

Infectious Disease Team Review Using Antibiotic Switch and Discharge Criteria Shortens the Duration of Intravenous Antibiotic: A Single-Center Cluster-Randomized Controlled Trial in Thailand

Thanyarak Wongkamhla,¹ Buddharat Khan-asa,² Sasima Tongchai,³ and Nasikarn Angkasekwinai^{1,*}

¹Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand, ²Pharmacy Department, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand, ³Department of Research and Development, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

Background. Strategies have been recommended to optimize early antibiotic (ATB) switching from intravenous (IV) to oral ATB. This study aimed to determine whether infectious disease (ID) team review using ATB switch and discharge criteria would shorten the duration of IV ATB and length of hospital stay (LOS).

Methods. This cluster-randomized controlled trial was conducted in 8 general medical wards as cluster units at Siriraj Hospital during January–October 2019. The ID team review with checklist criteria was performed on the third, fifth, and seventh day of IV-ATB treatment to determine (1) the suitability of switching to oral ATB or outpatient parenteral ATB therapy and (2) early discharge for patients receiving IV-ATB versus control. The primary outcomes were LOS and the duration or days of therapy (DOT) or defined daily dose (DDD) of IV-ATB therapy.

Results. Four wards each were randomly assigned to the intervention and control groups (46 patients/cluster, 184 patients/arm). No significant difference was observed between intervention and controls for median duration of IV-ATB therapy (7 vs 7 days) and LOS (9 vs 10 days). A significantly shorter duration of IV ATB was observed in patients without sepsis in the intervention group when measured by DOT (7 vs 8 days, $P = .027$) and DDD (7 vs 9, $P = .017$) in post hoc analysis.

Conclusions. Infectious disease team review using checklist criteria did not result in a shorter duration of IV-ATB and LOS in overall patients. Further study is needed to determine whether faster culture turnaround time or advanced testing will reduce the duration of IV-ATB therapy.

Keywords. antibiotic switch; checklist criteria; early discharge; randomized controlled trial; shortening.

Hospitalized patients with infections generally receive intravenous (IV)-antibiotic (ATB) therapy. However, the available evidence suggests that IV-ATBs are frequently unnecessary and may cause harmful complications, such as line-related infection or injury and prolonged length of hospital stay (LOS) [1]. Administration of IV-ATBs is essential in critically ill patients, such as those with septic shock [2]; those who have specific site of infection that requires IV-ATBs, such as meningitis [3]; or when microbial susceptibility testing shows the

effectiveness of only an IV-ATB agent. Multiple antimicrobial stewardship programs (ASPs) have been designed to improve the appropriate use of ATBs by promoting the selection of the optimal antimicrobial regimen, the best route of administration, and the optimal duration of ATB treatment [4]. Hospital ASP could increase infection cure rates while reducing adverse effects, hospital costs, and LOS [5]. Early switching from IV to oral ATB therapy is one of the important components of ASP initiatives with the intended aim of optimizing antimicrobial therapy while limiting toxicity and resistance [6]. The input of infectious disease (ID) specialists in the assessment of infection severity and the management of ATBs is important for both quality of care and cost containment [5].

Several previous studies and guidelines recommended switching from IV to oral ATBs in hospitalized patients with several infectious diseases, including community-acquired pneumonia, acute pyelonephritis, skin and soft tissue infections, and intra-abdominal infections [1, 6]. Early switching can shorten the duration of IV-ATB therapy and LOS with no negative effect on patient outcome [7, 8]. In addition, significant cost saving from the use of early IV to oral ATB switch therapy

Received 12 August 2020; editorial decision 26 October 2020; accepted 27 October 2020.

Correspondence: Nasikarn Angkasekwinai, MD, Associate Professor of Medicine, Division of Infectious Diseases and Tropical Medicine, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, 2 Wanglang Road, Bangkoknoi, Bangkok 10700, Thailand (nasikarn@gmail.com).

Open Forum Infectious Diseases® 2020

© The Author(s) 2020. Published by Oxford University Press on behalf of Infectious Diseases Society of America. This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs licence (<http://creativecommons.org/licenses/by-nc-nd/4.0/>), which permits non-commercial reproduction and distribution of the work, in any medium, provided the original work is not altered or transformed in any way, and that the work is properly cited. For commercial re-use, please contact journals.permissions@oup.com
DOI: 10.1093/ofid/ofaa539

(IVOST) or outpatient parenteral ATB therapy (OPAT) and discharge was demonstrated in previous studies [5, 9].

Many strategies and tools have been recommended to promote and optimize early ATB switching and early discharge for hospitalized patients, such as electronic reminders, questionnaires, and checklists [10–13]. A possible pathway towards increasing the appropriateness of ATB use could be a formal reassessment of ATB therapy after 2–4 days when culture results allow for re-evaluation [7]. However, there are a limited number of randomized controlled trials (RCTs) from low- and middle-income countries that have investigated the efficacy and efficiency of this ATB reassessment process.

