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Trends and influencing factors of hospitalization costs among patients with tetanus: a retrospective analysis based on a tertiary hospital in Northeast China, 2013-2025

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Research Article

Keywords: tetanus, hospitalization costs, mechanical ventilation, influencing factors, pneumonia

Posted Date: September 27th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-10786697/v1

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Additional Declarations: No competing interests reported.

Abstract

Background

Tetanus is a rare but life-threatening toxin-mediated infectious disease that imposes a substantial financial burden on healthcare systems and affected families. Despite its clinical severity, empirical evidence regarding the determinants of hospitalization costs for tetanus remains scarce. This study aimed to examine the temporal trends in hospitalization costs and to identify key cost-driving factors among tetanus inpatients treated at a tertiary hospital in Northeast China over a 13-year period, so as to provide evidence for optimizing resource allocation and cost-containment strategies.

Methods

We retrospectively collected clinical and cost data from 319 adult patients diagnosed with tetanus and hospitalized between 2013 and 2025. Patients were stratified into non-mechanical ventilation (non-MV, n = 185) and mechanical ventilation (MV, n = 134) groups. We analyzed the composition and annual dynamics of hospitalization costs, and applied multiple linear regression to identify independent factors associated with total medical expenditures.

Results

Total hospitalization costs were significantly higher in the MV group than in the non-MV group. Over the study period, costs in both groups exhibited a fluctuating pattern of initial increase followed by a decline. Medication expenses consistently represented the largest cost component and closely paralleled the trajectory of total costs. Multivariate regression revealed that total length of hospital stay (TLOS), hospital-acquired pneumonia (HAP), and age were independent cost drivers in non-MV patients, with TLOS exerting the predominant influence (standardized $\beta = 0.631$). Among MV patients, independent cost determinants included MV duration, TLOS, Ablett grade, ventilator-associated pneumonia (VAP), and sex, with MV duration being the strongest predictor (standardized $\beta = 0.523$).

Conclusions

Tetanus treatment poses a heavy economic burden, particularly for severe cases requiring intensive care and prolonged ventilation. TLOS, MV duration, disease severity, and pulmonary complications are major cost drivers that offer actionable targets for cost control. From a health service management perspective, reducing hospital and ventilation days through standardized clinical pathways, preventing ICU-related pneumonia, and rationalizing pharmaceutical use can effectively curb expenditures. At the population level, enhancing tetanus vaccination coverage among high-risk groups remains a fundamental strategy to reduce incident cases and the attendant societal economic burden. These

findings have direct implications for hospital administrators, payers, and policymakers in designing value-based care models and resource-efficient service delivery frameworks.

Background

Tetanus is an acute, specific, and toxin-mediated infectious disease caused by *Clostridium tetani*. The pathogen invades the human body through breaks in the skin or mucous membranes, proliferates under anaerobic conditions and produces exotoxins, which lead to persistent tonic contraction of systemic skeletal muscles, paroxysmal spasms and autonomic nervous system dysfunction. This disease is associated with a relatively high mortality rate [1, 2]. Along with increased vaccination coverage against neonatal tetanus, the global burden of tetanus decreased substantially between 1990 and 2019: disability-adjusted life years (DALYs) lost and mortality fell by 93% and 88%, respectively [3]. Nevertheless, the incidence of tetanus remains as high as 3.43 per 100,000 population in sub-Saharan Africa [4]. It is estimated that 23,000 people die of tetanus worldwide each year[3], imposing a substantial burden on both societies and individual families. Muscle spasms caused by tetanus typically last for 3 to 4 weeks, and clinical recovery relies on the regeneration of new axonal nerve terminals [5, 6]. Patients with tetanus usually require prolonged hospitalization, and the corresponding hospitalization costs remain high. To date, studies focusing on the medical expenses of tetanus treatment are scarce at home and abroad. This study analyzed 13 consecutive years of inpatient data on tetanus patients from Jilin Provincial People's Hospital in Northeast China. We explored the composition and temporal trends of hospitalization costs, as well as potential influencing factors. The findings aim to provide a theoretical basis for formulating rational strategies to control medical expenses among tetanus inpatients.

Methods

Data collection

We retrospectively reviewed medical records and hospitalization cost data from adult inpatients diagnosed with tetanus at Jilin Provincial People's Hospital between January 2013 and December 2025. All enrolled patients received comprehensive physical examinations and met the tetanus diagnostic criteria formulated by the World Health Organization (WHO) [1]. The corresponding diagnostic code based on the International Classification of Diseases, 10th Revision (ICD-10) was A35.X01. Two specially trained researchers extracted relevant patient data from the hospital’s electronic medical record system. A total of 371 hospitalized patients with tetanus were included in this study. To avoid bias in medical cost analysis caused by an excessively short TLOS that may indicate incomplete treatment, and to minimize the confounding effects of early death, discharge against medical advice due to financial constraints, or transfer to another hospital, the following exclusion criteria were established.: (1) Ablett grade Ⅵwith a TLOS of < 48 hours; (2) Ablett grade Ⅴ with a TLOS of < 5 days; and (3) Ablett grades Ⅲ–Ⅳ with a TLOS of < 10 days. Most cases meeting the above criteria were those who left hospital prematurely for economic reasons or died at an early stage due to critical illness, failing to receive full standard treatment. Their hospitalization costs could not truly reflect the overall economic burden of

tetanus treatment, and thus these cases were excluded. Finally, a total of 319 valid cases were included in this study. A retrospective analysis was conducted to analyze the demographic characteristics, clinical manifestations, treatment indicators and hospitalization costs of enrolled tetanus inpatients. Demographic data included gender, age, occupation and payment type (medical insurance or self-payment). Clinical characteristics consisted of etiology, Ablett grade, presence of concurrent pneumonia, receipt of MV, and discharge outcomes (cured/improved, uncured or death). Treatment indicators included MV duration, ICU length of stay (ICU LOS), TLOS and total hospitalization costs.According to the 2016 IDSA/ATS guidelines [7], hospital-acquired pneumonia (HAP) was defined as pneumonia occurring ≥ 48 hours after admission in non-ventilated patients, while ventilator-associated pneumonia (VAP) was defined as pneumonia occurring ≥ 48 hours after endotracheal intubation or MV, including cases within 48 hours after extubation. Clinical diagnosis for both entities was based on: (1) fever > 38.0℃; (2) leukocytosis > 10×10^9/L or leukopenia < 4×10^9/L; and (3) purulent respiratory secretions, combined with radiographic and microbiological findings.

All hospitalization cost data were directly extracted from the Hospital Information System (HIS). For analytical purposes, the original cost items were reclassified into six categories according to their clinical and service types: (1) Medication costs: Expenses for tetanus immunoglobulin, sedative and analgesic drugs, antibiotics, nutritional support agents and other pharmaceuticals; (2) Monitoring and nursing costs: Fees for hospital beds, inpatient examinations, nursing care, general medical services, oxygen inhalation, and standard preventive nursing interventions such as pressure ulcer prevention and positioning care; (3) Diagnostic and procedural costs: Charges for tracheotomy, debridement and dressing change, central venous catheterization, fiberoptic bronchoscopy, and invasive arterial blood pressure monitoring; (4) Laboratory testing costs: Expenses for routine blood tests, biochemical assays, arterial blood gas analysis, microbial culture and other laboratory examinations; (5) Imaging costs: Fees for computed tomography (CT), magnetic resonance imaging (MRI), X-ray, ultrasonography and other imaging examinations, and (6) Consumable costs: Expenses for high-value medical supplies and disposable medical materials. Raw hospitalization costs were recorded in Chinese Yuan (CNY). To facilitate international comparison, all cost values were converted into United States Dollars (USD) using the annual average official exchange rates released by the National Bureau of Statistics of China for the study period from 2013 to 2025. The overall average exchange rate across 2013–2025 was 1 US dollar = 6.68 Chinese Yuan (1 CNY ≈ 0.15 USD).

