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Authors
Huttner, Benedikt
Jones, Makoto
Madaras-Kelly, Karl
et al.

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Initiation and termination of antibiotic regimens in Veterans Affairs hospitals

Benedikt Huttner[1,2]†, Makoto Jones[1,2]*, Karl Madaras-Kelly[3,4], Melinda M. Neuhauser[5], Michael A. Rubin[1,2], Matthew Bidwell Goetz[6,7] and Matthew H. Samore[1,2]

[1]*VA Salt Lake City Health Care System, IDEAS Center, Salt Lake City, UT 84148, USA;* [2]*Division of Epidemiology, University of Utah, Salt Lake City, UT 84132, USA;* [3]*Boise VA Medical Center, Boise, ID 83702, USA;* [4]*College of Pharmacy, Idaho State University, Meridian, ID 83713, USA;* [5]*Department of Veterans Affairs Pharmacy Benefit Management Services, Hines, IL, USA;* [6]*VA Greater LA Healthcare System, Los Angeles, CA 90073, USA;* [7]*David Geffen School of Medicine at UCLA, Los Angeles, CA 90024, USA*

*Corresponding author. VA Salt Lake City Health Care System, 500 Foothill Drive, Salt Lake City, UT 84148, USA. Tel: +1-801-582-1565, ext. 4474; Fax: +1-801-582-5640; E-mail: makoto.jones@va.gov
†Present address: Infection Control Programme and Division of Infectious Diseases, Geneva University Hospitals and Faculty of Medicine, Rue Gabrielle Perret-Gentil 4, 1211 Geneva, Switzerland.

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Objectives: To assess rates of starting or stopping antibiotics across different hospitals.

Methods: We used barcode medication administration data to measure antibiotic use on acute-care wards in 128 Veterans Affairs medical centres (VAMCs) in 2010. A treatment day (TD) was defined as the administration of any antibiotic on a given day. A treatment period (TP) was defined as an interval of inpatient antimicrobial therapy with gaps of ≤1 day in TDs. The rate of starting antibiotics was calculated for inpatients who had not yet started antibiotics, as the number of start events divided by the 'person-time at risk'. The rate of stopping antibiotics was calculated analogously for inpatients that were on antibiotics. Once individuals had stopped antibiotics they were removed from further analysis. Per-day start and stop rates were also calculated for each day of hospitalization.

Results: The hospital mean rate of starting the first TP was 18.1 start events/100 days at risk (range 8.4–25.6/100 days at risk). The mean hospital stopping rate was 21.1 stop events/100 days at risk (range 13.3–29.5/100 days at risk). The ratio of a facility's starting and stopping rates was highly correlated with overall antibiotic use in TDs/1000 patient-days ($r_s = 0.92$, $P < 0.001$), while starting and stopping rates individually were only moderately correlated ($r_s = 0.39$, $P < 0.001$).

Conclusions: VAMCs with similar antibiotic use showed marked differences in their starting and stopping rates of antibiotics. It may be useful to target empirical therapy when starting rates are high and definitive therapy when stopping rates are low.

Keywords: antibiotic use, practice variation, infectious diseases

Introduction

In a recent policy statement advanced by US infectious disease and infection control societies, 'antimicrobial stewardship' was defined as 'coordinated interventions designed to improve and measure the appropriate use of antimicrobial agents'.[1] Measuring appropriate use of antimicrobials faces several challenges, however.[2] First, there is no clear consensus regarding what defines 'appropriate use' of antibiotics. Indeed, even guidelines about very common infectious conditions may vary importantly in their recommendations.[3] A further obstacle is the scarcity of detailed patient-level data in most settings. Currently available measures of antibiotic use are often derived from aggregated data sources (e.g. pharmacy dispensing data), which makes them relatively context-free and difficult to interpret. Even metrics derived from patient-level data, such as antimicrobial days/1000 patient-days (PDs), may only confer limited information about the quality of antibiotic use.