METHODS

Study Setting and Design

A cluster RCT was performed in general medical wards as cluster units at Siriraj Hospital (Bangkok, Thailand) during January 2019 to October 2019. Specialty units, such as the intensive care unit, cardiac care unit, respiratory care unit, or special unit for hematologic patients, were excluded. Each included ward has a capacity of 20 beds. This study aimed to evaluate the impact of ID team review for the suitability of early IVOST, OPAT, and early discharge using checklist criteria for patients receiving IV ATBs versus control group. This trial was not registered elsewhere because the study does not involve a drug or device. Furthermore, the intervention in this study related less to included patients and more to the acceptance (or not) of the ATB suggestion offered by the researchers to the treating physicians.

Study Participants

Eligible patients were adults aged 18 years or older who were admitted to participating wards and who received IV-ATBs for not more than 72 hours. We excluded patients who required a prolonged duration of IV-ATB therapy, such as (1) central nervous system infection, infective endocarditis, or vascular infection, (2) neutropenic patients, (3) patients who discontinued ATB treatment within 24 hours, and (4) patients who refused to participate in the study.

Patient Consent Statement

The study protocol was approved by the Siriraj Institutional Review Board (COA numbers Si 030/2019), and written consent was obtained from patients.

Randomization and Masking

The unit of randomization was general medical wards in the Department of Medicine. Participating wards were randomly allocated into 2 groups: intervention groups and control groups. The nature of the study design and intervention made masking of physicians and researchers impossible.

Control and Intervention

Most of the ATBs at Siriraj Hospital can be prescribed by any physician, except for restricted ATBs that require ID approval before dispensing (preprescription authorization), such as colistin, linezolid, sitafloxacin, and tigecycline. Another group of ATBs that are called controlled ATBs, including piperacillin/tazobactam, meropenem, and imipenem, require ID review and authorization after 72 hours (postprescription review and authorization). The responsible physician was required to complete the drug-use evaluation form for these controlled ATBs. In the present study, the intervention research team was composed of the ID team (1 ID specialist and 1 ID fellow) and the clinical pharmacist team who work with the medical, nursing, and healthcare team in each ward. All patients who received IV-ATB for less than 72 hours according to the records kept by the ward pharmacist were approached for recruitment into this study. Patients determined to be eligible for recruitment by the ID team that were willing to participate were enrolled consecutively until we reached the target number of patients per cluster.

In the control wards, management of ATBs (either converting IV to oral ATBs or OPAT) was left entirely to the judgment of the attending or primary physician. In the intervention wards, after obtaining written informed consent, the assessment was performed prospectively at enrollment (day 1 to day 3 of IV ATBs), day 5, and day 7 of ATB therapy using checklist criteria to define patient suitability for IV to oral ATB switching, OPAT, or discontinuation of ATB, as well as patient discharge. The types of drugs and doses of switched ATBs were also recommended by the ID team. The checklist criteria and the suggestions for treatment or discharge were placed in the patient's chart. In addition to placing the recommendation in the patient's chart, the ID team also had a verbal discussion with the responsible primary physician team regarding the reasons behind the provided recommendation. However, the final decision to discontinue the ATB, switch to oral ATB or OPAT, or discharge as recommended by the ID team was left to the discretion of the treating physician.

The checklist criteria for suitability of ATB switching is shown in [Supplementary Table S1](#). In brief, the infection was improving if there was a resolution of fever, decrease in white blood cell (WBC) counts, ability to absorb and tolerate oral ATB, and the absence of any other major factor preventing discharge. When an attending physician did not switch a patient to oral ATBs despite meeting all checklist criteria for doing so, he was asked to indicate the reason in a free text box on the checklist. Otherwise, there were no additional interventions by or formal consultations with the ID team.

Outcome and Data Collection

The primary outcomes were duration of IV ATBs in the hospital and length of stay (LOS). The duration of IV ATBs in the hospital was defined as the number of days that patients receives

IV ATBs for index infection, irrespective of the number of different drugs, until stopping ATBs or changing to an oral form or OPAT. Antibiotic use was also quantified by days of therapy (DOT) and defined daily dose (DDD). The DOT was measured by the sum of the number of days that a patient received each ATB for index infection, regardless of the dose. The DDD was defined as the assumed average maintenance dose per day for a drug used for its main indication [14]. Secondary outcomes were 30-day mortality, readmission rate within 30 days, recurrent infection rate at 14 days after the end of treatment, ATB cost, and total hospital cost during admission. The rate of reinfection and readmission were retrieved from electronic medical record. Patients discharged before 30 days after enrollment were contacted by telephone to document their outcome at 30 days. Data collected included the following: demographic characteristics of patients; presumed site of infection; presence of sepsis, defined as Quick Sequential Organ Failure (qSOFA) score of 2 or more; microbiological results at enrollment, day 5, and day 7; and information about the ATBs selected, including the type, route of administration, susceptibility of ATB, modification of the ATB regimen occurring from enrollment to the end of therapy, planned duration of treatment, and acceptance rate with a suggestion from the ID team. The total duration of ATB therapy, including both IV and oral courses for index infection, was also obtained.

