In 2016/17, we successfully sustained coordinated interventions to use antimicrobials responsibly.

Our activities included:

- Expansion of the PHC Antimicrobial Stewardship phone App
- Creation of a work shadowing program for nurse practitioners
- Optimal treatment of *Clostridium difficile* colonization and infection
- Implementation of a systematic penicillin allergy de-labeling program
- Audit and feedback for antimicrobial prescriptions
- Promotion of diagnostic test stewardship using urine cultures as a prototype
- Participation in rounds with General Surgery and Intensive Care
- Educational rounds for medical students, residents and pharmacists
- Institution of a collaborative daptomycin use evaluation

Positive measures of our collaborative efforts include:

- Achieving the lowest to date PHC-associated incidence rate of *Clostridium difficile* infection (4.8 cases per 10,000 patient days)
- De-labelling penicillin allergy in 350 patients
- Decreasing utilization of targeted antimicrobials

We would like to thank all prescribers at PHC for participating in activities to practice antimicrobial stewardship.
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.
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.
The antimicrobial stewardship subcommittee meets monthly to discuss antimicrobial utilization issues and provide feedback on antimicrobial utilization guidelines.
Clinical Activities

Each year, we reassess the value of our clinical activities to determine if we can improve existing processes, or implement new approaches to systematically improve antibiotic use at Providence Health Care.

In this section we highlight our coordinated set of actions designed to use antimicrobials in ways that ensure sustainable access to effective therapy for all who need them.
Prospective audit and feedback is a cornerstone of our antimicrobial stewardship program. Based on work lists containing targeted antibiotics stratified by duration of therapy, we review the medical chart and diagnostic test results. We make an assessment and discuss with the prescribing team when opportunities for change in any of the following areas are identified:

- Choice of antibiotic therapy (empiric, pathogen directed, syndrome directed susceptibility guided)
- Antibiotic dosing considering both host and pathogen factors
- Duration of antibiotic therapy
- Delivery method such as intravenous versus enteral administration of antibiotics
- Discontinuation of antibiotics
- Infectious diseases consultation

**Did you know?**

Each year we review over 1000 patient-cases and acceptance rates for our recommendations are ~80%.
Penicillin Allergy De-labeling

Patients are frequently labeled as being allergic to penicillin. Despite the high prevalence of this label (~15% of patients seen at PHC), most patients are not allergic and can tolerate penicillin and other beta-lactam antibiotics.

When managing patients with a designated penicillin allergy, prescribers tend to avoid beta-lactams and choose to prescribe alternative antibiotics. However, this practice has been associated with adverse patient outcomes such as increased lengths of stay, increased costs of care, increased rates of *C. difficile* infection and colonization with multidrug-resistant bacteria.

Two years ago, we collaborated with the Division of Allergy and Immunology to pilot a systematic allergy de-labeling program. The program was successful in de-labeling 2 to 5 patients weekly.

We have since formalized the penicillin allergy de-labeling program to include:

- A widely available and simple to use questionnaire to triage patients
- Weekly penicillin skin testing/oral challenge
- Formalized documentation of de-labeling in the local pharmacy information system and the provincial Pharmanet system
- Patient education regarding penicillin allergy de-labeling
The program has been successfully in labeling over 120 patients this past year. We have shared our program implementation ideas with other health authorities so that more patients can benefit from having a more accurate medication allergy record.

In our second year of developing the PHC Antimicrobial Stewardship Phone App (Spectrum Localized Antimicrobial Stewardship), we have updated the content and made the App available for free download on both the Apple and Google Play stores.

**Key features:**
- Direct phone connection to the PHC Antimicrobial Stewardship Pharmacist and Physician
- Locally relevant guidelines for managing common infections
- Decision support features incorporated into guidelines
- Antimicrobial information (contains most antimicrobials in the hospital formulary)
- Recent PHC antibiogram

There are 700 to 1000 active users monthly.

**Clinical Activities**

Download on the App Store
Get it on Google Play
View the Web Version
Diagnostic test stewardship involves modifying the process for ordering, performing and reporting diagnostic tests to improve the treatment of infections and other conditions.

The process or ordering and interpreting diagnostic tests is complex. Physicians may order common tests for patients without symptoms specific for the disease process (e.g. urine cultures from patients without symptoms referable to the urinary tract).

The problem with ordering tests in the setting of low pretest likelihood of disease is false positive results (or colonization rather than true infection). This may lead to unnecessary therapy (e.g. antibiotics for asymptomatic bacteriuria) and the associated harm.

