slivengood@campbell.edu

Development and Assessment of a Process to Describe the Timing of Antibiotic Changes in Adult Inpatients

CAMPBELL UNIVERSITY | College of Pharmacy & Health Sciences

aset Duke Antimicrobial Stewardship and Evaluation Team

Spencer Livengood[1], Richard Drew[1,2,3], Rebekah Moehring[2,3] Dustin Wilson[1,4], Justin Spivey[4]

1- Campbell University College Of Pharmacy & Health Sciences, Buies Creek, NC, USA;
2- Duke Antimicrobial Stewardship Outreach Network, Durham, NC, USA; 3- Division Of Infectious Diseases,
Duke University Medical Center, Durham, NC, USA; 4- Department of Pharmacy, Duke University Hospital, Durham, NC, USA

Duke Center for Antimicrobial Stewardship and Infection Prevention

Abstract

Background/Purpose: Hospital antimicrobial stewardship programs (ASP) perform prospective audit and feedback to optimize use of antimicrobials; however, workflow inefficiency continues to be a distinct challenge. We developed a method to describe the volume and timing of antimicrobial changes to inform decisions on optimal timing of ASP review and intervention.

Methods: This retrospective study was performed at Duke University Hospital using anonymized antibiotic administration records from the DASON central database. Eligible antibiotic courses were administered to inpatients > 18 years of age and had received > 2 antibiotics administrations for > 24 hours of treatment. A 2-month exploratory cohort (September to October 2017) was used to develop an antibiotic spectrum ranking and decision algorithm which was applied to a 1-year cohort (November 2017 to October 2018) for analysis of total change in antibiotic orders by day of the week. For each interval, the sum of antibiotic ranks was calculated and applied using specified definitions to determine the type of change occurring. The primary outcome was the number of total antibiotic changes that occurred on each day of the week. Secondary outcomes included the number and type (initiations, discontinuations, de-escalations, and escalations) of change. Descriptive statistics were used to describe the outcomes by day of the week.

Results: The ranking and decision algorithm were applied to 16,993 unique antibiotic courses. Total changes occurred most on Wednesday (14,971, 16.2% [95% CI 15.7-17.1%]) and Friday (14,349, 15.6% [95% CI 15.0-16.2%]). Compared to intervals on weekdays (0.407 mean changes per patients on antibiotics [95% CI 0.401-0.413]), weekends had a lower number of changes (0.363 mean changes per patients on antibiotics [95% CI 0.349-0.377]). Initiations occurred most frequently on Tuesday (3,078, 18.1% [95% CI 16.3-19.9%]), and discontinuations on Wednesday (3,179, 18.7% [95% CI 17.4-20.5%]).

Conclusion/Clinical Relevance: We developed and applied a method to characterize antimicrobial changes. In our institution, the reductions in the number of changes observed on weekends provide an opportunity for ASP involvement to be incorporated and help facilitate appropriate antimicrobial changes.

Background

- A growing concern in healthcare is the overuse and misuse of antibiotics, leading to consequences including antibiotic resistance, treatment failure, and increases in antibiotic-related adverse events and costs.[1]
- One of the keys to optimizing the use of antibiotics is through assisting clinicians at the crucial moments of antibiotic-decision making. These moments include initial determination if antibiotic therapy is warranted, evaluation of appropriateness, need for discontinuation or de-escalation, and optimal duration of therapy.[2]
- Although multidisciplinary antimicrobial stewardship programs (ASP) perform prospective audit and feedback as a proven method to optimize use of antimicrobials, there is no standard method to determine workflow.

Objectives

- **Primary**: To describe the total change in antibiotic orders between pre-selected time intervals in adult inpatients
- **Secondary**: To describe the number of initiations, de-escalations, escalations, and discontinuations for pre-selected time intervals and unit-specific totals

