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A point-prevalence survey of antimicrobial utilisation within New Brunswick hospitals to focus antimicrobial stewardship efforts and decrease low-value care

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RESUME

Introduction: Il est important de minimiser le gaspillage et les risques associés aux soins sans valeur. La gestion de l'utilisation des antimicrobiens vise à optimiser leur emploi et doit être adaptée au milieu et à sa population.

Objectifs: Évaluer les profiles d'utilisation actuels des antimicrobiens et fixer des objectifs pour les interventions en matière de gestion des antimicrobiens.

Méthode: Vingt-et-un hôpitaux du Nouveau-Brunswick offrant des soins de courte durée en médecine générale, en chirurgie et en pédiatrie ont pris part à une enquête sur la prévalence ponctuelle. Tous les patients admis aux hôpitaux participants et ayant reçu au moins un antimicrobien systémique ont été inscrits à l'étude. Les principaux critères d'évaluation étaient le profil d'utilisation, selon l'indication et l'antimicrobien prescrit, le bienfondé de l'utilisation et la durée de la prophylaxie chirurgicale. Des statistiques descriptives et un test d'indépendance X^2 furent utilisés pour l'analyse de données.

Résultats: L'enquête a été menée de juin à août 2012. Un total de 2244 patients ont été admis pendant la durée de l'étude et 529 (23,6%) ont reçu un antimicrobien. Au total, 691 antimicrobiens ont été prescrits, soit 587 (85%) pour le traitement et 104 (15%) pour la prophylaxie. Les antimicrobiens les plus souvent prescrits pour le traitement (n=587) étaient des classes suivantes : quinolones (25,6%), pénicillines à spectre étendu (10,2%) et métronidazole (8,5%). Les indications les plus courantes du traitement étaient la pneumonie (30%), les infections gastro-intestinales (16%) et les infections de la peau et des tissus mous (14%). Selon des critères définis au préalable, 23% (n=134) des ordonnances pour le traitement étaient inappropriées et 20% (n=120) n'avaient aucune indication de documentée. Les domaines où les ordonnances étaient inappropriées étaient les suivants : défaut de passage de la voie intraveineuse à la voie orale (n=34, 6%), mauvaise dose (n=30, 5%), traitement d'une bactériurie asymptomatique (n=24, 4%) et doublement inutile (n=22, 4%). Dans 33% (n=27) des cas, les ordonnances pour la prophylaxie chirurgicale étaient pour une période de plus de 24 heures.

Conclusions: Les résultats démontrent que les efforts de gestion des antimicrobiens doivent se concentrer sur les interventions conventionnelles de gestion de l'utilisation des antimicrobiens, l'amélioration de la documentation, l'optimisation de l'utilisation des quinolones et la réduction au minimum de la durée de la prophylaxie chirurgicale.

Mots clés: gestion de l'utilisation des antimicrobiens, prévalence ponctuelle, utilisation des antimicrobiens, utilisation appropriée, soins sans valeur

ABSTRACT

Introduction: Low-value practices should be stopped as they lead to waste and possible harm. Antimicrobial stewardship (AS) aims at optimizing antimicrobial prescribing and should be tailored to local needs.

Objectives: To assess current patterns of antimicrobial utilisation and identify targets for AS interventions.

Methods: A point prevalence survey was completed in 21 hospitals in New Brunswick, Canada. All admitted patients at the time of the survey and receiving at least one systemic antimicrobial were included. Main outcome measures included patterns and appropriateness of utilisation, and duration of surgical prophylaxis. Descriptive statistics and Chi-squared test of independence were used to analyse data.

Results: The survey was completed between June and August 2012. Of 2244 eligible patients, 529 (23.6%) were on antimicrobials. A total of 691 antimicrobials were prescribed, 587 (85%) for treatment, 104 (15%) for prophylaxis. Within the treatment group (n=587) the most frequently prescribed classes were fluoroquinolones (25.6%), extended-spectrum penicillins (10.2%) and metronidazole (8.5%). The most common treatment indications were pneumonia (30%), gastrointestinal infections (16%), and skin and soft tissue infections (14%). Based on predefined criteria 23% (n=134) of the treatment orders were inappropriate and 20% (n=120) had no documented indication. Areas of inappropriateness included not switched from IV-to-PO (n=34, 6%), inappropriate dose (n=30, 5%), treatment of asymptomatic bacteriuria (n=24, 4%) and inappropriate duplication (n=22, 4%); 33% (n=27) of surgical prophylaxis orders exceeded 24 hours.

Conclusions: The findings support AS efforts focused on established AS interventions, improved documentation, optimised fluoroquinolone use, and minimized length of surgical prophylaxis.

Keywords: antimicrobial stewardship, point prevalence survey, antimicrobial utilization, appropriateness of utilization, low-value care

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LIST OF ABBREVIATIONS

AHFS	American Hospital Formulary Services
AS	Antimicrobial Stewardship
ASC	Anti-Infective Stewardship Committee
CAD	Canadian Dollars
CDAD	*Clostridium difficile*-Associated Diarrhoea
CDC	Center for Disease Control and Prevention
CPS	Canadian Paediatric Society
C&S	Culture and sensitivity
CI	Confidence Interval
CSHP	Canadian Society of Hospital Pharmacists
D&T	Drugs and Therapeutics Committee
eGFR	Estimated Glomerular Filtration Rate
ECDC	European Centre for Disease Control and Prevention
ESAC	European Surveillance of Antimicrobial Consumption
EU	European Union

GDP	Gross Domestic Product
HIV	Human immunodeficiency virus
ICU	Intensive Care Unit
ID	Infectious Diseases
IDS	Infectious Diseases Service
IDSA	Infectious Diseases Society of America
IV	Intravenous
MRSA	Methicillin-Resistant *Staphyloccocus aureus*
NB	New Brunswick
PO	Oral
PPS	Point Prevalence Survey
ROP	Required Organizational Practice
SD	Standard Deviation
SHEA	Society for Healthcare Epidemiology of America
US	United States
VRE	Vancomycin-Resistant Enterococcus

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CHAPTER 1. INTRODUCTION

New Brunswick (NB), with a population of approximately 750,000, was recently amalgamated into two health authorities: Horizon Health Network (Horizon) and Vitalité Health Network (Vitalité). Horizon, a 1606-bed multi-hospital network, is the largest health-care organization in Atlantic Canada, serving NB, northern Nova Scotia and Prince Edward Island. Vitalité is also a multi-hospital network, serving primarily the francophone population of the province. Both regions include university hospitals, tertiary services and well as community hospitals. Within this context, systems from the various regions are entering into new affiliation agreements and their care practices are being reviewed and harmonized, therefore moving the province towards a more fully integrated health care system.

An important example of such harmonization is the NB Provincial Drugs and Therapeutics (D&T) Committee with its subcommittee, the NB Provincial Health Authorities Anti-Infective Stewardship Committee (ASC). The latter has the mandate to advise on all matters relating to the use of antimicrobials within the regional health authorities (Appendix 1). Its purpose is to make evidence-informed recommendations to the provincial D&T Committee regarding effective, safe and cost-effective choices of anti-infective agents to include within the provincial hospital formulary as well as the conditions and/or criteria for their use when appropriate, therefore acting as steward of this limited therapeutic resource. The ASC also has the mandate to develop and maintain an Antimicrobial Stewardship Program and to undertake reviews of antimicrobial utilisation with the goal to ensure their most clinically appropriate use with

regards to efficacy, toxicity and resistance patterns and make recommendations as appropriate. Ideal drug usage has been described as using "the right drug, administered by the best route, in the right amount, at the optimal interval, for the appropriate period, after an accurate diagnosis". (1) Recognizing that local, regional, national and international variations in antimicrobial prescribing practices exist and they are influenced by both cultural and behavioural determinants (2), the AS program aims towards interventions that are measurable and guided by international as well as local evidence.

Creating an AS program requires acquiring baseline information, including institutional use. (3) This helps identify recurrent problems with antimicrobial use at the institution-level and frame the problems that need to be addressed (e.g. failure to discontinue surgical antibiotic prophylaxis, vancomycin therapy for a single coagulase-negative *Staphylococcus* species blood culture, combination therapy for all gram-negative infections). (3, 4) Prior to this project no data were available to accurately assess antimicrobial utilisation within NB hospitals. Without these data, the NB Provincial Health Authorities ASC had no baseline against which to develop targeted AS interventions and against which to measure the effectiveness of such interventions. As a means to acquire these data, the ASC recommended the completion of a point prevalence survey in all eligible NB hospitals and across all services. To our knowledge, this is the first time such a large number of antimicrobial orders were reviewed over such a broad area of care within a health system in Canada.

CHAPTER 2. LITERATURE REVIEW

2.1 Influencing Prescribing Patterns

Research has shown that in the absence of a clear diagnosis, physicians oftentimes prescribe antimicrobials to be "on the safe side" or to prevent secondary bacterial infections. (5,6) Prescribing by physicians is believed to be influenced by factors such as cultural beliefs of the patient and the prescriber, patient-driven demand, socioeconomic factors, clinical autonomy as well as diagnostic uncertainty. (2, 6, 7) Strategies that have been used to influence prescribing include production of guidelines, development of multidisciplinary teams and an emphasis on education. (8) Despite such measures, personal experience has been shown to have a high degree of influence on physician prescribing patterns, at times contradicting evidence-based literature, and has led to less than optimal perceptions regarding such guidelines. (8)

A recent Cochrane review was performed and included interventions aimed at improving antimicrobial prescribing. (9) Both persuasive and restrictive interventions were reviewed. The persuasive interventions advised physicians on how to prescribe and provided them with feedback on their prescriptive habits; whereas the restrictive interventions aimed at limiting their prescriptive autonomy. An example of a restrictive intervention is the need for a physician to obtain approval from an infectious diseases (ID) specialist prior to or shorting after initiating an antimicrobial order. Restrictive interventions were found to have a significantly greater impact on prescribing outcomes at one month (32%, 95% confidence interval (CI) 2-61%, p=0.03) and on microbial outcomes at 6 months (53%, 95% CI 31-75%, p=0.001) but this

difference was no longer apparent at 12 or 24 months. (9). The authors performed a meta-analysis and concluded that restrictive interventions are most effective when the need is urgent but that after six months, persuasive and restrictive interventions are equally effective. In their review of the effectiveness of the persuasive audit and feedback intervention, Ivers and colleagues performed a multivariable meta-regression analysis and reported that feedback may be more effective when the baseline performance is low, the source of the feedback is a colleague or a superior, the feedback is provided several times and in multiple formats (verbal/written) and includes explicit targets and an action plan. (10) Any choice of intervention requires baseline data against which to measure its effectiveness. (2)

2.2 Low-Value Health Care: Disinvestment

Headlines throughout the developed world reflect concern related to the swelling cost of providing health services. In Canada, during the period from 1998 to 2008, public-sector spending on health grew at more than double the rate of revenue growth. (11) Total spending on health care in Canada was projected to reach $200 billion (CAD) in 2011, representing a health to gross domestic product (GDP) ratio of 8.1 percent. (11) Total expenditures for hospital services alone were $49.5 billion (CAD) in 2008 and were expected to rise to $58.4 billion (CAD) in 2011 or 3.4% of the GDP. (12) Older data estimate the annual costs of managing a methicillin-resistant *Staphylococcus aureus* (MRSA) colonized or infection patient to be $1363 (CAD) and $14 360 (CAD) respectively, the total for all Canadian hospitals being $42-$59 million (CAD). (13) Incremental costs for managing vancomycin-resistant enterococcus (VRE)-colonized patients were estimated at $6732 (CAD) per patient or $5 to $16 million for all Canadian

hospitals. (13) A model to assess the financial cost of antimicrobial resistance estimates the resistant microorganisms add approximately $25 to $40 million (CAD) annually in direct hospitalization costs in Canada (13)

