MUHC ASP | Antimicrobial Stewardship Program

ANNUAL REPORT 2019-2020

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EXECUTIVE SUMMARY

Following a restructuring of the MUHC Antimicrobial Stewardship Program (ASP) in January 2019, a small but skilled operational team has been working to promote appropriate antimicrobial use within the institution through a set of coherent activities, with oversight from a multidisciplinary committee. Our goals are consistent with the patient safety mandate and the tertiary and quaternary care mission of the MUHC.

We have developed a series of thoughtful and practical guidelines for the management of common infectious syndromes, in collaboration with a diverse group of clinical staff members. These guidelines are now available on a newly created ASP website. We have been prospectively reviewing patient cases on selected wards, and interacting with prescribers to provide immediate feedback on antimicrobial prescriptions. Over the past year, we have reviewed over 900 individual cases and provided formal ASP recommendations in the form of a consultation. In addition we continue to provide longitudinal pharmacokinetic services to all inpatients and selected outpatients on specific antimicrobial agents, enabling immediate dosage adjustments and minimizing toxicity and adverse events.

We have begun monitoring antimicrobial usage data across the institution. Though we do not yet have sufficient data to assess the specific impact of our activities on overall trends across the entire institution, our interventions lead to discontinuing or changing one third of the antibiotic prescriptions we review.

We believe an expansion of our activities will have substantial benefit in terms of clinical and cost outcomes, with some key investments. In this report we present the MUHC ASP's activities for 2019-2020, the trends we have noted, the indicators we follow, the strategic priorities we propose for next year, and the gaps we need to urgently address.

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BACKGROUND

Every year, an estimated 18,000 patients develop drug-resistant infections in Canadian hospitals; over 5,000 deaths per year are directly attributable to Antimicrobial Resistance (AMR). The global emergence of AMR and antibiotic-associated infections such as *C. difficile* have significant impacts on patient morbidity, mortality, healthcare costs, as well as staggering public health and economic implications. As significant as these impacts are now, they will worsen if resistance to current first and second-line antimicrobials continues to increase over time. In acute care settings with effective Infection Prevention and Control policies and programs, as is the case at the MUHC, spread of pathogens between patients is now limited - the major driver of AMR is now our excessive use of antimicrobials. At the MUHC, the costs of antimicrobials are close to 3 million CAD annually representing around 10% of the total pharmacy budget. The indirect costs of antimicrobial overuse (costs of colonization and infection with multi-drug resistant pathogens; costs of additional diagnostic tests or procedures; increased length of stay in hospital, etc.) have not been quantified, but are likely considerable.

The goal of our Antimicrobial Stewardship Program is to promote the optimal use of antimicrobials in ways that ensure access for patients that need antimicrobials, improve their outcomes, while minimizing patient- and institutional-level unfavourable effects.

The Antimicrobial Stewardship Program (ASP) of the MUHC evolved from the antibiotic subcommittee of the P&T committee. Initially, core activities consisted of: i) restricting the use of certain antimicrobials on the institutional formulary to infection experts (ID); ii) performing point-prevalence surveys of antimicrobial use (AMU) within global point-prevalence survey initiatives; iii) providing educational sessions to clinicians; iv) conducting AMR surveillance and clinical research projects. Since a restructuring of the program and the committee in January 2019, a small but dedicated operational team conducts the daily stewardship activities and a multidisciplinary ASP committee has oversight on the team's activities. The ASP committee chair is a sitting member of the P&T committee; the program is co-led by an infectious diseases (ID) physician and a clinical pharmacist, who are each accountable to the MUHC Director of Infectious Diseases and the Chief of Pharmacy, respectively.

VISION AND MISSION

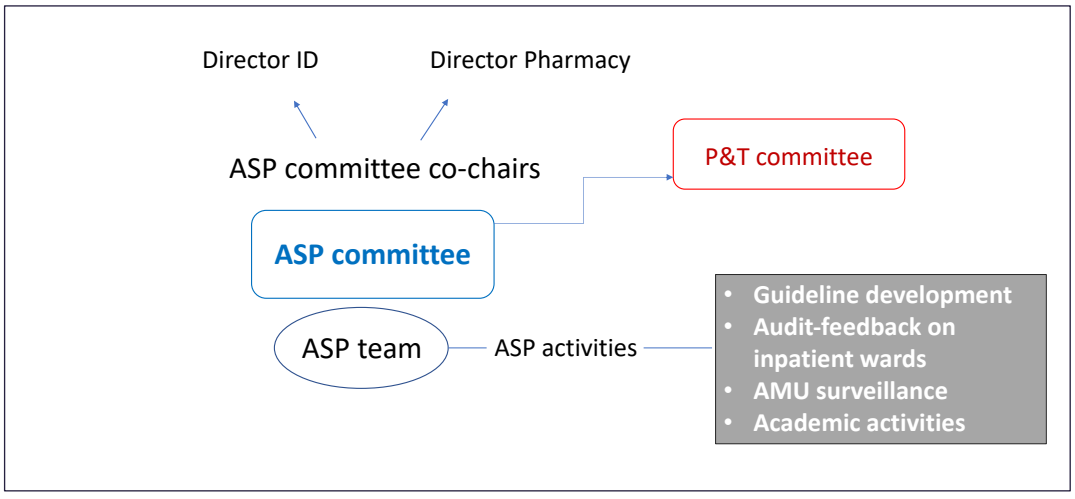
Optimize antimicrobial effectiveness while minimizing the potential for adverse events, antimicrobial drug resistance and costs

