The use of antibiotics in the treatment of skin and soft tissue infections in selected Canadian First Nations communities

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Abstract

Methicillin-resistant Staphylococcus aureus (MRSA) is a growing concern in Canada especially in Aboriginal communities in remote regions. The northern and remote communities possess some or many of the risk factors that are identified in previous research to be associated with Community-Associated Methicillin-resistant Staphylococcus aureus (CA-MRSA) infections such as overcrowding, challenges in maintaining personal hygiene and limited access to healthcare. CA-MRSA spreads rapidly in the communities. It is known to be associated with high morbidity and mortality rates. Furthermore, antibiotic resistance in CA-MRSA is increasing in Canada. It is known that inappropriate and greater use of antibiotics is associated with increased antibiotic resistance. To reduce and to control the antibiotic resistance, monitoring the prevalence of CA-MRSA and the changing antibiotic susceptibility profiles at the population level, especially in highly affected communities, is crucial. To our knowledge, there was no community-based study that examined the epidemiology of CA-MRSA skin and soft-tissue infections (SSTIs) in First Nations communities in Canada at large scale, and the knowledge on the risk factors, outcomes and antibiotic susceptibility profiles is still very limited.

This study aimed to describe the local epidemiology of SSTIs at the community level in selected First Nations communities as well as to describe the antibiotic use to treat SSTIs and the antibiotic susceptibility patterns of CA-MRSA. A retrospective chart review was conducted in 12 nursing stations in the First Nations communities across 5 provinces in Canada. The charts of individuals over 18 years of age who had received service at the nursing station in the previous 12 months, were reviewed in this study. Each antibiotic prescription that was noted in the chart in this period prior to chart review was recorded in the antibiotic tracking case report form. Data collected included demographics, indication for antibiotic use, antibiotic prescription parameters

and patient outcomes. In total, of 372 patient charts reviewed, 224 patient charts contained at least one case (an encounter that resulted in an antibiotic prescription during the study period). Of those 224 charts, 459 cases were recorded and, of those, 137 cases had a diagnosis of an SSTI. The prevalence of SSTI among the selected First Nations communities in 2012-2013 was estimated at almost 37%. In the 137 SSTI cases, 55 cases were identified as MRSA infections either by laboratory test such as wound culture or by history of colonization documented in the chart. The overall prevalence of MRSA in all SSTI cases was estimated at 40.1% (55 confirmed MRSA positive cases / 137 cases of SSTIs). The majority of SSTIs were purulent infections and wounds. We also found that a wound culture and susceptibility test were performed only in 29% of all SSTI cases. An orally administered antibiotic was most frequently used (in 71.5% of treatments). The majority of MRSA isolates in this study were susceptible to clindamycin and co-trimoxazole (90.5% and 95.2%), but only 29% were susceptible to erythromycin. In general, higher rates of SSTIs were seen in communities where overcrowding and poor access to running water are more prevalent. In this study, we found that the diagnostic tests such as wound culture and sensitivity test was not ordered very often and there was also lack of follow-up or lack of documentation of the follow-up. More research is needed to better understand the challenges and risk factors associated with CA-MRSA infections in remote communities. Developing a national-level surveillance system that can help with monitoring the epidemiology of SSTIs and the antibiotic susceptibility test results of CA-MRSA at community level would be essential for better prevention, control, and management. Furthermore, adopting other initiatives such as antibiotic stewardship programs at community and healthcare settings as well as addressing the socio-environmental factors such as housing and access to water would be all very important in the steps to curb antibiotic resistance.

Background

Staphylococcus aureus (*S. aureus*) is a gram-positive bacteria which is the leading pathogen responsible for causing skin and soft tissue infections (SSTI) (1–5). It is frequently found in the human respiratory tract and on the skin and can be part of the normal human flora (6–8). The colonization is very common in healthy people. It is thought that generally one out of every three people would be colonized (9,10). *S. aureus* is transmitted by direct skin-to-skin contact between people or indirectly by touching a contaminated object or surface (11,12). Moreover, *S. aureus* has a great ability to adapt to the antibiotics used against it. Over the past 60 years, epidemics and pandemics of antibiotic-resistant *S. aureus* were seen globally (13). *S. aureus* gained resistance against penicillin shortly after its introduction as a treatment, and penicillin-resistant *S. aureus* became pandemic throughout the 1950s and 1960s (13). The next choice of antibiotic treatment for infections caused by penicillin-resistant *S. aureus* was semi-synthetic penicillin (methicillin, oxacillin and cloxacillin) (14). Within two years following the introduction of these semi-synthetic penicillins as treatment, strains of *S. aureus* resistant to methicillin were found (13,14). Methicillin-resistant *S. aureus* (MRSA) then spread across the world over the last several decades and by the late 1960s, more than 80% of the *S. aureus* isolates found in hospitals were resistant to methicillin (15). These strains were named methicillin-resistant *Staphylococcus aureus* (MRSA). For many years, MRSA was seen almost exclusively as a nosocomial pathogen (11). However, since the 1990s, MRSA has also emerged in communities, causing SSTIs, necrotizing pneumonia, necrotizing fasciitis and sepsis (14). These MRSA strains found in the community were named Community-Associated MRSA (CA-MRSA) (16). The standardized case definition of CA-MRSA, created by the US Centers for

Disease Control and Prevention (CDC), specifies that CA-MRSA is a MRSA infection caused in a person who has none of the risk factors related to healthcare settings (risk factors of Healthcare-Associated MRSA (HA-MRSA)) (16):

- A positive culture of MRSA after 48 hours of admission to a hospital;
- History of hospitalization, surgery or residency in a long-term care facility in the past year;
- Presence of an indwelling percutaneous devices or catheters; or
- Prior isolation of MRSA.

This standardized case definition has some limitations, as HA-MRSA and CA-MRSA strains co-circulate in communities and in healthcare facilities (15,17,18). Because HA-MRSA and CA-MRSA strains are different from one another genotypically (19–21), molecular markers can be used to define MRSA isolates as "CA" or "HA". When genotyping testing is not available/not practiced in local laboratories, the distinction between HA- and CA- MRSA infection is done based on the place of acquisition of infection (not always the same as the pathogen's place of acquisition) (22). CA- and HA- MRSA not only differ genetically, but they also put different populations at risk (23) and have different risk factors (3,24,25). Although it is not yet clearly established, some known risk factors for CA-MRSA are low socioeconomic status, existing skin conditions (cuts, abrasions or wounds), scratches and insect bites, previous antibiotic use, poor hygiene, sharing of personal items and overcrowding (26–36). Also, some specific population groups are at higher risk of having CA-MRSA infections, such as people who inject drugs, men who have sex with men, military personnel, inmates of correctional facilities and Native or Aboriginal Canadians (14,37). Additionally, the Alberta Health and Wellness

department has proposed the “five C’s” of CA-MRSA transmission: lack of **C**leanliness, **C**rowding, close **C**ontact, sharing **C**ontaminated personal items and **C**ompromised skin (38). Certain groups of the population, such as Aboriginal Canadians, are particularly vulnerable to CA-MRSA because they share some or many of these risk factors.

CA-MRSA is now a global concern, not only because CA-MRSA infections have been reported around the world, (8) but also because it mainly affects a young and previously healthy population who have no predisposing nosocomial infections, (39) and it is associated with more severe disease (40–42). In Canada, there is an increasing concern about CA-MRSA because the rates of MRSA found in the communities have been rising dramatically over the past decade (10,43–45). The Canadian Nosocomial Infection Surveillance Program (CNISP) is a program which supports monitoring of healthcare-acquired infections at 52 sentinel sites of the Canadian Hospital Epidemiology Committee (CHEC). The CNISP reported that from 1995 to 2007 the proportion of CA-MRSA strains (from the MRSA infected cases counted in CNISP hospitals) increased from 6% to 23% (46). The results of CNISP reports show that the MRSA strains that are known to be community-associated have been increasing (Figure 1). It is clear that the number of MRSA isolates that are community-associated is rising in Canada. Although this is probably an underestimated number because the CNISP program only surveys inpatients at the sentinel sites, usually in large urban centres. The rates in northern and remote communities are expected to be higher because of the risk factors such as overcrowding, poor housing and limited access to healthcare. It has been identified that broader population-level surveillance is a priority in order to update and increase the knowledge and understanding of CA-MRSA in Canada (14).

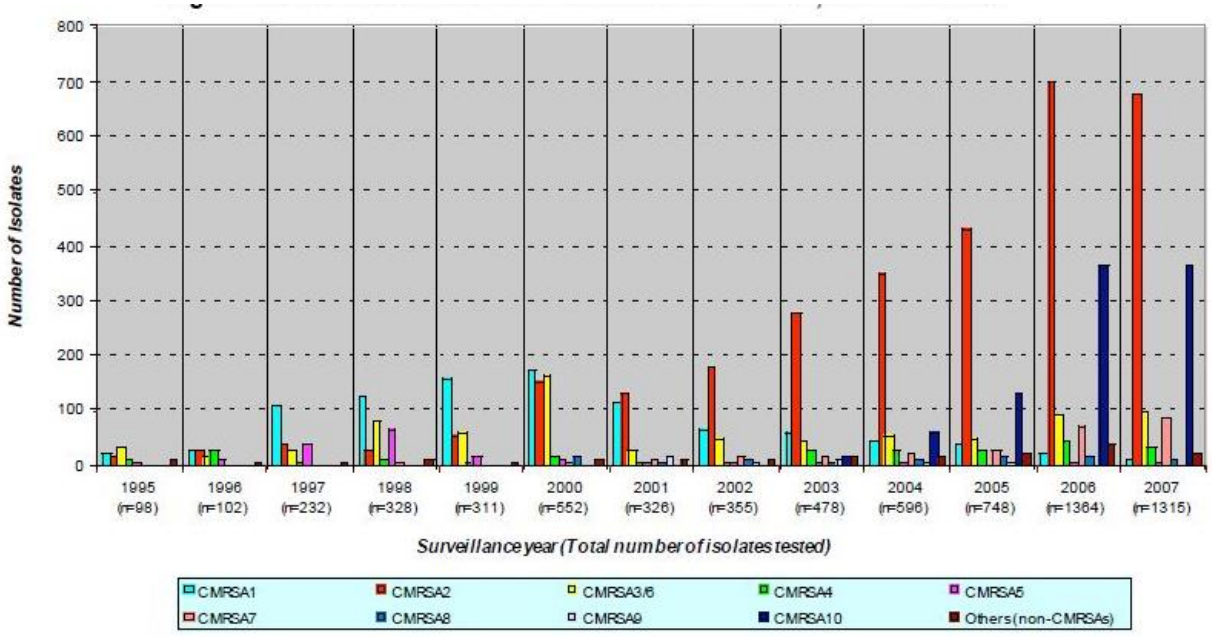

Figure 1: Distribution of MRSA strains from infected cases, CNISP 1995-2007 (47).

This increasing concern about CA-MRSA in Canada is further amplified by a combination of multiple issues. CA-MRSA is particularly well adapted to survive and transmit rapidly in community settings. Some of the known specific characteristics that contribute to this are the Panton-Valentine Leukocidin (PVL) genes which have cytolytic pore-forming activity that damages human immune cells, the smaller size of SCCmec IV element giving the CA-MRSA strains better fitness to survive as well as bacteriocin (a type of toxin) and ACME (Arginine Catabolic Mobile Element), which contributes to the CA-MRSA's enhanced growth and survival within its host (3,13,14,48,49). Furthermore, CA-MRSA has a higher attack rate in outbreak settings and infections occur in the general population, including healthy and young individuals (14). In addition, CA-MRSA infections put a greater burden on the health of the general population as well as increasing economic cost. Studies have found that resistant-Skin and Soft-Tissue Infections (SSTIs) (presumably caused by CA-MRSA) result in increased morbidity and mortality as well as in increased healthcare costs due to longer hospitalization and

higher hospital charges (1,50,51). In a study conducted by Salgado et al., the colonization period of community-associated strains of MRSA was about 700 times longer than that of the healthcare-associated strains: 36.9 billion annual person-days of MRSA colonization in the communities compared to 50.4 million annual person-days of colonization in the hospital (29). Moreover, studies have shown that HA-MRSA and CA-MRSA strains now co-circulate in communities and in healthcare facilities (15,17,18). The community-associated strains have now entered healthcare facilities and there are mathematical models predicting that CA- strains will eventually displace the HA- strains in healthcare settings (52,53). The barrier between communities and healthcare settings has become permeable. With this co-circulation of CA- and HA-MRSA strains in healthcare and community settings, infection control activities need to be coordinated between the two settings. Finally, there is also an increased concern about the multi-resistance to antibiotics and some studies have suggested that control at the community level will have a direct effect on the control in the hospitals. Successful control of nosocomial antibiotic resistance depends on the absence of the introduction of new community strains into healthcare settings (54). As MRSA is rapidly evolving and becoming more and more common in both community and healthcare settings, it is essential to monitor its changing prevalence, distribution as well as its antibiotic susceptibility patterns (55,56).

To date in Canada, the prevalence of CA-MRSA and the antibiotic susceptibility patterns have not been formally studied by a community-based study at the national level. Data on CA-MRSA is available from the CNISP where the proportion of CA-MRSA strains (from the MRSA isolates obtained from the inpatients of CNISP hospitals) is assessed (57). Many studies recommend different strategies to better prevent, control and treat the infections caused by CA-MRSA: infection prevention strategies (58), developing a surveillance program (14), infection

control practices in healthcare facilities (59) and adopting an antimicrobial stewardship program (49,60). Assessing the prevalence in the community and identifying and understanding some of the risk factors involved in high risk population, such as in northern and remote communities, are crucial to the success of all of these strategies to prevent and control infections caused by MRSA.

This study aims to describe the local epidemiology of skin and soft tissue infections presumably caused by MRSA in selected First Nations communities across five provinces and to describe the patterns of prescription and use of antibiotics in the treatment of skin and soft tissue infections in the selected communities. The patient outcomes and the antibiotic susceptibility patterns were to be assessed where possible. Finally, the results of this study were to serve as the information source to update and develop some specific recommendations for the healthcare facilities in remote communities concerning the use of antibiotics for the treatment of patients presenting with skin and soft tissue infections in these communities.