In this study, we aimed to leverage the detailed patient-level data available in the Veterans Affairs (VA) health care system to explore two classes of measures that map to clinical decision processes: the starting and stopping rates of antibiotic regimens. The ultimate goal of these efforts is to develop antibiotic use metrics that may assist antibiotic stewards in their efforts to identify targets for intervention.

Methods

Design and setting

One-hundred-and-fifty-two Veterans Affairs medical centres (VAMCs) provide care to approximately half a million hospitalized veterans each year. We studied antibiotic administration on acute medical–surgical and neurological wards (MedSurg wards) and ICUs. Wards and facilities not observed to have provided any inpatient acute-care medical or surgical services were excluded. The cohort was restricted to facilities with ≥10 operational acute-care beds during fiscal year 2010. We retrospectively analysed systemic antibiotics administered via barcode medication administration (BCMA) during hospitalizations for which the discharge occurred during calendar year 2010. Hospitalizations with >365 PDs on acute-care wards during the study period were excluded. This study was approved by the Research Review Committee of the VA Salt Lake City Health Care System and Institutional Review Board of the University of Utah.

Data

BCMA documents the administration of medications at the bedside and stores all information electronically with a time stamp.[4] BCMA data were analysed within the VA Information and Computing Infrastructure (VINCI) environment. The quality of the data was analysed as described previously.[5]

Measures

We included the systemic administration of all antibiotics of the J01 class of the Anatomical Therapeutic Chemical (ATC) classification (version 2011) with the exception of methenamine, but including rifampicin, oral metronidazole, oral vancomycin and nafcillin. Antibiotic consumption was expressed as 'treatment days' (TDs) and 'treatment periods' (TPs).[6] A TD (synonym 'length of therapy' or 'PD receiving antimicrobials') is the administration of *any antibiotic* on a given day independent of the number, strength or route of the individual doses or the number of different antibiotics given.[7,8] A TP represents an interval of uninterrupted antimicrobial