Statistical Analysis

From 104 patients admitted to 3 medical wards during June 2018 in Siriraj Hospital, the mean duration of IV-ATB in the hospital was 6.6 days, with a standard deviation (SD) of 5.30 days. The sample size was calculated based on the duration of IV-ATBs in the hospital. To detect 2 days shorter duration of IV-ATBs, and assuming an SD of 5.30, 80% power, and a 5% significance level, the total sample size required under individual randomization was 224 patients. Assuming an intracluster correlation of 0.01 and 20% loss to follow-up with 8 clusters, a minimum of 46 patients per cluster was required for a total sample size of 368 patients or 184 patients per arm.

Descriptive statistics were used to characterize the sample data. Qualitative data were presented as frequency and percentage, whereas quantitative data were presented as median and range. Comparison of baseline demographics, clinical characteristics, and outcomes was performed between the control and intervention groups and between those who survived and those who did not survive. The Mann-Whitney *U* test was used to compare quantitative data, and Pearson's χ^2 , Yates' continuity correction, or Fisher's exact test was used to compare qualitative data, as appropriate. Subgroup analysis of sepsis, culture proven from any site or from blood and mortality was performed in a post hoc manner. Marginal logistic regression model using generalized estimating equations was used to examine for association between factors and 30-day mortality. Statistical analysis

was performed using PASW Statistics 18.0 (SPSS, Inc., Chicago, IL) and Stata version 14 (StataCorp, College Station, TX). All statistical tests were 2-sided, with $P < .05$ indicating statistical significance.

RESULTS

Among the 664 patients who were on IV-ATB therapy, 296 patients were excluded. The reasons for exclusion are shown in [Figure 1](#). A total of 368 patients who still required IV-ATB therapy were included, with 184 patients in wards randomized to the intervention arm and 184 patients in wards randomized to control. Baseline characteristics were similar in both groups ([Table 1](#)). Sepsis and septic shock were found in 46 (25%) and 25 cases (13.6%), respectively, and equally in both groups. Bacteremia was observed in 68 patients (18.5%).

Antibiotic Management and Physician Acceptance Rate in the Intervention Ward

After assessment within 72 hours of IV-ATBs, 13 cases (7%) had no indication to continue ATBs, and 13 cases (7%) met the criteria for IVOST or OPAT. By day 7 of IV-ATBs, only half of patients still required ATBs. The overall physician acceptance rate with ID suggestions was 95.1%, 91.2%, and 91.5% on the day of enrollment, on day 5, and on day 7 of IV-ATBs, respectively ([Table 2](#)). However, acceptance of the suggestion from the ID team varied depending on the type of suggestion. Acceptance of a suggestion to stop ATBs or switch to oral ATBs was highest (89.2%) on day 7. The main reasons for not accepting with ATB switching suggestions, which were available in 31 of 36 episodes, included team and hierarchical issues (17 of 31, 54.8%), such as nonagreement by the primary physician and believing that IV ATBs are stronger than oral ATBs (14 of 31, 45.2%). The 3 main causes of delayed hospital discharge were unresolved or additional care required for comorbidities, the need for time to prepare home support, and waiting for forthcoming medical or surgical procedures before discharge. The median turnaround time (TAT) for culture results was 4 days (range, 2–8). [Supplementary Table S2](#) shows the types of pathogens by the site of infection, types of ATBs, and the duration of treatment for index infection.

Primary and Secondary Outcome

Overall, ID team review using predefined checklist criteria for IVOST or OPAT did not reduce the duration of IV-ATB therapy (7 days vs 7 days, $P = .327$) or LOS (9 days vs 10 days, $P = .951$) compared with the control group. The duration of total ATBs, including IV and oral ATBs, for index infection was similar in both groups regardless of measurement method ([Table 3](#)). Post hoc analysis of a subgroup of patients categorized by presence of sepsis, positive culture from any site, or positive culture from blood is shown in [Table 4](#). It is notable that patients without sepsis in the intervention group received a significantly shorter