Literature review

Clinical impacts of CA-MRSA: Skin and Soft-Tissue Infections

The most common clinical manifestation of Community-Associated Methicillin-resistant *Staphylococcus aureus* (CA-MRSA) is skin and soft tissue infections (SSTIs). About 90% of the cases of infections caused by CA-MRSA are SSTIs, and about 90% of them are abscesses or cellulitis with purulent drainage (4,5,10,61). Methicillin-resistant *Staphylococcus aureus* (MRSA) SSTIs can vary from mild, self-resolving infections to severe and life-threatening infections (62). The majority of these infections caused by CA-MRSA are mild to moderate purulent SSTIs such as furuncles, carbuncles, abscesses or purulent cellulitis (4,63,64). However, it has been reported that in some cases CA-MRSA can cause very severe and invasive infections such as severe sepsis, necrotizing pneumonia, necrotizing fasciitis, toxic shock syndrome, empyema and septic thrombophlebitis of large veins (13,14,25,65–68). Some of these more severe conditions are associated with a high mortality rates: necrotizing fasciitis and necrotizing pneumonia have been associated with 20% and 75% of mortality rates, respectively (25,65,69). Prior to the emergence of MRSA in communities, reports of these invasive and fatal diseases caused in healthy individuals were very rare; there are now many cases of outbreaks that have shown high morbidity and hospitalization associated with CA-MRSA. In the 1990s, a French study on community-acquired *S. aureus* pneumonia showed a mortality rate of 63% (37), and in the United States, there was an MRSA outbreak that caused the deaths of four children in the Midwest (55). The University of California at Los Angeles (UCLA) also reported that 4 of 14 adults diagnosed with necrotizing fasciitis caused by MRSA had no preexisting medical

condition (37). Moreover, the CDC reports that in 2005 about 94,000 persons developed their first invasive MRSA infection, and the mortality rate was about 20% (70). They also found that of those infections, about 14% were community-associated (70). In 2007, CA-MRSA caused the deaths of six previously healthy adults and children because of necrotizing pneumonia (71). These invasive infections caused by CA-MRSA have a high mortality rate, even when treated with the best adequate therapeutics (37).

Treatment of SSTIs

Once a patient visits a healthcare professional with a SSTI, the treatment can vary depending on the severity of the infection and the characteristics of the infected individual (e.g. young infants or immune-compromised people). The use of antimicrobial agents and surgical incision and drainage (I&D) procedure are the basis of treatment (72). Minor SSTIs (uncomplicated and superficial) may be treated just by incision and drainage without antimicrobial therapy or with topical antimicrobial agents (e.g. topical mupirocin or bacitracin, or topical antiseptics) (14,72), whereas more complicated SSTIs may be treated with systemic antibiotics (e.g. parenteral vancomycin) (58,72).

The I&D procedure is recommended for treatment of SSTIs based on the principle of source control and/or physical removal of infectious foci (64,73,74). It has been associated with high rates of cure or improved health outcomes (62). The IDSA practice guidelines recommend the incision and drainage procedure to treat abscesses, carbuncles large furuncles, and cellulitis (73,74), and since the majority of MRSA SSTIs are purulent, the I&D procedure is often

indicated for treatment (64). Some studies have shown the effectiveness of I&D only treatment (without antibiotics) of uncomplicated abscesses (62,75–77).

In Canada, the primary health care in First Nations communities is either provided by the federal government, provincial government or sometimes regulated by the bands. The majority of Aboriginal reserves are served by nursing stations under the First Nations and Inuit Health Branch (FNIHB) from the federal government. FNIHB provides clinical practice guidelines (CPG) to the nursing stations in the reserves (78). The current standard of treatment of SSTIs at the FNIHB nursing stations in northern communities is based on the FNIHB CPG. A summary of recommended treatment for SSTIs (in adults) by the FNIHB CPG as well as the IDSA clinical guidelines is available in Appendix A.

Community-associated MRSA infections in First Nations communities in Canada

Historically, in Canada, the first cases of outbreaks of CA-MRSA were seen in the late 1990s in the Aboriginal communities of Alberta, Manitoba and Nunavut (79–84). In a retrospective survey conducted in five hospitals in central Canada, Embil and colleagues have found that 62% of the patients who were MRSA-positive at admission were First Nations patients (82). Dalloo et al. found in their study, conducted in 2006-2007 which investigated the initial MRSA outbreak in a northern Inuit community in Nunavut, that 83% of MRSA isolates met the case definition of CA-MRSA (79). In that Inuit community, the incidence of MRSA was about 60% higher than the nosocomial CNISP incidence (7.4 cases per 1,000 patient admissions), but comparable to the numbers reported in other remote communities in northern Saskatchewan and Manitoba (39,79,80,85). Furthermore, the incidence of CMRSA7 (one of the

predominant strains of CA-MRSA) increased in the Aboriginal communities in Manitoba (80), Saskatchewan (84) and in Nunavut (79). For example, in Manitoba, the crude rates increased from 1 infection per 10,000 in 2003 to 13 infections per 10,000 in 2006 (80). Many studies in the past have shown that the rates of CA-MRSA have been high in the Aboriginal population in remote, northern communities (26,83,84,86–90). In a recent report on the rates of CA-MRSA in Northwestern Ontario, Muileboom et al. found that there was an 80% increase of CA-MRSA strains in *S. aureus* isolates between 2008 and 2012; it is also noticeable that 25% of the infections were reinfections (91). The authors identified that the risk factors in the remote communities such as overcrowding, inadequate housing and poor sanitation may be contributing to the high reinfection rates (91).

Traditional risk factors of nosocomial MRSA infection are known to be recent hospitalization, dialysis and the presence of an indwelling device (37). The risk factors of CA-MRSA differ from the risk factors of HA-MRSA. The important increases in incidences and spread of CA-MRSA in Canadian Aboriginal communities might be associated with some of these particular risk factors of CA-MRSA: overcrowding, frequent skin-to-skin contact, existing skin conditions, household exposure to someone with a skin condition, scratches/insect bites, participation in activities that result in damaged skin, sharing potentially contaminated objects, challenges in maintaining personal hygiene, limited access to healthcare and lower socio-economic status (26,31,33,34,83,85). Aboriginal people in Canada experience many of the CA-MRSA risk factors (e.g. overcrowding – about 10 times more frequent among First Nations, low socioeconomic status, limited access to healthcare) or environments or conditions that are associated with the risk factors (e.g. markers for poorer health status – lower life expectancy, higher infant mortality rate, higher hospitalization rates) (58,79,92,93). In fact, Canadian

Aboriginals were six times more likely to have had CA-MRSA isolated than were non-Aboriginals (83). It's clear that CA-MRSA infections are a growing concern in First Nations communities, but there is a lack of adequate surveillance data on rates and impact of MRSA in the communities: many reports have suggested more research is needed to reduce and prevent CA-MRSA infections in aboriginal communities and to make better recommendations and guidelines for adequate treatment (58,83,93,94).

The antibiotic resistance

Another alarming issue associated with MRSA infections is the growing antimicrobial resistance worldwide and in Canada. Antimicrobial resistance (AMR) is the resistance of a microorganism to an antibiotic to which it was previously susceptible (95). The resistant organisms are able to withstand the standard antibiotic treatments and consequently infections persist and may spread to others (95). The World Health Organization (WHO) recognizes AMR as a global concern because it results in prolonged illness and greater risk of death, in increased healthcare costs as more expensive therapies must be used and it also threatens a return to pre-antibiotic era where many infectious diseases risk becoming uncontrollable (95,96). The WHO identifies some of the factors that contribute to increase the AMR as following (95):

- Lack of a comprehensive and coordinated response;
- Weak or absent antimicrobial resistance surveillance and monitoring systems;
- Inadequate systems to ensure quality and uninterrupted supply of medicines;
- Inappropriate use of antimicrobial medicine;

- Poor infection prevention and control practices;
- Insufficient diagnostic, prevention and therapeutic tools.

In a recently published report on antimicrobial resistance by the World Health Organization, they identify the antimicrobial resistance as a global public health threat that requires action; coordinated surveillance systems across nations were recommended to reduce the gaps that exist presently (8).

In Canada, virtually all *S. aureus* are resistant to penicillin and ampicillin, but not to methicillin and cephalosporins; the *S. aureus* resistant to methicillin and cephalosporins are MRSA (37,49). CA-MRSA strains are susceptible to a wider range of antibiotics than HA-MRSA strains, for example, trimethoprim-sulfamethoxazole, clindamycin and doxycyline (14,97). For example, 79% of HA-MRSA isolates are resistant to clindamycin, but CA-MRSA has a low baseline resistance to clindamycin in comparison to HA-MRSA (3,14) (Figure 2). According to the 2012 national antimicrobial testing results by the Canadian Antimicrobial Resistance Alliance (CANWARD), 85.4% of CA-MRSA was susceptible to clindamycin (98).

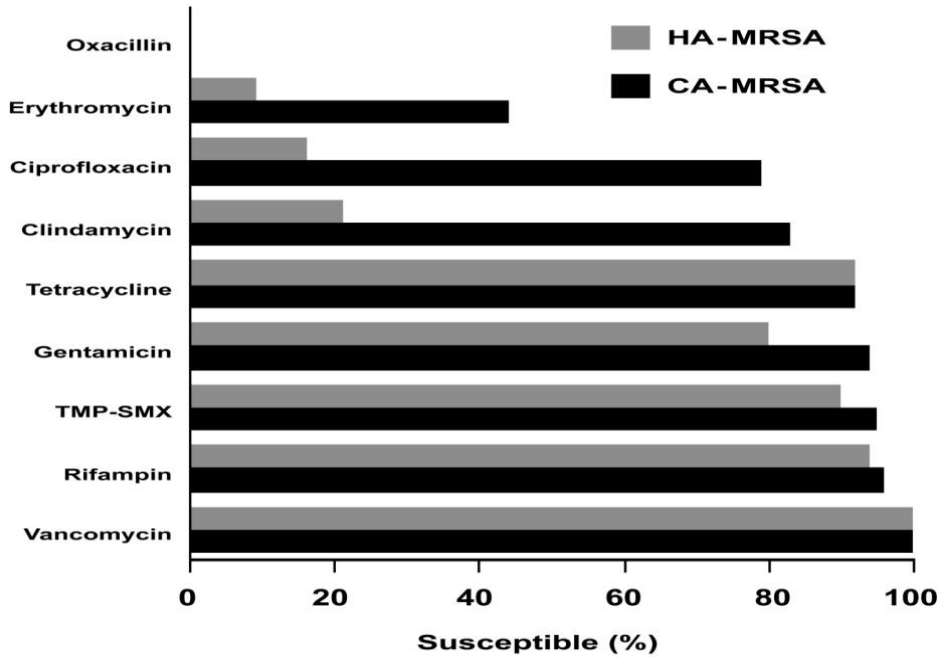

Figure 2: Antimicrobial susceptibilities for CA- and HA- MRSA (3)

Furthermore, not only is the antimicrobial resistance in CA-MRSA growing in Canada, but there has been some cases of clinical failures in CA-MRSA infections treated with clindamycin (99,100). There is a general consensus that the inappropriate and greater use of antibiotics are both associated with increased antibiotic resistance (101,102). Resistant SSTIs are difficult to treat; they result in increased morbidity and mortality, as well as increased healthcare costs (longer hospitalization, higher hospital charges) (1,50,51). In a recent study by Muileboom, the researchers have identified that the empiric treatment for cellulitis in Northwestern Ontario used to be cephalexin but the options for empiric treatment now have to be reconsidered because of the changing antibiotic resistance profiles of CA-MRSA (97).

To reduce and minimize antibiotic resistance, various initiatives were suggested: infection prevention strategies (58), developing a surveillance program (14), infection control practices in healthcare facilities (59) and adopting an antimicrobial stewardship (49,60).

A surveillance system is defined by the CDC as an ongoing systematic collection, analysis and interpretation of health data essential to the planning, implementation, and evaluation of public health practice as well as the timely dissemination to those who need to know (57). The general objectives of such system are to:

1) Monitor the number of cases for unusual changes and trends (risk, manifestation, affected population and geographic area);

2) Monitor occurrence with/without intervention, planning, and further study;

3) Identify abnormal events.

Currently in Canada, the CNISP and the CANWARD both monitor the antimicrobial resistance in CA-MRSA at the national level, although their data is based only on isolates obtained from sentinel sites or tertiary care centers, therefore it may not be completely representative of smaller northern remote communities (103,104).

The antimicrobial stewardship is a set of coordinated interventions which promote the appropriate use of antimicrobial agents (right choice of agent, right dose, route of administration and duration of therapy) for the right bacterial infection at the right time (49,60,105). This type of program is designed to optimize antimicrobial use in treating infections to achieve better health outcomes, to minimize adverse events and to reduce selective pressure on bacteria to reduce antimicrobial resistance. The Infectious Diseases Society of America (IDSA) and the Society for Healthcare Epidemiology of America (SHEA) presented guidelines for developing institutional programs to promote antimicrobial stewardship (105). They also identify two goals of the antimicrobial stewardship:

1) Optimize clinical outcomes and minimize adverse consequences of antimicrobial use;

2) Reduce costs related to healthcare system without impacting the quality of care (105).

Brief summary of the guidelines are presented in Appendix B.

Ethics

This study was reviewed by the Health Canada Research and Ethics Board (REB) and the Ottawa Health Science Network Research Ethics Board (OHSN-REB). The project was determined to be a quality assurance or quality improvement project with established standards of care for the use of antibiotics in nursing stations by the Health Canada REB. The purpose of the project was to contribute in establishing better practices in nursing stations, i.e. by ensuring adherence to available guidelines, and update these guidelines to better reflect local epidemiology.

Health Directors in the communities where data collection took place were contacted by the project coordinator. Furthermore, the consent from the Regional Nurse Officers (RNOs) was sought. The RNOs signed a concurrence form to approve that nursing stations in the region will participate in the project on a voluntary basis. This concurrence form was to replace the individual consent forms from each nursing station. The RNOs have also assisted in the selection of participating communities, which was done on a voluntary basis. Finally, the Nurse in Charge (NIC) and staff of nursing stations were informed of the project and were given the time frame for data collection. NICs in all participating communities have supported the project by accommodating the visiting investigators and coordinating the data collection processes.

In addition, the regions and the selected nursing stations were assigned specific codes, to protect the identity of the community and no information to identify a specific prescriber or

client were recorded during the data collection process. Only the project coordinator has the master list of the facility codes. This process ensured that the communities, prescribers and clients are not identifiable in the project.

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The use of antibiotics in the treatment of skin and soft tissue infections in selected Canadian First Nations communities

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Abstract

Background: The rate of MRSA infection has been rising in Canada with First Nations (FN) populations at higher-risk. To date, the prevalence of MRSA and the antibiotic susceptibility patterns have not been assessed by a community-based study at the national level. This study aimed to describe the local epidemiology of skin and soft tissue infections (SSTIs) in FN communities and also to describe antibiotic use.

Methods: This study was a retrospective chart review at 12 nursing stations in FN communities across 5 provinces. People over 18 who visited the nursing station in the previous 12 months were included. Each encounter that resulted in an antibiotic prescription during the study period was captured as a "case". Demographic information, indication for therapy, details of antibiotic use, microbiological data and treatment appropriateness were assessed.

Results: In total, 372 charts were reviewed, 459 cases were recorded and 137 of these represented SSTI. The prevalence of SSTI among the FN communities in 2012-2013 was estimated at 37%. The prevalence of MRSA in SSTI was 40.1%. Most MRSA isolates in this study were susceptible to clindamycin and co-trimoxazole (90.5% and 95.2%), with only 29% susceptible to erythromycin. The majority of SSTIs were purulent infections and wounds. Wound cultures were performed in only 29%. Thirty percent of antibiotic prescriptions were judged to be inappropriate. 72% of infections were treated orally. Higher rates of SSTIs were seen in communities where overcrowding and poor access to running water are more prevalent.