To achieve our primary aim of improving quality of patient care and safety, we employ a systematic approach focused on:

- ***Advising*** best practice: policies and treatment guidelines for the use of antimicrobial agents at the MUHC
- ***Tracking*** *(surveillance)* antimicrobial use within the institution
- ***Reporting*** *(feedback)* information on antibiotic use and resistance profiles to relevant clinical and administrative staff
- ***Educating*** health professionals on matters related to antimicrobials and their appropriate use
- ***Researching*** the impact of specific interventions on antimicrobial use at the MUHC

TEAM MEMBERS

The MUHC ASP is structured and governed as depicted below:



The **operational team** is composed of pharmacists (weekly rotation), ID physicians (assigned to specific wards, longitudinal) and part-time administrative personnel (website maintenance, database set-up and data monitoring)

Pharmacists	MD (ID)	Admin/research
Qian Li Daniel Thirion François Bourdeau Van Dong Nguyen Raphaëlle Lauly Anh Thu Do Mireille Bédard (maternity leave) Derek Lee (Sep 2018 - 2019)	Makeda Semret (RVH C10/D10) Anne-Marie Bourgault (MGH surgical wards) Ruth Horn (RVH C7/D7) Charles Frenette (RVH C9/D9)	Salvatore Moffat (part-time) Barbara Ann Jardin (part-time) Miraal Mavalvala (part-time Jan-Dec 2020)

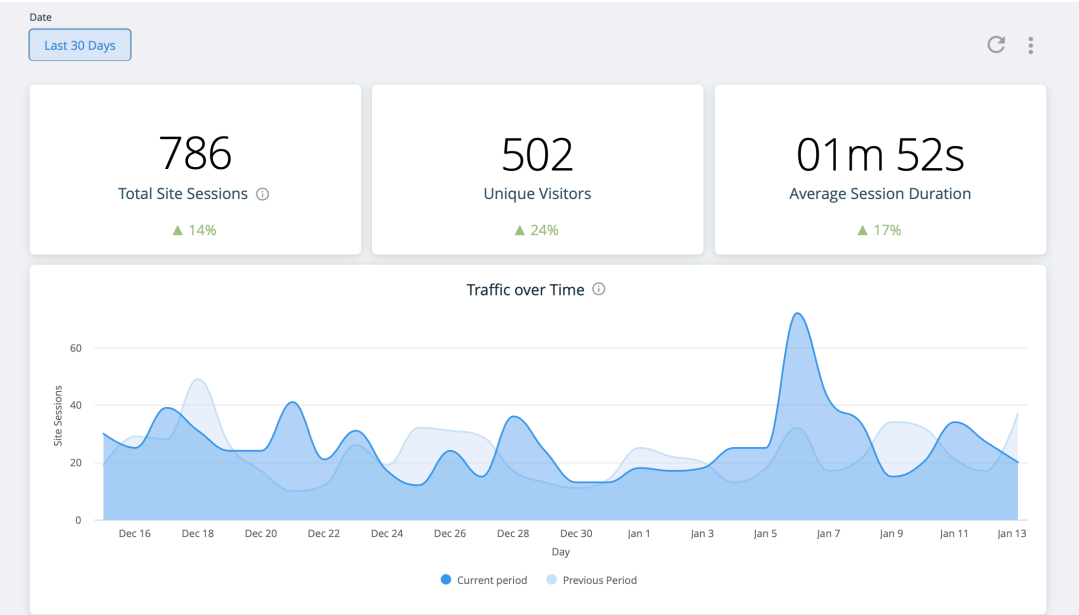
A multidisciplinary ASP committee which provides oversight over the team's activities consists of members with expertise in ID, Microbiology, pharmacotherapy, Infection Prevention and Control, and representatives from key divisions including General Internal Medicine, Emergency Medicine, Hematology-Oncology, Critical Care medicine, and General Surgery.
Members of the ASP committee are listed:

ACTIVITIES

Website creation

To enable easy access to MUHC treatment guidelines and increase the visibility of our program, we created a stand-alone ASP website that consolidates all relevant information in a single location (www.muhcasp.com). The decision to create a website rather than host relevant materials on the hospital intranet was based on feedback from clinicians. We conducted a survey in January 2019 and obtained responses from 150 clinicians with diverse practice profiles (ED, Medicine, Surgery) from all sites (RVH, MNI, MGH, Lachine). Of the respondents, 25% stated they had never referred to the intranet for antimicrobial treatment guidelines; only 25% were even aware guidelines existed on the intranet. Most respondents expressed a need for antimicrobial treatment guidelines with the caveat these needed to be easily accessible from all areas of the hospital and remotely, and that a combination website + smartphone application would be ideal.

The ASP website was launched in March 2020. Traffic was initially slow, but sharply increased following the release of our first version of COVID-19 management guidelines in April 2020. We currently have close to 800 visits per month though the number fluctuates (increases specifically following announcements of updates to the COVID-19 guidelines). Of note, our website attracts visitors from outside Canada (USA, Europe, Africa, Middle East, etc.). The figure below illustrates website traffic for the period Dec 15, 2020 to Jan 13, 2021 with a peak immediately after updates to COVID guidelines on Jan 6, 2021.