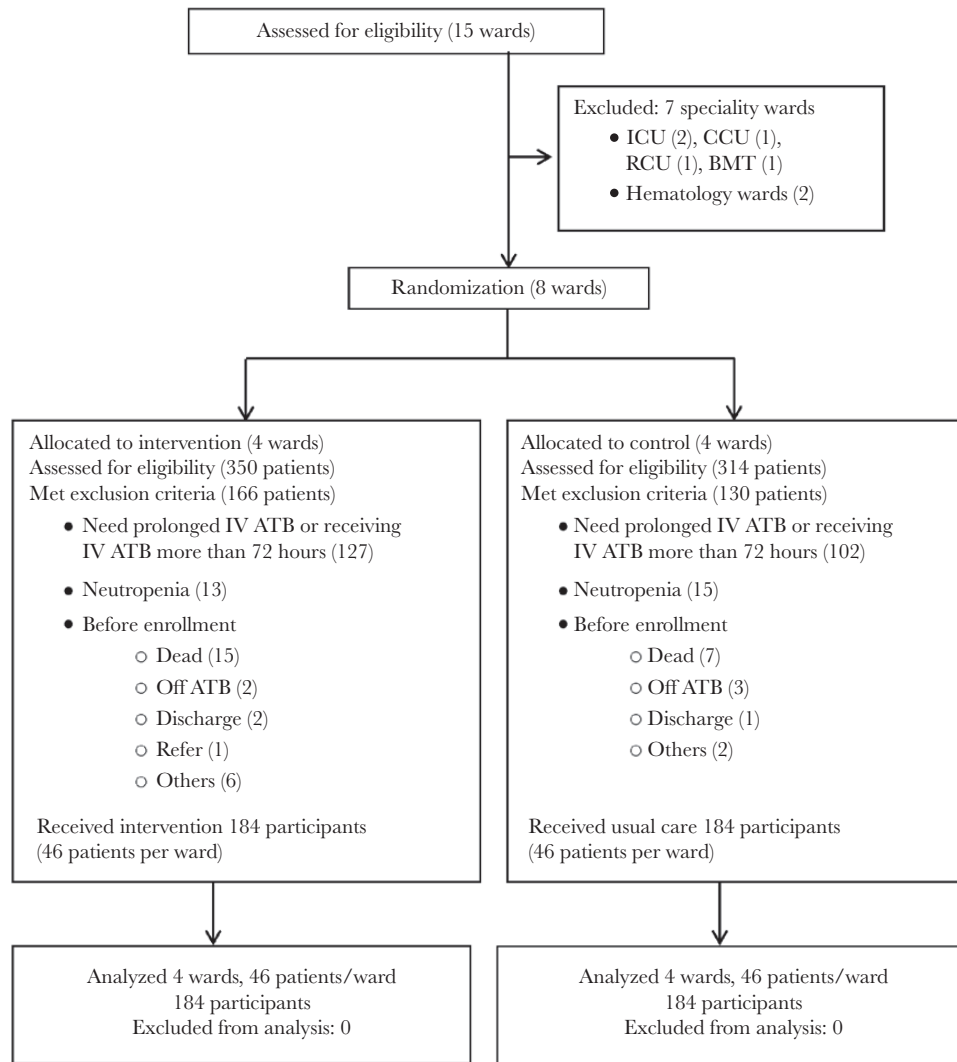


Figure 1. CONSORT flow diagram showing patient enrollment and flow through the study. ATB, antibiotic; BMT, *bone marrow transplant unit*; CCU, cardiac care unit; ICU, intensive care unit; IV, intravenous; RCU, respiratory care unit.

duration of IV ATBs than in the control group when quantified by DOT (7 days vs 8 days, $P = .027$) and DDD (7 days vs 9 days, $P = .017$). Although patients without bacteremia in the intervention group tended to have a shorter duration of IV ATBs (7 vs 9, $P = .273$), shorter DOT (8 days vs 10 days, $P = .456$), and lower DDD (8.7 vs 9.1, $P = .815$) than in the control group, the differences between groups did not achieve statistical significance.

Factors Associated With 30-Day Mortality

The mortality rate of patients in the intervention group was markedly lower than that in the control group (39 cases [21.7%] vs 58 cases [32.2%], $P = .032$). Eleven of 39 patients (28.2%) in the intervention group and 23 of 58 patients (39.6%) in the control group died within 7 days of enrollment. When excluding those who died within 7 days of enrollment, there were no significant differences in the duration of IV-ATB therapy between

groups. There was no difference in the 30-day readmission rate, total cost of ATBs, or total cost of admission (Table 3). Baseline characteristics compared between survivors and nonsurvivors are shown in Supplementary Table S3. Almost all factors from univariate analysis, including age (adjusted odds ratio [aOR], 1.1; 95% confidence interval [CI], 1.0–1.1), hematologic malignancy (aOR, 3.9; 95% CI, 1.6–9.6), solid malignancy (aOR, 2.5; 95% CI, 1.2–4.9), and presence of sepsis (aOR, 2.9; 95% CI, 1.6–5.7), were independently associated with mortality in multivariable analysis. Alternatively, female gender (aOR, 0.7; 95% CI, 0.5–0.9), diabetes mellitus (aOR, 0.5; 95% CI, 0.3–0.9), and intervention (aOR, 0.5; 95% CI, 0.39–0.66) were shown to be protective factors against death.