Conclusions: SSTIs, specifically due to MRSA, are common in FN communities in Canada. Appropriate prevention and treatment of SSTIs in these communities require a better understanding of the unique challenges faced by these communities as well as establishment of surveillance systems and antimicrobial monitoring programs.

Introduction

In Canada, there is increasing concern about Community-Associated Methicillin-Resistant *Staphylococcus aureus* (CA-MRSA) because the rates of MRSA found in communities have been rising dramatically over the past decade (10,43–45). The Canadian Nosocomial Infection Surveillance Program (CNISP) is a program which supports the monitoring of healthcare-acquired infections at 52 sentinel sites of the Canadian Hospital Epidemiology Committee (CHEC). The CNISP reported that from 1995 to 2007 the proportion of CA-MRSA strains, from the MRSA infected cases counted in CNISP hospitals, increased from 6% to 23% (46). It is clear that the number of MRSA isolates that are community-associated is rising in Canada, although this is probably an underestimated number, because the CNISP program only surveys inpatients of the sentinel sites, usually in large urban centres. The rates in northern and remote communities are expected to be higher because of the risk factors such as overcrowding, poor housing and limited access to healthcare. It has been identified that broader population-level surveillance is a priority to update and increase the knowledge and understanding of CA-MRSA in Canada (14).

This increasing concern about CA-MRSA in Canada is further amplified by a combination of multiple issues. CA-MRSA is particularly well adapted to survive and transmit rapidly in community settings (3,13,14,48,49). Furthermore, CA-MRSA has higher attack rate in outbreak settings and infections occur in the general population including healthy and young individuals (14). In addition, CA-MRSA infections put a greater burden on the health of the general population and create higher economic costs. Studies have found that resistant Skin and Soft-Tissue Infections (SSTIs), presumably caused by CA-MRSA, result in increased morbidity and mortality as well as in increased healthcare costs due to longer hospitalization and higher

hospital charges (1,50,51). In a study conducted by Salgado et al., the colonization period of community-associated strains of MRSA was about 700 times longer than that of the healthcare-associated strains: 36.9 billion annual person-days of MRSA colonization in the communities compared to 50.4 million annual person-days of colonization in the hospital (29). Moreover, studies have shown that HA-MRSA and CA-MRSA strains now co-circulate in communities and in healthcare facilities (15,17,18). The community-associated strains have now entered healthcare facilities, and there are mathematical models predicting that CA- strains will eventually displace the HA- strains in healthcare settings (52,53). The barrier between communities and healthcare settings has become permeable, and with this co-circulation of CA- and HA-MRSA strains in the healthcare and community settings, the infection control needs to be coordinated between the two settings. Finally, there is also an increased concern about the multi-resistance to antibiotics, and some studies have suggested that control at the community level will have a direct effect on the control in the hospital – successful control of nosocomial antibiotic resistance depends on the absence of the introduction of the new community strains into the healthcare settings (54). As MRSA is rapidly evolving and becoming more and more common in both community and healthcare settings, it is essential to monitor its changing prevalence, distribution as well as its antibiotic susceptibility patterns (55,56).

The prevalence of CA-MRSA and the antibiotic susceptibility patterns have not been formally studied by a community-based study at the national level in Canada. Data on CA-MRSA is available from the Canadian Nosocomial Infections Surveillance Program where the proportion of CA-MRSA strains (from the MRSA isolates obtained from the inpatients of CNISP hospitals) is assessed (57). Assessing the prevalence in the community and identifying and

understanding some of the risk factors involved in the high risk population, such as in northern remote communities, are crucial to better prevent and control infections caused by MRSA.

Staphylococcus aureus (*S. aureus*) is a gram-positive bacteria which is the pathogen most responsible for SSTIs (1–5). *S. aureus* is transmitted by direct skin-to-skin contact between people or indirectly by touching a contaminated object or surface (11,12). Moreover, *S. aureus* has a great ability to adapt to the antibiotics used against them; over the past 60 years infections caused by resistant *S. aureus* were considered to be exclusively healthcare- or hospital-associated (HA-) (14). However, since the 1990s, MRSA has also emerged in the communities, especially in North America (14). These MRSA strains found in the community were named Community-Associated MRSA (CA-MRSA) (16). According to the CDC case definition, CA-MRSA is an MRSA infection in a person who has none of the risk factors for HA-MRSA: a positive culture of MRSA after 48 hours of admission to a hospital; history of hospitalization, surgery or residency in a long-term care facility in the past year; presence of an indwelling percutaneous devices or catheters; or prior isolation of MRSA (16). This standardized case definition has some limitations, as HA-MRSA and CA-MRSA strains co-circulate in the communities and in healthcare facilities (15,17,18). Furthermore, CA- and HA- MRSA not only differ genetically, but they also put different populations at risk (23) and have different risk factors (3,24,25). Although it is not yet clearly established, some risk factors for CA-MRSA are: low socioeconomic status, existing skin conditions (cuts, abrasions or wounds), scratches and insect bites, previous antibiotic use, poor hygiene, sharing of personal items and overcrowding (26–36). Also, some specific population groups are at higher risk of having CA-MRSA infections such as injection drug users, men who have sex with men, military personnel, inmates of correctional facilities and Native or Aboriginal Canadians (14,37).

The most common clinical manifestation of CA-MRSA is skin and soft tissue infections (SSTIs): about 90% of the cases of infections caused by CA-MRSA are SSTIs, and about 90% of them are abscesses or cellulitis with purulent drainage (4,5,10,61). Although the majority of these infections caused by CA-MRSA are mild, it has been reported that in some cases CA-MRSA can cause very severe and invasive infections such as severe sepsis, necrotizing pneumonia, necrotizing fasciitis, toxic shock syndrome, empyema, endocarditis and septic thrombophlebitis of large veins (13,14,25,65–68). Prior to the emergence of MRSA in communities, reports of these invasive and fatal diseases caused in healthy individuals were very rare. The University of California at Los Angeles (UCLA) also reported that 4 of 14 adults diagnosed with necrotizing fasciitis caused by MRSA had no preexisting medical condition (37). In addition, some of these conditions are associated with a high mortality rates: necrotizing fasciitis and necrotizing pneumonia have been associated with 20% and 75% of mortality rates, respectively (25,65,69). These invasive infections caused by CA-MRSA have a high mortality rate, even when treated with the best available therapeutics (37).

Once a patient visits a healthcare professional with a SSTI, the treatment can vary depending on the severity of the infection and the characteristics of the infected individual (e.g. young infants or immune-compromised individuals). The use of antimicrobial agents and surgical incision and drainage (I&D) are the basis of treatment (72). Minor SSTIs that are uncomplicated and superficial may be treated by I&D without the antimicrobial therapy or with topical antimicrobial agents (e.g. topical mupirocin or bacitracin or topical antiseptics) (14,72), whereas more complicated SSTIs may be treated with systemic antibiotics (e.g. parenteral vancomycin) (58,72).

The antibiotic resistance of CA-MRSA is growing in Canada, and there have been some cases of clinical failures in CA-MRSA infection treated with clindamycin (99,100). There is a general consensus that inappropriate and greater use of antibiotics are both associated with increased antibiotic resistance (101,102). Resistant SSTIs are difficult to treat; they result in increased morbidity and mortality as well as in increased healthcare costs due to longer hospitalization and higher hospital charges (1,50,51). To reduce and minimize antibiotic resistance, various initiatives were suggested such as infection prevention strategies (58), developing a surveillance program (14), infection control practices in healthcare facilities (59) and adopting an antimicrobial stewardship program (49,60).

The antimicrobial stewardship program is a set of coordinated interventions which promote the appropriate use of antimicrobial agents (right choice of agent, right dose, route of administration and duration of therapy) for the right bacterial infection at the right time (49,60,105). The Infectious Diseases Society of America (IDSA) and the Society for Healthcare Epidemiology of America (SHEA) presented guidelines for developing institutional programs to promote antimicrobial stewardship (105). They also identify two goals of the antimicrobial stewardship: 1) optimize clinical outcomes and minimize adverse consequences of antimicrobial use; 2) reduce costs related to healthcare system without impacting the quality of care (105).

Historically in Canada, the first cases of outbreaks of CA-MRSA were seen in Aboriginal communities (79–84). In a retrospective survey conducted in five hospitals in central Canada, Embil and colleagues have found that 62% of the patients who were MRSA positive at admission were First Nations patients (82). Furthermore, the incidence of CMRSA7 (one of the predominant strains of CA-MRSA) increased in the Aboriginal communities in Manitoba (80), Saskatchewan (84), and in Nunavut (79): for example, in Manitoba, the crude rates increased

from 1 infection per 10,000 in 2003 to 13 infections per 10,000 in 2006 (80). These important increases in incidence and spread of CA-MRSA in Canadian Aboriginal communities might be associated with some of the common risk factors of CA-MRSA which were identified in previous research (31,106,107): overcrowding, frequent skin-to-skin contact, participation in activities that result in damaged skin, sharing potentially contaminated objects, challenges in maintaining personal hygiene, limited access to healthcare and lower socio-economic status (31,33,34,83,85). Aboriginal people in Canada experience many of these risk factors of CA-MRSA (e.g. overcrowding – about 10 times more frequent among First Nations, low socioeconomic status, limited access to healthcare). In addition, environments or conditions that are associated with the risk factors (e.g. lower life expectancy, higher infant mortality rate, higher hospitalization rates) are more common (58,79,92,93). In fact, Canadian Aboriginals were six times more likely to have had CA-MRSA isolated than were non-Aboriginals (83). It's clear that CA-MRSA infections are a growing concern in First Nations communities. As CA-MRSA can spread rapidly in the communities and can cause severe and fatal diseases in otherwise healthy individuals, research to identify risk factors associated with CA-MRSA infections in these communities are necessary for effective treatment and prevention strategies. The knowledge of local MRSA infection and antibiotic resistance rates are especially needed for the adequate management of SSTIs (66). In Canada, the primary health care in First Nations communities is either provided by the federal government, provincial government or sometimes regulated by the bands. A band is defined by the Aboriginal Affairs and Northern Development Canada (AANDC) as: "A body of Indians for whose collective use and benefit lands have been set apart or money is held by the Crown, or declared to be a band for the purposes of the *Indian Act*. Each band has its own governing band council, usually consisting of one chief and several

councillors. Community members choose the chief and councillors by election, or sometimes through custom (…)" (108). The majority of the Aboriginal reserves are served by the nursing stations under the First Nations and Inuit Health Branch (FNIHB) from the federal government. FNIHB provides a clinical practice guidelines (CPG) to the nursing stations in these reserves (78). The current standard of treatment of SSTIs at the FNIHB nursing stations in the northern communities is based on the FNIHB CPG.

This study will add to the knowledge of the prevalence of MRSA infections in some of the First Nations communities, which are part of the at-risk populations for outbreaks of MRSA infections (37,79,80,82,109). The authors of a cross-sectional study looking at the prevalence of MRSA in Ottawa shelters identified in their work that more prevalence studies in high-risk populations in Canada are needed to detect the changing epidemiology of MRSA and to guide empirical treatment of suspected MRSA infections in those populations (94). The epidemiological data on SSTIs and the data on antibiotic utilization in these communities could be used to monitor the changing prevalence and susceptibility profiles of CA-MRSA in Canada.

Developing the recommendations for an antimicrobial stewardship program will also contribute to optimizing antibiotic utilization in local healthcare facilities, which will reduce and prevent the antibiotic resistance, control the spread of CA-MRSA, decrease healthcare costs related to SSTIs as well as improve health outcomes. Many studies have already suggested that evidence-based guidelines on antimicrobial utilization in healthcare facilities should be implemented (15,26,49,93). This study will be able guide the development of evidence-based empirical treatment strategies specific to the selected First Nations communities in Canada.

Methods

Population

This study consisted of a retrospective chart review at selected nursing stations in the First Nations communities across five provinces in Canada (AB, SK, MB, ON and QC). Twelve nursing stations in total were selected to be included in this study based on the sample size calculation. The participation of communities was on a voluntary basis. The Health Canada Regional Nursing Officers (RNOs) assisted in the selection of participating communities. During the recruitment phase, the regional and community representatives at Health Canada nursing stations received an information letter containing the summary of the study and were asked to communicate with the study coordinator at the FNIHB Headquarters if they were interested in participating. After all 12 nursing stations were selected to participate in the study, they were sent details about the data collection such as the number of charts to be reviewed at the selected nursing station and the chart selection procedure including clearly defined selection criteria.

Selection criteria for chart review

Inclusion criteria:

1. Client 18 years of age or older;
2. Any client who has received a service at the nursing station over the past 12 months, starting retrospectively from the date of data collection.

Sample size

The sample size was calculated by using a two-stage cluster sample with stratification. At stage 1, the number of nursing stations needed was determined: as each nursing station represents a cluster and each province containing nursing stations represents a stratum, it was calculated that selecting 12 nursing stations across six provinces[1] would give estimates of ± 12% with 95% confidence. The allocation of nursing stations is done by a $\sqrt{N}$-proportional allocation, where *N* represents the stratum population sizes. To ensure that at least one nursing station is sampled in each stratum, the number of nursing stations sampled in each stratum are: 1, 2, 3, 2, 2, 2. At stage 2, the number of patients' charts to review at each nursing station was calculated. In order to estimate the proportion of correct antibiotic treatment within a margin of error of 10%, the minimum number of infections required to sample is n=100. This n is then multiplied by a factor of 4, because it is known from an audit (conducted in 2011 at Health Canada) that 1 in 4 patient charts, antibiotics were prescribed for treatment. Then, it was determined that 400 charts (n=100*4=400) across 12 sampled nursing stations were needed to be reviewed. About 20 charts were selected per 1000 population. Although the sample size was calculated based on the assumption that one in four charts would have a case of antibiotic use, in the actual data collection, approximately one in two charts had a case of antibiotic use. Hence the sample size of 372 charts was adequate to proceed with the analysis.

[1] Originally, six provinces were to participate in this project, but only five provinces were actually included in the project. The sample size is still statistically valid because the total number of charts reviewed is adequate.

Data collection

This study was a cross-sectional survey, using clients' charts at the nursing station for review. A simple random sample of patient charts was employed to select the charts to be reviewed from each of the selected nursing stations. The auditor chose a random starting point and selected the number of charts in an evenly-spaced manner. The inclusion criteria was used to select the charts to be reviewed. If a chart was pulled and it did not meet the inclusion/exclusion criteria, the next chart meeting the criteria was selected. One or two days prior to the date of arrival of the investigator at the nursing station for data collection, the Nurse In Charge (NIC) designated support staff at the nursing station to randomly select the specified number of charts for the project.

Charts were reviewed retrospectively covering a one year period, starting from the date the investigator arrived at the nursing station for data collection. Any time an antibiotic was prescribed during this one year period, it was captured in the Antibiotic Tracking Case Report Form (CRF) for analysis. The charts were reviewed for data on patient encounters that resulted in an antibiotic prescription(s).

Each time a client received a service at the nursing station which resulted in a prescription of at least one type of antibiotic within the previous year, it was defined as one case. So as the charts were reviewed, each antibiotic treatment for an infection during the study period was captured as a "case". Each case was captured in the Antibiotic Tracking Case Report Form (CRF) (see Appendix C) for analysis.