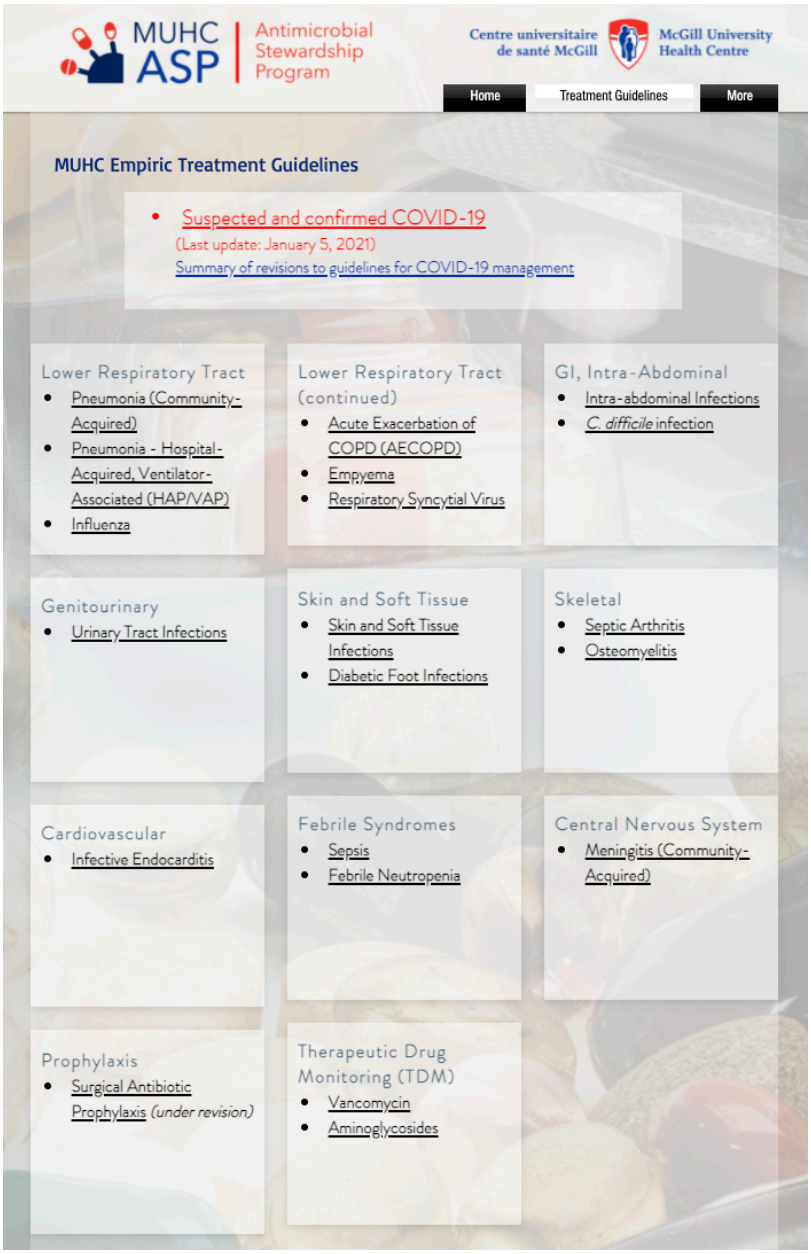


Guideline development

Previously, treatment choices for common infectious conditions (pneumonia, urinary tract infections, etc.) were listed in a single document (in a table format) accessible on the intranet under Pharmacy/treatment guidelines/infectious diseases. In order to increase readability and therefore compliance, we have prioritized the development of individual documents for each condition, and include recommendations on microbiological workup in addition to antimicrobial management. We strive for the content to be relevant and educational, and for the format to be succinct (and legible on smartphones). Most importantly, we include input from clinician stakeholders in the process of guideline development to ensure “buy-in”.

Guidelines are first drafted by a member of the operational team with references to best available evidence. They are then reviewed by the ASP co-leads, circulated to selected relevant stakeholders, discussed by the ASP committee, and finally endorsed by P&T.

Currently 21 guidelines that are thoughtful and practical have been finalized and uploaded onto **www.muhcasp.com/treatment-guidelines**.



Cumulative antibiograms 2019

We have compiled rates of susceptibility to antibiotics of organisms commonly isolated (all specimens) from our patient population (RVH and MGH). These data, presented as cumulative antibiograms for 2019, were used to support empiric antimicrobial treatment choices in the empiric treatment guidelines and will be useful to monitor overall resistance trends over time. Further work is underway to provide specimen- and site-specific antibiograms for analyses of trends.

Compiled through LUMED platform

- GRAM positive
- GRAM negative

Gram positive	Gram negative
Staphylococcus aureus	*Acinetobacter baumanii*
Methicillin-resistant staphylococcus aureus (MRSA)	*Citrobacter freundii*
Enterococcus faecalis	*Escherichia coli*
Enterococcus faecium	*Haemophilus influenzae*
Streptococcus anginosus	*Klebsiella oxytoca*
Streptococcus mitis	*Klebsiella pneumoniae*
Streptococcus pneumoniae	*Proteus mirabilis*
Staphylococcus epidermidis	*Pseudomonas aeruginosa*
Staphylococcus heamolyticus	*Serratia marcescens*
Staphylococcus lugdunensis	*Stenotrophomonas maltophilia*

AVAILABLE ON www.muhcasp.com/muhc-antibiograms

Prospective audit-feedback activities

We previously used to conduct periodic point-prevalence surveys of antimicrobial use selectively, e.g. by request from Infection Prevention and Control following an MDRO outbreak on a particular ward. After data analysis, ward- and department-level feedback would be delivered as an educational activity. Because the impact of educational sessions is generally modest (necessary but not sufficient to drive behavior change), and prescribers tend to be mostly residents rotating throughout the institution, we have shifted our focus to **real-time** audits of antimicrobial use **with direct and immediate feedback** to individual prescribing physicians. Prospective audit-feedback is now a core activity of our program, with the feedback presented as a formal ASP consultation on O-word.

