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ORIGINAL RESEARCH

Effect of ICU Quality Control and Secondary Analysis: A 12-Year Multicenter Quality Improvement Project

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Background: China's aging population and increasing demand for critical care pose significant challenges to ICU quality improvement (QI). This study evaluates the impact of a 12-year multicenter QI initiative on ICU performance and patient outcomes in the context of resource constraints.
Methods: A pre-post intervention study was conducted across 75 ICUs in Beijing from January 2011 to December 2022. Key interventions included the establishment of QI teams, infection prevention protocols, pain and sedation management, nutritional support, and early mobilization strategies based on the PDCA cycle, as well as regular training and feedback. Primary outcomes included ICU mortality, standardized mortality ratio (SMR) (ratio of observed to expected deaths, adjusted for risk), and healthcare-associated infections (HAIs), such as VAP, CLABSI, and CAUTI rates. Secondary outcomes included unplanned extubation rates, reintubation within 48 hours, and ICU readmission rates within 48 hours.
Results: Analysis of 425,534 patient records from 5396 reports revealed significant improvements. The proportion of ICU admissions among total inpatients increased from 4.1% in 2011 to 7.3% in 2022 ($P < 0.001$), and the proportion of patients with APACHE II scores ≥15 rose from 52.0% to 67.5% ($P < 0.001$). Compliance with 3-hour and 6-hour sepsis bundles increased ($P < 0.001$), and microbiological testing before antibiotic administration also improved ($P < 0.001$). Outcome indicators showed significant reductions in CRBSI and CAUTI rates ($P < 0.001$), ICU mortality ($P < 0.001$), and SMR ($P < 0.001$). VAP rates decreased from 6.29 to below 5.0 per 1000 ventilator days. ICU readmission rates and unplanned transfers slightly increased but remained low ($P > 0.05$).
Conclusion: The study highlights the importance of addressing structural, process, and outcome indicators for effective ICU management. Continued monitoring and targeted interventions for high-risk ICUs are essential to sustaining quality improvements.
Keywords: intensive care unit, quality improvement, data analysis, patient prognosis, mortality rate

Introduction

Critical care medicine has made significant progress globally, driven by advances in medical technology, diverse diagnostic and therapeutic approaches, and improved nursing standards.[1] These developments have substantially enhanced the survival and quality of life of critically ill patients. However, alongside this progress, countries such as China face unique challenges due to rapid societal changes, particularly the aging population and associated healthcare demands.[2] China's population is aging at an unprecedented rate. According to the National Bureau of Statistics, individuals aged 65 years or older are projected to account for approximately 30% of the population by 2035.[3] This demographic shift has led to a sharp increase in the prevalence of chronic diseases and the frequency of acute disease outbreaks, directly driving the demand for specialized intensive care unit (ICU) resources.[4] Consequently, balancing the growing need for critical care services with the constraints of existing healthcare resources has become a pressing challenge. Addressing these issues requires not only expanding ICU capacity but also improving service quality through systematic approaches.[5]

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Healthcare-associated infections (HAIs), such as ventilator-associated pneumonia (VAP), catheter-related bloodstream infections (CRBSI), and catheter-associated urinary tract infections (CAUTI), are critical indicators for evaluating ICU quality and patient safety.[6] VAP, defined as pneumonia occurring between 48 hours after the initiation of mechanical ventilation and 48 hours post-extubation, significantly increases patient morbidity, length of hospital stay, and healthcare costs, while complicating weaning and, in severe cases, threatening lives.[7,8] CRBSI, caused by bloodstream infections related to intravascular catheters, is closely linked to catheter use and maintenance practices. Its prevention not only reduces patient suffering and economic burden but also reflects hospital infection control quality.[9] Similarly, CAUTI, a urinary tract infection associated with catheter use, affects patient comfort and recovery, while contributing to the overuse of antibiotics and antibiotic resistance.[10] Monitoring and reducing the incidence of these HAIs are essential to improving ICU care quality and ensuring patient safety.

In recent years, global attention to quality improvement in ICU has grown significantly. Pronovost et al demonstrated that the implementation of multifaceted, safety culture–based interventions can markedly reduce catheter-related bloodstream infections in the ICU, thereby providing robust empirical evidence for quality improvement efforts.[5] Meanwhile, Rhodes et al introduced a set of prospectively defined quality indicators aimed at enhancing patient safety and the overall quality of care in critically ill patients, a framework that has been widely adopted across European ICU.[11] Despite global efforts to address HAIs and improve ICU care, most existing studies are limited to short-term interventions or single-center settings. There is a lack of comprehensive evaluations of long-term, multicenter quality improvement (QI) initiatives. Addressing this gap, our study evaluates the impact of a 12-year multicenter QI initiative on ICU quality indicators, including VAP, CRBSI, and CAUTI rates, as well as other key clinical outcomes such as ICU mortality and standardized mortality ratio (SMR). This initiative aimed to optimize ICU service processes and management systems through evidence-based protocols, staff training, and real-time performance monitoring. By focusing on long-term, large-scale interventions, this study not only fills a critical gap in the literature but also provides evidence for implementing sustainable improvements in ICU care. It highlights the potential for systematic QI measures to enhance patient safety, reduce HAIs, and improve ICU performance in resource-constrained settings.

Methods

Study Design

This evaluation leverages a comprehensive dataset from the Beijing Intensive Care Medical Quality Control and Improvement Center's quality enhancement project, spanning a 12-year timeframe from January 2011 to December 2022. This study is exempt from ethical review in accordance with Section 32 of the https://www.gov.cn/zhengce/zhengceku/2023-02/28/content_5743658.htm This retrospective study collected information data on a per ICU basis, without involving personal information, and could not be used to identify or trace back to specific individuals, thus posing no impact on individuals. The Beijing Friendship Hospital Research Ethics Committee has confirmed that no ethical approval is required.

Subjects and Populations

ICUs met the following requirements were included: 1. having more than five beds. 2. be capable of diagnosing and treating medical conditions such as VAP, CRBSIs, and CAUTIs. 3. complying with China's equipment, construction, and management standards [13].

This study employed a retrospective design, utilizing data from 75 ICUs in Beijing. It included adult patients (aged ≥18 years) admitted to any of the 75 participating ICUs over the 12-year study period, excluding those with significant missing data that precluded effective analysis.

Intervention

This study includes a comprehensive quality improvement initiative focused on four key interventions aimed at enhancing ICU patient outcomes: infection prevention, pain and sedation management, nutritional support, and early mobilization. Each intervention follows established guidelines to ensure scientific rigor and practical feasibility.

Infection Prevention Measures

Infection prevention is prioritized and implemented immediately upon ICU admission. Measures include proper hand hygiene, sterile techniques for invasive procedures, and daily environmental cleaning, with weekly ultraviolet disinfection. Surveillance for catheter-associated infections and multi-drug-resistant organisms is conducted regularly. Monthly audits by infection control specialists ensure compliance (WS/T 509–2016).[12]

Pain and Sedation Management Strategies

Pain management follows national guidelines and includes assessments using the Critical-Care Pain Observation Tool. Mild pain is treated with NSAIDs, while moderate to severe pain requires short-acting opioids like fentanyl. Non-pharmacological methods, such as psychological counseling, are combined with pharmacological treatments when necessary. Pain management is initiated upon ICU admission and adjusted based on daily CPOT scores (Chinese Guidelines for Pain and Sedation in Adult ICU Patients).[1,13]

Nutritional Support Programs

Nutritional support follows national guidelines, with enteral nutrition starting within 24–48 hours for patients with functional gastrointestinal tracts. Energy and protein intake are tailored based on individual needs, and parenteral nutrition is used if enteral feeding is not tolerated. Regular monitoring of blood glucose and electrolytes is conducted to adjust nutrition plans (Chinese Guidelines for Nutrition Assessment and Monitoring of Adult ICU Patients).[14]

Early Mobilization Practices

Early mobilization is initiated once hemodynamic and respiratory parameters stabilize. Interventions include passive joint exercises, sitting at the bedside, or walking, depending on the patient's condition. Sessions last 15–30 minutes and are conducted 1–2 times daily. The intensity of mobilization is gradually increased based on the patient's progress (Expert Consensus on Early Rehabilitation and Mobilization of Adult ICU Patients).[15]

Outcome

Primary Outcomes

Patient Mortality

Defined as all-cause mortality occurring during ICU admission. Mortality data will be sourced from hospital records and confirmed through follow-up communications with patient relatives or outpatient care providers. To account for differences in patient severity, the SMR is also calculated, which is defined as the ratio of observed mortality to expected mortality based on severity scores, such as the Acute Physiology and Chronic Health Evaluation II score.[16,17] The APACHE II score is a widely accepted quality control indicator in ICU settings, providing a robust method to assess patient severity and predict mortality risk. Its correlation with ICU mortality rates helps evaluate the effectiveness of ICU interventions and identify areas for improvement.

