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Evaluation of the impact before and after the application of an antimicrobial stewardship program at Dong Thap General Hospital, Vietnam, from 2017 to 2021

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SUMMARY

Background: Vietnam has one of the highest rates of antibiotic resistance in Asia. In 2020, the Vietnam Minister of Health introduced new legislation for the implementation of an antimicrobial stewardship program (ASP). The evidence for the effectiveness of ASP in small hospitals and hospitals located in provinces was limited compared with larger-scale and central city hospitals.

Aim: Evaluation of the impact before and after the introduction of an antimicrobial stewardship program at Dong Thap General Hospital, from 2017 to 2021.

Methods: Retrospective data was collected from June 2017 to June 2021. The impact of the ASP on changes in antibiotic use and the clinical outcome associated with the implementation of the ASP was evaluated using autoregressive integrated moving average modelling of controlled interrupted time-series analysis.

Results: There was a significant and sustained decrease in antibiotic consumption level (step change) in 2 indicators, DOT/1000PD (129.55; $P<0.01$) and LOT/1000PD (99.95, $P<0.01$), immediately after the ASP intervention. There were no statistically significant changes identified in terms of consumption with DDD/1000PD, or in the clinical outcomes. The results showed no statistically significant change in consumption trend (ramps) in all evaluated indicators. No statistically significant changes in consumption levels and trends were observed in the control group.

Conclusion: The ASP implemented in Dong Thap General Hospital from 2017 to 2021 showed a considerable influence on antibiotic consumption as indicated by the DOT/1000

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PD and LOT/1000 PD during the initial stages. Moreover, controlling antibiotic consumption did not negatively impact patient outcomes.

Introduction

The inappropriate use of antibiotics has become a significant concern in global healthcare, leading to an increase in antibiotic resistance (AMR), longer courses of treatment, and increased mortality rates [1]. In 2019, a study estimated that the global burden of antibiotic resistance resulted in approximately 4.95 million deaths (3.62—6.57), of which 1.27 million (0.911—1.71) were directly attributed to resistance [2]. To address these concerns, the World Health Organization (WHO) and many countries have established and developed antimicrobial stewardship programs (ASP) [3,4]. The implementation of ASP plays a crucial role in optimising the use of antibiotics and has contributed to slowing down the progression of antibiotic resistance. Overall, the implementation of ASP has had a positive impact on reducing total antibiotic consumption, shortening the duration of treatment, and increasing the appropriate use of antibiotics [5,6]. According to research by the Organization for Economic Co-operation and Development (OECD), the implementation of ASP helps to manage antibiotic use and combat antibiotic resistance, which could prevent 1.6 million deaths by 2050 and generate annual savings of $4.8 billion [6].

Vietnam is among the countries in Asia with the highest prevalence of antibiotic resistance, resulting in thousands of deaths annually [7]. The frequent and indiscriminate use of antibiotics in the community, along with inappropriate prescriptions in hospitals, are the two main reasons leading to increased antibiotic resistance [8,9]. In 2020, the Vietnam Minister of Health introduced legislation for the implementation of ASP in hospitals [10].

However, the evidence of the effectiveness of ASP in small and provincial hospitals has remained limited compared to larger hospitals. Dong Thap hospital is an important provincial-level hospital with limited facilities and personnel. It was selected as the study site to evaluate the effectiveness of ASP when implemented in a provincial hospital, using the WHO practical toolkit 2019 and guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America an evaluation indicator [4,11,12].

Methods

Study setting

This study was conducted in Dong Thap General Hospital, a provincial 1000-bed hospital, located in the Dong Thap province, Mekong Delta.

Ethical approval

Approval was obtained from Research Ethics Committee (No. 3092/BVĐT/TB) at Dong Thap General hospital.

Study design

This quasi-experimental study evaluated the ASP impact on changes in antibiotic use and clinical outcome associated with the implementation of the program at a provincial hospital using autoregressive integrated moving average (ARIMA) modelling — a statistical analysis model for trends — of controlled interrupted time series analysis.

Antibiotic use and other outcomes were collected before and after the ASP for admissions that met the specific selection criteria (systemic parenteral or oral antimicrobial agents and admission with hospital length of stay was at least one day). The clinical outcome of an inpatient was based on one of five discharge statuses which comprised: (1) recovered, (2) improved, (3) unchanged, (4) worsened, or (5) deceased. The three statuses 'unchanged', 'worsened' and 'deceased' were grouped into one group called 'cases with no improvement' to assess the ASP clinical outcome impact. We hypothesised there would be an immediate decrease in both the antibiotic consumption and the percentage of cases with no improvement (clinical outcome) as well as continued downward trends for these results after the intervention.

Intervention

The national ASP was introduced and implemented in Dong Thap General hospital in July 2020. In this study, the pre-intervention period was from July 2017 to June 2020 (pre-ASP), and the post-intervention period was from July 2020 to June 2021 (post-ASP). The process of setting up an ASP program to reduce total antibiotic use and to improve patient outcome included.