The audit-feedback team consists of a 1:1 pairing of ID specialist to pharmacist conducting weekly audits of antimicrobial use on target wards at the MGH and RVH.

Target Wards

- MGH: all surgical services (thoracic surgery, orthopaedic surgery, neurosurgery, general surgery, oral and maxillofacial surgery, plastic surgery, other)
- RVH:
    - All surgical services: cardiac surgery, vascular surgery, general surgery, urologic surgery, miscellaneous (oral and maxillofacial surgery, plastic surgery)
    - Medical wards: coronary care unit (CCU), internal medicine, hematology-oncology, transplant medicine

The ID physicians are assigned specific wards, while pharmacists rotate on a weekly basis. Cases to be audited are first identified using prespecified inclusion criteria:

Inclusion Criteria for 2019 - 2020

- Active parenteral **antibiotic** prescriptions
- Active oral broad-spectrum antibiotic prescriptions (i.e. amoxicillin-clavulanate, TMP-SMX, fluoroquinolones, third-generation cephalosporins)

Exclusion Criteria for 2019 - 2020

- Patients actively followed by ID service, or previously followed by ID service and treating team still following ID treatment plan

- Discharge imminent i.e. < 24 hours
- Antifungals, antivirals, prophylactic antibiotics

The ASP team then reviews the clinical information available in the medical records to identify opportunities to optimize antimicrobial use. The antimicrobial stewardship consultation on O-word provides specific recommendations for the antimicrobial(s). In cases considered too complex for ASP recommendations, we suggest to consult the clinical ID service. The ASP recommendations fall under 3 main categories:

- **Continue** current antimicrobial with a timeline for reassessment;
- **Change** the current antimicrobial (dose, route, or type);
- **Discontinue** the current antimicrobial.

The consultation is printed and flagged in the patient chart, but the ASP team does not change medication orders. The pharmacist monitors whether or not recommendations were accepted by the treating team.

Indicators:

We have been systematically collecting data on:

- Number of antimicrobial prescriptions audited;
- Types of recommendations issued;
- Acceptance of our recommendations by treating teams.

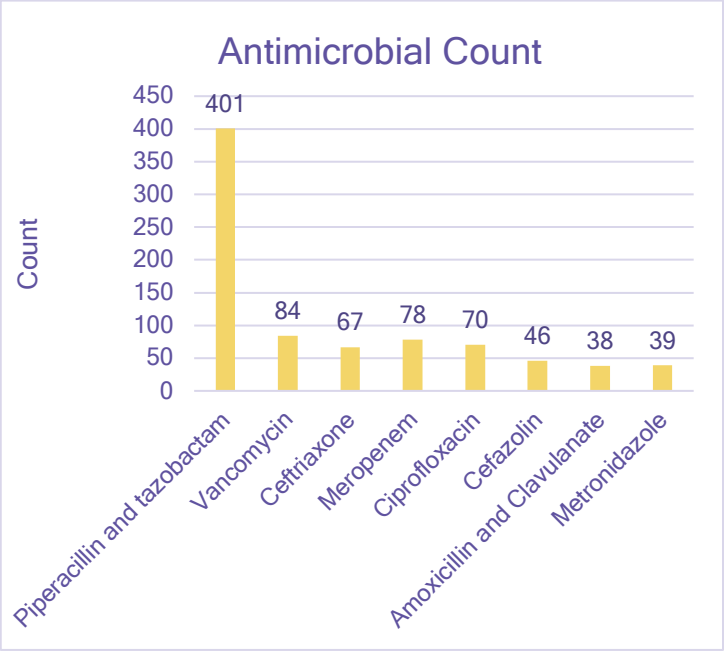
All data are manually entered into a secure web-based database (REDCap) in order to monitor and evaluate our activities.

Results:

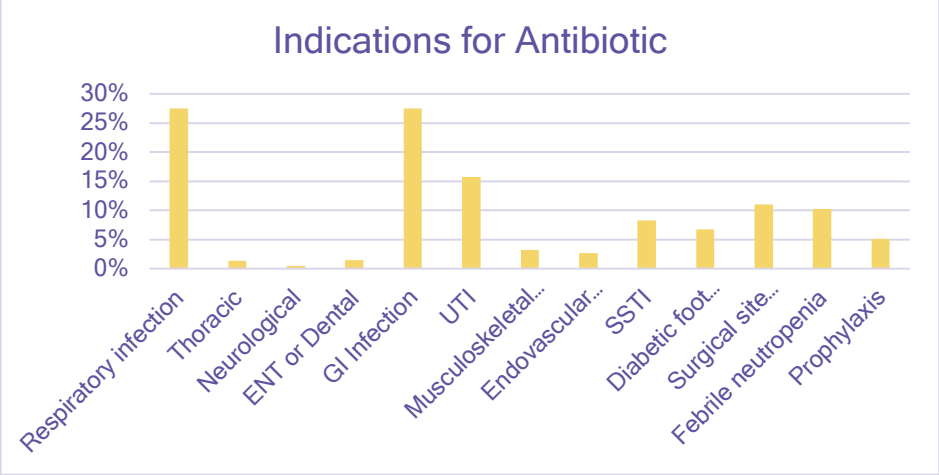
Between February 2019 and October 2020, we audited close to 800 prescriptions of antibiotics (no audits were conducted between March and August 2020 due to the COVID-19 pandemic) at the RVH and MGH.

