

# Effect on Duration of Antimicrobial Therapy of Removing and Re-establishing an Automatic Stop Date Policy

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## ABSTRACT

**Background and Objective:** In July 2000, the Pharmaceuticals and Therapeutics Committee at a 452-bed teaching hospital recommended discontinuation of its 7-day automatic stop order (ASO) policy, which applied to all drugs used in the hospital. Retrospective audits of duration of antimicrobial therapy were performed just before discontinuation of the 7-day ASO (ASO-7d) and 1 year after the ASO was removed (ASO-none). Because the duration of antimicrobial therapy increased over this 1-year period, a 5-day ASO was instituted (ASO-5d). Six months later, another audit was performed. The purpose of this study was to determine the influence of discontinuing and subsequently re-establishing an ASO on the duration of antimicrobial therapy.

**Methods:** Antimicrobial orders were categorized on the basis of duration of therapy: 1 to 8 days (standard), 9 to 20 days (intermediate), and more than 20 days (long). The percentages of orders continuing on each consecutive day after initiation of therapy in the 3 periods (ASO-7d, ASO-none, and ASO-5d) were compared. Statistical analysis consisted of the Cochran–Armitage trend test for ordinal data, with a Bonferroni correction for multiple comparisons.

**Results:** The percentage of orders categorized as standard therapy was 88.2% in the ASO-7d audit period, 82.8% in the ASO-none audit period, and 84.4% in the ASO-5d audit period. The percentage of orders categorized as intermediate in duration was 10.9% in the ASO-7d audit period, 15.0% in the ASO-none audit period, and 14.2% in the ASO-5d audit period. The percentage of orders categorized as long duration was 0.9% in the ASO-7d audit period, 2.2% in the ASO-none audit period, and 1.4% in the ASO-5d audit period. The trends for each of the 3 durations of therapy (1–8 days, 9–20 days, and more than 20 days) were significantly different from one another.

**Conclusions:** The percentage of orders that were continued for 8 days or less (standard therapy) was greater during the ASO-7d audit period than in the ASO-none and ASO-5d audit period.

## RÉSUMÉ

**Historique :** En juillet 2000, le Comité de pharmacologie d'un hôpital d'enseignement de 452 lits a recommandé l'abandon de sa politique d'ordonnance avec durée de validité (ODV) de 7 jours, qui s'appliquait à tous les médicaments utilisés dans cet hôpital. Des vérifications rétrospectives de la durée des traitements antimicrobiens ont été réalisées juste avant l'abandon de l'ODV de 7 jours (ODV-7j) et une année après l'abandon effectif de l'ODV (ODV-nil). Parce que la durée des traitements antimicrobiens s'est allongée durant cette période d'une année, une ODV de 5 jours a été mise en oeuvre (ODV-5j). Six mois plus tard, on a effectué une autre vérification. Le but de cette étude était de déterminer l'influence de l'abandon puis de la réintroduction subséquente d'une ODV sur la durée des traitements antimicrobiens.

**Méthodes :** Les ordonnances d'antimicrobiens ont été divisées en trois groupes, sur la base de la durée de la thérapie : de 1 à 8 jours (standard), de 9 à 20 jours (intermédiaire), et plus de 20 jours (prolongée). On a comparé le pourcentage d'ordonnances toujours en vigueur à chaque journée consécutive durant les trois périodes (ODV-7j, ODV-nil, ODV-5j). Le test des tendances de Cochran-Armitage pour les données ordinales, avec une correction de Bonferroni pour les comparaisons multiples, a été utilisé comme analyse statistique.