(1) Training and mentoring courses organised throughout the planning and implementation phases for doctors, pharmacists, microbiologists, and nurses;
(2) Restructuring the ASP board by adding representatives from the Hospital Leadership Board, and the Head of the Finance and Accounting Department;
(3) Undertaking the ASP in specific specialised departments. The ASP was responsible for monitoring and developing prioritised antibiotic guidelines with other departments, in compliance with national legislation, and quarterly reporting to the Drug and Treatment Council in the hospital on issues related to antibiotic use and actions to be taken.

Data collection and outcomes

Retrospective patient-level data from June 2017 to June 2021 were extracted and analysed to evaluate the effectiveness of the ASP. The primary outcome was the change in antibiotic consumption measured by: (1) Defined Daily Dose per 1000 patient-day (DDD/1000PD); (2) Day of Therapy per 1000

patient day (DOT/1000PD); (3) Length of Therapy per 1000 patient day (LOT/1000PD), calculated monthly. The DDD is the average maintenance dose per day for the drug used [4]. The DOT is defined by any amount of a specific agent administered on a calendar day to a particular patient as documented in the electronic medication administration record. The LOT differs from DOT in that the number of antimicrobials is irrelevant [13]. Total paracetamol consumption, expressed by DDD/1000PD/month and DOT/1000PD/month, was selected to be the negative control group with the hypothesis that paracetamol use was not affected by the ASP intervention. The secondary outcome was the patient clinical outcome (percentage of cases with no improvement) on discharge, collected at a monthly rate.

In addition, to provide a comprehensive overview of antibiotic usage in the hospital before and after the intervention, demographic data such as age and gender were obtained, as well as the number of admissions; and the percentage of antibiotic use in the 2021 WHO AWaRe classification; list of prioritised antibiotics for management detailed in the national legislation; antibiotic routes of administration. The Anatomical Therapeutic Chemical (ATC) classification system was applied to detect antibiotics — J01 (Antibacterials for systemic use) — in the patients' medications usage database. Information regarding antibiotic ATC code and its WHO-DDD unit were identified via https://www.whocc.no/atc_ddd_index/.

Statistical analysis

All statistical analyses were performed using R software (https://www.r-project.org/), version 4.1.2.

The primary and secondary outcomes were assessed by ARIMA model in interrupted time series analysis. We utilised the corrected Akaike Information Criterion (AICc) to select the most appropriate ARIMA (p, d, q) model. The AIC serves as a tool to compare various models for dataset analysis and identify the best fit, and AICc is a version of AIC corrected for small sample sizes. The most suitable model, which has the smallest AICc value, would be selected. We estimated two main intervention variables which were step change and ramp. Where step change is a sudden, sustained change where the time series is shifted either up or down by a given value immediately following the intervention and ramp is a change in slope that occurs immediately after the intervention [14]. Ljung-Box test was used to assess whether the residuals of the selected model were a white noise series.

This study used a Q-Q plot to test for normal distribution. To test for statistically significant differences between the mean and median values of the measures, we use the t-test for variables with normal distribution and the Mann-Whitney test for variables with no normal distribution. Categorical variables were assessed using the Chi-square test.

All tests of significance where a *P*-value was less than 0.05 was considered statistically significant.

Results

Patient characteristics

From June 1, 2017, to June 30, 2021, Dong Thap Hospital had 2,024,938 hospitalisations, of which 31.25% were treated with antibiotics. The number of inpatients with antibiotic treatment time of 24 hours or more in the study sample accounted for 24% of the total number of patients using antibiotics at the hospital. The medical records that met the pre-ASP and post-ASP selection criteria were 113,719 and 38,212 records, respectively (Table I see Figure 1). In both periods, there were no statistically significant differences in gender, age, and all treatment outcomes ($P>0.05$). Most patients were adults between the ages of 18 and 60 (pre-ASP: 41.4%, post-ASP: 43.5%).

Among the groups of antibiotics classified by ATC code, in both periods, the most used group was J01D subgroup (cephalosporins, carbapenems, and monobactams group) with the consumption rate was 55.65% and 56.96% in pre-ASP and post-ASP, respectively. In contrast, J01A subgroup had the lowest percentage of use with the figures for pre-ASP and post-ASP were approximately 0.08%.

According to the AwaRe classification, most prescribed antibiotics for inpatients in both periods were in Watch subgroup, 82.20% in pre-ASP and 78.60% in post-ASP. After the implementation of ASP, the antibiotic rate of Access subgroup slightly increased from 16.90% to 20.60%. The Reserve subgroup had the lowest percentage of inpatient prescriptions in both periods with 0.40% in pre-ASP and 0.50% in post-ASP.

According to the antibiotic classification in the national legislation (Decision no. 5631/2020 of the Ministry of Health-Vietnam), the antibiotic groups, except for group 1 and group 2, which were not given priority for management or monitoring, showed the highest usage rate (70.44% in pre-ASP and 68.98% in post-ASP). However, there was no significant difference in usage rates of these groups between the two periods.

