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ORIGINAL RESEARCH

# Impact of Enhanced Infection Control Measures on Hospital-Acquired Carbapenem-Resistant *Klebsiella pneumoniae, Escherichia coli, Pseudomonas aeruginosa*, and *Acinetobacter baumannii*

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**Background:** Carbapenem-resistant organisms (CROs) represent a major cause of healthcare-acquired infections. This study aims to evaluate the impact of enhanced infection control measures on the incidence of hospital-acquired carbapenem-resistant *Klebsiella pneumoniae, Escherichia coli, Pseudomonas aeruginosa*, and *Acinetobacter baumannii* infections. Given resource constraints, other CROs were excluded from the analysis.

**Methods:** This study was conducted at a tertiary hospital in China. The baseline period (Period 1) spanned from January 1, 2022, to December 31, 2023. Starting January 1, 2024, an enhanced intervention (Period 2) was implemented, comprising weekly active surveillance for CROs, coupled with immediate notification and on-site audit with feedback to ensure prompt implementation of contact isolation for positive cases. The study compared the trends of CROs, incidence rates of hospital-acquired CROs infections, contact isolation order compliance rates, and the consumption intensity of carbapenems between the two periods. An interrupted time-series analysis was used to assess the intervention effect.

**Results:** The incidence of CROs increased by 0.101 cases per 1000 patient-days per quarter in period 1 (95% CI: 0.006–0.209, $p = 0.043$), whereas it decreased by 0.179 cases per 1000 patient-days per quarter in period 2 (95% CI: −0.331 to −0.026, $p = 0.025$). Similarly, the rate of hospital-acquired CROs infections increased by 0.021 cases per 1000 patient-days per quarter in period 1 (95% CI: 0.008–0.0327, $p = 0.003$), but declined by 0.034 cases per 1000 patient-days per quarter in period 2 (95% CI: −0.051 to −0.017, $p = 0.001$). Concurrently, compliance with contact isolation orders improved markedly from 35.37% to 78.83% ($p < 0.001$). In contrast, carbapenem consumption showed a sustained upward trend throughout the study period, increasing by 1.012 defined daily doses per 1000 patient-days per quarter ($p = 0.003$), with no significant difference in trend between the two periods ($p = 0.105$).

**Conclusion:** Enhanced infection control measures were associated with a reduction in hospital-acquired CROs infections.

**Keywords:** carbapenem-resistant organisms, hospital-acquired, infection control, contact isolation, antimicrobial consumption

## Introduction

Healthcare-associated infections (HAIs) represent one of the most frequent adverse events in clinical settings, substantially contributing to increased morbidity, mortality, and healthcare costs.[1–3] The worldwide dissemination of carbapenem-resistant Gram-negative bacilli has become a pressing global public health challenge.[4] Among these, carbapenem-resistant

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*Enterobacteriaceae* (CRE), carbapenem-resistant *Acinetobacter baumannii* (CRAB), and carbapenem-resistant *Pseudomonas aeruginosa* (CRPA) constitute major etiological agents of HAIs and pose an escalating threat to public health globally.[5]

The World Health Organization has classified CRE and CRAB as critical-priority pathogens, while CRPA is classified as a high-priority drug-resistant bacterium.[6,7] Within CRE, *Klebsiella pneumoniae* and *Escherichia coli* are the predominant species producing carbapenemases.[5] In 2019, each of these pathogens, carbapenem-resistant *Klebsiella pneumoniae* (CRKP), carbapenem-resistant *Escherichia coli* (CREC), CRPA, and CRAB was associated with more than 250,000 deaths attributable to antimicrobial resistance (AMR), with *Escherichia coli* accounting for the highest mortality, followed by *Klebsiella pneumoniae* and *Acinetobacter baumanni*i.[8] The rising mortality linked to these carbapenem-resistant Gram-negative bacteria is a grave concern.[9]

Evidence-based preventive measures targeting carbapenem-resistant *Acinetobacter* and *Enterobacterales* remain limited, particularly at the population level.[10] Many currently recommended strategies are extrapolated from studies on methicillin-resistant *Staphylococcus aureus* or rely on facility-based control measures initiated after identifying a common source.[10,11] Although multifaceted interventions including hand hygiene, contact precautions and environmental cleaning have been advocated,[12–14] their real-world effectiveness in reducing hospital-acquired CROs infections remains uncertain.[15]

