# Table of Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Executive Summary</td>
<td>5</td>
</tr>
<tr>
<td>Background</td>
<td>6</td>
</tr>
<tr>
<td>Team</td>
<td>7</td>
</tr>
<tr>
<td>Clinical Activities &amp; Projects</td>
<td>11</td>
</tr>
<tr>
<td>Education</td>
<td>20</td>
</tr>
<tr>
<td>Guidelines</td>
<td>21</td>
</tr>
<tr>
<td>Research</td>
<td>23</td>
</tr>
<tr>
<td>Metrics</td>
<td>25</td>
</tr>
<tr>
<td>Awards</td>
<td>26</td>
</tr>
<tr>
<td>Financials</td>
<td>27</td>
</tr>
<tr>
<td>Appendix 1</td>
<td>31</td>
</tr>
<tr>
<td>Appendix 2</td>
<td>36</td>
</tr>
</tbody>
</table>
Acknowledgements

The continued success of Providence Health Care's Antimicrobial Stewardship Program has been possible thanks to the ongoing support of many teams and individuals at Providence.

We would like to specifically thank the following individuals and groups for their unique contributions to our program:

» Salomeh Shajari for volunteering her time in developing our audit and feedback database, and for extracting information from the database for our presentations.

» Dr. David Patrick and his “Do Bugs Need Drugs?” team for providing guidance in measuring antimicrobial utilization trends.

» Surgeons and fellows in the Division of General Surgery for letting us participate in weekly surgery rounds.

» Physicians and fellows in the Division of Critical Care Medicine for letting us develop antimicrobial stewardship “bullet rounds” in the Intensive Care Unit.

We would also like to thank the following groups for their engagement in improving our program this year:

» All prescribers at PHC

» Clinical pharmacists

» Medical Microbiology Laboratory

» Physicians, residents and medical students

» Nurse practitioners

» Medical microbiologists

» Division of Infectious Diseases physicians

» PHC Infection Prevention and Control (IPAC)

» Vancouver Coastal Health’s Antimicrobial Stewardship team (ASPIRES)
1.1
Executive Summary | Background
The Antimicrobial Stewardship Program (ASP) at Providence Health Care (PHC) was implemented April 1, 2013.

Now in our second year, our interdisciplinary program continues to coordinate interventions to guide the judicious use of antimicrobials and strives to optimize patient safety and reduce costs.

In 2014, ASP’s financially sustainable initiatives included the following:

- Ongoing audit and feedback of antimicrobial prescriptions. We made 1316 interventions with an 84% acceptance rate.
- Participation in two new sets of rounds: antimicrobial “bullet rounds” in the Intensive Care Unit and weekly multidisciplinary rounds with the Division of General Surgery at St. Paul’s Hospital.
- Collaboration and research with the Medical Microbiology Laboratory to improve appropriateness and timeliness of antimicrobial therapy for patients with bloodstream infections.
- Partnership with Infection Prevention and Control (IPAC) to address comprehensive management of urinary tract infections in residential care and *Clostridium difficile* infection among in-patients
- A variety of education sessions for medical students, residents and physicians.
- Development of high yield and locally relevant guidelines for infectious syndromes and antibiotic prophylaxis in surgeries.

Measures of success have included:

- Significant decrease in specific antibiotic utilization.
- Direct cost savings of $214,935 in antimicrobial expenditures.
- The lowest reported PHC-associated *C. difficile* infection incidence rate (5.6 cases/10,000 patient days).
- Improved timing of antibiotic prophylaxis administration for selected surgeries.
- Continued dialogue and engagement with prescribers around “Bugs and Drugs.”

This report describes the significant progress that ASP has made in achieving its goal of improving health outcomes and reducing antimicrobial resistance.

Sincerely,

Antimicrobial Stewardship Program
1.1 Background

We are facing an era of increasing antimicrobial resistance threats.

The Antimicrobial Stewardship Program believes appropriate antimicrobial prescribing can be achieved through multifaceted approaches that engage prescribers in dialogue on “bugs and drugs,” provide relevant and timely results from diagnostic tests, and educate prescribers at the point-of-care.

The ASP’s Vision and Mission guide how we effectively move towards our goal of improved health outcomes and reduced antimicrobial resistance.

VISION
To use innovative evidence-informed strategies to transform antimicrobial prescribing.

MISSION
To ensure patients and residents at Providence Health Care receive timely, effective, and safe antimicrobial therapy.

The misuse of antibiotics has contributed to the growing problem of antibiotic resistance, which has become one of the most serious and growing threats to public health.
2.0 Team

St. Paul’s Hospital
Antimicrobial Stewardship Program success is dependent on strong leadership support and multidisciplinary team participation.

*Did you know?* Antimicrobial Stewardship Program success is dependent on strong leadership support and multidisciplinary team participation.