Coupled with increases in costs and utilisation are questions relating to the effectiveness of many of the services provided. In the early 1990's reports suggested that 20% to 25% of patients received treatments deemed unnecessary and possibly harmful while 30% to 40% of patients did not receive treatment with proven effectiveness. (14, 15) It is generally recognized that up to 50% of antimicrobial use may be inappropriate, adding considerable cost to patient care and microbial resistance. (16-18) In the hospital environment 30 to 50% of antimicrobial use may be unnecessary or inappropriate, the broadest spectrum antimicrobials are commonly used and the most dangerous drug resistance is seen. (19, 20) Despite this, there are limited processes in place to identify, reduce or withdraw health technologies and practices which are obsolete, ineffective or inappropriate therefore remaining unnoticed by those who are involved in administrative and policy decision and resulting in suboptimal care and ineffective resource allocation. (21, 22)

The term disinvestment first appears in the health care literature about 20 years ago and it advocates a more objective, evidence-informed approach to resource allocation. (15) Efforts such as the Choosing Wisely initiative in the United States (US) (www.choosingwisely.org) , the

"Do Not Do" recommendations from the United Kingdom National Institute for Health and Care Excellence (www.nice.org) and recently the Canadian version of the Choosing Wisely campaign (www.choosingwiselycanada.org) are all proponents of health care provision that is based in evidence and critical of low-value interventions. While value in health care has been defined as "the framework for performance improvement" (23), low-value care has been defined as care that delivers "marginal benefit, be it through overuse, misuse or waste." (14) Disinvestment as understood in the context of low-value interventions should be considered part of a broader agenda to improve appropriateness, efficiency and quality, ensuring that the right patient receive the right care at the right time, at the right place and in the right way by the right person. (15)

2.3 Antimicrobial resistance

Despite the availability of antimicrobials, infectious diseases remain the second-leading cause of death world-wide, the third leading cause of death in the US (16) and the seventh in Canada. (17) Infections caused by antimicrobial-resistant organisms have been associated with increased length of hospital stay, increased mortality and increased costs of care. (19, 28) Use of antimicrobials selectively favours the propagation of resistant organisms and hospitals play a key role in this. (29, 30) In Europe, bloodstream infections due to third-generation cephalosporin-resistant *Escherichia coli* resulted in an increase in 30-day all-cause and hospital-stay mortality and an estimated 5-day increase in hospital stays. (28) In similar settings, MRSA patients had higher hospital-stay mortality, 30-day all-cause mortality and an 8.6-day increase

in length of stay compared to patients with methicillin-sensitive *Staphylococcus aureus*. (31)

In Canada, MRSA was first reported in 1981. (30) Data from the Canadian Nosocomial Infection Surveillance Program report increases in MRSA isolates from 0.95 per 100 isolates in 1995 to 8.1 per 100 isolates in 2002. (30) The first isolate of VRE appeared in Canada in 1993. (30) While the rate of VRE in Canada has not attained that of the US, it has been isolated in all 10 provinces. (30) Between 1998 and 2002, the rate of VRE in Canadian hospitals, while increased, was at 0.5 per 1000 patients admitted compared to the US data of 12 per 100 patients admitted. (32) Incident rates of penicillin-, trimethoprim-sulfamethoxazole-, macrolide-, clindamycin- and fluoroquinolone-resistant *Streptococcus pneumoniae* have increased markedly. (33) During the period between 1988 and 2001, rates of penicillin resistance increased from zero to 7% and rates of trimethoprim-sulfamethoxazole resistance increased from 3.7% to 12%. (33) Incidence of macrolide- and clindamycin-resistant isolates of *Streptococcus pneumoniae* has increased from 1.2% to 13.1% and 1.2% to 5.8% respectively during the same 13-year period. (33) Canada reports resistance rates to ciprofloxacin, levofloxacin and moxifloxacin of 1.8%, 0.7% and 0.3% respectively. (33) In patients 65 years of age or older, the rates of levofloxacin- and ciprofloxacin-resistant *Streptococcus pneumoniae* increased from zero to 4.3% and from zero to 7.2% respectively. (33) At present, the major multi-drug resistant gram-negative pathogen isolated in Canadian hospitals is *Pseudomonas aeruginosa.* (34, 35) About 30% of *Pseudomonas* isolates from Canadian and US intensive care units (ICU) are resistant to fluoroquinolones. (34) In Canada, 14% of intensive care unit (ICU)

Pseudomonas isolates demonstrate carbapenem resistance and about 13% of ICU *Pseudomonas* isolates are multi-drug resistant. (34)

Internationally, use of fluoroquinolones has been associated with increased rates of *Staphylococcus aureus* and *Pseudomonas* resistance to fluoroquinolones but also to carbapenems, amikacin and other antimicrobial classes of drugs. (36-38) The European Surveillance of Antimicrobial Consumption (ESAC) reports that during the period 2000-2005, the use of fluoroquinolones increased by 15% or more in almost half of the participating countries. (39) Concomitantly, fluoroquinolone resistance in *E. coli* increased from 5% to 14% during the period 2001-2004 and from 4% in 2005 to 8% in 2008 for *Klebsiella pneumoniae* isolates. (39)

Three general categories of antimicrobial-related drivers of resistance have been identified: the inappropriate or over-use of antimicrobials, sub-therapeutic exposure to an antimicrobial for long treatment periods and the use of low-potency antimicrobials. (30, 34-35) The emergence of antimicrobial-resistant organisms has prompted organizations such as the US Center for Disease Control and Prevention (CDC) (www.cdc.org), the European Centre for Disease Control and Prevention (ECDC) (www.ecdc.europa.eu) and the World Health Organization (www.who.org) and recently the Canadian Paediatric Society (CPS) (www.cps.ca) to send call to arms messages to heighten awareness of the public health concerns linked to the mismanagement of antimicrobials. These organizations caution that without a more judicious

approach to antimicrobial utilisation, antibiotic resistance threatens to return us to an era when even simple infections were fatal.

2.4 Pathogenic Selection

Another unintended consequence of antimicrobial use is the selection of pathogenic organisms. (40) Patients who are hospitalized and prescribed antimicrobials are at increased risk of developing *Clostridium difficile*-associated-diarrhoea (CDAD) due to normal intestinal flora disturbance. (41) In 2003, over 7000 cases of nosocomial CDAD were reported in Quebec hospitals. (42) In 2005, the reported incidence from 30 Quebec hospitals was 15 cases or more per 10,000 patient days, 5 times higher than the historic incidence. (42) A multivariate analysis of these data identified age, duration of hospitalization, a previous episode of CDAD and having received fluoroquinolones, cephalosporins, macrolides, clindamycin or intravenous beta-lactam/beta-lactamase inhibitors as independent risk factors to the development of CDAD. (42) Prolonged (7 days or longer) use of fluoroquinolones, first-generation cephalosporins, cefuroxime, clindamycin and macrolides also increased the risk of CDAD. (42) It is estimated that for every 10 patients that acquire CDAD in hospital, 1 patient will die. (43) The estimated increase in risk of dying in patients with hospital-acquired CDAD is 3-fold. (43) Patients with CDAD are more likely to have prolonged hospital stays; they are more likely to remain in hospital at 7 and 28 days compared to non-infected patients (Canadian data). (44) The median increase in length of stay attributable to CDAD is 6 days. (44)

While increasing antimicrobial resistance has created a critical need for the development of new antibiotics with novel mechanisms of action, the pharmaceutical industry has paradoxically been abandoning this area of research to focus on chronic disease therapies. (4, 26, 34) Since 1998, only ten new antimicrobials had been approved in the US and only two of these (linezolid and daptomycin) actually had new targets of action. (20) The main reasons cited for this decrease in interest are that "drug development is risky and expensive and drugs to treat infections are not as profitable as those that treat chronic disease." (20)

2.5 Antimicrobial Stewardship

Antimicrobial stewardship (AS) has been defined as ensuring patients get the right antimicrobials when they need them (and only when they need them). (17) It has been described as optimal antimicrobial utilisation by using "the right antimicrobial at the right time, at the right dose and for the right duration". (45) Similarity with the themes of disinvestment of low-value care are striking and reflect a need for an evidence-based approach to prescribing resulting in optimal utilisation as defined by Brundtland. (1)

Recognizing every antimicrobial order represents a balance of benefits and risks, AS efforts focus on appropriate use of antimicrobials while attempting to limit unwanted consequences of their use such as antimicrobial resistance, pathogenic selection and drug-related or administration-related adverse reactions. (17, 46). In 2007, the Infectious Diseases Society of

America (IDSA) published guidelines for supporting AS programs as a means to conserve the antimicrobials currently available. (17) A recent review of the literature on the impact of AS programs in critical care areas supports the conclusion that within these areas of care they result in improved antimicrobial utilisation, rates of resistance and limited adverse events while not negatively impacting short-term clinical outcomes. (19)

Antimicrobial stewardship interventions include such activities as clinical audit and feedback, a formulary of targeted antimicrobials and approved indications, education, antimicrobial order forms, guidelines and clinical pathways for antimicrobial utilization, strategies for streamlining or de-escalation of therapy, dose optimization and intravenous (IV) to oral (PO) conversion where appropriate. (17, 40)

2.6 Antimicrobial Stewardship Efforts in Canada

Although widespread resistance to first line antimicrobials is accelerating rapidly worldwide, rates differ considerably from country to country and among geographic regions of larger nations such as Canada. (47) While Canada still enjoys considerably lower rates of resistance than the US, it has substantially higher rates than other developed nations such as Denmark and Iceland. (48)

Systematic efforts for controlling antimicrobial resistance in Canada began in 1997 following a national consensus conference held in Montreal entitled “Controlling Antimicrobial Resistance: An Integrated Action Plan for Canadians”. (13) The conference, co-sponsored by Health Canada and the Canadian Infectious Disease Society, developed a plan which emphasized three core areas: AS, surveillance to monitor resistance trends and infection prevention and control. (13) In the 2012 edition, Accreditation Canada’s Qmentum Program updated its Managing Medications section to include a new Required Organizational Practice: ROP 1.3: “the organization has a program for AS to optimize antimicrobial use”. (40)

Because death rates from hospital-acquired infections are higher than those associated with most community-acquired infections, and rates of antimicrobial use are generally higher in patients admitted to critical care units, most of the AS efforts in Canada and elsewhere have been focused in the critical care environment. (19, 49-52) Studies in Canada have reported improved microbiologically targeted antimicrobial utilisation, decreased antimicrobial costs, decreased use of antipseudomonal agents and improved documentation following the introduction of AS programs within the intensive care area in both tertiary and community hospitals. (51-52)

2.7 Point Prevalence Surveys

Point prevalence surveys (PPS) have been used to provide information about antimicrobial use and to assess the impact of interventions such as antibiotic policies. (53-54) Such surveys have been documented for over 30 years; they can identify targets for improvement in antimicrobial prescribing. (54-55) PPS can help stewardship teams focus on clinical scenarios where overuse is common, where opportunities to de-escalate are missed, and where it can be possible to stop antimicrobial therapy when appropriate. (56) Repeated PPS have been used for the evaluation of infection control programs, to follow trends in hospital-acquired infections, determine rates of device utilisation and antibiotic usage, for intra-hospital comparisons, to measure adverse effects of hospital-acquired infections and to measure costs associated with these infections. (56-57) In Canada, PPS have focused primarily on surveillance of nosocomial infection rates through the Canadian Nosocomial Infection Surveillance Program (www.phac-aspc.gc.ca/nois-sinp/survprog-eng.php) and one article was identified in the literature that reports on the prevalence of nosocomial infections within Canadian adult acute-care hospitals. (56) While not focusing on overall antimicrobial utilisation, the authors do report on the percent of patients admitted to the participating hospitals who were on antimicrobials and the most frequently used antimicrobials (burden of utilisation). No Canadian PPS reports on antimicrobial utilisation with appropriateness evaluation were found in the literature.