Novel Gram-negative antibiotics are projected to substantially reduce mortality between 2025 and 2050, it is estimated that even under optimistic assumptions, approximately 28.03 million (23.7–32.8) annual AMR-related deaths will still occur by 2050.[10] This underscores that while developing drugs for the most difficult-to-treat infections is critical, it is insufficient alone to address the AMR crisis, as the emergence of further resistance appears inevitable A diversified portfolio of interventions is urgently needed to curb the transmission of carbapenem-resistant Gram-negative bacteria.

Before 2024, contact isolation orders at our institution were often delayed following positive CROs culture results, with poor compliance. In our institution, enhanced infection control measures were implemented, including the introduction of a weekly active surveillance program initiated in 2024. Now, two years following its introduction, we aim to evaluate its impact on the incidence of hospital-acquired CROs events, addressing the gap in evidence regarding the effectiveness of active surveillance combined with timely feedback in routine clinical practice.

# Materials and Methods

## Setting

This retrospective study investigated the epidemiology of hospital-acquired carbapenem-resistant organisms in the Affiliated Guangdong Second Provincial General Hospital of Jinan University. This tertiary care institution in Guangzhou, China, has a capacity of approximately 1,730 beds. The study period is divided into two parts, where period 1 (1 January 2022 to 31 December 2023) is the baseline and period 2 (1 January 2024 to 31 December 2025) is the intervention, with the enhancement in the infection control measures. Our enhanced infection control measures focused specifically on hospital-acquired infections caused by carbapenem-resistant *Klebsiella pneumoniae, Escherichia coli, Pseudomonas aeruginosa*, and *Acinetobacter baumannii*. Given resource constraints, other carbapenem-resistant organisms were excluded from the analysis.

## Baseline Period (Period 1)

Contact isolation was initiated only after attending physicians placed an order following positive CROs culture results. No systematic active surveillance was in place. Routine hand hygiene and environmental cleaning were performed according to hospital standards, but no structured audit-and-feedback system was implemented. Compliance with isolation orders was not systematically monitored or reported.

## Enhanced Infection Control Measures (Period 2)

Starting January 1, 2024, an enhanced intervention (Period 2) was implemented. The core components consisted of weekly active surveillance, immediate notification, on-site audit and feedback, and monthly performance reporting.

## Weekly Active Surveillance

Our Infection Prevention and Control (IPC) team has conducted weekly active surveillance for CROs, including CRKP, CREC, CRPA, and CRAB. Weekly active surveillance was conducted for all inpatients with submitted clinical microbiological specimens, including sputum, bronchoalveolar lavage fluid, urine, whole blood, wound swabs, and other specimen types. Screening specimens were not used for active surveillance in 2024.

## Immediate Notification

For inpatients identified as CROs-positive without existing contact isolation orders, the IPC team promptly notifies the attending physicians via Office Automation (OA) email, WeChat or telephone to ensure that appropriate isolation measures are implemented.

## On-Site Audit and Feedback

Targeted on-site audits are carried out weekly for all detected CROs cases, encompassing both colonization and infection. During these audits, immediate feedback is provided to reinforce the consistent application of bedside isolation precautions. A standardized Multidrug-Resistant Organism (MDRO) Prevention and Control Joint Inspection Form (Table S1) was developed to record and score compliance with infection prevention measures. Using the standardized Multidrug-Resistant Organism (MDRO) Prevention and Control Joint Inspection Form, the on-site inspections evaluated several key components of infection control, including adherence to isolation protocols, correct use of personal protective equipment, hand hygiene compliance, dedicated use of medical devices, environmental cleaning and disinfection practices, training and education and appropriate antimicrobial stewardship. The standardized audit tool was implemented during Period 2 as part of the enhanced intervention. As the tool was not in use during Period 1, comparative baseline audit scores were not available; therefore, the primary analysis focused on outcome indicators consistently measured across both periods.