*Left to Right:* Dr. Peter Phillips, Dr. TC Yang, Dr. Victor Leung, Dr. Tom Havey, Allison Kirkwood, Dr. Chantal Leger, Dr. Sylvie Champagne, Dr. Marc Romney, Luciana Frighetto, Dr. Mark Hull, Dr. Glen Brown. *Missing:* David Thompson
2.0 Team

**CLINICAL TEAM**

Allison Kirkwood and Dr. Victor Leung conduct the daily activities of the program. They are accountable for:

- ensuring visibility of the program across the organization.
- designing and implementing new ASP projects.
- liaising with external organizations to promote antimicrobial stewardship.

**OPERATIONAL TEAM**

Luciana Frighetto and David Thompson provide high-level management of the program. They are responsible for:

- ensuring the ASP meets targets.
- approving program scope, resources and budgets.
- informing the Senior Leadership Team and the PHC Board of Directors on the overall status of the program.

You can contact the ASP Physician (778-879-2339) or the ASP Pharmacist (604-809-0087) for all antimicrobial stewardship questions.
Team

ANTIMICROBIAL STEWARDSHIP SUBCOMMITTEE

The Antimicrobial Stewardship Subcommittee meets monthly to address antimicrobial utilization topics and provide feedback on ASP guidelines.
3.0 Clinical Activities & Projects
A majority of our clinical activities use the “audit and feedback” approach. The clinical ASP team prospectively audits the charts of patients and residents receiving targeted antimicrobials to determine opportunities to:

- Modify empiric therapy.
- Target therapy to specific pathogens.
- Optimize dose of antimicrobial therapy.
- Shorten the duration of antimicrobials.
- Discontinue antimicrobials.
- Transition to oral administration.
- Involve the Division of Infectious Diseases consult service.

Feedback is based on our review of the medical chart and diagnostic test results, and discussed with the prescriber.

We use a database to collect variables, such as indication for antimicrobials, and track the acceptance rate of our feedback and recommendations. The database generates individualized form letters highlighting our assessment and recommendation, and the letter is left in the interdisciplinary section of the patient chart.

This year we recorded 1316 audit and feedback interventions. The acceptance rate was 84%.
Clinical Activities & Projects

INTENSIVE CARE UNIT – ANTIMICROBIAL STEWARDSHIP BULLET ROUNDS

In collaboration with the Division of Critical Care Medicine (CCM), we started biweekly “bullet rounds” to review all patients receiving antimicrobials in the Intensive Care Unit (ICU) at St. Paul’s Hospital.

These bullet rounds allow ASP to better understand local CCM approaches to prescribing antimicrobials. The ASP clinical team meets with the ICU clinical pharmacist and the CCM Fellow to review each case, and recommendations for changing therapy are discussed.

We will use these findings to develop more targeted approaches to assist in judicious prescribing. Thus far, feedback from the CCM fellows has been positive.
Clinical Activities & Projects

GENERAL SURGERY ANTIMICROBIAL STEWARDSHIP ROUNDS

Thanks to a collaboration with the Division of General Surgery, we now participate in weekly multidisciplinary rounds to review all patients admitted to surgery. Antibiotic recommendations or infectious diseases referrals are discussed. The surgery clinical pharmacist and the clinical ASP team help ensure therapeutic modifications and facilitate a patient’s discharge from hospital.
Clinical Activities & Projects

BLOODSTREAM INFECTION ALERTS

Bloodstream infections are critical laboratory results. We are fortunate to have an onsite Medical Microbiology Laboratory which we collaborate with to review blood cultures. These results drive part of ASP's audit and feedback interventions.

The use of matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) identification directly from blood cultures, combined with direct antimicrobial susceptibility testing, offers prescribers the opportunity to initiate early and appropriate antimicrobial therapy.

During quarter two of this fiscal year, Dr. Tom Havey, Antimicrobial Stewardship Research Fellow, started a project to assess the relative impacts of using MALDI-TOF MS used alone or combined with audit and feedback interventions (see Research section).

Microbiology technologist working with blood cultures

Dr. Romney reviews MALDI-TOF MS results from direct blood cultures
Clinical Activities & Projects

“WAR ON THE SPORE” CLOSTRIDIUM DIFFICILE INFECTION MANAGEMENT

Prevention and management of Clostridium difficile infection (CDI) is a priority at PHC. In collaboration with Infection Prevention and Control (IPAC), we have expanded the “War on the Spore” project and started to prospectively review all inpatient cases of laboratory confirmed C. difficile. The assessment includes:

- Determination of CDI versus C. difficile asymptomatic colonization.
- Review of concurrent antimicrobials.
- Severity assessment based on regional CDI guidelines.
- Review of other medications that may influence CDI symptom duration.

All reviews are discussed with the medical team and documented in our database. Notes are left in the patient’s chart using our audit and feedback mechanisms.