The European Surveillance of Antimicrobial Consumption (ESAC) was established in 2000 and the initial phase included hospital-based information from only 15 hospitals and did not provide reliable data regarding bed occupation or patient admissions. (54) The second phase of the

project aimed at capturing more detailed information related to hospital utilisation and to establish the first standardized European PPS. (54)

CHAPTER 3. OBJECTIVES AND RESEARCH QUESTIONS

Despite the fact that NB has access to information-generating technologies, no database is currently available that allows accurate assessment of antimicrobial utilisation within NB hospitals. Analysis of these data to assess appropriateness is the baseline required to develop targeted AS interventions and against which to measure the effectiveness of these interventions.

3. 1 Research Questions

1. What are the current patterns of antimicrobial usage within NB hospitals with respect to patient characteristics, indication, prescribed daily dose, route and prescriber?

2. Based on antimicrobial usage patterns, where do opportunities exist to improve patient outcome and safety through implementation of targeted AS interventions within NB hospitals?

3.2 Primary research objective

Determine antimicrobial usage patterns within all NB hospitals with 10 or more acute care beds.

3.3 Secondary research objectives

Determine the proportion of antimicrobial orders within NB hospitals that are appropriate based on pre-defined criteria.

Determine the proportion of antimicrobial orders within NB hospitals that would be appropriate for targeted antimicrobial stewardship interventions.

CHAPTER 4. METHOD

4.1 Study Design

A point prevalence survey (PPS) method and data collection tool (see Appendix 2) were adapted from the ESAC PPS described by Ansari et al. and modified to meet local needs. (54) The survey was designed to gather data about all systemic antimicrobials prescribed within NB hospitals, including the antimicrobial itself, the indication(s) for the therapy, the patient and any patient-specific characteristics that could potentially influence the choice, the route of administration or the dose of the antimicrobial, the timing of the first dose with respect to the patient's hospitalisation, whether the antimicrobial was used for therapeutic purposes or for prophylaxis, the type of prescriber, whether prescribers had access to or had utilised the support of an ID specialist and whether microbiological data were utilised to support antimicrobial choices as appropriate. Microbiology culture reports were deemed relevant if representative of the site being treated and if the cultures were taken within 120 hours (5 days) of the start of the therapy. Review and analysis of this information was used to determine whether the orders met pre-defined inappropriateness criteria and to identify antimicrobial stewardship interventions that could be implemented to improve on this use. This study was not designed to assess the rates of either community-acquired infections or hospital-acquired infections in the province.

4.2 Study Setting and Population

The chairperson of the NB Anti-Infective Stewardship Committee sent a memo to all eligible NB hospital chief executives and medical advisory committees explaining the objectives of the PPS

and inviting them to participate. A letter of support from the directors of pharmacy from both health regions was also forwarded to the pharmacy departments of all NB hospitals asking for administrative support if needed by the research team.

The PPS was performed during the months of June, July or August 2012 and all eligible NB hospitals where in-patient acute, general medical, surgical or paediatric services are provided agreed to participate. Surgical units were surveyed on Tuesday, Wednesday or Thursday to capture information regarding prophylactic antimicrobial orders prescribed during the previous 24 hours. Medical units were surveyed on Monday, Tuesday, Wednesday or Thursday. Depending on the number of beds and staff availability, the survey could be completed in each participating hospital over 1 or more days; however, all patients admitted to an administrative unit (e.g. all patients admitted to a specific general surgery unit) were surveyed in a single day. On the day of the survey, eligible patients were identified using daily pharmacy services-generated patient-specific medication profiles and/or through daily admission census reports.

4.2.1 Inclusion Criteria

- All adult and paediatric patients admitted to a participating hospital patient care unit at the time of the survey and receiving at least one systemic[1] antimicrobial[2].

[1] Systemic was defined as an antimicrobial administered via one of the following routes: oral, intravenous or intramuscular.

[2] Antimicrobial was defined as those agents included in the American Hospital Formulary Service (AHFS) Pharmacologic-Therapeutic Classification System classes 08:12 (Antibacterials), 08:14 (Antifungals), 08:16 (Rifampin only), 08:30 (Metronidazole only), and 08:36 (Urinary Anti-Infectives)

4.2.2 Exclusion Criteria

- Patients admitted to an emergency department

4.3 The Research Team and Project Funding

The research team was comprised of two ID specialist physicians, one from each health network, three hospital pharmacists with experience in infectious diseases (including the author), two from Horizon and one from Vitalité a biostatistician and two university students. An unrestricted research grant was received from Medbuy Canada(www.mebbuy.ca) to cover student salaries and travel costs. The research protocol was authored primarily by the author with content support provided by the other expert team members. The statistical analysis method was developed with the support of the biostatistician. The funding agency had no direct or indirect influence on the content of the protocol, the data collection process or the data analysis and reporting process.

4.4 Inappropriateness Criteria

To the author's knowledge, no validated tool exists to measure appropriateness of antimicrobial prescribing. The choice of the inappropriateness criteria was based on the ISDA Antimicrobial Stewardship Guidelines. (17, http://www.idsociety.org)

These guidelines developed by the Infectious Diseases Society of America (IDSA) and the Society for Healthcare Epidemiology of America (SHEA) have become the cornerstone of most

North American AS programs. (17) They aim to developing AS programs that focus on appropriate selection, dosing, route and duration of antimicrobial therapy with a goal towards optimal clinical outcomes with minimal unintended consequences such as toxicity, selection of pathogenic organisms and emergence of resistance. (17) They have as a premise that there is a direct link between antimicrobial utilization and antimicrobial resistance and that the frequency of inappropriate antimicrobial use is an acceptable surrogate marker for avoidable resistance development. (17) Amongst the core elements of an AS Program, the following were deemed appropriate for baseline assessment with the use of a PPS: streamlining or de-escalation of therapy, dose optimization, parenteral to oral conversion. (17) Streamlining or de-escalating of therapy encourages review of culture results and other patient specific characteristics such as immunocompetence, co-morbidities and changing the spectrum of antimicrobial coverage as appropriate through either a switch to a less broad-spectrum agent or to a single agent from dual therapy (removal of redundant therapy as appropriate). (17) Dose optimization is as a result of the review of patient-specific characteristics such as age, renal function, immunocompetence, site of infection, and pharmacokinetic and pharmacodynamic characteristics of the drug. (17) Within this element is evaluation of the route of administration. Oral therapy may not be appropriate for the treatment of such infections as endocarditis, meningitis, osteomyelitis, or bacteraemia. (17) For antimicrobials with excellent oral bioavailability, a conversion from parenteral to oral therapy may be indicated provided clinical improvement (decrease in white blood cell count, the patient is haemodynamically stable, shows improved signs and symptoms), afebrile for at least 48 hours, has no evidence if gastrointestinal malabsorption, is not undergoing continuous nasogastric suctioning, has not

undergone a gastrectomy or ileostomy, does not have a malabsorption syndrome or a gastrointestinal obstruction. (17) Patients are not candidates for an intravenous to oral conversion program if they are being treated for endocarditis, a central nervous system infection, osteomyelitis, bacteraemia, a severe abcess, cystic fibrosis or are febrile neutropenic. (17) Because the reason an antimicrobial agent is prescribed should be documented in the patient chart, the presence of such information is deemed important as a measure of appropriateness. (12) The lack of information is considered as inappropriate since no relevant documentation supports the therapy. (12)

Very little good evidence exists regarding duration of therapy with antimicrobial agents. (http://www.idsociety.org) Evidence-based guidelines do however exist regarding duration of surgical prophylaxis and therefore this survey aimed at gathering information regarding length of antimicrobial prophylaxis in surgical patients. (http://www.idsociety.org)

4.4.1 Inappropriateness Criteria for Treatment or Medical Prophylaxis

(Table 1 and also see Appendix 2, 3 and 4)

Table 1. Inappropriateness Criteria for Treatment or Medical Prophylaxis

Code	Inappropriateness Criteria	Definition
A0	Does not meet other criteria	Does not meet other inappropriateness criteria
A1	Inappropriate therapy duplication	e.g. Dual beta-lactam therapy; inappropriate double coverage (i.e. double coverage when culture and sensitivity (C&S) results are available)
A2	Opportunity to de-escalate	Relevant C&S results available to allow de-escalation to a more narrow antimicrobial agent (if allergy profile permits)
A3	Bug-drug mismatch	Patient on antimicrobial to which relevant C&S reports show resistance
A4	Inappropriate dose	Inappropriate dose based on patient characteristics (e.g. eGFR) and/or indication
A5	Opportunity for intravenous (IV) to oral (PO) stepdown	Patient must meet all criteria for stepdown[3]
A6	Treatment of asymptomatic bacteriuria	Treatment of a positive urine C&S in a non-pregnant asymptomatic patient
A7	Inappropriate route	Inappropriate route for indication being treated (e.g. endocarditis, deep abscess, central nervous system infection)
A8	Inappropriate second line therapy	Inappropriate use of second-line therapy based on erroneous allergy information
A9	No documented indication	Therapy with no documented or identifiable indication

[3] *Stepdown criteria*

- IV therapy for treatment and not surgical prophylaxis
- Clinically improved, tolerating oral feeds and medications, no evidence of malabsorption
- Not treated for endocarditis, central nervous system infection, osteomyelitis, bacteraemia, abcess or cystic fibrosis
- Not febrile neutropenia

4.4.2 Inappropriateness Criteria for Surgical Antimicrobial Prophylaxis

Duration of surgical prophylaxis for a period of over 24 hours.

4.5 Data Collection

To ensure a consistent approach to data collection, a data collection form was developed which included pre-defined parameters and definitions. (Appendix 2 and 3) Prior to the start of the PPS, pilot surveys were completed to identify areas to improve the data collection process. Training sessions on the methods of PPS and the use of the data collection tool and database were completed for the survey team and assisting pharmacy services staff. The training was provided by the two hospital pharmacists from Horizon Health Network. All data were collected by a member of the research team at the time of the survey and added to an Excel spreadsheet by the students. All data were checked twice at the time of entry. At the beginning of the survey, the students were included in the data collection group. It became quickly obvious that to ensure accuracy, consistency and efficiency, the hospital pharmacists were better equipped to locate the data needed and to navigate the patient chart (either paper-based or electronic chart). The majority of the data were therefore collected by the three hospital pharmacists on the survey team. For surgical patients, details regarding prophylactic antimicrobials received in the previous 24-hours were also recorded and the documented intended duration of the order post-operatively. This allowed coding of the duration of prophylaxis as either 1 dose, 24-hours or less or greater than 24-hours. No effort was made to ensure the documented duration was in fact the final duration of the therapy. A decision was

made to exclude discussion with clinical staff regarding treatment options for any given patient. This decision was made by the research team based on the geographic magnitude of the survey (the entire province of NB) and the fact that the intent was not to interfere with or provide guidance on the therapy choices. This decision was supported by the literature that indicates that PPS do not generally include such discussion (55) therefore, no discussion regarding appropriateness of therapy was permitted between the members of the survey team and either the attending physician or other members of the care team. Members of the survey team were permitted to request additional information from members of the care team for clarity purposes only.