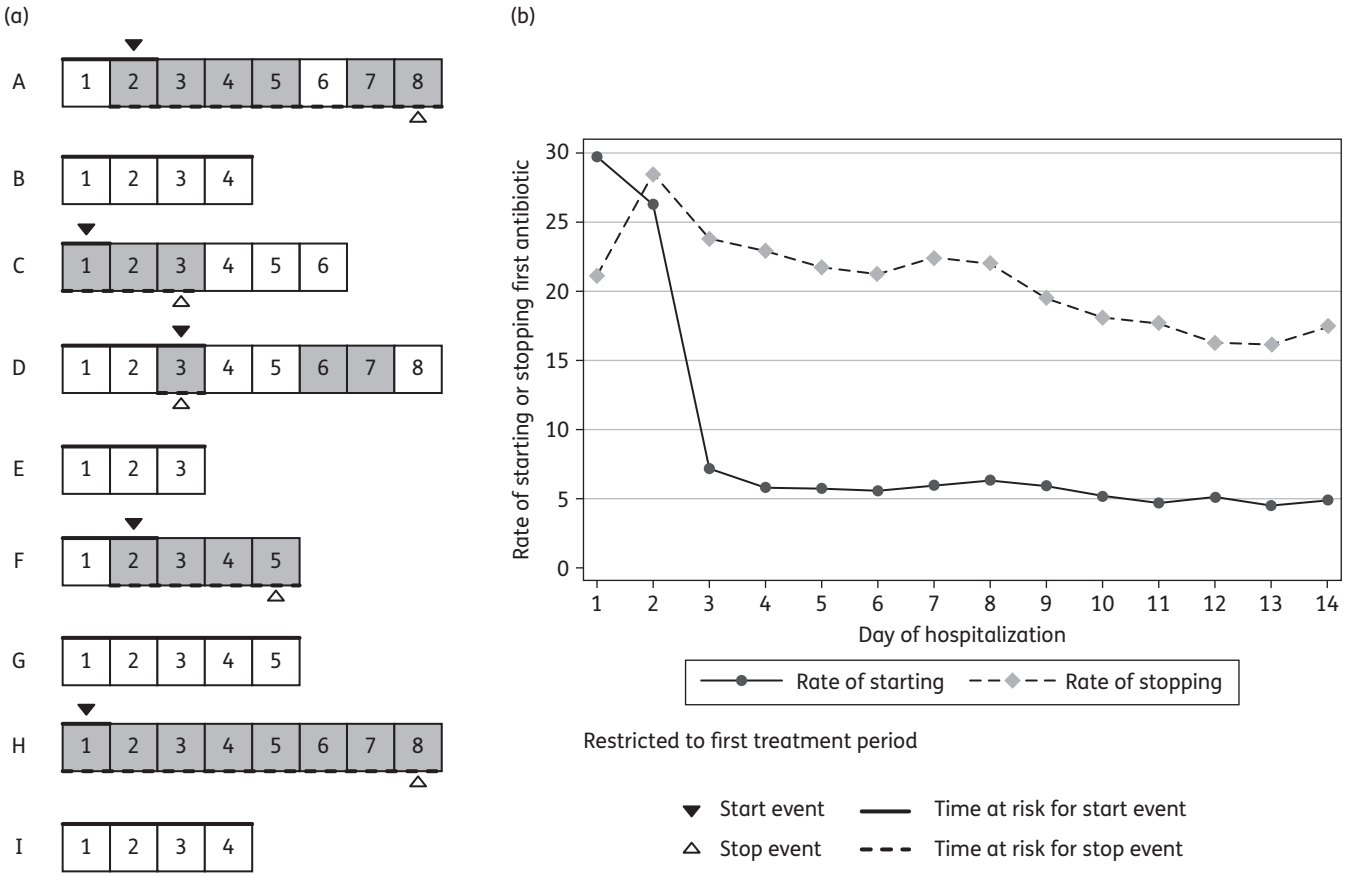

Figure 1. (a) Scheme for calculating starting and stopping rates based on hypothetical hospitalizations. Letters A–I indicate different hospitalizations. Squares represent days of hospitalization. Numbers inside the squares indicate the *n*th day of hospitalization (admission=day 1). Grey shading indicated days when a systemic antibiotic was administered. Black triangles indicate the first day during a hospitalization when a systemic antibiotic was administered (= start event). White triangles identify the day when the first antibiotic TP was considered stopped (either because of discharge the next day or no antibiotics during the following 2 days of hospitalization=stop event). Black solid lines identify days at risk of a start event. Black dashed lines identify days at risk of a stop event. In this example a first antibiotic TP is administered during five out of nine hospitalizations (A, C, D, F and H). In three of these five hospitalizations the stopping event is due to a discharge the next day (A, F and H). In the remaining two of these five hospitalizations (C and D) the stopping event is identified due to ≥2 consecutive days without antibiotic administration. Starting and stopping rates in this example would be calculated as follows: starting rate=5 starting events/25 days at risk=20/100 days at risk; and stopping rate=5 stopping events/23 days at risk=22/100 days at risk. (b) Overall starting and stopping rates of the first antibiotic TP by day of hospitalization in 128 VAMCs (expressed as start/stop events/100 days at risk).