## Monthly Performance Reporting

Monthly internal reports are issued to summarize identified deficiencies and rank departmental performance.

## Hospital-Acquired Carbapenem-Resistant Organisms Events

The incidence rates of the selected carbapenem-resistant, including CRKP, CREC, CRPA, and CRAB expressed as 1000 patient days from 2022 Q1 to 2025 Q4, were analyzed. Each patient was assigned a unique hospital identification number. For the same patient and the same infection site, only the record with the earliest specimen collection date was included in the analysis. CROs incidence was defined as the detection of CRKP, CREC, CRPA, or CRAB from any clinical specimen (eg., sputum, urine, blood, wound swab) regardless of whether the patient met clinical criteria for infection. Cases identified through screening specimens (eg., rectal swabs) were not included in the incidence calculation.

Hospital-acquired carbapenem-resistant organisms events were jointly confirmed by the attending physicians and the infection prevention and control staff. In this study, hospital-acquired CROs events were defined as infections occurring more than 48 hours after admission, with confirmation of the targeted resistant pathogens through culture of clinical specimens. If the same patient experienced multiple HAIs events caused by the same pathogen, only the first episode was recorded. The incidence rates of hospital-acquired carbapenem-resistant organisms events were expressed as the number of episodes per 1,000 patient-days.

## Contact Isolation Orders Compliance

Patients who were hospitalized and required contact isolation orders were included in the analysis. For any patient with bacterial culture positivity for CRKP, CREC, CRPA, or CRAB, regardless of specimen source (eg., urine, blood, sputum) or clinical classification as infection or colonization, a contact isolation order was mandated in the long-term medical instructions. Patients discharged on or before the date of the final laboratory report were excluded. Additionally, contact isolation orders initiated prior to the report due to other pathogen infections or clinical reasons were not included in the statistical evaluation. Cases involving specimen contamination were also excluded.

## Carbapenem Consumption Before and After the Enhancement of Infection Control Measures

This study analyzed the quarterly consumption of carbapenems (ertapenem, meropenem and imipenem/cilastatin) from 2022 to 2025, expressed in defined daily doses (DDD) per 1000 patient-days, and compared the change in antimicrobial use between period 1 and period 2.

## Ethics Approval and Consent Statement

All methods in this study were carried out in accordance with relevant guidelines and regulations. This study was conducted in strict compliance with the Declaration of Helsinki. The study was approved by the Ethics Committee of The Affiliated Guangdong Second Provincial General Hospital of Jinan University, Guangzhou, China (Approval No. 2025-KY-KZ-459-01). Due to the retrospective nature of the study and the use of a de-identified database, the Ethics Committee of The Affiliated Guangdong Second Provincial General Hospital of Jinan University waived the need of obtaining informed consent.

## Data Collection

The medical records of inpatients were retrieved from the hospital's Intelligent Infection Management System (Shanghai Lilian Information Technology Co., Ltd.) and the Blue-Dragonfly Hospital Infection Real-Time Monitoring and Management System 6.0. The selected microorganisms comprised *Klebsiella pneumoniae, Escherichia coli, Pseudomonas aeruginosa*, and *Acinetobacter baumannii*, along with their corresponding antimicrobial susceptibility profiles. Antimicrobial susceptibility testing was interpreted as susceptible, intermediate, or resistant according to the Clinical and Laboratory Standards Institute (CLSI) guidelines (M100, 33rd edition, 2023). All clinical isolates underwent identification using the automated VITEK 2 Compact system (bioMérieux, France). Susceptibility testing was performed using the dedicated VITEK 2 GP639 susceptibility card (bioMérieux). All AST results generated during the study were interpreted retrospectively using the unified standard of the CLSI M100, 33rd edition (2023) breakpoints. For carbapenems, susceptibility was determined for meropenem, imipenem, and ertapenem using minimum inhibitory concentration breakpoints defined by CLSI. Isolates with resistance to at least one carbapenem agent were classified as carbapenem-resistant.