DISCUSSION

In the present study, ID team review for the suitability of IVOST and early discharge using checklist criteria did not result in a

Table 1. Baseline Demographic and Clinical Characteristics Compared Between the Control and Intervention Groups (N = 368)

Characteristics	Control (n = 184)	Intervention (n = 184)	P Value ^a
Age (years), median (range)	70 (18–101)	68 (18–93)	.383
Male gender, n (%)	92 (50.0%)	92 (50.0%)	1.000
ID attending ^b , n (%)	14 (7.6%)	12 (6.5%)	.839
ID consultation ^c , n (%)	27 (14.7%)	22 (12.0%)	.361
Underlying disease, n (%)	159 (86.4%)	172 (93.5%)	.024
HT	107 (58.2%)	98 (53.3%)	.401
Dyslipidemia	74 (57.8%)	54 (42.2%)	.038
DM	63 (34.2%)	67 (36.4%)	.744
CKD	45 (24.5%)	50 (27.2%)	.634
Solid malignancy	22 (12.0%)	37 (20.2%)	.044
Hematologic malignancy	13 (7.1%)	10 (5.4%)	.667
Autoimmune disease	12 (6.5%)	17 (9.2%)	.568
Steroid use	10 (5.4%)	12 (6.5%)	.826
Chronic Liver disease	10 (5.4%)	14 (7.6%)	.526
HBV or HCV infection	9 (4.9%)	14 (7.6%)	.389
Chronic lung disease	8 (4.3%)	24 (13%)	.006
Old TB	8 (4.3%)	10 (5.4%)	.629
HIV infection	6 (3.3%)	2 (1.1%)	.284
Sepsis, n (%)	46 (25.0%)	46 (25.0%)	1.000
Septic shock, n (%)	25 (13.6%)	25 (13.6%)	1.000
Site of infection, n (%)			
Pneumonia	76 (41.3%)	86 (46.7%)	.345
UTI	31 (16.8%)	35 (19.0%)	.684
IAI	30 (16.3%)	29 (15.8%)	1.000
Primary bacteremia	13 (7.1%)	13 (7.1%)	1.000
SSTI	12 (6.5%)	6 (3.3%)	.227
Others	22 (12%)	15 (8.2%)	.298
Any culture positive, n (%)	63 (34.4%)	72 (39.6%)	.364
Received susceptible ATB, n (%)	53 (84.1%)	59 (81.9%)	.915
Positive blood culture, n (%)	33 (17.9%)	35 (19.0%)	.673

Italic text means P value less than .05.

Abbreviations: ATB, antibiotic; CKD, chronic kidney disease; DM, diabetes mellitus; ID, infectious diseases; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; HT, hypertension; IAI, intra-abdominal infection; SSTI, skin and soft tissue infection; TB, tuberculosis; UTI, urinary tract infection.

^aP < .05 indicates statistical significance.

^bID attending was defined as the attending physician who acted as the primary physician and also is a specialist in infectious diseases.

^cID consultation was defined as the patients who had a formal ID consultation from primary physician.

shorter duration of IV-ATBs in the hospital or LOS despite the fact that one fourth of patients in the intervention wards could discontinue all ATBs within 7 days. We enrolled adult patients who had been receiving IV-ATBs for not more than 72 hours. Therefore, the time of enrollment would be day 1 to day 3 of IV-ATBs, and we assessed the patients' condition on day 5, which is appropriate timing for reassessment of clinical and laboratory data. This result is in contrast to a previous meta-analysis that showed a reduction in the duration of ATB treatment by 1.95 days from 11 days to 9.1 days, and reduced LOS by 1.12 days from 12.9 days to 11.8 days by using a number of stewardship interventions. Those interventions included either single or combined intervention, such as education on ATB use (enabling), review and feedback, or restrictive intervention [8]. However, the studies included in that meta-analysis were published over a 70-year period (1947–2015), and many studies in and recommendations for shorter duration of ATBs have been published over time [15, 16]. In the present study, even in the control group, the median duration of IV-ATBs and LOS was 7 days and 10 days, respectively, which is shorter than the findings in the intervention group reported in the aforementioned meta-analysis. Another previous meta-analysis to determine the effectiveness of AMS interventions in low- and middle-income countries [10, 17] had no strong conclusion regarding the effectiveness of intervention due to the low quality of the study, risk of contamination, and publication bias.

