by the annual sum of patient-days and multiplying by 1000. The same calculation was performed for *K. pneumoniae* and *P. aeruginosa*. Crude relative risk (RR) and 95% confidence interval (CI) were also calculated by dividing the incidence rates for the two different years. Segmented regression analysis of an interrupted time-series was used to assess the changes in incidence rates from before to after the intervention. In this method, each segment or time interval was defined by level and trend [19,22]. A change in level was the difference between the observed rate at the first point of the post-intervention period and the rate predicted by the pre-intervention time trend. A change in trend was identified as a difference between the post- and pre-intervention slopes, with a negative change in level and slope indicating a reduction in the rates. The two-segment model was constructed with a pre-intervention period of 43 months (January 2011 to July 2014) and a post-intervention period of 29 months (August 2014 to December 2016). For all tests, $P < 0.05$ was considered statistically significant. All modelling and statistical tests were performed using Software R (R Core Team, Vienna, Austria).

Results

The study isolated 202 new cases of MDR-GNB among ICU-admitted patients over a period of 35,909 patient-days. Of these isolates, 100 were caused by *K. pneumoniae* (83 ESBL and 17 carbapenemase-producing strains) and 102 were caused by XDR *P. aeruginosa* (82 non-VIM-carbapenemase producers and 20 VIM-carbapenemase). The overall incidences of MDR-GNB in the pre- and post-intervention periods were 9.15 and 2.20 per 1000 patient-days, respectively. This yielded an RR between both periods of 0.24 (95% CI: 0.17–0.34). Analysis of the crude RRs between consecutive years showed a statistically

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significant increase in total MDR-GNB rates in 2012 and 2013, followed by a statistically significant decrease in 2015, by which time the new protocols were established. However, the crude RRs for MDR-GNB rose in 2016, mainly due to two outbreaks. This was due to infection caused by a new strain of carbapenemase-producing *K. pneumoniae*, which was traced to neurosurgery wards, and the other was caused by XDR *P. aeruginosa* between January and April 2016, but only affected one of the units. Figure 2 and Table I summarizes the changes in the annual number of cases and rates.

Segmented regression analysis of the interrupted time-series

The slope before the intervention showed a statistically significant ascendance for MDR-GNB rates, especially for MDR *K. pneumoniae* (MDR *P. aeruginosa* rates were not significantly ascendant). During the post-intervention period, no changes in the slopes were observed on any of the analyses (Figure 2 and Table I). Overall, the intervention was associated with statistically significant changes in the incidence rates when

