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Antimicrobial Stewardship

Annual Report 2016-2017

Prepared by the Fraser Health Antimicrobial Stewardship Program

June 2017

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Contents

Executive Summary

The Fraser Health Antimicrobial Stewardship Program (ASP) is a small but thriving program. Our highly skilled team works closely with other clinical staff members who are already championing antimicrobial stewardship on the front line. We have continued to grow as a program, currently comprised of four specialized pharmacists and one Infectious Diseases consultant.

Our purpose is to promote appropriate antimicrobial use within Fraser Health. To accomplish this, we have set three goals which guide all of our program activities: to optimize patient care through appropriate antimicrobial use, to slow the emergence of antimicrobial resistance, and to improve health care efficiency. These goals are consistent with the patient safety mandate to minimize preventable harm to patients.

With our team of ASP clinicians, we are routinely reviewing patient cases involving targeted antibiotics and interacting with prescribers in a systematic fashion at multiple acute care sites. Over the past year, our team has reviewed 6,241 patient cases and made specialized clinical interventions in 3,173 patient cases. Our recommendations were accepted in 82% of cases.

We have continued to expand our FH specific ASP Handbook, which is a consolidated, evidence-based reference for treatment of common infections. This year we have released chapters to support and guide clinicians in management of in-hospital sepsis and urinary tract infections.

The ASP is involved in development and revision of pre-printed order sets that include antimicrobials. Pre-printed orders (PPO) help standardize care across Fraser Health in line with best practices. This year, we took the initiative to update the community acquired pneumonia PPO to reflect our updated ASP Handbook guidance. We also provided feedback on pre-printed orders for inpatient sepsis, sepsis in the emergency department, febrile neutropenia, and peritoneal dialysis peritonitis. We are also collaborating with multiple clinical groups on updating antimicrobial prophylaxis recommendations on peri-operative order sets.

Our program's activities have shown a positive impact on antimicrobial usage trends. Usage of our targeted restricted antimicrobials (carbapenems, linezolid, daptomycin) has been reduced. Usage of fluoroquinolones has also dropped, which may positively impact *C. difficile* infection rates.

Improving health care efficiency is one of our three goals to ensure taxpayer money is used wisely and effectively. Fraser Health has seen a $336,934 reduction in antimicrobial expenditure in FY2016-17 compared to FY2015-16 – a 3.5% reduction.

This report provides further details on our program's initiatives, as well as the various performance measures we follow. We've learned a great deal from our clinicians and staff, and have been tremendously fortunate to have such broad support. We look forward to any comments or questions regarding this report. As we strive to use antimicrobials wisely in today's patients, we hope to prolong their effectiveness for tomorrow's patients.

Background

The rise of antimicrobial resistance is a significant threat to patient care and public health. An estimated 18,000 Canadians every year develop drug-resistant infections within our hospitals.[1] The emergence of antimicrobial resistance impacts patient morbidity and mortality, leading to increased healthcare costs. Major problems include the rise of methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus faecium* (VRE), and multidrug-resistant gram-negative organisms, including *Pseudomonas*, *Acinetobacter*, and carbapenem-resistant Enterobacteriaceae (CRE). Unchecked, mortality attributable to antimicrobial resistance is estimated to increase to over 300,000 annually in North America by 2050.[2]

Concurrently, the healthcare system has had to manage the rise of *Clostridium difficile* infection (CDI). Concerted efforts at reducing CDI include improving infection prevention and control practices, as well as promoting appropriate use and selection of antimicrobials through an antimicrobial stewardship program (ASP).

ASP has been shown to improve antimicrobial usage, improving the quality of patient care through more appropriate selection and dosing of antimicrobials. Patient safety is also improved through reduced toxicity and adverse events from antimicrobial misuse. Institution of an effective ASP can decrease CDI, as well as put downward pressure on the rise of antimicrobial resistance. Furthermore, all of these benefits can be realized while saving the healthcare system money.

The ASP purpose and goals are as follows:

Purpose:
The ASP promotes appropriate use of antimicrobials within Fraser Health (FH).

Goals:
The goals of the program are threefold:

a. To optimize patient care through appropriate selection and use of antimicrobials, while minimizing adverse events
b. To slow the emergence of antimicrobial resistance by limiting selection pressure from antimicrobial misuse
c. To improve health care efficiency by reducing unnecessary antimicrobial use

[1] Public Health Agency of Canada. Antimicrobial resistance and use in Canada: A federal framework for action. Can Commun Dis Rep. 2014;40 Suppl 2:2-5.
[2] Review on Antimicrobial Resistance. Antimicrobial resistance: tackling a crisis for the health and wealth of nations. 2014. Available from http://amr-review.org/Publications.

ASP Team Members

Clinical Team

The clinical team conducts the daily activities of the ASP. This includes performing audit and feedback of antimicrobial prescribing, providing education for clinicians, undertaking quality improvement initiatives, and liaising with stakeholders and leaders across the health authority.

Members of the clinical team include:

Dr. Kevin Afra	*ASP Medical Director & ID Consultant*
Dr. Vivian Leung	*Pharmacy Coordinator, Antimicrobial Stewardship*
Dr. Colin Lee	*Clinical Pharmacy Specialist, Antimicrobial Stewardship*
Dr. Ivy Chow	*Clinical Pharmacy Specialist, Antimicrobial Stewardship*
Dr. Tim Leung	*Clinical Pharmacy Specialist, Antimicrobial Stewardship*

Administrative support for the program is provided by Julie Reynolds.

Executive Oversight

Dr. Kevin Afra, medical director of the ASP, is accountable to Linda Dempster (VP Patient Experience) and Dr. Roy Morton (VP Medicine) who provide executive-level guidance and oversight for the program. They also inform the Fraser Health Executive, the Board of Directors, and provincial stakeholders on the status of the ASP.

Dr. Vivian Leung (Pharmacy Coordinator) is accountable to Dr. Adil Virani (Manager, Pharmacy Services), who reports to Linda Morris (Director, Pharmacy Services).

Regional ASP Committee

The Regional ASP Committee is an inter-disciplinary group of clinicians and leaders within the health authority. The Committee discusses, develops, promotes, and evaluates strategies utilized by the ASP to meet its program goals.

Members of the Regional ASP Committee include:

Dr. Kevin Afra (chair)	*ASP Medical Director & ID Consultant*
Dr. Yasemin Arikan	*ID Consultant, RCH*
Wendy Bowles	*Regional Department Head, Nurse Practitioners*
Dr. Elizabeth Brodkin	*Executive Medical Director, Infection Control & MHO*
Dr. Michael Chapman	*ID Division Head & ID Consultant, SMH*
Sarah Derman	*CNS, Surgical Network*
Dr. John Diggle	*Regional Department Head, Medicine*
Dr. Sayeeda Hudani	*Regional Department Head, Hospitalists*
Dr. Vivian Leung	*ASP Pharmacy Coordinator*
Dr. Neil Mina	*Medical Microbiologist*
Dr. Anurag Markanday	*ID Consultant and Internal Medicine Head, ARHCC*
Dr. Laurenna Peters	*ID Consultant, BH*
Julie Reynolds	*Administrative Assistant*
Dr. Steven Reynolds	*Program Medical Director, Critical Care*
Dr. Adil Virani	*Manager, Pharmacy Services*

Ackowledgements

The ASP would like to thank the countless individuals who have supported our program. We have been encouraged by our growing collaboration with the FH Executive Team, Site Medical Directors, and Site Executive Directors. We are fortunate to enjoy a strong partnership with Pharmacy Services. It is a privilege to support our front-line Physicians, Nurse Practitioners, and Pharmacists as we strive towards excellence in patient care.

Our special thanks also goes to:

- Regional ASP Committee members who have moved on or changed to ad hoc roles: Michele Babich
- Division of Infectious Diseases
- Medical Microbiology
- Infection Prevention and Control
- Medication Use and Evaluation Team (Anthony Tung, Dr. Angus Kinkade, and Dr. Aaron Tejani)
- Our colleagues from other antimicrobial stewardship programs, including the Antimicrobial Stewardship Programs of Providence Health Care and Vancouver Coastal Health.
- The Provincial Antimicrobial Stewardship Clinical Expert Group (PACE)

Program Activities

Audit and Feedback

Prospective audit and feedback is one of the core activities of an ASP. It involves case-by-case assessment of antimicrobial use with direct feedback to the prescribing physician. Patients receiving targeted antimicrobials are identified prospectively. One of our team members will review the patient's medical record and investigation results to identify opportunities to optimize antimicrobial use, namely:

- Optimal drug (appropriate spectrum for identified infection and investigation results)
- Optimal dosing
- Optimal route (encouraging oral therapy when safe and appropriate)
- Optimal duration

If an opportunity for optimization is identified, a note with our suggestions is left in the medical record. We also strive to discuss the case with the prescribing physician. Our audit and feedback service does not change medication orders without the express permission of the most responsible provider.

For fiscal year 2016-2017, our team performed the following:

Patient Cases Reviewed	Patient Cases Intervened Upon	Acceptance Rate
6,241	3,173	82%

Quality Improvement (QI) Projects

The ASP has become involved in a number of quality improvement projects in partnership with others throughout the health authority.

Community Acquired Pneumonia

We have partnered with Hospitalist groups at BH, RCH, and SMH to focus on antimicrobial prescribing for patients admitted with community acquired pneumonia. Our goal is to improve the process of antimicrobial prescribing at admission and on day 3, where many patients can switch to oral therapy. The project encourages guideline-concordant therapy, improved communication, and timely step-down to oral therapy.

Feedback is provided to individual prescribers to regular audit and feedback. Aggregate statistics are also shared with each group regularly. Early results have been promising and we hope to expand to more sites in the coming fiscal year.

Clostridium difficile Infection

We are collaborating with Infection Prevention and Control and Pharmacy on a novel process to identify patients with *Clostridium difficile* infection who may have guideline-discordant care. This process will expedite involvement of Pharmacy or Infectious Diseases specialists in patient care. Our goal is to improve the treatment of patients with *Clostridium difficile* infection, which also reduces the risks of transmission to other vulnerable patients.

We have developed an algorithm for Infection Prevention and Control Practitioners to identify patients who would benefit from escalation to Pharmacy. Likewise, a clinical reference has been developed to support Pharmacists' review of CDI cases, and guide further escalation to ASP or Infectious Diseases.

Implementation of the pilot phase will begin in early FY2018.

Urinary Tract Infection in Residential Care

In an effort to expand the role of ASP beyond acute care, we have partnered with Residential Care on a project targeting asymptomatic bacteriuria. Asymptomatic bacteriuria is common in residential care, and in the vast majority of cases antimicrobial therapy is unnecessary may result in side effects, *Clostridium difficile* infection, or emergence of antimicrobial resistance.

Our working group has developed an algorithm to differentiate symptomatic from asymptomatic bacteriuria and guide appropriate collection of urine cultures. A form has been developed to standardize the clinical algorithm and aid communication between care staff and prescribers. Treatment recommendations for prescribers are provided in our new ASP Handbook chapter on Urinary Tract Infections. Building on our positive experience with audit and feedback in acute care, a similar process is also being trialed with this QI project. We look forward to reviewing the results at our pilot sites this coming fiscal year.