4.6 Study variables

The following variables, chosen to support analysis of the appropriateness of prescribing as described by the IDSA guidelines (17), were collected for all eligible patients directly from the patient record:

- Patient demographics: age, sex, weight, estimated glomerular filtration rate (eGFR), co-morbidities as defined by the Charlson Comorbidity Index[4], allergies, immunosuppressive therapy[5]
- Date of admission/ date of survey

[4] The Charlson Comorbidity Index is a validated index that provides a measure of the burden of comorbid disease. Nineteen major conditions are included in the Charlson Index and are weighted based on their strength of association with mortality. (58)

[5] Immunosuppression was defined as a patient with either a haematological or solid tumour, having received or receiving chemotherapy, who has a congenital immunodeficiency or long-term immunosuppressive therapy (equivalent to prednisone 20mg/day or more for at least 2 weeks or patients with HIV infection with CD4 count less than 200. (www.cdc.org)

- Number of antimicrobials per patient
- Type of antimicrobial prescribed
- Dose, route and frequency
- Documented indication
- Anatomical site of infection
- Prescriber type
- Community- vs. Hospital[6] - acquired infection treatment vs. Prophylactic therapy
- Relevant microbiological cultures
- Documented infectious diseases consultation
- Admission to an intensive care unit
- Mechanical ventilation insertion
- Presence of a urinary catheter
- Stepdown criteria (see Data Collection Tool, Appendix 2)
- Urinary tract infection criteria (see Data Collection Tool, Appendix 2)

4.7 Data Analysis

Assessment of the appropriateness of therapy was performed independently by the infectious disease specialists and the hospital pharmacists with experience in infectious disease through the application of pre-defined criteria (Appendix 4). Final conclusions regarding attribution of the inappropriateness criteria were reached through consensus. No information was retained

[6] Hospital-Acquired infection was defined as symptoms starting > 48 hours after admission and/or procedure performed in hospital as per the US CDC (www.cdc.org)

regarding the number of assessments that required discussion as the overall number was very low. Of interest, the hospital pharmacists were more apt to accept documented symptoms (e.g. “acute abdomen”, “Increased frequency”) as a diagnosis than the physicians were. Following discussion early in the review process, symptom only documentation was deemed inadequate and therefore judged to have no documented indication.

Throughout the data analysis four denominators were used: patients, indications for therapy (treatment vs. prophylaxis), diagnosis and antimicrobial administered. Each patient could have more than one indication or diagnosis and could have more than one antimicrobial prescribed. Only those orders with a documented indication were included in the inappropriateness criteria analysis.

Descriptive statistics (mean and standard deviation) were used to describe the patient population and to compare between-hospital and between-health region point estimates of antimicrobial use. Sums and percentages were used to describe antimicrobial utilisation patterns. Chi squared test of independence was performed to assess the impact of an infectious diseases consultation. A p value < 0.05 was deemed statistically significant.

Data were analysed using R language for statistical computing. (59)

4.8 Research Ethics Approval

This project was submitted to and received ethical approval from both the Horizon Health Network Research Ethics Board (Appendix 5) and the *Comité d'éthique de la recherche du Réseau de santé Vitalité* (Appendix 6).

CHAPTER 5. RESULTS

5.1 Results

The PPS was completed between June and August 2012. Twenty-one of 22 (95.5%) NB hospitals met the eligibility criteria and were included in the survey. A total of 2244 patients were admitted at the time of the survey and 529 (23.6%) were on systemic antimicrobial therapy. (Table 1) 211/2244 patients (9.4%) were receiving treatment for hospital-acquired infections. The mean age of the patients included was 67.1, the mean Charlson index value was 6.2 and the mean number of antimicrobials prescribed per patient was 1.3.

A total of 691 antimicrobials were prescribed: 326 (47.2%) for community-acquired infections, 261 (37.8%) for hospital-acquired infections, 82 (11.9%) for surgical prophylaxis and 22 (3.2%) for medical prophylaxis. (Table 2) The majority of patients were prescribed one antimicrobial (390/529, 73.7%), 119/529, 22.5% were prescribed two antimicrobials and 20/529, 3.8% were on three or more agents. The average number of antimicrobial per patient was 1.3. Of the patients receiving three or more antimicrobials, 9/20, 45% met the criteria for being immunocompromised.

The majority (238/691, 34.4%) of antimicrobial prescriptions were ordered by members of the family practice category of physicians. (Table 3) Surgeons ordered 173/691 (25.0%) and internal medicine specialists (excluding infectious diseases) ordered 99/691 (14.3%) of the

antimicrobials prescribed, followed by hospitalists (56/691, 8.1%), infectious diseases specialists/microbiologists (49/691, 7.1%), emergency room physicians (45/691, 6.5%), intensivists (23/691, 3.3%), geriatricians (7/691, 1.0%) and other, undefined (1/691, 0.1%).

Table 2. Patient Characteristics

Categorical variable	Number (N=529)	Percentage
Gender		
Female	284	53.7
Male	245	46.3
Admitted to ICU[7]		
Yes	48	9.1
No	481	90.9
Documented ID[8] **Consult**		
Yes	63	11.9
No	466	88.1
Immunosuppression		
Yes	79	14.9
No	450	85.1
Number of antimicrobials/patient		
1	390	73.7
2	119	22.5
≥ 3	20	3.8
Continuous variable	Mean	SD[9]
Age	67.1	18.8
Charlson Index	6.2	4.0
Antimicrobials/patient	1.3	0.56

[7] ICU = Intensive Care Unit

[8] ID = Infectious Diseases

[9] SD = Standard Deviation

Table 3. Number of Prescribed Antimicrobials by Indication

Indication	Number (N=691)	Percentage
Treatment	587	85
Community-acquired infection	326	47.2
Hospital-acquired infection	261	37.8
Prophylaxis	104	15
Surgical prophylaxis	82	11.9
Medical prophylaxis	22	3.2

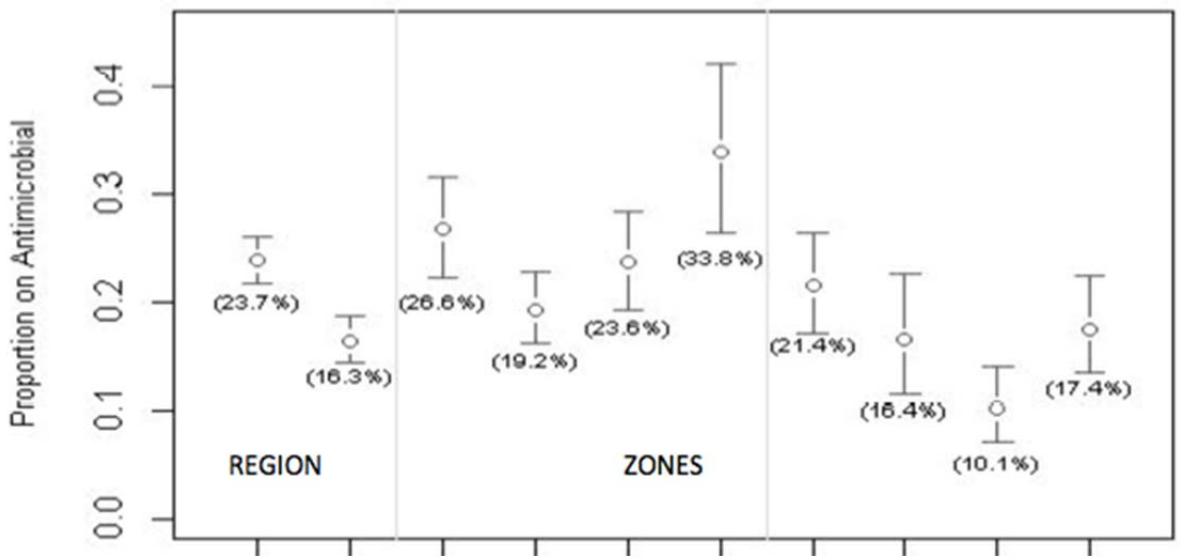
Table 4. Number of Prescribed Antimicrobials by Prescriber Type

Prescriber type	Number (N=691)	Percentage
Family Medicine	238	34.4
Surgeon	173	25.0
Internal Medicine	99	14.3
Hospitalist	56	8.1
Infectious Diseases/Microbiologist	49	7.1
Emergency Room Physician	45	6.5
Intensivist	23	3.3
Geriatrician	7	1.0
Other (not defined)	1	0.1

Variability was seen when an analysis of the proportion of patients who were estimated to be on antimicrobial therapy at the time of the PPS was performed, both between regions and between zones.[10] (Figure 1)

[10] A zone is defined by a geographically distinct section of the province; each zone is comprised of either a university hospital centre or community hospital with tertiary services plus at least one smaller community hospital. Each region is comprised of 4 zones.

Figure 1. Proportion of Patients on Antimicrobials by Region/Zone



5.2 Patterns of Antimicrobial Utilisation for Prophylaxis Orders

5.2.1 Medical Prophylaxis orders

Seventeen patients, 7/17 (41.2%) were women and 10/17 (58.5%) were men, had 22 orders defined as medical prophylaxis. The mean age of this group was 65 years (range 40-92). Thirteen patients (76.5%) were immunocompromised based on the US CDC definition as having one of: a haematological or solid tumour, having received chemotherapy, having congenital immunodeficiency, or long-term immunosuppressive therapy (e.g. equivalent to prednisone 20 mg/day for 2 weeks or more) or an infection with human immunodeficiency virus (HIV). The most frequently prescribed antimicrobials were: cotrimoxazole 7/22, 31.8%, ciprofloxacin 3/22, 13.6%, fluconazole 2/22, 9.1%, doxycycline 2/22, 9.1%, dapsone 2/22, 9.1%, and voriconazole

2/22, 9.1%. The remaining 4/22, 18.2% orders were for rifampin, tetracycline, azythromycin and cefoxitin. (Table 5)

Table 5. Medical Prophylaxis - Antimicrobials Prescribed

Antimicrobial	Number (n=22)	Percentage
Cotrimoxazole	7	31.8
Ciprofloxacin	3	13.6
Fluconazole	2	9.1
Doxycycline	2	9.1
Dapsone	2	9.1
Voriconazole	2	9.1
Miscellaneous	4	18.2

5.2.2 Surgical Prophylaxis Orders

Of the 82 antimicrobials prescribed for surgical prophylaxis, 34/82, 41.5% were for orthopaedic surgery, 19/82, 23.2% for gastrointestinal surgery , 12/82, 14.6% for cardiovascular surgery, 7/82 for surgery within the urinary tract and the remaining 4/82, 4.9% were for neurosurgery, ear, nose and throat surgery, ophthalmic surgery and one without a documented indication. The most frequently prescribed antimicrobials were cefazolin (50/82, 61%), ciprofloxacin (9/82, 11%), clindamycin (9/82, 11%), metronidazole (6/82, 7.3%) and cefoxitin (4/82, 4.9%). The remaining 4 orders (4/82, 4.9%) were for cephalexin, penicillin, vancomycin and piperacillin/tazobactam. (Table 6)

Table 6. Surgical Prophylaxis - Antimicrobials Prescribed

Antimicrobial	Number (n=82)	Percentage
Cefazolin	50	61
Ciprofloxacin	9	11
Clindamycin	9	11
Metronidazole	6	7.3
Cefoxitin	4	4.9
Miscellaneous	4	4.9

5.3 Patterns of Antimicrobial Utilisation for Treatment Orders

Of the 587 antimicrobials prescribed for the treatment of either a community-acquired or a hospital-acquired infection, the top 7 most frequently prescribed classes were the fluoroquinolones (150/587, 25.6%) , extended spectrum penicillins (60/587, 10.2%), metronidazole (50/587, 8.5%), third-generation cephalosporins (49/587, 8,3%), aminopenicillins (46/587, 7.8%), first-generation cephalosporins (34/587, 5.8%) and second-generation cephalosporins (31/587, 5.3%). (Table 7) These 7 classes accounted for 71.5% of the antimicrobials prescribed for treatment. Sixteen other classes of antimicrobials accounted for the remaining 167/587 (28.5%) of orders (see Appendix 7 for further detail)

Table 7. Treatment-Prescribed Antimicrobials by Class

Antimicrobial Class	Number (n=587)	Percentage
Fluoroquinolones	150	25.6
Extended Spectrum Penicillins	60	10.2
Metronidazole	50	8.5
3rd Generation Cephalosporins	49	8.3
Aminopenicillins	46	7.8
1st Generation Cephalosporins	34	5.8
2nd Generation Cephalosporins	31	5.3
Others	167	28.5