Statistical analyses

We performed all statistical analyses using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were tested for normality using the Shapiro-Wilk (S-W) test. Data following a normal distribution were presented as mean ± standard deviation (SD), and between-group comparisons were performed using the t-test. Non-normally distributed quantitative data were expressed as median (interquartile range, IQR). The Mann-Whitney U test was used for comparisons between two independent groups, including gender, payment type and concurrent pneumonia. The Kruskal-Wallis H test was

applied for comparisons across multiple independent groups, such as etiology and Ablett grade. Spearman's rank correlation analysis was conducted to explore the relationships between continuous variables (age, MV duration, ICU LOS and TLOS) and total hospitalization costs.Given the obvious right-skewed distribution of hospitalization costs, natural logarithmic transformation was performed to normalize the data. Variables that achieved statistical significance in univariate analysis were entered into the multiple linear regression model. The assignment of independent variables was defined as follows: gender (male = 0, female = 1); payment type (medical insurance = 0, self-payment = 1); Ablett grade (non-ventilated group: Grade I = 1, Grade II = 2, Grade III = 3; ventilated group: Grade III = 1, Grade IV = 2); pneumonia (absent = 0, present = 1). Age, TLOS, MV duration and ICU LOS were directly incorporated as continuous variables. Multivariate linear regression analysis was performed to identify independent factors associated with hospitalization costs. A P value < 0.05 was considered statistically significant.

Ethics statement

This study was approved by the Ethics Committee of Jilin Provincial People's Hospital (Approval No.: 2026047). This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Since this was a retrospective study and all data used were anonymized clinical records, the requirement for written informed consent from patients was waived by the Ethics Committee.

Results

Baseline characteristics of the study population

A total of 319 adult patients with tetanus were enrolled in this study. Regarding demographic characteristics, 230 patients (72.1%) were male, the mean age was 56.1 ± 10.4 years, and the majority were farmers (242 cases, 75.9%). Most patients were covered by medical insurance (250 cases, 78.4%). In terms of clinical characteristics, trauma was the leading cause of tetanus (285 cases, 89.3%). According to the Ablett classification, 70 patients (21.9%) were grade I, 100 (31.3%) grade II, 104 (32.6%) grade III, and 45 (14.1%) grade IV. A total of 124 patients (38.9%) had complicated pneumonia. At discharge, 307 patients (96.2%) achieved cure or improvement .Among the 134 patients receiving MV, the median MV duration was 18.0 (11.3, 23.7) days, and the median ICU LOS was 20.0 (13.8, 26.3) days.The mean age was 58.6 ± 9.6 years in the non-MV group and 52.2 ± 10.6 years in the MV group, showing a statistically significant difference (t = 3.760, P < 0.001). The proportion of patients with medical insurance was 75.7% in the non-MV group and 87.3% in the MV group (χ^2 = 6.722, P = 0.010). Pneumonia was present in 4.3% of the non-MV group compared with 86.6% of the MV group (χ^2 = 222.846, P < 0.001). The median TLOS was 15.0 (12.0–19.0) days in the non-MV group and 29.5 (24.0–36.0) days in the MV group (Z = − 11.372, P < 0.001). The median total hospitalization cost was 4,804.58 (3,109.80–7,690.88) USD in the non-MV group and 21,627.00 (15,877.95–28,468.33) USD in the MV group (Z = − 14.506, P < 0.001).See Table 1 for details.

Annual trends in total hospitalization costs

Annual trends of total hospitalization costs among non-MV tetanus patients

The total hospitalization costs of patients in the non-MV group showed a skewed distribution. Mild outliers were observed in each year, while no extreme outliers were detected. The median total hospitalization costs exhibited a fluctuating pattern, with an initial increase followed by a decline. From 2013 to 2018, the median cost increased progressively from 3127.67 USD in 2013 to a peak of 7799.51 USD in 2018. After 2018, the median cost declined with fluctuations, and dropped to a relatively low level of 2799.97 USD in 2025. Box plots revealed obvious differences in box width and whisker length across different years, indicating varied dispersion of hospitalization costs. The dispersion of cost distribution was relatively high from 2017 to 2019. Among all cost components, medication costs accounted for the largest proportion and changed in strong accordance with total hospitalization costs. Monitoring and nursing costs, diagnostic and procedural costs, disposable medical supply costs, laboratory testing costs and imaging costs remained at relatively low levels with slight annual fluctuations; in particular, diagnostic and procedural costs stayed consistently low throughout the study period. See Fig. 1 and Fig. 2.

Annual trends of total hospitalization costs among MV tetanus patients

The median total hospitalization costs in the MV group was markedly higher than that in the non-ventilated group, with a greater dispersion of cost distribution. Extreme high outliers were observed in multiple years. Overall, the median cost presented a fluctuating upward trend. It stood at 16216.91 USD in 2013, and rose obviously to 24140.32 USD from 2013 to 2015. Afterwards, it dropped to the lowest level of 15176.29 USD in 2017, then increased with fluctuations again and reached the peak of 31580.19 USD in 2022. From 2023 to 2025, the median cost gradually declined to 17221.79 USD. In terms of cost components, medication costs consistently accounted for the largest proportion and showed a trend highly consistent with total hospitalization costs. Diagnostic and procedural costs increased rapidly in the later stage with a prominent growth rate after 2021. Monitoring and nursing costs, laboratory testing costs and disposable medical supply costs remained stable or rose slowly with minor annual fluctuations. Imaging costs took up the smallest share throughout the study period and exhibited no obvious annual changes. See Fig. 3 and Fig. 4.

Analysis of factors influencing total hospitalization costs in non-MV tetanus patients

Univariate analysis of total hospitalization costs in the non-MV group

Age was significantly correlated with total hospitalization costs (r = 0.16, P = 0.031). The median total cost was 6618.31 (3842.46-9816.09) USD for self-paying patients and 4496.60 (3094.42-10800.96) USD for patients with medical insurance, with a statistically significant difference between the two groups (Z = 2.99, P = 0.030). Statistically significant differences in median total hospitalization costs were also found across different Ablett grades (H = 37.68, P < 0.001). The cost increased progressively with higher grades. The median cost of Grade III patients reached 12147.96 (7894.54-13837.10) USD, which was markedly higher than that of Grade I and Grade II patients. The median total cost was 9566.66 (5706.78-13539.08) USD in patients with HAP and 4729.16 (3098.29-7070.92) USD in those without HAP, showing a significant inter-group difference (Z = 2.74, P = 0.006). TLOS had a significant correlation with total hospitalization costs (r = 0.73, P = 0.031). No significant differences in hospitalization costs were observed between different genders or etiologies (P > 0.1). See Table 2.

