ASCENSION

# Universal Implementation of Antimicrobial Stewardship Program Leads to Reduction in Antibiotic Use and Cost Savings: Pilot Results from a Large U.S. Health System

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## BACKGROUND

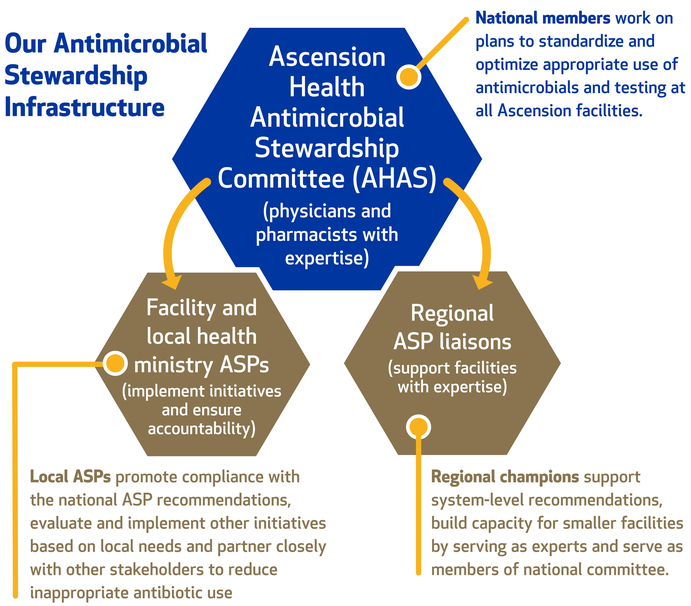
Antimicrobials are often used inappropriately, either to treat syndromes that do not represent bacterial infections or for a longer period of time than is appropriate to treat the targeted infection. With increased antibiotic resistance resulting from unnecessary antibiotic use, antimicrobial stewardship (AS) in the United States has become a national priority.

The White House developed *The National Strategy for Combating Antibiotic-resistant Bacteria (CARB),* which calls for hospitals and healthcare systems to implement antimicrobial stewardship programs (ASPs). A system approach fosters accountability and encourages standardization at the hospital level. We describe the impact of establishing ASPs at the system and hospital levels on antimicrobial use and cost.

## Center of Excellence

ANTIMICROBIAL STEWARDSHIP AND INFECTION PREVENTION

### Our Antimicrobial Stewardship Infrastructure




## METHODS

Every hospital developed an AS team, co-led by a physician and pharmacist, to ensure compliance with evidence-based antimicrobial use, culture orders and standardized disease management processes. Evidence-based indications were developed for aztreonam, ceftaroline, daptomycin, linezolid, tigecycline and ertapenem. Utilization over time by defined daily dose (DDD)/1,000 patient days was shared with each facility monthly to review successes and opportunities as well as to a develop plan of action. In addition, we directly engaged with opportunity hospitals through phone calls and site visits.

### Daptomycin Utilization Criteria

- Treatment of bacteremia or endocarditis or severe systemic infection caused by methicillin-resistant *Staphylococcus aureus* (MRSA) with documented severe allergy and intolerance to vancomycin[1]
- Treatment of MRSA-associated bacteremia or serious systemic infections (other than pneumonia) with vancomycin MIC ≥ 2 mcg/mL and no clinical improvement
- Treatment of vancomycin-resistant enterococci (VRE)-associated bacteremia
- Treatment of vancomycin-refractory MRSA bacteremia or endocarditis as evidenced by clinical decompensation after four days therapy despite optimized vancomycin therapy (e.g., trough level 15-20 mcg/mL)

### Linezolid Utilization Criteria

- Documented MRSA infection in a patient with severe allergy to vancomycin[1]
- Documented severe intolerance or resistance to daptomycin
- Documented vancomycin-refractory pneumonia after two to three days of therapy, evidenced by worsening infiltrate or pulmonary status
- Vancomycin-refractory pneumonia as evidenced by MIC ≥ 2mcg/mL and no clinical improvement
- Documented MRSA bacteremia refractory to vancomycin and daptomycin as evidenced by failure to clear culture after seven days of therapy despite optimized vancomycin dosing
- Documented VRE bacteremia or severe skin and soft tissue infection (SSTI)

### Tigecycline Utilization Criteria

- Salvage therapy for MRSA/VRE infections on a case-by-case basis
- Multidrug-resistant, gram-negative organisms, including *Acinetobacter* spp. and *Stenotrophomonas maltophilia* on a case-by-case basis
- Documented intra-abdominal infections in patients with contraindications to both fluroquinolones and beta-lactams

Tigecycline: black box warning – to be reserved only for situations where no other alternative is available

### Ceftaroline Utilization Criteria

- Approved indications for community-acquired pneumonia and skin and skin structure infections
- However, use should be very limited because other drugs with longstanding history of safety and efficacy provide adequate coverage.
- Because of its activity against MRSA, it is differentiated from other cephalosporins and should be reserved for use in very select situations related to severe MRSA infections, where the standard therapy fails or there is no other alternative due to intolerance.