Incidence of Complications

Complications are significant adverse events during the ICU stay that negatively impact patient outcomes. This study focuses on major complications, including VAP, catheter-associated urinary tract infections, central line-associated bloodstream infections. These complications will be documented daily by clinical staff and periodically reviewed for accuracy. VAP: Diagnosed based on the Centers for Disease Control and Prevention and National Healthcare Safety Network surveillance definitions for specific types of infections;[18] CAUTIs: Identified per CDC/NHSN criteria, requiring clinical symptoms such as fever, urgency, or dysuria, confirmed by positive urine culture; CLABSIs: Determined using CDC/NHSN definitions, with positive blood cultures and no other identifiable source of infection; Pressure Ulcers: Includes stage II or higher ulcers as per the National Pressure Injury Advisory Panel classification system.[19] Each of these complications is a critical quality indicator in ICU care, with direct implications for patient recovery and mortality. Monitoring these complications allows for targeted interventions and continuous quality improvement efforts in ICU settings.

Secondary Outcomes

The secondary outcomes include unplanned extubation rates, reintubation rates within 48 hours, and ICU readmission rates within 48 hours. Unplanned extubation is defined as the percentage of patients who experience unplanned extubation during their ICU stay, with data collected from electronic medical records and verified through clinical documentation. Reintubation rates within 48 hours refer to the percentage of patients requiring reintubation within 48 hours of extubation, with data gathered from patient records and confirmed through follow-up assessments. ICU readmission rates within 48 hours measure the percentage of patients readmitted to the ICU within 48 hours after initial discharge, with data obtained from electronic medical records and supplemented by follow-up communications with outpatient care providers to ensure accurate documentation of readmissions. These secondary outcomes are pivotal in assessing the immediate impact of ICU care on patient recovery and the effectiveness of discharge protocols. Monitoring these outcomes helps optimize ICU patient management and reduce preventable readmissions.

Sample Size and Power

Due to the retrospective nature of the study, no formal sample size calculation was performed. However, with data encompassing 75 ICUs and over 420,000 patient records, the study provides robust statistical power for detecting meaningful trends and associations.

Statistical Analysis

Statistical analysis was performed using advanced statistical software such as R and SPSS to ensure robust evaluation of the data. The one-sample Kolmogorov–Smirnov test was employed to assess the normality of measurement data. Data conforming to a normal distribution were expressed as mean ± standard deviation, whereas non-normally distributed data were presented as median (interquartile range). Enumeration data were described using frequencies and composition ratios. To compare differences between groups, the Mann–Whitney *U*-test was used for non-parametric data, while t-tests were applied to parametric data. For repeated-measures data, two-way repeated-measures ANOVA was performed when data showed normal distribution and homogeneity of variance; otherwise, the Scheirer-Ray-Hare test was utilized. Time-series analysis was employed to evaluate temporal variations and predict trends in quality indicators over the 12-year period. Multivariable regression models were constructed to adjust for potential confounders such as patient demographics, baseline severity (APACHE II scores), and comorbidities. All statistical tests were two-tailed, and a P value of less than 0.05 was considered statistically significant. This integrated statistical approach enabled a comprehensive analysis of both short-term and long-term impacts of the quality improvement interventions on ICU performance and patient outcomes.

In 2010, the Beijing Center for Quality Control and Improvement of Critical Care Medicine established nine ICU QC indicators, with data collection commencing in 2011. On April 10, 2015, the National Health Commission recommended six additional indicators,[20] and we incorporated them into data collection in 2018 (Table 1). QI specialists submitted data to the Beijing Center for Quality Control and Improvement of Critical Care Medicine (https://bj.ccmqc.com). The Center extracted and reviewed the data, including numerical range assessment and logical verification. Indicators were calculated based on raw data (Table 1).

Results

Quality Improvement Over the Past 12 Years

From January 2011 to December 2022, we collected QC data encompassing 75 ICUs, which yielded 5396 reports pertaining to 425,534 patients.

The structural indicators (proportion of ICU in total inpatients (bed occupancy), proportion of APACHE II score ≥ 15 in all ICU patients) gradually increased over the last 12 years. The process indicators (3h and 6h SSC bundles compliance, microbiology detection before antibiotics, and proportion of DVT prophylaxis) also progressed. The outcome indicators (unplanned endotracheal extubation, CRBSI, CAUTI, and pressure sore incidence rate) improved. However, unplanned transfer to ICU, reintubation, and ICU re-admission rates within 48 hours have increased recently.

Table 1 Quality Control Indicators, Definitions, Data Collection Period and Trend P Value

Indicators	Definition	Collection Period	Coefficient	Trend *P* Value
Proportion of ICU in total inpatients (%)	(patients admitted to the ICU)/(patients admitted to hospital during the same period)	2018–2022	0.097	0.000
Proportion of ICU in total inpatient bed occupancy (%)	(days of ICU bed occupancy by patients)/(days of hospital bed occupancy by patients during the same period)	2018–2022	0.150	0.000
Proportion of APACHE II score ≥ 15 in all ICU patients (%)	(no. of patients with APACHE II score ≥ 15 during the first 24 h in the ICU)/((no. of patients admitted to the ICU during the same period)	2018–2022	0.069	0.002
3 h SSC bundles compliance (%)	(no. of septic shock patients who received the 3-h SSC bundle treatment)/ (no. of septic shock patients admitted to the ICU during the same period)	2018–2022	0.081	0.001
6 h SSC bundles compliance (%)	(no. of septic shock patients who received the 6-h SSC bundle treatment)/ (no. of septic shock patients admitted to the ICU during the same period)	2018–2022	0.076	0.002
Microbiology detection before antibiotics (%)	(no. of patients with microbiology detection before antibiotics)/(no. of patients who received antibiotics during the same period)	2018–2022	0.113	0.000
Proportion of DVT prophylaxis (%)	(no. of patients who received DVT prophylaxis treatment)/(no. of patients admitted to the ICU during the same period).	2018–2022	0.071	0.001
Unplanned transfer to ICU (%)	(no. of patients with unplanned transfer to the ICU from other wards)/(no. of patients transferred to the ICU from other wards during the same period)	2018–2022	0.153	0.000
Unplanned endotracheal extubation (%)	(no. of patients with unplanned endotracheal extubation)/(no. of patients with endotracheal extubation during the same period)	2011–2022	−0.042	0.003
Reintubation rate within 48 h (%)	(no. of patients reintubated within 48 h after endotracheal extubation)/(no. of patients with endotracheal extubation during the same period)	2011–2022	0.069	0.000
ICU re-admission rate within 48h (24h) (%)	(no. of patients readmitted to the ICU within 24h(48) h after discharge from the ICU)/(no. of patients discharged from the ICU during the same period)	ICU re-admission rate within 24 h (%) in 2011–2018; ICU re-admission rate within 48 h (%) in 2018–2022	0.035	0.011
VAP incidence rate (%)/1000 ventilator days	(no. of patients with VAP)/(no. of patients with mechanical ventilation during the same period)	2011–2022	−0.026	0.056
CRBSI incidence rate (%)/1000 line days	(no. of patients with CRBSI)/(no. of patients with a central venous catheter during the same period)	2011–2022	−0.097	0.000
CAUTI incidence rate (%)/1000 line days	(no. of patients with CAUTI)/(no. of patients with a urinary catheter during the same period)	2011–2022	−0.089	0.000
Pressure sore incidence rate (%)	(no. of patients with pressure sore incidence in the ICU)/(no. of patients admitted to the ICU during the same period)	2011–2018	−0.103	0.000
ICU Mortality rate (%)	(no. of patients who died in the ICU)/(no. of patients who discharged or died from the ICU during the same period)	2011–2018 Data for 2018–2022 was also collected	−0.082	0.000
Expected mortality rate (%)	(the sum of expected mortality rates for all patients admitted to the ICU) / (no. of patients admitted to the ICU during the same period). Expected mortality was calculated based on APACHE II score.	2018–2022 Data for 2011–2018 was also collected	−0.019	0.175
Standardized mortality ratio (SMR)	(no. of patients who died in the ICU)/ the sum of expected mortality rates for all patients admitted to the ICU); Expected mortality was calculated based on APACHE II score.	2011–2022	−0.165	0.000