The reasons why ID team review for the suitability of IVOST and early discharge using checklist criteria did not reduce the duration of IV-ATBs might be due to several reasons. The first reason could be the delay in TAT for culture results (4 days), which led to difficulty in making suggestions on oral ATBs or OPAT before getting the results of antimicrobial susceptibility testing. The TAT in a prior study conducted in high-income countries using similar interventions was only 3 days, which is shorter than the TAT in our study [13]. Further studies are needed to determine whether a faster TAT of culture or advanced testing will be able to reduce the duration of IV-ATB therapy in resource-limited settings. In addition, the switching

Table 2. Summary of ID Suggestions on Antibiotic Management and Physician Acceptance in the Intervention Ward

ID Suggestion	Stop, n (%)	Oral ATB, n (%)	OPAT, n (%)	Continue IV, n (%)	Discharge, n (%)
Day of ATB					
D2–3 (n = 184)	13/184 (7.0%)	11/184 (6.0%)	2/184 (1.1%)	158/184 (85.9%)	3/184 (1.6%)
Accept (n = 175)	9/13 (69.2%)	8/11 (72.7%)	0/2 (0%)	158/158 (100.0%)	3/3 (100.0%)
D5 (n = 170)	26/170 (15.3%)	36/170 (21.2%)	6/170 (3.5%)	102/170 (60.0%) ^a	23/170 (13.5%)
Accept (n = 155)	22/26 (84.6%)	28/36 (77.8%)	5/6 (83.3%)	100/102 (98.0%)	20/23 (86.9%)
D7 (n = 141)	37/141 (26.2%)	24/141 (17.0%)	6/141 (4.3%)	74/141 (52.5%) ^a	18/141 (12.8%)
Accept (n = 129)	33/37 (89.2%)	19/24 (79.2%)	3/6 (50.0%)	74/74 (100.0%)	11/18 (61.1%)

Abbreviations: ATB, antibiotic; D, day; ID, infectious disease; IV, intravenous; OPAT, outpatient antibiotic therapy.

^aSuggested escalating antibiotic for 5 cases on D5 (comply 100%) and 4 cases on D7 (comply 100%).

Table 3. Primary and Secondary Study Outcomes Compared Between the Control and Intervention Groups (N = 368)

Outcomes	Control (n = 184)	Intervention (n = 184)	P Value
Primary Outcome			
IV ATB for Index Infection			
Duration of IV ATB, days	7 (2–30)	7 (2–35)	.327
Days of IV ATB, days	8 (2–68)	7.5 (2–62)	.205
DDD of IV ATB	9 (0.8–98)	8 (1.2–51)	.534
Total ATB for Index Infection			
Duration of IV ATB, days	8 (2–34)	8 (2–35)	.784
Days of IV ATB, days	11 (2–68)	11 (2–62)	.292
DDD of IV ATB	11 (0.7–200)	11 (1.2–88.3)	.534
Length of stay, days	9 (1–92)	10 (1–104)	.951
Secondary Outcome			
30-day mortality, n (%)	58 (32.2%)	39 (21.7%)	.032
30-day readmission rate, n (%)	25 (13.8%)	30 (16.5%)	.573
Recurrent infection ^a , n (%)	26 (14.1%)	20 (10.9%)	.344
Same infection site, n (%)	14 (53.8%)	9 (45%)	.463
Total ATB cost, baht	3024 (138–90 886)	2879 (69–51 892)	.621
Total cost of admission, baht	60 995.5 (3416–893 0041 893 004.2)	62 836.0 (5415–670 0751 670 075.7)	.681

Italic text means *P* value less than .05.

Abbreviations: ATB, antibiotic; DDD, defined daily dose; IV, intravenous.

NOTE: Quantitative data are reported as median (minimum, maximum) unless stated otherwise. *P* < .05 indicates statistical significance.

^aRecurrent infection was defined as re-emergence of infection at 14 days after end of treatment.

criteria required not only clinical criteria, but also a decrease in WBC count of less than 12 000 cells/mm³. However, we did not routinely check WBC counts. Finally, although patients may have met the switching criteria, complex conditions of patients admitted in medical department, such as comorbidities, and issues of home support could prevent early discharge.

The rate of physician acceptance with ID team suggestions using the checklist criteria was higher than 90% in this study. This suggests that ID team review and suggestions did not adversely affect communication and trust among the care team, as mentioned in previous studies [8].

It is notable that a significant decrease in the duration of IV ATBs was observed in patients without sepsis in the intervention ward. A duration of ATB therapy of 7–10 days is generally adequate for sepsis patients, and longer courses are necessary only in some patients, such as those with slow clinical response or with undrainable foci [18]. A shorter duration of ATB therapy even in sepsis patients is safe without affecting treatment success [19]. Decisions on the duration of ATB should be considered depending on patient-related factors and the type of infection [20]. However, the subgroup of patients with sepsis was analyzed in a post hoc manner, so the results should be interpreted with caution until confirmed in future study.