Overall there were 587 orders for combined community-acquired infections or hospital-acquired infections. Of these, 113 (19.3%) did not have a documented indication and therefore no anatomic site of infection could be assigned. Of the remaining 474 orders, the top 6 anatomic sites of infection were: pneumonia (140/474, 29.5%), gastro-intestinal (74/474, 15.6%), skin and soft tissue (68/474, 14.3%), cystitis (55/474, 11.6%), bronchitis (35/474, 7.4%) and bone and joint (22/474, 4.6%) (Table 8) (see Appendix 8 for further detail)

Table 8. Anatomical Sites for Community- and Hospital-Acquired Infections

Anatomic site	Number (n=474)	Percentage
Pneumonia	140	29.5
Gastro-Intestinal	74	15.6
Skin and Soft Tissue	68	14.3
Cystitis	55	11.6
Bronchitis	35	7.4
Bone and Joint	22	4.6
Other	80	16.8

The top 6 treatment-prescribed antimicrobials were: ciprofloxacin (95/587, 16.2%), piperacillin-tazobactam (59/587, 10.1%), metronidazole (50/587, 8.5%), moxifloxacin (43/587, 7.3%), amoxicillin (includes amoxicillin-clavulanate) (39/587, 6.6%) and ceftriaxone (38/587, 6.5%) (Table 9) (see Appendix 9 for further detail)

Table 9. Treatment Prescribed Antimicrobials

Antimicrobial	Number (n=587)	Percentage
Ciprofloxacin	95	16.2
Piperacillin-Tazobactam	59	10.1
Metronidazole	50	8.5
Moxifloxacin	43	7.3
Amoxicillin	39	6.6
Ceftriaxone	38	6.5
Other	263	44.8

Of the 95 orders identified for ciprofloxacin, 31/95 (32.6%) had no documented indication, 19/95 (20%) were for the treatment of cystitis, 17/95 (20%) for gastro-intestinal infections, 9/95 (9.5%) for pneumonia, 7/95 (7.4%) for skin and soft tissue infections, 7/95 (7.4%) for the treatment of pyelonephritis and 5/95 (5.4%) for miscellaneous other indications. (Table 7)

Table 10. Ciprofloxacin Use by Anatomic Site

Anatomic Site	Number	Percentage
No documented indication	31	32.6
Cystitis	19	20.0
Gastro-Intestinal	17	17.9
Pneumonia	9	9.5
Skin and Soft Tissue	7	7.4
Pyelonephritis	7	7.4
Miscellaneous	5	5.4

5.4 Appropriateness of Prophylaxis Orders

5.4.1 Appropriateness of Medical Prophylaxis Orders

The 17 patients who were receiving medical antimicrobial prophylaxis were admitted to hospitals for indications which appeared unrelated to the reason they were prescribed

antimicrobials for prophylaxis. This was surmised based on the types of treatment antimicrobials they received at the time of the PPS and the documented indications for this treatment. Limited information was documented regarding the reason for the medical prophylaxis. No further appropriateness assessment was made on the medical prophylaxis orders due to the lack of documentation and clear guidelines with respect to the appropriateness of such orders.

5.4.2. Appropriateness of Surgical Prophylaxis Orders

Eighty-two antimicrobials were prescribed for surgical prophylaxis (Table 11). These orders were categorized based on the following durations: 1 dose only, 24-hour or less, greater than 24 hours. Sixty-seven percent of orders were deemed appropriate and 32.9% inappropriate based on the IDSA 2013 guidelines (http://www.idsociety.org) that suggest that the duration of prophylaxis should be 24 hours or less for most procedures. Table 12 provides information regarding the duration of surgical prophylaxis based on anatomic site. No other appropriateness assessment was planned for surgical prophylaxis orders during this PPS.

Table 11. Duration of Surgical Prophylaxis

Duration of Prophylaxis	Number	Percentage
≤ 24 hours	37	45.1
> 24 hours	27	32.9
1 dose	18	21.9

Table 12. Duration of Surgical Prophylaxis by Anatomic Site

Anatomic Site	1 dose n (%)	≤ 24 hours n (%)	> 24 hours n (%)	Total
Central nervous system	0 (0.0)	0 (0.0)	1 (100)	1
Cardiovascular	2 (16.7)	8 (66.7)	2 (18.7)	12
Ear/Nose/Throat	0 (0.0)	0 (0.0)	1 (100)	1
Eye	0 (0.0)	1 (100)	0 (0.0)	1
Gastrointestinal	5 (26.3)	2 (10.5)	12 (63.2)	19
Obstetrics/Gynecology	5 (83.3)	1 (16.7)	0 (0.0)	6
Bone/Joint	3 (8.9)	25 (73.5)	6 (17.6)	34
Urinary Tract	2 (33.3)	0 (0.0)	5 (66.7)	7
Not documented	1 (100)	0 (0.0)	0 (0.0)	1

5.5 Appropriateness of Treatment Orders

Based on pre-defined criteria, 254/587 (43.3%) of treatment orders were either inappropriate 134/587, 22.9% or had no documented indication, 120/587, 20.4%. (Table 13) Three hundred and thirty-three orders, 56.7%, did not meet any of the inappropriateness criteria.

Table 13. Appropriateness of Therapy

Code	Inappropriateness Criteria	Number	Percentage
A0	Did not meet criteria	333	56.7
A1	Inappropriate duplication of therapy	22	3.7
A2	Opportunity to de-escalate	13	2.2
A3	Bug-drug mismatch	11	1.9
A4	Inappropriate dose	24	4.1
A5	Opportunity for IV to PO stepdown	34	5.8
A6	Inappropriate treatment of bacteriuria	24	4.1
A7	Inappropriate route	0	0
A8	Inappropriate 2nd line therapy	0	0
A9	No documented indication	120	20.4

There were significantly more antimicrobial orders that met inappropriateness criteria A1 through A9 when no infectious diseases service(IDS) (defined as one or more physicians with expertise in infectious diseases) was available at the hospital where the data were collected (X^2 = 15.62, df = 1, p<0.001) (Table 14). Of note, at the time of the PPS and currently IDS are available only in those hospitals with on-site ID specialists. Telehealth or other off-site consultation services are not provided.

Table 14. Influence of Infectious Diseases Services (IDS) and Inappropriateness Codes

	Code A0 n (%)	Codes A1-A9 n (%)	Totals
IDS	**201 (65.0)**	108 (35.0)	309
No IDS	145 (48.8)	**152 (51.2)**	297
Total	346	260	606

(X^2 = 15.62, df = 1, p<0.001)

CHAPTER 6. DISCUSSION AND RECOMMENDATIONS FOR PRACTICE AND POLICY MAKING

This PPS was performed to assess whether antimicrobial usage within NB hospitals was appropriate, based on pre-defined criteria, for the treatment of community- and hospital-acquired infections or for medical or surgical prophylaxis and to assess whether differences exist between regions and geographic zones as a means to identify targets for AS activities.

No Canadian PPS reports on antimicrobial utilisation with appropriateness assessment were found in the literature and therefore comparisons will primarily be made with US, Australian and European survey results as their patient populations, while not identical, are more likely to resemble those in the Canadian context compared to Asian or Middle-Eastern surveys.

6.1 Burden of Utilisation

Of the 2244 patients who were admitted to the 21 surveyed hospitals during the survey period, 529 (23.6%) were on systemic antimicrobials. These data suggest that the burden of antimicrobial utilisation in NB hospitals was in the lower spectrum of that generally reported elsewhere. PPS performed in several European, Australian and one US university teaching hospital report usage ranging from 22.9% up to 48% (average 32%). (29, 39, 54-55, 60-67) The one Canadian study that reported on the burden of utilisation (56) reported that 36% of patients among the total patients surveyed were on at least one systemic antimicrobial. While not reported in either the Canadian or the international literature, it is interesting to note that

34.4% of all antimicrobial orders in NB were from members of the Department of Family Medicine. This should not be surprising given that within NB hospitals, approximately 30% of inpatient care is provided by members of this department.[11] An analysis of the proportion of patients estimated to be on an antimicrobial at the time of the PPS suggests between-zone and between-region variability. No regression analysis was performed to attempt to identify variables that could influence these prescribing patterns. Further research would be required to understand the root causes of these variations.

6.2 Antimicrobial Utilisation Based on Indications

A total of 691 antimicrobials were prescribed with 85% of these for the treatment of either community-acquired (47.2%) or hospital-acquired infections (37.8%). The remaining 15% were for either surgical (11.9%) or medical prophylaxis (3.2%). These findings were similar to those reported internationally, ranging from 70% to 84% for treatment indications and 16% to 30% for prophylaxis. (53-54, 62, 66) Only Ansari and colleagues (54) specifically reported on the rates of antimicrobials used to treat community-acquired infections (48.4%) and hospital acquired infections (30%) and for surgical prophylaxis (15%) and medical prophylaxis (6.7%). These results are similar to the NB findings.

The most frequent types of infections reported in this PPS included pneumonia (29.5%), gastro-intestinal infections (15.6%), skin and soft tissue infections (14.3%) and cystitis (11.6%). A study

[11] Personal communication, chairs of the Horizon and Vitalité Medical Advisory Committees

performed in Northern Ireland in 4 acute-care hospitals and using a very similar survey (53, 62) reported very comparable findings, with respiratory infections being most common (30%) followed by gastrointestinal infections (18%), skin and soft tissue infections (18%) and urinary tract infections (13%). Ansani and colleagues reported on the results of a PPS performed in 20 European hospitals in 2006. (54) Respiratory tract infections was also the most frequent indication (28.9%) followed by skin and soft tissue infections (18.8%), intra-abdominal infections (12.6%) and urinary tract infections (13.5%). (54) An Australian study comparing antimicrobial utilisation in private hospitals and state run hospitals reported that overall, the most frequent indications were respiratory infections (31.3%), skin and soft tissue infections (17.8%), urinary tract infections (12.1%) and bone and joint infections (12.1%). (60) Amadeo and colleagues (63) performed their PPS in paediatric hospitals; no direct comparison was made between their results and the NB results given that only 9 patients in the NB survey were less than 19 years of age. Other PPS performed in Europe did not report types of infections being treated. (29, 39, 61-62, 64-67) No other Canadian data were available for comparison.

6.3 Antimicrobial Utilisation Based on Antimicrobial Class

Fluroroquinolones were the most frequently ordered class of antimicrobials, and ciprofloxacin the most frequent of the fluoroquinolones, representing 25.6% and 16.2% respectively of all orders. The next closest class are extended-spectrum penicillins (10.2%). In their PPS for nosocomial infections in 7 Canadian hospitals, including one NB hospital, Gravel and colleagues reported that the overall most frequent antimicrobials ordered were cephalosporins (11.4%), fluoroquinolones (10.6%), metronidazole (6.6%) and penicillins (6.5%). (56) The apparent

difference in rates of fluoroquinolone prescribing in NB hospitals compared to the Canadian rates from 2002 is worth noting and is troublesome. Most European countries suggested an increase in fluoroquinolone use but were well below the rate reported here (range 3.9% to 14.9%) (29, 39, 53-54, 62, 66-67) save in France where reported rates were similar to NB's (23.6%) (65). This was described as an anomaly compared to the other countries in the European Union (EU) and the authors suggested a more focused survey would be required to attempt to elucidate the reasons for the variance. (65) This high use of fluoroquinolones in NB and in France are of concern since the ESAC and others have reported that an increase in use of fluoroquinolones has resulted in significant increases in rates of fluoroquinolone-resistant *E. coli*, *Klebsiella pneumoniae* and *Pseudomonas*. (36-38, 54) Fluroroquinolone and other broad-spectrum antibiotic use has also been identified as an independent risk factor for the development of CDAD. (42) When appropriateness criteria based on the Gyssens criteria (68) (see Table 15) were applied, fluoroquinolones have also been found to be an independent risk factor for inappropriate prescribing. (29) While different than the inappropriateness criteria applied in our survey, this could be an area of interest for future research. Seven classes of antimicrobials accounted for 72% of the orders. Sixteen classes therefore accounted for the remaining 28% of orders which suggests considerable variability in antimicrobials prescribed.

