

[ ORIGINAL ARTICLE ]

## Antimicrobials in the Hospital Are Unevenly Discontinued on Weekdays

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### Abstract:

**Objective** Amid the global spread of antimicrobial resistance, antimicrobial stewardship should be further promoted in the clinical setting. Our previous study suggested an intra-week disproportion of discontinuation of broad-spectrum antibiotics. We therefore explored the generalization of this prescription trend by investigating the use of all intravenous antibiotics.

**Methods** A retrospective, observational study.

**Patients** Between January 1, 2018, and December 31, 2020, we collected data on the initiation and discontinuation of intravenous antimicrobials on each day of the week and on days after holidays at Okayama University Hospital, Japan. We compared the monthly antimicrobial prescription initiation and discontinuation using the Kruskal-Wallis test and Mann-Whitney U-test with Bonferroni correction as a *post-hoc* procedure.

**Results** Data from 15,293 hospitalized cases were analyzed. The initiation of antimicrobials differed slightly among days of the week, although this trend was clinically insignificant. Compared with the initiations, antimicrobial discontinuations were disproportionately biased among the weekdays, tending to occur on Mondays ( $p < 0.001$ ) about twice as often as on other days. Similarly, antimicrobials were unevenly discontinued on the day after holidays compared to other days ( $p < 0.001$ ), with an approximately 2-fold difference. The use of antimicrobials in the hospital was thus unequally terminated on weekdays.

**Conclusion** To further promote antimicrobial stewardship, clinicians should be aware of the influence of behavioral, environmental, and social factors on antimicrobial prescription, which is seemingly beyond medical indications.

**Key words:** antimicrobial resistance, antimicrobial stewardship, antibiotics, weekdays, weekends

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### Introduction

Antimicrobial resistance (AMR) is a growing public health issue that should be promptly addressed worldwide. Multidisciplinary, multifaceted approaches are essential in reducing AMR, and antimicrobial stewardship (AST), advocating the rational use of antibiotics, is a particularly vital strategy in combatting the rising threat of AMR. Subsequent to the endorsement of the AMR Global Action Plan in May 2015 by the World Health Organization (1), the Japanese government launched the National Action Plan on AMR in April 2016 and has promoted the AST program in domestic

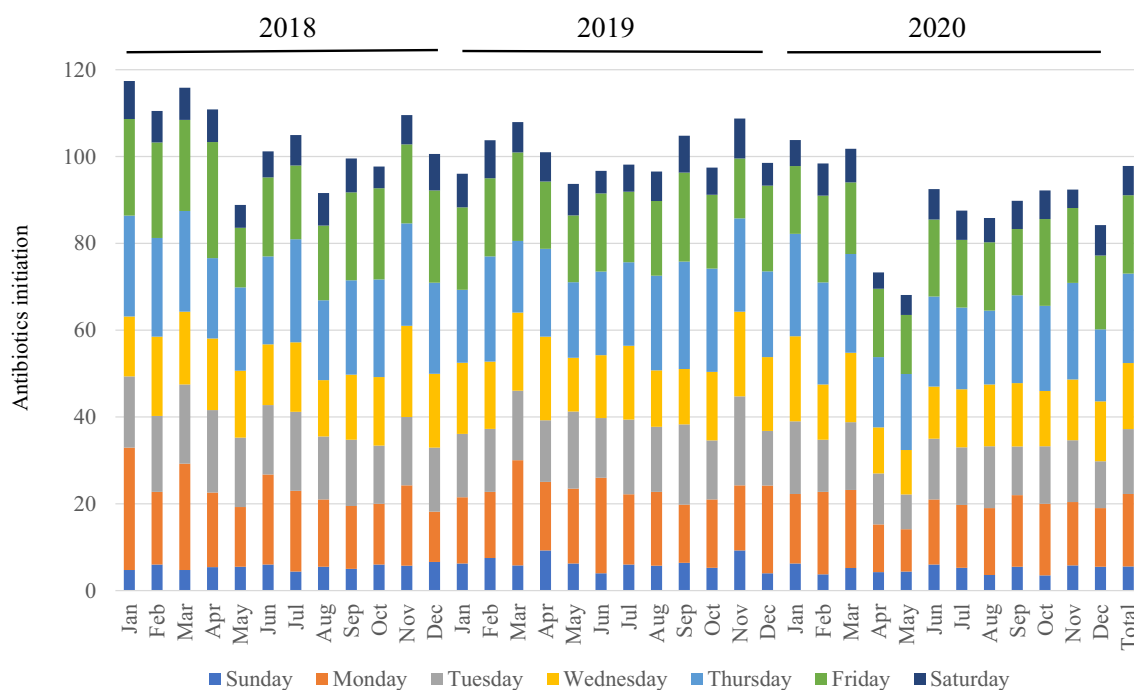
medical institutes (2).