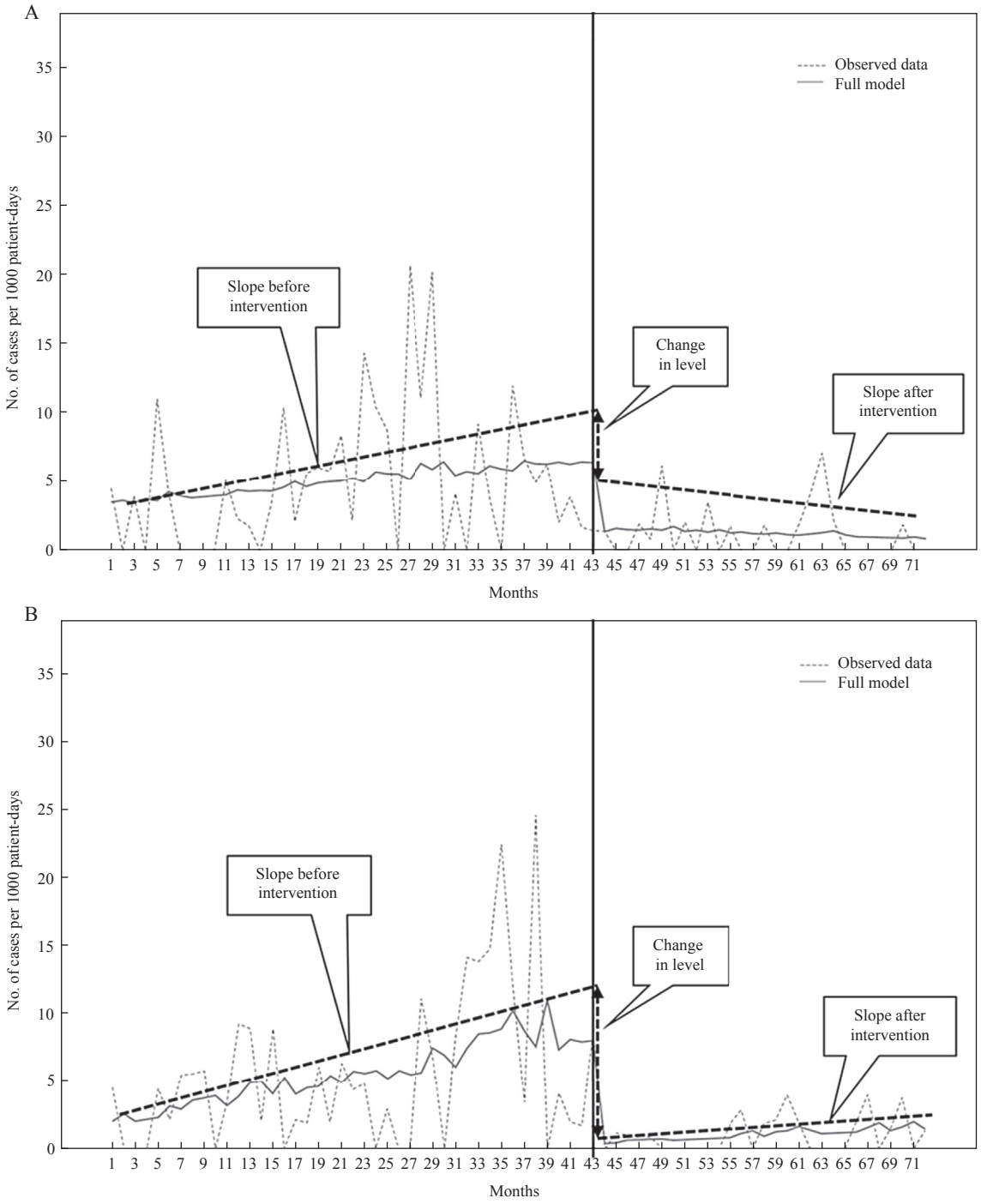

Figure 2. Changes in the incidence rates of multidrug-resistant bacteria in the intensive care units. (A) Multidrug-resistant *Pseudomonas aeruginosa*. (B) Multidrug-resistant *Klebsiella pneumoniae*. (C) Overall multidrug-resistant Gram-negative bacteria.