6.4 Appropriateness of Antimicrobial Utilisation

Although 587 antimicrobial orders were reviewed that were ordered for the treatment of either community- or hospital-acquired infections, 333 (56.7%) of these orders did not meet any of the applied inappropriateness criteria and were therefore not evaluable. A further 20.4% had

no documented indication that could be identified in the chart therefore limiting the data available for assessment. In comparing to similar surveys done elsewhere, lack of documentation has been identified as a key target for intervention with rates averaging 25%, above the NB incident of 20.4% (range 15.7% to 42%). (53, 55, 60-62, 64, 66) While apparently better than the rates reported in the literature, efforts to improve documentation should also be included in NB's stewardship efforts.

The remaining 22.6% of orders fell in one of 6 other inappropriateness criteria: opportunity for IV to PO stepdown (5.8%), inappropriate dose (4.1%), inappropriate treatment of bacteriuria (4.1%), inappropriate antimicrobial therapy duplication (3.7%), opportunity to de-escalate (2.2%) and bug-drug mismatch (1.9%) and are considered appropriate for targeted AS interventions. No comparison could be made with European and Australian published data in regards to the inappropriateness criteria used in this PPS as the criteria they used were dissimilar or appropriateness of utilisation was not one of the objectives of the study. One PPS performed in a tertiary care hospital in the US and available in abstract form only (57) used somewhat similar inappropriateness criteria and reported 22% of their orders were either unnecessary or overly broad. Within this 22% the most common reason for unnecessary antimicrobial use was for the treatment of asymptomatic bacteriuria (5.6%), failure to de-escalate (4.5%) and duplication of therapy (2.1%). This PPS did not report on such criteria as appropriateness of dosing and IV to PO stepdown. Comparison with the NB data must be made with caution because of these differences in criteria used but also since these data are from a

single tertiary centre and insufficient information in available to compare the patient characteristics and the hospital case load to enable an assessment of their degree of similarity.

Regardless of whether these results are comparable, the NB data point to areas of potential improvement and various possible strategies requiring various levels of resources including antibiotic policies, audit and feedback, clinical guidelines and the enabling of delegated functions to other members of the care team including clinical pharmacists.

It is generally accepted that there is no clinical reason to extend surgical prophylaxis beyond 24 hours post-surgery. (http://www.idsociety.org , 54) The ESAC group has gone so far as to recommend that "the target rate for duration of prophylaxis > 24-hours should be zero for all specialties." (54) Results of this survey indicate that 33% of the antimicrobial orders for surgical prophylaxis in NB hospitals were for a duration greater than 24 hours. In comparison, rates reported internationally range from 0 to 70%. (53, 54, 60-61, 63-67) From this comparison, NB results fall within the median of the reported rates; making surgical prophylaxis an appropriate target for stewardship interventions. Countries where surgical prophylaxis guidelines were used reported good adherence to the recommendations. (53, 61)

6.5 Study Limitations

This PPS is deemed exploratory as it only captures data from a moment in time and may not be reflective of the overall antimicrobial prescribing trends within NB's health networks. (69) No

definitive statement can be made based on the results of the survey but they may be indicative of where further efforts should be focussed. (69) While the overall number of patients who were on antimicrobials at the time of the survey (529/2244, 23.6%) is within the generally reported range, it does lie in the lower end of this range (22.9% - 48%). It may be that the timing of the survey (June-August) resulted in numbers that could have been strongly influenced by the practices of select clinicians or caseloads or practice sites. Not all surgical specialties were represented in the case mix identified during this PPS. Some NB hospitals close surgical suites or decrease surgical suite utilisation, therefore limiting the number of elective procedures performed. A certain degree of subjective judgement was used in attributing the inappropriateness criteria for the treatment antimicrobials and no inter-rater reliability test was performed to identify whether this was significant. No costing analysis was performed regarding possible savings should unnecessary therapies be prevented. Insufficient data were collected to perform such an analysis given the nature of a PPS. Actual medication utilisation would be necessary to assess potential savings i.e. the actual duration of the therapy and the doses used and this was deemed to be beyond the scope of this project. Fifty-seven percent of the orders retrieved “did not meet criteria” for evaluation of appropriateness. In this survey, “did not meet criteria” was not synonymous with either “appropriate” or “inappropriate”. A broader choice of inappropriateness criteria may have captured some of these orders and therefore could have added to the robustness of the results. The use of the Gyssens criteria (68) (see Table 12) to evaluate appropriateness of antimicrobial utilisation may have resulted in an increase in the number of reported inappropriate orders.

Table 15. Gyssens Criteria

1. Correct decision (appropriate use)
• No AMT[12] and no infection and no AMT needed • No AMT and infection and no AMT needed • AMT and infection and appropriate choice and appropriate use
2. Incorrect decision (inappropriate use)
• No AMT and infection and AMT needed • AMT and no infection and no prophylaxis and no AMT needed • No AMT and no infection and prophylaxis needed
3. Incorrect choice (inappropriate use)
• Divergence from guidelines
4. Missing data (insufficient information)
• No AMT and not enough diagnostic information about infection • Infection and not enough diagnostic information if AMT is needed • AMT and not enough diagnostic information about infection • Infection and not enough information about AMT

6.6 Study Strengths

While much work has been done in Canadian hospitals in regards to AS activities, most of this work has occurred in the intensive care area and in hospitals in other provinces and may not be generalisable to all hospital-care settings or to NB. (51-52) The most significant strength of this survey is the fact that it was done in NB to be used in NB and all eligible hospitals were included. It provides province-wide information over the full range of medical and surgical services. The inappropriateness criteria were pre-defined based on previous work done elsewhere and the design of the survey was based on work done extensively in Europe. All inappropriateness criteria were evaluated by two sets of reviewers: clinical pharmacists with extensive knowledge of antimicrobial therapy and infectious diseases specialty physicians.

[12] AMT = antimicrobial therapy

6.7 Future Research

Further research would be needed to attempt to investigate and evaluate the contribution of potential factors that may lead to deviation from optimal prescribing such as the extensive variability in the use of antimicrobials by class, the large percentage of treatment orders that were without an indication, the large percentage of orders for antimicrobial prophylaxis that had a duration of greater than 24 hours and the suggested inter-zone and inter-regional incidence of antimicrobial prescribing.

6.8 Recommendations for Practice and Policy Making

The results of this PPS support that AS efforts in NB should be focused on enabling IV to PO stepdown, de-escalation of therapy, appropriateness of dosing, halting treatment of asymptomatic bacteriuria in non-pregnant patients, halting of unnecessary duplicate therapies, improving documentation of indications within the patient record, improving adherence to surgical prophylaxis guidelines and improving antimicrobial selection overall. Specific efforts should be directed at decreasing the overall use of fluoroquinolones and other broad-spectrum antimicrobials when possible. Decision makers should focus their efforts on AS strategies that are supported by evidence such as antibiotic use policies, audit and feedback processes, clinical guidelines and the development of acceptable delegated function which enable other members of the care team to directly intervene on orders that do not meet pre-defined criteria for appropriateness. Furthermore, the results of this PPS indicate that in NB, efforts should also focus on increasing prescriber awareness on the importance of adherence to documentation standards, the risk of high rates of fluoroquinolone prescribing and prolonged

surgical prophylaxis i.e. increased antimicrobial resistance and enabling pathogenic selection. Resources should be sought to increase the number of infectious diseases specialists available to support prescribers. The PPS showed that there is a significant association between the availability of an infectious diseases specialist and appropriateness of prescribing, i.e., the presence of and infection diseases specialist resulted in fewer inappropriate treatment orders. Because of the important impact of family physicians on in-hospital care and the fact that they were the most frequent prescribers (34.4%), specific efforts should be directed towards providing this group of prescribers with tools to assist in optimizing antimicrobial prescribing.

Results of the PPS were presented to the NB Anti-Infective Stewardship Committee, the Horizon Health Network Regional Medical Advisory Committee, the Vitalité Health Network Regional Medical Advisory Committee and the Infectious Diseases specialists groups, various other physician groups, the Canadian Society of Hospital Pharmacists (CSHP) NB Branch annual education session (Moncton, NB) and the Dr. Donald MacLellan Research Day (Moncton, NB). Poster presentations were given at the CSHP National Annual Summer Education Session (Calgary, AB), the Canadian Agency for Drugs and Technologies in Health Annual Symposium (Gatineau, QC) the Capital Health Pharmacy Research and Education Day (Halifax, NS) and the Interprofessional Health Research Day (Saint John, NB).

Since the first presentation of the results of this PPS, several actions have been undertaken: a dedicated antimicrobial stewardship website is now available on the two regional Intranet

systems and four NB treatment guidelines have been developed and are currently in use: an provincial community-acquired pneumonia pathway, a provincial skin and soft tissue infections guidelines, a new urinary tract infections guideline with an emphasis towards using ciprofloxacin exclusively for the treatment of pyelonephritis if possible and a new *Clostridium difficile* treatment guideline. Three other provincial guidelines are in progress: an acute sinusitis treatment guideline, an acute exacerbation of chronic obstructive pulmonary disease treatment guideline and an intra-abdominal/diverticulitis treatment guideline. As well, an antimicrobial IV to PO conversion policy has been developed that enables hospital pharmacists throughout the province and other members of the healthcare team to step patients down to oral therapy when appropriate and safe. Two other studies have also been performed to add to the information derived from this PPS: a study of surgical prophylaxis in the larger Horizon hospitals with a broader range of inappropriateness criteria and a study to investigate the management of urinary track infections within Horizon hospitals.

CHAPTER 7. CONCLUSIONS

7.1 Conclusions

To effectively influence prescribing practices, institutions must aim at providing local utilisation evidence and relate this information to their clinicians. (9, 61) This PPS performed in NB hospitals provides contextual evidence supporting AS efforts enabling IV to PO stepdown, de-escalation, appropriate dosing, halting treatment of asymptomatic bacteriuria, halting unnecessary duplicate therapies, improving documentation, improving adherence to surgical prophylaxis guidelines and improving antimicrobial selection. The availability of an infectious diseases specialist was found to be statistically related to improved overall appropriateness of prescribing.

The results of this PPS indicate that the burden of antimicrobial utilisation in NB hospitals is within the lower range of that reported elsewhere. Antimicrobial utilisation by indication was similar to that reported elsewhere, with the majority for the treatment of either community-acquired infections or hospital-acquired infections and the remaining for surgical or medical prophylaxis. As well, the most frequent indications for antimicrobial therapy are similar to those reported internationally, with respiratory tract infections being the most common indication followed by gastrointestinal infections, skin and soft tissue infections and cystitis.

Fluroquinolones were found to be the most frequently prescribed class of drugs in NB hospitals. Given be that use of fluoroquinolones and ciprofloxacin in particular have been identified as independent risk factors for the development of multi-drug resistant organisms and in the selection of pathogenic organisms, efforts to modify prescribing patterns to limit the use of this class of antimicrobials must be supported and sustained. While not significantly different from that reported in the literature, lack of documentation is noteworthy and efforts to promote improvement should be considered essential. Efforts should also be directed towards improving compliance with recommended guidelines regarding use of antimicrobials in surgical prophylaxis.

Since receiving the results of this PPS, several changes have been implemented within NB hospitals. Regular repeated PPS would be an effective tool to evaluated the effectiveness of these changes.