The PHC-associated CDI incidence rate (5.7 per 10,000 patient days) has been the lowest reported at PHC. This is down 35% compared to last fiscal year.

Real time BBM alerts to the ASP Clinical team for all inpatients with laboratory confirmed C. difficile
Clinical Activities & Projects

RESIDENTIAL CARE URINARY TRACT INFECTIONS AND ASYMPTOMATIC BACTERIURIA

We continued our collaboration with Infection Prevention and Control (IPAC) to optimize the diagnosis of urinary tract infections (UTI) and asymptomatic bacteriuria (ASB). With implementation of a combined toolkit and management guidelines, there is a sustained decrease in the rate of urine cultures submitted to the Medical Microbiology Laboratory. This work was associated with decreased antibiotic prescriptions for treating UTIs and/or over-treating ASB.

Antibiotic therapy for asymptomatic bacteriuria offers no benefit and increases harm for persons in residential care.

Treatment of asymptomatic bacteriuria in residential care facilities exposes residents to unnecessary harm from antibiotics.

Urine cultures ordered at PHC residential care facilities. Since implementation of the project in 2013, there has been a significant decrease in urine cultures ordered.
Clinical Activities & Projects

CLINICAL & SYSTEMS TRANSFORMATION

Clinical & Systems Transformation (CST) is a joint undertaking between Providence, Vancouver Coastal Health and Provincial Health Services Authority. These organizations have committed to ensuring the CST project delivers an integrated electronic health record and standardized clinical practices.

Antimicrobial Stewardship was identified as one of the project priorities for CST. Our program worked on reviewing all antimicrobials within standardized order sets. We met with the CST project teams to help them understand our current state workflows.

Our hope is that CST can improve antimicrobial stewardship across all three health organizations.

ASP at PHC, VCH and PHSA collaborated to review all CST order sets with antimicrobial content.
5.0 Education

Our education program is focused on point-of-care dialogue, formal and informal rounds presentations, and supervision of trainees.

The following activities made up the delivery of our education program in 2014:

» Dialogue for teaching and learning with prescribers on the wards or during phone conversations during audit and feedback interventions

» Monthly rounds to residents and medical students rotating on the General Surgery service and Infectious Diseases Consultation service, and bimonthly rounds for the trainees on the Clinical Teaching Unit (Medicine).

» Evening Journal Clubs designed to raise awareness of the ASP with practicing physicians.

» Three fellows in the Division of Infectious Diseases and one Pharmacy doctoral candidate completed rotations under the supervision of the ASP clinical team.
Guidelines

We expanded our guidelines and pathways in 2014 by engaging relevant specialist services to target high-yield antimicrobial stewardship opportunities. We used local epidemiology to rationalize antimicrobial use and produced guidelines for the following scenarios:

» Empiric therapy of intra-abdominal infections
» Intravenous antimicrobial to oral conversions
» *Staphylococcus aureus* bacteremia
» *Clostridium difficile* infection
» Penicillin allergy.
» Pre-operative and intraoperative antimicrobial prophylaxis (VCH/PHC combined)

Guidelines are posted on our ASP website. The guidelines for *S. aureus* bacteremia and *Clostridium difficile* infection are attached directly to patient results on the patient electronic health record. (See appendix for copies of the guidelines).
7.0 | 8.0 | 9.0
Research | Metrics | Awards
Research

We supervised or co-supervised three research projects with final results available next fiscal year. We will continue to study drug utilization trends before and after implementation of ASP using interrupted time series analyses (see Metrics section).

**USING MATRIX-ASSISTED LASER DESORPTION/IONIZATION TIME-OF-FLIGHT MASS SPECTROMETRY (MALDI-TOF MS) COUPLED WITH AUDIT AND FEEDBACK TO IMPROVE ANTIMICROBIAL TREATMENT FOR PATIENTS WITH BLOODSTREAM INFECTIONS**

Dr. Tom Havey, an Antimicrobial Stewardship research fellow, conducted a three-phase quality improvement project to assess the impacts of a new laboratory technology combined with an ASP audit and feedback approach on improving appropriate antimicrobial treatment for patients with bloodstream infections.

MALDI-TOF MS can be used to identify organisms directly from positive blood cultures. During the course of this study, the frequency of using MALDI-TOF for direct blood culture identification progressed from intermittent to twice daily for all positive blood cultures identified during weekdays. The results of the MALDI-TOF identification were either linked to routine microbiology laboratory notification or systematic audit and feedback interventions.

This project was supervised by doctors Marc Romney and Victor Leung and funded by a post-residency research award from the Association of Medical Microbiology and Infectious Disease (AMMI) Canada.
Research

DAPTOMYCIN USE EVALUATION AT PROVIDENCE HEALTH CARE

Emma Kim, a fourth year pharmacy student, participated in a daptomycin use evaluation.