**Résultats :** Le taux d'ordonnances tombant dans la catégorie standard était de 88,2 % durant la période ODV-7j, de 82,8 % durant la période ODV-nil, et de 84,4 % durant la période ODV-5j. Celui tombant dans la catégorie intermédiaire était de 10,9 % durant la période ODV-7j, de 15,0 % durant la période ODV-nil, et de 14,2 % durant la période ODV-5j. Celui tombant dans la catégorie prolongée était de 0,9 % durant la période ODV-7j, de 2,2 % durant la période ODV-nil, et de 1,4 % durant la période ODV-5j. Les tendances pour chacune des trois catégories de durée de thérapie (1–8 jours, 9–20 jours, et plus de 20 jours) étaient significativement différentes d'une à l'autre.

**Conclusions :** Le taux d'ordonnances en vigueur durant huit jours ou moins (thérapie standard) était supérieur dans le groupe



Conversely, a smaller percentage of orders in the ASO-7d audit period were of intermediate or long duration. This suggests that a 7-day ASO is the most beneficial in terms of controlling duration of antimicrobial therapy.

**Key words:** automatic stop order, antimicrobial, stop date

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## BACKGROUND

Automatic stop order (ASO) policies for antimicrobial agents and other medications are in effect in many institutions. ASOs are intended to ensure that both physicians and pharmacists regularly review drug therapy that is prescribed without a specified duration. The advantages of ASOs include promoting safe and rational drug use, preventing inappropriate duration of therapy, and reducing drug costs.<sup>1</sup> These advantages are particularly important for antimicrobials, the misuse of which can be associated with increased resistance.<sup>2,3</sup> However, enforcement and monitoring of ASOs can be time consuming.<sup>1,4</sup> In addition, inadvertent discontinuation of therapy can occur if a drug order reaches its stop date and is not renewed even when it is appropriate to do so; in this situation, the patient is deprived of necessary treatment.<sup>1</sup>

In July 2000, the Pharmaceuticals and Therapeutics Committee at the authors' 452-bed teaching hospital removed the ASO policy that applied to all drugs used in the institution. Until that time, the ASO had taken effect at 7 days for antimicrobials (ASO-7d) and at various durations of therapy for other drug classes. The ASOs for all medications (including antimicrobials) were discontinued because some medications were not being reordered in a timely fashion by housestaff, which resulted in a greater workload for both nursing staff and pharmacists and possible harm to patients as a result of missing doses for medications that had reached their stop date. At the same time, the Antimicrobial Use Working Group expressed concern that, without an ASO, the duration of antimicrobial therapy might become inappropriately lengthy in some patients.

An initial audit was performed just before removal of the ASO-7d to establish a baseline; the audit procedure was repeated 1 year after the ASO was removed

ODV-7j que dans les groupes ODV-nil et ODV-5j. Inversement, le taux d'ordonnances en vigueur pour une durée intermédiaire et prolongée était plus faible durant la période ODV-7j. Ces données portent à croire qu'une validité d'ordonnance de 7 jours est la plus bénéfique pour contrôler la durée du traitement antimicrobien.

**Mots clés :** durée de validité, antimicrobien, date d'arrêt

(ASO-none), to determine any effect on the duration of antimicrobial therapy. During this 1-year period, the mean duration of therapy increased; consequently, in December 2001, the ASO was reimplemented, but with a 5-day duration (ASO-5d). Five days was assumed to be a reasonable point at which to reassess the need for continuation of therapy, change from empiric therapy, or step down to oral therapy (for drugs being administered intravenously). The purpose of this study was to determine the influence of discontinuing and subsequently re-establishing an ASO on the duration of antimicrobial therapy.

## METHODS

A drug use evaluation (DUE) query was performed through the General Electric Medical Systems Information Technologies Centricity Pharmacy computer system. The DUE query extracts all patient-specific orders within the system for particular time periods according to parameters set by the user. For the purpose of this study, all antimicrobial agents, with the exception of antiviral and topical antifungal agents for human immunodeficiency virus infection, were chosen. The data identified by the initial query were then subjected to further selection on the basis of certain variables using Actuate software (Actuate Corporation, San Francisco, California) a program that filters Centricity Pharmacy data into a report that can be read and distributed. The selected variables were patient name, drug, dose, frequency, attending physician service, and start and stop dates. The data were then downloaded into Excel (Microsoft, 1997 version) for further manipulation. For the ASO-7d audit, 4 months preceding the July 2000 removal of the ASO policy were chosen (February, March, April, and June 2000) to determine the baseline duration of antimicrobial