N=792 antibiotic prescriptions audited
(median 1/patient; range 1-4)

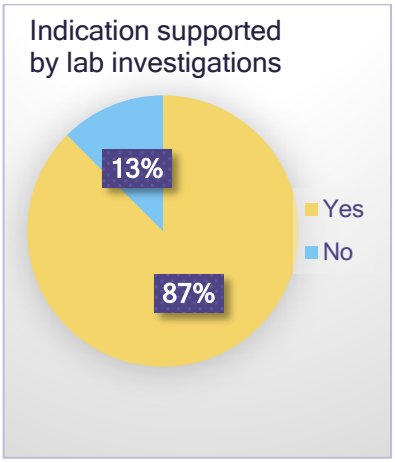
Site	Proportion (%)
RVH	59
MGH	41
Main reason for admission	**Proportion (%)**
Sepsis or suspected infection	26
Medical disease	21
Elective or semi-elective surgery	19
Emergency surgery	12
Malignancy	14
Cardiac disease	4
Polytrauma	4

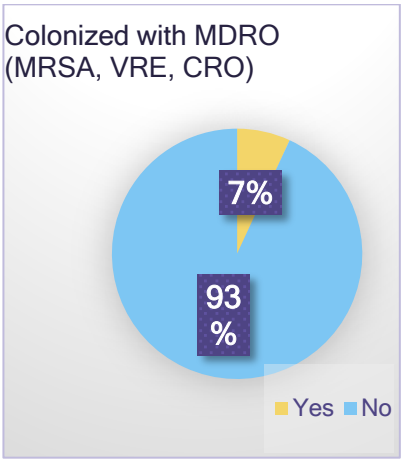


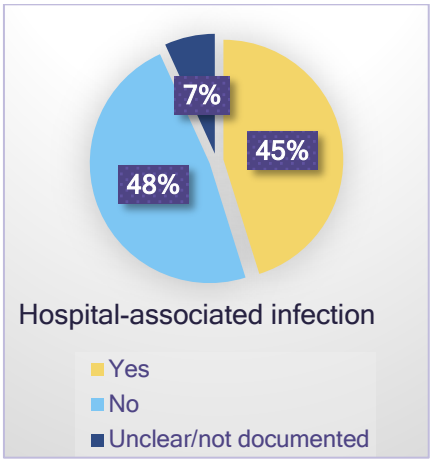
Piperacillin-tazobactam is by far the most frequently prescribed antibiotic on our audited wards followed by vancomycin, then meropenem. The most common indications for antibiotic prescriptions among inpatients in our target wards are respiratory and gastro-intestinal infections (GI infections more frequent at the RVH than at the MGH).



We find that diagnostic workup for infectious syndromes is generally quite appropriate; the documented indication is supported by lab investigations in 87% of cases. Suspected hospital-associated infections account for 45% of antimicrobial prescriptions, and 7% of patients are colonized with drug-resistant organisms at the time of audits.

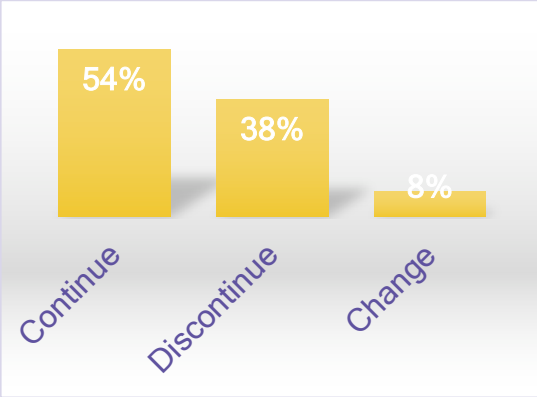






ASP recommendations for antibiotic prescriptions

Between 2019-2020, the ASP team found 46% of prescriptions to be inappropriate and hence recommended to **discontinue or change** the prescriptions, while 54% of prescriptions were deemed appropriate



Reasons for recommendations to discontinue antibiotics:

- Treatment duration sufficient (34%)
- Indication not evident based on medical record (24%)
- Diagnosis not supported by investigations (13%)
- Does not follow MUHC treatment guidelines (7%)
- Other (22%)

Reasons for recommendations to change antibiotics:

- Inappropriate antimicrobial choice (based on microbiology or indication) (57%)
- Dosing inappropriate (25%)
- Route inappropriate (12%)
- Safety considerations (allergies, organ dysfunction, etc.) (1%)
- Other (5%)

Acceptance of ASP recommendations

Overall, 73% of the ASP recommendations were accepted by treating teams. The lowest acceptance rates were noted in situations when the ASP team was not able to connect with members of the treating team or the clinical ward pharmacist at the time of the ASP consultation.

Pharmacokinetic (PK) services

The ASP pharmacists ensure continuous PK services for vancomycin, aminoglycosides, voriconazole and posaconazole for inpatients at the RVH and the MGH, and some selected outpatient clinics (CF and TB clinics). Based on drug levels, patient characteristics and treatment indication, dosages are adjusted on a continuous basis to optimize therapeutic efficacy and minimize toxicity.

We did not formally monitor this activity in 2019-2020, but note from our audit-feedback activities that dosing of antimicrobials has been generally very adequate at our institution.