Daptomycin utilization has been increasing since it was first approved by the PHC Pharmacy & Therapeutics (P&T) committee on August 1, 2008. Daptomycin was our top antimicrobial expenditure in 2014.

The primary objective of this study is to describe the spectrum of daptomycin prescribing practices. The findings will help inform revisions of the PHC P&T formulary restrictions for Daptomycin.

This study was supervised by Allison Kirkwood and Dr. Victor Leung.

COMPARATIVE EFFECTIVENESS OF CLOXACILLIN OR CEFAZOLIN VERSUS VANCOMYCIN EMPIRIC THERAPY IN PATIENTS WITH METHICILLIN-SUSCEPTIBLE STAPHYLOCOCCUS AUREUS (MSSA) BACTEREMIA

Dr. Davie Wong, a fourth year Infectious Diseases Fellow, will study whether empiric therapy with cloxacillin or cefazolin compared to vancomycin is associated with differences in survival and microbiological cure in patients with MSSA bacteremia.

The findings of this study may inform revision of our S. aureus bacteremia guidelines.

This study was supervised by Dr. Victor Leung.
8.0 Metrics

AUDIT AND FEEDBACK
- We audited 1610 patient charts and 1316 of these required interventions
- The most frequently reviewed syndromes included intra-abdominal infections, bloodstream infections, pneumonia, urinary tract infections and skin and soft-tissue infections

CLOSTRIDIUM DIFFICILE INFECTION
- We audited 77 in-patient cases of laboratory confirmed C. difficile and 56 of the cases required intervention

BACTEREMIA REVIEWS
- We audited 237 bloodstream infections and 202 required interventions

ANTIMICROBIAL UTILIZATION DATA
We developed the capacity to better extract drug dispensing data from our pharmacy information systems and convert the results to Defined Daily Doses (DDDs).

The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults. It provides a fixed unit of measurement, independent of price and dosage form, which enables us to assess trends in drug consumption.

The final metric is a rate expressed as DDDs/10000 patient days.

To assess trends more rigorously before and after implementation of ASP, we received guidance from the “Do Bugs Need Drugs?” team to use interrupted time series analyses.

Details of DDDs/10000 patient days for specific antimicrobials can be found here.

Information Systems Pharmacist, Josh Batterink, extracts and analyzes drug utilization trends
Awards

Dr. Victor Leung submitted a project proposal, which was developed with multiple specialists at PHC during an ASP-sponsored journal club, on “Improving care delivery and optimizing outcomes for diabetic foot infections” to the Specialist Services Committee (SSC).

The SCC provided a $10,000 grant to support the development of a stage two proposal with specialists in the Fraser Health Authority.

SSC is a Partnership of Doctors of BC and the Ministry of Health.

http://www.sscbc.ca/
10.0 Financials
Financials

Financial saving is not the main goal of the program but we know that successful implementation of an ASP can have significant cost savings. One concrete measure of these savings is antimicrobial expenditures.

Fiscal sustainability is one of our guiding principles. Antimicrobial expenditures decreased by $214,935 (taking into account the decrease in the antimicrobial budget by $208,000).

Antimicrobial expenditures decreased by $214,935

The Antimicrobial Stewardship Program implemented in 2013 is fiscally sustainable.
10.0 Financials

FISCAL YEAR 2014 - 2015 ANTIMICROBIAL EXPENDITURES

<table>
<thead>
<tr>
<th>FISCAL PERIODS</th>
<th>Actual Expenditure</th>
<th>Budgeted Expenditure</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>$2,000,000</td>
<td>$800,000</td>
</tr>
<tr>
<td>2</td>
<td>$1,800,000</td>
<td>$1,600,000</td>
</tr>
<tr>
<td>3</td>
<td>$1,600,000</td>
<td>$1,400,000</td>
</tr>
<tr>
<td>4</td>
<td>$1,400,000</td>
<td>$1,200,000</td>
</tr>
<tr>
<td>5</td>
<td>$1,200,000</td>
<td>$1,000,000</td>
</tr>
<tr>
<td>6</td>
<td>$1,000,000</td>
<td>$0</td>
</tr>
<tr>
<td>7</td>
<td>$800,000</td>
<td>$600,000</td>
</tr>
<tr>
<td>8</td>
<td>$600,000</td>
<td>$400,000</td>
</tr>
<tr>
<td>9</td>
<td>$400,000</td>
<td>$200,000</td>
</tr>
<tr>
<td>10</td>
<td>$200,000</td>
<td>$0</td>
</tr>
<tr>
<td>11</td>
<td>$0</td>
<td>$0</td>
</tr>
<tr>
<td>12</td>
<td>$0</td>
<td>$0</td>
</tr>
<tr>
<td>13</td>
<td>$0</td>
<td>$0</td>
</tr>
</tbody>
</table>
## 10.0 Financials