Notes: ≥: Greater than or equal to. h: Hours. Statistical Terms: Coefficient: The estimated slope from the time-series analysis indicating the direction and magnitude of change over time. Trend P value: The statistical significance derived from the time-series analysis; a lower P value suggests a more statistically robust trend.
Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II; SCC, Surviving Sepsis Campaign; DVT, Deep Venous Thrombosis; VAP, Ventilator-Associated Pneumonia; CRBSI, Catheter-Related Bloodstream Infections; CAUTI, Catheter-Associated Urinary Tract Infections.

VAP incidence and expected mortality rate compared between 2010 and 2022 were approximative, while SMR and ICU mortality rate declined. Above all, the QI indicator's varieties across 12 years reflect advancements in ICU management (Figure 1).

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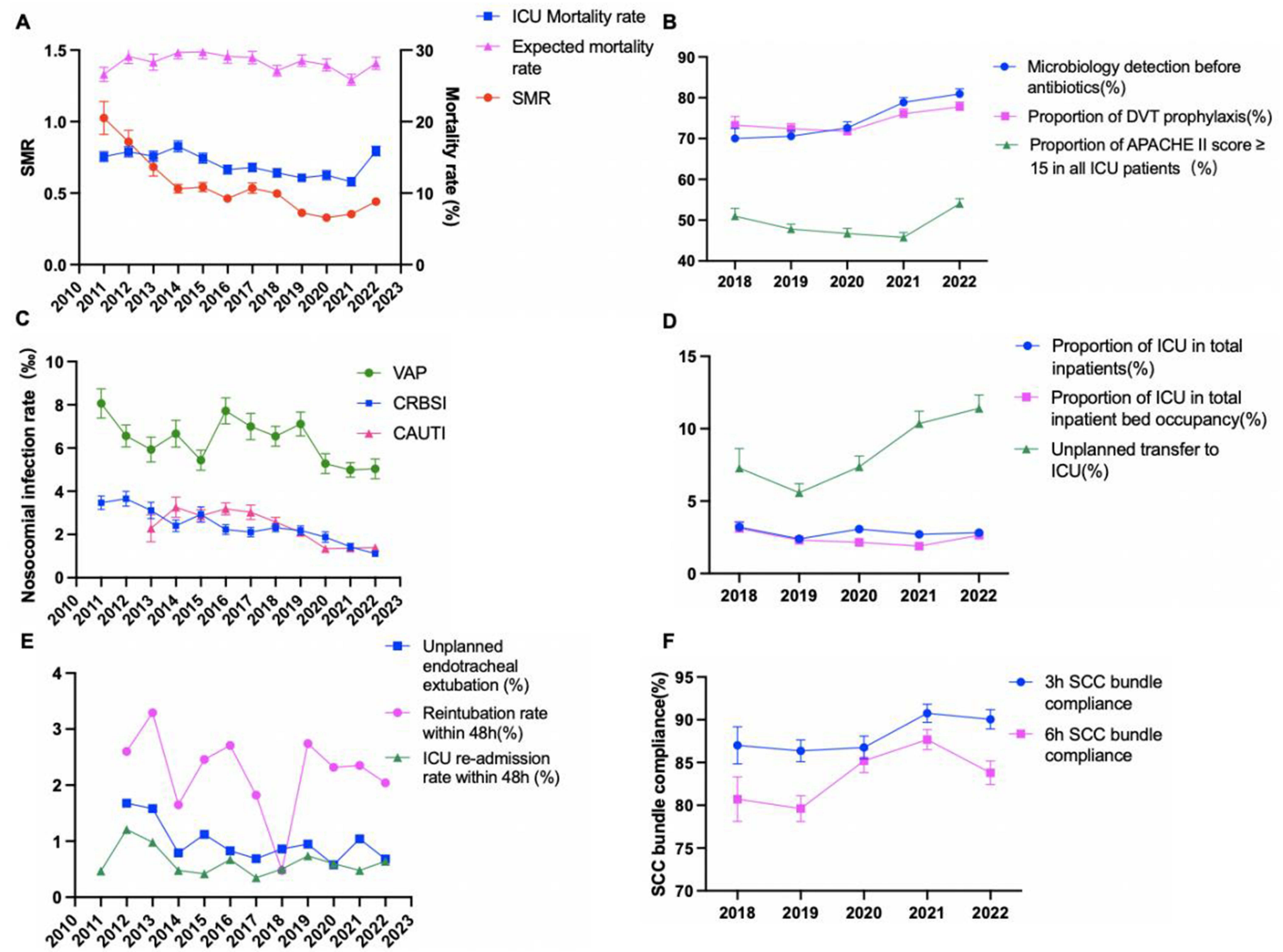

Figure 1 The QI indicator's varieties across 12 years. (**A**). SMR, ICU Mortality Rate, and Expected Mortality Rate: The Standardized Mortality Ratio (SMR) (red line) shows a decline over time, while ICU mortality rate (blue) and expected mortality rate (pink) remain relatively stable with minor fluctuations. (**B**). Microbiology Detection Before Antibiotics, DVT Prophylaxis, and APACHE II Scores: There is an upward trend in the proportion of microbiology detection before antibiotics (green), DVT prophylaxis (blue), and patients with APACHE II scores ≥ 15 (purple), reflecting improved clinical practices and increasing patient acuity in the ICU. (**C**). Nosocomial Infection Rates: The rates of ventilator-associated pneumonia (VAP), catheter-related bloodstream infections (CRBSI), and catheter-associated urinary tract infections (CAUTI) show a consistent decline, signaling improvements in infection control practices in the ICU. (**D**). ICU Bed Occupancy and Transfers: The proportion of ICU patients relative to total inpatient beds (blue) peaked and then stabilized, while unplanned transfers to the ICU (green) fluctuated over time. This suggests evolving ICU admission and transfer protocols. (**E**). Unplanned Endotracheal Extubation, Reintubation, and Readmission Rates: Unplanned endotracheal extubation (pink) fluctuates significantly, while reintubation rates within 48 hours (green) and ICU readmission rates within 48 hours (blue) show minor changes, indicating areas for improvement in airway management. (**F**). Compliance with 3-hour and 6-hour SSC Bundles: Compliance with both 3-hour (blue) and 6-hour (pink) SSC bundles improved over time, demonstrating effective implementation of quality improvement protocols aimed at reducing sepsis-related complications.

Policies Spurred ICU Management

The QI project started in 2011—however, national ICU QC indicators were introduced in April 2015. Since new policies promote management enhancement, we categorized the nine initial indicators into the early phase (2011–2015) and the later phase (2016–2022). Scheirer-Ray-Hare (SRH) test analyzes the influence of official guidance.