Optimizing the length of antimicrobial therapy is of great importance for AST. Recently, the non-inferiority and safety of short-course treatment for various bacterial diseases have been reported. For example, a single-facility retrospective observational study demonstrated that short-course (7-11 days) antimicrobial therapy was as effective as a prolonged course (12-21 days) for uncomplicated *Pseudomonas aeruginosa* blood stream infection (3). Two randomized controlled studies further suggested the non-inferiority of one-week antimicrobial treatment compared to a two-week course in patients suffering from Gram-negative bacteremia (4). In this manner, the feasibility of short antibiotic treatment has been

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**Figure 1.** The numbers of antimicrobial prescriptions initiated monthly by day of the week through the study period.

corroborated.

However, social and environmental factors, such as staffing shortages and limited medical resources, are known to influence prescribing antibiotics beyond the medical indication (5, 6). Our previous studies have also demonstrated the intra-week disproportion of antibiotic termination; however, those studies included only patients receiving broad-spectrum antimicrobials (7, 8). To clarify the generalizability for this prescription tendency, we performed another study that comprehensively covered all antimicrobial agents in a hospital, regardless of their spectrum.

## Materials and Methods

This was a single-facility retrospective observational study conducted at the Okayama University Hospital, Japan, referring to our previous studies (7, 8). The study period was between January 1, 2018, and December 31, 2020 (3 years), during which we collected administrative data on the in-hospital use of all the intravenous antimicrobials (both antibiotics and antifungals). We included only cases treated for more than four consecutive days, excluding those who received antimicrobials for three days or fewer. The study protocol adhered to the tenets of the Declaration of Helsinki and the Ethical Guidelines for Medical and Health Research Involving Human Subjects, which was approved by the institutional review boards of the hospital (No. 2001-013). The need for informed consent from each patient was waived because the data were fully anonymized.

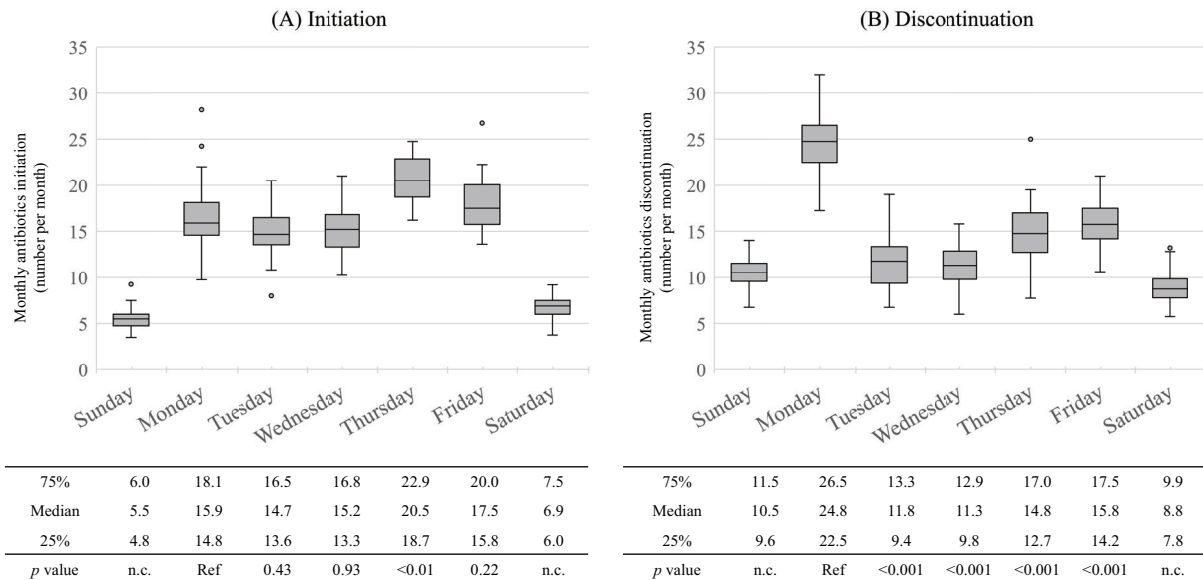
We counted the initiation and discontinuation of antimicrobial administration on (i) each day of the week and (ii) days after holidays and calculated the number of antimicro-