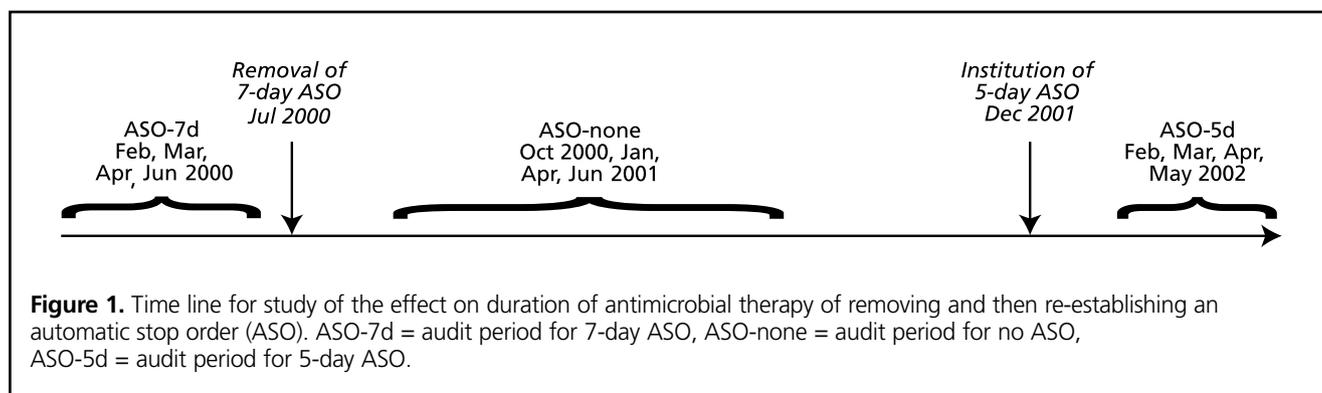
treatment. For the ASO-none audit, 4 months evenly spaced throughout the year after discontinuation of the ASO policy were chosen: October 2000 and January, April, and June 2001. For the ASO-5d audit, 4 consecutive months after establishment of the 5-day ASO were chosen: February, March, April, and May 2002. The months chosen for the first audit did not exactly parallel those for the last audit, because the computer-generated data for May 2000 were incomplete (Actuate files had been “lost” from the system and were irretrievable); data for June 2000 were used instead. The use of antimicrobials does not differ between May and June at this institution, primarily because few respiratory tract and other infections are identified in the spring and summer months. The timeline for the study is presented in Figure 1.

All patient-specific orders written during the specified time periods and dispensed by the pharmacy department were identified. Only orders for the treatment of infection were included; orders for surgical prophylaxis were excluded. In addition, the following orders for other types of prophylaxis were excluded: all orders for IV antimicrobials for adults not generated through the IV room that were for less than 48 h duration and that were written by a surgical service; all orders for cotrimoxazole or trimethoprim written by the urology service (when accompanied by IV gentamicin), since these medications are commonly used within this institution for postoperative prophylaxis; all orders for nystatin oral suspension of 100 000 IU 4 times daily administered to adult patients (considered a prophylactic dose); all orders for nitrofurantoin given once daily; and orders for pediatric chemotherapy patients receiving cotrimoxazole 3 times per week. As well, any antimicrobials dispensed by the Community Care IV service (a service providing antimicrobials to discharged patients that was operated by the pharmacy department) were excluded, as this service was discontinued during

the course of the study. Certain areas of the hospital (the Intensive Care Unit and the Neonatal Intensive Care Unit) have historically retained antimicrobials as ward stock items, and orders from these units were therefore excluded from the analysis.