## Statistical Analyses

All statistical analyses were performed using IBM SPSS statistical software (version 29.0). An interrupted time-series analysis (ITSA) was conducted using segmented linear regression to evaluate the impact of enhanced infection control measures on the incidence of hospital-acquired carbapenem-resistant organism events and inpatient contact isolation orders. The model was specified as:

$$Y = \beta_0 + \beta_1 \times \text{time} + \beta_2 \times \text{intervention} + \beta_3 \times \text{time\_after} + \varepsilon$$

where Y represents the outcome variable (incidence of CROs, hospital-acquired CROs infection rate, or contact isolation compliance rate) at time t; time is a continuous variable indicating the quarter number (from 1 to 16); intervention is a binary variable indicating pre-intervention (0 for Period 1, 1 for Period 2); and time_after is a continuous variable counting quarters since the intervention began (0 for Period 1, and 1 to 8 for Period 2). $\beta_0$ represents the baseline level, $\beta_1$ represents the pre-intervention slope, $\beta_2$ represents the immediate effect of the intervention, and $\beta_3$ represents the change in trend after the intervention compared with the pre-intervention period. $\varepsilon$ represents the random error. The *Durbin-Watson* test was used to assess autocorrelation. All statistical analyses were evaluated at the statistical significance level of $p < 0.05$ (two-sided).

# Results

## Trends of Carbapenem-Resistant Organisms

From the first quarter of 2022 to the fourth quarter of 2023 (Period 1), the overall incidence of CROs, encompassing CRKP, CREC, CRPA, and CRAB, was 2.468 cases per 1,000 patient-days (95% confidence interval [CI]: 1.947–2.680). From the first quarter of 2024 to the fourth quarter of 2025 (Period 2), the corresponding CROs incidence declined to

1.331 cases per 1,000 patient-days (95% CI: 1.165–1.642). The difference between the pre-intervention and post-intervention periods was statistically significant ($p < 0.001$).

In period 1, the quarterly incidence of CROs increased by 0.101 cases per 1000 patient-days (95% CI: 0.006–0.209, $p = 0.043$). In contrast, in Period 2, it declined by 0.179 cases per 1000 patient-days per quarter (95% CI: −0.331 to −0.026, $p = 0.025$). Figure 1 illustrates the trends in the incidence of CROs, including CRKP, CREC, CRPA, and CRAB, expressed as cases per 1000 patient-days from the first quarter of 2022 to the fourth quarter of 2025. The *Durbin-Watson* test result was 1.782 ($p= 0.557$), indicating no significant autocorrelation in the model residuals.

## Hospital-Acquired Carbapenem-Resistant Organisms Events

The incidence of hospital-acquired CROs infections was 0.183 cases per 1000 patient-days (95% CI: 0.104–0.310) in period 1, compared with 0.083 cases per 1000 patient-days (95% CI: 0.055–0.164) in period 2, a difference that was statistically significant ($p = 0.002$).

For hospital-acquired CROs infections, the rate increased at a pace of 0.021 (95% CI: 0.008–0.0327, $p = 0.003$) cases per 1000 patient-days per quarter in period 1, while it decreased by 0.034 (95% CI: −0.051 to −0.017, $p = 0.001$) cases per 1000 patient-days per quarter in period 2. Figure 2 presents the incidence rates of hospital-acquired infections caused by CROs, including CRKP, CREC, CRPA, and CRAB, expressed as cases per 1000 patient-days from 2022 Q1 to 2025 Q4. The *Durbin-Watson* test result was 2.479 ($p= 0.950$), indicating no significant autocorrelation in the model residuals.

## Contact Isolation Compliance Rate

The contact isolation compliance rate was 35.37% (95% CI: 29.27–41.46%) during the pre-intervention period and increased to 78.83% (95% CI: 74.08–83.57%) in the post-intervention period, a statistically significant improvement ($p < 0.001$). However, the trend of compliance did not differ significantly between the two periods, indicating that compliance remained stable after the initial improvement. Figure 3 illustrates the contact isolation compliance rate from the first quarter of 2022 to the fourth quarter of 2025.