In 2013, we introduced a toolkit and management algorithm for urinary tract infections (UTIs) and asymptomatic bacteriuria (ASB) in PHC residential care homes. In the last 4 years, we have sustained a significant decrease in collection of unnecessary urine cultures and antibiotic treatment for asymptomatic bacteriuria. By targeting the diagnostic process at the upstream steps, we have avoided multiple downstream consequence of inappropriate testing.
To understand current practice in acute care, we conducted a baseline 3-month audit of urine culture testing from medical and surgical wards at St. Paul’s Hospital.

We found that:

- 690 urine cultures were ordered for 476 patients over 3 months.
- 68.6% of urine cultures were ordered inappropriately based on guideline-concordant indications.
- 36.8% of asymptomatic bacteriuria cases were treated with antibiotics unnecessarily.
- $9,257 of wasted laboratory expenditures (supplies and labour costs) associated with inappropriate testing over 3 months.

We need to improve the appropriate ordering of urine cultures on medical and surgical wards at SPH.

Our goal is to continue to work with the laboratory and clinicians to practice better diagnostic test stewardship.

Clinical Activities
We continued the “War on the Spore” collaboration with Infection Prevention and Control (IPAC) and the Medical Microbiology lab. This year we expanded the use of rapid alerts to communicate the diagnosis and management of outpatients with laboratory tests positive or indeterminate for *Clostridium difficile*. The communication channels connecting the laboratory, IPAC and ASP help strengthen our comprehensive approach to preventing transmission and controlling infection with *C. difficile*.

Our positive impact is demonstrated in the lowest to date PHC-associated incidence rate of *C. difficile* infection at 4.8 cases per 10,000 patient days.

**Did you know?**

We achieved the lowest to date *C. difficile* infection rate at 4.8 cases per 10,000 patient days.

By expanding our program to outpatients in addition to hospitalized patients and residents, we have been successfully preventing hospital readmissions for *C. difficile* infection.
The appropriate utilization of rapid diagnostic tests (RDTs) can enhance antimicrobial stewardship practice. At PHC, we have worked with the Medical Microbiology laboratory to implement three RDTs to help with interventions in optimizing antimicrobial therapy.
Bloodstream Infections

Timeliness and appropriateness of empirical and susceptibility guided antimicrobial therapy can be improved if pathogen identification and antimicrobial susceptibility testing can be done expeditiously. Compared to many other hospitals, the PHC Medical Microbiology laboratory is able to provide rapid identification and preliminary antibiotic susceptibility results for positive blood cultures.

The microbiology laboratory is continuously improving the use of matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) and more recently the FilmArray blood culture identification (BCID) panel. In addition, the use of direct antibiotic susceptibility testing from blood cultures aids in early phenotypic identification of resistance.

The antimicrobial stewardship clinical team rounds with the medical microbiologists daily to expedite the reporting of blood culture results to physicians. The goal is to quickly institute appropriate empiric antimicrobial and susceptibility guided therapy for our patients.
The PHC Medical Microbiology laboratory provides daily rapid testing to diagnose viral respiratory tract infections. We wanted to encourage physicians to act on these results and discontinue antibiotics when there was a confirmed diagnosis of a viral respiratory tract infection. We also wanted to optimize the use of Oseltamavir for those diagnosed with influenza.

We conducted a quasi-experimental audit and feedback intervention of adult inpatients with a positive polymerase chain reaction for a respiratory virus. Audit and feedback was implemented based on 2 criteria: absence of positive bacterial cultures and absence of consolidation on chest imaging. A chart review was conducted to assess for days of antibiotics post viral diagnosis. The balancing measures included:

- length of stay
- intensive care unit admission within 14 days
- mechanical ventilation within 14 days
- antibiotics prescribed within 14 days
- *Clostridium difficile* infection diagnosed within 30 days
- readmission within 30 days
Antimicrobial stewardship recommendations for hospitalized patients with viral respiratory tract infections were accepted for 77% of cases. This targeted approach based on easily assessed parameters translated into a 1.3 day decrease in mean days (95% confidence interval, 0.3-2.3; P < 0.01) of antibiotics postviral diagnosis compared with the previous year without systematic interventions. Compared with the previous year, no differences were identified for adverse outcomes associated with the intervention.


Did you know?
Rapid viral diagnostics coupled with direct feedback to physicians facilitates shorter antibiotic duration for respiratory tract infections.
Timely and accurate diagnosis of *Clostridium difficile* colonization and infection is key to ensuring proper patient management and institution of infection control measures to prevent transmission.

This past year, the Medical Microbiology lab improved *C. difficile* diagnosis by implementing a two staged testing approach that includes an in-house molecular based method (PCR) followed by toxin detection test (enzyme immunoassay).