ASP Handbook

The ASP has created a Handbook to consolidate in a single reference our guidance on treatment of common infectious conditions and important antimicrobial use issues. This inter-disciplinary collaboration is created by the ASP in conjunction with the Regional ASP Committee, the Division of Infectious Diseases, Medical Microbiology, and our clinicians. The Handbook integrates best available medical literature, recommendations from professional organizations, regional antimicrobial resistance (our antibiogram), and regional formulary.

This fiscal year, we have continued to develop and publish content:

- Inpatient Sepsis
- Urinary Tract Infections

This adds to our previously released content on:

- Community acquired pneumonia
- Aspiration pneumonia
- Pediatric infections
- Vancomycin dosing and therapeutic monitoring

Multiple new chapters are planned for the coming fiscal year. Existing chapters will be reviewed annually for updates taking into account evolving practice standards, local antimicrobial resistance, and formulary.

ASP Website

The ASP created a website on the Fraser Health intranet in order to improve visibility of our program and consolidate all our communication and reports in a single location (**Figure 1**). Our website includes our ASP Handbook, local antibiograms, our reports, and contact information for our clinical teams across the region.

Check out our internal website here.

In order to improve accessibility for clinicians, we have successfully released our content on the externally accessible Fraser Health Medical Staff website (**Figure 2**). Click here to take a look.

Figure 1. Antimicrobial Stewardship intranet website

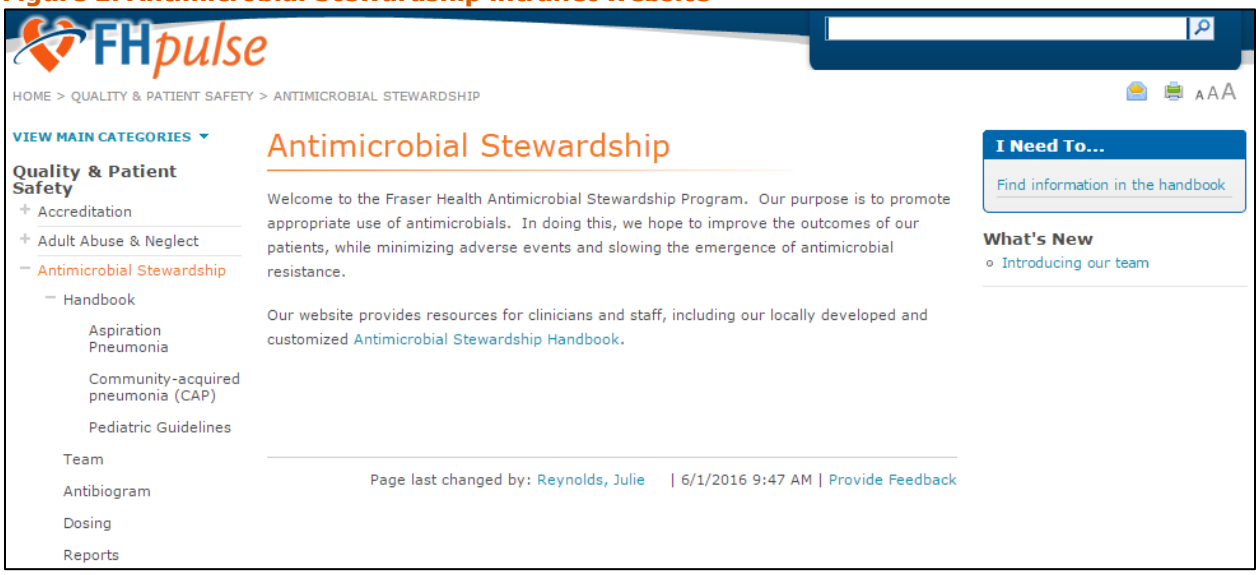
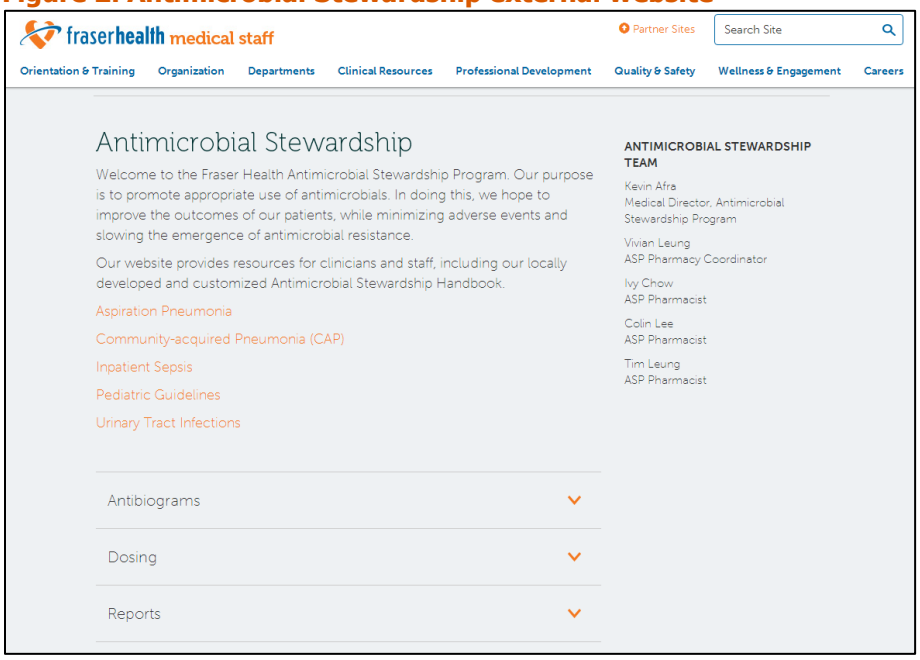


Figure 2. Antimicrobial Stewardship external website



Pre-Printed Order Revisions

The ASP acts as a regional resource and reviewer for antimicrobials on pre-printed orders (PPO's) undergoing development or revision. Some of these are initiated by the ASP, while others are at the request of other clinical departments or divisions within the Fraser Health. We collaborate with representatives from relevant specialties and stakeholder groups to review the best available medical literature, recommendations from professional organizations, regional antimicrobial resistance, and local resource availability.

This fiscal year, we have been involved in revision/development of the following PPO's:

- Community acquired pneumonia
- Inpatient sepsis
- Sepsis in the Emergency Department
- Febrile neutropenia
- Peritoneal dialysis peritonitis
- Implantable cardiac devices peri-operative
- Cardiac surgery peri-operative
- Hepatobiliary surgery peri-operative
- Spinal surgery peri-operative

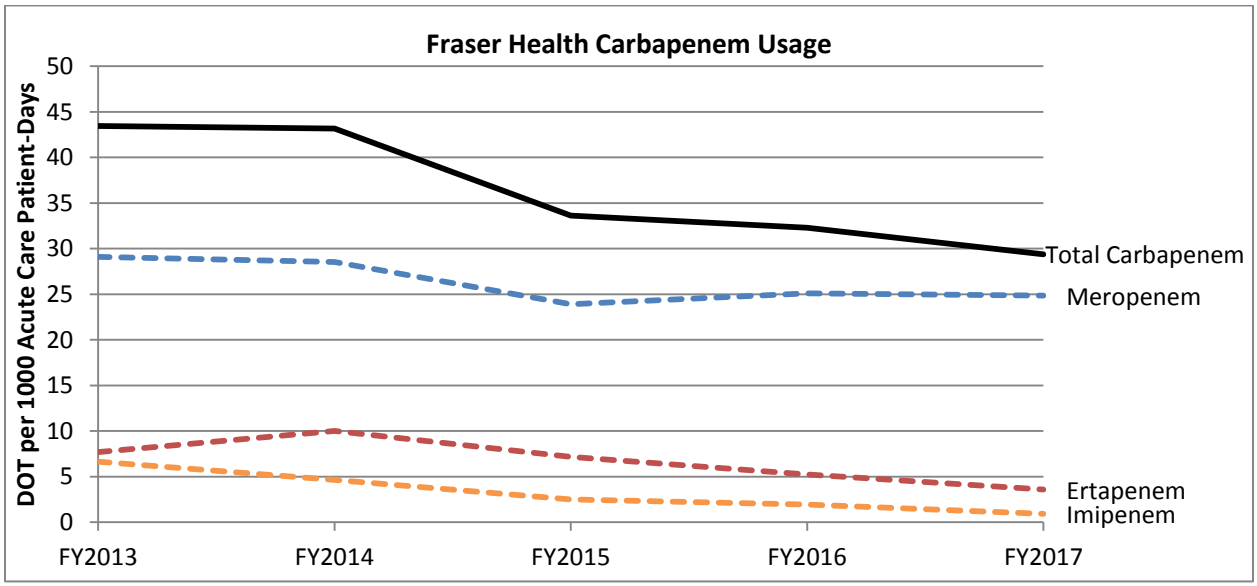
Antimicrobial Usage Trends

The ASP reviews usage trends of targeted antimicrobials on an ongoing basis. This year, we have converted our primary drug usage metric to days of therapy (DOT). DOT is the number of days that a patient receives an antimicrobial agent regardless of dose. This is the most accurate and preferred measure of antimicrobial use, endorsed by the Centers for Disease Control and the US National Healthcare Safety Network.[3] Total DOT is then normalized to the common denominator of 1,000 patient-days. The resulting unit of measure, "DOT per 1,000 patient-days", does not account for interhospital differences in case mix and patient acuity. However, it is a metric that accounts for hospital size and patient volume, and is used by many other institutions.

Usage data reflects admitted inpatients only. It does not reflect treatment of non-inpatients through emergency departments, day-medicine/infusion centres, or the home IV program.

Carbapenems are one of our most potent class of antimicrobials. Resistance to carbapenems in gram-negative infections is a serious public health threat and a strong impetus for antimicrobial stewardship. Carbapenem usage has dropped by 32% since FY2013 (**Figure 3**), and by 9% compared with FY2016. Furthermore, meropenem comprises a greater proportion of our carbapenem usage, which the ASP views favourably given its lower daily cost compared to imipenem and ertapenem.

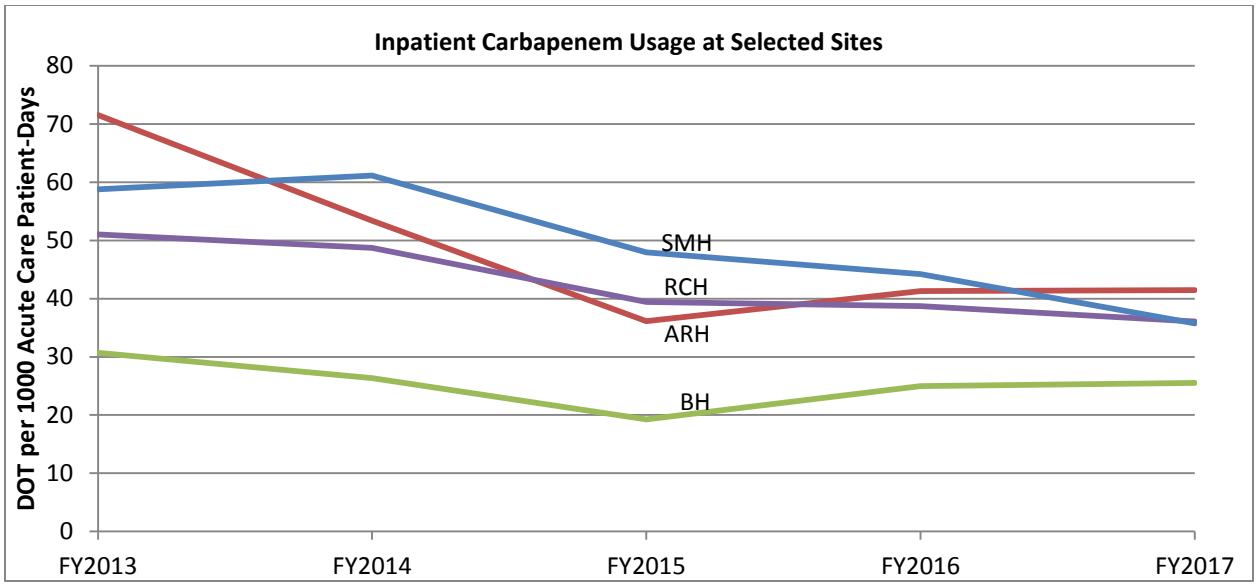
Figure 3. Inpatient carbapenem usage.