Data collection tool

During the data collection phase, the Antibiotic Tracking CRF was used to collect pertinent information from the patients' charts. Patients' names and unique identifier numbers (e.g. health card or Band number) were not captured on the Antibiotic Tracking CRF. Each chart was assigned a number in ascending order. The collected data from the each patient's chart included:

- Coded location
- Patient's assigned number for the study
- Prescriber type: RN, NP, MD, dentist
- Date of antibiotic prescription
- Demographic information about the patient: gender, age, weight, creatinine or creatinine clearance, allergy status
- Other relevant medical conditions of the patient: diabetes, COPD, cardiac disease, pregnancy, immunocompromised, alcoholism, asplenia, liver disease, renal disease, other
- Presence of medical devices: urinary catheter, central line, other
- Indication for use of antibiotic: fever, urinary tract infection symptoms, respiratory infections symptoms (upper, lower, ear), diarrhea, skin/wound infection, sexually transmitted infection, eye infection, dental infection, other
- Diagnostic tests: blood culture, urine culture, urinalysis, sputum test, throat culture, stool culture, chest x-ray, CBC, wound culture, vaginal swab, other

- Presence of a resistant organism and laboratory test results (including the antibiotic susceptibility if available)
- Outcomes: clinical outcomes, adverse events, disposition
- Presence of other treatment procedures: adjunctive therapy, incision and drainage procedure, wound care
- Information on antibiotic use: the prescribed antibiotic, dose, route, frequency, duration, presence of combination therapy.

Analysis

Primary outcomes measures such as demographic information of the patients, the diagnosis (the reason for visit of the primary health care facility), the antibiotic utilization patterns and the clinical outcomes were collected from the medical charts. Information was gathered from the nursing notes and the doctor's notes. When available, antibiotic susceptibility profiles from laboratory reports linked to the existing patient medical chart were also recorded. Secondary outcome measures such as antibiotic appropriateness was assessed by looking at the antibiotic utilization patterns (antibiotic used, dose, route and frequency of administration and duration of treatment) and the appropriateness was assessed in seven different categories: appropriate agent, appropriate dose, appropriate route of administration, appropriate frequency of administration, appropriate duration of treatment, appropriate combination therapy and overall appropriateness of treatment.

The appropriateness of the antibiotic prescribed was determined by using the FNIHB Clinical Practice Guidelines (CPG) (78) and by using the Infectious Diseases Society of America's (IDSA) Clinical Practice Guidelines (110) (Appendix A), based on the client's pre-existing medical conditions, the clinical symptoms and availability of the diagnostic test results including culture and susceptibility when available. In cases where an antibiotic was used in combination with another antibiotic, the appropriateness of this combination therapy was determined. Finally, the overall appropriateness of each antibiotic use was determined. The overall appropriateness of each antibiotic treatment was evaluated as:

- Inappropriate use but not resulting in ineffective therapy;
- Appropriate use;
- Inappropriate use and resulting in ineffective therapy;
- Unable to assess (the appropriateness).

Inappropriate use but not resulting in ineffective therapy was defined as an antibiotic prescription in higher doses or longer duration than necessary, or choice of a second-line agent when a first-line agent was available, or unnecessary broad spectrum agent used. Inappropriate use and resulting in ineffective therapy was defined as duration shorter than the recommended duration, prescription dose lower than the recommended dose, use of narrow-spectrum agent when broad spectrum agent or combination therapy indicated, or mismatch between antibiotic and available culture results.

Data was analyzed using SAS statistical software (version 9.3, ©2002-2010 SAS Institute Inc., Cary, NC, USA) for analysis.

Patient demographics and other variables of primary outcome measures (including predisposing health conditions and patient outcomes) were analyzed by using descriptive statistics. The patient's clinical outcome was considered as "treatment failure" when it was noted in the charts that patients returned to the nursing stations for treatment as they were clinically not improving on the prescribed antibiotic, they were experiencing adverse reactions or side effects to the prescribed antibiotic, or they admitted being non-adherent to taking the antibiotic.

The proportion of SSTIs that are caused by MRSA was calculated as below to describe local epidemiology of SSTI in the selected communities:

$$\text{Prevalence of MRSA} = {}^{MRSA\ positives}/_{Total\ number\ of\ SSTI\ cases}$$

The prevalence of SSTIs, proportions of different antibiotics used, proportions of resistance to antibiotics, as well as the overall clinical outcomes and the antibiotic utilization patterns (antibiotic used, route of administration, mean duration of treatment, and antibiotic appropriateness) were analyzed.

The prevalence of SSTIs in the patient population was calculated as below:

$$\text{Prevalence of SSTIs} = {}^{Number\ of\ SSTI\ cases}/_{Total\ number\ of\ charts\ reviewed}$$

Results

Description of study population

Chart selection and case rate

Figure 3 presents a diagram of the process of chart selection for the retrospective chart review at the nursing stations in selected First Nations communities. Of the 372 charts randomly selected across 12 nursing stations in five provinces, 224 charts contained at least one case, defined as a charted encounter where an antibiotic prescription was provided in the past 12 months. From those charts, 459 cases of antibiotic prescriptions were recorded on the case report forms and were analyzed (i.e. some charts contained more than one case). There were 137 cases with the diagnosis of a Skin and Soft-Tissue Infection (SSTI) in total, from 65 patient charts. Separate analyses for SSTIs were performed with this data. In total, 569 antibiotic prescriptions were written at the nursing stations.

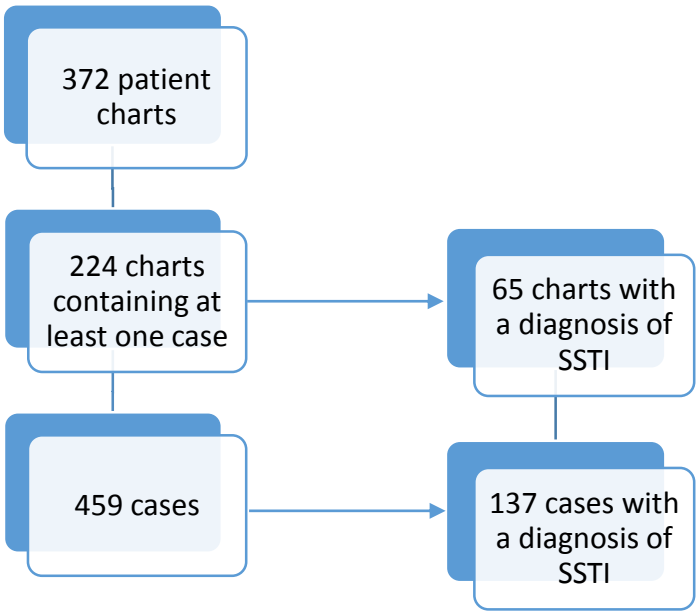

Figure 3. Diagram of patient charts, number of cases and antibiotic prescriptions.

Table 1 presents the total number of charts reviewed in each province and the respective number of cases recorded from those provinces. The case rate was calculated based on the number of cases recorded in each province divided by the number of charts reviewed in each province.

Table 1: Number of charts reviewed and number of cases recorded in the five provinces

Province	**Number of charts reviewed**	**Number of cases recorded**	**Case rate**
Ontario	100	126	1.26
Alberta	60	77	1.28
Manitoba	120	170	1.42
Saskatchewan	70	63	0.9
Quebec	22	23	1.05
Total	372	459	1.23

Patient demographics

The patient characteristics were analyzed from the 224 patients whose charts contained at least one case from the total of 372 charts that were reviewed; 65 patients whose charts contained at least one case of SSTI were analyzed separately. Table 2 shows characteristics of the study sample. Most of the demographic characteristics are similar between all patients and SSTI patients. The only noticeable difference was in gender distribution: there were more cases involving females than males (60% vs. 40%, respectively). For SSTI patients, the distribution is more equal between females and males (48% vs. 52%, respectively). More than 80% of the study population (83% and 89% for all patients and SSTI patients, respectively) was under the age of 50, and persons under the age of 30 represented the largest group for which antibiotics were prescribed. Demographic information (gender and age distribution) from the communities was not available for comparison. In both all patients and SSTI patients, the prevalence of impaired renal function was low (less than 5%). Diabetes was present in at least one fifth of the population in both groups. Cardiac disease was present in more than 15% of all patients (almost 19% for all patients and 15% in SSTI patients) and reported alcohol misuse was present in one fifth of the population in all patients and in 30% of SSTI patients, respectively. “Other disease” is present in 40% of the SSTI patients: this included depression, schizophrenia, asthma, hypertension, osteoarthritis, etc. Presence of indwelling devices such as urinary catheters or permanent intravenous access devices, which increase the risk of infection, was rare in both all patients and SSTI patients. The “other device (n=1)” in SSTI patients was a cochlear implant.

Table 2: Study population characteristics

	All patients (N total=224)	***SSTI patients (N total=65)***	**p-value**
	N (%)	***N (%)***	
Gender			
Male	91 (40.6 %)	34 (52.3 %)	0.0942[a]
Female	133 (59.4 %)	31 (47.7 %)	
Age (years)			
18 to 30	95 (42.4 %)	32 (49.2 %)	0.3247[a]
31 to 40	51 (22.8 %)	11 (16.9 %)	
41 to 50	40 (17.9 %)	15 (23.1 %)	
51 to 60	20 (8.9 %)	6 (9.2 %)	
61 to 70	12 (5.4 %)	0	
70+	6 (2.7 %)	1 (1.5 %)	
Creatinine Clearance (GFR)			
<60mL/min	10 (4.5 %)	3 (4.6 %)	1.000[b]
>60mL/min	197 (88.0 %)	57 (87.7 %)	
Missing	17 (7.6 %)	5 (7.7 %)	
Pre-existing medical conditions			
COPD	6 (2.7 %)	2 (3.1 %)	1.000[b]
Diabetes	48 (21.4 %)	13 (20.0 %)	0.8038[a]
Pregnancy	12 (5.4 %)	0	0.0746[b]
Cardiac disease	42 (18.8 %)	10 (15.4 %)	0.5340[a]
Immunocompromised	3 (1.3 %)	1 (1.5 %)	1.000[b]
Alcoholism	40 (17.9 %)	20 (30.8 %)	0.0238[a]
Asplenia	0	0	-
Liver disease	10 (4.5 %)	3 (4.6 %)	1.000[b]
Renal disease	13 (5.8 %)	3 (4.6 %)	1.000[b]

Other disease	103 (46.0 %)	26 (40.0 %)	0.3930[a]
Presence of medical device			
Urinary catheter	1 (0.5 %)	0	1.000[b]
Central line	0	0	
Other device	5 (2.2 %)	1 (1.5 %)	

[a]P-value calculated from Chi-Square Test of Independence

[b]P-value calculated from Monte Carlo estimate for the Fisher's Exact Test

Skin and soft tissue infections

Prevalence of SSTIs

There were 137 of cases of SSTIs in the 372 charts reviewed. This means that the proportion of SSTIs in total population (reviewed charts) was: 137 SSTI cases / 372 charts reviewed across 12 nursing stations in the First Nations reserves. At least one case of SSTI, for which an antibiotic prescription was made, was found in 36.8% of the patient charts. This cross-sectional proportion of SSTIs in the total population can be used to estimate the prevalence of SSTIs among selected First Nations communities at almost 37%.

Prevalence of *S. aureus*

The proportions of SSTIs caused by *S. aureus* were estimated for 137 cases of SSTIs. Table 3 shows the proportions of SSTIs caused by *S. aureus*.

Table 3: *Staphylococcus aureus* in SSTIs

	N	***%***
MSSA	5	3.65
MRSA	55	40.15
Other organism	8	5.84
Unknown organism	69	50.36

N total=137 cases of SSTI

The proportions of SSTI cases that were caused by Methicillin-resistant *Staphylococcus aureus* (MRSA) were determined by confirmed wound cultures or presumed by history of colonization as documented in the chart. In the 55 cases that were MRSA positive, 27 cases were confirmed by a wound culture during the current infection. For the remainder of cases, MRSA-positive status was known from previous wound culture results or as indicated in the patient's chart; meaning that the patient was colonized with MRSA. The proportion of MRSA positive cases in the total number of SSTIs that were treated with antibiotics can be used to estimate the prevalence of MRSA in all SSTI cases. Overall, the prevalence of MRSA in all SSTI cases was estimated at 40.1%. It is important to note that the etiologic agent remained unknown in more than 50% of the SSTI cases.

Other organisms isolated from wound cultures included Group A streptococcus (n=6), Viridans group streptococcus (n=1), Enterobacter cloacae (n=2), and Serratia marcescens (n=1).

MRSA susceptibility and profiles

The susceptibility of MRSA to different antibiotics was analyzed from culture and susceptibility results, when available in patient charts. It's important to note that the panels of antibiotics tested differ across regions and not all isolates are tested against every antibiotic listed. Only 29% of MRSA isolates in this study were susceptible to erythromycin, but most were susceptible to clindamycin and co-trimoxazole (90.5% and 95.2% respectively). Antibiogram for MRSA and MSSA is presented in table 4.

Table 4: Antibiogram for *S. aureus*/MRSA

Antibiotic susceptibility	Number of isolates[2]	Erythromycin	Clindamycin	Tetracycline	Co-trimoxazole	Vancomycin	Oxacillin	Gentamicin	Linezolid	Cefazolin	Penicillin
		Percentage of isolates that are susceptible									
Staphylococcus aureus	4	50	50	-	100	100	100	100	-	100	0
MRSA	21	28.6	90.5	100	95.2	100	0	100	100	0	0

Characteristics of SSTIs

Characteristics of SSTIs were collected when data was available in the charts. It was possible to categorize the 137 cases of SSTIs in four groups: purulent infections, non-purulent infections, skin-breakdowns and wounds. Purulent infections included abscesses, boils,

[2] Not all isolates tested against every antibiotic listed.
"-" :The isolate was not tested against this antibiotic

folliculitis, impetigo and open wounds or sores with pus or purulent discharge. Non-purulent infections included cellulitis and any infections with swelling or redness, but no pus or discharge. Skin breakdowns included lacerations, rashes, scabs, warts and abrasions. Only the cases where it was described in the chart as having a purulent discharge was categorized as purulent infections. Open sores, ulcers, bite wounds and surgical site infections were grouped into "wounds". Different proportions are shown in Table 5. Approximately 27% of SSTI cases could not be classified due to lack of information available in the charts. Purulent infections and wounds were most common; each representing almost one quarter of all cases.

