Infection and Drug Resistance

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ORIGINAL RESEARCH

Economic Burden of Carbapenem-Resistant Organisms in Critically Ill Patients: A Multicenter, Retrospective Cohort Study

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Background: Carbapenem-resistant organisms (CROs) are a growing threat in intensive care units (ICUs) worldwide due to the limited treatment options and high risk of morbidity and mortality. While previous studies have assessed the clinical implications of CROs, few have systematically quantified their economic burden.

Aim: This study aimed to evaluate the economic burden attributable to CROs compared with carbapenem-susceptible organisms (CSOs) among critically ill patients in China.

Methods: We conducted a retrospective cohort study including 7,232 ICU patients from two tertiary hospitals in Western China (2019–2024). Patients were assigned to either the CRO group or the CSO group and matched using a 1:1 propensity score matching (PSM) approach. ICU length of stay (LOS), hospital LOS, and total hospitalization cost were compared between the two groups, followed by generalized linear models (GLMs) to assess the independent impact of CRO status. Institutional-level opportunity costs were estimated based on excess ICU occupancy.

Results: Among the 7,232 patients, 379 (5.24%) developed CRO, with carbapenem-resistant Acinetobacter baumannii (CRAB) being the predominant pathogen. PSM produced 379 pairs of CRO and CSO patients. The CRO group had significantly longer ICU LOS (median 11.0 vs 5.0 days, $P<0.001$), longer hospital LOS (median 24.0 vs 13.0 days, $P<0.001$), and higher total hospitalization costs (median CNY 99,549 vs CNY 50,279, $P<0.001$) than the CSO group. GLMs showed that CRO independently predicted longer ICU LOS (OR: 2.37; 95% CI: 2.03–2.76), longer hospital LOS (OR: 1.97; 95% CI: 1.70–2.27), and higher total hospitalization costs (OR: 1.99; 95% CI: 1.78–2.23). An estimated 321 hospital admissions and 459 ICU admissions were lost over six years due to excess bed occupancy by CRO patients, resulting in a total institutional financial loss of approximately CNY 134,000 per year.

Conclusion: CROs are associated with substantially increased economic burden in ICU patients. These findings support the implementation of early screening, targeted prevention, and stewardship strategies to mitigate the impact of CROs.

Keywords: carbapenem-resistant organisms, CROs, intensive care units, ICU, economic burden, hospitalization cost, length of stay, propensity score matching, PSM, generalized linear models, GLM

Background

Carbapenem-resistant organisms (CROs)are bacteria that have developed resistance to carbapenem antibiotics, which are considered powerful, "last-line" or "reserve" antibiotics for serious infections caused by multidrug-resistant bacteria.[1] CROs mainly include carbapenem-resistant Acinetobacter baumannii (CRAB), carbapenem-resistant Enterobacteriaceae (CRE), and Pseudomonas aeruginosa (CRPA).[1] These bacteria have been listed as critical priority pathogens for new antibiotic development by the World Health Organization (WHO) due to their antibiotic-resistant characteristics and the lack of effective treatment. CROs pose a serious and growing challenge to intensive care units (ICUs) worldwide due to limited treatment options, vulnerability of ICU patients, and rapid spread of resistance.[2–4] In China, the prevalence of

Received: 23 July 2025
Accepted: 19 November 2025
Published: 20 December 2025

CROs in ICUs has risen dramatically, with CRAB being identified as the dominant pathogen in many hospitals.[5–7] Emerging evidence demonstrates that CROs are associated with increased mortality, prolonged mechanical ventilation, extended ICU and hospital stays, and elevated medical costs.[6,8] As antimicrobial resistance continues to escalate, the control and management of CROs have become national priorities in many healthcare systems, including China.[4,5,9]

Existing studies have predominantly focused on the clinical outcomes and risk factors associated with individual types of CROs, such as CRAB, CRKP, or CRPA.[1,7,10–14] Numerous studies have identified predictors of CRO colonization or infection, including prior antibiotic exposure, mechanical ventilation, prolonged hospital stay, and comorbidities.[10,11,13] However, most of these studies examine CRO colonization and CRO infection separately and rarely consider their collective burden as a group of multidrug-resistant pathogens. Moreover, current evidence is heavily weighted toward clinical outcomes, with limited attention paid to the broader economic consequences of CROs. This is particularly concerning in resource-constrained ICU settings, where the institutional impact—such as bed occupancy, cost escalation, and service inefficiencies—can be profound but is often underappreciated. As China's ICUs face increasing patient volumes, constrained bed capacity, and rising antimicrobial costs, understanding institutional-level burden has become both urgent and essential for health policy and hospital management.[9,15] Some recent research in China hasdemonstrated significantly increased hospital stays and healthcare costs associated with CROs, highlighting the urgency and importance of addressing CROs in hospitals.[16,17] Investigating the economic burden of CROs in critically ill patients has significant policy implications for healthcare systems, public health, and research and development. A better understanding of the costs associated with these infections is crucial for justifying increased investment in infection control, antimicrobial stewardship, rapid diagnostics, and the development of new drugs.