Multiple linear regression analysis of total hospitalization costs in the non-MV group

Variables with a P value less than 0.1 in the univariate analysis were included in the multiple linear regression model, namely age, payment type, Ablett grade, HAP and TLOS. The final model exhibited good goodness-of-fit, with an R^2 of 0.558, an adjusted R^2 of 0.545, an overall F value of 45.168 and P < 0.001. The results revealed that age had a statistically significant effect on total hospitalization costs (b = 0.008, t = 2.447, P = 0.015). The presence of HAP was also a significant influencing factor (b = 0.426, t = 2.542, P = 0.012). In addition, TLOS was significantly associated with hospitalization costs (b = 0.066, t = 10.783, P < 0.001). According to the standardized regression coefficients, TLOS had the highest value of 0.631, which was identified as the most critical factor affecting hospitalization costs. See Table 3.

Univariate analysis of total hospitalization costs in the MV group

The median total hospitalization costs was 22930.29 (16286.77-28868.44) USD for male patients and 18270.56 (15041.82-25679.41) USD for female patients, with Z = 1.80 and P = 0.072. The median cost was 20583.25 (14894.69-27401.01) USD for patients with Ablett Grade III and 22930.29 (17496.88-32167.86) USD for those with Grade IV, with Z = 1.74 and P = 0.083. A statistically significant difference was found between patients with and without VAP. The median cost was 23208.22 (17325.92-29061.23) USD in patients complicated with VAP and 14230.17 (10647.19-16493.93) USD in those without VAP (Z = 4.68, P < 0.001). Significant correlations were observed between total hospitalization costs and MV duration (r = 0.76, P < 0.001), ICU LOS (r = 0.76, P < 0.001), as well as TLOS (r = 0.67, P < 0.001). No significant associations were detected between hospitalization costs and age, payment type or etiology (P > 0.1). See Table 4.

Multiple linear regression analysis of total hospitalization costs in the MV group

In view of clinical causal relationships, ICU LOS acted as a mediating variable between MV duration and total hospitalization costs. Given the strong causal association and collinearity among these indicators, ICU LOS was excluded from the multiple linear regression model. Variables with a univariate $P < 0.1$, including gender, Ablett grade, VAP, MV duration and TLOS, were enrolled into the regression model to screen for independent risk factors affecting hospitalization costs. The final model showed good goodness-of-fit, with an R^2 of 0.743, an adjusted R^2 of 0.733, an overall F value of 73.967 and $P < 0.001$. The results demonstrated that gender ($b = -0.096$, $t = -2.038$, $P = 0.044$), Ablett grade ($b = 0.127$, $t = 2.744$, $P = 0.007$), VAP ($b = 0.213$, $t = 3.280$, $P = 0.001$), MV duration ($b = 0.025$, $t = 9.231$, $P < 0.001$) and TLOS ($b = 0.015$, $t = 6.905$, $P < 0.001$) all exerted statistically significant effects on total hospitalization costs. According to the standardized regression coefficients, MV duration had the highest value of 0.523, which was the most critical factor influencing total hospitalization costs. See Table 5.

Table 1
Baseline characteristics of hospitalized patients with tetanus 2013–2025

Characteristics	Total (n = 319)	Non MV (n = 185)	MV (n = 134)	t/Z/χ2	*P* value
Demographic characteristics					
Male, n (%)	230 (72.1)	134 (72.4)	96 (71.6)	0.024	0.877
Age (years), Mean ± SD	56.1 ± 10.4	52.2 ± 10.6	58.6 ± 9.6	-3.760	< 0.001
Occupation, n (%)				1.063	0.588
Farmer	242 (75.9)	137 (74.1)	105 (78.4)		
Worker	10 (3.1)	7 (3.8)	3 (2.2)		
Others	67 (21.0)	41 (22.2)	26 (19.4)		
Payment type, n (%)				6.722	0.010
Medical insurance	257 (80.6)	140 (75.7)	117 (87.3)		
Self-payment	62 (19.4)	45 (24.3)	17 (12.7)		
Clinical characteristics					
Etiology, n (%)				4.059	0.131
Trauma	285 (89.3)	168 (90.8)	117 (87.3)		
Spontaneous infection	19 (6.0)	7 (3.8)	12 (9.0)		
Others	15 (4.7)	10 (5.4)	5 (3.7)		
Ablett grade, n (%)					—
Grade I	70 (21.9)	70 (37.8)	0		
Grade II	98(30.7)	98 (53.0)	0		
Grade III	109 (32.2)	17(9.2)	92 (68.7)		
Grade IV	42 (13.2)	0	42 (31.3)		
HAP/VAP, n (%)	124 (38.9)	8 (4.3)	116 (86.6)	222.846	< 0.001

Note: A total of 134 mechanically ventilated (MV) patients were analyzed for duration of mechanical ventilation and ICU length of stay (ICU LOS). Ablett grades I and II generally indicate milder disease, and patients with these grades in this cohort did not require mechanical ventilation; an additional 17 patients with Ablett grade III did not receive mechanical ventilation due to economic and other reasons. All patients receiving mechanical ventilation were Ablett grade III or IV. Comparisons of Ablett grade distribution between groups were not performed due to the non-overlapping severity stratification between the MV and non-MV groups.

Characteristics	Total (n = 319)	Non MV (n = 185)	MV (n = 134)	t/Z/$\chi 2$	*P* value
Discharge outcome, n (%)				8.923	0.012
Cured/improved	307 (96.2)	183 (98.9)	124 (92.5)		
Unhealed	4 (1.3)	1 (0.5)	3 (2.2)		
Death	8 (2.5)	1 (0.5)	7 (5.2)		
Treatment indicators					
MV duration (days), median (IQR)	NA	NA	18.0 (11.3–23.7)		
ICU LOS (days), median (IQR)	NA	NA	20.0 (13.8–26.3)		
TLOS(days), median (IQR)	20.0 (14.0–29.0)	15.0 (12.0–19.0)	29.5 (24.0–36.0)	-11.372	< 0.001
Total hospitalization costs (USD), median (IQR)	9338.15 (4431.12-18829.40)	4804.58 (3109.80-7690.88)	21627.00 (15877.95-28468.33)	-14.506	< 0.001

Note: A total of 134 mechanically ventilated (MV) patients were analyzed for duration of mechanical ventilation and ICU length of stay (ICU LOS). Ablett grades I and II generally indicate milder disease, and patients with these grades in this cohort did not require mechanical ventilation; an additional 17 patients with Ablett grade III did not receive mechanical ventilation due to economic and other reasons. All patients receiving mechanical ventilation were Ablett grade III or IV. Comparisons of Ablett grade distribution between groups were not performed due to the non-overlapping severity stratification between the MV and non-MV groups.

Note

Circles (○) indicate mild outliers beyond 1.5 times the interquartile range. The numbers represent case IDs, facilitating data traceability and verification.

Note

Circles (○) represent mild outliers (> 1.5×IQR), asterisks (*) represent extreme outliers (> 3×IQR). Numbers indicate case IDs for data traceability.