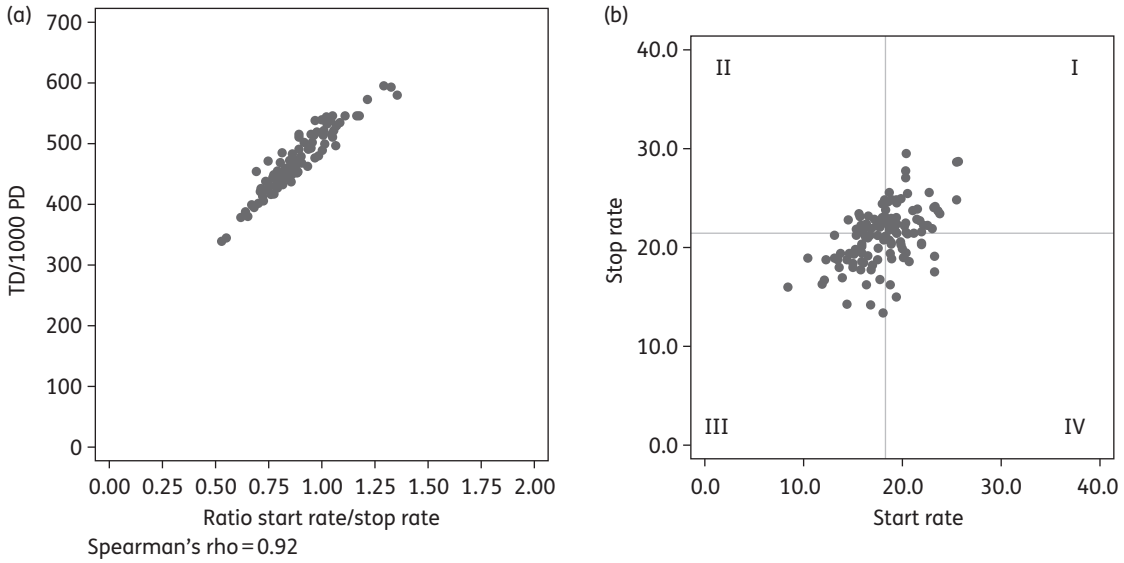

Figure 2. (a) Correlation of the ratio of the starting and stopping rates for the first antibiotic TP with overall antibiotic use in TDs/1000 PDs for each VAMC. (b) Correlation of starting and stopping rates (in start/stop events/100 days at risk) by VAMC. Lines represent the median starting and stopping rates. Roman numbers label the quadrants.

therapy regardless of the number of different antibiotics administered.[9] The end of a TP ('stop event') is determined by detecting gaps of >1 calendar day in TDs (i.e. a day when any antibiotic was given) or a discharge the following day (ignoring outpatient therapy). TDs, TPs and PDs were determined using a midnight census approach and TDs were normalized to 1000 PDs.

Starting and stopping rates

TDs/1000 PDs is a prevalence measure of inpatient antibiotic use. Its value depends on relative rates of treatment initiation and termination during hospitalization. We defined two supplementary metrics to capture the dynamic processes that underlie the TD statistic. The rate of starting antibiotics was calculated for inpatients that had not yet started antibiotics. The rate of stopping antibiotics was calculated for inpatients that were on antibiotics. Termination of an inpatient antibiotic regimen occurs via two different mechanisms. The first way is to end antibiotic treatment, presumptively through an order process such as expiration or cancellation. The second way is discharge, which terminates inpatient treatment if not already ended because it removes the patient from the hospital. These mechanisms are mutually exclusive in that termination by one type of event precludes the occurrence of the other type of event. Of note, once individuals fulfilled the criteria for an antibiotic stop event they were removed from further analysis, meaning that only the first TP was examined.

Antibiotic start rates were calculated by dividing the number of start events by the 'person-time at risk', consisting of days of hospitalization until the day the first systemic antibiotic was administered (Figure 1a). Similarly, stop rates were calculated by dividing the number of stop events by the 'person-time at risk', consisting of patients on antibiotics. While there are by definition equal numbers of start and stop events in each hospital, the person-time at risk differs for start and stop rates, meaning that stop rates can be quite different from start rates at the same hospital (Figure 1a). Per-day start and stop rates were also calculated for each day of hospitalization. These measures were computed to assess the extent to which hospitals with the same TDs/1000 PDs varied with respect to starting and stopping rates. Spearman's rank correlation coefficient was calculated for the correlation between the ratio of the starting and stopping rates of the first TP with overall antibiotic use in TDs/1000 PDs. All analyses were performed using STATA 11 (College Station, TX, USA).