Most inpatients were prescribed parenteral antibiotics. The rate of using parenteral antibiotics was 70.20% and the rate of using oral antibiotics was 29.80% in pre-ASP; 75.20% and 24.80% in post-ASP (Appendix 1).

The cost of antibiotics in pre-ASP and post-ASP was 59,102,011,066 VND and 24,266,221,270 VND, respectively, corresponding to 42.80% and 42.36% of the total drug usage cost ($P>0.05$).

Antibiotic consumption

The purpose of this study was to analyse the Defined Daily Dose (DDD), Days of Therapy (DOT), and Length of Therapy (LOT) indices for antibiotic consumption in a cohort of 75,604 patients in the pre-ASP period and 27,478 patients in the post-ASP period. Hospitalised paediatric patients who were prescribed antibiotics were excluded from the study as these indices are not applicable to this demographic. The findings indicate that the DDD/1000 PD in the pre-ASP and post-ASP periods were 1467.27 and 1355.44, while the DOT/1000 PD were 1179.57 and 1082.73, and the LOT/1000 PD were 867.50 and 808.80 (Table II).

Among the different antibiotic groups, cephalosporins were the most frequently used in both periods, with 625.25 DDD/1000 PD and 656.91 DOT/1000 PD in pre-ASP and 475.39 DDD/1000 PD and 578.20 DOT/1000 PD in post-ASP. Fluoroquinolones were the second most used antibiotic group in pre-ASP, with 378.05 DDD/1000 PD and 230.23 DOT/1000 PD, and penicillin in post-ASP, with 394.39 DDD/1000 PD and 181.08 DOT/1000 PD. Ceftazidime, a third-generation cephalosporin, had the highest percentage of use in both periods, with 14.36% (DDD/1000 PD)

Table I
Patient characteristics for inpatients whose duration of antibiotic treatment from 24 hours upwards during the pre- and post-intervention periods (Pre-ASP and Post-ASP)

Characteristics	Pre-ASP (n=113,719)	Post-ASP (n=38,212)	*P*
Gender			
Male	49,300 (43.35)	16,799 (43.96)	0.93
Female	64,419 (56.65)	21,413 (56.04)	
Age			
Median (Q1-Q3)	31 (5—60)	35 (9—63)	0.69
< 18 years	38,115 (33.52)	10,734 (28.09)	0.49
From 18 to < 60 years	47,092 (41.41)	16,628 (43.52)	0.81
≥ 60 years	28,512 (25.07)	10,850 (28.39)	0.65
Hospitalisation (No. Cases)			
Treatment results (%)			
Recovered	56.73	56.2	0.98
Improved	34.04	33.31	0.98
Unchanged	5.95	5.48	0.54
Worsened	3.22	4.96	0.88
Deceased	0.06	0.05	0.97
Length of stay			
Median (Q1 — Q3)	5 (3—8)	5 (3—7)	<0.01
Min — Max	1—85	1—88	
The rate of 1 infection episode (%)	99.37%	99.50%	
The use of antibiotics classified by ATC code (WHO) (%)			
J01A (Tetracyclines)	0.08	0.08	
J01C (Beta-lactam antibacterials, Penicillins)	10.53	13.35	
J01D (Other Beta-lactam antibacterials)	55.65	56.96	
J01E (Sulfonamides and Trimethoprim)	0.12	0.2	
J01F (Macrolides, Lincosamides, Streptogramins)	2.35	2.29	
J01G (Aminoglycoside antibacterials)	4.26	6.73	
J01M (Quinolone antibacterials)	19.85	17.06	
J01X (Other antibacterials)	6.76	2.7	
Others	0.39	0.64	
The use of antibiotics classified by AwaRe classification (%)			
Access	16.9	20.59	
Watch	82.17	77.96	
Reserve	0.45	0.52	
Not recommended	0.5	0.94	
The use of antibiotics classified by national legislation- Decision no. 5631 (%)			
Group 1 — priority management	5.45	6.22	
Group 2 — monitored when using	24.1	23.8	
Others	70.44	69.98	
The use of two antibiotic administration routes (%)			
Parenteral	70.2	75.2	
Oral	29.8	24.8	
Cost of antibiotics (VND)			
%/Total drug usage cost	42.80	42.36	

and 21.30% (DOT/1000 PD) in pre-ASP and 16.83% and 21.70% in post-ASP (Table II).