Therefore, this study aimed to quantify the economic burden associated with CRO colonization or infection in ICU patients using real-world data from two tertiary hospitals in Western China. Previous economic evaluations frequently rely on unadjusted comparisons or basic regression methods, which may not adequately control for confounding variables.[8,14] This study employed more methodologically robust techniques, propensity score matching (PSM) and generalized linear models (GLMs), to isolate the actual economic burden attributable to CROs. By combining PSM and GLM approaches, we evaluated the impact of CRO status (including both colonization and infection) on ICU LOS, hospital LOS, and total hospitalization cost. We also estimated institutional-level opportunity costs based on excess ICU occupancy. Our findings may support evidence-based infection control and resource planning strategies in high-risk care settings.

Methods

Study Design and Setting

This multicenter, retrospective, propensity score−matched cohort study was conducted in the central ICUs of two tertiary general hospitals in Sichuan Province, China, between January 1, 2019, and December 31, 2024. Hospital A has a 32-bed ICU that admits approximately 1,000 patients per year, while Hospital B has a 28-bed ICU that admits about 900 patients per year. The study protocol received approval from the Institutional Review Boards (IRBs) of both hospitals (Approval No. 202452 and No. 2025KY004HY). Given the retrospective design and use of de-identified electronic medical records, the requirement for informed consent was waived. All procedures were conducted in accordance with the Declaration of Helsinki and relevant national regulations.

To provide a robust causal estimate of the economic burden, we adopted a two-stage methodological approach that explicitly addresses the dual challenges of selection bias and non-normal cost data. First, we used PSM to create a matched cohort of patients, effectively eliminating baseline confounding and mimicking a randomized experimental design. Unlike conventional regression, this design-stage process allowed us to assess covariate balance before outcome analysis transparently. Second, recognizing that healthcare expenditures are highly skewed, we applied a GLM with a gamma distribution and log-link function to the newly balanced sample. This two-step process ensures that our findings are not only free from selection bias but also accurately model the complex distributional nature of economic data, representing a significant methodological advancement over single-method approaches.