Data from 2016 to 2022 showed significant reductions in the expected mortality rate, ICU mortality rate, SMR, and unplanned endotracheal extubation rate (Table 2). Improvements were predominantly in mortality-related indicators, implying that standardized management positively influenced medical procedures.

Infectious-related indicators, specifically CRBSI and CATIU, markedly decreased (Table 2), which may be partially attributed to medical technology advancements.

ICU re-admission rate within 48h was the only indicator affected by time and group interaction (Table 2), underscoring the comprehensive progress of diagnostic and therapeutic competencies.

Table 2 Group×time Interaction Analysis

	Group		Time		Group×Time	
	H	*P*	*H*	*P*	*H*	*P*
Expected mortality rate (%)	4.3551	0.037	21.4825	0.029	9.1808	0.605
ICU Mortality rate (%)	41.148	0.000	17.102	0.105	3.608	0.980
Standardized Mortality Ratio (SMR)	60.848	0.000	3.993	0.970	5.976	0.875
ICU re-admission rate within 48h (24h) (%)	1.0594	0.303	5.8728	0.882	25.996	0.007
Unplanned endotracheal extubation rate (%)	5.0039	0.025	5.473	0.906	6.3589	0.844
Reintubation rate within 48h (%)	2.4278	0.119	5.1951	0.921	3.0836	0.990
VAP incidence rate (‰)	3.7648	0.976	0.188	0.665	6.3302	0.850
CRBSI incidence rate (%)/1000 line days	5.474	0.906	44.704	0.000	7.413	0.765
CAUTI incidence rate (%)/1000 line days	2.2221	0.998	17.5077	0.000	8.551	0.664

Notes: ‰: Per thousand. (24h)(48h): Hours. Statistical Terms: H: Test statistic (eg, from a nonparametric test such as the Kruskal–Wallis test). P: P-value indicating the level of statistical significance.
Abbreviations: VAP, Ventilator-Associated Pneumonia; CRBSI, Catheter-Related Bloodstream Infections; CAUTI, Catheter-Associated Urinary Tract Infections.

Secondary Analysis of the QI Indicators

Among 75 ICUs, 48 (64.0%) and 27 (36.0%) were from tertiary and secondary hospitals, respectively; 53 (70.7%) were comprehensive, and 22 (29.3%) were specialized; 58 (77.3%) in urban areas, while 17 (22.7%) in suburban areas. The above classifications served as a fundament for secondary analysis to unearth the management parallels and disparities among ICUs. As shown in Table 3 and Figure 2

Tertiary hospital ICUs prioritize monitoring the incidence rates of VAP, CRBSI, and CAUTI. In contrast, secondary hospitals emphasize compliance with 3-hour sepsis care bundles (SSC), pre-antibiotic microbiology detection, ICU readmission rates within 48 hours, occurrences of unplanned endotracheal extubation, reintubation rates within 48 hours, unplanned ICU transfers, and pressure sore rates. General ICUs concentrate on adherence to both 3-hour and 6-hour SSC bundles, unplanned endotracheal extubation incidents, the proportion of DVT prophylaxis, and the incidence rates of VAP, CRBSI, and CAUTI. Conversely, specialized ICUs are chiefly concerned with unplanned ICU transfers. Urban ICUs direct their attention to VAP, CRBSI, CAUTI incidence rates, DVT prophylaxis proportions, and pressure sore rates. Meanwhile, ICUs in suburban areas prioritize microbiology detection before antibiotic administration.

Time-Series Analysis and Prediction

The analysis of our time-series data has shown how the quality control (QC) indicators have changed over the past twelve years. The readmission rate to the ICU within 48 hours (24 hours) (Figure 3A) has decreased, especially during the winter months, and has stabilized around 1.0% since 2021. The proportion of ICU bed occupancy relative to total inpatient beds (Figure 3B) peaked in 2018 and has remained stable at around 5% due to stricter ICU admission standards for critically ill patients. An increasing proportion of ICU patients with APACHE II scores ≥ 15 since 2021 supported the assumption (Figure 3O), likely due to hospital expansions and increased bed availability. The unplanned endotracheal extubation rate (Figure 3K) has shown a consistent decline over the twelve-year observation period, indicating improvements in patient management and safety protocols. Initially, the rate exhibited significant volatility, peaking around 2013. However, since 2016, the rate has gradually decreased with smaller fluctuations. The forecast suggests that the rate will stabilize below 10‰, reflecting advancements in clinical practices and the implementation of preventive measures.

The volatility in the proportion of ICU patients relative to total inpatients (Figure 3C) has decreased since 2020, with future estimates suggesting it will stabilize between 8.5% and 9% as hospital scales reach equilibrium. The rate of unplanned transfers to the ICU (Figure 3D) has gradually increased with minimal fluctuations.

The 3-hour SSC bundle (Figure 3E) has revealed periodic oscillations, while the 6-hour bundle (Figure 3F) has shown a slight downward trend. The incidence rates of VAP, pressure sores, CAUTI per 1000 line days, and CRBSI per 1000 line days have all decreased (Figure 3G-J). Significantly, the incidence rates of VAP and pressure sores may remain

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Table 3 Secondary Analysis of the QI Indicators [Median(Q1,Q3) Mean(SE)]