In the 2016-17 fiscal year our program expansion has brought on-site regular audit and feedback service to the four largest FH hospitals: ARH, BH, RCH, and SMH. Through these efforts, carbapenem usage has plateaued or been reduce at these four large sites (**Figure 4**). Our experience continues to show the importance of regular, on-site, audit and feedback in order to see reductions in antimicrobial usage.

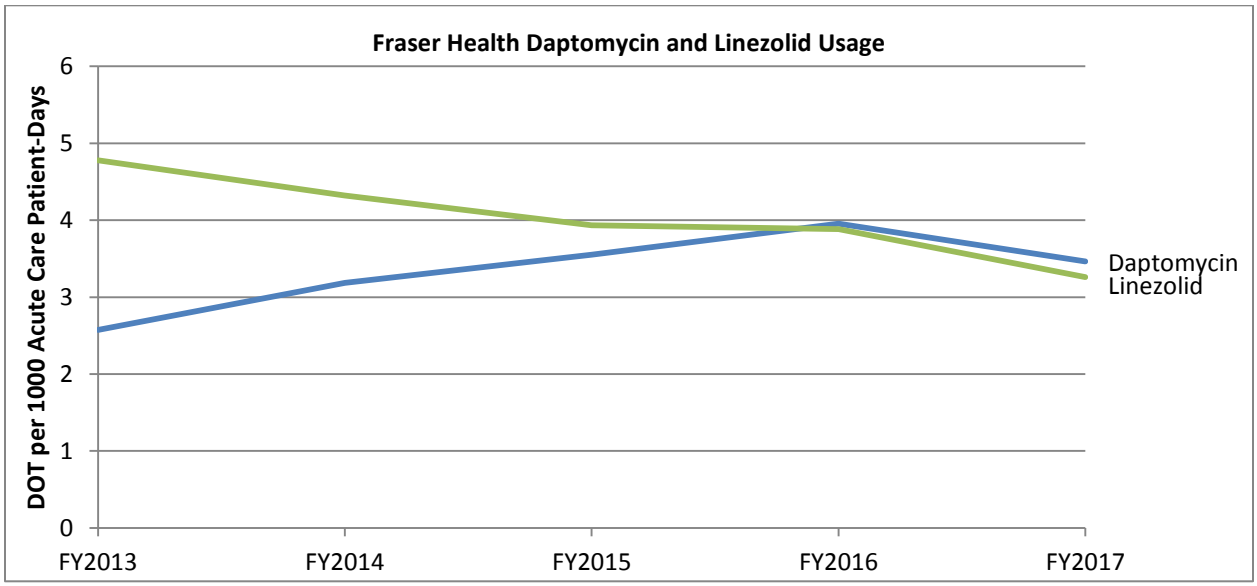
Figure 4. Inpatient carbapenem usage at selected sites.

[3] https://www.publichealthontario.ca/en/eRepository/Antimicrobial_Stewardship_Metrics_Evaluation_2014.pdf



The ASP also tracks usage of two restricted drugs used for resistant gram-positive organisms: linezolid and daptomycin. For the first time, we have seen concomitant reductions in daptomycin and linezolid usage by 13% and 15% respectively (**Figure 5**).

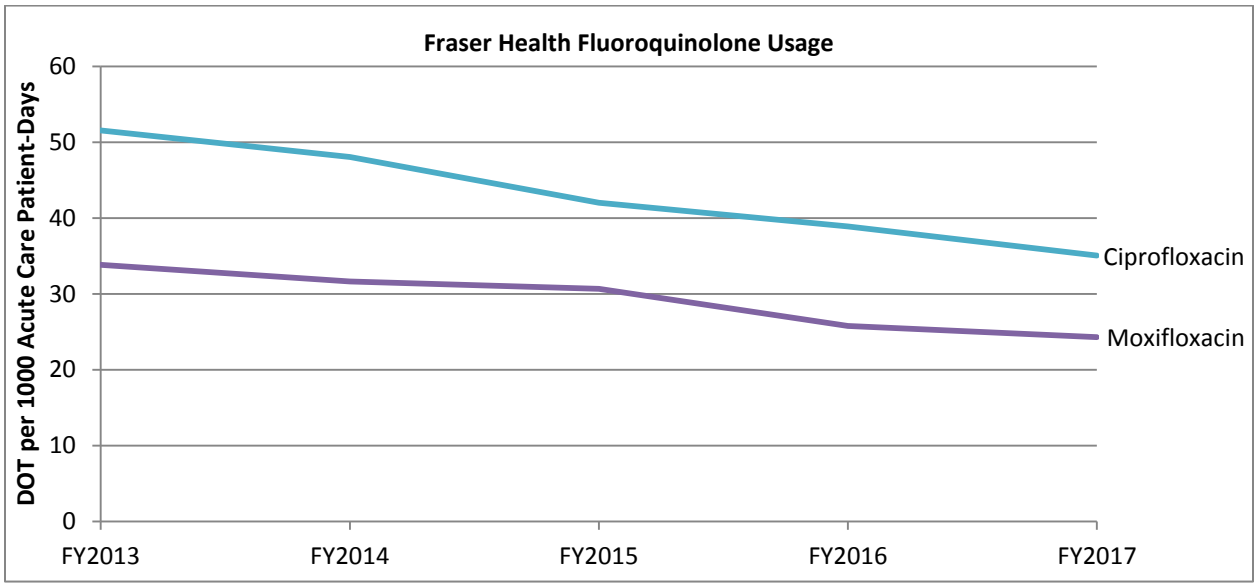
Figure 5. Inpatient linezolid and daptomycin usage.



Fluoroquinolones have come under heightened scrutiny recently due to increased appreciation of their side-effects[4] and strong epidemiological association with *Clostridium difficile* infection.[5] While not a high priority for audit and feedback interventions, the ASP has utilized education, guidelines, and pre-printed orders to guide appropriate use of fluoroquinolones. Ongoing reduction in fluoroquinolone usage is viewed favourably (**Figure 6**).

[4] See https://www.fda.gov/Drugs/DrugSafety/ucm511530.htm and http://www.hc-sc.gc.ca/dhp-mps/medeff/reviews-examens/fluoroquinolones2-eng.php.
[5] Dingle KE et al. Effects of control interventions on *Clostridium difficile* infection in England: an observational study. Lancet Infect Dis. 2017;17:411-421.

Figure 6. Inpatient fluoroquinolone usage.



Please refer to the statistical appendix for hospital-specific usage of targeted antimicrobials.

Financials

Antimicrobial expenditures are presented for combined inpatient and outpatient antimicrobial usage based on pharmacy data. The expenditures exclude some patients on our home IV program as they are supplied by the vendor Calea.

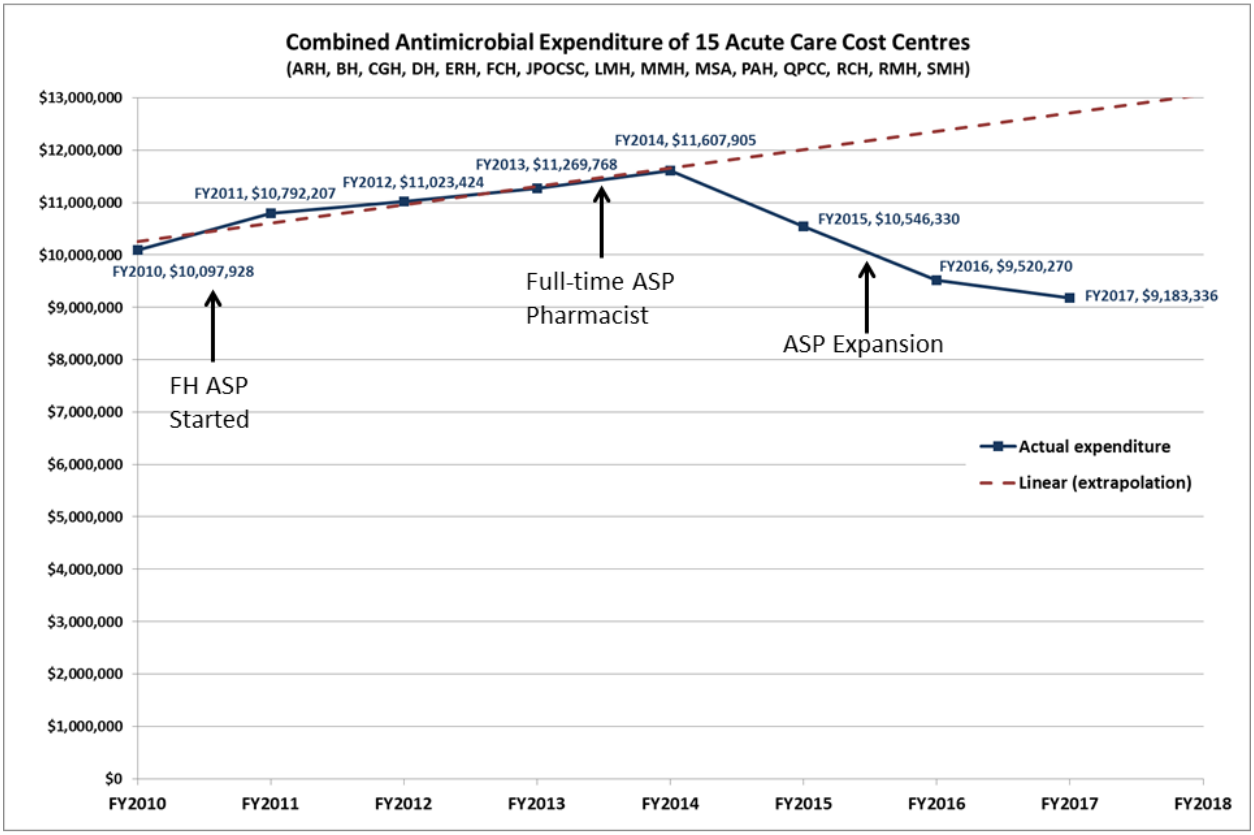
Daptomycin continues to be our agent with the highest expenditure (**Table 1**). However, contract pricing and lower usage of carbapenems has contributed to a net reduction in the combined cost of five restricted antimicrobials drugs.