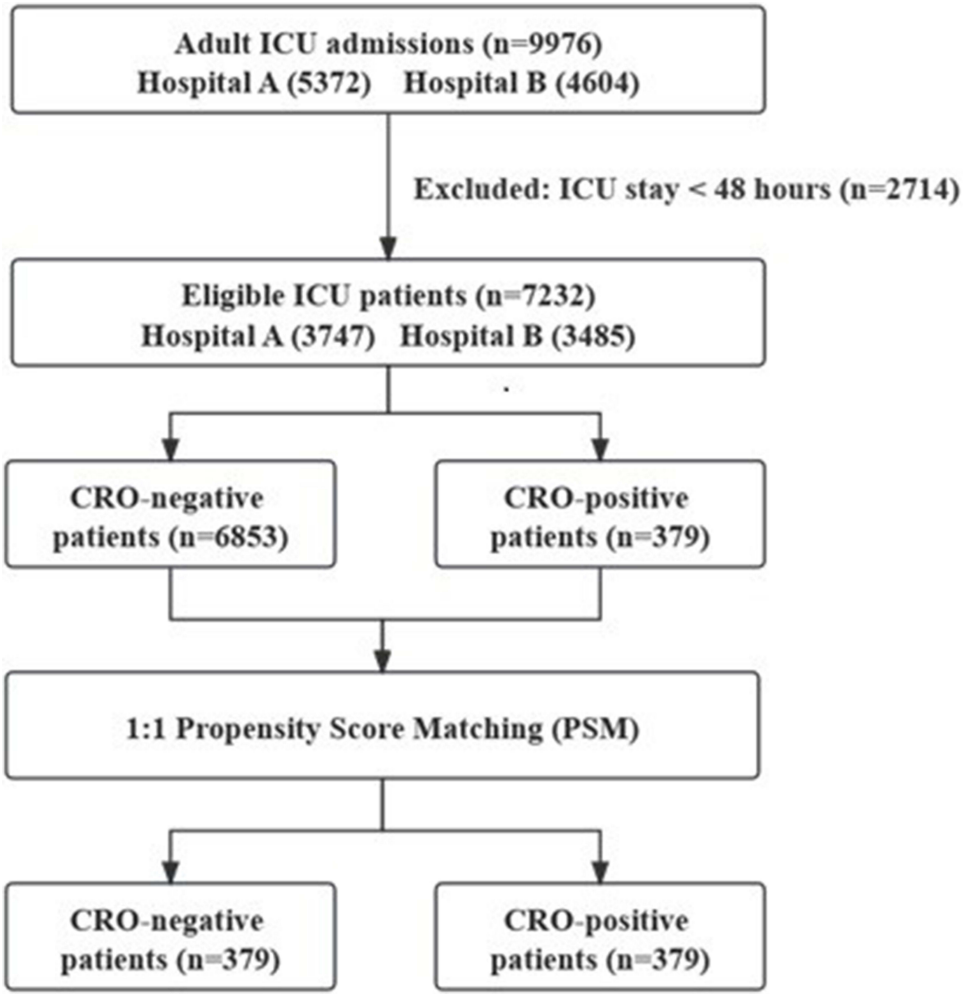

Figure 1 Flow chart of patient inclusion.

Inclusion and Exclusion Criteria

Our study included patients who satisfied the following inclusion criteria: (1) patients admitted to the ICUs between January 1, 2019, and December 31, 2024, (2) aged 18 years or older, and (3) with an ICU LOS of at least 48 hours. We chose 48 hours as a cutoff for ICU LOS to ensure that assessment of exposure status (CRO colonization or infection) occurs within the ICU, and to ensure a sufficient observation window to evaluate resource consumption and economic burden.[18] Patients were excluded if more than 30% of all baseline study variables were missing or if their total hospital LOS exceeded 365 days to reduce the impact of outliers. After applying these criteria, 7,232 patients remained from the initial 9,976 ICU admissions, including 3,747 from Hospital A and 3,485 from Hospital B (Figure 1).

Data Collection

Data from 2019 to 2024 were retrospectively extracted from electronic hospital information systems of both ICU centers using a standardized electronic case report form. Data were collected by a trained team comprising infection control personnel and data engineers, who conducted dual independent review and cross-validation to ensure data accuracy and completeness. All data were anonymized before analysis to maintain patient confidentiality.

Exposure

CRO colonization or infection status was determined by microbiological culture results. Microbial colonization is the presence and multiplication of microbes on a host surface without causing disease or a host immune response, while

infection is a more serious process where microbes invade host tissues, leading to pathological changes and signs of illness, such as fever, pain, redness, swelling, elevated white blood cell count, etc.[19] CRO colonization or infection was defined as the isolation of CRAB, CRE (including carbapenem-resistant Klebsiella pneumoniae), or CRPA from any clinical specimen obtained during a patient's hospitalization. Microbiological identification and antimicrobial susceptibility testing (AST) were performed using the VITEK 2 Compact system (bioMérieux, France). The requisite materials were obtained from commercial suppliers as follows: culture media (Autobio Diagnostics Co., Ltd., China), aerobic/anaerobic blood culture bottles (BD, USA), and AST-specific cards including the AST-N panels (bioMérieux, France).

Outcomes

To comprehensively assess the economic impact of CRO colonization or infection, both individual-level and institutional-level outcomes were evaluated.Individual-level outcomes primarily included LOS and total hospitalization costs. LOS was defined as the duration from hospital admission to discharge, encompassing both ICU LOS (the number of days spent in the ICU) and hospital LOS (the number of days spent in general wards). Hospitalization costs were calculated from itemized billing recordsand included all itemized hospitalization expenses, such as medications, examinations, therapies, consumables, nursing care, and rehabilitation. At the institutional level, we evaluated the hospital economic burden through two key metrics: (1) the reduction in patient admission capacity due to prolonged hospital stays caused by CROs, calculated as: Reduced admissions = (Number of CRO cases × (Median LOS of CRO group - Median LOS of CSOgroup)) / Median LOS of CSO group; and (2) the associated financial loss caused by reduced admissions was estimated as: opportunity costs= Reduced admissions × (Median hospitalization cost × 5% marginal profit rate).[20] The 5% marginal profit rate was chosen as a conservative estimate to prevent an overestimation of the economic burden associated with CROs. While the actual profit margins for Chinese tertiary hospitals can range from 3% to 8%, due to variations in region, medical insurance policies, and cost structures, using a middle-ground percentage helps ensure the final estimate is robust.

Covariates

We also extracted the following covariates: (1) demographic characteristics, including year of ICU admission, study hospital, age, and gender; (2) clinical characteristics, including illness severity at admission assessed by Acute Physiology And Chronic Health Evaluation (APACHE) II scoresand comorbidities with common chronic diseases, such as hypertension, diabetes, Chronic heart diseases (CHD), and chronic lung disease; (3) invasive procedures, including central venous catheterization, mechanical ventilation, urinary catheterization, and surgery.