Table 5: Characteristics of SSTIs

	N	***%***
Purulent	34	24.82
Non-purulent	15	10.95
Skin breakdown	17	12.41
Wounds	34	24.82
Unknown	37	27.01

N total=137 cases of SSTI

Diagnostic testing, treatment procedures and outcomes in SSTIs

Diagnostic testing was performed in 44% of all cases (n=459). In the 137 cases of SSTIs, around 39% of them had at least one diagnostic test performed. Table 6 presents the frequency of diagnostic testing in the 137 cases of SSTIs. Wound culture and susceptibility test was done in only 29% of SSTI cases. However, some SSTI may have been non-purulent such as cellulitis or erysipelas. 40% of cases presenting with SSTI were previously known or confirmed to be MRSA positive. When we assessed frequency of wound culture and susceptibility test by different SSTI

categories, the group with the highest frequency of wound culture is the "unknown" SSTIs, with almost 49% of the cases. Since all the cases that did not have any information on the chart indicating the characteristics of the infection were grouped into this "unknown" SSTIs group, we can only speculate that some of these were purulent infections requiring a wound culture. For some patients no wound culture was obtained, as they were treated empirically based on their previous test results indicating positive MRSA status.

Table 6: Frequency of diagnostic testing in SSTIs

	N	***%***
Performance of diagnostic tests		
Blood culture	2	1.46
CBC	4	2.92
Wound culture	40	29.20
Purulent	9	26.47[3]
Non-purulent	3	20.00[4]
Skin breakdown	1	5.88[5]
Wounds	9	26.47[6]
Unknown	18	48.65[7]
Diagnostic test summary		
No test performed	84	61.31
Test with positive result	38	27.74
Test with negative result	8	5.84
Test result missing	7	5.11

N total=137

[3] 26.47% of all purulent infections (n=34) had wound culture performed
[4] 20% of all non-purulent infections (n=15) had wound culture performed
[5] 5.88% of all skin breakdowns (n=17) had wound culture performed
[6] 26.47% of all wounds (n=34) had wound culture performed
[7] 48.65% of all "unknown" SSTIs (n=37) had wound culture performed

In addition to antibiotic treatment, use of adjunctive treatment measures were also noted from the patient charts. These include incision and drainage (I&D) procedure and wound care. Around 49% of the patients received wound care at the clinics and about 9% of all SSTI cases received incision and drainage procedure. However, when we assess use of adjunctive measures by SSTI category, the group "purulent infections" had the highest proportion where I&D procedure was performed. 8 out of 12 incision & drainage procedures were performed for purulent SSTI cases. Wound care usually involved wound cleansing and a change of dressing and debridement in some situations. The proportion of combined-antibiotic treatment (i.e. two or more antibiotic agents were prescribed for the same infection) as well as the proportion of cases which were treated with topical antibiotics were documented. Combination therapy was most commonly prescribed using cephalexin and co-trimoxazole, particularly in one community. 26% of SSTIs were treated with topical antibiotics: 18% of SSTIs were treated with topical antibiotics only and 9% of SSTIs were treated with a dual treatment consisting of both topical and oral antibiotics. Clinical outcomes were also noted from the charts. Table 7 shows the frequency of other treatment procedures and the clinical outcomes for SSTI cases. For the majority of cases, the clinical outcome is unknown. There are some possible explanations for the unknown outcomes:

- Clients usually do not return to the nursing station after their initial visit
- Follow-up appointments are not documented in the charts
- The population is somewhat transient[8] making the process of follow-up difficult.

[8] There were a few cases of patients who are "visiting" the communities and presented themselves to the nursing station. I was also seen in some of the patient charts that the patient doesn't visit the nursing station often and sometimes there was no documentation for years.

Table 7: Outcomes, adjunctive therapy and combination therapy for SSTIs

	N	***%***
Clinical outcomes		
Cure	16	11.68
Failure	19	13.87
Unknown	84	61.31
Improvement	17	12.41
Adjunctive therapy		
Yes	68	49.64
No	69	50.36
Incision & drainage		
Yes	12	8.76
Purulent	8	23.53[9]
Non-purulent	1	6.67[10]
Skin breakdown	0	0
Wounds	0	0
Unknown	3	8.11[11]
No	125	91.24
Wound care		
Yes	67	48.91
No	70	51.09
Combination therapy		
Yes	41	29.93
No	96	70.07
Treatment with topical antibiotics	36	26.28

[9] 23.53% of all purulent infections (n=34) had incision & drainage performed
[10] 6.67% of all non-purulent infections (n=15) had incision & drainage performed
[11] 8.11% of "unknown" SSTIs (n=37) had incision & drainage performed

In combination with oral antibiotics	12	8.76
Topical antibiotic treatment alone	24	17.52

N total=137

Distribution of SSTIs by region

Table 8 shows the distribution of SSTIs across provinces. The rates of SSTIs were calculated based on the number of SSTI cases found in the communities for each province divided by the total number of charts reviewed in the provinces. Although the rate of SSTIs per community is not shown to ensure confidentiality, analysis for SSTI rate per community was performed. In general, higher rates of SSTIs[12] were seen in the communities where patients are known to experience overcrowding and less access to running water (residents in the three communities with the highest rate of SSTI did not have access to running water).

Table 8: Distribution of SSTIs by province

	N of cases	***N of charts***	***Rate of SSTI per chart***
Province			
Ontario	34	100	0.34
Alberta	8	60	0.13
Manitoba	60	120	0.5
Saskatchewan	21	70	0.3
Quebec	14	22	0.64*

N total=137

*Note: The rate of SSTI per chart in QC is high. However it is representative of one community that mainly uses topical antibiotic for minor skin infections.

[12] Top 3 highest rates of SSTI per chart by community are: 0.725, 0.7 and 0.5

Antibiotic utilization for Skin and Soft Tissue Infections

Antibiotics prescribed for SSTIs

Table 9 presents all the antibiotics prescribed for the 137 cases of SSTIs in this study. The top seven most prescribed antibiotics for skin and soft tissue infections were (from highest to lowest): cephalexin (n=45), co-trimoxazole DS (n=26), Polysporin ointment (n=9), ceftriaxone (n=7), azithromycin (n=5), cloxacillin (n=5), and ciprofloxacin (n=5). Clindamycin was rarely used in the treatment of SSTI. Combination treatments using cephalexin and co-trimoxazole were prevalent in some communities.

Table 9: Antibiotic utilization for SSTIs

Antibiotic prescribed	***N***	***%***
Cephalexin	45	32.85
Co-trimoxazole DS	26	18.98
Polysporin ointment	9	6.57
Ceftriaxone	7	5.11
Azithromycin	5	3.65
Cloxacillin	5	3.65
Ciprofloxacin	5	3.65
Cefazolin	4	2.92
Bacitracin	4	2.92
Amoxicillin	3	2.19
Nitrofurantoin[13]	3	2.19
Amoxicillin/Clavulanic acid	3	2.19
Clindamycin	2	1.46
Penicillin V	2	1.46

[13] Cases with dual diagnosis: SSTI and UTI; they were still included in the analysis as SSTI cases.

Mupirocin ointment	2	1.46
Clotrimazole cream	2	1.46
Bactroban ointment	2	1.46
Erythromycin ointment	1	0.73
Cefixime	1	0.73
Ciprodex drops[14]	1	0.73
Doxycycline	1	0.73
Fucidin cream	1	0.73
Permethrin lotion	1	0.73
Sofracort ear drops[15]	1	0.73
Bacitrin ointment	1	0.73

N total=137 cases of SSTI

Route, duration and frequency

The most frequent route of antibiotic administration was orally administered, with 71.5% of SSTI cases treated with orally administered antibiotics. There was 18.3% of SSTI cases treated with topical antibiotic and 8.8% of SSTI cases received an antibiotic administered intravenously. The prescribed frequency of antibiotic was variable. The frequency of admission prescribed most often was QID (four times a day), with 37.2%, followed by BID (twice a day), with 32.9%.

The indicated duration of antibiotic treatment was variable; from one day of treatment (usually topical antibiotic applied at the nursing station on the day of the visit) to 3, 4, 5, 7, 10,

[14] Cases with dual diagnosis: SSTI and ear infections; they were still included in the analysis as SSTI cases.
[15] Cases with dual diagnosis: SSTI and UTI; they were still included in the analysis as SSTI cases.

and 14 days of treatment. The most frequently prescribed duration of treatment was 7 days (n=53; 39%) followed by 10 days of treatment (n=33; 24%).

For some antibiotic prescriptions, information on the dose, duration and frequency was not available as it was not recorded in the charts.

Use of topical antibiotics was highly variable for indications, duration and frequency. For SSTIs, the duration of topical antibiotic treatment ranged from one day to 14 days. Five to ten days of topical antibiotic treatment was typical for SSTIs. In 36% of prescriptions, the duration of treatment was unknown. The frequency of application varied from a one-time application and once daily to four times a day. Twice a day was the most commonly prescribed frequency of application.

Appropriateness of treatment for SSTIs

Table 10 presents the overall appropriateness of treatment for SSTIs. Inappropriate therapy resulting in ineffective treatment was far more common in SSTIs due to MRSA[16]. Overall appropriateness was judged based on the appropriateness of the choice of antibiotic, dose, duration, frequency, use of combination therapy as well as a client's predisposing medical conditions by using IDSA guidelines.

[16] Note that some "MRSA" cases are assumed by colonization and not with firm proof through wound culture.

Table 10: Overall appropriateness of treatment for SSTIs

	Inappropriate NOT resulting in ineffective therapy	**Appropriate**	**Inappropriate resulting in ineffective therapy**	**Unable to assess**
SSTIs (total)	20 (14.93%)	82 (61.19%)	20 (14.93%)	12 (8.96%)
MRSA	11 (18.64%)	30 (50.85%)	15 (25.42%)	3 (5.08%)

N total of SSTIs = 137

Table 11 shows appropriateness of the different patterns in the antibiotic utilization for treating SSTIs assessed based on two different guidelines. Appropriateness was assessed by using the FNIHB Clinical Practice Guidelines (CPG) and the Infectious Diseases Society of America (IDSA) Clinical Practice Guidelines (110) (Appendix A). Note that because NPs and MDs do not have to adhere by FNIHB CPG, judging appropriateness based on FNIHB CPG was often inapplicable. Appropriateness of the choice of the antibiotic prescribed, the prescribed dose of the antibiotic, the route and the frequency of administration, the duration of the prescription and the combination therapy was evaluated. Appropriateness evaluated based on IDSA guidelines showed that the inappropriate use in treating SSTIs was the highest in the choice of antibiotic (22.63%), followed by the dose of antibiotic (8.03%) and the combination therapy (8.03%). When appropriateness was judged based on the CPG, the highest inappropriate use in treating SSTIs was in the duration of the prescription (27.74%), followed by the dose of antibiotic (16.06%), the choice of antibiotic (14.6%) and the frequency of administration (14.6%). The inappropriate route of administration was low (11.68% and 0%, based on CPG and IDSA, respectively).

Table 11: Appropriateness of antibiotic utilization patterns for treating SSTIs

	N	***%***
Choice of antibiotic: Appropriateness by CPG		
Not appropriate	20	14.6
Appropriate	104	75.91
Not applicable	13	9.49
Choice of antibiotic: Appropriateness by IDSA		
Not appropriate	31	22.63
Appropriate	106	77.37
Unable to assess	0	0
Dosing of antibiotic[17]: Appropriateness by CPG		
Not appropriate	20	14.60
Appropriate	77	56.20
Not applicable	40	29.20
Dosing of antibiotic[18]: Appropriateness by IDSA		
Not appropriate	6	4.38
Appropriate	127	92.70
Unable to assess	4	2.92
Duration of prescription: Appropriateness by CPG		
Not appropriate	38	27.74
Appropriate	37	27.01
Not applicable	61	44.53
Missing	1	0.73
Duration of prescription: Appropriateness by IDSA		
Not appropriate	7	5.11
Appropriate	109	79.56
Unable to assess	21	15.33

[17] The "dosing" of antibiotic was calculated by combining the appropriateness rates for dose, route and frequency.
[18] The "dosing" of antibiotic was calculated by combining the appropriateness rates for dose, route and frequency.

Combination therapy: Appropriateness by CPG		
Not appropriate	7	5.11
Appropriate	15	10.95
Not applicable	115	83.94
Combination therapy: Appropriateness by IDSA		
Not appropriate	11	8.03
Appropriate	26	18.98
Unable to assess	100	72.99

N total=137 cases of SSTI

Appropriateness was also analyzed separately for SSTIs treated with cephalexin (N total=45) and for SSTIs treated with co-trimoxazole DS (N total=26). The appropriateness of the utilization patterns of cephalexin for SSTI treatment is presented in table 12 (only showing the appropriateness assessed based on IDSA guidelines). Although it is not shown on the table, the appropriateness for SSTIs treated with cephalexin assessed based on CPG guidelines showed similar results. For SSTIs treated with cephalexin, the proportion of inappropriate use was highest in the choice of antibiotic, with almost 30%. Based on the overall appropriateness of all cephalexin utilization for treating SSTIs, more than 20% of them was inappropriate resulting in ineffective therapy.

Table 12: Appropriateness of cephalexin utilization patterns for treating SSTIs

	N	***%***
Choice of antibiotic: Appropriateness by IDSA		
Not appropriate	13	28.89
Appropriate	32	71.11
Unable to assess	0	0

Dosing of antibiotic[19]: Appropriateness by IDSA		
Not appropriate	2	4.44
Appropriate	43	95.56
Unable to assess	0	0
Duration of prescription: Appropriateness by IDSA		
Not appropriate	0	0
Appropriate	44	97.78
Unable to assess	1	2.22
Combination therapy: Appropriateness by IDSA		
Not appropriate	4	8.89
Appropriate	7	15.56
Not applicable	34	75.56
Overall appropriateness		
Not appropriate but not resulting in ineffective therapy	2	4.44
Appropriate	31	68.89
Not appropriate resulting in ineffective therapy	10	22.22
Unable to assess	1	2.22
Missing	1	2.22

N total=45

Table 13 shows appropriateness of co-trimoxazole DS utilization patterns in SSTIs assessed based on IDSA guidelines. Appropriateness assessed based on CPG showed similar results, but not presented in this table. As with cephalexin utilization, the inappropriate use of co-trimoxazole was highest in the choice of antibiotic, at about 15%. However, based on the overall appropriateness analysis, most of the inappropriate use of co-trimoxazole DS did not result in

[19] The "dosing" of antibiotic was calculated by combining the appropriateness rates for dose, route and frequency.

ineffective therapy. Only about 8% of all co-trimoxazole utilization for treating SSTIs was inappropriate resulting in ineffective therapy.

Table 13: Appropriateness of co-trimoxazole DS utilization patterns for treating SSTIs

	N	***%***
Choice of antibiotic: Appropriateness by IDSA		
Not appropriate	4	15.38
Appropriate	22	84.62
Unable to assess	0	0
Dosing of antibiotic[20]: Appropriateness by IDSA		
Not appropriate	0	0
Appropriate	24	92.31
Unable to assess	2	7.69
Duration of prescription: Appropriateness by IDSA		
Not appropriate	1	3.85
Appropriate	22	84.62
Unable to assess	3	11.54
Combination therapy: Appropriateness by IDSA		
Not appropriate	0	0
Appropriate	8	30.77
Not applicable	18	69.23
Overall appropriateness		
Not appropriate but not resulting in ineffective therapy	3	11.54
Appropriate	18	69.23
Not appropriate resulting in ineffective therapy	2	7.69
Unable to assess	2	7.69
Missing	1	3.85

N total=26

[20] The "dosing" of antibiotic was calculated by combining the appropriateness rates for dose, route and frequency.