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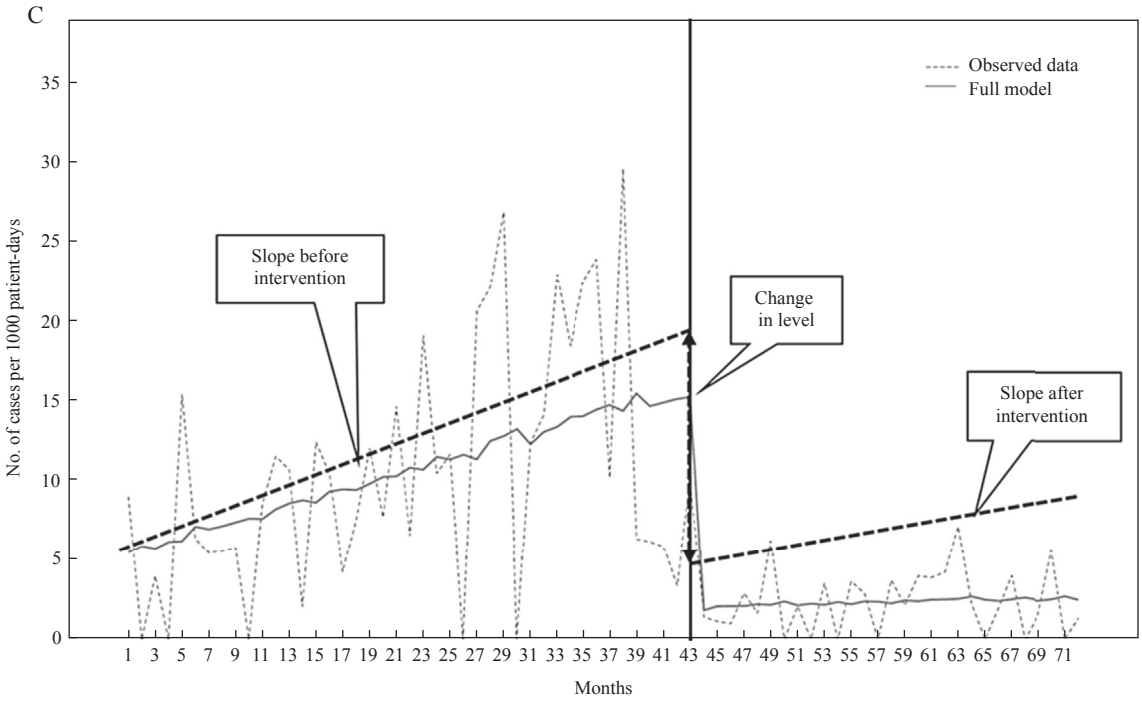

Figure 2. (*continued*).

compared with the pre-intervention period, with changes in level of −13.638, −8.680, and −4.969 for total MDR-GNB, MDR *K. pneumoniae*, and MDR *P. aeruginosa* rates, respectively (Table II).

Discussion

The removal of sinks from patients' rooms and the implementation of other water-safe strategies in our ICU were associated with improvements in endemic MDR-GNB rates. Interestingly, the intervention had the greatest impact on reducing new cases of *K. pneumoniae*, rather than of *P. aeruginosa*, which is the micro-organism classically associated with water and moist environments in critical care units [23–26]. Although this finding is difficult to interpret, it could reflect differences in the adhesion to biofilm, which would favour *P. aeruginosa* spreading further down into the wastewater drainage. By contrast, *K. pneumoniae* would remain in the proximal drains, facilitating faster elimination.

Several studies have demonstrated the role of contaminated sinks in sporadic colonization of patients after an outbreak or during prolonged outbreaks of MDR-GNB in ICU [9,12,17,27]. To control new cases, most of these introduced chemical disinfection and/or sink replacement. As evidenced by their results, these strategies helped to control the grade of sink contamination but often failed to eliminate contamination because MDR bacteria tended to reappear [9,10,12,15,28–30]. This suggests that persistent colonization remained further down in the pipes in most water systems. In our case, we decided to remove the sinks from patient rooms based on two main arguments. First, since their installation, the sinks in our ICU were used for handwashing, patient daily hygiene, and discarding dirty water from colonized patients, which probably meant that we had high rates of contamination throughout the system. Second, there was insufficient evidence about the best agent, volume, and time of exposure for optimal chemical disinfection.

Notably, despite the number of new acquisitions decreasing after introducing our intervention, we failed to eliminate MDR-GNB transmission in our wards. This could explain the difficulties in avoiding outbreaks caused by new strains from other parts of the hospital.