PSM

PSM was conducted using a 1:1 nearest-neighbor matching algorithm without replacement, which reduces the total sample size but ensures that each matched pair is unique. The caliper width was set to 0.2 times the standard deviations of the logit-transformed propensity score. This value is a commonly recommended "gold standard"in PSM research, as it minimizes the mean squared error of the estimated treatment effect, ensuring that only sufficiently similar subjects are matched.[21] Matching variables included ICU admission year, hospital, age, gender, APACHE II score, comorbidities, and invasive procedures. Covariate balance was assessed using standardized mean differences (SMD), with all values below 0.1, suggesting that an adequate balance was achieved after matching (Supplementary Table 1). Matching was performed using R software (version 4.4.2) with the MatchIt package (v4.6.5), and balance was evaluated via the cobalt package (v4.5.2). Visualization of matching quality was created using ggplot2 (v3.5.1) with love plots and density plots. Ultimately, 379 CRO patients were matched to 379 CSO patients (total, n = 758), as illustrated in Figure 1.

Data Analysis

All statistical analyses were conducted using SPSS software (version 27.0). In our study, only two variables had missing data: the APACHE II score (6.5% of missing data) and hospitalization costs (8% of missing data), which were imputed using the average means. Baseline characteristics of the propensity score-matched groups (CRO vs CSO) were described and compared. The Skewness-Kurtosis (SK) test was initially performed to determine whether continuous variables were

normally distributed,followed by Q-Q plots for visualization (Supplementary Figure 1). Normally distributed data were expressed as means ± standard deviations (SDs) and compared using Student's *t*-test. In contrast, non-normally distributed data were presented as medians and interquartile ranges (IQRs) and compared using the Wilcoxon Rank-Sum test. Categorical data are presented as counts with percentages (%) and compared using the Chi-square test or Fisher's exact test for group comparisons.

To assess the independent association between CRO status and outcomes, GLMs were applied. Hospital LOS, a count variable exhibiting overdispersion, was modeled using a negative binomial distribution with a log link function. Total hospitalization cost, a continuous and right-skewed variable, was analyzed using a gamma distribution with a log link function. Covariates used in PSM were included to adjust for potential confounding and enhance model robustness. All statistical tests were two-sided with a significant threshold of 0.05.

Results

Patient Characteristics and Pathogen Distribution

Among 7,232 ICU patients included in the final analysis, 379 (5.24%) developed CROs based on microbiological cultures. Details of the CROs' incidence by year are shown in Supplementary Table 2. CRAB-only accounted for 64.6% (245/379) of CRO cases, followed by CRE-only (56/379, 14.8%), CRPA-only (39/379, 10.3%), and ≥2 CROs (39/379, 10.3%) (Table 1). Notably, Hospital A had a significantly higher proportion of CRAB than Hospital B (143/3747, 3.8% vs 102/3485, 2.9%, P<0.001).

Following 1:1 PSM, 379 CRO patients were matched to 379 CSO counterparts, forming a final analytic cohort of 758 patients (Figure 1). Baseline characteristics were well-balanced across the matched groups (all SMDs < 0.1; Figure 2, Table 1).

LOS and Hospitalization Cost

The CRO group had significantly longer ICU LOS (median, 11 vs 5 days, $P < 0.001$) and hospital LOS (median, 24 vs 13 days, $P < 0.001$) than the control group (Table 2). The total hospitalization costs were nearly twice as high in the CRO group compared to the CSO group (median CNY 99,549 vs CNY 50,279, $P < 0.001$). Specifically, antimicrobial expenditure and medication costs were 274% and 142% higher in the CRO group compared to the CSO group. Additional cost domains such as diagnostics, consumables, and nursing also showed a significant difference between the two groups.

Multivariable Model Estimates

Generalized linear models confirmed CRO status as an independent predictor of LOS and hospitalization costs (Table 3). CRO independently predicted longer hospital LOS (OR = 1.97, 95% CI: 1.70–2.27),longer ICU LOS (OR = 2.37, 95% CI: 2.03–2.76), and highertotal hospitalization cost (OR = 1.99, 95% CI: 1.78–2.23) as compared to CSO (Table 4).

Table 1 Proportions of CROs by Bacterial Species

	Total		Hospital A		Hospital B	
	n	%	n	%	n	%
CRAB-only	245	64.64	143	58.13	102	76.69
CRE-only	56	14.78	48	19.51	8	6.02
CRPA-only	39	10.29	28	11.38	11	8.27
≥2 CROs	39	10.29	27	10.98	12	9.02
Total	379	100.00	246	100.00	133	100.00

Abbreviations: CRO, Carbapenem-Resistant Organism; CRAB,carbapenem-resistant Acinetobacter baumannii;CRE, carbapenem-resistant Enterobacteriaceae;CRPA, Pseudomonas aeruginosa.