Interrupted time series analysis

Antibiotic consumption

The ARIMA model (1,1,0) is considered appropriate for the DDD/1000 PD index, DOT/1000 PD index, and LOT/1000 PD index (Appendix 2). Interrupted time series analysis (ITS) revealed a sudden decrease in consumption level (step change) by 5.4 DDD/1000PD and a monthly decrease of 7.4 DDD/1000PD after ASP (ramp), but this did not reach statistical significance (P=0.84, P=0.59). For DOT/1000PD, ITS showed a significant decrease in the level of antibiotic use (step change) by 129.55 DOT/1000 PD immediately after the intervention (P<0.01). However, there was a slight increase of 1.45 days per month in the period after ASP (ramp) (P=0.88), but this was statistically insignificant. There was also an immediate decrease of LOT/1000 PD, which exhibited a decrease of 99.95 days after the intervention (step change) (P<0.01), with a further non-significant increase of 2.53 days every month in the period after ASP (ramp) (P=0.54). (Table III, Figure 2).

Clinical outcomes

After analysing the data of the proportion of cases with no improvement in treatment results, the study determined that

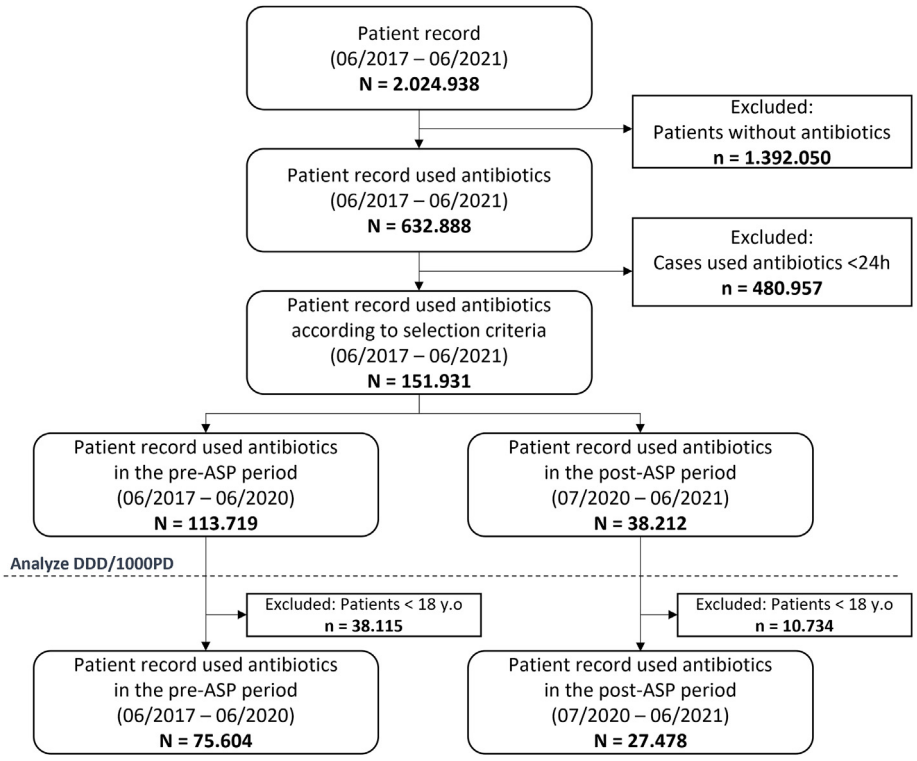


Figure 1. Data collection.

the most appropriate ARIMA model was ARIMA (4,1,1) (see Appendix 1 for details). The results indicated that there was a non-significant decrease in the proportion of cases with no improvement in treatment results immediately after the implementation of ASP, 1.34% in July 2020 (step change) (P=0.08). On the other hand, the data also showed an increasing trend of 0.08% per month in the period after ASP for the ramp variable, but these changes failed to reach statistical significance with a P-value of 0.47 (Table III and Figure 2).

Control group

The assessment of consumption variables in the control group did not show any statistically significant changes. The values of step change variable showed that there significantly was a sudden decrease in consumption level in indicator DDD/1000 PD immediately by 7.76 DDD/1000 PD (P=0.82) (Table III). Simultaneously, there was a trend of increasing consumption by 2.1 DDD per month after ASP (ramp) (P=0.76) (Table III). Meanwhile, the results of DOT/1000 PD also demonstrated a sudden and sustained increase of 7.52 DOT/1000 PD after intervention (step change) (P=0.63) (Table III), accompanied by a trend towards a decrease of 2.23 days of antibiotic treatment per month after ASP (ramp) (P=0.27) (Table III, Figure 2).

Discussion

The findings indicated that the intervention did not have a significant impact on the rates of antibiotic subgroups. The Watch subgroup accounted for 82.2% and 78.0% in pre-ASP and post-ASP, respectively. This failed to reach the WHO's target for the Access subgroup, which aims to account for at least 60% of total [15]. A similar case was reported in a study conducted at the Hospital for Tropical Diseases in Ho Chi Minh City, Vietnam, where the Watch subgroup accounted for 78.1% [16]. Additionally, Eili Y. *et al*. showed that the global consumption of Watch subtype antibiotics increased to 90.9% in 76 countries from 2000 to 2015, indicating an upward trend in antibiotic use worldwide [17]. In Vietnam, the antibiotic resistance situation is complicated due to the overuse and misuse of antibiotics, not only in hospitals but also in the community [18]. High levels of consumption of the Watch subgroup were detected and mentioned within the community [19]. Moreover, Nga Do *et al*. showed that a percentage of antibiotics' self-medication without prescription in Vietnam was 55.2%, which was the highest among six low- and middle-income countries [19]. The main reasons were the convenience of treating mild conditions, the least expensive and most timely way to obtain antibiotics in drug stores (community) compared to hospitals [18–20]. Hence, intervention strategies for antibiotic use are needed in the community in addition to the hospitals in Vietnam to effectively to control the consumption among antibiotic subgroups.