From previous systematic review [8], interventions for improving ATB prescription for hospital inpatients were effective without adversely affecting mortality (11% in both arms). In our study, the patients in the intervention wards had 33% lower mortality than those in the control wards (39 cases [21.7%] vs 58 cases [32.2%], *P* = .032, respectively); however, there was

no difference in the readmission rate, the cost of ATBs, or the total cost of care between groups. Recruitment bias is an unlikely explanation for the mortality benefit because the patient characteristics were very similar between groups. Intervention was also shown to be a protective factor against mortality in multivariate analysis. This finding might be explained by early ID consultation, and that ID physicians are more likely to select the type and optimum duration of appropriate ATBs for individual patients. However, we did not find any difference in the proportion of susceptible ATB therapy, duration of IV, or total ATBs for index infection in our study. Several previous studies reported mortality benefit of early ID consultation [21, 22]. Because there are no good explanations for the difference in mortality between groups, the possibility of false relationship may have existed.

The intervention in our study is partially similar to postprescription review and feedback [23], but our intervention focused on evaluation of the patients' condition to determine whether they were reaching a status according to the checklist criteria where they could be safely switched to oral ATB or OPAT or discharged. Although clinical judgment specific to making treatment recommendations was permitted in our study design, uncertainty and variation in clinical judgement in medicine exists in all forms. A technical document, such as a checklist, is developed based on the current literature and best practice. A checklist is a list of action items arranged in a logical and consistent manner; therefore, it allows the evaluator to record the presence or absence of the individual items listed. Therefore, the checklist criteria are not only useful as a

Table 4. Study Outcomes Categorized by Presence of Sepsis, and Culture Results Compared Between the Control and Intervention Groups (N = 368)

Study Outcomes	Control (n = 184)	Intervention (n = 184)	P Value
Duration of IV ATB, Days			
Presence of Sepsis			
Yes (n = 92)	7 (2–30)	8.5 (3–30)	.329
No (n = 276)	7 (2–30)	7 (2–35)	.076
Culture-Proven			
Yes (n = 135)	9 (4–30)	8 (3–32)	.085
No (n = 230)	7 (2–30)	7 (2–35)	.745
Positive Culture			
Blood (n = 68)	10 (4–30)	10 (3–32)	.198
Nonblood (n = 67)	9 (4–30)	7 (3–21)	.273
Days of IV ATB, Days			
Presence of Sepsis			
Yes (n = 92)	9 (2–54)	11 (2–62)	.284
No (n = 276)	8 (2–68)	7 (2–44)	.027
Culture-Proven			
Yes (n = 135)	11 (4–68)	9.5 (3–43)	.135
No (n = 230)	7 (2–59)	7 (2–62)	.460
Positive Culture			
Blood (n = 68)	12 (4–54)	12 (3–42)	.237
Nonblood (n = 67)	10 (4–68)	8 (3–43)	.456
DDD of IV ATB			
Presence of Sepsis			
Yes (n = 92)	8.5 (2–89.75)	11.6 (2.3–51)	.144
No (n = 276)	9 (0.8–98)	7 (1.16–51)	.017
Culture-Proven			
Yes (n = 135)	10.7 (0.8–98)	9.7 (3–47)	.253
No (n = 230)	7.8 (1.5–47)	7.1 (1.2–51)	.266
Positive Culture			
Blood (n = 68)	14 (2.8–89.7)	10 (3–28.5)	.086
Nonblood (n = 67)	9.1 (0.8–98)	8.7 (3–47)	.815

Italic text means P value less than .05.

Abbreviations: ATB, antibiotic; DDD, defined daily dose; IV, intravenous.

NOTE: Quantitative data are reported as median (minimum, maximum) unless stated otherwise. P < .05 indicates statistical significance.

mnemonic device, but also as a tool to achieve standardization of process, and it enhances the objectivity and reproducibility of an assessment.

A key strength of the present study is the study design with cluster RCT, which could minimize contamination of the intervention compared with a traditional RCT design. Our study design may also have increased physician acceptance with ID team suggestions because the intervention was implemented at the ward level. In addition, the patients in our study had a variety of conditions compared with prior studies that focused on a specific infection, pathogen, or population. The limitations of our study include the limited generalizability of our findings to other hospital settings, because our center is a national referral center that is commonly provided care to complicated cases, with multiple comorbidities, and with more risk of acquisition of or infection with multidrug-resistant pathogen. Therefore, the checklist criteria for IVOST or OPAT and discharge criteria may not be applied in different settings or hospitals, such as in the surgical department, pediatric patients, or in rural hospitals.

CONCLUSIONS

In conclusion, ID team review using checklist criteria did not result in a shorter duration of IV-ATB or LOS in overall patients. However, and notably, the duration of IV-ATB therapy in the intervention group was significantly reduced among nonsepsis patients. Further studies are needed to determine whether a faster TAT of culture or advanced testing will be able to reduce the duration of IV-ATB therapy.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases online*. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Acknowledgments

We gratefully acknowledge Dr. Pinyo Rattanaumpawan (Division of Infectious Diseases and Tropical Medicine, Department of Medicine,

Faculty of Medicine Siriraj Hospital, Mahidol University) for sample size calculation and all of the clinical pharmacists working on the general medical wards of the Department of Medicine for assistance with notifying patients who were on intravenous antibiotics.