Combined antimicrobial expenditure across 15 acute care cost centres has continued a strong downward trend over the past three fiscal years **(Figure 7)**. Antimicrobial expenditures in Fraser Health have been reduced by $2,424,569 from their peak in FY2013-14, a 20.9% reduction. Over the past year, antimicrobial expenditures have been reduced by $336,934, a 3.5% reduction

Table 1. Combined cost of five restricted antimicrobial drugs.

Restricted Antimicrobials	Total Inpatient & Outpatient Expenditure (excluding Home IV supplied by Calea)				Difference (FY2017 vs. FY2016)
	FY2014	FY2015	FY2016	FY2017	
Daptomycin	$1,547,352	$1,526,455	$1,827,867	$1,427,050	↓ $400,817
Ertapenem*	$1,425,784	$1,362,119	$1,073,966	$960,607	↓ $113,359
Meropenem*	$1,053,891	$917,240	$531,317	$408,425	↓ $122,892
Linezolid	$717,889	$611,506	$148,025	$67,538	↓ $80,487
Imipenem*	$395,985	$199,474	$69,278	$23,885	↓ $45,393
Total	**$5,140,901**	**$4,616,793**	**$3,650,453**	**$2,887,505**	↓ **$762,948**
*Carbapenems	$2,875,660	$2,478,833	$1,674,561	$1,392,917	↓ $281,644

Figure 7. Combined antimicrobial expenditure of 15 acute care cost centres.



Statistical Appendix

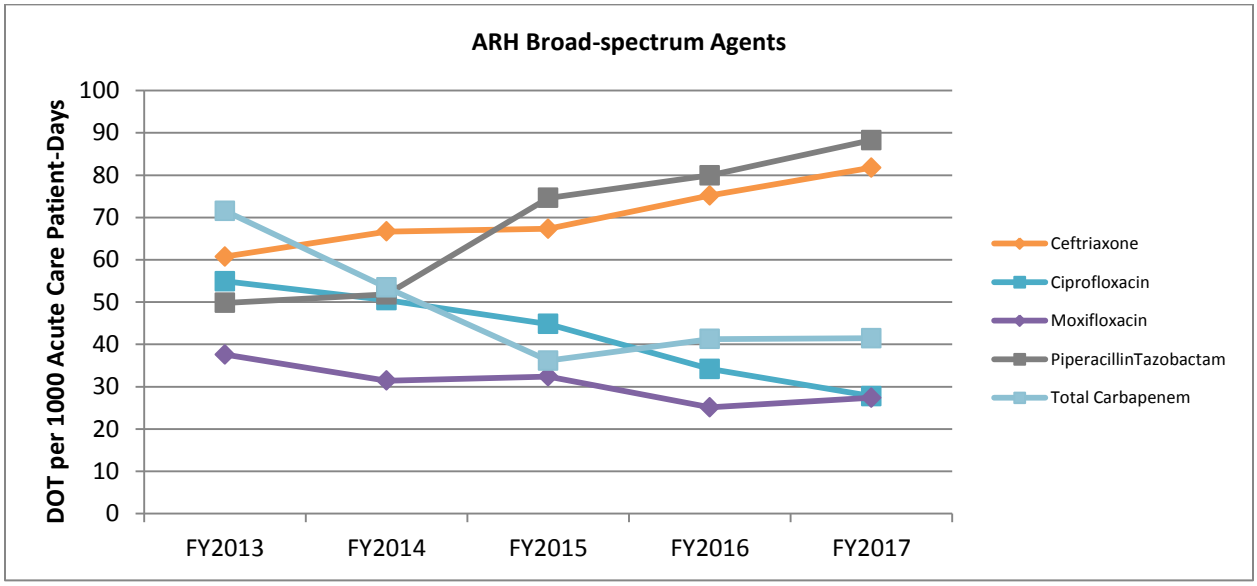
Notes to Interpretation

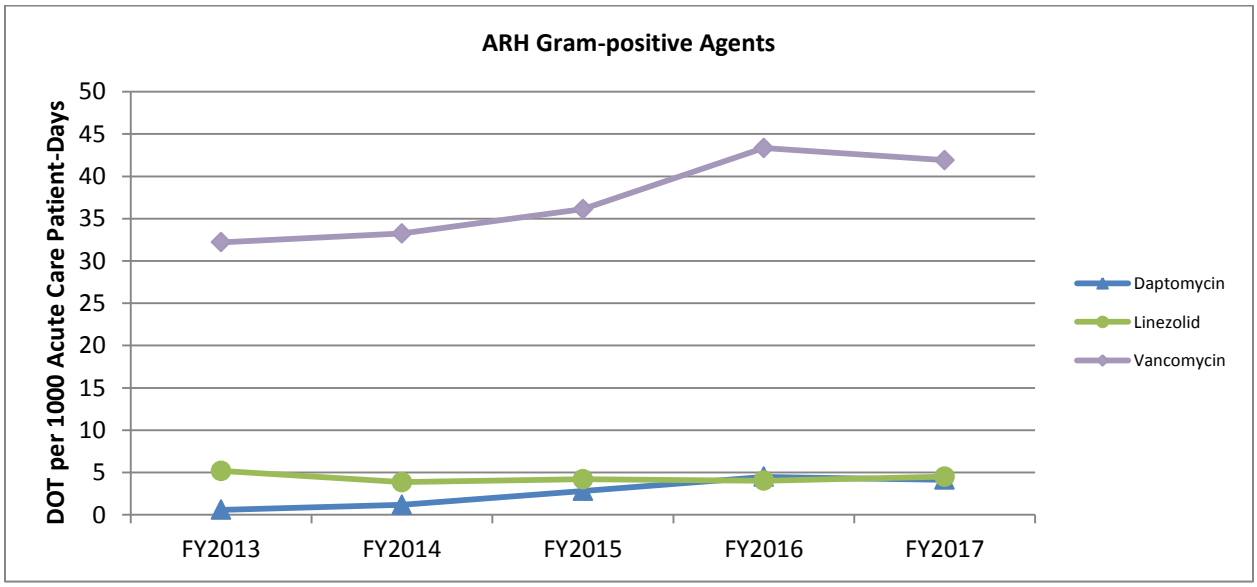
Antimicrobial usage data is expressed in days of therapy (DOT) per 1,000 acute care patient-days. Usage data reflects admitted inpatients only. It does not reflect treatment of non-inpatients through emergency departments, day-medicine/infusion centres, or the home IV program.

The vertical axis for all graphs has been set to the same scale to provide consistency between sites. Broad-spectrum agents active against gram-negative infections are shown separately from gram-positive agents.

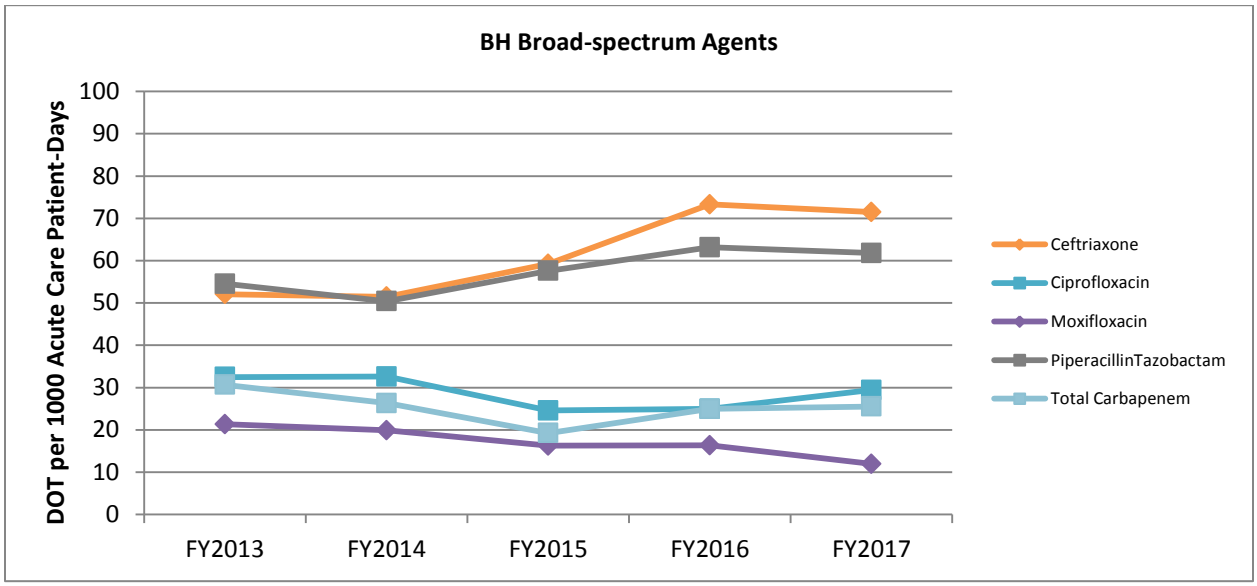
Restricted Antimicrobial Usage by Site

ARH





BH


BH Broad-spectrum Agents
DOT per 1000 Acute Care Patient-Days
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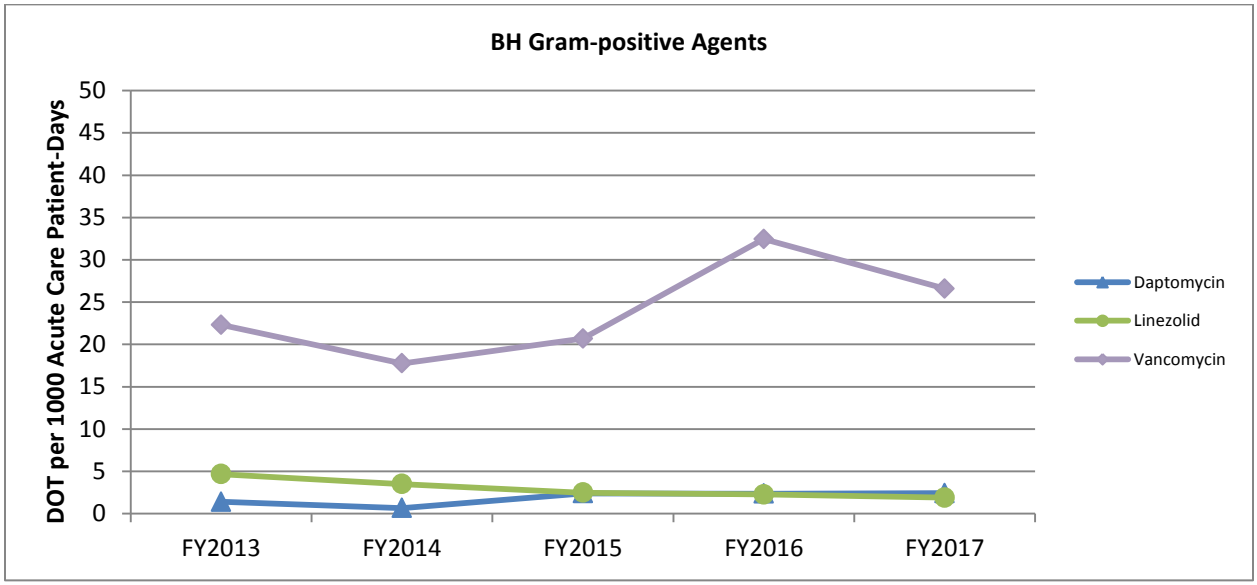
Moxifloxacin
PiperacillinTazobactam
Total Carbapenem