Table 2
Comparison of hospitalization costs among tetanus patients with different clinical characteristics in the non-MV group 2013–2025

Characteristics	**n**	**Costs (USD), median (IQR)**	***Z/H/r* value**	***P* value**
Gender			0.33	0.564
Male	134	4700.84 (3094.97-7905.56)		
Female	51	5474.82 (3555.52-6818.83)		
Age (years)			0.16	0.031
Payment type			2.99	0.030
Medical insurance	140	4496.60 (3094.42-10800.96)		
Self-payment	45	6618.31 (3842.46-9816.09)		
Etiology			5.63	0.600
Trauma	168	4753.96 (3106.14-7126.53)		
Spontaneous infection	7	7751.63 (6077.18-12401.35)		
Others	10	4701.19 (3080.87-12718.82)		
Ablett grade			37.68	< 0.001
Grade I	70	3514.71 (2581.50-5055.08)		
Grade II	98	5129.86 (3742.75-7510.92)		
Grade III	17	12147.96 (7894.54-13837.10)		
HAP			2.74	0.006
No	177	4729.16 (3098.29-7070.92)		
Yes	8	9566.66 (5706.78-13539.08)		
TLOS(days)			0.73	< 0.001

Table 3
Multiple linear regression analysis of hospitalization costs for tetanus patients in the non-MV group 2013–2025

Variable	**B**	**SE**	**β**	***t* value**	***P* value**	**95% *CI***
Constant	8.349	0.284	-	29.447	< 0.001	7.790–8.909
Age	0.008	0.003	0.124	2.447	0.015	0.002–0.014
Payment type	0.129	0.082	0.082	1.576	0.117	-0.032-0.290
Ablett grade	0.117	0.117	0.109	1.899	0.059	-0.005-0.239
HAP	0.426	0.168	0.128	2.542	0.012	0.095–0.757
TLOS	0.066	0.006	0.631	10.783	< 0.001	0.054–0.078
Note: R^2 = 0.558, adjusted R^2 = 0.545, F = 45.168, P < 0.001.						
Note: B, unstandardized regression coefficient; SE, standard error; β, standardized regression coefficient; CI, confidence interval. Dependent variable: log-transformed total hospitalization costs.						

Table 4
Comparison of hospitalization costs among tetanus patients with different clinical characteristics in the MV group 2013–2025

Characteristics	n	Costs (USD), median (IQR)	*Z/H/r* value	*P* value
Gender			1.80	0.072
Male	96	22930.29 (16286.77-28868.44)		
Female	38	18270.56 (15041.82-25679.41)		
Age (years)			0.07	0.434
Payment type			0.59	0.555
Medical insurance	118	21754.71 (15993.46-28470.77)		
Self-payment	16	20356.90 (11829.09-28363.27)		
Etiology			2.24	0.326
Trauma	117	20447.62 (15450.27-28706.87)		
Spontaneous infection	12	24743.18 (22853.93-28363.27)		
Others	5	19250.02 (17848.87-25252.35)		
Ablett grade			1.74	0.083
Grade III	92	20583.25 (14894.69-27401.01)		
Grade □	42	22930.28 (17496.88-32167.86)		
VAP			4.68	< 0.001
No	18	14230.17 (10647.19-16493.93)		
Yes	115	23208.22 (17325.92-29061.23)		
MV duration			0.76	< 0.001
ICU LOS (days)			0.76	< 0.001
TLOS(days)			0.67	< 0.001

Table 5
Multiple linear regression analysis of hospitalization costs for tetanus patients in the MV group 2013–2025

Variable	B	SE	β	*t* value	*P* value	95% *CI*
Constant	10.471	0.181		57.759	< 0.001	10.113–10.830
Gender	-0.096	0.047	-0.092	-2.038	0.044	-0.188 to -0.003
Ablett grade	0.127	0.046	0.126	2.744	0.007	0.035–0.219
VAP	0.213	0.065	0.155	3.280	0.001	0.084–0.341
MV duration	0.025	0.003	0.523	9.231	< 0.001	0.020–0.031
TLOS	0.015	0.002	0.343	6.095	< 0.001	0.010–0.020
Note: R^2 = 0.743, adjusted R^2 = 0.733, F = 73.967, P < 0.001.						
Note: B, unstandardized regression coefficient; SE, standard error; β, standardized regression coefficient; CI, confidence interval. Dependent variable: log-transformed total hospitalization costs.						

Discussion

In this study, we analyzed inpatient data and hospitalization costs from 319 tetanus patients treated at a tertiary referral center in Northeast China over a 13-year period (2013–2025), with the goal of identifying temporal cost trends and key drivers of healthcare expenditure from a health services research perspective. Our findings revealed substantial cost stratification according to disease severity. The median total cost in the MV group was 21,627.00 USD, approximately 4.5 times higher than that in the non-MV group (4,804.58 USD). This marked disparity reflects the intensive resource utilization required for severe tetanus, including prolonged MV support, high-dose sedative and analgesic therapy, continuous ICU monitoring, specialized nursing care, and invasive diagnostic and therapeutic procedures.

Comparisons with previous studies highlight considerable cross-country variation in tetanus-related hospitalization costs. Yen et al. [8] reported a median cost of 166,259 USD among 15 adult tetanus patients in the United States, while a South Korean single-center study documented a median of 18,011 USD [9]. A Vietnamese ICU-based study reported a substantially lower median of 2,590 USD [10]. These differences likely reflect disparities in healthcare financing models, unit costs of ICU services, pharmaceutical pricing, and labor costs across health systems. A Chinese multicenter study by Yu et al. [11] in Suzhou reported median costs of 19,062.8 USD for severe cases and 4,291.1 USD for non-severe cases, closely aligning with our findings and suggesting relative consistency within the Chinese context. According to the National Bureau of Statistics of China, the per capita disposable income of Chinese residents was 6,507 USD in 2025, with per capita medical expenditure at 386 USD [12]. When benchmarked against these figures, the hospitalization costs observed in our cohort—particularly for

severe cases—represent a catastrophic health expenditure for average families, underscoring the urgent need for cost-containment strategies within China's healthcare system.

Regarding temporal trends, the median total hospitalization costs in both groups exhibited a fluctuating pattern of initial increase followed by a decline. Medication expenses consistently comprised the largest proportion of total costs and closely paralleled the trajectory of overall expenditures, indicating that pharmaceutical costs are the primary lever influencing total hospitalization costs. The upward trend from 2013 to 2018 may be attributed to improved survival rates among severe tetanus patients and the introduction of newer, more expensive sedative and analgesic agents (e.g., dexmedetomidine) that enhanced clinical management but increased pharmaceutical expenditure. However, after 2018, the inclusion of key sedative drugs such as dexmedetomidine and propofol in China's national centralized volume-based procurement (VBP) program [13, 14] significantly reduced unit drug prices, driving a synchronous decline in total hospitalization costs. Concurrently, the National Healthcare Security Administration (NHSA) piloted and scaled up Diagnosis-Related Groups (DRG)-based payment reforms starting in 2019, which multiple studies have confirmed effectively curb unnecessary hospitalization costs by incentivizing efficiency in resource utilization [15, 16]. The convergence of these two policy interventions—pharmaceutical pricing reform and value-based payment models—likely underpins the observed cost decline after 2018. Notably, in the MV group, diagnostic and procedural costs increased after 2021, primarily driven by increased utilization of fiberoptic bronchoscopy and central venous catheterization in severe cases, yet total costs continued to decrease overall, suggesting that medication cost savings outweighed increases in procedural expenditure.