### FINANCIAL STATEMENT 2014-2015

<table>
<thead>
<tr>
<th>LABOUR</th>
<th>ACTUAL ($)</th>
<th>BUDGET ($)</th>
<th>VARIANCE ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASP Physician</td>
<td>163,000</td>
<td>163,000</td>
<td>--</td>
</tr>
<tr>
<td>ASP Pharmacist</td>
<td>122,715</td>
<td>122,715</td>
<td>--</td>
</tr>
<tr>
<td>Analyst</td>
<td>--</td>
<td>42,384</td>
<td>42,384</td>
</tr>
<tr>
<td>Clerk</td>
<td>--</td>
<td>4,999</td>
<td>4,999</td>
</tr>
<tr>
<td>Total Labour</td>
<td>285,715</td>
<td>333,099</td>
<td>47,384</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>NON-LABOUR</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Office supplies</td>
<td>414</td>
<td>--</td>
<td>(414)</td>
</tr>
<tr>
<td>Conference</td>
<td>--</td>
<td>1,500</td>
<td>1,500</td>
</tr>
<tr>
<td>Phones</td>
<td>753</td>
<td>300</td>
<td>(453)</td>
</tr>
<tr>
<td>Purchased salaries</td>
<td>--</td>
<td>360</td>
<td>(360)</td>
</tr>
<tr>
<td>Consultants</td>
<td>4,400</td>
<td>--</td>
<td>4,400</td>
</tr>
<tr>
<td>Travel</td>
<td>1,049</td>
<td>5,000</td>
<td>3,951</td>
</tr>
<tr>
<td>Computer Fee</td>
<td>2,276</td>
<td>--</td>
<td>(2,276)</td>
</tr>
<tr>
<td>Total Non-Labour</td>
<td>9,253</td>
<td>6,800</td>
<td>(2,452)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TOTAL EXPENSES</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>294,968</td>
<td>339,899</td>
<td>44,932</td>
</tr>
</tbody>
</table>

### ANTIMICROBIALS

<table>
<thead>
<tr>
<th>ANTIMICROBIALS</th>
<th>ACTUAL ($)</th>
<th>BUDGET ($)</th>
<th>VARIANCE ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1,848,777</td>
<td>1,855,712</td>
<td>6,935</td>
</tr>
</tbody>
</table>

Note: 2014/15 budget was reduced by $208,000 to fund the program.
11.0

APPENDIX I - GUIDELINES
Facility-specific treatment recommendations, based on national guidelines and local susceptibilities and formulary options can optimize antibiotic selection and duration, particularly for common indications for antibiotic use. We added the following guidelines this year:

**Suspected Penicillin Allergy in Patients Undergoing Surgery**

**KEY MESSAGES**

- Cephalosporins may be prescribed to patients with reported penicillin allergy if physicians use the clinical decision support algorithm below.
- If the reaction to penicillin occurred more than 10 years ago, the likelihood of a reaction to cephalosporin is low due to diminished IgE levels.
- Only 10% of all patients who report a penicillin allergy are diagnosed as skin-test positive. Of those who are skin-test positive, there is only a 2% cross-reactivity rate with cephalosporins for patients who have a true penicillin allergy (i.e. 0.2% of all patients reporting allergy).
- Overall, there is less than a 1 in 100,000 risk of anaphylaxis with a cephalosporin in patients reporting a penicillin allergy.

**ASSESS THE TYPE OF REACTION TO PENICILLIN**

- **Stevens Johnson Syndrome OR Toxic Epidermal Necrolysis**
  - Do NOT administer beta-lactam.
  - Consider alternative antibiotic.
  - For vancomycin, please make note on OR booking form.

- **Anaphylaxis within past 10 years (dyspnoea, facial swelling, shock, immediate hives)**
  - Referral to allergist for preoperative testing.
  - Do NOT administer beta-lactam.
  - Consider alternative antibiotic.
  - For vancomycin, please make note on OR booking form.

- **Anaphylaxis more than 10 years ago**
  - Proceed with administering cephalosporin in a monitored perioperative setting. Consider referral to allergist for preoperative testing.
  - Consider physician supervision for first dose depending on clinical history.

- **Unknown reaction OR Patient unable to recall**
  - Proceed with administering cephalosporin in a monitored perioperative setting.
  - Consider physician supervision for first dose depending on clinical history.