The observed differences between the DDD/1000PD and the DOT/1000PD can be explained by the fact that the DDD index has been shown in numerous studies to overestimate antibiotic consumption compared to the actual levels [21–24]. The percentage difference between the forecasted "counterfactual" value and the actual value at the end of the corresponding research period for the impact of the program on the four indices of DDD/1000PD, DOT/1000PD, and LOT/1000PD, and the proportion of cases with no improvement was 2.95%, 7.98%, 7.02%, and -7.83%, respectively (Appendix 3). Additionally, there was a high proportional use of the parenteral route with 70.2% and 75.2% for pre-ASP and post-ASP, respectively).

Table II
Total antibiotic consumption measured by defined daily dose per 1000 patients-days (DDD/1000 PD) and days of therapy per 1000 patients-days (DOT/1000 PD)

Antibiotics	ATC code	DDD/1000 patients-day		DOT/1000 patients-day	
		Pre-ASP	Post-ASP	Pre-ASP	Post-ASP
Penicillins					
Penicillins + beta-lactamase inhibitors		***244.88***	***221.31***	***52.66***	***51.46***
Amoxicillin	J01CA04	244.88	221.31	52.66	51.46
Beta-lactamase-sensitive penicillins		***1.04***	***13.21***	***6.52***	***18.11***
Cloxacillin	J01CF02	0.07	6.07	0.09	11.82
Oxacillin	J01CF04	0.99	7.14	6.43	6.29
Penicillins + beta-lactam inhibitors		***85.87***	***159.87***	***58.69***	***74.11***
Ampicillin -sulbactam	J01CR01	2.71	0.05	3.31	0.08
Amoxicillin - sulbactam	J01CR02	30.77	0.00	8.92	0.00
Amoxicillin - clavulanic acid	J01CR02	47.80	159.82	42.53	74.03
Piperacillin - tazobactam	J01CR05	4.59	0.00	3.93	0.00
Cephalosporin					
Second-generation cephalosporins		***275.34***	***47.78***	***116.99***	***51.56***
Cefoxitin	J01DC01	7.93	9.57	13.08	14.61
Cefuroxime	J01DC02	267.41	38.21	103.91	36.95
Third-generation cephalosporins		***342.20***	***409.34***	***509.60***	***491.15***
Cefotaxime	J01DD01	47.92	53.36	0.00	3.62
Cefotiam	J01DC07	0.00	2.42	171.82	177.92
Ceftazidime	J01DD02	210.74	228.18	251.24	234.91
Ceftriaxone	J01DD04	36.41	31.35	40.53	24.19
Cefixime	J01DD08	46.42	92.03	43.93	46.91
Cefpodoxime	J01DD13	0.21	0.00	0.88	0.25
Cefoperazone - sulbactam	J01DD62	0.50	2.00	1.20	3.35
Fourth-generation cephalosporins		***7.88***	***18.27***	***30.32***	***35.49***
Cefepime	J01DE01	5.94	17.79	27.58	34.87
Cefpirome	J01DE02	1.94	0.48	2.74	0.62
Carbapenems		***13.65***	***40.77***	***15.87***	***40.62***
Meropenem	J01DH02	3.70	8.74	5.77	10.06
Ertapenem	J01DH03	0.41	5.94	0.30	4.09
Imipenem - cilastatin	J01DH51	1.35	0.00	9.80	26.47
Aminoglycosides		***29.49***	***46.85***	***52.48***	***74.81***
Gentamicin	J01GB03	3.38	1.24	13.51	4.82
Amikacin	J01GB06	24.30	44.83	33.82	68.86
Netilmicin sulfate	J01GB07	1.81	0.78	5.15	1.13
Phosphonic		*0.09*	*0.00*	*0.07*	*0*
Fosfomycin	J01XX01	0.09	0.00	0.07	0.00
Tetracycline		*4.31*	*4.13*	*0.96*	*0.84*
Doxycycline	J01AA02	3.86	4.13	0.81	0.84
Tetracycline	J01AA07	0.45	0.00	0.15	0.00
Macrolide		*5.11*	*5.51*	*27.15*	*24.40*
Spiramycin	J01FA02	0.02	0.00	0.03	0.00
Roxithromycin	J01FA06	0.02	0.04	0.07	0.03
Clarithromycin	J01FA09	1.24	1.02	0.30	0.22
Azithromycin	J01FA10	3.80	4.35	26.75	24.15
Lincosamide		*0.03*	*0.10*	*0.58*	*0.69*
Clindamycin	J01FF01	0.03	0.10	0.58	0.69
Fluoroquinolone		*378.05*	*343.43*	*230.23*	*181.08*
Ofloxacin	J01MA01	91.51	66.97	27.60	20.07
Ciprofloxacin	J01MA02	201.25	182.82	164.71	116.15
Levofloxacin	J01MA12	17.79	3.35	36.11	34.08
Moxifloxacin	J01MA14	2.61	15.57	1.81	10.78
Glycopeptides		*26.77*	*20.65*	*60.93*	*20.85*
Teicoplanin	J01XA02	0.69	6.08	0.58	5.58
Vancomycin	J01XA01	26.08	14.57	4.35	15.27
Polymyxin		*2.44*	*3.89*	*4.68*	*5.47*