ANTIMICROBIAL UTILISATION

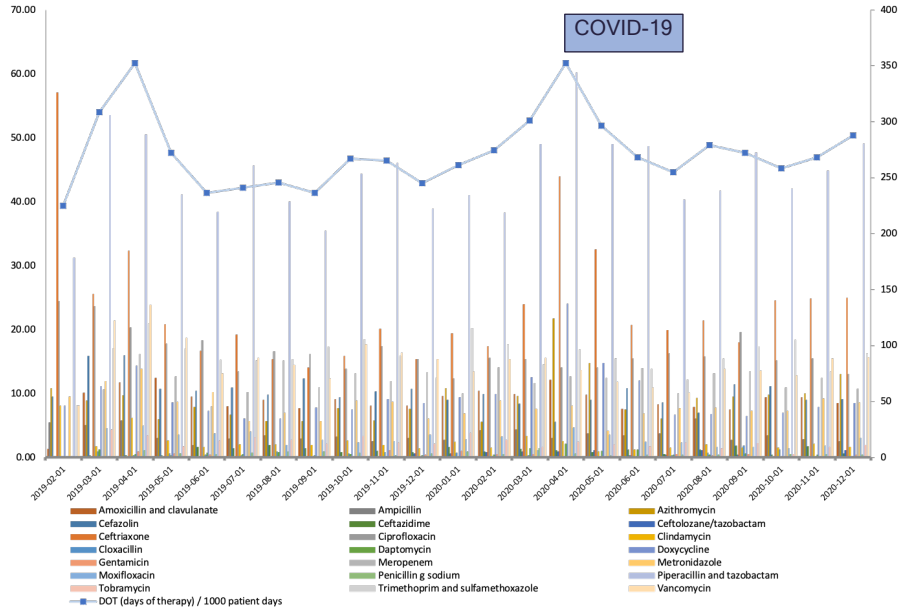
Measurement tools

Prior to 2019, measuring antimicrobial utilisation (AMU) across the institution was a technically challenging task that could only be performed by IT. We are now able to directly compile AMU metrics from the DATA feature of the LUMED platform. We have adopted Days of Therapy (DOT) as our preferred metric, as it is the most accurate measure of AMU endorsed by healthcare safety networks and international agencies. We further normalize DOT to the common denominator of 1000 patient-days.

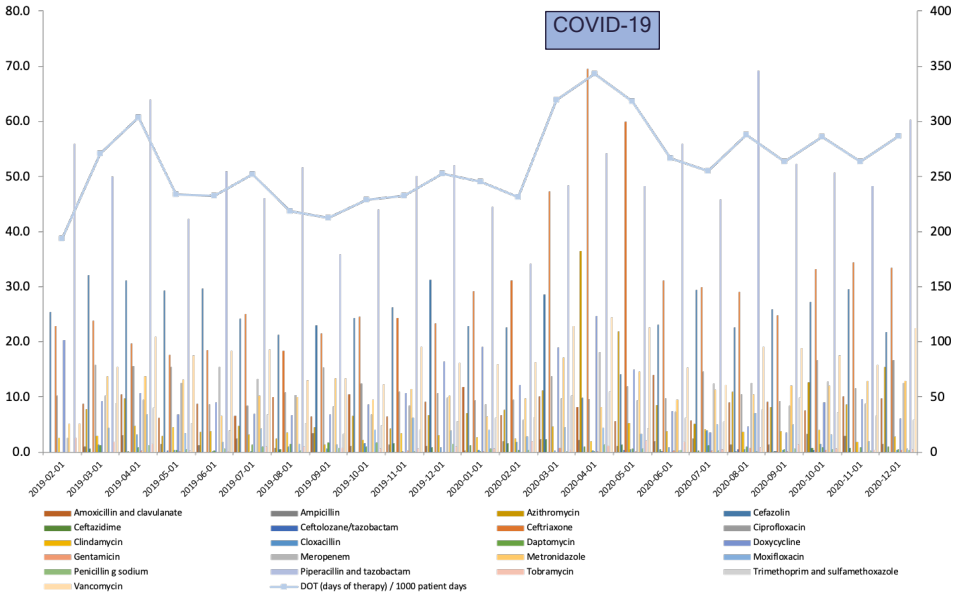
Trends

In this report we present monthly AMU data (DOT/1000 patient-days) for each hospital site. The blue line represents total AMU (all antibiotics), while individual antibiotic DOT are shown as colored bars. We note increase in total AMU at both sites in April-June 2020, coinciding with the first wave of COVID-19 when all audit-feedback activities had ceased.