Discussion

This study was a cross-sectional survey of a representative sample of First Nations communities across Canada to assess the prevalence of Community-Associated Methicillin-resistant *Staphylococcus aureus* (CA-MRSA) infections in the remote and northern regions. The rate of CA-MRSA Skin and Soft-Tissue Infections (SSTIs) and the antibiotic prescribing patterns and appropriateness have not been studied at the community level in Canada. Although the sample size is not big, we tried to portray a representative picture of the epidemiology of CA-MRSA SSTIs in the Aboriginal communities by sampling data from 12 Aboriginal communities across five provinces.

The results show that the gender distribution of SSTI patients were almost equal between females and males (48% vs. 52%, respectively). However, the gender distribution in the selected communities or the gender distribution of the patients visiting the nursing stations were not available for comparison. Almost 50% of the SSTI patients were aged between 18 and 30 and the patient population had few predisposing chronic medical conditions, although 30% of the SSTI patients were reported to misuse alcohol. This is consistent with other research that shows that the affected population tend to be young and previously healthy (25,29,49,67,84,97,111–113).

To our knowledge, this study was the first to assess the prevalence of CA-MRSA SSTIs at the community level at large, especially in the Aboriginal communities where the population is considered to be a high-risk group for CA-MRSA infections. According to the retrospective chart review, the prevalence of CA-MRSA SSTIs among First Nations communities in Canada in 2012-2013 was estimated at almost 37%.

Furthermore, this research shows that MRSA was found in 40.2% of all SSTI cases, and Methicillin-Susceptible *Staphylococcus aureus* (MSSA) was found in 3.7% of all SSTI cases. The prevalence of MRSA in SSTIs may even be higher than this number because of the etiologic agent remains unknown in the majority of SSTI cases (50.4%). In a recent retrospective medical record review by Pate et al., conducted in the United States at an urban community hospital, 46.5% of the *S. aureus* isolates were MSSA and 53.5% of the *S. aureus* isolates were MRSA (113). Other studies have also showed that MRSA is now identified as the primary cause of SSTIs (63,114).

In our study, only 28.6% of CA-MRSA isolates were susceptible to erythromycin, compared to the susceptibility of 58% found in the Northwest Ontario (91). However, susceptibilities to clindamycin, co-trimoxazole and tetracycline were high (90.5%, 95.2% and 100%, respectively) and were similar to the findings of different studies: in 2011, Muileboom et al. found CA-MRSA susceptibility of almost 100% to clindamycin, co-trimoxazole and tetracycline, and CANWARD found, in 2012, CA-MRSA susceptibility of 85.4% to clindamycin and 100% to co-trimoxazole (91,98).

Our findings show that the SSTIs caused by CA-MRSA in communities were mostly purulent infections (24.8%) and wounds (24.8%). It was not possible to identify the characteristics of SSTIs in the 27% of the cases from the charts. Almost 50% of all SSTI cases were purulent infections or wounds and this finding is comparable to the findings in previous research that the majority of MRSA infections manifest as mild to moderate purulent SSTIs (4,62,64). Furthermore, the diagnostic testing of SSTIs was fairly low at the nursing stations in the communities. Only 29% of SSTI cases had wound culture and susceptibility test done. This is a low proportion considering that almost 50% of the SSTI cases were either purulent infections

or wounds; in addition, 49% of the “unknown” SSTI cases were sent for wound culture and susceptibility test, suggesting that almost half of the “unknown” SSTI cases may have been purulent infections or wounds.

The findings of this study suggest that the performance of incision and drainage (I&D) procedure as treatment for SSTIs in northern communities was low: only 9% of all SSTI cases received I&D procedure. Although only the cases with an antibiotic prescription were recorded in this study, it was rare to find a case of SSTI treated only with I&D procedure or wound care. Almost all SSTI cases requiring treatment at the nursing station have received an antibiotic treatment. In the present study, the clinical outcome is unknown for the majority of the cases, and we were unable to assess the effectiveness of I&D procedure. However, many studies have shown in the past that I&D is associated with positive clinical outcomes for purulent SSTIs (115–117) and some studies suggest that antibiotic use does not improve clinical outcomes of patients with uncomplicated MRSA SSTIs (75,76).

In Aboriginal communities, cephalexin was identified as the most used antibiotic agent for treatment of SSTIs, which is known to be the typical choice of antibiotic for empiric treatment of cellulitis in northern regions (97). Co-trimoxazole was also used frequently. The antibiotic prescribing patterns were described in this study in terms of route, duration and frequency: oral administration was the most frequently seen, most frequently prescribed duration of treatment was 7 days and the frequency of QID (four times a day) was seen the most often. Data on topical antibiotic use was usually inconsistent across the regions. The appropriateness of antibiotic prescribing patterns were also assessed in this study: overall, about half (50.9%) of MRSA SSTI infections had received an appropriate treatment. The overall appropriateness was assessed based on IDSA guidelines.

In this study, we were unable to assess the correlation between the rate of SSTIs and some of the CA-MRSA risk factors such as overcrowding, poor housing, and sanitation, due to the retrospective nature of the study. However, the environmental information at the community level was sought, and higher rates of SSTIs were found in the communities where access to running water and overcrowding were a common issue for the population. It is also known that overcrowding and poor housing are commonly experienced by people living in northern remote communities. Moreover, some of the major challenges that these communities face include the remote location of the communities (limited access to laboratories and healthcare centres; often limited by no road access and unstable flight schedules dependent on the weather) which can lead to slow and uncertain access to tests and drugs, and compromised storage or transport of samples. In terms of distance between the communities and laboratory facilities, the distance can vary greatly depending on the region (e.g. from 50km to 400km or more). But more importantly, in terms of flights (as some communities are only accessible by flights), travel can take from 30 minutes to 4-8 hours depending on distance and weather.

The nursing stations in the First Nations communities operate either under FNIHB or under the First Nations themselves. The biggest difference pertaining to this study between the FNIHB Health Canada managed nursing stations and the Band managed nursing stations in the transferred communities is that the nurses at FNIHB nursing stations have to adhere to FNHIB CPG and the prescriptions are limited to the drugs listed in FNIHB Nursing Station Formulary; the Band-managed nursing stations do not have to adhere to FNIHB CPG.

We can also think about seasonality and latitude as possible factors causing higher prevalence of SSTIs in these communities. In terms of this study, we were not able to capture

these data but in the future, it would be interesting to investigate the relationship between SSTIs and injuries and trauma caused by cold weather, etc.

There are several limitations to this study. While this study attempted to evaluate the epidemiology of SSTI and the antibiotic susceptibility profiles of CA-MRSA in Aboriginal communities, the results may not be applicable to all First Nations communities across Canada. Since participation of communities was voluntary, maybe communities with higher SSTIs or MRSA problem were more or less likely to participate in the study. In addition to the voluntary selection of participating communities, British Columbia and the Maritime provinces were not part of the study. This project only captured the adult population as well. Because of the nature of the retrospective chart review, not all data was available all the time, there was no control over the existing data and the availability of data varied across different sites. Limitations in the data collection included the inconsistent microbiology available, the lack of consistent description of the clinical presentation in the chart as well as the lack of follow-up or the documentation of follow-up (thereby the lack of information on patient outcomes). Other missing information on the charts included the patient's allergies (missing or not updated), patient's current prescriptions (e.g. for chronic diseases) and patient's weight and height. Performance of diagnostic tests and clinical outcomes of the patients were largely unknown as well. This large proportions of missing information may have biased the results. For example, missing information on the etiologic agent (only about 40% of SSTI cases were confirmed as MRSA infections[21] and the etiologic agent remained unknown in 50% of the cases) might underestimate the prevalence of

[21] SSTI cases were either MRSA confirmed by wound culture results or presumed to be caused by MRSA when patient had a history of MRSA colonization

MRSA in SSTIs and the true proportion might actually be higher than estimated in this study. The antibiotic susceptibility profiles of MSSA and MRSA were analyzed from small numbers of isolates because of the lack of information, thus limiting some conclusions that can be drawn from the antibiogram. Efforts should be put together to understand why diagnostic tests, such as wound swab culture and susceptibility test, are not performed very often for SSTI patients in the communities as to encourage and improve the diagnostic testing. Accurate picture of the MRSA prevalence and the susceptibility profiles are crucial to control and reduce the SSTIs in the communities. Currently laboratories across provinces do not have a same panel of antibiotics for antibiotic susceptibility tests; streamlining laboratory services to use a standard panel of antibiotics would be the first step to more accurate picture of MRSA susceptibility profiles in Canada.

Furthermore, the antibiotic utilization patterns were only assessed in terms of the prescriptions. We were not able to collect information on patient antibiotic utilization patterns, therefore unable to comment on the adherence to the treatment of the population and to further link to clinical outcomes. Only a few cases of non-adherence by patients were recorded in the reviewed patient charts. In the future, the documentation in the patient charts of follow-up process when antibiotics are prescribed as well as the clinical outcomes should be improved in order to better measure patient outcomes.

The sociocultural information about the patients were only captured in some of the patient charts (when the "well-woman health examination" form was available in the chart). Environmental factors such as overcrowding, adequate housing, and access to clean running water remained unknown for each individual case. Future studies should aim to collect more complete information on the environmental factors and risk factors such as access to running

water, crowding, housing conditions, available dental services and exposure to smoke in these communities because the risk factors associated with the spread of CA-MRSA in the northern remote communities may be different compared to factors identified in studies involving large urban centres where cultural, socio-economic, medical and environmental conditions are different (26).

Conclusion

This study was one of the first community-based research to examine the epidemiology of Community-Associated Methicillin-resistant *Staphylococcus aureus* (CA-MRSA) Skin and Soft-Tissue Infections (SSTIs) in First Nations communities in Canada. Results of this study have shown different characteristics of the SSTI patients in communities, with the population being young and previously healthy in general. The prevalence of SSTIs and MRSA in communities as well as the susceptibility profiles are presented in the study. The antibiotic prescribing patterns and other treatment measures for SSTIs were described as well as the appropriateness of treatment. Overall, environmental factors such as access to running water and overcrowding seemed to be associated with high rates of SSTIs. The results of this study are useful for the better understanding of the antibiotic utilization at the primary healthcare facilities in the North, for improving the prevention, management and control strategies targeting CA-MRSA infections. It was also shown in this study that diagnostic testing was underperformed in the majority of cases, and follow-up with patients were often undocumented or missing. There is currently no system to monitor the wound culture and susceptibility test results of CA-MRSA at the community level. Developing a surveillance system that can help with monitoring the epidemiology of SSTIs and the changing antibiotic susceptibility patterns in communities would be essential for effective management of SSTIs in the community settings. Surveillance and antimicrobial stewardship programs should be evaluated and implemented where possible, to better support clinicians at nursing stations for effective treatment of MRSA infections. Other tools such as point-of-care testing, standardization of use of specific antibiotic regimen, region-specific antibiograms, and continuing education for practitioners would also be beneficial.

Final Conclusion

Community-Associated Methicillin-resistant *Staphylococcus aureus* (CA-MRSA) is a growing problem in the remote and northern Aboriginal communities in Canada. Previous research have shown that CA-MRSA rates in remote communities are higher than the nosocomial Canadian Nosocomial Infection Surveillance Program (CNISP) rates, calculated from large, urban healthcare centres (39,79,80,85). Although there were some recent studies addressing this issue in remote communities (91,97), the prevalence of Skin and Soft -Tissue Infection (SSTI), CA-MRSA and the antibiotic susceptibility patterns have not been formally studied at the community level. This community-based study attempted to capture the local epidemiology of SSTIs in the selected First Nations communities, and to gather information from a more representative sample (nursing stations across five provinces). The major challenge that we encountered was the lack of information on the microbiology data due to underperformance of diagnostic tests and on the patient outcomes due to low number of follow-ups or documentation of follow-ups. This study was able to estimate the prevalence of SSTIs and MRSA with the available data, identify some of the SSTI patient characteristics, assess the antibiotic utilization for the treatment of SSTIs and the appropriateness of this utilization as well as the antibiotic susceptibility profiles of CA-MRSA. Due to the nature of the retrospective review, it was not possible to identify the risk factors associated with individual cases. However, we were able to see that, as identified as risk factors of CA-MRSA in the previous research (26,31,33,34,83,85), overcrowding and lack of running water seemed to be related to higher rates of SSTIs in the communities. These environmental factors as well as other social determinants of

health need to be considered and efforts should be put together to try to understand these factors to improve the management, control and prevention.

In future studies, it would be beneficial to conduct a prospective study where good documentation of follow-up as well as gathering more information on individual risk factors would be possible. Future work should also aim to include communities from all regions in Canada in order to best represent the epidemiology of SSTIs and the antibiotic susceptibility patterns in First Nations communities across Canada. It would be also beneficial to create a system for an up-to-date surveillance on the epidemiology of SSTIs (and other common infections at the community level) and the emergence of resistant organisms. Effectiveness of antimicrobial stewardship programs in remote communities could also be assessed.

Summary

This study aimed to describe the local epidemiology of Skin and Soft-Tissue Infections (SSTIs) in the selected nursing stations in the remote and northern First Nations communities in Canada. Although it doesn't include all regions, the sample was obtained from 12 different communities across five provinces. Some of the important findings of this study include the high prevalence of SSTIs and Methicillin-resistant *Staphylococcus aureus* (MRSA), the demographic characteristics of individuals with SSTIs, the antibiotic utilization patterns for SSTI treatment as well as the antibiotic susceptibility profiles. It was also shown that some environmental factors were related to higher rates of SSTIs. The study population found to be generally young with little predisposing morbidity. The prevalence of SSTIs was estimated at 37% and the prevalence of MRSA was estimated at 40%. More than half of the SSTIs were purulent infections and wounds. Oral antibiotics were most frequently prescribed antibiotics (between oral, topical and IV) and cephalexin was the most prescribed antibiotic, followed by co-trimoxazole DS. Other than the antibiotic treatment, around 49% of the cases had received wound care, but only 9% had received incision & drainage procedures. The diagnostic testing, wound swab culture and sensitivity test was not often performed. Only 29% of all the SSTI cases had a wound culture and sensitivity test done. According to the MRSA susceptibility profiles assessed in this study, most MRSA were susceptible to clindamycin and co-trimoxazole, but only about 29% of MRSA was susceptible to erythromycin. In this study we were unable to assess the individual risk factors of Community-Associated MRSA (CA-MRSA), but, at the community-level, overcrowding and lack of running water were associated with SSTIs. The residents in the three communities with

the highest rate of SSTI did not have access to running water. In the future, it would be important to monitor the prevalence of CA-MRSA and the antibiotic susceptibility at the community level.

There is a great need of knowledge in CA-MRSA risk factors and challenges particular to northern, remote settings, especially to improve the performance of diagnostic testing and follow-ups. It is important to evaluate and develop different programs such as surveillance programs or antimicrobial stewardship programs that could improve the management, control and prevention of CA-MRSA infections in the remote communities. Finally, addressing the socio-environmental factors such as housing and access to water in coordination with different programs and activities are also essential to improve health, quality of care and health outcomes of the population.