	Total	**Secondary Hospitals**	**Tertiary Hospitals**	**P**	**General ICU**	**Specialized ICU**	**P**	**Urban ICU**	**Suburban ICU**	**P**
Proportion of ICU in total inpatients (%)	2.01(1.06,3.02) 2.78(0.08)	1.83(1.22,2.45) 2.13(0.09)	2.13(0.85,3.31) 3.07(0.11)	0.007	2.18(1.43,3.22) 3.22(0.11)	1.20(0.38,2.53) 1.77(0.09)	0.000	1.98(0.82,3.05) 2.95(0.11)	2.05(1.36,2.97) 2.38(0.07)	0.007
Proportion of ICU in total inpatient bed occupancy (%)	1.55(0.98,2.38) 2.34(0.08)	1.48(1.16,1.93) 1.73(0.06)	1.63(0.84,2.63) 2.61(0.11)	0.031	1.78(1.27,2.66) 2.64(0.99)	1.01(0.47,1.62) 1.66(0.14)	0.000	1.59(0.83,2.60) 2.41(0.10)	1.51(1.21,1.87) 2.18(0.13)	0.389
Proportion of APACHE II score ≥ 15 in all ICU patients (%)	48.22 (24.34,70.73) 48.82(0.59)	67.54 (50.00,85.71) 65.02(0.95)	38.66 (19.63,59.87) 41.89(0.66)	0.000	52.00 (27.58,74.07) 51.83(0.72)	43.28 (18.75,61.54) 42.45(0.99)	0.000	46.30 (23.24,70.38) 47.85(0.70)	53.38 (27.23,71.81) 51.39(1.08)	0.004
3h SSC bundles compliance (%)	100.00 (90.00,100.00) 88.45(0.58)	100.00 (83.33,100.00) 84.49(1.27)	100.00 (91.67,100.00) 90.17(0.62)	0.002	100.00 (86.67,100.00) 86.69(0.76)	100.00 (95.00,100.00) 92.42(0.78)	0.000	100.00 (90.08,100.00) 89.43(0.64)	100.00 (85.71,100.00) 85.93(1.28)	0.561
6h SSC bundles compliance (%)	100.00 (80.00,100.00) 83.80(0.67)	100.00 (75.00,100.00) 82.15(1.29)	100.00 (80.00,100.00) 84.55(0.78)	0.106	100.00 (75.00,100.00) 81.95(0.86)	100.00 (83.33,100.00) 87.95(0.98)	0.001	100.00 (80.00,100.00) 84.04(0.77)	100.00 (75.00,100.00) 83.30(1.32)	0.610
Microbiology detection before antibiotics (%)	89.53 (60.00,100.00) 75.26(0.66)	85.19 (46.23,96.30) 69.28(1.33)	91.95 (64.29,100.00) 78.03(0.73)	0.000	89.29 (60.00,100.00) 75.68(0.79)	90.00 (61.20,100.00) 74.93(1.17)	0.949	92.31 (65.37,100.00) 78.47(0.71)	80.75 (44.88,97.14) 67.34(1.42)	0.000
Proportion of DVT prophylaxis (%)	87.38 (56.24,97.05) 74.40(0.60)	90.00 (68.09,95.65) 77.90(0.99)	85.71 (51.27,97.59) 72.84(0.75)	0.237	86.96 (60.53,97.55) 76.19(0.68)	87.50 (45.45,95.24) 70.59(1.18)	0.001	85.71 (52.22,96.60) 73.06(0.72)	90.11 (65.79,97.83) 77.81(1.08)	0.002
Unplanned endotracheal extubation (%)	0.00(0.00,0.00) 0.94(0.05)	0.00(0.00,0.00) 1.07(0.11)	0.00(0.00,0.00) 0.88(0.06)	0.000	0.00(0.00,0.00) 0.99(0.07)	0.00(0.00,0.00) 0.82(0.09)	0.016	0.00(0.00,0.00) 0.89(0.06)	0.00(0.00,0.00) 1.10(0.12)	0.293
Reintubation rate within 48 h (%)	0.00(0.00,0.00) 2.11(0.09)	0.00(0.00,0.00) 2.50(0.19)	0.00(0.00,0.00) 1.92(0.10)	0.000	0.00(0.00,0.00) 2.23(0.11)	0.00(0.00,0.00) 1.83(0.15)	0.701	0.00(0.00,0.00) 2.17(0.11)	0.00(0.00,0.00) 1.90(0.15)	0.084
Unplanned transfer to ICU (%)	0.00(0.00,7.93) 8.53(0.38)	0.00(0.00,14.09) 13.07(0.96)	0.00(0.00,6.35) 6.66(0.36)	0.004	0.00(0.00,7.41) 7.78(0.44)	0.00(0.00,8.82) 10.10(0.75)	0.003	0.00(0.00,8.00) 9.13(0.48)	0.00(0.00,7.57) 6.97(0.57)	0.790
ICU re-admission rate within 48 h (%)	0.00(0.00,0.00) 0.63(0.05)	0.00(0.00,0.00) 0.85(0.12)	0.00(0.00,0.00) 0.53(0.04)	0.000	0.00(0.00,0.00) 0.65(0.06)	0.00(0.00,0.00) 0.60(0.08)	0.360	0.00(0.00,0.00) 0.53(0.04)	0.00(0.00,0.00) 0.93(0.14)	0.391
VAP incidence rate (%)/1000 ventilator days	0.00(0.00,8.52) 6.29(0.15)	0.00(0.00,6.90) 5.40(0.27)	1.76(0.00,9.17) 6.70(0.18)	0.000	0.00(0.00,8.77) 6.68(0.20)	0.00(0.00,8.06) 5.47(0.23)	0.002	0.00(0.00,8.63) 6.20(0.17)	0.00(0.00,8.20) 6.55(0.35)	0.002
CRBSI incidence rate (%)/1000 line days	0.00(0.00,2.59) 2.34(0.07)	0.00(0.00,0.00) 2.30(0.15)	0.00(0.00,3.29) 2.36(0.08)	0.000	0.00(0.00,3.21) 2.49(0.09)	0.00(0.00,0.00) 2.20(0.12)	0.000	0.00(0.00,3.01) 2.25(0.08)	0.00(0.00,0.00) 2.62(0.19)	0.000
CAUTI incidence rate (%)/1000 line days	0.00(0.00,3.09) 2.28(0.08)	0.00(0.00,2.79) 2.22(0.16)	0.00(0.00,3.13) 2.30(0.09)	0.000	0.00(0.00,3.64) 2.75(0.11)	0.00(0.00,0.00) 1.26(0.08)	0.000	0.00(0.00,3.42) 2.55(0.10)	0.00(0.00,1.88) 1.43(0.09)	0.000
Pressure sore rate (%)	0.00(0.00,0.00) 0.62(0.04)	0.00(0.00,0.00) 0.65(0.07)	0.00(0.00,0.00) 0.60(0.04)	0.000	0.00(0.00,0.00) 0.63(0.04)	0.00(0.00,0.00) 0.60(0.07)	0.285	0.00(0.00,0.00) 0.71(0.05)	0.00(0.00,0.00) 0.31(0.04)	0.000

ICU Mortality rate (%)	10.00 (3.13,20.00) 14.03(0.19)	15.79 (7.64,25.87) 18.77(0.36)	7.50 (2.13,17.14) 11.85(0.22)	0.000	12.86 (5.56,23.08) 16.20(0.24)	4.41 (1.33,12.82) 9.45(0.30)	0.000	9.09 (2.50,20.00) 13.78(0.23)	12.50 (5.36,20.83) 14.80(0.34)	0.000
Expected mortality rate (%)	24.72 (14.56,38.00) 28.24(0.26)	31.20 (21.20,45.45) 34.40(0.47)	21.00 (12.20,34.37) 25.48(0.30)	0.000	27.38 (16.00,39.82) 29.57(0.30)	19.00 (12.00,32.42) 25.24(0.49)	0.000	23.18 (13.07,38.16) 27.88(0.31)	26.82 (19.56,37.68) 29.33(0.43)	0.000
Standardized mortality ratiio (SMR)	0.3239 (0.1481,0.5966) 0.5282(0.0130)	0.3850 (0.1943,0.6622) 0.6439(0.0308)	0.2970 (0.1328,0.5620) 0.4767(0.0127)	0.000	0.3744 (0.1939,0.6618) 0.5881(0.0166)	0.2089 (0.0888,0.4379) 0.3940(0.0195)	0.000	0.3098 (0.1410,0.5801) 0.5116(0.0142)	0.3691 (0.1755,0.6431) 0.5790(0.0298)	0.000

Notes: %: Per hundred. Statistical Terms: P: P-value indicating the level of statistical significance.

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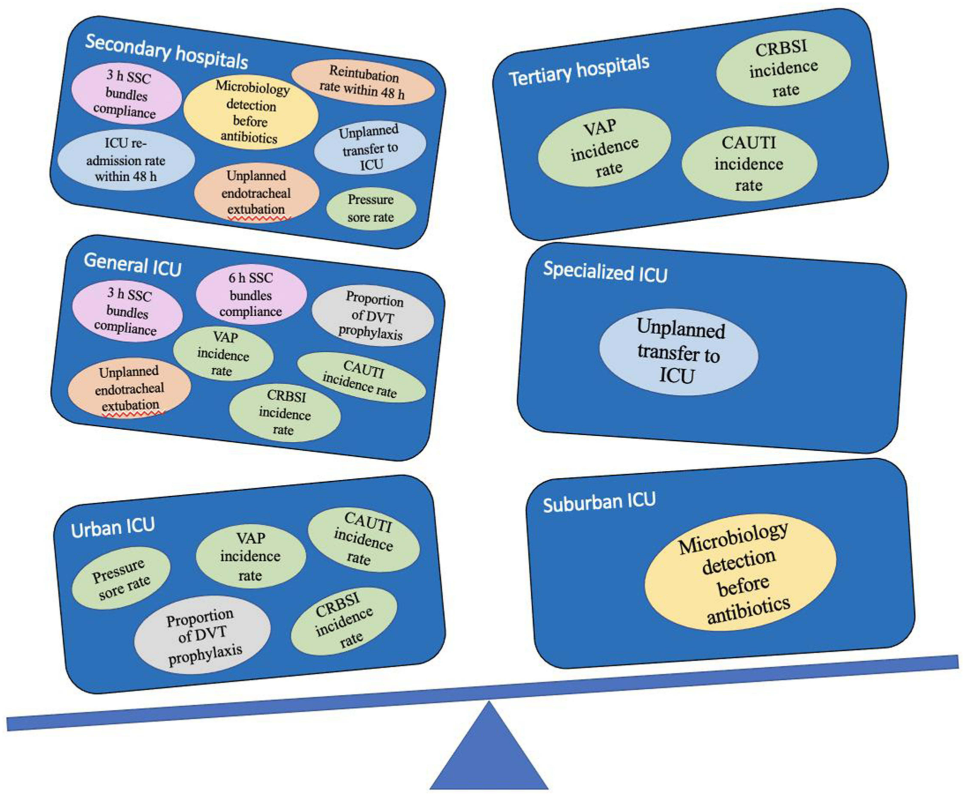

Figure 2 The focus of quality control in ICUs differs based on different characteristics and geographical regions.

below 5‰ and 0.1%, respectively, highlighting the improvement in ICU care quality. The proportion of DVT prophylaxis (Figure 3M and N) has shown fluctuations over time, with a general trend towards improvement. A notable drop is observed around 2022, followed by stabilization. Future projections suggest that the proportion will remain steady, indicating enhanced adherence to preventive measures.