Table II (*continued*)

Antibiotics	ATC code	DDD/1000 patients-day		DOT/1000 patients-day	
		Pre-ASP	Post-ASP	Pre-ASP	Post-ASP
Colistin	J01XB01	2.44	3.89	4.68	5.47
Imidazole		*39.13*	*3.76*	*31.75*	*2.82*
Metronidazole	J01XD01	39.09	3.68	31.73	2.74
Tinidazole	J01XD02	0.04	0.08	0.02	0.08
Oxazolidinone		*0.98*	*0.25*	*0.73*	*0.16*
Linezolid	J01XX08	0.98	0.25	0.73	0.16
Combinations of antibacterials		*10.02*	*16.40*	*5.84*	*8.80*
Spiramycin -metronidazole	J01RA04	6.68	10.89	4.43	6.70
Sulfamethoxazole - trimethoprim	J01EE01	3.34	5.51	1.41	2.10
Total		1467.27	1355.44	1179.57	1082.73

*Inpatients aged < 18 years using antibiotics were excluded when calculating and examining DDD because this indication is only applied to adults.

Table III
ARIMA model for total antibiotic use measured in DDD/1000 PD, DOT/1000 PD, LOT/1000 PD, the proportion of cases with no improvement for intervention and DDD/1000 PD, LOT/1000 PD for control group

Unit	Step change	*P*	Ramp	*P*
Intervention				
DDD/1000PDs	-5.40 [-138,58; 128,32]	0.84	-7.24 (-37,94; 21,58)	0.59
DOT/1000PDs	-129.55 [-196,72; -62,38]	<0.01	1.45 [-13,43; 16,42]	0.84
LOT/1000PDs	-99.95 [-136,77; -63,12]	<0.01	2.53 [-5,53; 10,59]	0.54
The proportion of cases with no improvement	-1.34 [-2,88; 0,16]	0.08	0.08 [-0,15; 0,32]	0.47
Control				
DDD/1000PDs	7,76 [-58,03; 73,52]	0.82	2,10 [-12,33; 16,53]	0.76
LOT/1000PDs	7,52 [-23,42; 38,46]	0.63	-2,23 [-6,20; 1,75]	0.27

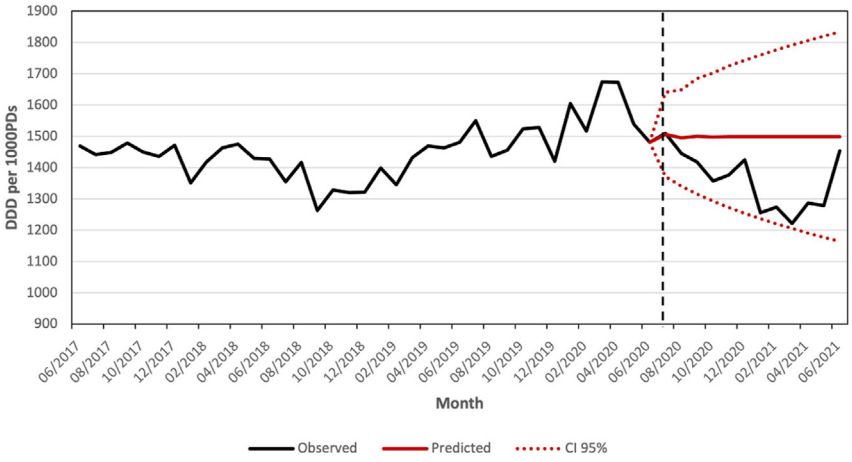
ARIMA, autoregressive integrate moving average; DDD, defined daily doses; DOT, Day of Therapy; LOT, Length of Therapy; PD, patient-days. *The results were presented as mean (95% confidence interval) if not stated otherwise.*

A study conducted by Vallès *et al.* has demonstrated that using the DDD for surveillance can lead to errors for patients with severe illnesses [21]. Therefore, evaluating antibiotic consumption beyond the actual levels through the DDD may impact on the effectiveness of ASP and could result in higher consumption levels than the reality, leading to an inaccurate assessment of changes in consumption during the post-ASP stage (step change), as indicated by the observed results in the DOT.