**Non-severe reactions**
- Delayed rash (more than 24 hrs from taking drug)
- Testing
- GI intolerance
### PHC Guidelines for Empiric Treatment of Intra-Abdominal Infections (IAI)

**Developed by the Antimicrobial Stewardship Program and the Division of General Surgery**

<table>
<thead>
<tr>
<th>IAI Infection Type</th>
<th>Source control less than 24 hours and no anti-seed therapy and no malignancy</th>
<th>Ceftriaxone 1 g IV Q24H</th>
<th>N/A</th>
<th>Total Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complicated</td>
<td>Ceftriaxone 1 g IV Q24H + Metronidazole 500 mg IV Q12H</td>
<td>Amoxicillin/Clsulinate 875 mg PO BID 5-7 days</td>
<td>Discontinue post-op</td>
<td></td>
</tr>
<tr>
<td>Uncomplicated or CA</td>
<td>Ceftriaxone 1 g IV Q24H + Metronidazole 500 mg IV Q12H</td>
<td>N/A</td>
<td>Discontinue post-op</td>
<td></td>
</tr>
<tr>
<td>HCA early onset</td>
<td>Ceftriaxone 1 g IV Q24H + Metronidazole 500 mg IV Q12H</td>
<td>Amoxicillin/Clsulinate 875 mg PO BID 5-7 days</td>
<td>Discontinue post-op</td>
<td></td>
</tr>
<tr>
<td>HCA late onset or Critically ill</td>
<td>Piperacillin/Tazobactam 3.375 g IV Q6H</td>
<td>Amoxicillin/Clsulinate 875 mg PO BID 5-7 days</td>
<td>Discontinue post-op</td>
<td></td>
</tr>
<tr>
<td>Uncomplicated or CA</td>
<td>Ceftriaxone 1 g IV Q24H</td>
<td>N/A</td>
<td>Discontinue post-op</td>
<td></td>
</tr>
<tr>
<td>HCA early onset</td>
<td>Ceftriaxone 1 g IV Q24H + Metronidazole 500 mg IV Q12H</td>
<td>Amoxicillin/Clsulinate 875 mg PO BID 5-7 days</td>
<td>Discontinue post-op</td>
<td></td>
</tr>
<tr>
<td>HCA late onset or Critically ill</td>
<td>Piperacillin/Tazobactam 3.375 g IV Q6H</td>
<td>Amoxicillin/Clsulinate 875 mg PO BID 5-7 days</td>
<td>Discontinue post-op</td>
<td></td>
</tr>
<tr>
<td>Uncomplicated or CA</td>
<td>Ceftriaxone 1 g IV Q24H + Metronidazole 500 mg IV Q12H</td>
<td>N/A</td>
<td>Discontinue post-op</td>
<td></td>
</tr>
<tr>
<td>HCA early onset</td>
<td>Ceftriaxone 1 g IV Q24H + Metronidazole 500 mg IV Q12H</td>
<td>Amoxicillin/Clsulinate 875 mg PO BID 5-7 days</td>
<td>Discontinue post-op</td>
<td></td>
</tr>
<tr>
<td>HCA late onset or Critically ill</td>
<td>Piperacillin/Tazobactam 3.375 g IV Q6H</td>
<td>Amoxicillin/Clsulinate 875 mg PO BID 5-7 days</td>
<td>Discontinue post-op</td>
<td></td>
</tr>
<tr>
<td>Uncomplicated or CA</td>
<td>Ceftriaxone 1 g IV Q24H</td>
<td>N/A</td>
<td>Discontinue post-op</td>
<td></td>
</tr>
<tr>
<td>HCA early onset</td>
<td>Ceftriaxone 1 g IV Q24H + Metronidazole 500 mg IV Q12H</td>
<td>Amoxicillin/Clsulinate 875 mg PO BID 5-7 days</td>
<td>Discontinue post-op</td>
<td></td>
</tr>
<tr>
<td>HCA late onset or Critically ill</td>
<td>Piperacillin/Tazobactam 3.375 g IV Q6H</td>
<td>Amoxicillin/Clsulinate 875 mg PO BID 5-7 days</td>
<td>Discontinue post-op</td>
<td></td>
</tr>
<tr>
<td>Not critically ill</td>
<td>Piperacillin/Tazobactam 3.375 g IV Q6H + Vancomycin loading dose 30 mg/kg IV then maintenance dose</td>
<td>Based on culture results</td>
<td>Based on response to therapy</td>
<td></td>
</tr>
<tr>
<td>Critically ill</td>
<td>Meropenem 500 mg IV Q6H + Vancomycin loading dose 30 mg/kg IV then maintenance dose + MBC/Min 100 mg IV Q12H</td>
<td>Based on culture results</td>
<td>Based on response to therapy</td>
<td></td>
</tr>
</tbody>
</table>

**UNCOMPlicated**: icomes from surgery only without an anatomic disruption or WACOMPLICATIONS extend beyond source organ causing peritonitis or abscess. **CRITICALLY ILL**: severe shock. **COMMUNITY ASSOCIATED**: MSA associated with healthcare setting and no known healthcare exposure. **HOSPITAL ASSOCIATED** (HCA): acquired more than 48 hours post-admission, non-hospitalization, surgery, dialysis, residence in long-term care facility within last 12 months. Can be EARLY (less than 5 days) or LATE (more than 5 days) onset.
11.0

Management of Staphylococcus Aureus Bacteremia

**KEY MESSAGES**
- S. aureus is the leading cause of bacteremia with high associated mortality.
- Early Infectious Disease consultation is strongly recommended & associated with better outcomes.
- It is essential to control the source of S. aureus bacteremia and institute urgent treatment.