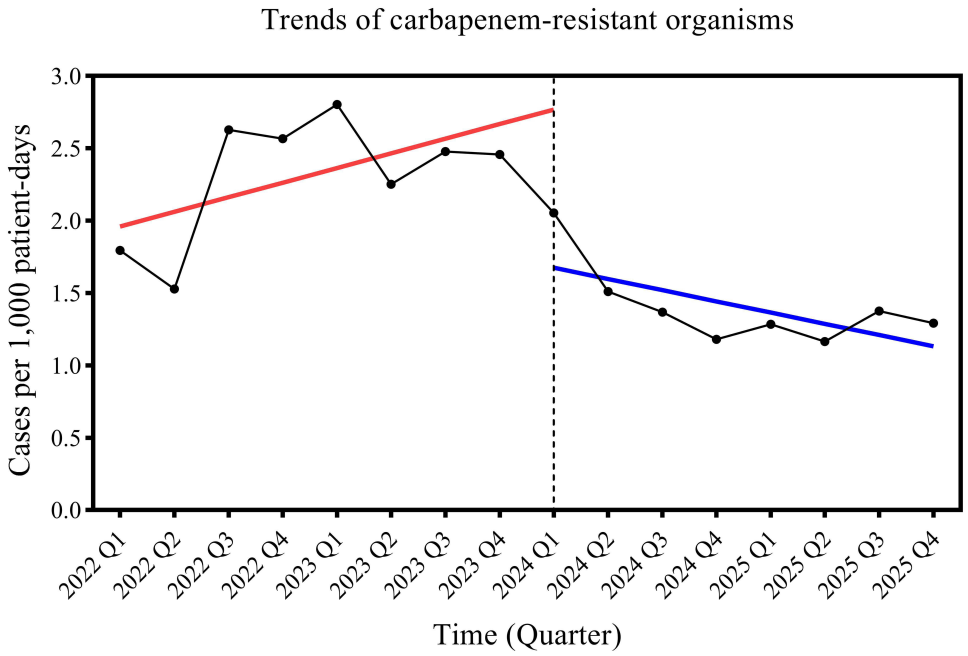


**Figure 1** Trends of carbapenem-resistant organisms from 2022 Q1 to 2025 Q4. Black line represents carbapenem-resistant organisms, red line represents the pre-intervention trend line, and blue line represents the post-intervention trend line.


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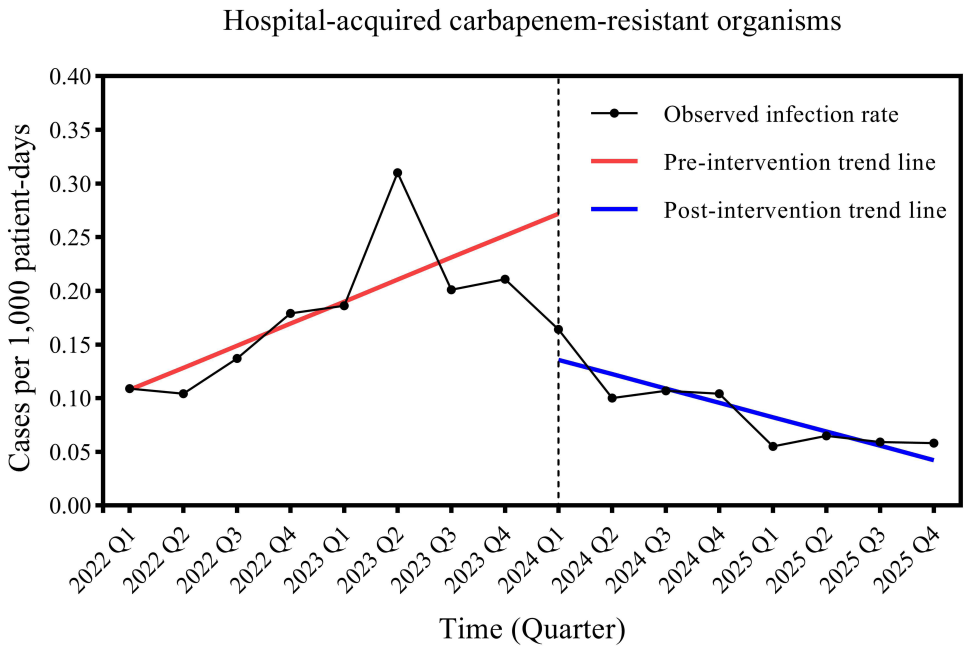


**Figure 2** Hospital-acquired CROs events from 2022 Q1 to 2025 Q4. Black line represents the observed infection rate, red line represents the pre-intervention trend line, and blue line represents the post-intervention trend line.