bials administered monthly. Holidays in this study were defined as Japanese national days off (Supplementary material 1). In the hospital, antimicrobials were those ordered by attending physicians and residents but not by nurse practitioners or other healthcare professionals. During weekdays (Monday to Friday), an infection control team consisting of an infectious disease physician and pharmacists conducts prospective audits and feedback their discussion as an AST activity, but not during weekends (Saturday and Sunday) or on holidays.

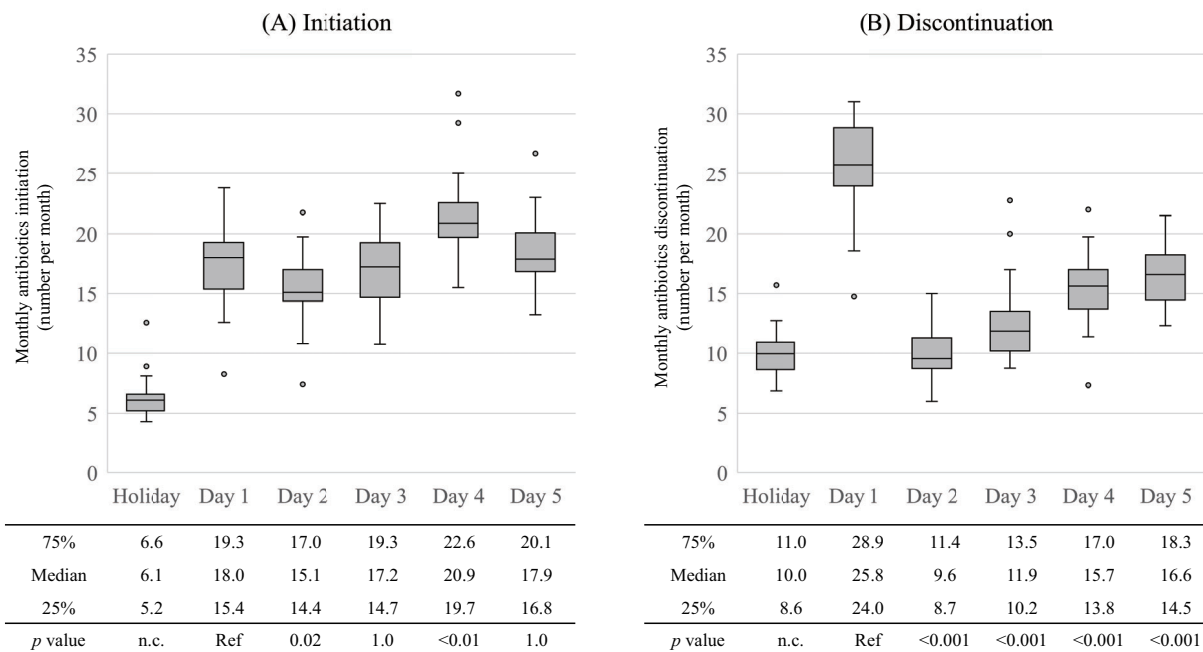
The numbers of antimicrobials initiated or discontinued monthly were summarized as the median and interquartile range (IQR) and compared among days of the week and days after holidays. In particular, we focused on the difference in the numbers between Monday and other days of the week as well as on the day immediately following a holiday and later days. We applied the Kruskal-Wallis test and Mann-Whitney U-test with Bonferroni correction as a *post-hoc* procedure. Analyses were performed using the EZR software program (version 3.5.2), which is a graphical user interface for R (the R Foundation for the Statistical Computing, Vienna, Austria) (9). Statistical significance was set at a *p* value <0.05.