BH Gram-positive Agents
DOT per 1000 Acute Care Patient-Days
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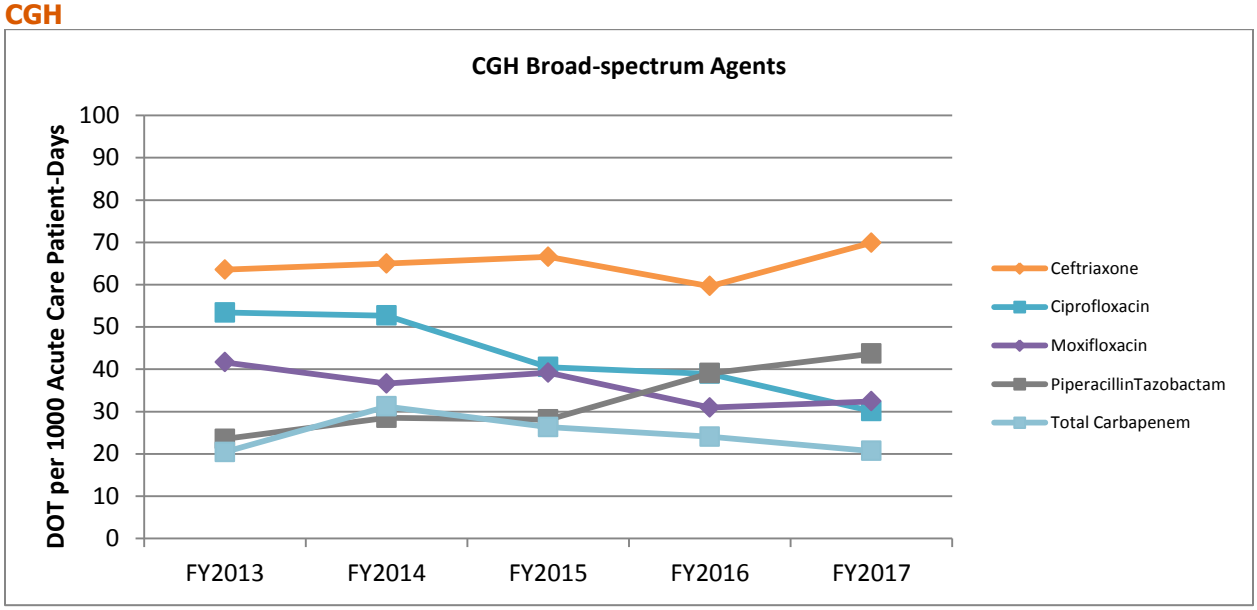
Daptomycin
Linezolid
Vancomycin

CGH


CGH Broad-spectrum Agents
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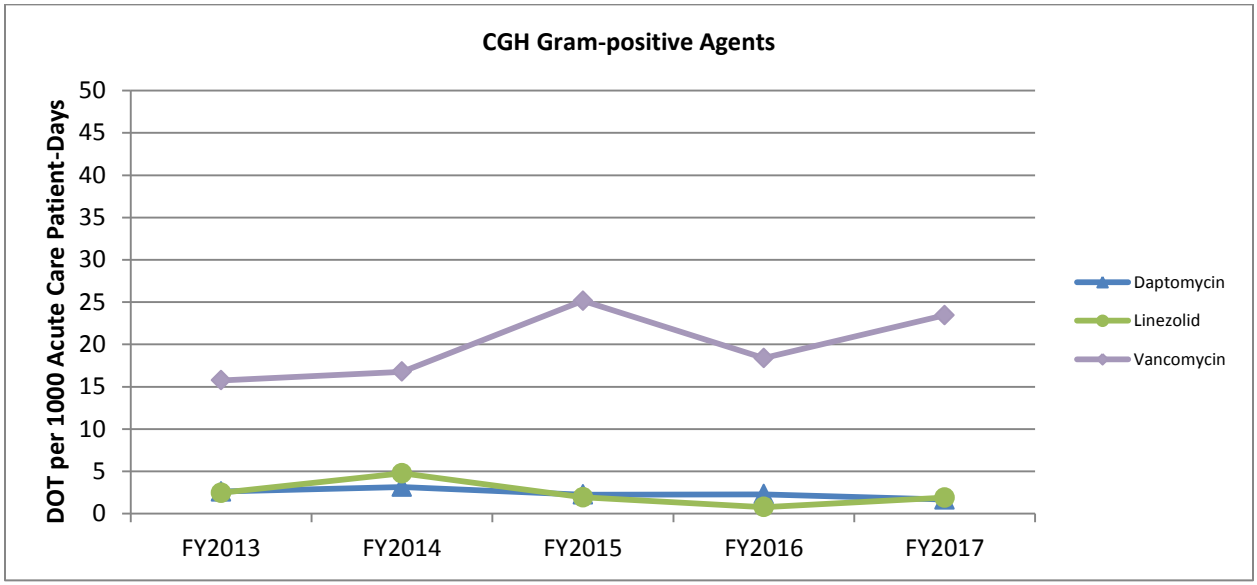
Moxifloxacin
PiperacillinTazobactam
Total Carbapenem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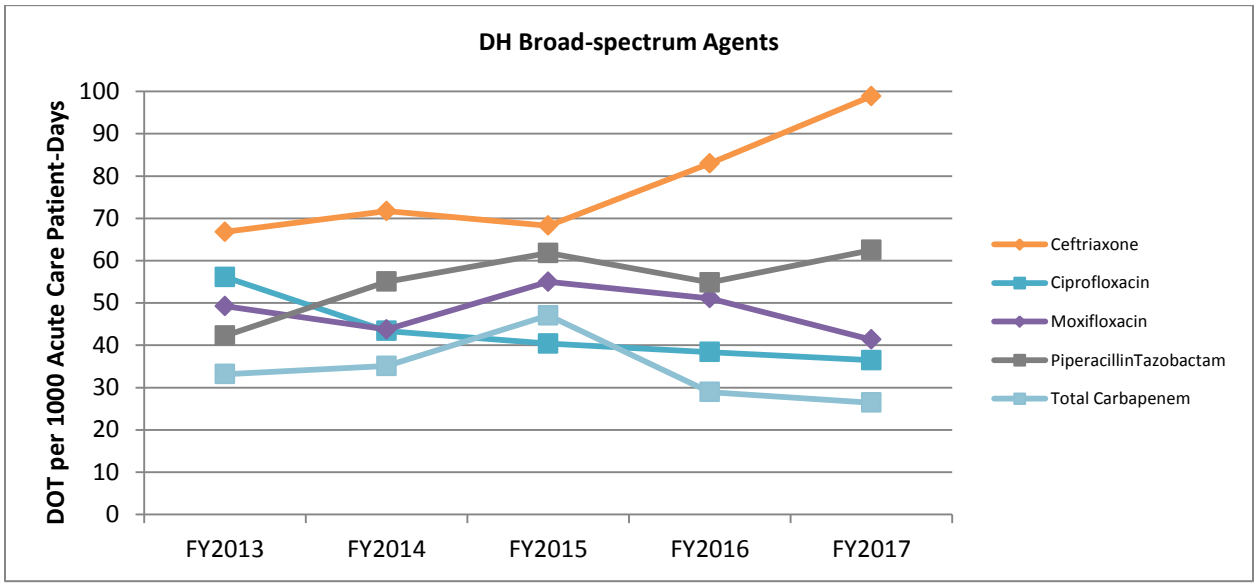
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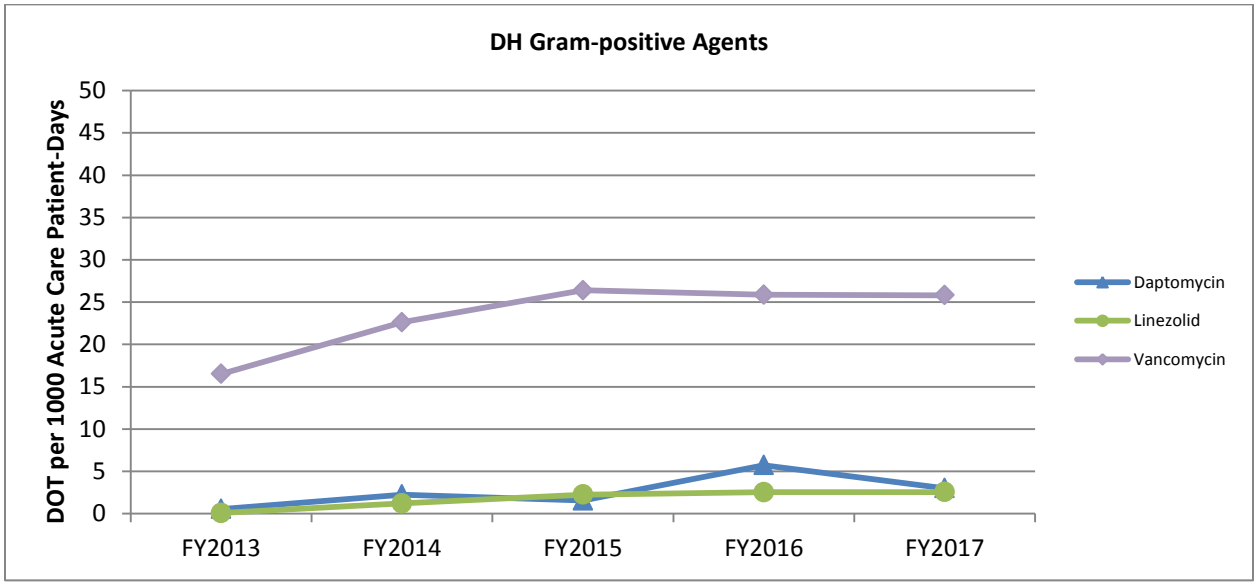
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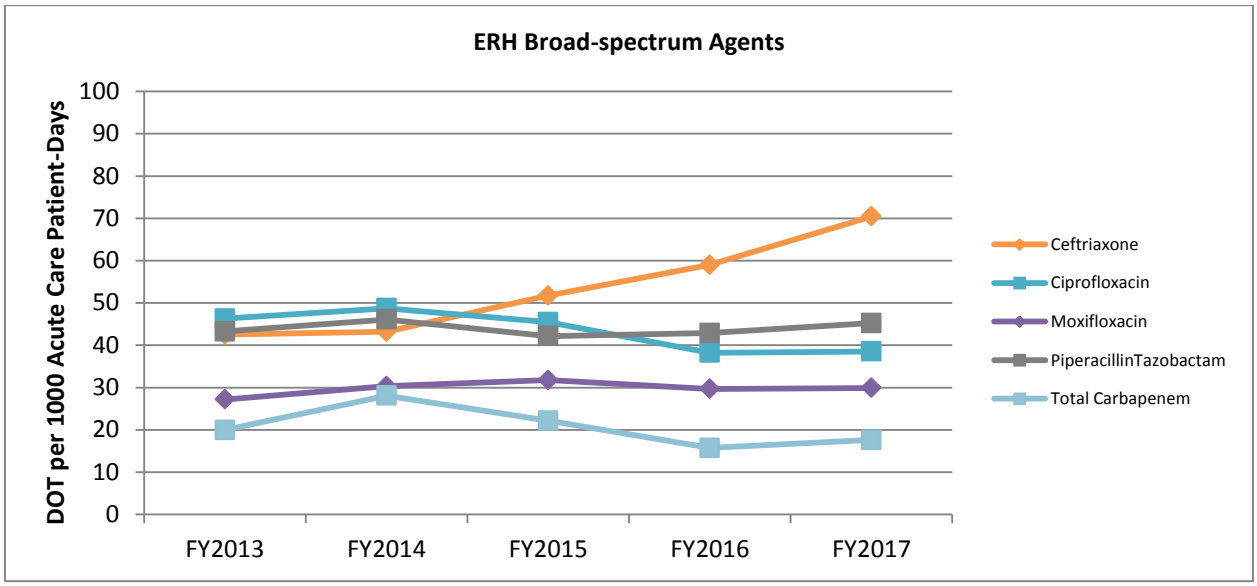
Vancomycin

