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Brief Report

The effectiveness of formulary restriction and preauthorization at an academic medical center

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The impact of formulary restriction and preauthorization (FRPA) on prescribing trends was examined over a 5-year period at an academic medical center. Ordinary least squares regression was used to identify hospital units demonstrating statistically significant trends in prescription of restricted agents. Significant decreases in restricted drug use were seen on 2 of 7 medicine units subject to FRPA, whereas a significant increase was seen in 1 of 4 surgical units subject to FRPA.

Antibiotic stewardship programs (ASPs) exist to promote appropriate use of antimicrobials in addressing increasing resistance seen in many microbial species. Appropriate use ensures therapy is effective while limiting the use of agents with unnecessarily broad coverage. The Infectious Disease Society of America (IDSA) and the Society for Healthcare Epidemiology of America, Inc (SHEA) have published guidelines endorsing formulary restriction and preauthorization (FRPA) as a leading evidence-based method that may be employed by ASPs to promote appropriate antimicrobial use in the inpatient setting. With FRPA, prescribing physicians must obtain approval from ASP staff prior to administration of a restricted or non-formulary drug.[1] ASP interventions such as FRPA have been shown to decrease rates of multidrug resistant gram-negative organisms, methicillin-resistant *Staphylococcus aureus*, and *Clostridium difficile* infection.[2]

The Virginia Commonwealth University Health System (VCUHS) is an 865-bed academic tertiary care facility with an ASP that has been in place for approximately 20 years. A comprehensive FRPA program has been in place for the majority of this time period. Members of the ASP team, including clinical pharmacists and infectious diseases fellows, share responsibility for approving restricted agents between 8:00 AM and 9:00 PM, 7 days per week. Overnight antimicrobial orders are not subject to FRPA and providers may enter orders for restricted antimicrobials through 8:00 AM of the following day. FRPA at VCUHS applies to all medical and surgical wards, with pediatric wards being exempt. All restricted antimicrobials included in this study were restricted throughout the entire study period. The objective of this study was to determine the longitudinal effectiveness of FRPA at our hospital.

METHODS

Antimicrobial use data were available for each agent prescribed at the unit level in days of therapy (DOT) per 1,000 patient-days between August 2012 and June 2017. DOT for restricted and non-restricted drugs were summed within each month, forming the primary analysis variables: total restricted and total non-restricted antimicrobial use. Restricted drugs included ampicillin-sulbactam, aztreonam, cefotaxime, ceftaroline, ceftazidime, ceftazidime-avibactam, ceftolozane-tazobactam, colistimethate, daptomycin, ertapenem, fidaxomicin, fosfomycin, imipenem-cilastatin, isavuconazonium, linezolid, micafungin, moxifloxacin, posaconazole, telavancin, tigecycline, and voriconazole. Ordinary least squares regression was then applied to the

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monthly time series of total restricted and non-restricted drug use according to Equation 1 and Equation 2:

$$\frac{DOT_{Restricted}}{1,000\,patient-days} = Intercept + \#\,Months\,since\,August\,2012 \quad (Equation1)$$

$$\frac{DOT_{Non\text{–}Restricted}}{1,000\,patient-days} = Intercept + \#\,Months\,since\,August\,2012 \quad (Equation2)$$

The coefficient and *P* value associated with the months since August 2012 regression variable ("time trend") provides an estimate of the direction, magnitude, and statistical significance associated with the time trend of total restricted and non-restricted use during the period studied. Data on case composition by ward and other demographic details were not available, thus regression analysis only accounts for time trend.

Analysis was completed using SAS software version 9.4 (SAS Institute, Cary, NC).

RESULTS

Statistically significant negative time trends in antibiotic use were observed in 2 of 7 of medical units (medical intensive care unit [ICU], medicine-progressive) and 0 of 4 surgical units. A statistically significant negative trend was also seen on 1 of 4 pediatric units (neonatal ICU). One surgical unit (burn ICU) demonstrated a statistically significant increasing time trend in restricted use. In total, 2 of 11 (18%) adult units subject to FRPA demonstrated statistically significant decreases in restricted antimicrobial use during the study period, compared to 1 of 4 (25%) pediatric units (Fig 1 and Table 1).

Table 1
Ordinary least squares regression results for time trend variable, restricted, and non-restricted antimicrobials.

		Restricted		Non-Restricted	
Type	Unit	Time trend	*P* value	Time trend	*P* value
Medical	Hematology-oncology	0.64	.092	−0.68	.586
	Med-acute care	0.39	.406	0.29	.757
	Cardiac ICU	−0.37	.106	−0.58	.465
	Medical ICU	−2.06	.000	0.36	.681
	Bone marrow transplant	0.52	.500	−3.99	.000
	Digestive health	−0.14	.300	−2.12	.037
	Medicine-progressive	−0.93	.000	−3.53	.000
Surgical	Surgery-acute care	−0.30	.157	−0.60	.333
	Burn ICU	0.84	.002	2.83	.003
	Cardiac surgery ICU	−0.50	.277	0.84	.418
	Surgical trauma ICU	−0.52	.102	4.36	.000
Pediatric	General pediatrics	−0.36	.136	−2.12	.000
	Neonatal ICU	−0.29	.001	0.32	.540
	Pediatric ICU	−0.12	.785	−3.70	.000
	Ped-progressive	−0.29	.099	−1.48	.064

ICU, intensive care unit; *Med*, medical; *Ped*, pediatrics.