Disclaimer. The funding source had no role in the study design, data collection, analysis, or interpretation, conclusions drawn, or preparation of the manuscript.

Financial support. This work was funded by a Siriraj Grant for Research Development and Medical Education, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand (Grant Number R016233011; to N. A.).

Potential conflicts of interest. All authors: no reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

References

1. Li HK, Agweyu A, English M, Bejon P. An unsupported preference for intravenous antibiotics. *PLoS Med* **2015**; 12:e1001825.
2. Levy MM, Evans LE, Rhodes A. The surviving sepsis campaign bundle: 2018 update. *Intensive Care Med* **2018**; 44:925–8.
3. Sigfrid L, Perfect C, Rojek A, et al. A systematic review of clinical guidelines on the management of acute, community-acquired CNS infections. *BMC Med* **2019**; 17:170.
4. Barlam TF, Cosgrove SE, Abbo LM, et al. Implementing an antibiotic stewardship program: guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. *Clin Infect Dis* **2016**; 62:e51–77.
5. Desai M, Franklin BD, Holmes AH, et al. A new approach to treatment of resistant gram-positive infections: potential impact of targeted IV to oral switch on length of stay. *BMC Infect Dis* **2006**; 6:94.
6. Dellit TH, Owens RC, McGowan JE Jr, et al; Infectious Diseases Society of America; Society for Healthcare Epidemiology of America. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clin Infect Dis* **2007**; 44:159–77.
7. Waagsbø B, Sundøy A, Quist Paulsen E. Reduction of unnecessary IV antibiotic days using general criteria for antibiotic switch. *Scand J Infect Dis* **2008**; 40:468–73.
8. Davey P, Brown E, Charani E, et al. Interventions to improve antibiotic prescribing practices for hospital inpatients. *Cochrane Database Syst Rev* **2013**; 4:CD003543.
9. Balinsky W, Nesbitt S. Cost-effectiveness of outpatient parenteral antibiotics: a review of the literature. *Am J Med* **1989**; 87:301–5.
10. Dryden M, Saeed K, Townsend R, et al. Antibiotic stewardship and early discharge from hospital: impact of a structured approach to antimicrobial management. *J Antimicrob Chemother* **2012**; 67:2289–96.
11. Beeler PE, Kuster SP, Eschmann E, et al. Earlier switching from intravenous to oral antibiotics owing to electronic reminders. *Int J Antimicrob Agents* **2015**; 46:428–33.
12. Nathwani D, Lawson W, Dryden M, et al. Implementing criteria-based early switch/early discharge programmes: a European perspective. *Clin Microbiol Infect* **2015**; 21:S47–55.
13. Mertz D, Koller M, Haller P, et al. Outcomes of early switching from intravenous to oral antibiotics on medical wards. *J Antimicrob Chemother* **2009**; 64:188–99.
14. Brotherton AL. Metrics of antimicrobial stewardship programs. *Med Clin North Am* **2018**; 102:965–76.
15. Hayashi Y, Paterson DL. Strategies for reduction in duration of antibiotic use in hospitalized patients. *Clin Infect Dis* **2011**; 52:1232–40.
16. Tansarli GS, Andreatos N, Pliakos EE, Mylonakis E. Antibiotic treatment duration for bacteremia due to Enterobacteriaceae: a systematic review and meta-analysis. *Antimicrob Agents Chemother* **2019**; 63:e02495–18.
17. Van Dijck C, Vlieghe E, Cox JA. Antibiotic stewardship interventions in hospitals in low- and middle-income countries: a systematic review. *Bull World Health Organ* **2018**; 96:266–80.
18. Dellinger RP, Schorr CA, Levy MM. A users' guide to the 2016 surviving sepsis guidelines. *Intensive Care Med* **2017**; 43:299–303.
19. Arulkumaran N, Khpal M, Tam K, et al. Effect of antibiotic discontinuation strategies on mortality and infectious complications in critically ill septic patients: a meta-analysis and trial sequential analysis. *Crit Care Med* **2020**; 48:757–64.
20. Vincent JL, Bassetti M, François B, et al. Advances in antibiotic therapy in the critically ill. *Crit Care* **2016**; 20:133.
21. Schmitt S, McQuillen DP, Nahass R, et al. Infectious diseases specialty intervention is associated with decreased mortality and lower healthcare costs. *Clin Infect Dis* **2014**; 58:22–8.
22. Schmitt S, MacIntyre AT, Bleasdale SC, et al. Early infectious diseases specialty intervention is associated with shorter hospital stays and lower readmission rates: a retrospective cohort study. *Clin Infect Dis* **2019**; 68:239–46.
23. Tamma PD, Avdic E, Keenan JF, et al. What is the more effective antibiotic stewardship intervention: preprescription authorization or postprescription review with feedback? *Clin Infect Dis* **2017**; 64:537–43.