https://doi.org/10.2147/IDR.S555843

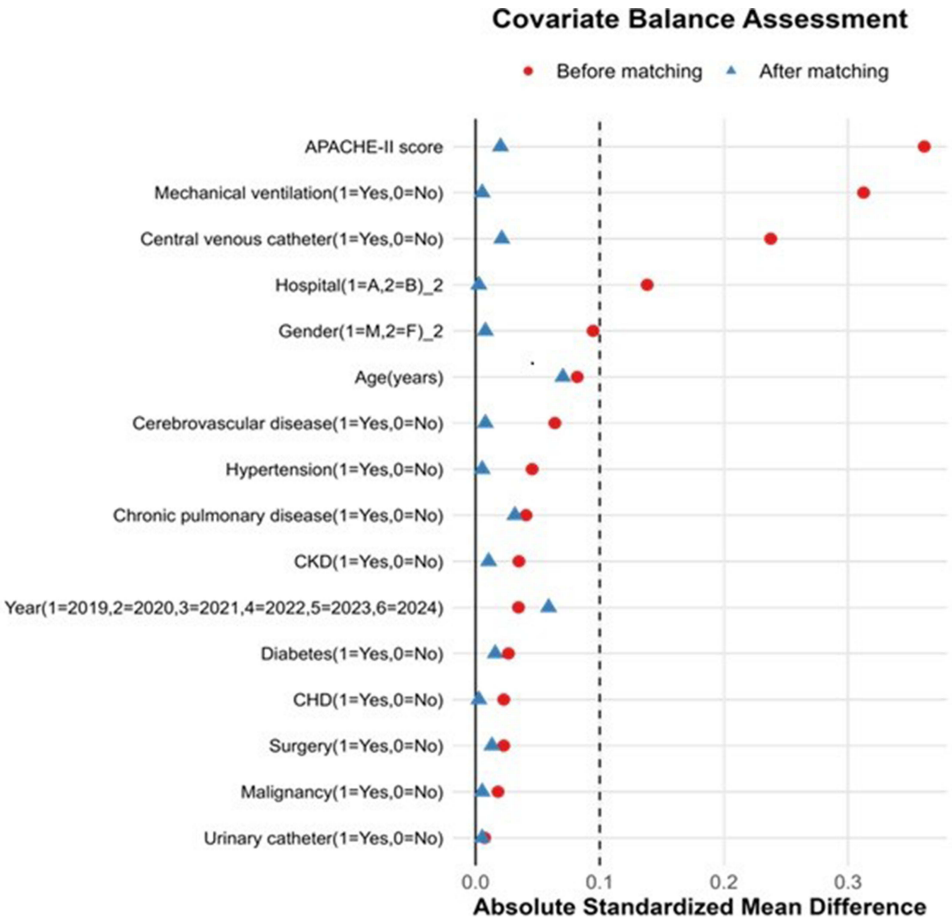

Figure 2 Covariate Balance Before and After Matching.

Institutional-Level Economic Burden

Excess ICU occupancy among CRO patients was projected to result in 459 missed ICU admissions and 321 missed hospital admissions over six years. Based on a conservative 5% marginal profit assumption, this corresponds to cumulative institutional opportunity costs of approximately CNY 134,000 per year. These estimates reflect opportunity costs alone and exclude direct expenditures related to CRO prevention and control (such as staffing, training, medical equipment, and medicines). We performed further sensitivity analyses by using different matching algorithms (eg, nearest-neighbor vs kernel matching) and different GLM distributions and link functions for the cost outcome (eg, Gamma or inverse Gaussian distributions with a log-link), and the results remained consistent.

Discussion

With the growing threat of global antimicrobial resistance, CROs are accounting for an increasingly larger proportion of ICU-acquired infections, especially in low- and middle-income countries where healthcare systems are more fragile.[5,7] This study, based on a large ICU cohort from two tertiary hospitals in Western China, employed PSM and GLM to systematically evaluate the impact of CRO colonization or infection on economic burden at both individual and institutional levels. The results demonstrated that CRO predicted longer ICU LOS, longer hospital LOS, and higher hospitalization costs as compared to CSO. Additionally, CRO is projected to result in an institutional opportunity loss of approximately CNY 134,000 per year. These findings are consistent with trends observed in both domestic and international studies, underscoring the substantial economic burden imposed by CROs.[8,12,14]

Our study detected an incidence of 5.24% for CROs among ICU patients, and further microbiological analysis revealed that CRAB was the most common pathogen among CRO patients, especially in mixed infections. This finding