Methods

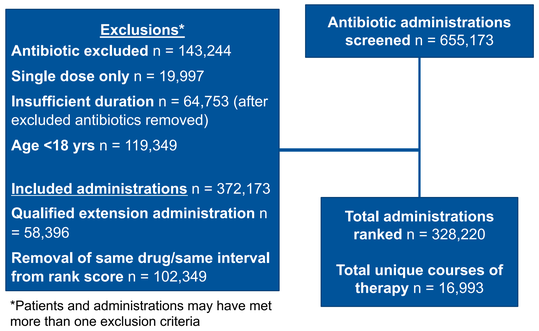
- **Design**: Retrospective, single center, cohort study
- **Population:**
  - Inclusion
    - Inpatient at Duke University Hospital
    - ≥ 18 years of age
    - Administered > 1 antibiotic for > 24 hours between November 1, 2017 and October 31, 2018 (September 1, 2017 to October 31, 2017 for exploratory cohort)
    - Antibiotic indicated for empiric or directed treatment of a bacterial infection
  - Exclusion
    - Administrations of any antibiotic not included in the "Antibiotic Rank" table (see Table 1)
    - Administrations missing the following data points: antibiotic name or administration time and date
- **Data Collection and Analysis**
  - Subjects were screened for eligibility using existing deidentified data presently stored in the DASON central database
  - Data fields collected: DASON subject number, age in years, gender, antibiotic name, administration time and date, route, dose at time of last order, ordering provider, and patient unit
  - Antibiotic rank (see Table 1) was determined for each drug and calculated for each interval by adding each individual antibiotics rank together that was administered within the interval or if an interval fell within an antibiotic's dosing window (i.e. q24hr drugs were counted for AM and PM between administrations). Duplicate administrations of the same antibiotic within an interval were not counted twice.
  - Antibiotic changes were identified via a change in antibiotic rank and are defined below. A decision tree was utilized to determine if an antibiotic's rank was continued for intervals outside of its administration interval.
  - An exploratory cohort was used to validate the described methodology of applying intervals and ranks.
  - Descriptive statistics were utilized for analysis .
- **Key Definitions:**
  - **Change**: any of the following: initiation, escalation, de-escalation, or discontinuation of an antibiotic occurring within an antibiotic course to a given patient as evidenced by bar coded administration data (as defined below)
  - **Antibiotic rank:** sum of all currently administered antibiotic ranks for a patient on the same calendar day and interval. (see Table 1)
  - **Interval:** AM and PM of each day of the week - 14 total intervals
  - **Initiation**: first antibiotic administration to a patient without antibiotic administrations within the prior > 72 hours
  - **Discontinuation:** last antibiotic administration to a patient without subsequent antibiotic administration for > 72 hours
  - **De-escalation**: reduction in the antibiotic rank within an antibiotic course from one interval to the next
  - **Escalation**: increase in the antibiotic rank within an antibiotic course from one interval to the next

Table 1. Antibiotic Rank

Spectrum Category	Narrow Spectrum	Broad Spectrum	Extended spectrum, including MDRO and Pseudomonas	Protected
Rank	1	2	3	4
Antibacterials included	amoxicillin cephalosporins – 1st and 2nd generation doxycycline metronidazole nafcillin nitrofurantoin oxacillin penicillin trimethoprim/ sulfamethoxazole	amoxicillin/ clavulanate ampicillin/sulbactam azithromycin cephalosporins – ceftriaxone and oral 3rd generation clarithromycin clindamycin	aminoglycoside aztreonam cefepime ceftazidime ertapenem fluoroquinolones piperacillin/ tazobactam vancomycin (IV only)	ceftaroline ceftazidime/avibactam ceftolozane/tazobactam colistin daptomycin imipenem/cilastatin linezolid meropenem meropenem/vaborbactam polymyxin tedizolid tigecycline

Results

Figure 1. Patient Screening and Enrollment



*Patients and administrations may have met more than one exclusion criteria

Table 2. Patient Course Characteristics (n=16,993)

Age in years – median (IQR)	62 (24)
Duration of therapy in days – mean (SD)	7.0 (11.6)
Initiations of rank 3 and 4 antibiotics	
- Weekend – mean per day (95% CI)	44.2 (42.3-46.2)
- Weekdays – mean per day (95% CI)	60.6 (59.2-62.0)
Discontinuations of rank 3 and 4 antibiotics	
- Weekend – mean per day (95% CI)	25.5 (23.2-27.7)
- Weekdays – mean per day (95% CI)	35.0 (33.8-36.1)
Mean changes per patients on antibiotics	
- Weekend – mean (95% CI)	0.363 (0.349-0.377)
- Weekdays – mean (95% CI)	0.407 (0.401-0.413)
Total changes weekend	
- AM weekend – mean per interval (95% CI)	103.4 (99.6-107.3)
- PM weekend – mean per interval (95% CI)	101.8 (96.5-107.2)
Total changes weekday	
- AM weekday – mean per interval (95% CI)	133.5 (130.9-136.2)
- PM weekday – mean per interval (95% CI)	132.1 (129.6-134.5)
ICU total changes	
- Weekend – mean per day (95% CI)	27.2 (26.2-28.2)
- Weekdays – mean per day (95% CI)	31.9 (31.3-32.5)