**ANTIMICS (Diagnosis Identification of S. aureus)**
- Vancomycin 30 mg/kg IV Loading dose
  - Long-term infusion: 30 mg/kg IV per 8h, adjusted based on serum levels
  - trough levels should be >10 mg/L

**TREATING ANTIMICS**
- Methicillin-resistant S. aureus (MRSA)
- Methicillin-susceptible S. aureus (MSSA)
- Vancomycin (30 mg/kg IV loading dose)
- Frequency depends on serum levels
  - Target trough at 10-20 mg/L

**INVESTIGATIONS**
- Through physical examination, culture, and imaging studies.
- Blood cultures should be obtained in all suspected cases.
- Empirical treatment should be initiated pending laboratory results.

**HOSPITAL POLICIES**
- Blood cultures should be obtained in all suspected cases.
- Empirical treatment should be initiated pending laboratory results.

**RECOMMENDATIONS**
- Start with TTE.
- Consider TEE if discussion with cardiology is required.

**DURATION**
- 72 hours after negative blood cultures.
- Patients with acute bacteremia can be discharged from the hospital.
- Patients with sepsis or severe sepsis should be discharged on appropriate antibiotic therapy.
- Long-term antibiotic treatment may be needed for patients who have complicated S. aureus bacteremia in the hospital.

**RECOMMENDATIONS**
- Repeat blood cultures are recommended to determine clearance of bacteremia. Order repeat blood cultures on day 2, then every 1-2 weeks until negative.
- Blood cultures should be obtained in all suspected cases.
- Empirical treatment should be initiated pending laboratory results.
- Early intensive care admission is strongly recommended for all patients with persistent bacteremia.
Clostridium difficile Infection (CDI) Clinical Management Algorithm

**KEY MESSAGES**

- Clostridium difficile is a common cause of infective diarrhoea in hospitals.
- Treatment is with an initial single dose of oral vancomycin or metronidazole.
- Other agents should be reserved for patients with severe CDI or in those who have not responded to initial treatment.
- Ingestion of probiotics or FOS (fructo-oligosaccharides) may be used as an adjunct to antibiotic therapy.
- Lack of available CDI clinical guidelines for various settings can lead to variability in treatment approaches.
- Surveillance and reporting of CDI is important to track the incidence and impact of the infection.

**SUSPECTED OR CONFIRMED CDI**

- Enterotoxin test for stool samples.
- Stool culture for CDI.
- Stool PCR for CDI.
- Blood cultures for CDI.
- Urine cultures for CDI.
- Stool ELISA for CDI.
- Other tests may be required based on clinical presentation.

**CLINICAL PRESENTATION**

- Mild to moderate: self-limiting
- Moderate: persistent or relapsing diarrhea
- Severe: severe diarrhea, fever, hypotension, electrolyte disorders, and/or organ failure
- FULMINARY (one of the following):
  - Fluid management
  - Intravenous antibiotics
  - Enteric prophylaxis
  - Nutritional support
  - Symptomatic management

**INVESTIGATE AND TREAT APPEARING SOURCES**

- CT scan for abscesses
- Colonoscopy for suspected CDI
- Biopsy for CDI
- Blood cultures for CDI
- Urine cultures for CDI
- Stool cultures for CDI

**FIRST STEP TREATMENT (ACTIVE OR MODERATE)**

- Oral vancomycin 125 mg PO BID for 10-14 days
- Oral metronidazole 500 mg PO BID for 10-14 days
- Folic acid 5 mg PO daily for 10-14 days
- Lubiprostone 2 mg PO BID for 10-14 days
- Metronidazole 500 mg PO TID for 10-14 days

**SECOND STEP TREATMENT (SEVERE)**

- Oral vancomycin 125 mg PO BID for 10-14 days
- Oral metronidazole 500 mg PO TID for 10-14 days
- Folic acid 5 mg PO daily for 10-14 days
- Lubiprostone 2 mg PO BID for 10-14 days
- Metronidazole 500 mg PO TID for 10-14 days
- Intravenous vancomycin 125 mg PO BID for 10-14 days
- Intravenous metronidazole 500 mg PO TID for 10-14 days
- Folic acid 5 mg PO daily for 10-14 days
- Lubiprostone 2 mg PO BID for 10-14 days
- Metronidazole 500 mg PO TID for 10-14 days

**THIRD STEP TREATMENT (FULMINARY)**

- Intravenous vancomycin 125 mg PO BID for 10-14 days
- Intravenous metronidazole 500 mg PO TID for 10-14 days
- Folic acid 5 mg PO daily for 10-14 days
- Lubiprostone 2 mg PO BID for 10-14 days
- Metronidazole 500 mg PO TID for 10-14 days

**REFERENCES**

APPENDIX II – DRUG UTILIZATION
Appendix II – Drug Utilization

The following pages contain detailed drug utilization graphs.