Table 2 General Information Before and After Matching

Variable	Before matching				After matching			
	CSO (n=6853)	CRO (n=379)	t/χ^2	*P*	CSO (n=379)	CRO (n=379)	t/χ^2	*P*
Year			65.836	<0.001			24.563	<0.001
2019	801(11.70%)	76(20.10%)			53(14.00%)	76(20.10%)		
2020	951(13.90%)	24(6.30%)			52(13.70%)	24(6.30%)		
2021	1119(16.30%)	41(10.80%)			51(13.50%)	41(10.80%)		
2022	1374(20.00%)	55(14.50%)			77(20.30%)	55(14.50%)		
2023	1302(19.00%)	109(28.80%)			78(20.60%)	109(28.80%)		
2024	1306(19.10%)	74(19.50%)			68(17.90%)	74(19.50%)		
Hospital			27.475	<0.001			0.006	0.939
A	3501(51.10%)	246(64.90%)			247(65.20%)	246(64.90%)		
B	3352(48.90%)	133(35.10%)			132(34.80%)	133(35.10%)		
Age (M ± SD)	68.29 ± 14.80	69.35 ± 12.95	−1.539	0.124	70.26 ± 14.02	69.35 ± 12.95	0.929	0.353
Sex			13.520	<0.001			0.057	0.811
Male	4143(60.50%)	265(69.90%)			268(70.70%)	265(69.90%)		
Female	2710(39.50%)	114(30.10%)			111(29.30%)	114(30.10%)		
APACHE II score (M ± SD)	26.06 ± 9.82	29.29 ± 8.93	−6.810	<0.001	29.11 ± 10.00	29.29 ± 8.93	−0.261	0.795
Hypertension	2147(31.30%)	136(35.90%)	3.449	0.063	134(35.40%)	136(35.90%)	0.023	0.879
Diabetes	1464(21.40%)	91(24.00%)	1.492	0.222	97(25.60%)	91(24.00%)	0.255	0.614
CHD	1490(21.70%)	91(24.00%)	1.082	0.298	90(23.70%)	91(24.00%)	0.007	0.932
Chronic Lung Disease	1801(26.30%)	115(30.30%)	3.044	0.081	103(27.20%)	115(30.30%)	0.927	0.336
CKD	1117(16.30%)	75(19.80%)	3.177	0.075	71(18.70%)	75(19.80%)	0.136	0.713
Cerebrovascular Disease	1678(24.50%)	117(30.90%)	7.847	0.005	120(31.70%)	117(30.90%)	0.055	0.814
Malignancy	630(9.20%)	28(7.40%)	1.415	0.234	26(6.90%)	28(7.40%)	0.080	0.778
Central Venous Catheter	2078(30.30%)	205(54.10%)	93.910	<0.001	213(56.20%)	205(54.10%)	0.341	0.559
Mechanical Ventilation	2813(41.00%)	274(72.30%)	143.336	<0.001	272(71.80%)	274(72.30%)	0.026	0.871
Urinary Catheter	6722(98.10%)	369(97.40%)	0.993	0.319	371(97.90%)	369(97.40%)	0.228	0.633
Surgery	1837(26.80%)	93(24.50%)	0.944	0.331	98(25.90%)	93(24.50%)	0.175	0.676

Abbreviations: CRO, Carbapenem-Resistant Organism; CSO, Carbapenem-Susceptible Organism; M ± SD, Mean ± Standard Deviation; APACHE II, Acute Physiology And Chronic Health Evaluation II; CHD, Coronary Heart Disease; CKD, Chronic Kidney Disease.

Table 3 LOS and Hospitalization Costs Between the CRO and CSO Groups

Variable	CSO	CRO	z	*P*
Length of hospital stay (days)	13.00(7.00, 24.00)	24.00(15.00, 43.00)	−9.878	<0.001
Length of ICU stay (days)	5.00(3.00, 9.00)	11.00(7.00, 21.00)	−12.109	<0.001
Total hospitalization cost (CNY)	50279.00(32102.60, 88040.35)	99548.58(56321.68, 185156.00)	−10.156	<0.001
Medication cost (CNY)	13210.42(6381.82, 23360.47)	31974.35(16515.44, 58491.54)	−12.228	<0.001
Antimicrobial drug cost (CNY)	1390.48(488.88, 2955.20)	5191.94(2065.68, 11529.85)	−12.900	<0.001
Examination cost (CNY)	48381.27(3744.00, 101038.20)	83477.74(5787.00, 230946.76)	−5.889	<0.001
Treatment cost (CNY)	10,454.00(5567.50, 19594.50)	23425.00(13011.14, 48936.63)	−10.883	<0.001
Surgery cost (CNY)	175.00(0.00, 1120.00)	175.00(0.00, 1225.00)	−0.175	0.861
Anesthesia cost (CNY)	255.00(80.00, 1113.00)	355.00(40.00, 1835.25)	−1.774	0.076
Laboratory test cost (CNY)	9361.00(5924.00, 14213.00)	15517.00(9774.75, 26674.50)	−10.363	<0.001
Nursing cost (CNY)	1030.50(600.00, 1962.50)	2532.00(1346.63, 4618.50)	−11.847	<0.001
Medical consumables cost (CNY)	1030.50(600.00, 1962.51)	6159.99(2864.15, 18086.32)	−4.062	<0.001