Improvements are also indicated by declines in unplanned endotracheal extubation (Figure 3K) and the reintubation rate within 48 hours (Figure 3L), reflecting advancements in diagnostic and treatment capabilities. The trends in the expected mortality rate (Figure 3P) and the ICU mortality rate (Figure 3Q) have been consistent, and predictions suggest they will remain elevated. However, the SMR has declined (Figure 3R), signifying ongoing medical progress. Details of time-Series Analysis are listed in Table 4.

Discussion

The 12-year multicenter QI project in this study demonstrated significant improvements in ICU care, notably reducing mortality and the SMR. These findings highlight the success of implementing evidence-based interventions across diverse ICU settings in Beijing. Structural indicators, such as ICU admissions among inpatients and the proportion of patients with APACHE II scores ≥15, increased over time, reflecting a growing focus on critical care for severe cases. Process improvements, including adherence to the 3-hour and 6-hour sepsis care bundles and infection prevention measures, significantly contributed to the reduction of HAIs, such as VAP, CRBSI, and CAUTI. For instance, the mean VAP incidence rate decreased to 6.29 per 1000 ventilator days, which is lower than the national benchmarks of 8–11 per 1000 ventilator days and previous reports of 12–18 per 1000 ventilator days.[21,22] This achievement underscores the effectiveness of targeted infection prevention protocols and standardized care practices in mitigating HAIs. These results align with global trends, emphasizing the importance of multidisciplinary and long-term QI initiatives.

According to the Donabedian framework, quality control indicators can be classified into structural, process, and outcome domains, which systematically evaluate and improve healthcare quality.[23] Structural indicators assess the allocation and efficiency of resources required for care delivery, including physical and organizational attributes such as facilities, equipment, and staffing.[24] Process indicators reflect the quality and effectiveness of actions taken by healthcare providers (eg, adherence to clinical guidelines, patient management strategies, and the execution of medical practices) and the dynamic functioning of institutions.[25] Outcome indicators measure the results of healthcare interventions (eg, recovery rates, complication rates, and overall patient health status) and provide a final assessment of organizational structure and operational quality. This study incorporated process indicators only after 2018, and outcome indicators still dominate the composition of quality metrics, highlighting the need for further refinement in indicator composition.[26]

This study demonstrated a significant reduction in ICU mortality and SMR over the 12-year QI period, consistent with findings from previous studies. For instance, Pronovost et al reported a notable decline in ICU mortality through enhanced hand hygiene and infection control measures.[27] Similarly, this study effectively reduced patient mortality through multidisciplinary team collaboration, early intervention strategies, and optimized treatment pathways. However, the SMR reduction (−0.165) in this study was slightly lower compared to the results reported by Wang et al, likely due to the increased severity of cases admitted.[28] During the study period, the proportion of patients with APACHE II scores

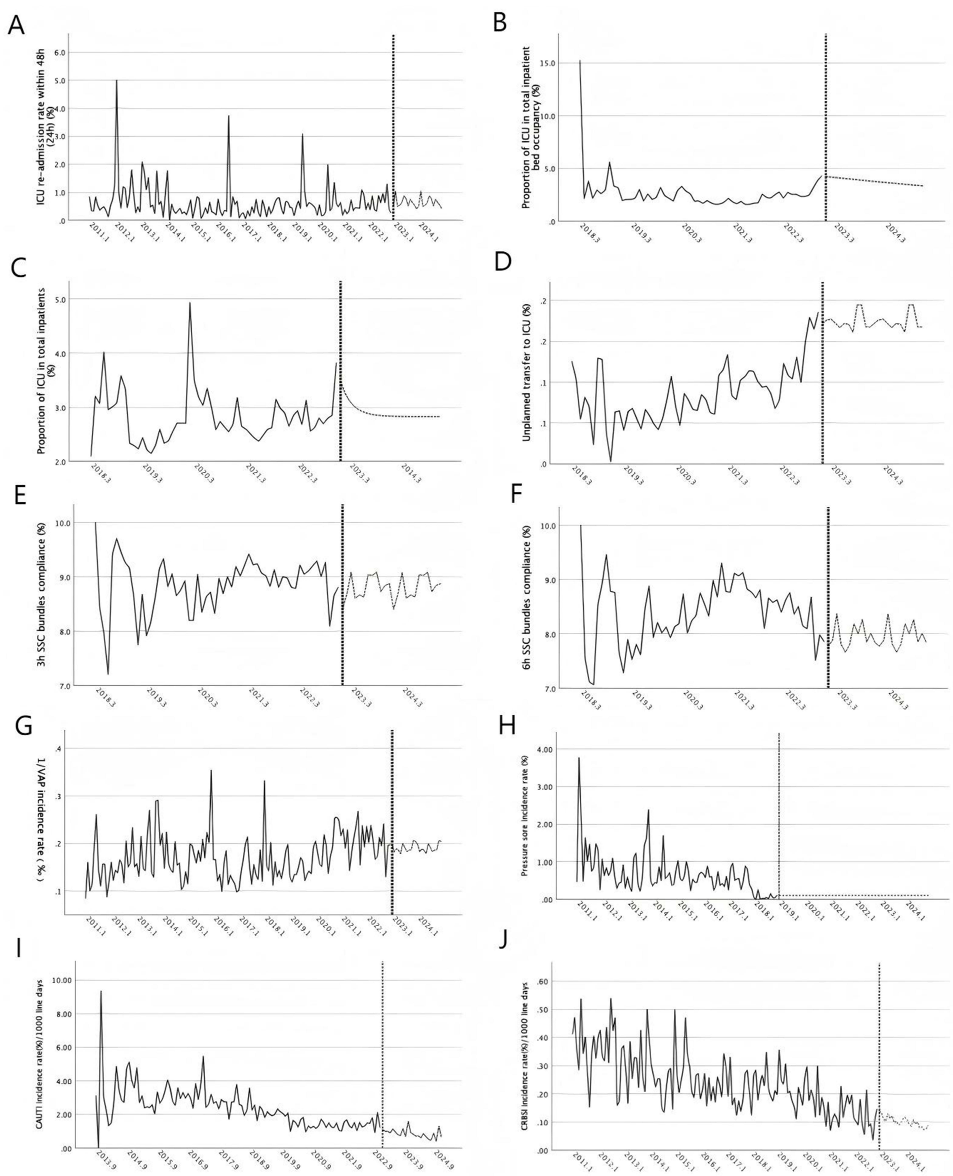

Figure 3 Continued.