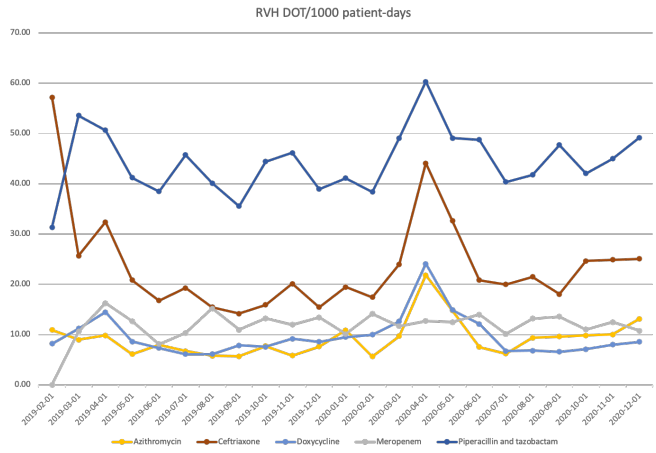
DOT per 1000 Patient days RVH

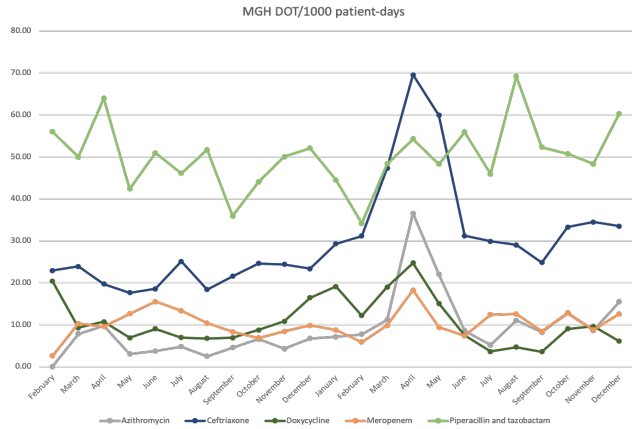


DOT per 1000 Patient days MGH



Of note, while piperacillin-tazobactam is generally the most utilized antibiotic throughout the year, during the spring of 2020 the increase in AMU was predominantly driven by ceftriaxone, azithromycin and doxycycline - the very antibiotics that, at the time, were recommended in our guidelines for the initial management of COVID-19. The figures below show trends for selected antibiotics (ceftriaxone, azithromycin, doxycycline, piperacillin-tazobactam, meropenem)



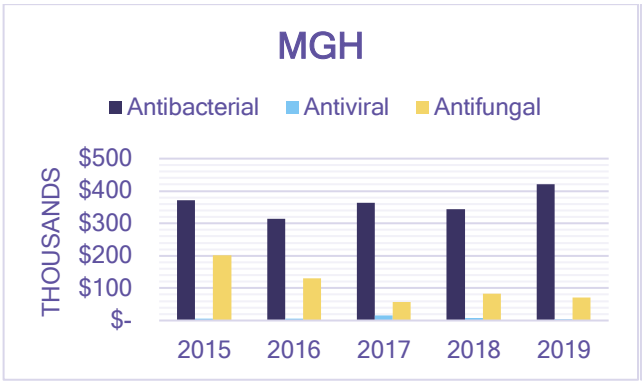


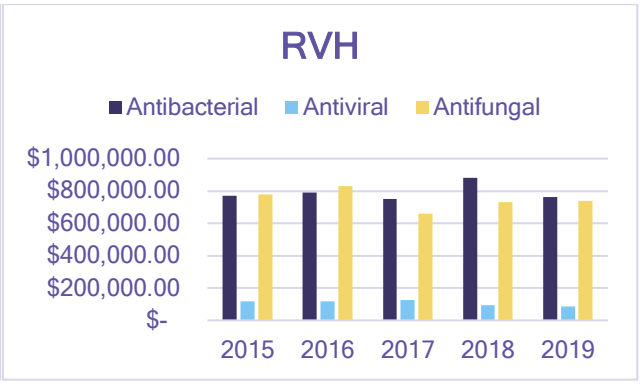
This suggests that MUHC clinicians follow treatment guidelines in terms of **initial choice** of antimicrobial therapy, but are less likely to discontinue antibiotics on their own, even in the absence of confirmed bacterial infection. This confirms the importance of sustained audit-feedback activities to reduce or optimize AMU.

ANTIMICROBIAL EXPENDITURES

Data on antimicrobial (class 8 drugs) expenditures are presented for 2015-2019, based on pharmacy data and reflecting mostly inpatient usage.

At the MGH antibacterials account for most of the antimicrobial expenditures, particularly since the transfer of hematology-oncology care to the Glen site in 2015. At the RVH, antifungals account for **nearly half** of the total antimicrobial expenditures. Although there is to date insufficient data to assess the impact of our activities on overall antimicrobial expenditures, it is unlikely our activities will have significant impact on costs **until we include antifungals** in prospective audit-feedback activities.





SUMMARY

Since 2019, we have reorganized our structure, engaged a truly multidisciplinary oversight committee, consolidated a small but skilled operational team, and focused on successfully implementing core activities. We have adopted a process for guideline development that involves relevant experts and stakeholders, and produced guidelines that clinicians consider useful. We have directed our efforts and focused our core activities in the sectors that we believe will have higher long-term impacts.

We now systematically monitor antimicrobial use (AMU) at the RVH and MGH, in addition to expenditures. At present, there is insufficient data to detect trends or accurately assess the impact of our activities on AMU. We do however have compelling preliminary evidence that MUHC clinicians are increasingly accessing the ASP website and complying with newly developed antimicrobial therapy guidelines.

Piperacillin-tazobactam remains the “workhorse” and is the most frequently prescribed antibiotic by a wide margin. This is not surprising since healthcare-associated infections are frequent; the use of broad-spectrum antibiotics is generally driven by legitimate concerns the MUHC patient population carries a high-risk of complicated and drug-resistant infections. We find that clinical and laboratory investigations are generally appropriate and support treatment indications. Yet, despite the complexity of the MUHC cases, we identify that antibiotics can safely be discontinued in over one third of cases audited. Our feedback is generally well received, but acceptance of our recommendations will likely improve through greater communication with treating teams.