Notes: Conversion based on PBOC rates, June 14, 2025: CNY1 = $0.1393; CNY1 = €0.1204.
Abbreviations: ICU, Intensive Care Unit; CRO, Carbapenem-Resistant Organism; CSO, Carbapenem-Susceptible Organism.

https://doi.org/10.2147/IDR.S555843

Table 4 Results of Generalized Linear Model Analysis for LOS and Hospitalization Costs

Variable	OR	95% CI	*P*	Increase
Hospital LOS	1.970	1.704–2.274	<0.001	0.970
ICU LOS	2.368	2.031–2.762	<0.001	1.368
Total hospitalization cost	1.994	1.783–2.230	<0.001	0.994

Abbreviations: ICU, Intensive Care Unit; LOS: Length of Stay; OR, Odds Ratio; CI, Confidence Interval.

aligns with previous studies and may be explained by the strong ability of CRAB to persist in the environment and form biofilms.[6,8] CRAB can survive for a long time on various surfaces, allowing the bacteria to colonize and persist in hospital environments, thereby increasing the likelihood of transmission and infection.[22] In addition, CRAB can easily form biofilms, which makes it more resistant to antibiotics and disinfectants, further reinforcing its survival and the spread of infections.[22] Therefore, it is crucial to adhere to stringent infection control measures, including environmental cleaning, surface disinfection, and hand hygiene, to prevent the transmission of CRAB.[23]

Our study showed that the CRO group had significantly longer ICU and hospital LOS than the CSO group. GLM further confirmed that CRO independently predicted significant increases in hospital LOS, ICU LOS, and total hospitalization costs. CROs drive an increased economic burden through multiple mechanisms, including higher treatment costs, prolonged hospitalizations, and indirect economic impacts. The carbapenem-resistant nature of CROs forces clinicians to use "last-resort" antibiotics, such as polymyxins (eg, colistin) and tigecycline, which are significantly more expensive and often have more side effects than standard carbapenem therapies.[24–26] Treatment for CRO infections typically requires a combination of multiple antibiotics to overcome resistance, further increasing medication costs.[24–26] Additionally, CROs are associated with a longer length of hospitalization, higher intensity of care, and increased resource utilization, which are key drivers of total healthcare costs.[11,14,22] Furthermore, the higher mortality rate and prolonged hospitalizations associated with CRO infections lead to significant indirect economic costs from lost wages and productivity, both for the patient and their family.[27] All these factors contribute to a significantly higher financial burden, indicating the need to promote appropriate antimicrobial stewardship and enhance infection control to curb the development and spread of CROs.

In addition, this study innovatively evaluated the indirect financial impact of CROs on healthcare institutions. We estimated a significant cumulative loss of ICU and hospital admissions, resulting in an annual economic loss of approximately CNY 134,000 These findings shift our understanding of CRO-related consequences from individual clinical outcomes to the broader hospital system, with a focus on resource inefficiencies. This comprehensive perspective provides a quantitative foundation for targeted investment in institutional infection control and for effective health policy planning and implementation. The mechanisms underlying the increased institutional costs of CRO are multifaceted. These include prolonged empirical antimicrobial therapy, repeated microbiological testing, extensive diagnostic and imaging studies, and increased nursing intensity.[1,24,28] In addition, treatment of CRO infections is often associated with a higher risk of antibiotic-related adverse events, which can further complicate the clinical course and delay the implementation of other treatment plans.[29–31] Our findings underscore the importance of preventing and effectively treating CROs to mitigate financial losses and optimize healthcare resources. Our results highlight the importance of prudent antibiotic use, robust infection control measures, and effective diagnostic practices in mitigating the overall burden on the healthcare system.

Our study represents the first attempt to quantify the economic burden of CROs at both the individual and institutional levels by combining PSM with GLM modeling. Our approach offers robust statistical control and parameter estimation, filling a crucial gap in the CRO burden literature, particularly in the Chinese healthcare context. However, this study also has some limitations. First, the retrospective study design is subject to multiple biases, including selection bias, information bias, and confounding bias, which may limit the external validity of the study findings. Future prospective longitudinal studies are needed to provide a stronger basis for establishing causality and minimizing the impact of biases.

Second, our study presented the total combined infection and colonization costs without distinguishing between infection and colonization status, which may lead to an overestimation of the economic burden of CROs. Future studies should integrate multiple data sources to accurately distinguish between them and utilize advanced statistical and financial modeling to characterize the different patient populations better. Third, the analysis did not include post-discharge indirect costs, such as those related to readmissions, rehabilitation, or outpatient treatment, thereby underestimating the total burden of CRO to some extent. Future studies should incorporate these costs to obtain a more comprehensive picture of the overall economic impact of CROs. Fourth, the study lacked data on clinical outcomes, such as mortality, functional status, and quality-adjusted life years (QALYs), preventing a more comprehensive assessment that encompasses both economic burden and patient prognosis, including cost-effectiveness analyses. Future studies should incorporate survival and health utility measures to assess the value of CRO prevention strategies better.