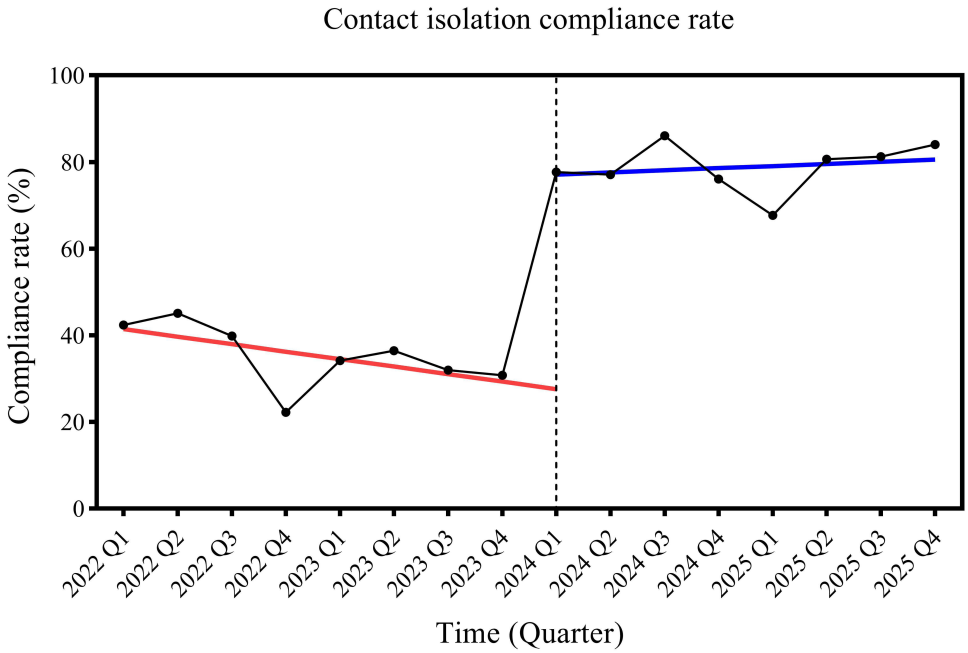


**Figure 3** Contact isolation compliance rate from 2022 Q1 to 2025 Q4. Black line represents the contact isolation compliance rate, red line represents the pre-intervention trend line, and blue line represents the post-intervention trend line.

## Carbapenem Consumption

The consumption of carbapenems (ertapenem, meropenem, and imipenem/cilastatin), expressed in defined daily doses (DDD) per 1000 patient-days, was 37.96 (95% CI: 26.26–47.25) during the pre-intervention period and 44.09 (95% CI: 39.12–48.59) in the post-intervention period, with no statistically significant difference in trend observed between the two periods ($p = 0.105$). Overall, carbapenem use increased at a rate of 1.012 DDD per 1000 patient-days per quarter (95%