Bibliography

1. Dryden M. Complicated skin and soft tissue infections caused by methicillin-resistant Staphylococcus aureus: epidemiology, risk factors, and presentation. Surg Infect (Larchmt) [Internet]. 2008 Jan [cited 2013 Mar 21];9 Suppl 1(1):s3–s10. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18844473

2. Diekema DJ, Pfaller M a, Schmitz FJ, Smayevsky J, Bell J, Jones RN, et al. Survey of infections due to Staphylococcus species: frequency of occurrence and antimicrobial susceptibility of isolates collected in the United States, Canada, Latin America, Europe, and the Western Pacific region for the SENTRY Antimicrobial Surveillanc. Clin Infect Dis [Internet]. 2001 May 15;32 Suppl 2(Suppl 2):S114–32. Available from: http://www.ncbi.nlm.nih.gov/pubmed/11320452

3. Naimi TS, Ledell KH, Como-sabetti K, Borchardt SM, Boxrud DJ, Johnson SK, et al. Comparison of Community- and Health Care–Associated Methicillin-Resistant Staphylococcus aureus Infection. J Am Med Assoc. 2003;290(22):2976–84.

4. Fridkin SK, Hageman JC, Morrison M, Sanza LT, Como-sabetti K, Jernigan J, et al. Methicillin-Resistant Staphylococcus aureus Disease in Three Communities. N Engl J Med. 2005;352:1436–44.

5. Liu C, Graber CJ, Karr M, Diep BA, Basuino L, Schwartz BS, et al. A population-based study of the incidence and molecular epidemiology of methicillin-resistant Staphylococcus aureus disease in San Francisco, 2004-2005. Clin Infect Dis [Internet]. 2008 Jun 1 [cited 2013 Mar 27];46(11):1637–46. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18433335

6. PHAC. Fact Sheet: Methicillin-Resistant Staphylococcus aureus [Internet]. Public Health Agency of Canada. 2008. Available from: www.phac-aspc.gc.ca/id-mi/mrsa-eng.php

7. PHAC. Fact Sheet: Community-Acquired Methicillin-Resistant Staphylococcus aureus (CA-MRSA) [Internet]. Public Health Agency of Canada. 2008. Available from: www.phac-aspc.gc.ca/id-mi/camrsa-eng.php

8. WHO | Antimicrobial resistance: global report on surveillance 2014. World Health Organization; [cited 2014 Apr 30]; Available from: http://www.who.int/drugresistance/documents/surveillancereport/en/

9. CDC. S.aureus and MRSA Surveillance Summary. Centers for Disease Control and Prevention. 2011.

10. Purcell K, Fergie J. Epidemic of Community-Acquired Methicillin-Resistant Staphylococcus aureus Infections: A 14-Year Study at Driscoll Children's Hospital. ARCH PEDIATR ADOLESC MED. 2005;159(3):980–5.

11. Adam HJ, Allen VG, Currie A, Mcgeer AJ, Simor AE, Richardson SE, et al. Community-associated methicillin-resistant Staphylococcus aures: prevalence in skin and soft tissue infections at emergency departments in the Greater Toronto Area and associated risk factors. 2009;11(5):439–46.

12. CDC. FAQs about Methicillin-Resistant Staphylococcus aureus [Internet]. Vital. 2008 Sep. Available from: http://www.nature.com/doifinder/10.1038/vital850

13. DeLeo FR, Otto M, Kreiswirth BN, Chambers HF. Community-associated meticillin-resistant Staphylococcus aureus. Lancet [Internet]. Elsevier Ltd; 2010 May 1 [cited 2013 Mar 4];375:1557–68. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3511788&tool=pmcentrez&rendertype=abstract

14. Barton M, Hawkes M, Moore D, Conly J, Nicolle L, Allen U, et al. Guidelines for the prevention and management of community-associated methicillin-resistant Staphylococcus aureus: A perspective for Canadian health care practitioners. Can J Infect Dis Med Microbiol. 2006;17 Suppl C:4C–24C.

15. Fast M, Bunzeluk K. Population-level interventions to reduce the development and transmission of community-associated antimicrobial resistance : A perspective from the National Collaborating Centre for Infectious Diseases. Can J Infect Dis Med Microbiol. 2010;21(3):119–20.

16. Morrison M a, Hageman JC, Klevens RM. Case definition for community-associated methicillin-resistant Staphylococcus aureus. J Hosp Infect [Internet]. 2006 Feb [cited 2013 Mar 26];62(2):241. Available from: http://www.ncbi.nlm.nih.gov/pubmed/16289455

17. Furuya EY, Lowy FD. Antimicrobial-resistant bacteria in the community setting. Nat Rev Microbiol [Internet]. 2006 Jan [cited 2013 Mar 26];4(1):36–45. Available from: http://www.ncbi.nlm.nih.gov/pubmed/16357859

18. Zaoutis TE, Toltzis P, Chu J, Abrams T, Dul M, Kim J, et al. Clinical and molecular epidemiology of community-acquired methicillin-resistant Staphylococcus aureus infections among children with risk factors for health care-associated infection: 2001-2003. Pediatr Infect Dis J [Internet]. 2006 Apr [cited 2013 Feb 27];25(4):343–8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/16567987

19. Eady EA, Cove JH. Staphylococcal resistance revisited: community-acquired methicillin resistant Staphylococcus aureus--an emerging problem for the management of skin and soft tissue infections. Curr Opin Infect Dis [Internet]. 2003 Apr [cited 2013 Mar 21];16(2):103–24. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12734443

20. Carleton H a, Diep BA, Charlebois ED, Sensabaugh GF, Perdreau-Remington F. Community-adapted methicillin-resistant Staphylococcus aureus (MRSA): population

dynamics of an expanding community reservoir of MRSA. J Infect Dis [Internet]. 2004 Nov 15;190(10):1730–8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15499526

21. Okuma K, Iwakawa K, Turnidge JD, Warren B, Bell JM, Brien FGO, et al. Dissemination of New Methicillin-Resistant Staphylococcus aureus Clones in the Community. J Clin Microbiol. 2002;40(11):4289–94.

22. INSPQ. Perspective quant à la pertinence et la faisabilité d'un système de surveillance des infections à staphylococcus aureus résistant à la méthicilline communautaire. 2012.

23. Herold BC, Immergluck LC, Maranan MC, Lauderdale DS, Gaskin RE, Boyle-vavra S, et al. Community-Acquired Methicillin-Resistant Staphylococcus aureus in Children With No Identified Predisposing Risk. J Am Med Assoc. 2003;279(8):593–8.

24. Iyer S, Jones DH. Community-acquired methicillin-resistant Staphylococcus aureus skin infection: a retrospective analysis of clinical presentation and treatment of a local outbreak. J Am Acad Dermatol [Internet]. 2004 Jun [cited 2013 Mar 6];50(6):854–8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15153884

25. Gillet Y, Issartel B, Vanhems P, Fournet J, Lina G, Bes M, et al. Association between Staphylococcus aureus strains carrying gene for Panton-Valentine leukocidin and highly lethal necrotising pneumonia in young immunocompetent patients. Lancet. 2002;359:753–9.

26. Golding GR, Levett PN, McDonald RR, Irvine J, Nsungu M, Woods S, et al. A comparison of risk factors associated with community-associated methicillin-resistant and -susceptible Staphylococcus aureus infections in remote communities. Epidemiol Infect [Internet]. 2010 May [cited 2013 Mar 21];138(5):730–7. Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=20092664

27. Mainous III A, Hueston W, Everett CJ, Diaz V. Nasal Carriage of Staphylococcus aureus and Methicillin-Resistant S aureus in the United States, 2001-2002. Ann Fam Med. 2006;4(2):132–7.

28. Jernigan JA, Pullen AL, Flowers L, Jarvis WR. Prevalence of and Risk Factors for Colonization with Methicillin- Resistant Staphylococcus aureus in an Outpatient Clinic Population. Infect Control Hosp Epidemiol. 2003;24(6):445–50.

29. Salgado CD, Farr BM, Calfee DP, Salgado D, Farr M. Community-Acquired Methicillin-Resistant Staphylococcus aureus: A Meta-Analysis of Prevalence and Risk Factors. Clin Infect Dis. 2003;36(2):131–9.

30. Shahin R, Johnson IL, Jamieson F, Mcgeer A, Tolkin J, Ford-jones EL, et al. Methicillin-Resistant Staphylococcus aureus Carriage in a Child Care Center Following a Case of Disease. ARCH PEDIATR ADOLESC MED. 1999;153:864–8.

31. Baggett HC, Hennessy TW, Rudolph K, Bruden D, Reasonover A, Parkinson A, et al. Community-onset methicillin-resistant Staphylococcus aureus associated with antibiotic use and the cytotoxin Panton-Valentine leukocidin during a furunculosis outbreak in rural Alaska. J Infect Dis [Internet]. 2004 May 1;189(9):1565–73. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15116291

32. Baillargeon J, Kelley MF, Leach CT, Baillargeon G, Pollock BH. Methicillin-resistant Staphylococcus aureus infection in the Texas prison system. Clin Infect Dis [Internet]. 2004 May 1;38(9):e92–5. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15127360

33. Pan ES, Diep BA, Charlebois ED, Auerswald C, Carleton H a, Sensabaugh GF, et al. Population dynamics of nasal strains of methicillin-resistant Staphylococcus aureus--and their relation to community-associated disease activity. J Infect Dis [Internet]. 2005 Sep 1;192(5):811–8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/16088830

34. Young DM, Harris HW, Charlebois ED, Chambers H, Campbell A, Lee C, et al. An Epidemic of Methicillin-Resistant Staphylococcus aureus Soft Tissue Infections Among Medically Underserved Patients. Am Med Assoc. 2004;139.

35. Haley RW, Bregman D a. The role of understaffing and overcrowding in recurrent outbreaks of staphylococcal infection in a neonatal special-care unit. J Infect Dis [Internet]. 1982 Jun;145(6):875–85. Available from: http://www.ncbi.nlm.nih.gov/pubmed/7086199

36. Ellington MJ, Perry C, Ganner M, Warner M, McCormick Smith I, Hill RL, et al. Clinical and molecular epidemiology of ciprofloxacin-susceptible MRSA encoding PVL in England and Wales. Eur J Clin Microbiol Infect Dis [Internet]. 2009 Sep [cited 2013 Apr 12];28(9):1113–21. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19484277

37. David MZ, Daum RS. Community-Associated Methicillin-Resistant Staphylococcus aureus: Epidemiology and Clinical Consequences of an Emerging Epidemic. Clin Microbiol Rev [Internet]. American Society for Microbiology (ASM); 2010 Jul [cited 2013 Feb 28];23(3):616–87. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2901661&tool=pmcentrez&rendertype=abstract

38. AHW. Provincial Methicillin-Resistant Staphylococcus aureus (MRSA) Infection Prevention and Control Guidelines. 2007.

39. Mulvey MR, MacDougall L, Cholin B, Horsman G, Fidyk M, Woods S. Community-associated methicillin-resistant Staphylococcus aureus, Canada. Emerg Infect Dis. 2005;11(6):844–50.

40. Adam H, McGeer A, Simor A. Fatal case of post-influenza, community-associated MRSA pneumonia in an Ontario teenager with subsequent familial transmission. Canada

Commun Dis Rep [Internet]. 2007;33(04). Available from: http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/07vol33/dr3304a-eng.php

41. Castaldo ET, Yang EY. Severe Sepsis Attributable to Community-Associated Methicillin-Resistant Staphylococcus aureus: An Emerging Fatal Problem. 2007;

42. Vayalumkal J V, Whittingham H, Vanderkooi O, Stewart TE, Low DE, Mulvey M, et al. Necrotizing pneumonia and septic shock: suspecting CA-MRSA in patients presenting to Canadian emergency departments. [Internet]. Cjem. 2007. p. 300–3. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17626697

43. Kaplan SL, Hulten KG, Gonzalez BE, Hammerman W a, Lamberth L, Versalovic J, et al. Three-year surveillance of community-acquired Staphylococcus aureus infections in children. Clin Infect Dis [Internet]. 2005 Jun 15;40(12):1785–91. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15909267

44. Weese JS, Dick H, Willey BM, McGeer a, Kreiswirth BN, Innis B, et al. Suspected transmission of methicillin-resistant Staphylococcus aureus between domestic pets and humans in veterinary clinics and in the household. Vet Microbiol [Internet]. 2006 Jun 15 [cited 2013 Mar 26];115(1-3):148–55. Available from: http://www.ncbi.nlm.nih.gov/pubmed/16464540

45. Kurbis CA, Wylie JL. Community-based cluster of methicillin-resistant Staphylococcus aureus in Manitoba. Can J Infect Dis [Internet]. 2001;12(3):149–52. Available from: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=18159332

46. Simor AE, Gilbert NL, Gravel D, Mulvey MR, Bryce E, Loeb M, et al. Methicillin-resistant Staphylococcus aureus colonization or infection in Canada: National Surveillance and Changing Epidemiology, 1995-2007. Infect Control Hosp Epidemiol [Internet]. 2010 Apr [cited 2013 Mar 26];31(4):348–56. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20148693

47. PHAC. Results of the Surveillance of Methicillin-resistant Staphylococcus aures - from 1995 to 2009 - A project of the Canadian Nosocomial Infection Surveillance Program (CNISP). 2009.

48. Simons H, Alcabes P. A model for surveillance of methicillin-resistant Staphylococcus aureus. Public Health Rep [Internet]. 2008;123(1):21–9. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2099322&tool=pmcentrez&rendertype=abstract

49. Skov R, Christiansen K, Dancer SJ, Daum RS, Dryden M, Huang Y-C, et al. Update on the prevention and control of community-acquired meticillin-resistant Staphylococcus aureus (CA-MRSA). Int J Antimicrob Agents [Internet]. Elsevier B.V.; 2012 Mar [cited

2013 Mar 21];39(3):193–200. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22226649

50. Kaye KS, Engemann JJ, Mozaffari E, Carmeli Y. Reference group choice and antibiotic resistance outcomes. Emerg Infect Dis [Internet]. 2004 Jun;10(6):1125–8. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3323179&tool=pmcentrez&rendertype=abstract

51. Engemann JJ, Carmeli Y, Cosgrove SE, Fowler VG, Melissa Z, Trivette SL, et al. Adverse Clinical and Economic Outcomes Attributable to Methicillin Resistance among Patients with Staphylococcus aureus Surgical Site Infection. Clin Infect Dis. 2003;36(5):592–8.