Implications

Strategies for evidence-based infection control and resource planning to address the increased economic burden of CROs in ICU patients must be comprehensive and data-driven, focusing on prevention, surveillance, and efficient allocation of resources. Based on our findings, we propose the following strategies to prevent CRO infection and reduce the economic burden of infection. First, hospitals should reinforce strict adherence to hand hygiene protocols (eg, proper use of soap and water), enhance environmental cleaning (eg, adequate disinfection of high-touch surfaces), and implement contact precautions (eg, using gowns and gloves for all patient interactions). Second, hospitals should implement proactive surveillance and early detection of CRO infections by performing active surveillance testing using rapid diagnostic tools (eg, Xpert Carba-R assays) to routinely screen high-risk ICU patients for CRO colonization upon admission. During CRO outbreaks, hospitals should implement whole-genome sequencing (WGS) or other genotyping methods to identify and trace transmission chains quickly. Third, hospitals should optimize resources to offset the economic impact of CROs through adequate staffing and training. For instance, hospitals can assign specific nursing staff to exclusively care for CRO-positive patients during a shift to minimize the risk of cross-transmission to other patients. Ongoing, targeted training should be provided to all healthcare personnel on the prevention of CRO transmission and compliance with infection control guidelines. Finally, hospitals should regularly evaluate the cost-effectiveness of infection control interventions to prioritize and streamline initiatives. Hospitals can convert economic burden data into a Return on Investment (ROI) model for infection prevention and control and present the ROI as a positive financial return, emphasizing that the savings from reduced healthcare-associated infections (HAIs) make the investment worthwhile.

Conclusion

This study demonstrates that CRO colonization or infection among ICU patients significantly prolongs ICU and hospital length of stay, increases total hospitalization costs, and reduces bed utilization efficiency. The burden extends beyond the individual level to institutional impacts, as reduced bed turnover leads to financial loss and operational strain. These findings carrysignificant policy and resource planning implications in formulating national priorities, ensuring patient safety and quality, optimizing existing infrastructure, and promoting interdepartmental collaboration.

Our study underscores the importance of implementing early screening, stratified isolation, and antimicrobial stewardship interventions in high-risk ICU populations. Targeted prevention and control measures may yield substantial medical and economic benefits, offering evidence-based support for the design of more cost-effective strategies to mitigate antimicrobial resistance in critical care environments. While this study provides a robust framework for quantifying the economic burdens of CROs, it is essential to acknowledge certain limitations, such as the retrospective study design, the inability to distinguish between colonization and infection, the lack of other indicators and further analyses, which warrant future research.

Abbreviations

CROs, Carbapenem-resistant organisms; CSOs, Carbapenem-susceptible organisms; ICUs, Intensive care units; LOS, Length of stay; PSM, Propensity score matching; GLMs, Generalized linear models; CRAB, Carbapenem-resistant Acinetobacter baumannii; CRE, Carbapenem-resistant Enterobacteriaceae; CRKP, Carbapenem-resistant Klebsiella pneumoniae; CRPA, Carbapenem-resistant Pseudomonas aeruginosa; WHO, World Health Organization; APACHE II, Acute Physiology And

Chronic Health Evaluation II; CHD, Coronary heart disease; CKD, Chronic kidney disease; IRBs, Institutional Review Boards; OR, Odds ratio; CI, Confidence interval; AST, Antimicrobial susceptibility testing; CNY, Chinese Yuan; QALY, Quality-adjusted life year; PBOC, People's Bank of China; WGS, Whole-genome sequencing; ROI, Return on Investment; HAI, Healthcare-associated infections.

Data Sharing Statement

The data of this study are available on reasonable request from the corresponding author.

Ethical Approval of Studies and Consent for Publication

This retrospective study was approved by the Ethics Committees of Zigong First People's Hospital and Fushun People's Hospital (Approval No. 202452 and No. 2025KY004HY). All data were anonymized and de-identified before analysis, and no personally identifiable information was used. The requirement for informed consent was waived due to the retrospective nature of the study and the use of routinely collected clinical data.

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.

Funding

This study was funded by grants from the Youth Innovation Project of Sichuan Medical Association (Grant No. Q2024027), the Key Research Program of the Department of Science and Technology of Zigong (Grant No. 2023-YGY-2-04), and the research project of Zigong Philosophy and Social Science Key Research Base, Health Humanities Research Center (Grant No. JKRWY24-06).

Disclosure

The authors report no conflicts of interest in this work.

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