Because of the overwhelming amount of data, the medical records were not reviewed; as such, this study was strictly an audit of drug therapy orders, and each order was assumed to represent a course of therapy. Step-down to oral therapy and switching from one antimicrobial to another because of sensitivity were all considered as separate orders. Combined IV and oral therapy refers to total duration of antimicrobial therapy regardless of route of administration. It was not possible to determine if breaks in therapy were due to an antimicrobial not being ordered in a timely fashion after the ASO was reached or after an operative procedure. Consequently, for both the ASO-7d and the ASO-5d audits, orders for the same patient for the same drug were considered consecutive and were grouped together if there was 2 days or less between them. For ASO-none, this cutoff was shortened to 24 h, since this type of delay in therapy was expected to be of shorter duration when there was no stop date.

All orders processed in the time periods described above were downloaded into an Excel spreadsheet. Data were analyzed by determining the percentage of orders for antimicrobial therapy that were continued for 3 categories of duration: 1 to 8 days (standard), 9 to 20 days (intermediate), and greater than 20 days (long). These percentages were calculated for the pooled 4-month audit periods for combined (IV and oral) routes of administration and are presented in both tabular and graphic format. Statistical analysis was performed using the Cochran–Armitage trend test for ordinal data. This test compares 2 groups with values on an ordinal scale. Because multiple comparisons were made, a Bonferroni correction was used.



## RESULTS

Table 1 shows the percentage of orders for antimicrobial therapy that were continued in the 3 ASO periods for each duration category (1 to 8 days, 9 to 20 days, and greater than 20 days). A significantly higher percentage of orders were continued beyond 8 days in the ASO-none period than the ASO-7d period. Similarly, a significantly higher percentage of orders were continued beyond 8 days in the ASO-5d period than the ASO-7d period. Although the difference between the ASO-5d and the ASO-none periods in terms of percentage of orders continuing beyond 8 days was statistically significant, the relatively small absolute difference may not be clinically significant.

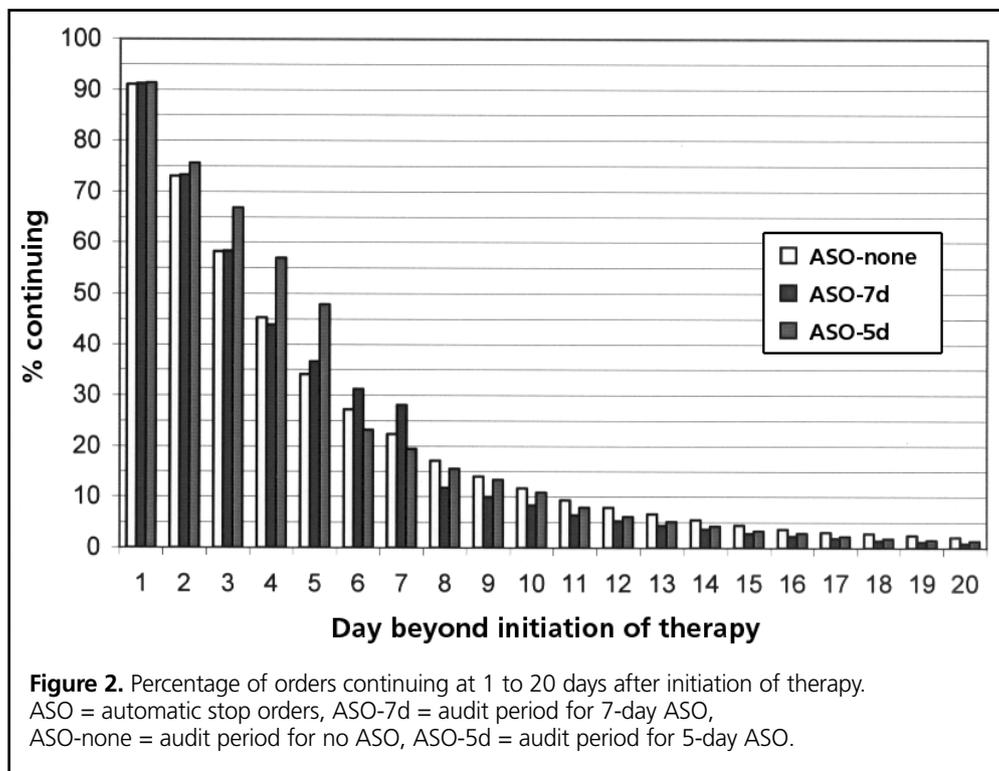
The percentage of orders that continued each day after initiation of therapy is presented in Figure 2. The