Multivariate regression analyses identified distinct cost-driving profiles between non-MV and MV patients. For non-MV patients, TLOS emerged as the predominant cost driver (standardized $\beta = 0.631$, $P < 0.001$), with each additional hospitalization day increasing total costs by approximately 6.6%. This finding aligns with the broader infectious disease economics literature [17, 18] and carries clear implications for hospital operations management: shortening length of stay through optimized clinical pathways—including early spasm control, structured nutritional support, and timely complication screening—represents the single most effective strategy to reduce costs for mild-to-moderate tetanus cases, without compromising patient safety. The median TLOS in our non-MV cohort was 15.0 days, comparable to the 17.5 days reported by An et al. [19], suggesting room for further pathway optimization.

HAP was another significant cost driver in non-MV patients ($\beta = 0.426$, $P = 0.012$), with affected patients incurring 102.3% higher median costs than those without HAP. Tetanus-related generalized muscle spasms frequently involve respiratory muscles, impairing sputum clearance and predisposing patients to hypostatic pneumonia [11, 20]. From a quality-of-care perspective, implementing evidence-based pneumonia prevention bundles—including semirecumbent positioning, enhanced oral hygiene, and early mobilization—could mitigate this modifiable cost driver. Age also independently influenced costs($\beta = 0.008$, $P = 0.015$), consistent with the well-documented higher complication rates and more complex care needs among elderly patients with comorbidities [21]. Importantly, the significant univariate association

between payment type and costs disappeared in multivariate analysis, indicating that the observed cost differential between insured and self-paying patients was confounded by disease severity and TLOS rather than directly attributable to insurance status per se—a reassuring finding for equity-oriented health financing policies.

For patients in the MV group, independent influencing factors for total hospitalization costs included ventilation duration, overall TLOS, Ablett grade, VAP, and gender. Approximately 50% of patients with severe tetanus require MV due to respiratory muscle spasm and airway secretion retention, with a reported median ventilation duration ranging from 16 to 23 days [18, 22, 23]. In the present study, 42.0% of patients received MV, with a median ventilation duration of 18 days, which was consistent with previous literature. Among these factors, MV duration exerted the strongest impact (standardized β = 0.523, $P < 0.001$), with each additional ventilator day increasing hospitalization costs by approximately 2.5%. Consistent with our findings, Bae et al [9] also demonstrated that ventilation-related expenditure constitutes the largest proportion of total hospitalization costs in tetanus patients. Increased consumption of medical supplies, continuous ICU monitoring, and the prevention and management of VAP are the primary drivers of elevated medical expenses. Furthermore, ICU LOS was highly correlated with ventilation time, and both indicators were significantly positively associated with hospitalization costs. These findings suggest that, from a health service management standpoint, reducing MV duration through standardized sedation vacations, daily spontaneous breathing trials, and multidisciplinary weaning teams can substantially reduce both ventilation time and associated costs, thereby alleviating the economic burden in severe tetanus patients.

Ablett grade and VAP also independently influenced costs in the MV group. Higher Ablett grades, reflecting more severe autonomic dysfunction and refractory spasms, required escalating doses of sedative, analgesic, and muscle relaxant agents, commensurately increasing pharmaceutical costs and complication risks. Kang et al. [24] similarly documented a positive correlation between tetanus severity and hospitalization costs ($r = 0.41$, $P < 0.05$). VAP occurred in 86.6% of MV patients in our cohort and conferred a 63.1% higher median cost compared with VAP-free patients. This exceptionally high incidence reflects the compounded effects of airway instrumentation, high-dose sedation impairing cough reflexes, and prolonged immobility [25–27]. VAP not only prolongs MV duration and ICU LOS but also generates substantial additional expenses for broad-spectrum antibiotics, microbiological diagnostics, and therapeutic bronchoscopy. Therefore, hospital-acquired infection control programs that prioritize VAP prevention—through standardized oral care, subglottic secretion drainage, and conservative transfusion strategies—can yield substantial cost savings while improving patient outcomes. Female patients exhibited significantly lower costs than males ($\beta = -0.096$, $P = 0.044$). This gender disparity may be partially explained by males' higher average body weight (necessitating larger weight-based medication doses) and higher smoking prevalence, which increases baseline pulmonary susceptibility. The specific mechanisms warrant further investigation.

Beyond its clinical implications, this study offers several actionable insights for health system stakeholders. For hospital administrators and clinical department heads, the strong association between

TLOS/MV duration and costs underscores the need for standardized clinical pathways, early rehabilitation protocols, and weaning algorithms that can simultaneously improve quality and reduce resource intensity. For health insurers and payers, the cost differential by severity and the disproportionate contribution of pharmaceutical and ventilation-related expenses suggest that DRG-based reimbursement rates for tetanus should be risk-adjusted to account for MV necessity and complication status, preventing financial disincentives for treating severe cases. For public health policymakers, the significant cost savings observed following the national centralized drug procurement and DRG reforms provide empirical support for continuing and expanding value-based pharmaceutical pricing and payment innovations. Moreover, the persistently high cost burden, particularly for severe cases, reinforces the public health imperative of primary prevention through expanded tetanus vaccination coverage among high-risk occupational groups such as farmers and construction workers—a measure that would reduce incident cases and, consequently, the aggregate societal economic burden.

Several limitations should be acknowledged. First, this was a single-center retrospective study at a tertiary referral hospital in Northeast China. The enrolled patients were predominantly middle-aged male farmers, which may limit generalizability to other regions, hospital levels, or demographic groups. Second, our cost analysis was restricted to direct in-hospital expenditures. Indirect costs—including transportation, accommodation, productivity losses for patients and caregivers, and out-of-pocket expenses for non-hospital medications—were not captured, potentially underestimating the full societal economic burden. Third, residual confounding from unmeasured factors such as baseline comorbidity severity, nutritional status, and pre-admission functional status cannot be ruled out. Future multicenter prospective studies incorporating diverse geographic regions, varying hospital tiers, and comprehensive costing frameworks (including both direct and indirect costs) are warranted to validate and extend our findings.

Conclusion

In conclusion, this study confirms that tetanus imposes a substantial and severity-stratified economic burden on patients and healthcare systems, with mechanically ventilated patients incurring costs approximately 4.5 times higher than their non-ventilated counterparts, driven predominantly by total length of stay, mechanical ventilation duration, disease severity (Ablett grade), and pulmonary complications (HAP/VAP). From a health service delivery and policy perspective, these findings underscore the need for multifaceted cost-containment strategies that operate at both the institutional and population levels: within hospitals, optimizing clinical pathways to safely shorten hospitalization and ventilation days, implementing evidence-based pneumonia prevention bundles, and rationalizing pharmaceutical use through formulary management can directly curb modifiable expenditures; simultaneously, the significant cost reductions observed following China's centralized drug procurement and DRG-based payment reforms provide empirical support for continued value-based pharmaceutical pricing and reimbursement innovations. Ultimately, however, the most fundamental and cost-effective approach to reducing the societal burden of tetanus lies in strengthening primary prevention—expanding vaccination coverage among high-risk occupational groups such as farmers and rural workers—thereby

reducing incident cases and the attendant downstream healthcare costs, while future multicenter prospective research incorporating indirect costs and long-term outcomes is warranted to further inform evidence-based resource allocation and health policy formulation.