DISCUSSION

These data suggest FRPA has been effective at our institution for adult medical units. In these units, we not only saw stable use of restricted agents but also significant declines for some units. In contrast, surgical units saw no significant decreases over the time period studied with a significant positive trend in use seen within the burn ICU.

Of the 4 pediatric units studied, the neonatal ICU demonstrated a statistically significant decrease in restricted antimicrobial use trend; this appears to be driven largely by changes in the pattern of cefotaxime use in recent years. In terms of the total consumption of restricted antimicrobials, this ward tends to make a relatively small contribution to total use within our health system.

Concern has been raised that restriction may promote increases in use of non-restricted agents that blunt any benefits derived from

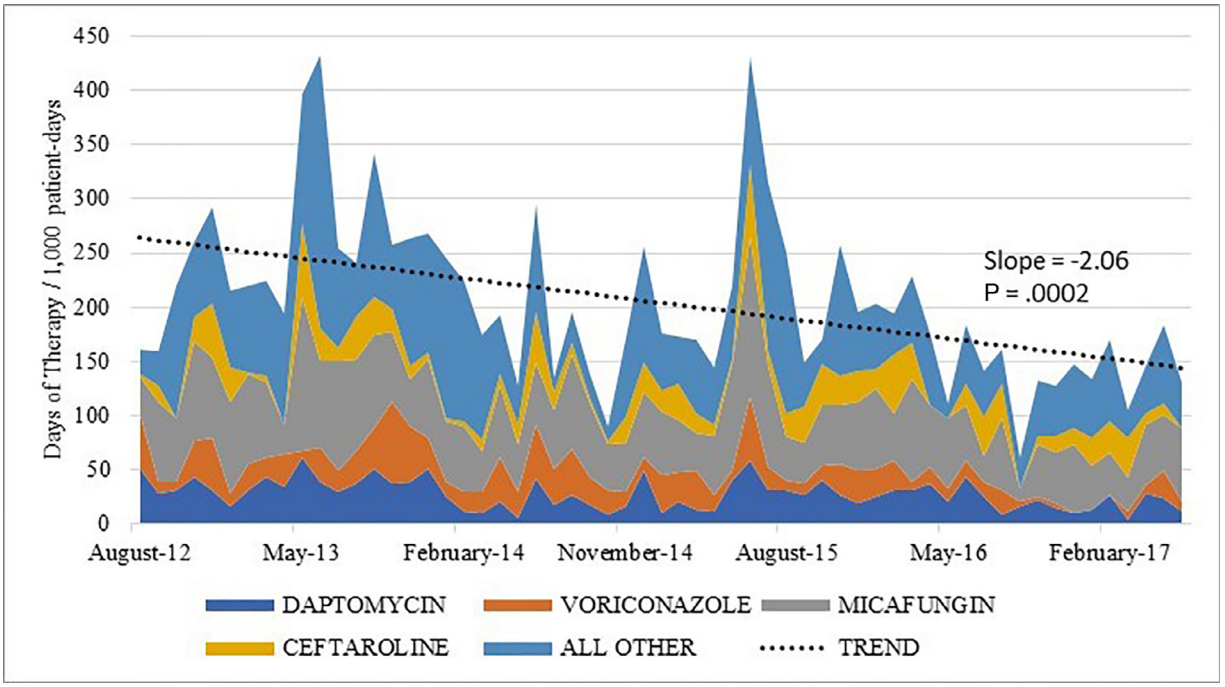

Fig 1. Total restricted antimicrobial use within the medical intensive care unit.

FRPA programs—the "squeezing the balloon" phenomenon.[3] Our data however do not suggest that any such effect has occurred within VCUHS during the period studied. Neither of the 2 medical wards showing negative trends in restricted drug use were associated with corresponding upward trends in non-restricted use.

Our study was limited by potential for confounding due to parallel ASP interventions. In addition to FRPA, adult patients were also subject to postantibiotic order review with provider feedback during the study period. It is not possible to discern the relative contributions of provider feedback versus FRPA or other ASP activities on unit-level antimicrobial use over the study period.

To carry out this study, we developed a novel method of tracking FRPA effectiveness. Many past studies have relied on analyzing a single agent or a small subset of agents to evaluate ASP performance.[4] However, ASP efforts often target dozens of drugs; trends observed in a smaller subset may not reflect broader patterns affecting the entire scope of agents targeted by an ASP. Our approach used unique methodology to aggregate multiple restricted drugs and analyze cumulative trends by applying regression analysis to aggregated time series data. We believe this approach provides a simple, comprehensive view of FRPA performance that may be of value to other institutions.

CONCLUSIONS

Our analysis suggests that our FRPA program has been effective at limiting the use (and in some cases reducing the use) of restricted agents, especially for medical units. We also describe a novel way of analyzing FRPA performance that may be of value to other programs. These data will inform FRPA efforts at our institution.

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