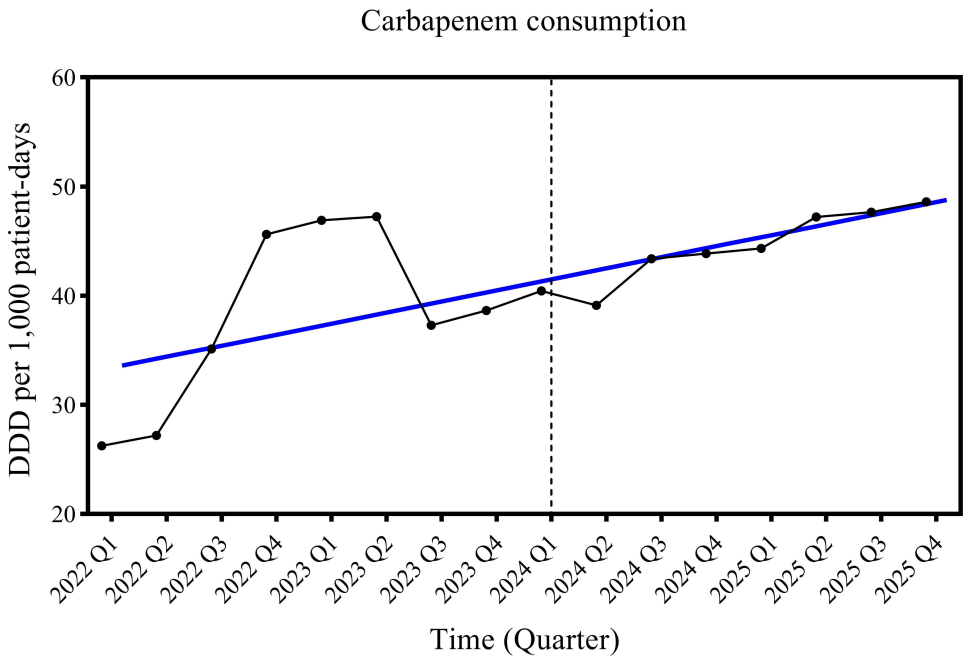


**Figure 4** Carbapenem consumption before and after the enhancement of infection control measures. Black line represents carbapenem consumption, and blue line represents the trend line.

CI: 0.409–1.617, $p = 0.003$) across both periods. Figure 4 illustrates carbapenem consumption before and after the enhancement of infection control measures from the first quarter of 2022 to the fourth quarter of 2025.

## Discussion

Our study suggests that, even amid increasing carbapenem consumption, enhanced infection control measures were associated with a reduction in the incidence of hospital-acquired carbapenem-resistant organisms. AMR infections represent a global public health crisis.[16] The management of severe infections such as pneumonia and bacteremia caused by carbapenem-resistant gram-negative bacteria poses substantial clinical challenges.[17] In 2019, an estimated 1.3 million deaths worldwide were directly attributable to AMR pathogens.[8] The escalating threat of antimicrobial resistance undermines the effectiveness of existing antimicrobial therapies for infection control,[18] contributing not only to a significant burden of clinical infections in high-risk patient populations,[19] but also to nosocomial transmission and outbreaks.[20,21]

Despite sustained efforts in antimicrobial stewardship, which have partially reduced overall antibiotic use intensity, a persistent upward trend in antimicrobial consumption, particularly of carbapenems, remains evident.[22] Consistent with this pattern, our study found that carbapenem use increased by 1.012 DDD per 1000 patient-days per quarter throughout the observation period. Correspondingly, the incidence of CROs increased by 0.101 cases per 1000 patient-days per quarter during period 1, and hospital-acquired CROs infections increased by 0.021 cases per 1000 patient-days per quarter in the same period. Importantly, the implementation of enhanced infection control measures was associated with a significant reduction in both CROs trends and hospital-acquired CROs infections. These findings underscore the necessity of prioritizing robust infection control and preventive strategies to mitigate the risk of nosocomial transmission of carbapenem-resistant organisms. Enhanced infection control measures including weekly active surveillance enabled early identification of colonized patients, allowing for prompt contact isolation. This likely reduced cross-transmission, which is a key driver of CRO dissemination in hospital settings. The substantial improvement in contact isolation compliance (from 35.37% to 78.83%) likely played a critical role in disrupting transmission chains. However, we acknowledge the limitation in interpreting these mechanisms. The absence of whole-genome sequencing data precluded confirmation of strain homology and transmission dynamics, which would have provided stronger evidence for the interruption of transmission chains.


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Various infection control measures have been advocated to curb the spread of CROs, including hand hygiene,[21] conversion from multi-bed wards to single isolation rooms,[23,24] single-room isolation with mandatory use of personal protective equipment (gloves, gowns, and surgical masks) by healthcare staff,[25] environmental cleaning and disinfection,[26] training and education,[27,28] daily chlorhexidine bathing,[29] and environmental surveillance-driven CROs IPC strategies,[30] among others. In this study, we systematically evaluated several key components of infection control through a structured on-site audit tool. This tool assessed adherence to isolation protocols, correct use of personal protective equipment, hand hygiene compliance, dedicated use of medical devices, environmental cleaning and disinfection practices, training and education (including patient awareness), and appropriate antimicrobial stewardship. Audits were conducted through direct observation and immediate feedback for inpatients with CROs.