Abbreviations

HAP
Hospital-acquired pneumonia
ICU LOS
Intensive care unit length of stay
IQR
Interquartile range
MV
Mechanical ventilation
SD
Standard deviation
TLOS
Total length of hospital stay
USD
United States dollars
VAP
Ventilator-associated pneumonia.

Declarations

Acknowledgements
Not applicable.

Authors' contributions

Conceptualization: YJW and HTS. Methodology: LLZ. Formal analysis and data curation: YJW, LLZ, and XJ. Validation: ZBX and HTS. Investigation: CLD, XJ, and LLZ. Writing - original draft preparation: CLD and ZBX. Writing - review and editing: YJW and HTS. Approval of final manuscript: All authors. The authors read and approved the final manuscript.

Funding

This study received no external funding.

Availability of data and materials
The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Jilin Provincial People's Hospital (Approval No.: 2026047). This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Due to the retrospective nature of the study and the use of anonymized clinical records, the requirement for written informed consent was waived by the Ethics Committee.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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References

1. World Health Organization. Tetanus. https://www.who.int/news-room/fact-sheets/detail/tetanus. Accessed 22 August 2026.
2. Brooks VB, Curtis DR, Eccles JC. Mode of action of tetanus toxin. Nature. 1955;175(4446):120–1.
3. Li J, Liu Z, Yu C, et al. Global epidemiology and burden of tetanus from 1990 to 2019: A systematic analysis for the Global Burden of Disease Study 2019. Int J Infect Dis. 2023;132:118–26.
4. Casey RM, Nguna J, Opar B, et al. Field investigation of high reported non-neonatal tetanus burden in Uganda, 2016–2017. Int J Epidemiol. 2023;52(4):1150–62.
5. Duchen LW, Tonge DA. The effects of tetanus toxin on neuromuscular transmission and on the morphology of motor end plates in slow and fast skeletal muscle of the mouse. J Physiol. 1973;228:157–72.
6. Duchen LW. The effects of tetanus toxin on the motor end-plates of the mouse. An electron microscopic study. J Neurol Sci. 1973;19:153–67.
7. Kalil AC, Metersky ML, Klompas M, et al. Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clin Infect Dis. 2016;63(5):e61–111.
8. Yen C, Murray E, Zipprich J, Winter K, Harriman K. Missed opportunities for tetanus postexposure prophylaxis—California, January 2008–March 2014. MMWR Morb Mortal Wkly Rep. 2015;64:243–6.
9. Bae S, Go M, Kim Y, Hwang S, Kim SW, Kwon KT, Jung SI, Chang HH. Clinical outcomes and healthcare costs of inpatients with tetanus in Korea, 2011–2019. BMC Infect Dis. 2021;21(1):247.
10. Hung TM, Van Hao N, Yen LM, et al. Vietnam ICU Translational Applications Laboratory (VITAL) Investigators. Direct Medical Costs of Tetanus, Dengue, and Sepsis Patients in an Intensive Care Unit in Vietnam. Front Public Health. 2022;10:893200.

11. Yu J, Zheng B, Liu N, et al. Trends and Hospitalization Outcomes of Tetanus Cases: A Multicenter Retrospective Study in Suzhou, 2013–2023. Risk Manage Healthc Policy. 2024;17:2729–39.
12. National Bureau of Statistics of China. Residents' Income and Consumption Expenditure in 2025. https://www.stats.gov.cn/sj/zxfb/202601/t20260119_1962321.html. Accessed 22 August 2026.
13. Sunshine Medical Procurement All-In-One. https://www.smpaa.cn/gjsdcg/2018/11/15/8511. shtml. Accessed 22 August 2026.
14. Sunshine Medical Procurement All-In-One. https://www.smpaa.cn/xxgk/gggs/2021/03/03/9914.shtml. Accessed 22 August 2026.
15. Du L, Fang S, Zhang Q. Trend analysis of medical expenses under DRG payment reform in China. Sci Rep. 2025;15:36961.
16. Li L, Yang W, Tang X, et al. The impacts of the diagnosis-related group payment reform on hospitalization-related medical expenses: evidence from China. Health Econ Rev. 2025;15:94.
17. Tang J, Yuan J, Wang H, et al. Evaluation of the disease burden of nosocomial infection among inpatients in a cancer hospital based on propensity score matching. Front Public Health. 2025;13:1572558.
18. Moradi S, Najafpour Z, Cheraghian B, et al. The Extra Length of Stay, Costs, and Mortality Associated With Healthcare-Associated Infections: A Case-Control Study. Health Sci Rep. 2024;7(11):e70168.
19. An Y, Guo Y, Li L, et al. Management and outcome of adult generalized tetanus in a Chinese tertiary hospital. Front Public Health. 2024;12:1301724.
20. Centers for Disease Control and Prevention. About Tetanus. https://www.cdc.gov/tetanus/about/. Accessed 19 August 2026.
21. Centers for Disease Control and Prevention (CDC). Tetanus surveillance --- United States, 2001–2008. MMWR Morb Mortal Wkly Rep. 2011;60(12):365–9.
22. Van Hao N, Yen LM, Davies-Foote R, et al. The management of tetanus in adults in an intensive care unit in Southern Vietnam. Wellcome Open Res. 2021;6:107.
23. Yasunaga H, Fushimi K, Matsui H, et al. Clinical features and outcomes of tetanus: Analysis using a National Inpatient Database in Japan. J Crit Care. 2018;44:388–91.
24. Kang Y, Mai G, Zhu X, et al. Epidemiological and Clinical Characteristics of Non-neonatal Tetanus Patients in Guangxi, China: An 11-year Retrospective Study (2011–2021). Biomed Environ Sci. 2023;36(9):880–5.
25. Mahieu R, Reydel T, Maamar A, et al. Admission of tetanus patients to the ICU: a retrospective multicentre study. Ann Intensive Care. 2017;7:112.
26. Phu VD, Nadjm B, Duy NHA, et al. Ventilator-associated respiratory infection in a resource-restricted setting: impact and etiology. J Intensive Care. 2017;5:69.
27. Loan HT, Parry J, Nga NT, et al. Semi-recumbent body position fails to prevent healthcare-associated pneumonia in Vietnamese patients with severe tetanus. Trans R Soc Trop Med Hyg. 2012;106:90–7.