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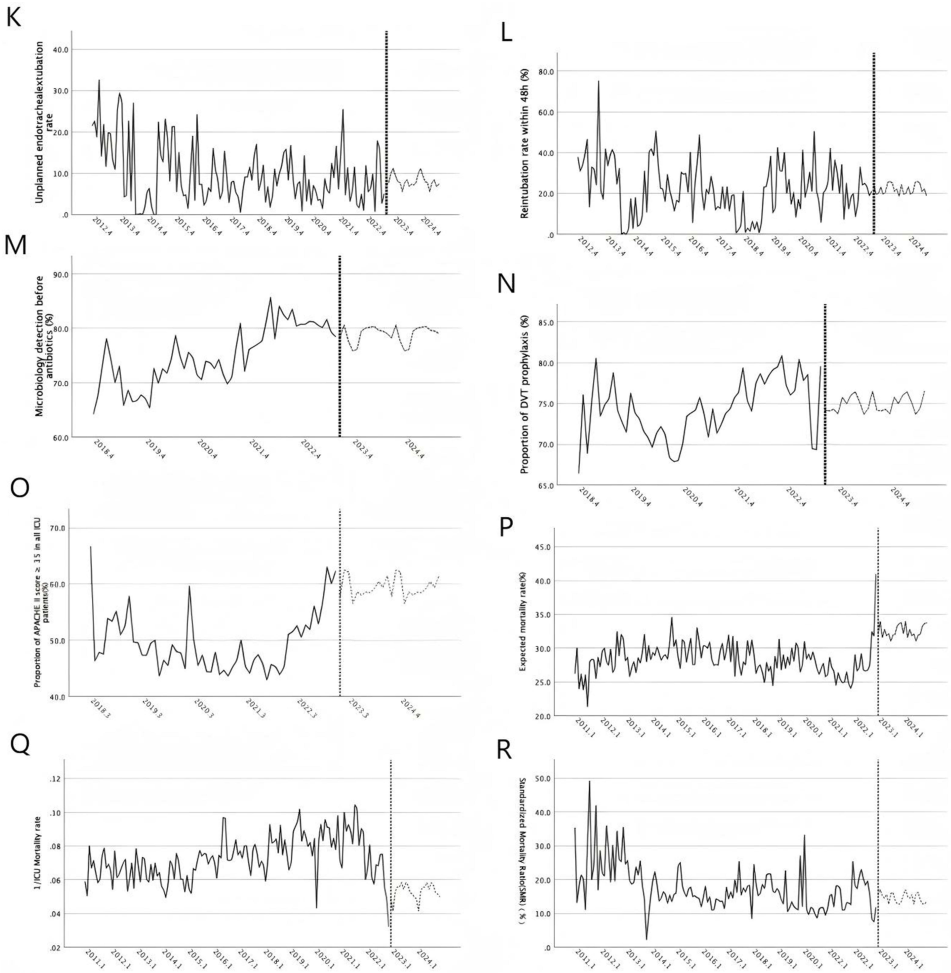

Figure 3 Trends in ICU quality control indicators over the past twelve years. (**A**). Readmission rate to ICU within 48 hours (24 hours). (**B**). ICU bed occupancy relative to total inpatient beds. (**C**). Proportion of ICU patients relative to total inpatients. (**D)**. Unplanned transfers to ICU. (**E**). 3-hour SSC bundle. (**F**). 6-hour SSC bundle. (**G)**. Ventilator-associated pneumonia (VAP) incidence per 1000 line days. (**H**). Pressure sores incidence per 1000 line days. (**I**). Catheter-associated urinary tract infections (CAUTI) per 1000 line days. (**J**). Catheter-related bloodstream infections (CRBSI) per 1000 line days. (**K)**. Unplanned endotracheal extubation. (**L)**. Reintubation rate within 48 hours. (**M**). Microbiology detection before antibiotics. (**N**).Proportion of DVT prophylaxis .(**O**).Proportion of ICU patients with APACHE II scores ≥ 15.(**P)**. Expected mortality rate. (**Q)**. ICU mortality rate. (**R**). Standardized Mortality Ratio (SMR).

≥15 increased from 52.0% to 67.5%, indicating a substantial rise in the complexity of cases treated in ICUs. Mechanistically, the introduction of multidisciplinary teams improved the precision of clinical decision-making, while the PDCA (Plan-Do-Check-Act) cycle reduced medical errors. Additionally, the implementation of structured workflows enhanced the early identification and intervention for critically ill patients, thereby lowering mortality risk in high-risk populations. Nevertheless, the increased severity of patient conditions partially limited the observed mortality reduction, suggesting that these improvements were achieved under increasingly challenging clinical conditions, further validating the scientific rigor and effectiveness of the QI measures.

The study also reported a reduction in VAP incidence to 6.29 per 1000 ventilator days, a result significantly better than the previously reported range of 12–18 per 1000 ventilator days.[21] Similarly, CRBSI and CAUTI also showed decreased incidence rates. The reduction in infection rates can be attributed to the standardization of aseptic procedures and the reinforcement of hand hygiene culture, consistent with the findings of Berenholtz et al on the impact of infection control culture.[29] Furthermore, Buetti et al highlighted that regular audits and feedback on care processes, infection rates, and provider education are critical tools for preventing CRBSI, with catheter removal being the primary treatment approach.[30] Catheter replacement has also been shown to effectively prevent CRBSI.[31] For VAP management, evidence-

Table 4 Time-Series Analysis

	Model Type	Stationary R-Squared	Ljung-Box Q (18)			
			Statistics	DF	*P*	Number of Outliers
ICU re-admission rate within 48h (24h) (%)	Simple Seasonal	0.707	9.382	16	0.897	<0.001
Proportion of ICU in total inpatient bed occupancy (%)	ARIMA(1,0,0)(0,0,0)	0.914	11.727	17	0.816	3
Proportion of ICU in total inpatients (%)	ARIMA(1,0,0)(0,0,0)	0.632	12.158	17	0.79	3
Unplanned transfer to ICU (%)	Simple Seasonal	0.679	17.794	16	0.336	<0.001
3h SSC bundles compliance (%)	Simple Seasonal	0.777	17.872	16	0.331	<0.001
6h SSC bundles compliance (%)	Simple Seasonal	0.738	23.932	16	0.091	<0.001
VAP incidence rate (‰)	Simple Seasonal	0.722	25.453	16	0.062	<0.001
Pressure sore incidence rate (%)	ARIMA(0,1,1)(0,0,0)	0.724	24.394	17	0.109	4
CAUTI incidence rate (%)/1000 line days	Winters' Additive	0.858	12.569	15	0.636	<0.001
CRBSI incidence rate (%)/1000 line days	Winters' Multiplicative	0.738	30.101	15	0.012	<0.001
Unplanned endotracheal extubation rate (%)	Simple Seasonal	0.749	23.44	16	0.102	<0.001
Reintubation rate within 48h (%)	Simple Seasonal	0.682	25.83	16	0.056	<0.001
Microbiology detection before antibiotics (%)	Simple Seasonal	0.721	13.715	16	0.62	<0.001
Proportion of DVT prophylaxis (%)	Simple Seasonal	0.682	25.83	16	0.056	<0.001
Proportion of APACHE II score ≥ 15 in all ICU patients (%)	Simple Seasonal	0.691	22.443	16	0.129	<0.001
Expected mortality rate (%)	Simple Seasonal	0.653	13.142	16	0.662	<0.001
ICU Mortality rate (%)	Simple Seasonal	0.616	12.323	16	0.721	<0.001
Standardized Mortality Ratio (SMR)	Simple Seasonal	0.781	13.34	16	0.648	<0.001

Notes: ‰: Per thousand. (24h)(48h): Hours. Statistical Terms: Stationary R-squared: Proportion of variance explained by the model using stationary data. Ljung-Box Q (18): Test statistic for autocorrelation at 18 lags (Statistics: numerical value of the test; DF: degrees of freedom; P: p-value indicating significance).
Abbreviations: ICU, Intensive Care Unit; SSC, Surviving Sepsis Campaign; DVT, Deep Vein Thrombosis; VAP, Ventilator-Associated Pneumonia; CRBSI, Catheter-Related Bloodstream Infection; CAUTI, Catheter-Associated Urinary Tract Infection; SMR, Standardized Mortality Ratio; ARIMA, Auto-Regressive Integrated Moving Average; Winters' Additive/Multiplicative, Seasonal time-series forecasting models.

based interventions such as elevating the head of the bed and regularly evaluating extubation criteria significantly reduced the risk of infection.[32]

Furthermore, this study observed an upward trend in ICU readmission rates and unplanned ICU transfer rates; however, the median values for these indicators remained 0%, limited to a small number of ICUs, and were consistently below national averages.[22] ICU readmission is associated with poorer outcomes,[33] with approximately one-third of ICU patients being readmitted within 90 days post-discharge and 53% within 12 months.[34] These findings contrast with studies like those by Mark E et al, which demonstrated declining ICU readmission rates.[35] In prior literature, optimization of discharge criteria and implementation of follow-up rehabilitation plans were often linked to reduced readmission risks.[36] By contrast, the results of this study suggest that there is still room for improvement in these areas within domestic ICUs.