ERH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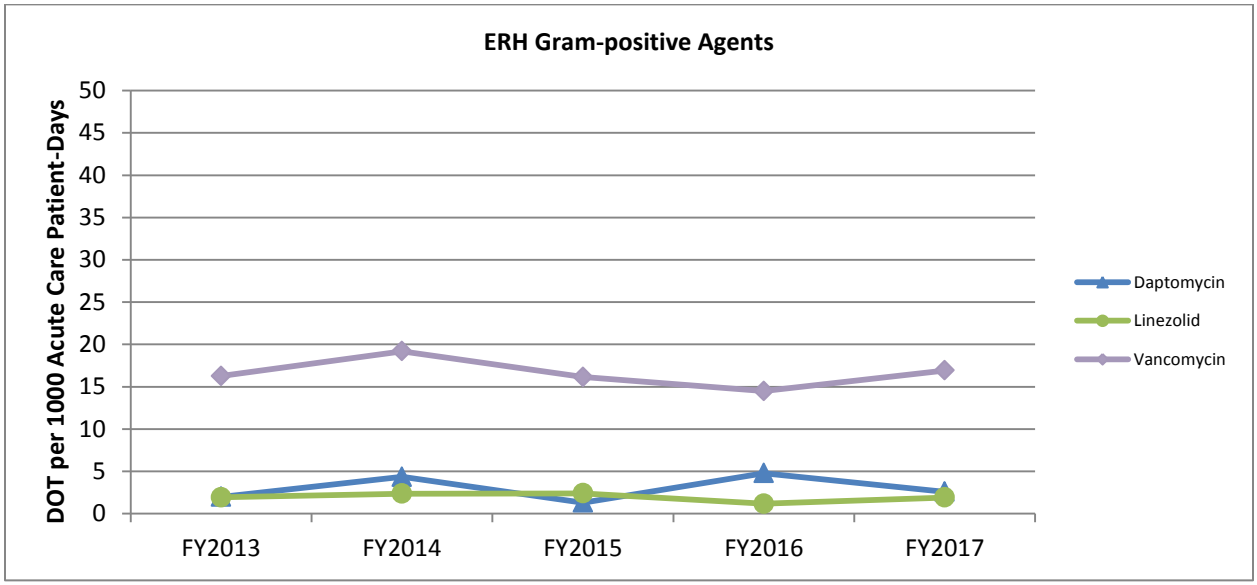
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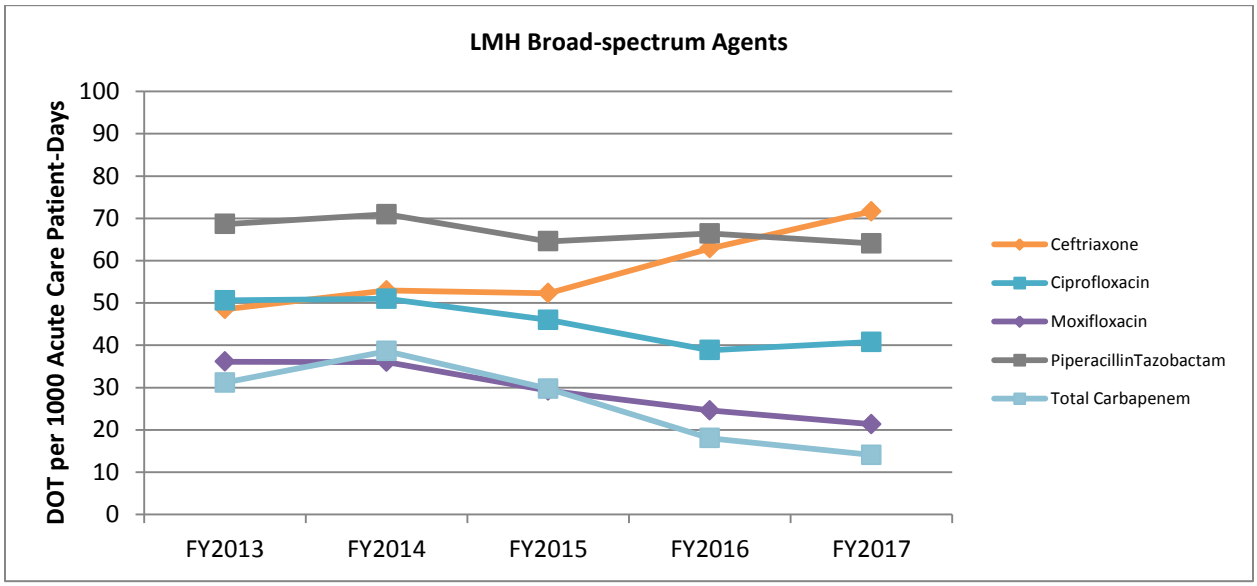
LMH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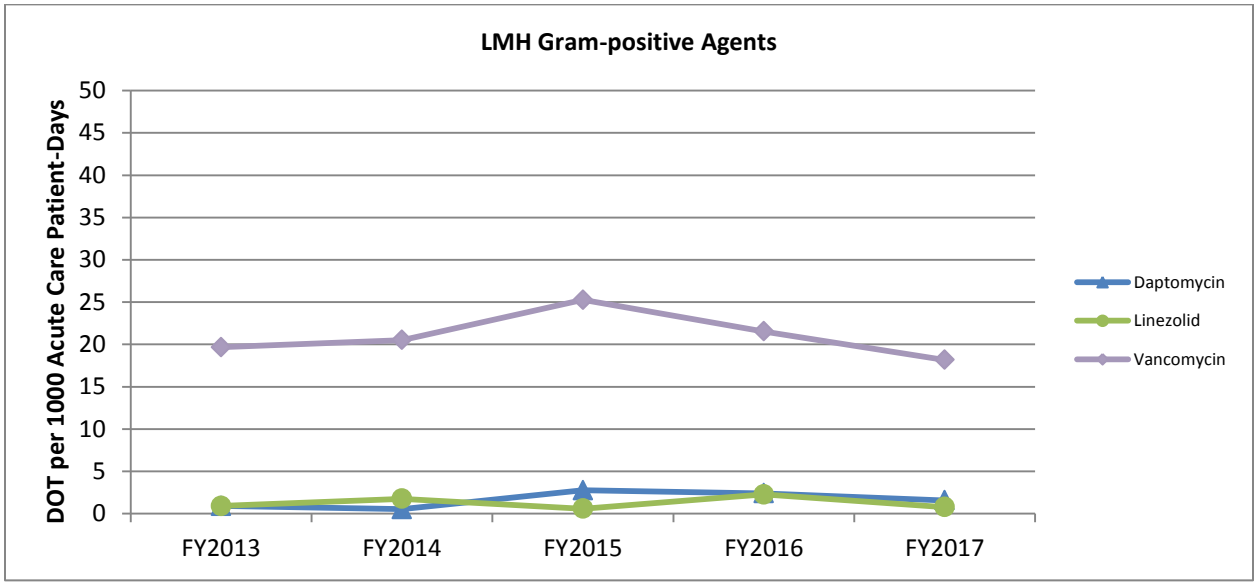
Total Carbapenem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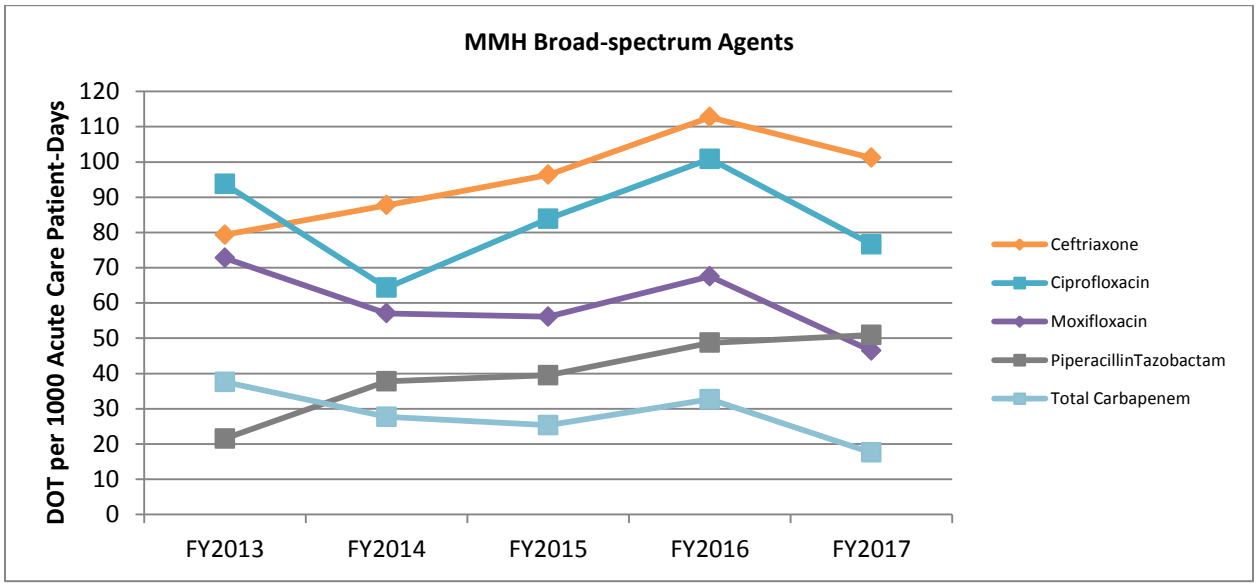
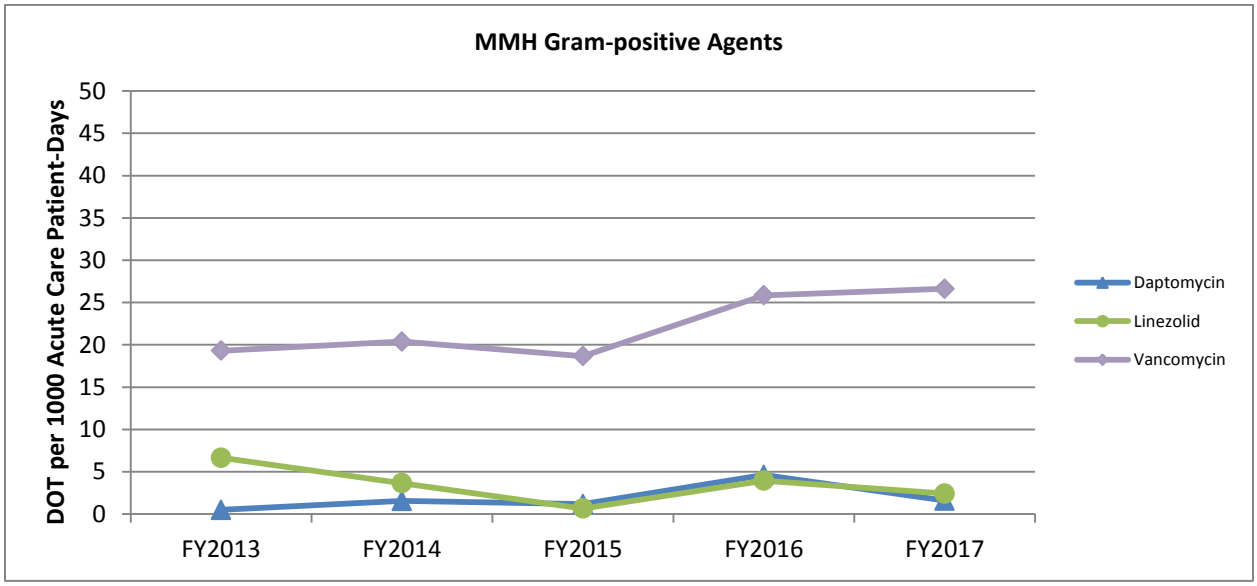
50
45
40
35
30
25
20
15
10
5
0
FY2013
FY2014
FY2015
FY2016
FY2017
Daptomycin
Linezolid
Vancomycin