Figures

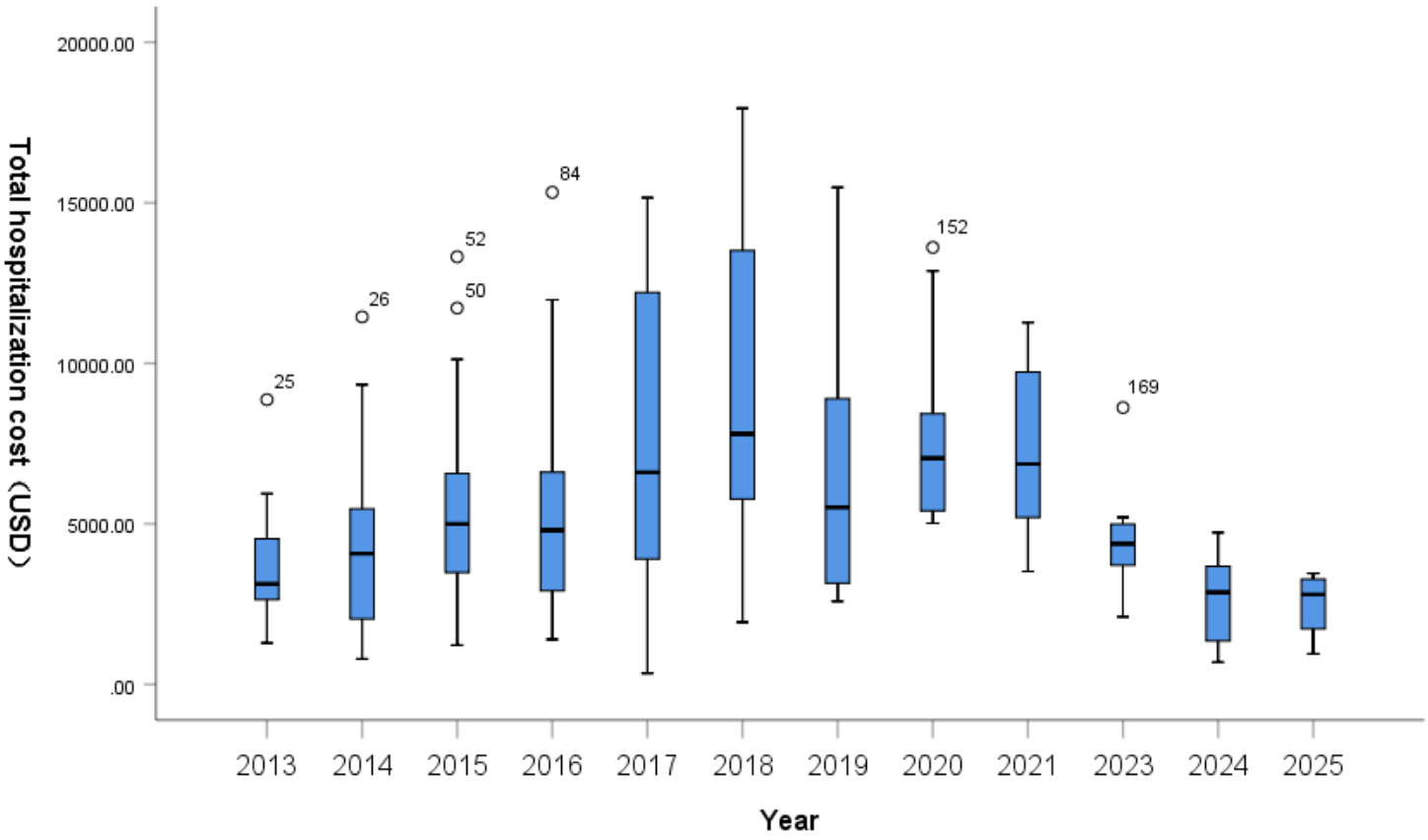


Figure 1

Boxplot of total hospitalization costs for tetanus patients in the non-MV group 2013–2025

Note: Circles (○) indicate mild outliers beyond 1.5 times the interquartile range. The numbers represent case IDs, facilitating data traceability and verification.

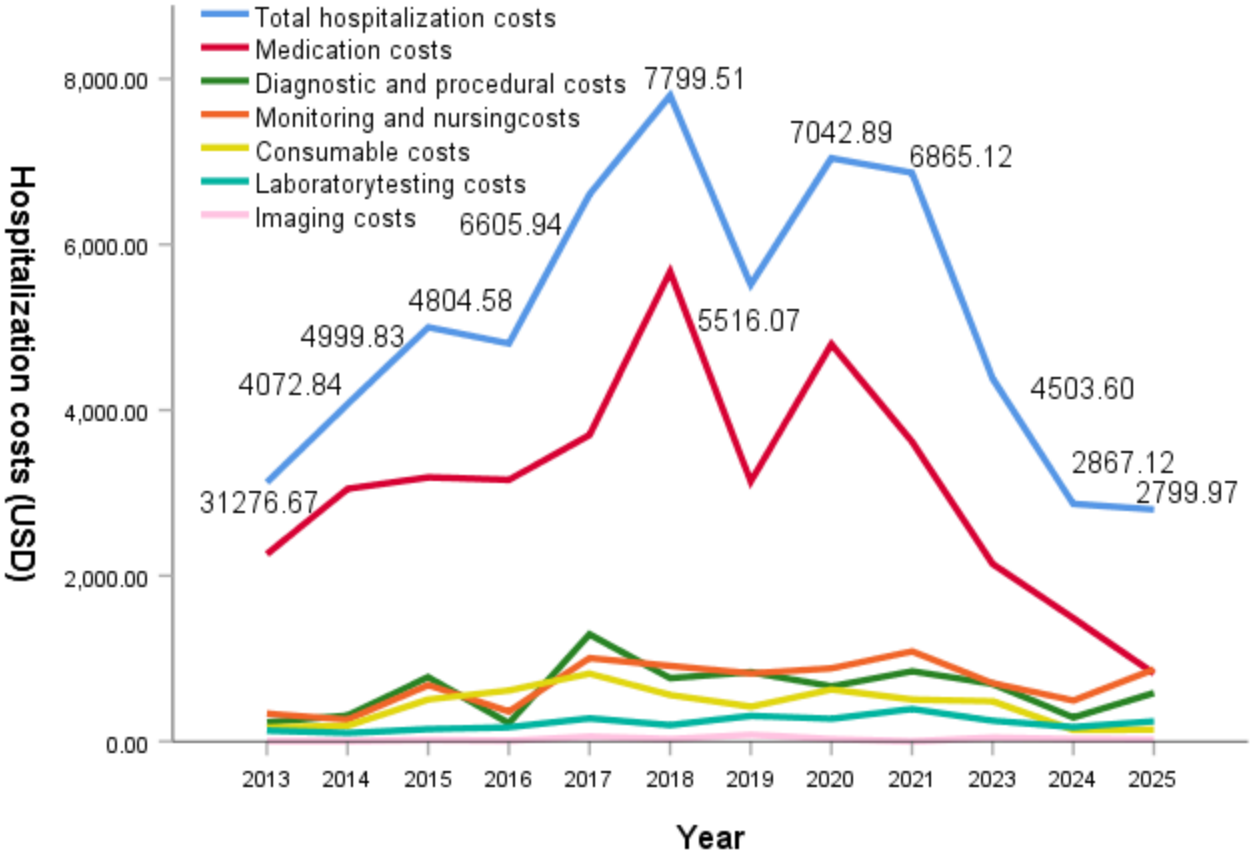


Figure 2

Median trends of total and sub-item hospitalization costs among tetanus patients in the non-MV group 2013–2025