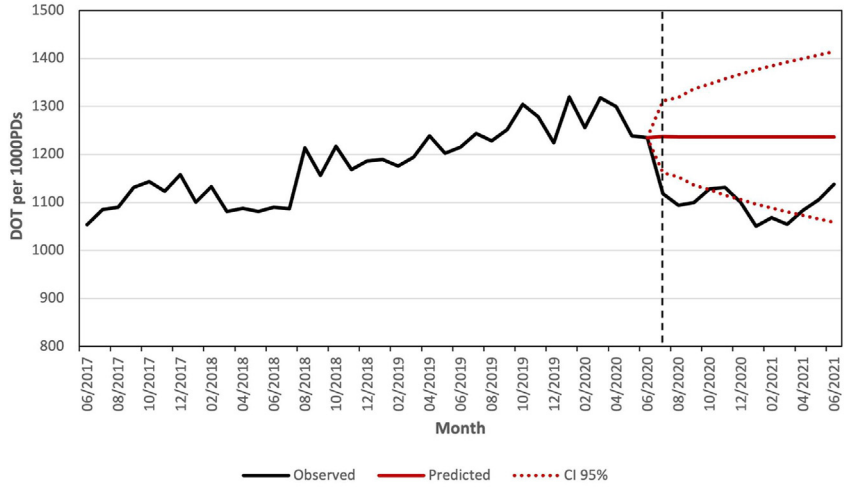
Additionally, the DDD fails to accurately assess patients with impaired renal function, as these individuals require antibiotic dosage adjustments, resulting in lower actual doses compared to other patients [25]. Moreover, the DDD measurement is not recommended for the paediatric population, which accounted for a third of the study population (33.52% and 28.09% in the pre-ASP and post-ASP periods, respectively) [16]. Therefore, it might not reflect the change in total antibiotic consumption for the overall population. Hence, to evaluate the effectiveness of ASP using the DDD or DDD/1000PD, it is necessary to control several factors (related to the study population and disease model) and emphasise the prioritisation of the DOT index in the study.

The study's findings on clinical outcomes align with a meta-analysis of 15 Asian countries that also found non-statistically significant changes in clinical outcomes resulting from ASP [26]. Although the goals of antibiotic management programs include reducing resistance and improving clinical outcomes, these are long-term issues that depend on several factors, such as a patient's condition, underlying disease, and medication adherence status, rather than just the clinical effects of rational antibiotic use. Therefore, the short-term expectation of the ASP in this study was to improve consumption rather than to change clinical outcomes. A three-year ASP implementation evaluation study at Osaka City University Hospital demonstrated significant improvements in clinical outcomes. Specifically, the study revealed that in-hospital mortality and 30-day mortality rates were significantly lower after the ASP implementation (24.8%—18.0% and 20.4%—10.5%, respectively) [27]. Hence, the hospital should extend the timescale of further studies to capture the outcomes that demonstrate the long-term impact of the ASP intervention.

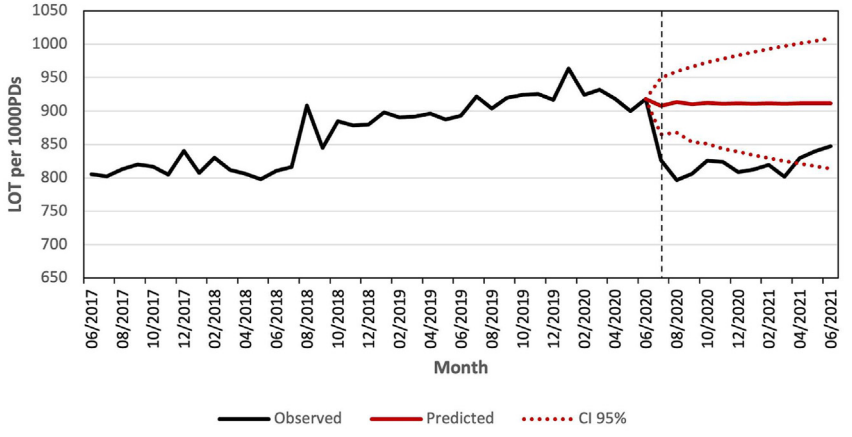
This study has several limitations. First, the duration of the post-ASP period in our study was short, limiting our ability to capture the long-term effectiveness of the program. Furthermore, our findings highlight the need for future investigations to consider additional indicators as recommended by the WHO, such as usage costs, microbiological outcomes, rates of route-switching, adherence to prescribed regimens, and prophylactic antibiotic utilisation in surgical settings [4].