Figure 2. Type of Changes per Day

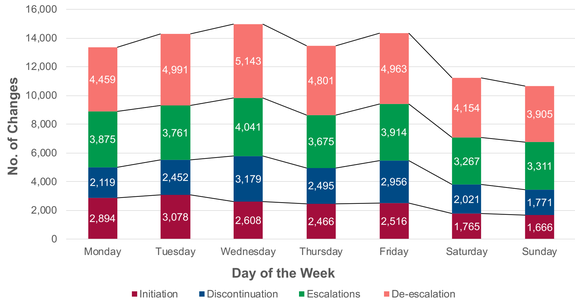


Table 3. Heat Map of Total Changes

	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
AM	6,456	7,205	7,567	6,648	7,512	5,788	5,177
PM	6,891	7,077	7,404	6,789	6,837	5,419	5,476
Total Changes	13,347	14,282	14,971	13,437	14,349	11,207	10,653

Discussion

- Unique methods of standardizing antibiotic changes with application of an antibiotic ranking system were utilized. These methods could be used at other institutions to analyze antimicrobial stewardship workflow.
- Similar definitions and antibiotic ranks have been proposed to predict antibiotic changes. Based on the assessment of an exploratory data set, our methods of calculating antibiotic rank were changed to better capture de-escalations.[3,4]
- Administration data was used utilized instead of order data and is thought to be in close proximity to timing of decision making. A decision tree was utilized to help determine approximate time of antibiotic change by providers.
- Observation of antibiotic changes appear to show a pattern of decreased overall trends on the weekend, as opposed to those shown during the week.
- Many changes appear to occur on Tuesdays (especially concerning initiation and escalations, which may be reflective of provider service changes at our institution).
- Lack of antimicrobial stewardship efforts performed by infectious diseases providers, stewardship pharmacists, and clinical pharmacists may play a role in the diminished changes seen on the weekend.

Limitations

- Data set is from a single center and may be difficult to extrapolate to other institutions.
- Admission and discharge data was unable to be obtained; however, these are treatment courses that are not anticipated to change over the weekend based on census data.

Conclusions

- Unique methods of standardizing antibiotic changes with application of an antibiotic ranking system may provide institutions with an effective way to analyze antimicrobial stewardship workflow.
- Observation of the data points to a decrease in antibiotic changes that occurred on the weekends when compared to weekdays.
- Due to the apparent stagnation of antimicrobial optimization on the weekend, this may provide an opportunity for antimicrobial stewardship involvement to be incorporated and help facilitate appropriate antimicrobial changes.

References

1. Wathne JS, Kleppe LKS, Harthug S, Blix HS, Nilsen RM, Charani E, Bergen Intervention Teams, Smith I. The effect of antibiotic stewardship interventions with stakeholder involvement in hospital settings: a multicentre, cluster randomized controlled intervention study. Antimicrob Resist Infect Control. 2018 10;7:109.
2. Tamma PD, Miller MA, Cosgrove SE. Rethinking how antibiotics are prescribed incorporating the 4 moments of antibiotic decision making into clinical practice. JAMA. 2019;321(2):139-140.
3. Developing Patient Safety Outcome Measures and Measurement Tools for Antibiotic Stewardship Programs Metrics Guide, 2017. (Accessed October 5, 2019, at https://dason.medicine.duke.edu/system/files/page-attachments/704/dason-cdcfinalanalysistool-r11-21.pdf)
4. Moehring RW, Ashley ED, Davis AE, Dyer AP, Parish A, Ren X, Lokhnygina Y, Hicks LA, Srinivasan A, Anderson DJ. Development of an electronic definition for de-escalation of antibiotics in hospitalized patients. Clin Infect Dis. 2020 Jul 8:ciaa932. doi: 10.1093/cid/ciaa932. Epub ahead of print. PMID: 32639558.

Conflict of interest: Nothing to disclose