The ASP clinical team provides feedback to prescribers on optimal management of *C. difficile* colonization and infection. The comprehensive program to fight *C. difficile* at PHC is known as “War on the Spore.”
The ASP Clinical team joins the weekly multidisciplinary rounds to review every patient admitted to the general surgery service. The clinical pharmacist and the ASP team help facilitate antimicrobial therapy plans to optimize treatment outcomes.

Intensive Care Unit

The ASP Clinical team meets with the ICU clinical pharmacist and the ICU Fellow on Tuesdays and Fridays every week to review patients prescribed antimicrobials. During these “bullet rounds” we discuss opportunities for optimizing antimicrobial treatment.

General Surgery

The ASP Clinical team joins the weekly multidisciplinary rounds to review every patient admitted to the general surgery service. The clinical pharmacist and the ASP team help facilitate antimicrobial therapy plans to optimize treatment outcomes.
Daptomycin is one of the last line drugs for treating infections caused by methicillin resistant Staphylococcus aureus (MRSA) and Vancomycin resistant Enterococcus (VRE). At PHC, Daptomycin constituted 19% of the overall antimicrobial budget. It is unclear if daptomycin use strictly follows the provincial restriction criteria.

Since January 1, 2017, we started a collaborative prospective daptomycin use evaluation (DUE) with antimicrobial stewardship teams at Vancouver Coastal Health and Fraser Health. In comparison to the 2 year retrospective DUE conducted at PHC, this DUE will include inpatients and outpatients. Furthermore, the reason for prescribing daptomycin will be elicited directly from the prescriber. All infectious diseases physicians and medical microbiologists in the three health authorities were given opportunities to review the protocol and provide feedback.

Some goals of the DUE include:
- promoting optimal daptomycin therapy
- preventing treatment related problems
- understand daptomycin use practice variations from both patient-outcome and resource utilization perspectives
- identify areas in which further information on daptomycin use is needed by health care providers

The interim and annual results of the DUE will be shared with prescribers to promote dialogue on optimizing daptomycin utilization.
Our main channel for delivering antimicrobial education continues to occur at the point of care during our audit and feedback activities. Having dialogue about cases in a timely manner provides learning opportunities for prescribers and the antimicrobial stewardship team. In addition to the point of care education, we have delivered education sessions throughout the year including:

- Supervision of infectious diseases and medical microbiology residents during their month long rotation
- Week long rotations for PHC Nurse Practitioners
- Job shadowing opportunities for clinical pharmacists and pharmacy residents
- Monthly teaching for trainees rotating on the Infectious Diseases consultation service
- Monthly orientation to trainees in General Surgery
- Bi-monthly noon rounds for the Clinical Teaching Unit
- Orientation for rotating first year residents in Family and Community Medicine program and the SPH rotating residency
- Journal club evening
Our successfully implemented Antimicrobial Stewardship Program has demonstrated concrete financial costs savings from decreased antimicrobial drug expenditures.

Although the primary goal of any ASP is to optimize patient safety and minimize harms from antimicrobial treatments, the positive downstream cost savings is significant and should be recognized. We continue to generate a positive return on investment that exceeds our original business case projecting financial sustainability.
Introduction
Drug utilization may be used as one of the metrics for the effectiveness of an ASP program. For example, demonstrating decreases in broad spectrum antibiotic use, and downward trends in antibiotic utilization, could suggest a positive change in antibiotic prescribing practices. The main limitation of any drug utilization metric is the inability to capture appropriateness of individual prescriptions. Furthermore, using the metric of defined daily dose (DDD) inflates drug utilization when using more appropriate antibiotic combinations. At Providence Health Care, we have chosen to use DDD because of the ability to capture this metric accurately and efficiently.

Drug Utilization
The following pages contain detailed drug utilization trends at Providence Health Care.

Measurements
Information on antibiotic use from April 1, 2005 to March 31, 2016 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 began July 2013 and the period before this was used as the control.
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. We generated models for both St. Paul’s Hospital (SPH) and Mount Saint Josephs 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 IV, PO, and PO Proportion (Ratio of PO to total systemic usage)
8. Ciprofloxacin IV, PO, and PO Proportion (Ratio of PO to total systemic usage)
9. Moxifloxacin IV, PO, and PO Proportion (Ratio of PO to total systemic usage)
10. Clindamycin PO and IV
A simple interrupted time series analysis can be specified using the equation \( Y_t = B_0 + B_1 t + B_2 X_1 + B_2 t_{\text{after}} \)

- \( Y_t \) = 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

In 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) have 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 been an increase in overall usage of antibiotics with WHO ATC J01 Classification. Multiple appropriate antibiotic utilization factors contribute to the increase in total DDD. These factors include:

- Increase in overall use of ceftriaxone instead of Piperacillin-Tazobactam
- Increase in Vancomycin utilization. We hypothesize that some of the utilization may be appropriate and related to modifications to the dosing nomogram revised in March 2016. However, inappropriate vancomycin utilization remains an opportunity to target improvement.
- Increase in cefazolin use from appropriate weight based dosing for pre-operative prophylaxis.
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 and sustained decrease in piperacillin-tazobactam usage at MSJ and SPH.
At SPH, after implementation of ASP in period 3, fiscal year 2014, there was a significant decrease in meropenem usage. No modeling of meropenem was done at MSJ because of high variability in usage. However, there is a trend toward increasing meropenem usage at both sites, which is a target for ongoing ASP interventions.
Appendix 1

Drug Utilization: Defined Daily Dose (DDD) Analysis

Vancomycin

There has been a significant increasing trend in vancomycin use at SPH. We hypothesize this is due to increasing empiric treatment of suspected MRSA infections (respiratory, skin and soft tissue, sepsis). Appropriate vancomycin use is a target for future improvement, and may be facilitated both by ASP interventions, and by introducing more rapid diagnostic technologies in the microbiology laboratory. There was no significant change in vancomycin usage at MSJ.
Three significant factors resulted in change in ceftriaxone usage. These were included in the model:

- In period 3, fiscal year 2008, ceftriaxone became the standard 3rd generation cephalosporin on 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. Since then, there has been a significant increase in ceftriaxone utilization at SPH. We hypothesize that the narrowing of broad-spectrum antibiotics (e.g. piperacillin-tazobactam and meropenem) to ceftriaxone, and the common use of the 2 gram dosing of the drug account for this increase.
Drug Utilization: Defined Daily Dose (DDD) Analysis

Appendix 1

Since fiscal year 2009, there has been a significant increasing trend in daptomycin use at SPH. A daptomycin drug utilization evaluation is under way in order to explain this increase. No modeling of daptomycin usage was done at MSJ because of intermittent and low usage.
Neither total azithromycin utilization nor the proportion of oral and parenteral azithromycin prescribed changed significantly before and after implementation of ASP. This is a target for future improvement, as highly bioavailable oral antimicrobials are the preferred agents in patients who can reliably take and absorb them.
Appendix 1

Drug Utilization: Defined Daily Dose (DDD) Analysis

Fluoroquinolones – Ciprofloxacin and Moxifloxacin

MSJ - IV Ciprofloxacin

SPH - IV Ciprofloxacin

MSJ - Oral Ciprofloxacin

SPH - Oral Ciprofloxacin

Immediate Effect
Not Significant

Stewardship
Slope Change: 0.277
P = 0.012

Immediate Effect
Not Significant
Appendix 1

Drug Utilization: Defined Daily Dose (DDD) Analysis

Fluoroquinolones – Ciprofloxacin and Moxifloxacin

MSJ - Ciprofloxacin

SPH - Ciprofloxacin
Appendix 1
Drug Utilization: Defined Daily Dose (DDD) Analysis

Fluoroquinolones – Ciprofloxacin and Moxifloxacin

MSJ - IV Moxifloxacin

SPH - IV Moxifloxacin

Immediate Effect
Not Significant

Stewardship
Slope Change
Not Significant

MSJ - Oral Moxifloxacin

SPH - Oral Moxifloxacin

Immediate Effect
Not Significant

Stewardship
Slope Change
Not Significant
Total fluoroquinolone utilization has steadily decreased since the implementation of ASP. This is likely due to the development of clinical practice guidelines based on local antibiogram data, which shows that resistance rates to fluoroquinolones in Enterobacteriaceae was >20%, making them suboptimal as empiric therapy. Furthermore, fluoroquinolones have been issued an FDA black box warning due to their association with serious adverse reactions (tendonitis and tendon rupture, peripheral neuropathy, and central nervous system effects). Physicians have been sensitized to the recommendation that they should be reserved for use in patients who have no alternative treatment options.

The proportion of oral and parenteral fluoroquinolone has not changed significantly before and after implementation of ASP. This is a target for future improvement, as highly bioavailable oral antimicrobials are the preferred agents in patients who can reliably take and absorb them.
Total clindamycin utilization has steadily decreased since the implementation of ASP. This is possibly related to the development of clinical practice guidelines based on local antibiogram data, which shows that resistance rates to clindamycin in Staphylococcus aureus was >40%, making it suboptimal as empiric therapy. Furthermore, clindamycin has been issued an FDA black box warning due to its association with severe and sometimes fatal Clostridium difficile-associated colitis. Physicians have been sensitized to the recommendation that they should be reserved for use in patients who have no alternative treatment options.