(A)

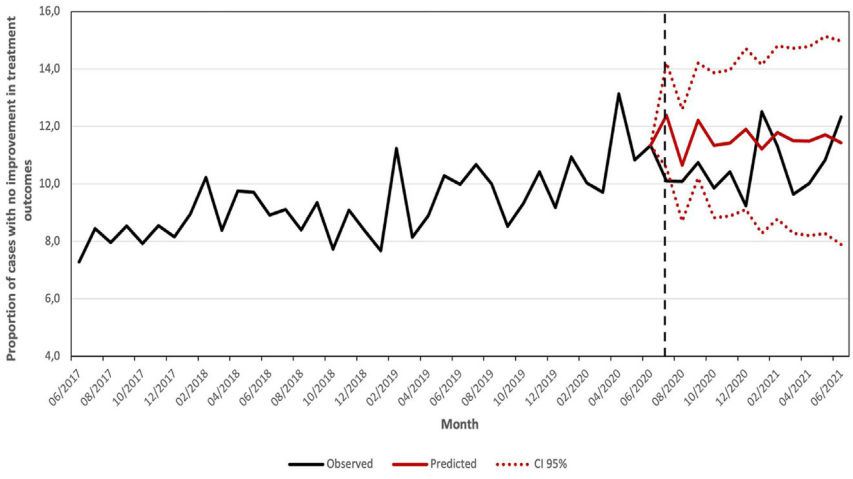


(B)

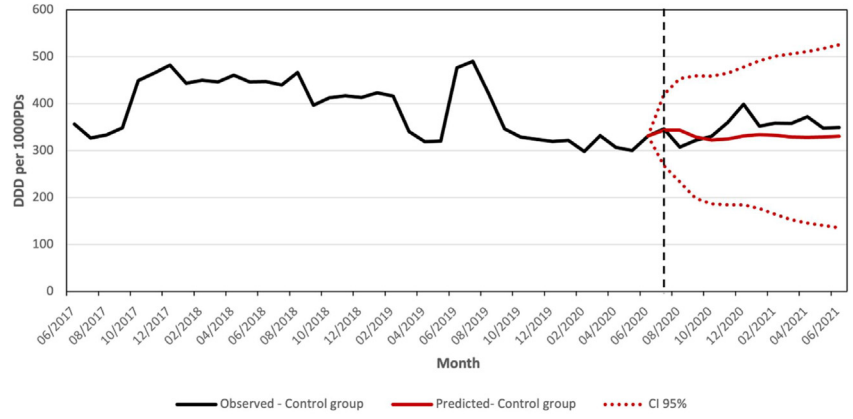


(C)

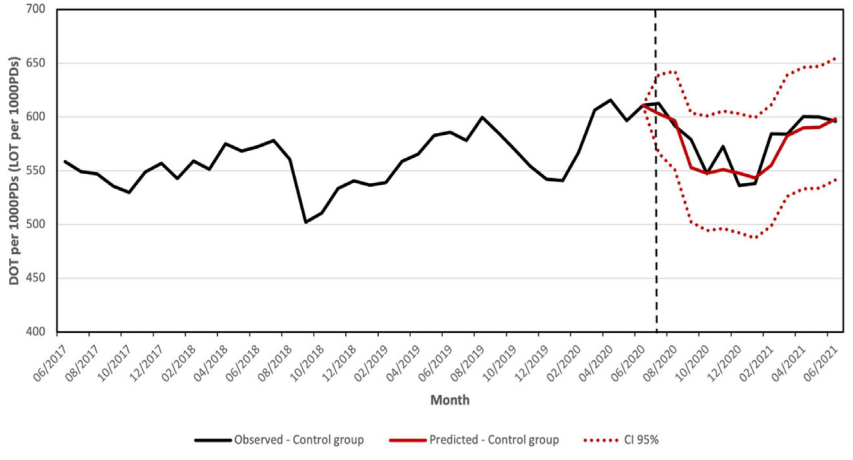
Figure 2. Total antibiotic use: DDD/1000 PD (A), DOT/1000 PD (B), LOT/1000 PD (C) and The proportion of cases with no improvement (D) in pre-ASP and post ASP; DDD/1000 PD (E), DOT/1000 PD (F) for control group. Each data point represents total DDD/1000 PD (DOT/1000 PD, LOT/1000 PD) or total cases with no improvement per month from June 2017-June 2021 in Dong Thap General Hospital. The implementation of ASP (represented by a dashed line) occurred in July 2020.



(D)



(E)



(F)

Figure 2. (*continued*).

Conclusions

The implementation of ASP resulted in a reduction in antibiotic consumption levels. However, the downward trend could not be maintained. Additionally, patient outcomes did not show a significant difference compared to before the ASP implementation. The DOT and LOT indices are appropriate indicators for evaluating the effectiveness of ASP in controlling the antibiotic consumption. Besides assessing antibiotic consumption and patient outcomes, supplementary indicators should be studied further to achieve a more comprehensive and detailed evaluation of the ASP's effectiveness.

Conflicts of interest

None.

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Authors' contributions

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Writing: all authors.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.infpip.2023.100311.

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