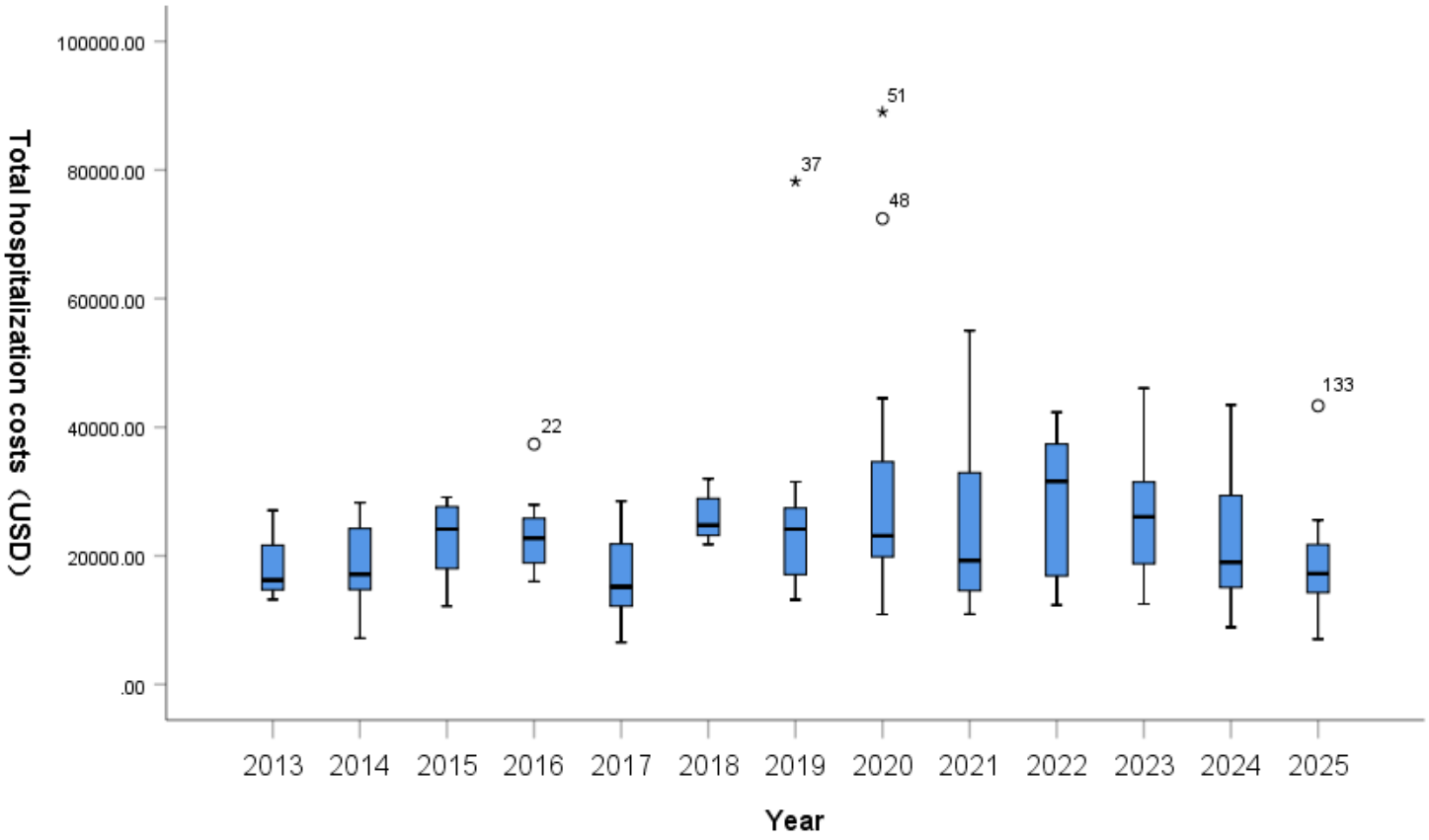


Figure 3

Boxplot of total hospitalization costs for tetanus patients in the MV group 2013–2025

Note: Circles (○) represent mild outliers (>1.5×IQR), asterisks (*) represent extreme outliers (>3×IQR). Numbers indicate case IDs for data traceability.

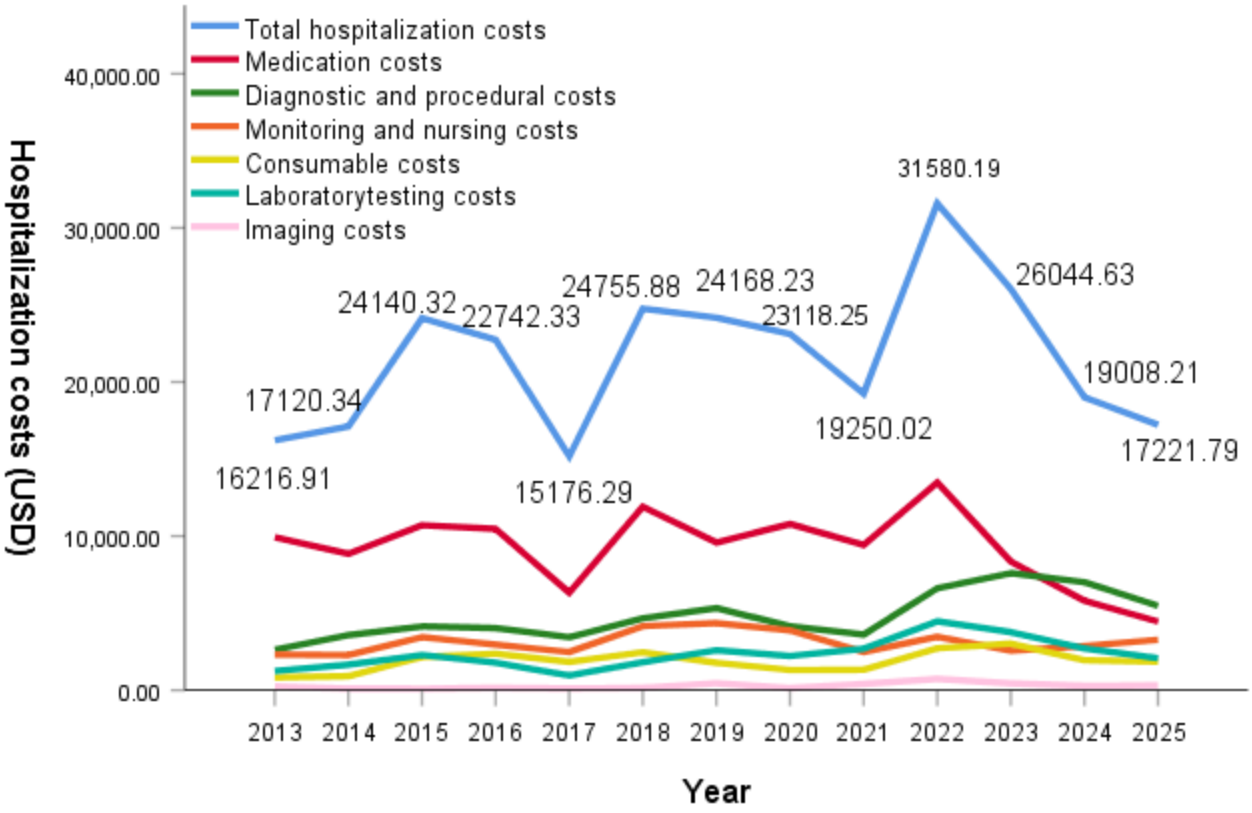


Figure 4

Median trends of total and sub-item hospitalization costs among tetanus patients in the MV group 2013–2025

Table 2 Comparison of hospitalization costs among tetanus patients with different clinical characteristics in the non-MV group 2013–2025