percentage of orders that were continued was similar for the three audit periods on both day 1 and day 2. Starting on day 3 and up to day 5, the percentage of orders that were continued during the ASO-5d audit period was higher than that in either the ASO-7d or ASO-none audit period. After 5 days, the percentage of orders that were continued in the ASO-5d audit period declined substantially (by nearly 25%) but remained sizable. The same phenomenon was observed for the ASO-7d audit period but was not as dramatic. After 7 days, the percentage of orders that were continued during the ASO-7d period declined by 16.5% and, after this point, was much smaller than for either the ASO-5d or ASO-none period. For the ASO-none period, there was a gradual decrease in the percentage of orders that were continued with each subsequent day.

**Table 1. Duration of Antibiotic Therapy before and after Discontinuation of a 7-Day Automatic Stop Order (ASO) and after Implementation of a 5-Day ASO\***

Duration of Antibiotic Therapy, days	Audit Period; No. (and %) of Therapeutic Courses					
	ASO-7d (n = 5046)		ASO-none (n = 5044)		ASO-5d (n = 5378)	
1-8	4453	(88.2)	4177	(82.8)	4541	(84.4)
9-20	548	(10.9)	758	(15.0)	762	(14.2)
>20	45	(0.9)	109	(2.2)	75	(1.4)

\*In all pairwise comparisons the difference was statistically significant. For ASO-7d v. ASO-none,  $p < 0.001$ ; for ASO-none v. ASO-5d,  $p = 0.01$ ; for ASO-7d v. ASO-5d,  $p < 0.001$ .



## DISCUSSION

Misuse of antimicrobial therapy may be characterized as use of inappropriate agents, inadequate dosage regimens, or inappropriate duration of treatment. Antibiotic use exerts selective pressure on bacterial populations, which can promote the emergence of antimicrobial resistance<sup>5</sup>; antibiotic misuse in particular may exacerbate this problem. Inappropriate duration of antimicrobial therapy has been cited by several authors as a factor contributing to resistance.<sup>2,3,6</sup> Historically, programs that restrict antimicrobial prescribing have been implemented to control costs.<sup>6</sup> One of the potential benefits of such programs is a decrease in the probability of emergence of resistant organisms; as a result of increasing concerns regarding antimicrobial resistance, this has become a more prominent objective of antibiotic control programs. Recent guidelines from the Society for Healthcare Epidemiology of America and the Infectious Diseases Society of America for the prevention of antimicrobial resistance advocate the implementation of infection control policies to restrict the spread of resistant organisms and antibiotic control policies that restrict prescribing.<sup>6</sup> One control mechanism suggested in the guidelines is the use of automatic stop orders.

There is a paucity of literature dealing with ASOs. Only one study has been published (and then only in abstract form) dealing with the effect of removing a stop date on the duration of antimicrobial therapy. Tierney and Brunet<sup>7</sup> described their experiences regarding the duration of antimicrobial therapy after removal of an ASO. A total of 181 courses of antimicrobial therapy before and 200 courses after ASO removal were included in the analysis. The mean treatment duration (and standard deviation [SD]) for combined therapy was 4.68 (SD 4.95) days before and 4.03 (SD 4.43) days after ( $p = 0.18$ ). The authors concluded that in the presence of effective clinical pharmacy services, ASOs do not necessarily control the length of antimicrobial therapy. However, not all antimicrobials administered in the hospital were included in the analysis, and the number of courses investigated was much smaller than in the present study.