## Results

In total, data from 15,293 cases were enrolled. During the study period, antibiotics prescriptions decreased in 2020 (especially April and May) in comparison with the preceding two years (Fig. 1). This was presumably due to the influence of fewer hospitalizations amid the coronavirus disease 2019 pandemic. The number of each antibiotic prescribed



**Figure 2.** The numbers of antimicrobials (A) initiated and (B) discontinued monthly on each day of the week. Data are shown as the median and box (interquartile range) and whisker (minimum and maximum within 1.5 times the interquartile range) plots. The Kruskal-Wallis test and Mann-Whitney U-test with Bonferroni correction were performed to evaluate the differences between Monday and other weekdays. n.c.: not compared



**Figure 3.** The numbers of antimicrobials (A) initiated and (B) discontinued monthly after holidays. Data are shown as median and box (interquartile range) and whisker (minimum and maximum within 1.5 times the interquartile range) plots. The Kruskal-Wallis test and Mann-Whitney U-test with Bonferroni correction were performed to evaluate the differences between Day 1 and other days. n.c.: not compared

during the study period is shown in Supplementary material 2.

The numbers of antimicrobials initiated and discontinued monthly on each day of the week are shown in Fig. 2. Over a week-long period, there were fewer antimicrobial initiations on weekends than weekdays. The initiating patterns on

weekdays appeared similar throughout the week, except for a nominal increase on Thursday compared with other days. However, conversely, antimicrobials were disproportionately discontinued on Monday compared to other weekdays ( $p < 0.001$ ), showing an approximately 2-fold difference (median number of antibiotics discontinued monthly: 24.8 on Mon-

day, 11.8 on Tuesday, 11.3 on Wednesday, 14.8 on Thursdays, and 15.8 on Friday).

Similarly, the monthly numbers for the initiation and discontinuation of antimicrobials after holidays are shown in Fig. 3 Compared to day 1 (immediately after a holiday), the numbers of antimicrobial initiation were lower on day 2 and higher on day 4, although the difference seemed clinically insignificant. With regard to discontinuation, the antimicrobials were also unevenly discontinued on day 1 compared to other days ( $p < 0.001$ ), showing an approximately 2-fold difference (median number of antibiotics discontinued monthly: 25.8 on Day 1, 9.6 on Day 2, 11.9 on Day 3, 15.7 on Day 4, and 16.6 on Day 5).

## Discussion

The present study revealed disproportionate discontinuation of all intravenous antimicrobials during weekdays at our hospital. Our previous studies showed that the administration of broad-spectrum antimicrobials was discontinued on Tuesday or day 2 after holidays (7, 8). As has been discussed in previous reports, infectious diseases occur on all days of the week; therefore, the initiation and discontinuation of their treatment should not be biased toward any particular day. However, our results again revealed the presence of beyond-the-medical-indication factors regarding the use of antimicrobials in hospitals.

In contrast to preceding data, the present study revealed that antimicrobials were frequently discontinued on Monday or day 1 after holidays. This study targeted all intravenous antimicrobials, not just broad-spectrum drugs. Patients receiving broad-spectrum antimicrobials tend to be in a critically ill or immunocompromised state, so the decision for antimicrobial discontinuation likely requires substantial discussion and permission from a senior doctor when young clinicians on duty are in charge, leading to a delay in drug discontinuation. AST may help promote the optimization of antimicrobial use (10, 11); however, our data suggested these efforts had relatively little impact on controlling the antimicrobial usage in our hospital. Notably, antibiotics were frequently started on Thursday or day 4 during the study period. Although this bias might be associated with the increased discontinuation of antibiotics on Monday or day 1, we could find no solid rationale to support this notion.

Limitations of the present study include the single-facility setting, absence of stratification by infectious diseases, and lack of patient outcomes. However, our attempt to comprehensively include all antimicrobial agents used in a tertiary-

care hospital successfully made it clear that the bias in terminating antimicrobial treatment likely applies across the board.

Collectively, to fight against the global AMR problem, the use of antimicrobials should be appropriately controlled. The influence of the day of the week exists to some extent in clinical settings around the world. Thus, our finding of disproportionate discontinuation of intravenous antimicrobials during weekdays may also be found in other healthcare settings. We hope that our data will help raise awareness concerning the ongoing biased use of antibiotics and will accelerate AST activities in hospitals worldwide.

**The authors state that they have no Conflict of Interest (COI).**

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