During the study period, as the complexity of cases admitted to ICUs increased—reflected by higher APACHE II scores—patients discharged from the ICU with severe conditions were more likely to experience clinical deterioration.[16] Additionally, deficiencies in discharge evaluation processes and limited capacity for recognizing critically ill patients in general wards could be critical factors contributing to the observed readmission rates. As the proportion of high-risk patients increased, the overall prognosis of discharged ICU patients became more precarious, and insufficient post-discharge support may have exacerbated clinical deterioration.

Moreover, in some centers, external factors such as bed shortages may have prompted premature discharge of high-risk patients, leading to increased readmission and unplanned ICU transfer rates. Weaknesses in early recognition and monitoring of critically ill patients in general wards may also have contributed to the rise in unplanned ICU transfers.[37]

McPeake et al, after screening nearly 9,000 studies, reported that in studies of critically ill populations from North America and Europe, nearly one-third of patients were readmitted within 90 days post-discharge, and 53% were readmitted within 12 months.[38] They identified comorbidities and frailty, events during the initial hospitalization, and post-discharge infections as the three key risk factors driving readmissions. To mitigate these risks, it is critical to strictly adhere to transfer and discharge criteria, ensuring that patients with foreseeable risks of deterioration are not discharged prematurely. This approach is essential for minimizing ICU readmission and unplanned transfer rates while improving overall patient outcomes.

The results of this study indicate that the reintubation rate within 48 hours showed an upward trend during the quality improvement process. However, the median value for this indicator remained 0, significantly lower than the national quality control benchmarks,[39] suggesting that most hospitals did not experience such adverse events, with only a small number of ICUs occasionally exhibiting elevated values. Accordingly, this study used both median (interquartile range) and mean (standard error) metrics to reflect the distribution of these values.[40]

Reintubation has been shown to be associated with significantly increased morbidity and mortality.[41] Although some ICUs in this study had begun implementing post-extubation support therapies, standardized management practices were not consistently applied across all centers. Insufficient post-extubation support, particularly for high-risk patients, is likely the primary factor contributing to the observed increase in reintubation rates. In some ICUs, failure to provide timely high-flow oxygen therapy or noninvasive ventilation (NIV) following extubation may have increased the risk of airway management failure. Thille AW et al demonstrated that for mechanically ventilated patients at high risk of extubation failure, the immediate use of nasal high-flow oxygen therapy combined with NIV after extubation significantly reduced the risk of reintubation compared to high-flow oxygen therapy alone.[42] Other studies have also suggested that the combination of NIV and humidification therapy post-extubation is more effective in preventing reintubation than high-flow oxygen therapy alone.[43]

Additionally, inadequate assessment of extubation criteria may have led to premature extubation in some cases. Variability in monitoring and intervention capabilities across different centers likely further exacerbated the observed differences in reintubation rates. These findings highlight that while pre-extubation management has improved, follow-up care and interventions after extubation remain areas requiring further strengthening.

Our findings align with and extend established ICU quality improvement models. For example, Pronovost et al[5] demonstrated that the implementation of evidence-based care bundles significantly reduced catheter-related bloodstream infections in the ICU, which is consistent with our observation that standardized protocols play a crucial role in improving patient outcomes. Similarly, Needham et al[44] reported that structured quality improvement initiatives can enhance long-term outcomes for ICU survivors, supporting our data that comprehensive quality control measures are beneficial. However, our study, based on a 12-year observational cohort, reveals broader trends in ICU performance that differ from the focused interventions examined in these earlier studies. Unlike the targeted approaches described by Pronovost et al and Needham et al, our results highlight ongoing challenges related to resource allocation and care standardization across diverse clinical settings. Additionally, while Kahn et al[45] identified specific operational barriers to ICU quality improvement, our findings suggest that addressing these challenges may require system-wide reforms and transformative policy changes. These discrepancies underscore the need for context-specific quality improvement strategies in critical care.

The strengths of this study lie in its large-scale, multicenter, and long-term design, encompassing data from 425,534 patients, which provides robust statistical power and broad external validity. Additionally, the use of standardized interventions and multidisciplinary collaboration validates the feasibility of quality improvement initiatives in diverse healthcare resource settings. This long-term, multicenter approach offers valuable insights into evaluating the impact of quality improvement efforts in complex healthcare systems and addresses a significant gap in the literature regarding the effects of prolonged interventions.

The study has several limitations that should be acknowledged. First, the absence of granular patient-level data limits insights into individual disease severity, treatment appropriateness, and specific patient outcomes. This confines the analysis to a macro-level evaluation, potentially obscuring variations in outcomes among subgroups. Second, data reporting was incomplete, with only 35–50 of the 75 ICUs submitting data monthly. This inconsistency may introduce reporting bias and limit the generalizability of the findings. Third, private hospitals were not included in the study,

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leaving a gap in understanding the quality of care across all ICU settings in Beijing. Although most critically ill patients seek care in public hospitals, the absence of private hospitals may restrict the comprehensiveness of the conclusions. Furthermore, methodological limitations exist. The standardization of interventions across diverse ICUs posed challenges, as variability in implementation may have influenced outcomes. Additionally, confounding factors, such as advances in medical technology, cumulative clinical experience, and concurrent hospital policy changes, may have contributed to outcome improvements, making it difficult to isolate the direct impact of the QI interventions. Finally, the awareness among healthcare providers of being observed as part of a QI initiative may have altered their behavior (Hawthorne effect), potentially influencing the results independently of the interventions. Despite these limitations, the study provides valuable insights into ICU quality improvement efforts in Beijing, but the findings should be interpreted with caution, considering these constraints. Future research should consider a prospective, multicenter approach, incorporating comprehensive data collection and enhanced quality control measures to improve transparency and rigor, while including more detailed patient-level data, expanding to private hospitals, and employing methods to better control for confounding factors and behavioral biases.

Conclusion

In this 12-year observational cohort study, we comprehensively evaluated the clinical characteristics and outcomes of ICU patients across 75 participating units. Our findings indicate significant trends in ICU patient demographics, treatment outcomes, and quality control indicators, highlighting both improvements in patient management and areas requiring further enhancement. Notably, our analysis revealed that rigorous quality control measures are associated with reduced mortality and improved patient recovery. Despite these advances, persistent challenges remain in optimizing ICU resource allocation and implementing standardized care protocols across diverse clinical settings. This study provides a robust foundation for future research; prospective studies are warranted to validate these findings and explore innovative strategies for ICU quality control. Ultimately, our findings support the formulation of evidence-based policies aimed at enhancing critical care services and ensuring sustainable improvements in patient outcomes. These insights can serve as a catalyst for transformative changes in ICU management and policy-making.

Data Sharing Statement

The datasets used and analysed during the current study available from the corresponding author on reasonable request.

Human Ethics and Consent to Participate

This study is exempt from ethical review in accordance with Section 32 of the https://www.gov.cn/zhengce/zhengceku/2023-02/28/content_5743658.htm. This retrospective study collected information data on a perICU basis, without involving personal information, and could not be used to identify or trace back to specific individuals, thus posing no impact on individuals. The Beijing Friendship Hospital Research Ethics Committee has confirmed that no ethical approval is required.

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 declared that they have no conflicts of interest regarding this work.

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