Cleary and Nolan<sup>1</sup> described experiences in their hospital with an ASO policy. In one year, 6 failures of antimicrobial therapy in 5 patients were attributed to antimicrobials not being reordered once the ASO had been reached. These patients missed between 2 and 7 days of therapy. Five of the failures were attributed to the ASO notice not being affixed to the physician's orders. Missed antimicrobial doses possibly contributed to 4 patients experiencing prolonged hospital stay and

to one death. There have been no such documented incidents at the authors' institution, but it is accepted that many medication incidents go unrecorded. The situation described by Cleary and Nolan<sup>1</sup> could occur in any institution and is an inherent disadvantage of ASOs.

When the 7-day ASO was removed in 2000, there was a concern that antimicrobial therapy would become inappropriately long, a possibility that was confirmed when the audit was repeated in 2001. This difference in treatment duration was statistically significant. As a result, a 5-day ASO was instituted in December 2001. The results of the final audit (for the ASO-5d period) were surprising: the percentage of orders that were continued for prolonged periods was higher than during the ASO-7d audit period but similar to that observed during the ASO-none audit period. As well, the number of patients remaining on treatment after day 5 dropped precipitously, which was also observed with the 7-day ASO but to a lesser degree. It is probable that with such a short ASO period, decisions to either discontinue or step down to oral therapy were not being made before the ASO was reached. This situation is likely due to prescribers not having enough confidence to make a change so early in therapy (clinicians were receiving reminder notices 48 h [before a weekend] or 24 h [on weekdays] before the ASO point was reached). As a result, patient care teams may have ordered a longer course of therapy to avoid being reminded after just a few days of therapy. For the ASO-7d period, ASO notices were sent 2 days later than was the case during the ASO-5d period. The trend for smaller percentages of orders to be continued during the ASO-7d period than during either the ASO-5d or the ASO-none period may indicate that patient care teams were more prepared to make a decision at that time.

The time required to police an ASO is an important issue. The patient-pharmacist ratio at the authors' institution is higher than that in many teaching hospitals, notwithstanding the fact that 3 pharmacist positions were vacant at the time of the audits. The increased duration of therapy during the 5-day ASO period may be partly attributed to the pharmacist shortage: less clinical coverage may have meant that fewer orders for antimicrobial agents underwent timely assessment. Tierney and Brunet<sup>7</sup> questioned the need for an ASO in the presence of clinical pharmacy services, and their point may be well taken. However, in this era of a pharmacist shortage, it may be difficult to maintain sufficient pharmacist human resources to obviate the need for an ASO.



This study had several limitations, including those inherent to a review of data. No medical records were reviewed, which necessitated many assumptions, as outlined previously. The acuity of the patients treated was unknown but might have influenced the longer duration of therapy observed during the ASO-5d and ASO-none audit periods.

## CONCLUSIONS

The elimination of a 7-day ASO had an adverse impact on antimicrobial therapy and led to a significant increase in the percentage of orders that were continued beyond 8 days. Once the 5-day ASO was implemented, the increase in the percentage of orders that continued beyond 8 days was maintained, contrary to what had been anticipated. This difference is attributed partially to lack of clinical confidence to make a change early in treatment and partially to limited availability of clinical services.

Future research should address the issue of whether the degree of increase in duration of therapy observed in this study can be correlated with increased rates of antimicrobial resistance and should identify other factors that might contribute to prolongation of duration of antimicrobial treatment during each of the audit periods.

To strike a balance among the need for patient care teams to reassess treatment, considerations of patient safety, and limited resources, the recommendation brought to the Pharmaceuticals and Therapeutics Committee, on the basis of these results, was to remove the "hard stop" of 5 days. At the time of writing, no ASO for antimicrobials was in place. If a decision is made to reinstitute an ASO, it will likely be for a 7-day period.

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