Results

Our study included 128 hospitals and 508978 hospitalizations. During 50.2% of hospitalizations at least one dose of antibiotics was administered before discharge. Of all hospitalizations where a systemic antibiotic was administered, 94.8% involved only a single TP. Figure 1(b) illustrates the overall start and stop rates for the first TP for each day of hospitalization.

The mean start rate for all 128 facilities was 18.1 start events/100 days at risk (range 8.4–25.6) and the mean stop rate was 21.1 stop events/100 days at risk (range 13.3–29.5/100 days at risk). The ratio of a facility's starting and stopping rates was highly correlated with overall antibiotic use in TDs/1000 PDs ($r_s = 0.92$, $P < 0.001$) (Figure 2a) while starting and stopping rates within a facility were only moderately correlated ($r_s = 0.39$, $P < 0.001$) (Figure 2b). While ICUs accounted for 16.1% of all PDs during the study period, overall 19.4% of starts and 11.1% of stops of the first TP occurred in the ICU. Of note, 72.3% of all stop events were coincident with discharge the next calendar day.

Discussion

In this study, we examined the relationship between starting and stopping rates of the first antibiotic TP and overall antibiotic use in 128 VA medical centres. We demonstrated that the two measures together tightly correlated with traditional aggregate antibiotic use metrics. By pairing an analysis of TDs with an analysis of its components, i.e. starting and stopping rates, we believe that it will be possible for antibiotic stewards to identify more efficiently which clinical decisions should be targeted.

One could imagine that, e.g. antibiotic stewards in facilities with high starting rates (Figure 2b, quadrants I and IV) should focus on improving empirical therapy (i.e. avoiding unnecessary antibiotic courses). Antibiotic stewards in facilities with low stopping rates (Figure 2b, quadrants III and IV) may try to intervene to shorten treatment duration. While the starting and stopping rate

metrics proposed in this study are still relatively crude, we believe that they represent a valuable first step towards a decision-based framework for antibiotic stewardship.

Our study has several limitations. Some doses of administered antibiotics may have been missed through circumvention of BCMA (e.g. prophylaxis administered in the operating room).[10] Compliance with BCMA is regularly monitored, however, and other data sources are prone to overestimation of antibiotic use.[11] In addition, our definition of TP is arbitrary and does not necessarily reflect treatment duration, particularly since we did not differentiate between end of an antibiotic TP and discharge of a patient. Further analyses taking into account outpatient therapy are therefore warranted. Our definition of TP also does not fully account for TPs where antibiotics may be appropriately dosed >1 day apart (e.g. vancomycin in patients with severely impaired renal function), but this most likely applies only to a very small population within each facility. The same applies to intermittently dosed long-term prophylaxis with antibiotics in certain patient populations (e.g. trimethoprim/sulfamethoxazole). A further limitation is the fact that the capture of prophylactic antibiotics for surgery by BCMA varies between centres. Antibiotics given in the operating room are usually not recorded by BCMA so that appropriate single-dose prophylaxis should not have a major influence on the proposed metrics.

Finally, the VA is a unique setting with a special patient population (e.g. a high proportion of old patients, few female patients) that limits the external generalizability of our findings. However, the overall concept is applicable to and reproducible by any hospital where individual-level antibiotic use data are available. Additional studies to compare the magnitude of inter-hospital variation in antimicrobial use across different multi-facility healthcare systems are warranted.

The detailed patient-level electronic data available in the VA system offer a unique opportunity to leverage these capacities to develop a deeper understanding of the reasons for variation in antibiotic use and implement interventions targeted to the particularities of each facility.

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Transparency declarations

None to declare.

Disclaimer

The views expressed in this article are those of the authors and do not necessarily reflect the views of the Department of Veterans Affairs, the US government or any of the affiliated institutions.

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