In our institution, although patients with CROs should ideally be placed in single isolation rooms, the majority in practice receive contact precautions at the bedside, which may elevate the risk of hospital-acquired transmission. Prior evidence indicates that susceptible patients have an average of 4.8 daily interactions with CROs-positive individuals under contact precautions.[15] Therefore, strengthening infection control measures, including the use of standardized checklists for real-time auditing and feedback, is essential to minimize the spread of CROs. This approach may also hold relevance for other healthcare settings, particularly in resource-limited regions.

At our hospital, contact isolation precautions are initiated only after a physician enters a contact isolation order in the electronic medical record following a positive CROs culture result. Our weekly active surveillance system helps identify inpatients with unreported or unordered contact isolation and promptly alerts the responsible clinicians to place the necessary orders, thereby activating appropriate infection prevention measures. Following the implementation of this enhanced intervention, contact isolation compliance improved significantly from 35.37% to 78.83%. Concurrently, the trend of carbapenem-resistant organisms decreased by 0.179 cases per 1000 patient-days per quarter in period 2, and hospital-acquired CROs infections declined by 0.034 cases per 1000 patient-days per quarter. These results suggest that active surveillance coupled with timely feedback can effectively shorten the window period between microbiological reporting and the implementation of isolation precautions. The use of multi-channel reminders (eg., OA system, WeChat, phone calls), combined with on-site audits and feedback, appears to facilitate meaningful changes in physician behavior.[15]

This study has several limitations. First, it is a single-center interrupted time-series descriptive study without a control hospital, which may limit the generalizability of the findings. Although interrupted time-series analysis accounts for underlying secular trends and strengthens causal inference, residual confounding from unmeasured factors cannot be entirely excluded. These include changes in patient case mix, seasonal variations, time-varying factors such as ward capacity and bed turnover rates, shifts in antimicrobial stewardship policies, and regional antimicrobial resistance patterns, none of which were specifically measured in this study. Second, the interaction between antimicrobial use and infection control measures is likely complex. Dynamic transmission modeling could help elucidate the relationships among antibiotic consumption, isolation compliance, and infection rates. Third, the absence of whole-genome sequencing precluded tracing strain homology and confirming the interruption of transmission chains. Fourth, organism-specific trends were not analyzed due to small sample sizes for individual species and the bundled nature of the intervention, which targeted all four organisms simultaneously. Further studies with larger sample sizes could explore organism-specific trends, as the intervention may have had differential effects on individual CRO species. Fifth, the use of quarterly rather than monthly data points may have reduced statistical power. Sixth, this study used a pre-post design without a concurrent control group, limiting causal inference. Finally, although carbapenem use continued to increase while CROs declined, we acknowledge that antibiotic selective pressure may exert delayed effects on resistance through longer-term evolutionary processes. The two-year post-intervention observation period may not be sufficient to capture such delayed effects, and longer-term surveillance is warranted.

## Conclusion

Enhanced infection control measures were associated with a reduction in hospital-acquired CROs infections. Key components included weekly active surveillance for CROs combined with immediate notification, on-site audit, and timely feedback to ensure prompt contact isolation. These findings suggest that enhanced infection control measures may be effective in reducing CROs transmission even in settings where antibiotic consumption continues to rise.

## Data Sharing Statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

## Ethics Approval and Consent Statement

All methods in this study were carried out in accordance with relevant guidelines and regulations. This study was conducted in strict compliance with the Declaration of Helsinki. The study was approved by the Ethics Committee of The Affiliated Guangdong Second Provincial General Hospital of Jinan University, Guangzhou, China (Approval No. 2025-KY-KZ-459-01). Due to the retrospective nature of the study and the use of a de-identified database, the Ethics Committee of The Affiliated Guangdong Second Provincial General Hospital of Jinan University waived the need of obtaining informed consent.

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

The authors declare they have no actual or potential competing financial interests and have given their approval for this version to be published.

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