STATISTICAL ANALYSIS

We conducted an interrupted time series analysis using methods previously described. Time series analysis differs from a regression analysis as values in a time series can be dependent on previous values (autocorrelated). Performing a regression analysis without accounting for autocorrelation results in inappropriate estimation of coefficients and statistical significance. We account for autocorrelation using a simple ARIMA model. Some models were found to have seasonal autocorrelation and this was also included in the model.

METHODOLOGY

Measurements

Information on antibiotic use from April 1, 2005 to March 31, 2015 was obtained from the pharmacy information system as World Health Organization defined daily doses (DDDs). The DDDs were available by fiscal period (13 periods per year, beginning in April). Patient census data was used to standardize the data to DDDs per 1000 patient-days. The Antimicrobial Stewardship Program was fully implemented in July 2013 and the period before this was used as the control.

We generated models for both St. Paul’s Hospital (SPH) and Mount Saint Joseph Hospital (MSJ) for the following antimicrobials:

1. All Antibiotic Use (defined as IV/oral medication with the WHO ATC classification of J01 (Antibacterials for systemic use)
2. Piperacillin/Tazobactam
3. Meropenem
4. Vancomycin IV
5. Ceftriaxone
6. Daptomycin
7. Azithromycin PO Proportion (Ratio of PO to total systemic usage)
8. Ciprofloxacin PO Proportion (Ratio of PO to total systemic usage)

9. Moxifloxacin PO Proportion (Ratio of PO to total systemic usage)

A simple interrupted time series analysis can be specified using the equation $Y_t = B_0 + B_1 t + B_2 X_1 + B_2^\text{after}$

- $Y_t$ = the outcome value
- $B_0$ = starting point/intercept
- $B_1, B_2$ = regression coefficients
- $X_1$ = Binary indicator of whether the time period is from before or after the intervention was implemented
- $t$ = number of fiscal periods since the onset of observation (13 fiscal periods /year)
- $t^\text{after}$ = number of fiscal periods since the onset of the intervention

The majority of the drugs that we modeled had the following regression coefficients.

- $B_0$ is the baseline DDD for the drug
- $B_1$ represents the underlying trend in DDD prior to the intervention
- $B_2$ represents the immediate change in DDD with the intervention
- $B_3$ represents the change in the DDD trend after the intervention (the sum of $B_1$ and $B_3$ is the post-intervention slope)

Some drugs (ceftriaxone and piperacillin-tazobactam) had had significant changes in usage during the time period investigated for reasons other than ASP. To model the effects correctly, additional time periods were included in the analysis.

The time-series analysis was performed using R statistical software and the forecast package.
ASP was fully implemented in period 3, fiscal Year 2014. There has so far been no significant change in overall usage of antibiotics with WHO ATC J01 Classification.
At the end of fiscal year 2009, there was a change in Piperacillin/Tazobactam restrictions resulting in increased usage at SPH. This change was incorporated into the model to appropriately fit the data. After implementation of ASP in period 3, fiscal year 2014, there was a significant decrease in Piperacillin/Tazobactam usage at MSJ and SPH.
The high variability in Meropenem usage at MSJ precluded us from performing modeling of the data. At SPH after implementation of ASP in period 3, fiscal year 2014, there was a significant decrease in Meropenem usage.
After implementation of ASP in period 3, fiscal year 2014, there was no significant change in Vancomycin usage. It is too early to determine whether there has been a significant change in trend of Vancomycin usage after the intervention.
Three significant factors resulted in change in Ceftriaxone usage. Theses were included in the model:

- In period 3, fiscal year 2008, Ceftriaxone became the standard 3rd generation cephalosporin on our formulary.
- In Period 7 fiscal year 2012, probenecid was discontinued from the market resulting in increased ceftriaxone usage in place of Cefazolin + Probenecid for skin and soft tissue infections
- ASP was implemented in period 3, fiscal year 2014. There was a significant decrease in Ceftriaxone usage at MSJ but not at SPH.
* No modeling was done for Daptomycin utilization at MSJ because of very low usage and high variability

Since fiscal year 2010, there has been a significant increasing trend in Daptomycin usage at SPH. There has been no significant impact in usage after implementation of ASP.
The percentage of PO to total Azithromycin usage was approximately 70% prior to ASP implementation and there was no significant effect after implementation.
Prior to ASP implementation the percentage of PO to total ciprofloxacin usage was approximately 70% at MSJ and 55% at SPH. There were no immediate effects after ASP implementation.
Prior to ASP implementation the percentage of PO to total moxifloxacin usage was approximately 70%. There were no immediate effects after ASP implementation.