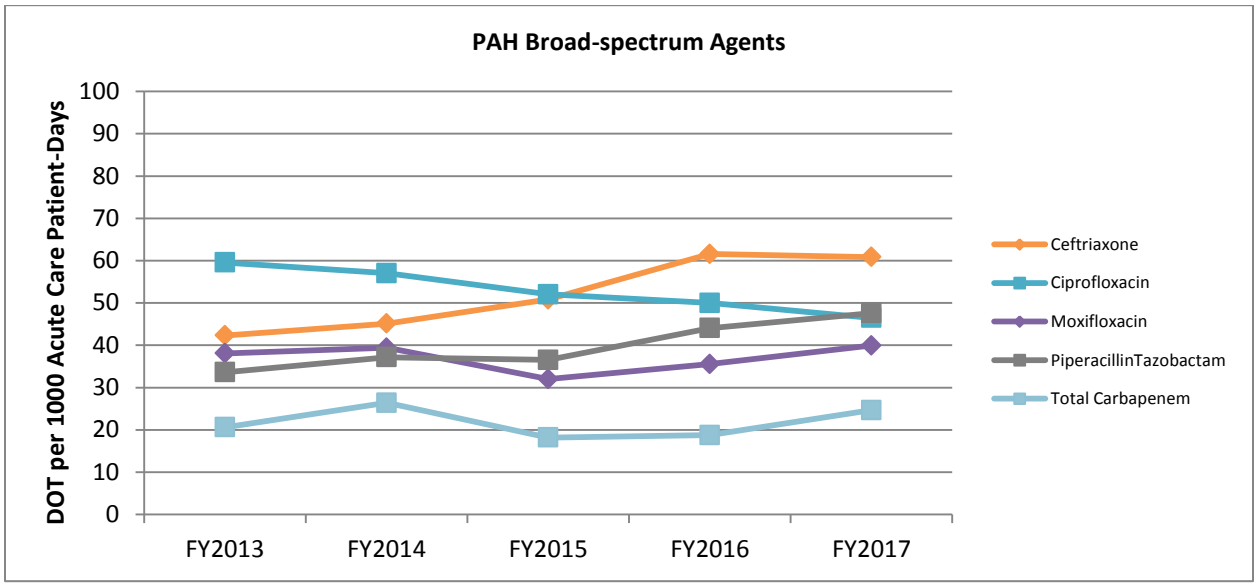
MMH

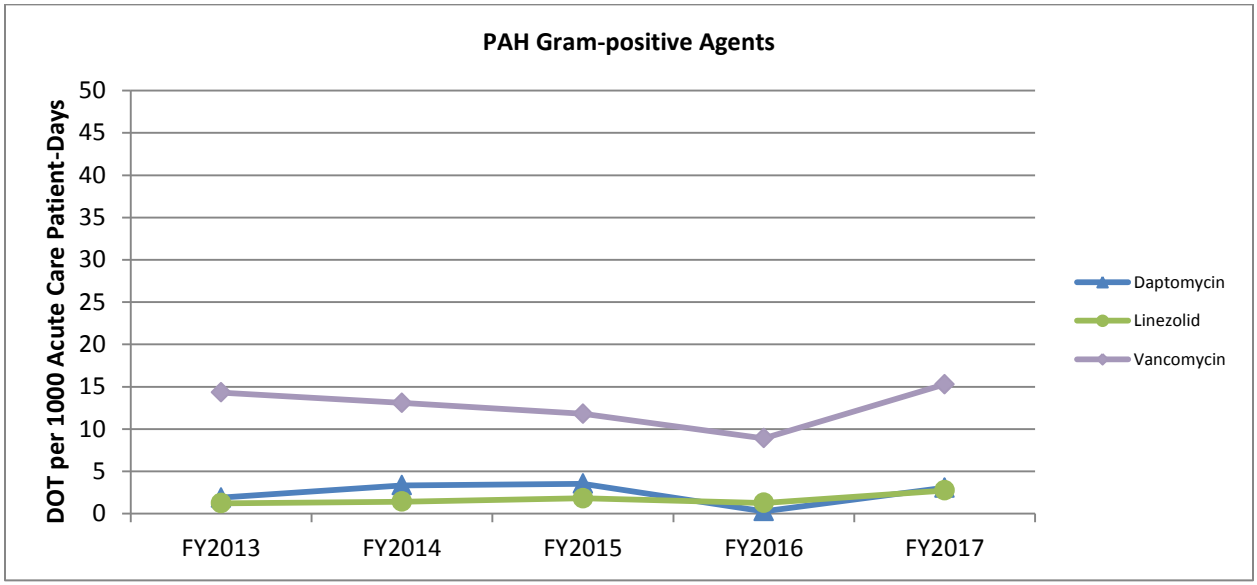


Note: Vertical axis scaled to 120 DOT per 1000 acute care patient-days.

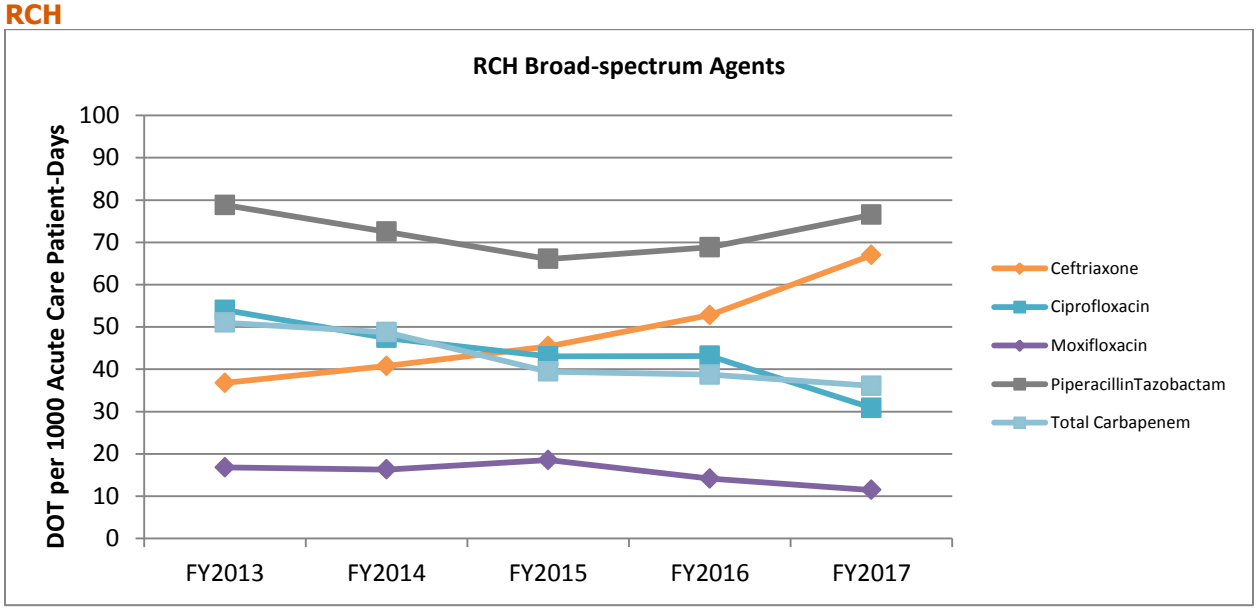


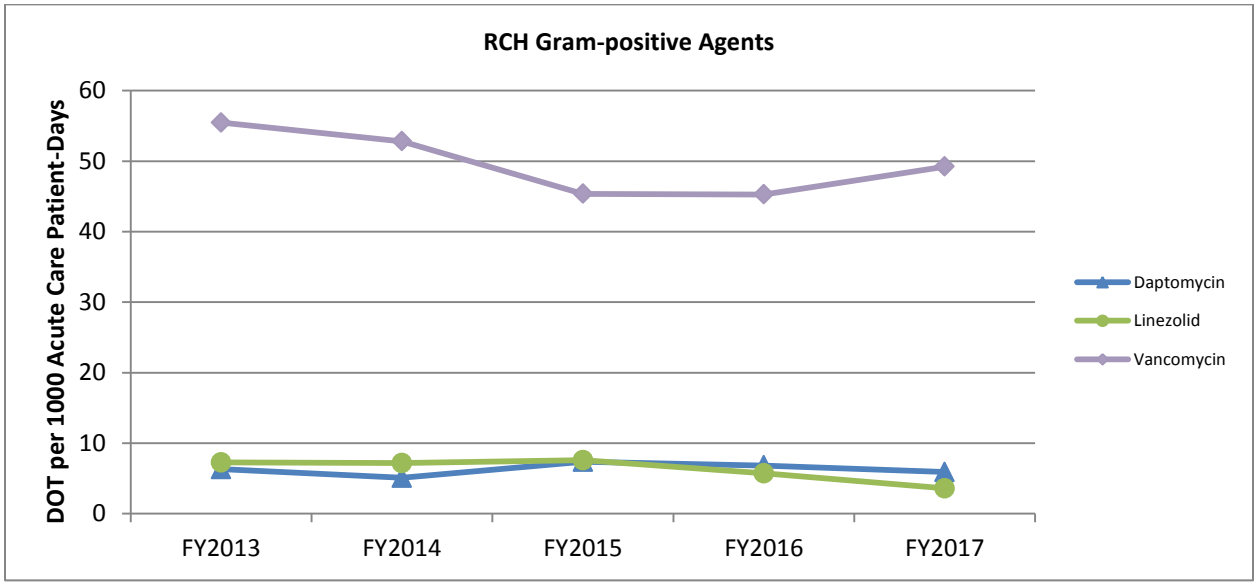
PAH


PAH Broad-spectrum Agents
DOT per 1000 Acute Care Patient-Days
100
90
80
70
60
50
40
30
20
10
0
FY2013
FY2014
FY2015
FY2016
FY2017
Ceftriaxone
Ciprofloxacin
Moxifloxacin
PiperacillinTazobactam
Total Carbapenem