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APPENDIX 1

ANTI-INFECTIVE STEWARDSHIP COMMITTEE TERMS OF REFERENCE

NB Provincial Health Authorities Anti-infective Stewardship Committee (ASC)

(Sub-committee to Drugs and Therapeutics (D&T) Committee)

Terms of Reference

PURPOSE

Makes recommendations to the Provincial D&T Committee regarding the formulary of anti-infective pharmaceuticals available for use within the New Brunswick regional health authorities, i.e. Vitalité Health Network (Vitalité) and Horizon Health Network (Horizon) including conditions and/or criteria for use where appropriate which reflects rational, evidence-informed, safe and cost-effective therapy.

Advises on all matters relating to the use of anti-infective pharmaceuticals within the regional health authorities.

VALUES

Evidence-informed decision making: The committee ensures that decisions are supported with the best available evidence and in consideration of the experiences of other jurisdictions.

Decision making criteria: The committee ensures that decisions support effective therapy consistent with best practice and evidence considering the needs of clients, staff, other service providers, and prescribing medical professionals, as well as safety, effectiveness, cost and the need to avoid product duplication[13].

Provincial Perspective: The committee includes representation from Vitalité and Horizon to ensure the committee structure is representative of each RHA.

COMPOSITION

The members of the committee are appointed by the D&T Committee with the Chair of the ASC, or at least one of the members of the committee, also being a member of the D&T Committee.

[13] Accreditation Canada Medication Management Standards 2010

Membership:

Chair (may be one of the following members)

Infectious Diseases physicians (3; with at least one from each RHA)

Laboratory Medicine Microbiology representative (2; one from each RHA)

Family Physician representative (2; one from each RHA)

Public Health representative (2; one from each RHA)

Infection Control representative (2; one from each RHA)

Drug Use Evaluation pharmacist (2; one from each RHA)

Clinical Staff pharmacist with speciality or interest in infectious disease (2; one from each RHA)

The committee has the authority to consult any member of the medical or regional health authority staff to act in an advisory capacity.

CONFLICT OF INTEREST DISCLOSURE

All members will be required to declare any conflict of interest as per the Provincial D&T Committee Conflict of Interest Guidelines. Conflict of interest declarations can be made at the meetings or prior to the meeting by notifying the Chair via fax or email.

The chair has the authority to determine if the circumstances or interests of a participant amount to a conflict of interest in respect to a submission that is before the committee. Participants shall not be involved in a submission in which they have sponsorship.

Names of members who have a conflict of interest shall be documented in the minutes.

FUNCTION

1. To make recommendations to the D&T Committee regarding the use (rationale, cost effectiveness and monitoring) of all anti-infective pharmaceuticals.

2. To undertake evidence-based evaluation of requests for changes to the Formulary with regard to anti-infective pharmaceuticals, including additions, deletions and criteria for use, and make recommendations to the D&T committee in this regard.

3. To recommend criteria for use, restrictions and policy and procedures for selected anti-infective pharmaceuticals to ensure safe and appropriate use within the regional health authorities.

4. To undertake regular review of the formulary, including drug utilization to ensure the anti-infective pharmaceuticals available are the most clinically appropriate (with regard to efficacy, toxicity and resistance patterns) and cost-effective to serve the patient population, and to make appropriate recommendations to the D&T Committee.

5. To review non-formulary drug utilization of anti-infective pharmaceuticals and make recommendations to the D&T committee for appropriate adjustments to the formulary.

6. To undertake regular evidence-informed reviews of RHA protocols that contain or are related to use of anti-infective pharmaceuticals (including but not limited to criteria for use, treatment guidelines, clinical order sets, pre-printed orders, etc.).

7. To monitor the patterns of sensitivity and resistance to anti-infective pharmaceuticals and to initiate appropriate drug use evaluation activities as needed in consultation with the D&T Committee.

8. To assist in implementation of education and control measures designed to improve the appropriateness, safety and cost-effectiveness of anti-infective use.

9. To provide guidance from a laboratory perspective with regards to current testing methodologies and options for testing and therapeutic monitoring that will influence formulary and anti-infective therapy decisions.

10. To incorporate the use of high-quality evidence-based resources in decision-making, including but not limited to Canadian Agency of Drugs and Technologies in Health (CADTH), Oregon Health and Science University's Drug Effectiveness Review Project (DERP) and Quebec's le Conceal des Medicaments.

MEETINGS AND MINUTES

The committee shall meet at least nine times per year at the call of the chair.

The committee shall maintain a permanent record of its proceedings and actions.

Quorum

A majority of the membership will constitute a quorum

Remuneration/Expenses

Fee-for-service physicians will be remunerated in accordance with Department of Health administrative policy and have travel expenses reimbursed in accordance with the provincial government travel policy.

Salaried physicians will have travel expenses reimbursed in accordance with the provincial government travel policy.

Regional Health Authority and Department of Health personnel will have travel expenses reimbursed in accordance with the provincial government travel policy by their respective organizations.

Other committee members will have travel expenses reimbursed in accordance with the provincial government travel policy.

Accountability (reporting)

The Anti-infective Stewardship Sub-Committee reports to the Provincial Drugs and Therapeutics Committee.

APPENDIX 2

Point Prevalence Survey Data Collection Form

Hospital:_____

Hospital Code:_____

Number of Beds:_____

Tertiary Centre: Yes___ No___

ID Service available on-site: Yes___ No___

Microbiology Support on-site: Yes___ No___

Administrative Unit	Total # of Pts on Unit on Survey Day	Total # of Pts on Antimicrobial Therapy on Survey Day	Survey Date (d/m/y)	Comments

Point Prevalence Survey Data Collection Form – Patient Data

* Survey Code (Hospital #/ Survey #/ Patient initials _____ * Auditor_____

Date of admission (D/M/Y) _____ Survey date (D/M/Y) _____ * Nursing Unit_____

*MRN _____ * Gender (M/F) _____ * Age_____ * Weight _____

* ICU Admission: Yes___ No___ * Mechanical Ventilation: Yes ___ No ___

* Attending Service_____ * Documented ID Consult (written or verbal): Yes___ No ___

*Urinary Catheter[1] Yes ___ No ___

*** Allergy[2]**	***Reaction**

Age Adjusted Charlson Co-Morbidity Index[3] _____		
☐ Myocardial Infarction[4]	☐ Congestive Heart Failure	☐ Peripheral Vascular Disease[5]
☐ Stroke (Cerebrovascular disease)[6]	☐ Dementia	☐ Chronic Obstructive Pulmonary Disease (COPD)
☐ Connective Tissue Disorder	☐ Peptic Ulcer Disease[7]	☐ Mild Liver Disease[8]
☐ Diabetes	☐ Hemiplegia	☐ Renal disease (eGFR <60)
☐ Diabetes/end organ damage	☐ Any tumour (within 5 years)	☐ Leukemia
☐ Lymphoma[9]	☐ Mod – Severe liver disease[10]	☐ Metastatic solid tumour
☐ AIDS		

Immunosuppression[11] Yes ___ No ___ Reason for Immunosuppression: _____

MDRD or eGFR: _____mL/min (most recent)

Systemic Antimicrobial	Unit Dose [12]	Doses per Day[13]	Route[14]	Order set?[15] (Y/N/NA)	Diagnosis Documented[16] (Y/N)	Diagnosis or Type of Surgery[17]	Prescriber[18]	Indication[19]	Culture Pre-Therapy[20] Y/N	Appropriateness/ Assessment Codes[21]

Antimicrobial Therapy

Stepdown criteria[22]					
☐ IV therapy and not surgical prophylaxis ☐ Clinically improved (WBC ↓, haemodynamically stable, improved signs & symptoms), afebrile at least 48 hours. ☐ Tolerating oral nutrition, enteral feeds and/or oral medications ☐ No evidence of malabsorption (e.g. diarrhoea/ vomiting) and none of the following: continuous NG suctioning, gastrectomy, malabsorption syndrome (i.e. short gut), GI obstruction, or ileostomy ☐ Not treated for endocarditis, CNS infection, osteomyelitis, bacteraemia, abscess or cystic fibrosis ☐ Not febrile neutropenia **All criteria for oral therapy met? Yes___ No___**					
UTI criteria					
Urinalysis done Y___ N ___ Nitrite: _____ Leukocyte esterase _____ Leukocyte urine _____					
☐ Fever	☐ ↑ WBC	☐ Frequency	☐ Urgency	☐ Dysuria	☐ Suprapubic pain
☐ CV angle pain or tenderness	☐ Pregnant	☐ Urological procedure/ TURP			

Explanatory Notes

1 To locate information refer to nursing notes

2 To locate information refer to physician order sheet, EMR or Home medication reconciliation form

3 To locate information refer to History and Physical section of the chart, Progress Notes or Consult Notes (Tim to calculate final index score).

4 Myocardial infarction includes patients with 1 or more definite or probable MI resulting in hospitalization, ECG changes and/or enzyme changes at any time.

5 Peripheral vascular disease includes patients with intermittent claudication or those who had a bypass for arterial insufficiency, those with gangrene or acute arterial insufficiency, and those with an untreated thoracic or abdominal aneurysm (6 cm or more).

6 Cerebrovascular disease includes patients with a history of a cerebrovascular accident with major but also minor or no residua and transient ischemic attacks.

7 Peptic ulcer disease consists of patients who have required treatment for ulcer disease, including those who have bled from ulcers.

8 Mild liver disease consists of cirrhosis without portal hypertension or chronic hepatitis.

9 Lymphoma includes patients with Hodgkins, lymphosarcoma, Waldenstroms's macroglobulinemia, myeloma and other lymphoma

10 Moderate liver disease consists of cirrhosis with portal hypertension without variceal bleeding. Severe liver disease consists of patient with cirrhosis with portal hypertension and a history of variceal bleeding.

11 As per CDC defined severe immunodeficiency: haematological and solid tumours, receipt of chemotherapy, congenital immunodeficiency, or long-term immunosuppressive therapy (e.g. equivalent to prednisone 20 mg/day for 2 weeks or more) or patients with HIV infection with CD4 count < 200

12 Grams per dose; for combination products record the total dose prescribed

(e.g. Amoxi/Clav: 500/125 = 0.625 g; Co-trimoxazole DS = 0.96 g)

13 Provide fractions of dose when necessary (e.g. q18h = 1.5 doses/day; q36h = 0.67 dose/day; q48 h = 0.5 dose/day)

14 IV, IM PO

15 From clinical order set, pathway or pre-printed orders when can be assessed

16 Diagnosis or indication for therapy was recorded in the notes or consult when started

17 See list for standardized nomenclature for diagnosis

18 Prescriber:

Family Medicine	FM	Infectious Disease Specialist/ Microbiologist	ID	Intensivist	ICU
Internal Medicine	IM	Surgeon	S	Paediatrician	P
Geriatrician	G	Pharmacist	RPh	Nurse Practitioner	NP

19 Indication Codes

A: Community Acquired Infection	Symptoms or antimicrobial started < 48 hours from admission		
B: Hospital Acquired Infection	Symptoms or antimicrobial started > 48 hours from admission		
C: Surgical Prophylaxis	C1: Single dose	C2: ≤ 24 hrs	C3: > 24 hrs
D: Medical Prophylaxis			

20 Relevant culture taken before antimicrobial treatment was started, representative of the site being treated. Print copies of culture results taken within 120 hours (5 days) of start of therapy and attach to form.

21 Assessment regarding appropriateness of therapy or potential for stewardship interventions, more than 1 may apply. To be completed by investigators following data collection.