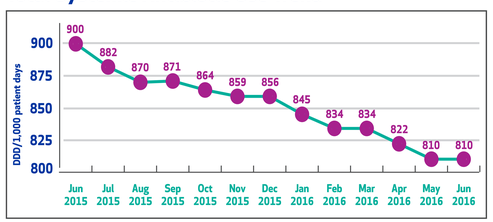
[1]*Anaphylaxis OR serious infusion-related reactions unresponsive to an increase in infusion time (two to three hours) and premedication OR drug fever OR adverse drug-related hematologic event (e.g., leukopenia).*

## RESULTS

### Table 1: Impact on Aggregate Targeted Antimicrobial Agent Use

| | FY15 | | | FY16 | | | Difference between FY15 and FY16 DDD/1,000 patient days | | |
|---|---|---|---|---|---|---|---|---|---|
| Antibiotic | DDD | Patient days | DDD/1,000 patient days | DDD | Patient days | DDD/1,000 patient days | Percent change | P-value | 95% CI |
| *n=85* | | | | | | | | | |
| Ceftaroline | 6,572 | 3,656,268 | 1.8 | 3,605 | 3,486,390 | 1.0 | -42.5% | p<0.001 | (0.71, 0.82) |
| Daptomycin | 46,190 | 3,656,268 | 12.6 | 27,360 | 3,486,390 | 7.8 | -37.9% | p<0.001 | (4.6, 4.9) |
| Linezolid | 17,919 | 3,656,268 | 4.9 | 13,162 | 3,486,390 | 3.8 | -23.0% | p<0.001 | (1.03, 1.22) |
| Tigecycline | 4,851 | 3,656,268 | 1.3 | 2,720 | 3,486,390 | 0.8 | -41.2% | p<0.001 | (0.5, 0.6) |
| Ertapenem | 19,690 | 3,656,268 | 5.4 | 17,240 | 3,486,390 | 4.9 | -8.2% | p<0.001 | (0.34, 0.55) |
| Aztreonam | 10,141 | 3,656,268 | 2.8 | 8,953 | 3,486,390 | 2.6 | -7.4% | p<0.001 | (0.13, 0.28) |
| All systemic | 3,443,342 | 3,656,268 | 941.8 | 3,006,379 | 3,486,390 | 862.3 | -8.4% | p<0.001 | (79.0, 79.9) |

### Total Systemic Antibiotic Use Trend




**10% Reduction**

### Table 2: Targeted Agent Use Reduction and Cost Avoidance

| Antibiotic | FY15 DDD/1,000 patient days | FY16 DDD/1,000 patient days | Cost Avoidance |
|---|---|---|---|
| Aztreonam | 3.7 | 3.1 | $300,000 |
| Ceftaroline | 1.7 | 1.1 | $700,000 |
| Daptomycin | 12.2 | 8.7 | $3,400,000 |
| Ertapenem | 6.6 | 5.4 | $30,000 |
| Linezolid | 4.7 | 4.1 | $40,000 |
| Tigecycline | 1.3 | 0.8 | $440,000 |

### Table 3: Total Antibiotic Cost Savings FY15 vs. FY16

| Year | Total acute spend: all drugs | Total acute spend: systemic antibiotics | % of total spend |
|---|---|---|---|
| FY15 | $401,000,000 | $30,000,000 | 7.5% |
| FY16 | $447,000,000 | $28,080,000 | 6.2% |

- Antibiotic cost inflation 20% in FY16, compared to overall pharmaceutical cost inflation of 9.5%
- If practices remained the same for FY16 as in FY15, a $6 million impact would have been seen.
- With antimicrobial stewardship activities, a decrease in spend was seen of $2 million.
- If inflation is removed, an $8 million total cost avoidance has been realized.

## DISCUSSION

Our System-wide antimicrobial stewardship efforts resulted in:

- **8.4% reduction,** from **941.8** DDD/1,000 patient days in **FY15** to **862.3** in **FY16** (p<0.001), in targeted antibiotic use (aztreonam, ceftaroline, daptomycin, ertapenem, linezolid and tigecycline) and **$4.9 million cost avoidance**
- **10% reduction,** from **900** DDD/1,000 patient days to **810**, in use of all systemic antibiotics and **$8 million savings**

Prospective monitoring, established utilization criteria, utilization monitoring and accountability led to our success.

## CONCLUSION

A System-wide antimicrobial stewardship effort, engaging hospitals with clear indications for use, is associated with the reduction of inappropriate antimicrobial use and cost.