PAH Gram-positive Agents
DOT per 1000 Acute Care Patient-Days
50
45
40
35
30
25
20
15
10
5
0
FY2013
FY2014
FY2015
FY2016
FY2017
Daptomycin
Linezolid
Vancomycin

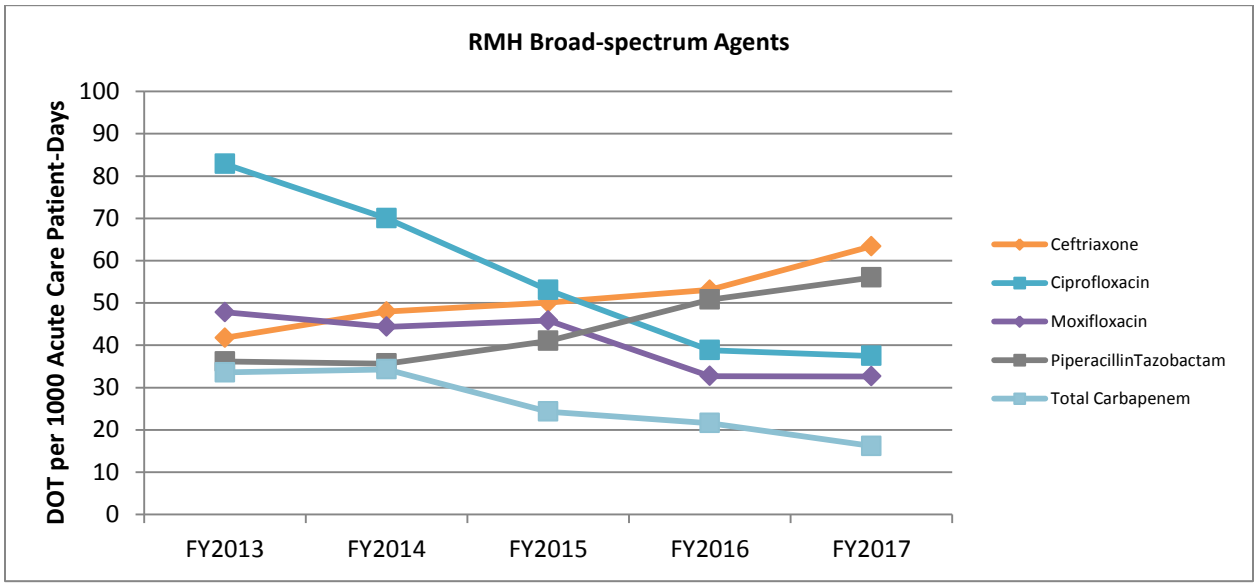
RCH

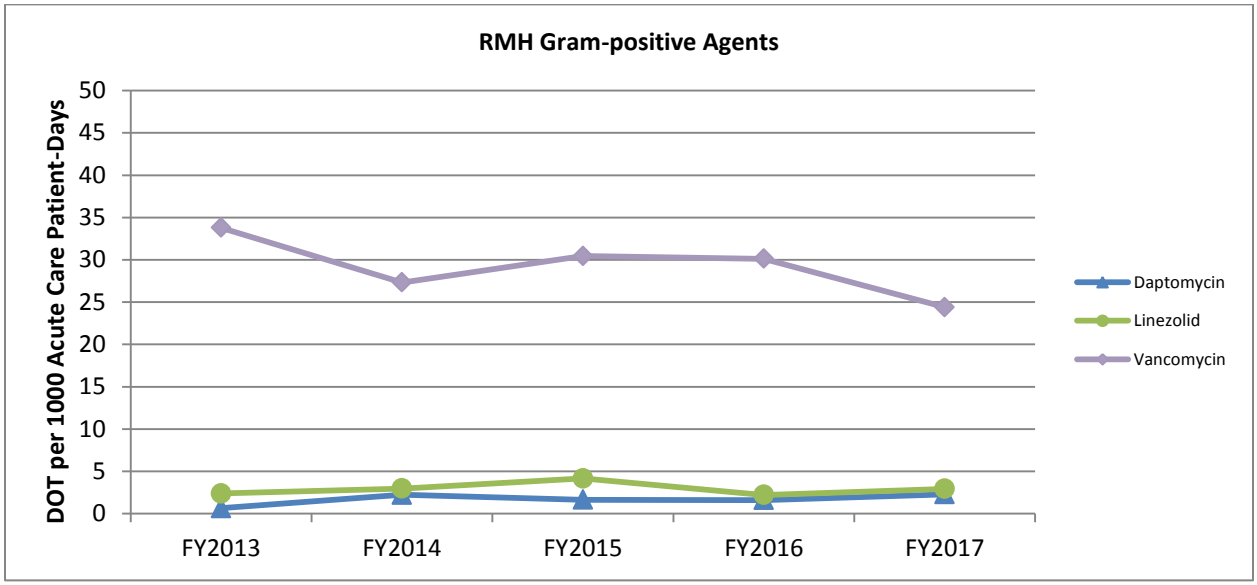




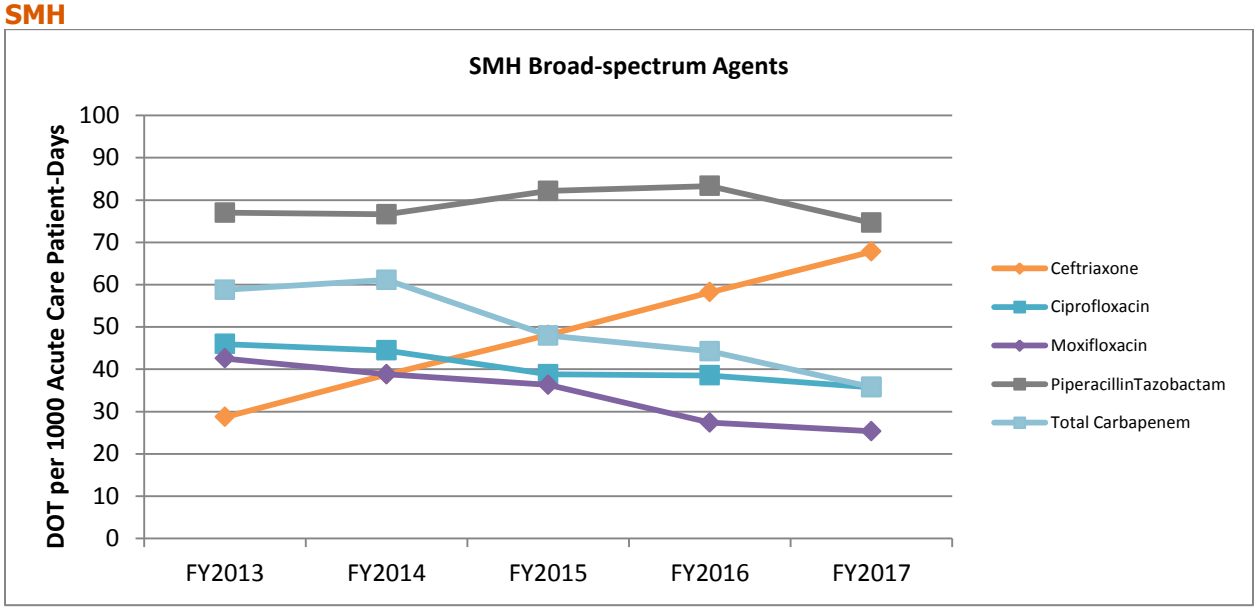
Note: Vertical axis scaled to 60 DOT per 1000 acute care patient-days.

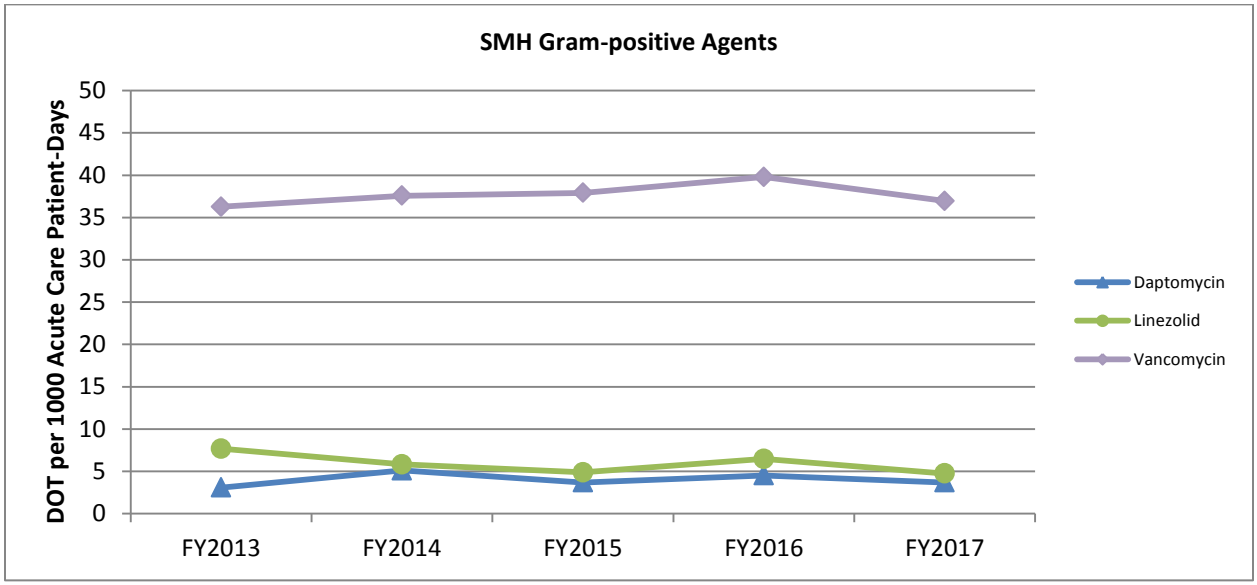
RMH


RMH Broad-spectrum Agents
DOT per 1000 Acute Care Patient-Days
100
90
80
70
60
50
40
30
20
10
0
FY2013
FY2014
FY2015
FY2016
FY2017
Ceftriaxone
Ciprofloxacin
Moxifloxacin
PiperacillinTazobactam
Total Carbapenem


RMH Gram-positive Agents
DOT per 1000 Acute Care Patient-Days
50
45
40
35
30
25
20
15
10
5
0
FY2013
FY2014
FY2015
FY2016
FY2017
Daptomycin
Linezolid
Vancomycin

SMH


SMH Broad-spectrum Agents
DOT per 1000 Acute Care Patient-Days
100
90
80
70
60
50
40
30
20
10
0
FY2013
FY2014
FY2015
FY2016
FY2017
Ceftriaxone
Ciprofloxacin
Moxifloxacin
PiperacillinTazobactam
Total Carbapenem


SMH Gram-positive Agents
DOT per 1000 Acute Care Patient-Days
50
45
40
35
30
25
20
15
10
5
0
FY2013
FY2014
FY2015
FY2016
FY2017
Daptomycin
Linezolid
Vancomycin