22 To locate information refer to nurses notes, graphic, EMR

APPENDIX 3

Definitions

Bug-Drug Mismatch	Patient on an antimicrobial to which the presumed causative organism is resistant based on relevant culture and sensitivity reports
Community Acquired Infection	Symptoms of antimicrobial therapy for presumed infection started < 48 hours after patient was admitted to hospital
Hospital Acquired Infection	Symptoms start > 48 hrs after admission to hospital and/or associated with treatments in performed hospital
Immunocompromised	As per CDC[14] defined severe immunodeficiency: haematological and solid tumours, receipt of chemotherapy, congenital immunodeficiency, or long-term immunosuppressive therapy (e.g. equivalent to prednisone 20 mg per day for 2 weeks or more) or patients with HIV infection with CD_4 count < 200/mm^3
Inappropriate Dose	Based on patient characteristics (e.g. eGFR) and/or indication (e.g. Meningitis dosing)
Inappropriate Route	Inappropriate route for indication being treated (e.g. oral route for endocarditis, CNS infection, deep abscess, high risk febrile neutropenia, etc.)
Inappropriate Therapy Duplication	Inappropriate double coverage (e.g. dual β-lactam therapy, double coverage when culture and sensitivity results available)
Inappropriate Treatment of Asymptomatic Bacteruria	Treatment of a positive urine culture and sensitivity in a patient without symptoms or signs referable to a urinary tract infection (fever; increased WBC; urinary frequency, urgency, and dysuria; suprapubic pain; costovertebral angle pain/tenderness) and patient not pregnant, having recent or planned urological procedure with mucosal bleeding or TURP[15]
Opportunity for De-escalation	Relevant culture and sensitivity report available that indicates appropriate de-escalation option to a narrower antimicrobial spectrum antimicrobial agent (if allergy profile permits)

[14] CDC = Centre for Disease Control www.cdc.gov

[15] TURP = Trans-Urethral Resection of the Prostate

Opportunity for IV to PO Conversion	An appropriate oral option exist and patient has met the following criteria for IV to PO conversion: has improved clinically (WBC ↓, haemodynamically stable, improved signs & symptoms) and has been afebrile for at least 48 hours; is tolerating oral nutrition, enteral feeds and/or other oral medications; is not showing evidence of malabsorption (e.g. diarrhoea/vomiting) and none of the following are present: continuous nasogastric suctioning, gastrectomy, malabsorption syndrome (i.e. short gut), GI obstruction, or ileostomy; is not being treated for an indication where parenteral therapy is clinically indicated (e.g. endocarditis, CNS infection, osteomyelitis, bacteraemia, abscess, cystic fibrosis); and does not have febrile neutropenia
Prescriber	Family Practice Physician, Internal Medicine Specialist, Infectious Disease Specialist/Microbiologist, Surgeon, Intensivist, Paediatrician, Geriatrician, Hospitalist, Pharmacist, Nurse Practitioner
Relevant culture	Sample taken before or during antimicrobial treatment and representative of the site of presumed infection being treated

APPENDIX 4

Inappropriateness Criteria – Treatment and Medical Prophylaxis

A0: Does not meet other criteria	Does not meet other assessment criteria
A1: Inappropriate Therapy Duplication	e.g. Dual β-lactam therapy; inappropriate double coverage (i.e. double coverage when culture and sensitivity results available)
A2: Opportunity for De-escalation	Relevant C&S results available for de-escalation to a more narrow antimicrobial agent (if allergy profile permits)
A3: Bug-Drug Mismatch	Patient on antimicrobial to which relevant C&S reports show resistance
A4: Inappropriate Dose	Inappropriate dose based on patient characteristics (e.g. eGFR) and/or indication (e.g. meningitis dosing)
A5: Opportunity for IV to PO	Apply to each antimicrobial therapy patient is receiving and to where appropriate oral option is available (see p.2 stepdown criteria on Patient data collection form)
A6: Inappropriate Treatment for Asymptomatic Bacteruria	Treatment of a positive urine C&S in a patient without S&S referable to a urinary tract infection (see p. 2 UTI criteria on Patient data collection form)
A7: Inappropriate route	Inappropriate route for indication being treated (e.g. oral route for treatment of endocarditis, central nervous system infection, deep abscess, high risk febrile neutropenia, etc.)
A8: Inappropriate 2nd Line Therapy	Inappropriate use of a second line antimicrobial therapy based on erroneous allergy information
A9: No Indication	Therapy with no documented or identifiable indication

Inappropriateness Criteria for Surgical Prophylaxis

C3: Duration longer than 24 hours	IDSA does not support duration longer than 24 hours for most surgical prophylaxis (www.idssociety.org)
C2: Duration of 24 hours or less	Acceptable duration based on IDSA
C1: One pre-operative dose	Acceptable duration based on IDSA

APPENDIX 5

Research Ethics Board Approval Letter –

Horizon Health Network

Horizon

Research Ethics Board

Horizon Health Network, [illegible]
400 University Avenue, Saint John, New Brunswick, Canada E2L 4L2
Research Office - [illegible]

May 17, 2012

Ms. Diane Brideau-Laughlin Bsc (Pharm) MSc (candidate)
Principal Investigator

Dear Ms. Brideau-Laughlin:

Re: "A Point Prevalence Survey of Antimicrobial Use Within Horizon Health Network: Benchmarking and Patterns of Use to Support Antimicrobial Stewardship Efforts".
Our File #: 2012-1722

The above noted proposal has been reviewed and approved via the delegated review process of the Horizon Health Network REB.
APPROVED:

- **Research Study Application:** signed and dated April 20, 2012 and
- **Protocol (including Appendices 1-6):** version 1 dated April 20.

Also received and on file:

- CVs for you, Tmothy MacLaggan and Dr. Joanne Salmon.

The Research Ethics Board for the Horizon Health Network is organized and operates according to the principles of the ICH Harmonized Tripartite Guidelines: Good Clinical Practice, Tri-Council Policy Statement and Division 5 of the Food and Drug Regulations. Re-approval should be initiated two months prior to the due date of May 17, 2013.

It should be noted that as a member of the Horizon Health Network REB, you were not involved in any way with the review and approval of this project.

Please do not hesitate to contact the office, if we can be of further assistance. Best wishes as you proceed.

With kind regards,

Chair, Horizon Health Network REB

RESEARCH - BUILDING THE FOUNDATION FOR QUALITY PATIENT CARE

APPENDIX 6

Research Ethics Board Approval Letter – Vitalité Health Network

Bureau de l'éthique
Ethics Office

Le 20 juin 2012

Diane Brideau-Laughlin

OBJET : A Point Prevalence Survey of Antimicrobial Use Within Horizon Health Network and Vitalité Health Network: Benchmarking and Patterns of use to Support Antimicrobial Stewardship Efforts

Investigateurs principaux : Diane Brideau-Laughlin et Timothy MacLaggan
Site : Réseau de santé Vitalité et Réseau de santé Horizon

Approbation finale

- Protocole, version 1, daté du 20 avril 2012

Mme Brideau-Laughlin,

À sa réunion du 13 juin 2012, le Comité d'éthique de la recherche a délibéré et a accordé une approbation finale pour l'étude ci-dessus mentionnée, et ce, avec quorum. Étant donné la nature de l'étude, une étude pour l'évaluation de la qualité, le CÉR accepte que le consentement ne soit pas utilisé auprès des patients. Cependant, le CÉR demande que vous lui transmettiez le nom des personnes désignées pour aller dans le dossier des patients.

Nous désirons vous rappeler que le Comité d'éthique de la recherche est organisé et fonctionne d'après les lignes directrices des bonnes pratiques cliniques.

Veuillez agréer, Mme Brideau-Laughlin, l'expression de mes salutations distinguées.

Présidente du Comité d'éthique
de la recherche

Bureau de l'éthique
Ethics Office
1750, promenade Sunset Drive
Bathurst NB E2A 4L7

ethique.ethics@vitalitenb.ca

APPENDIX 7

Antimicrobials Prescribed for the Treatment of Community- and Hospital-Acquired Infections by Antimicrobial Class

AHFS Class	Name	Number	%
8:12:18	Quinolones	150	25.6%
8:12:16:16	Extended Spectrum Penicillins	60	10.2%
8:31:32	Metronidazole	50	8.5%
8:12:06:23	3rd Generation Cephalosporins	49	8.3%
8:12:16:08	Aminopenicillins	46	7.8%
8:12:06:04	1st Generation Cephalosporins	34	5.8%
8:12:06:08	2nd Generation Cephalosporins	31	5.3%
8:12:12:92	Other Macrolides	27	4.6%
8:12:28:16	Glycopeptides	21	3.6%
8:14:08	Azoles	18	3.1%
8:12:28:20	Clindamycin	16	2.7%
8:12:07:08	Carbapenems	15	2.6%
8:12:20	Sulfonamides	15	2.6%
8:12:02	Aminoglycosides	12	2.0%
8:12:24	Tetracyclines	11	1.9%
08:12:16:12	Penicillinase Resistant Penicillins	8	1.4%
8:36	Urinary Anti-Infectives	7	1.2%
8:12:16:04	Natural Penicillins	7	1.2%
8:12:12:04	Erythromycin	4	0.7%
8:14:16	Echinocandins	3	0.5%
8:16;92	Dapsone	1	0.2%
8:12:28:24	Linezolid	1	0.2%
8:14:02	Terbinafine	1	0.2%
		587	100.0%

APPENDIX 8

Anatomic Sites for Community- and Hospital-Acquired Infections

Site	Number	%
PNEU	140	29.5%
GI	74	15.6%
SST	68	14.3%
Cyst	55	11.6%
BRON	35	7.4%
BJ	22	4.6%
BAC	18	3.8%
Pye	14	2.9%
SIRS	13	2.7%
IA	12	2.5%
ENT	11	2.3%
CV	7	1.5%
OBGY	2	0.4%
CNS	2	0.4%
Misc	1	0.2%
	474	99.8%

Definitions (Ansari 2009)

Code	Definition	Code	Definition
PNEU	Pneumonia	IA	Intra-abdominal infection
GI	Gastrointestinal infection	ENT	Ear/Nose/Throat infection
SST	Skin and soft tissue infection	SST	Skin and soft tissue infection
Cyst	Cystitis	CV	Cardiovascular infection
BRON	Bronchitis	BRON	Bronchitis
BJ	Bone and Joint	OBGY	Obstetrical or gynaecological infection
BAC	Bacteraemia	CNS	Central nervous system infection
Pye	Pyelonephritis	Misc	Miscellaneous
SIRS	Systemic inflammatory response		

APPENDIX 9

Treatment-Prescribed Antimicrobials

Antimicrobial	Number	%
Ciprofloxacin	95	16.2%
Piperacillin-Tazobactam	59	10.1%
Metronidazole	50	8.5%
Moxifloxacin	43	7.3%
Amoxicillin	39	6.6%
Ceftriazone	38	6.5%
Cefuroxine	30	5.1%
Cefazolin	23	3.9%
Azithromycin	21	3.6%
Vancomycin	21	3.6%
Fluconazole	17	2.9%
Clindamycin	16	2.7%
Cotrimoxazole	15	2.6%
Cephalexin	13	2.2%
Doxycycline	11	1.9%
Gentamicin	9	1.5%
Levofloxacin	9	1.5%
Ceftazidime	8	1.4%
Cloxacillin	8	1.4%
Imipenem	8	1.4%
Ampicillin	7	1.2%
Clarithromycin	6	1.0%
Meropenem	6	1.0%
Nitrofurantoin	6	1.0%
Penicillin	5	0.9%
Erythromycin	4	0.7%
Caspofungin	3	0.5%
Norfloxacin	3	0.5%
Cefotaxime	2	0.3%
Tobramycin	2	0.3%
Amikacin	1	0.2%
Cefixime	1	0.2%
Cefprozil	1	0.2%
Dapsone	1	0.2%
Ertapenem	1	0.2%
Linezolid	1	0.2%

Terbinafine	1	0.2%
Ticarcillin	1	0.2%
Trimethoprim	1	0.2%
Voriconazole	1	0.2%