The main limitation of this study is that we did not perform water-testing or other environmental screening before the intervention. However, in 2013 we explored sinks of one of the two ICU wards. The inspection showed deteriorated siphons which had a large amount of biofilm in the pipe light. The biofilm tested positive for different types of micro-organism such as *P. aeruginosa*, *Stenotrophomonas maltophilia*, and different ESBL-producing Enterobacteriaceae, although none of the isolates belonged to our endemic MDR bacteria. We contend that this previous finding — along with the sharp reduction of new acquisitions of MDR-GNB observed after removing sinks and changing water use policies — supports our pre-intervention hypothesis. That is, our endemic bacteria were ubiquitous in the ICU sinks and perpetuated the cycle of new colonization or infection of patients. In addition, the study design allowed us to measure the impact of specific components of the intervention because other infection control strategies did not change between the pre- and post-intervention periods. Indeed, there were no changes in either the antibiotic stewardship policy or the complexity of patients admitted to ICU during the study period, both of which could be potential confounders. As we previously reported, rates of *A. baumannii* infection fell rapidly after changing our cleaning procedures, though there was no change in the rates of other MDR-GNB [19]. These observations are consistent with the main

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Table I
Changes in the incidence rates of multidrug-resistant bacteria in the intensive care units

Variable	2011	2012	2013	2014	2015	2016
Sum of patient-days	5703	6161	2709	2221	6384	6795
Pseudomonas aeruginosa						
No. of new cases	15	35	21	14	8	9
Incidence rate × 1000 patient-days	2.63	5.68	7.76	1.73	1.25	1.31
Relative risk (95% CI)[a]		2.16 (1.18–3.95)	1.36 (0.79–2.34)	0.81 (0.41–1.60)	0.20 (0.08–0.47)	1.06 (0.41–2.74)
Klebsiella pneumoniae						
No. of new cases	17	25	23	20	7	8
Incidence rate × 1000 patient-days	2.98	4.06	8.50	2.48	1.10	1.18
Relative risk (95% CI)[a]		1.36 (0.73–2.52)	2.09 (1.19–3.69)	1.06 (0.58–1.93)	0.12 (0.05–0.29)	1.07 (0.39–2.96)
Total MDR-GNB						
No. of new cases	32	60	44	34	15	17
Incidence rate × 1000 patient-days	5.61	9.74	16.25	4.21	2.35	2.50
Relative risk (95% CI)[a]		1.74 (1.13–2.67)	1.67 (1.13–2.46)	0.94 (0.60–1.47)	0.15 (0.08–0.28)	1.07 (0.53–2.13)

CI, confidence interval; MDR-GNB, multidrug-resistant Gram-negative bacteria.
[a] Calculated as incidence rate of the current year/incidence rate of the previous year.

reservoir for *A. baumannii* being dry surfaces, and the main reservoir for other MDR-GNB being wet areas. In this regard, a recent study conducted in the Netherlands showed that removing sinks from patients' rooms and introducing water-free patient care improved the control of sporadic GNB transmission, including MDR-GNB, in settings with low levels of endemic GNB [31].

In conclusion, this is the first study to show that removing sinks from patients' rooms and implementing other water-safe measures can be effective tools in the fight against MDR-GNB in highly endemic ICU settings with poor control. The study also supports the argument that sinks have important roles in outbreaks and in maintaining high endemic rates in ICU settings.

Table II
Impact of the water-safe measures on the monthly incidence rates of multidrug-resistant Gram-negative bacteria [a]

Parameter estimates	Coefficient	Standard error	*P*-value
Pseudomonas aeruginosa			
Constant	3.400	1.379	0.016
Slope before intervention	0.075	0.055	0.174
Change in level after intervention	−4.969	2.152	0.024
Change in slope after intervention	−0.101	0.113	0.374
Klebsiella pneumoniae			
Constant	1.805	1.562	0.252
Slope before intervention	0.169	0.062	0.008
Change in level after intervention	−8.680	2.403	<0.001
Change in slope after intervention	−0.125	0.128	0.332
Total multidrug-resistant Gram-negatives			
Constant	5167	1854	0.007
Slope before intervention	0.245	0.073	0.001
Change in level after intervention	−13.638	2.892	<0.001
Change in slope after intervention	−0.226	0.152	0.140

[a] Segmented regression analysis of interrupted time-series.

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Conflict of interest statement
None declared.

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