PRIORITIES FOR 2021-2022

Building on our experience and learnings to date, we hope to tackle the following strategic priorities in the coming years:

Expansion of Audit and feedback activities

- **Clinical Teaching Units (Medicine CTU):** We had previously not targeted medical CTUs because CTUs had their own stewardship initiative, which is now defunct. Given the significant utilization of antimicrobials on these units and our manpower limitations, success will be dependent on sustained access to electronic platforms such as the LUMED clinical decision support system. We are currently working with the company to optimize this tool for our needs, such that some of our activities can be conducted remotely, in real time, and be less dependent on a physical review of the medical chart.
- **ICU:** The ICU poses a particular challenge. Providing feedback based on chart reviews would be labor-intensive and low yield due to the complexity of the cases and high prevalence of drug-resistant organisms in that setting. Targeting only specific drugs (e.g. carbapenems and antifungals) would be feasible, and could inform next steps.
- **Antifungals:** Antifungals represent a significant portion of our overall antimicrobial expenditures and are increasingly used particularly at the RVH. Evaluating current use and optimizing antifungal prescriptions in collaboration with the newly created ID-Hematology-Oncology-Transplant clinical service (ID-HOT) is a logical and important next step in our activities.

Guideline development

- **Surgical antibiotic prophylaxis:** The MUHC surgical antibiotic prophylaxis guidelines, which have not been reviewed since 2016, include agents such as single-dose aminoglycosides for some surgeries (e.g. cardiac and vascular). Reports of nephrotoxicity in these patients and concerns for patient safety have since emerged. We will work with surgical specialties to update pre-operative surgical prophylaxis guidelines, basing these on existing evidence and institutional (IPC) data on surgical site infection rates.
- **Antibiotic prophylaxis in vascular and interventional radiology (IR):** There are currently no MUHC guidelines for antibiotic prophylaxis during vascular and IR procedures. Divergent practices are commonly seen, with concerns of indiscriminate use of third-generation cephalosporins and aminoglycosides and questions of drug supply on

units. The development of these guidelines is therefore a priority together with the surgical prophylaxis guidelines.

- **Management of fungal infections:** We currently do not have MUHC guidelines for the treatment of superficial and invasive fungal infections. Though these are frequently managed by ID, guidelines will help set benchmarks for our planned assessment and optimization of antifungal use.
- **Other:** We will further develop guidelines relevant for the Montreal Neurological Institute *(Encephalitis, Nosocomial meningitis/ventriculitis),* Obstetrics/Gynecology Department *(Chorioamnionitis, endometritis, vulvovaginitis/cervicitis/PID),* and eventually surgical sub-specialities (ENT, Plastics, etc.). Of note, all MUHC empiric treatment guidelines will be updated periodically based on latest available evidence.

Education

- **Online ASP course for residents and MUHC clinicians:** Residents and faculty have expressed a need for educational sessions on antimicrobial stewardship. We will develop an online course to be hosted on the McGill MyCourses platform, that is focused on basic foundational knowledge of antimicrobials, fundamentals of microbiological workup and MUHC treatment guidelines for common infectious syndromes. We will work with the MUHC education office, residency program directors and CTU directors to ensure the course is available to all medical and surgical residents (with certification) prior to or upon starting their rotations at the MUHC.
- **Residency training and Clinical fellowship in ASP:** Infectious Diseases-Medical Microbiology residents now rotate in ASP at the MUHC as part of their core training. These residents will be assigned scholarly projects that include an educational component that will serve the institution. Further, the McGill ID-Microbiology training program and Post-Graduate Medical Education office have approved a 1-year clinical fellowship in Antimicrobial Stewardship for physicians. This fellowship is currently not funded, but we will work to identify potential funding streams to ensure our program attracts high-caliber candidates.

Quality / Research initiatives

- **Prescription report cards:** In addition to feedback provided to individual prescribers through audit-feedback, we will compile ward-specific aggregate statistics in terms of appropriateness of prescribing (based on compliance to guidelines, duration of treatment, appropriateness of diagnostic workup). These “report cards” will be an

opportunity for exchange between the ASP and ward treating teams, with a goal to identify specific challenges and areas for improvement.

- **Research:** Several members of the ASP committee and operational team are active researchers, already leading or participating in antimicrobial clinical trials including projects assessing shorter treatment durations. We will support and collaborate with MUHC-based research teams, but additionally are exploring the feasibility of scholarly projects involving trainees (ID and pharmacy residents) in 2021.

GAPS / CHALLENGES

We have been able to pursue many of the activities described in this report with the help of a part-time research assistant (whose salary is paid by Dr. Semret's research funds). More recently, the pharmacy department has provided secretarial support for committee meetings. While that has been very helpful, to expand our activities as described above and achieve meaningful clinical and cost outcomes, **investments in 2 key areas** is critical:

1) **Dedicated program admin:** creating such a position (at least part-time) is crucial to delegate some of the time-consuming tasks and liberate the operational team to focus their efforts on activities requiring expertise. The ideal candidate would be an MSc holder with a background in sciences (e.g. microbiology or pharmacy), and their tasks would include (but not limited to): basic analytics; website/app maintenance; meeting organization; outreach and communications; scheduling of core activities; preparation of courses; drafting reports and "report cards".
2) **Electronic platform:** with our manpower limitations, clinical decision-support tools are essential to increase the scope and frequency of activities with an impact on antimicrobial use. Since 2019, we have obtained access to the APSS function of the LUMED platform on a trial (pilot) basis. This function merges electronic medical records, laboratory results and prescription information and enables various analyses. While there are competing products in this area, we have found APSS-LUMED to be powerful, user-friendly and are currently working with the company to refine its functionality for our setting. Continued access to APSS, or purchase of an equivalent alternative, is critical to maintain and expand our activities.