52. D'Agata EMC, Webb GF, Horn MA, Moellering, Jr. RC, Ruan S. Modeling the Invasion of Community- Acquired Methicillin- Resistant Staphylococcus aureus into Hospitals. Clin Infect Dis [Internet]. 2009 Feb [cited 2014 Aug 14];48(3):274–84. Available from: http://cid.oxfordjournals.org/lookup/doi/10.1086/595844

53. Skov RL, Jensen KS. Community-associated meticillin-resistant Staphylococcus aureus as a cause of hospital-acquired infections. J Hosp Infect [Internet]. Elsevier Ltd; 2009 Dec [cited 2014 Aug 11];73(4):364–70. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19786313

54. Hiramatsu K, Cui L, Kuroda M, Ito T. The emergence and evolution of methicillin-resistant Staphylococcus aureus. Trends Microbiol [Internet]. 2001 Oct;9(10):486–93. Available from: http://www.ncbi.nlm.nih.gov/pubmed/11597450

55. Deresinski S. Methicillin-resistant Staphylococcus aureus: an evolutionary, epidemiologic, and therapeutic odyssey. Clin Infect Dis [Internet]. 2005 Feb 15;40(4):562–73. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15712079

56. Diep BA, Sensabaugh GF, Somboona NS, Carleton HA, Perdreau-Remington F. Widespread Skin and Soft-Tissue Infections Due to Two Methicillin-Resistant Staphylococcus aureus Strains Harboring the Genes for Panton-Valentine Leucocidin. J Clin Microbiol. 2004;42(5):2080–4.

57. Simor AE, Ofner-agostini M, Bryce E, Green K, Mcgeer A, Mulvey M, et al. surveillance. 2001;165(1):21–6.

58. Carson J. Methicillin-resistant Staphylococcus aureus in First Nations communities in Canada. Paediatr Child Heal [Internet]. 2005;10(9):557–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19668690

59. Irvine J, Society CP, Nations F, Committee MH. Staphylococcus aureus in Indigenous communities in Canada. 2012;17(7):395–6.

60. SHEA, IDSA, PIDS. Policy Statement on Antimicrobial Stewardship by the Society for Healthcare Epidemiology of America (SHEA), the Infectious Diseases Society of America (IDSA), and the Pediatric Infectious Diseases Society (PIDS). Infect Control Hosp Epidemiol [Internet]. University of Chicago PressChicago, IL; 2012 Apr [cited 2013 Mar 21];33(4):322–7. Available from: http://www.jstor.org/stable/info/10.1086/665010

61. Kaplan SL, Hulten KG, Gonzalez BE, Hammerman WA, Lamberth L, Versalovic J, et al. Three-Year Surveillance of Staphylococcus aureus Infections in Children. Clin Infect Dis. 2005;40(12):1785–91.

62. Forcade N a, Wiederhold NP, Ryan L, Talbert RL, Frei CR. Antibacterials as adjuncts to incision and drainage for adults with purulent methicillin-resistant Staphylococcus aureus (MRSA) skin infections. Drugs [Internet]. 2012 Feb 12;72(3):339–51. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22316350

63. Moran GJ, Krishnadasan A, Gorwitz RJ, Fosheim GE, McDougal LK, Carey RB, et al. Methicillin-Resistant S. aureus Infections among Patients in the Emergency Department. N Engl J Med. 2006;355(7):666–74.

64. Liu C, Bayer A, Cosgrove SE, Daum RS, Fridkin SK, Gorwitz RJ, et al. Clinical practice guidelines by the infectious diseases society of america for the treatment of methicillin-resistant Staphylococcus aureus infections in adults and children. Clin Infect Dis [Internet]. 2011 Feb 1 [cited 2014 Jul 11];52(3):e18–55. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21208910

65. Rieg G, Mehdi S, Perlroth J, Bayer AS, Tang AW, Phung TO, et al. Necrotizing Fasciitis Caused by Community-Associated Methicillin-Resistant Staphylococcus aureus in Los Angeles. N Engl J Med. 2005;352:1445–53.

66. Daum RS. Skin and Soft-Tissue Infections Caused by Methicillin-Resistant Staphylococcus aureus. N Engl J Med [Internet]. 2007;357(13):1357–1357. Available from: http://content.nejm.org/cgi/doi/10.1056/NEJMx070054

67. Bassetti M, Nicco E, Mikulska M. Why is community-associated MRSA spreading across the world and how will it change clinical practice? Int J Antimicrob Agents [Internet]. Elsevier B.V.; 2009 Jul [cited 2013 Mar 4];34 Suppl 1:S15–S19. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19560669

68. Kempker RR, Farley MM, Ladson JL, Satola S, Ray SM. Association of methicillin-resistant Staphylococcus aureus (MRSA) USA300 genotype with mortality in MRSA bacteremia. J Infect [Internet]. Elsevier Ltd; 2010 Nov [cited 2013 Mar 16];61(5):372–81. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2975870&tool=pmcentrez&rendertype=abstract

69. Chambers HF. Community-associated MRSA--resistance and virulence converge. N Engl J Med [Internet]. 2005 Apr 7;352(14):1485–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15814886

70. Klevens RM, Morrison M a, Nadle J, Petit S, Gershman K, Ray S, et al. Invasive methicillin-resistant Staphylococcus aureus infections in the United States. JAMA [Internet]. 2007 Oct 17;298(15):1763–71. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17940231

71. MMWR. Severe methicillin-resistant Staphylococcus aureus community-acquired pneumonia associated with influenza--Louisiana and Georgia, December 2006-January 2007. [Internet]. MMWR. Morbidity and mortality weekly report. 2007 Apr p. 325–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17963982

72. Nathwani D, Morgan M, Masterton RG, Dryden M, Cookson BD, French G, et al. Guidelines for UK practice for the diagnosis and management of methicillin-resistant Staphylococcus aureus (MRSA) infections presenting in the community. J Antimicrob Chemother [Internet]. 2008 May [cited 2013 Mar 13];61(5):976–94. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18339633

73. Stevens DL, Bisno AL, Chambers HF, Everett ED, Dellinger P, Goldstein EJC, et al. Practice guidelines for the diagnosis and management of skin and soft-tissue infections. Clin Infect Dis [Internet]. 2005 Nov 15 [cited 2014 Mar 19];41(10):1373–406. Available from: http://cid.oxfordjournals.org/content/41/10/1373.full

74. Gorwitz RJ, Jernigan DB, Powers JH, Jernigan JA. Strategies for Clinical Management of MRSA in the Community : Summary of an Experts ' Meeting Convened by the Centers for Disease Control and Prevention [Internet]. 2006 p. 1–24. Available from: http://stacks.cdc.gov/view/cdc/12423

75. Rajendran PM, Young D, Maurer T, Chambers H, Perdreau-Remington F, Ro P, et al. Randomized, double-blind, placebo-controlled trial of cephalexin for treatment of uncomplicated skin abscesses in a population at risk for community-acquired methicillin-resistant Staphylococcus aureus infection. Antimicrob Agents Chemother [Internet]. 2007 Nov [cited 2014 Aug 16];51(11):4044–8. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2151464&tool=pmcentrez&rendertype=abstract

76. Schmitz GR, Bruner D, Pitotti R, Olderog C, Livengood T, Williams J, et al. Randomized controlled trial of trimethoprim-sulfamethoxazole for uncomplicated skin abscesses in patients at risk for community-associated methicillin-resistant Staphylococcus aureus infection. Ann Emerg Med [Internet]. Elsevier Inc.; 2010 Sep [cited 2014 Aug 16];56(3):283–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20346539

77. Duong M, Markwell S, Peter J, Barenkamp S. Randomized, controlled trial of antibiotics in the management of community-acquired skin abscesses in the pediatric patient. Ann

Emerg Med [Internet]. Elsevier Inc.; 2010 May [cited 2014 Aug 16];55(5):401–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19409657

78. Government of Canada HCFN and IHB. Clinical Practice Guidelines for Nurses in Primary Care: Adult Care [First Nations and Inuit Health Branch, Health Canada, 2011] [Internet]. 2008 [cited 2014 Apr 17]. Available from: http://www.hc-sc.gc.ca/fniah-spnia/services/nurs-infirm/clini/adult/index-eng.php

79. Dalloo A, Sobol I, Palacios C, Mulvey M, Gravel D. Investigation of community-associated methicillin-resistant Staphylococcus aureus in a remote northern community, Nunavut, Canada. Canada Commun Dis Rep. 2008;34(5).

80. Larcombe L, Waruk J, Schellenberg J, Ormond M. Rapid emergence of methicillin-resistant Staphylococcus aureus (MRSA) among children and adolescents in northern Manitoba, 2003-2006. Canada Commun Dis Rep. 2007;33(02).

81. Taylor G, Kirkland T, Kowalewska-Grochowska K, Wang Y. A multistrain cluster of methicillin-resistant staphylococcus aureus based in a native community. Can J Infect Dis. 1990;1(4):121–6.

82. Embil J, Ramotar K, Romance L, Alfa M, Conly J, Cronk S, et al. Methicillin-resistant Staphylococcus aureus in tertiary care institutions on the Canadian prairies 1990-1992. Infect Control Hosp Epidemiol [Internet]. 1994 Oct;15(10):646–51. Available from: http://www.ncbi.nlm.nih.gov/pubmed/7844335

83. Ofner-Agostini M, Simor AE, Mulvey M, Bryce E, Loeb M, McGeer A, et al. Methicillin-resistant Staphylococcus aureus in Canadian aboriginal people. Infect Control Hosp Epidemiol [Internet]. 2006;27(2):204–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/16465642

84. Golding GR, Levett PN, Mcdonald RR, Irvine J, Quinn B, Nsungu M, et al. High Rates of Staphylococcus aureus USA400 Infection, Northern Canada. Emerg Infect Dis. 2011;17(4):722–6.

85. Mulvey M, Embil J, Horsman G, Irvine J, Paton S, Woods S. Identification of Risk Factors for the Acquisition of Community-Acquired Methicillin-Resistant Staphylococcus aureus (MRSA) associated infections versus Methicillin-Sensitive Staphylococcus aureus (MSSA) infections. 2009.

86. Wylie JL, Nowicki DL. Molecular Epidemiology of Community- and Health Care-Associated Methicillin-Resistant Staphylococcus aureus in Manitoba, Canada. J Clin Microbiol. 2005;43(6):2830–6.

87. Groom A V, Wolsey DH, Naimi TS, Smith K, Johnson S, Boxrud D, et al. Community-AcquiredMethicillin-Resistant Staphylococcus aureus inaRural American Indian Community. JAMA. 2001;286(10):1201–5.

88. Byrd KK, Holman RC, Bruce MG, Hennessy TW, Wenger JD, Bruden DL, et al. Methicillin-resistant Staphylococcus aureus-associated hospitalizations among the American Indian and Alaska native population. Clin Infect Dis [Internet]. 2009 Oct 1 [cited 2014 Aug 16];49(7):1009–15. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19725783

89. David MZ, Rudolph KM, Hennessy TW, Zychowski DL, Asthi K, Boyle-Vavra S, et al. MRSA USA300 at Alaska Native Medical Center, Anchorage, Alaska, USA, 2000-2006. 2Emerging Infect Dis. 2012;18(1):105–8.

90. Tong SYC, Bishop EJ, Lilliebridge R a, Cheng AC, Spasova-Penkova Z, Holt DC, et al. Community-associated strains of methicillin-resistant Staphylococcus aureus and methicillin-susceptible S. aureus in indigenous Northern Australia: epidemiology and outcomes. J Infect Dis [Internet]. 2009 May 15 [cited 2014 Aug 16];199(10):1461–70. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19392622

91. Muileboom J, Hamilton M, Parent K, Makahnouk D, Kirlew M, Saginur R, et al. Community-associated methicillin-resistant Staphylococcus aureus in northwest Ontario: A five-year report of incidence and antibiotic resistance. Can J Infect Dis Med Microbiol. 2013;24(2):42–4.

92. StatisticsCanada. Census 2006: Aboriginal Peoples in Canada in 2006: Inuit, Métis and First Nations, 2006 Census: Findings [Internet]. Statistics Canada. 2006 [cited 2013 Mar 26]. Available from: http://www12.statcan.gc.ca/census-recensement/2006/as-sa/97-558/index-eng.cfm

93. Irvine J. Community-associated methicillin-resistant Staphylococcus aureus in Indigenous communities in Canada. Paediatr Child Heal. 2012;17(7):385–6.

94. Szakacs T a, Toye B, Turnbull JM, Muckle W, Roth VR. Prevalence of methicillin-resistant Staphylococcus aureus in a Canadian inner-city shelter. Can J Infect Dis Med Microbiol [Internet]. Pulsus Group Inc; 2007;18(4):249–52. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21937829

95. WHO. WHO | Antimicrobial resistance. World Health Organization; [cited 2014 Mar 6]; Available from: http://www.who.int/mediacentre/factsheets/fs194/en/

96. PHO. About ASP [Internet]. [cited 2014 Mar 6]. Available from: http://www.publichealthontario.ca/en/BrowseByTopic/InfectiousDiseases/AntimicrobialStewardshipProgram/Pages/About_ASP.aspx#.Uxjkm_ldUdg

97. Muileboom J, Hamilton M, Kelly L. The changing face of cellulitis and MRSA in rural Canada: a clinical update. Can J Rural Med. 2013;18(4):137–9.

98. CANWARD. 2012 NATIONAL Antimicrobial Susceptibility Testing Results: Staphylococcus aureus, CA-MRSA [Internet]. 2014. Available from: http://www.can-r.com/study.php?study=canw2012

99. Siberry GK, Tekle T, Carroll K, Dick J. Failure of clindamycin treatment of methicillin-resistant Staphylococcus aureus expressing inducible clindamycin resistance in vitro. Clin Infect Dis [Internet]. 2003 Nov 1;37(9):1257–60. Available from: http://www.ncbi.nlm.nih.gov/pubmed/14557972

100. Frank AL, Marcinak JF, Mangat PD, Tjhio JT, Kelkar S, Staphylo- BM. Clindamycin treatment of methicillin-resistant Staphylococcus aureus infections in children. Pediatr Infect Dis J. 2002;21(6):530–4.

101. Tong SYC, McDonald MI, Holt DC, Currie BJ. Global implications of the emergence of community-associated methicillin-resistant Staphylococcus aureus in Indigenous populations. Clin Infect Dis [Internet]. 2008 Jun 15 [cited 2013 Mar 27];46(12):1871–8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18462175

102. Urth T, Hjort U, Søgaard M, Skov R. Successful control of CA-MRSA in Denmark: Mission impossible ? 1st International Conference on Prevention and Infection Control (ICPIC). Geneva, Switzerland; 2011.

103. PHAC. Canadian Nosocomial Infection Surveillance Program - 2010 - MRSA Surveillance Protocol - Surveillance for methicillin-resistant Staphylococcus aureus (MRSA) in CNISP health care facilities. 2009.

104. Zhanel GG, Adam HJ, Baxter MR, Fuller J, Nichol K a, Denisuik AJ, et al. Antimicrobial susceptibility of 22746 pathogens from Canadian hospitals: results of the CANWARD 2007-11 study. J Antimicrob Chemother [Internet]. 2013 May [cited 2014 Aug 16];68 Suppl 1:i7–22. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23587781

105. Dellit TH, Owens RC, McGowan JE, Gerding DN, Weinstein R a, Burke JP, et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. Clin Infect Dis [Internet]. Oxford University Press; 2007;44(2):159–77. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17173212

106. Khawcharoenporn T, Tice AD, Grandinetti A, Chow D. Risk factors for community-associated methicillin-resistant Staphylococcus aureus cellulitis--and the value of recognition. Hawaii Med J [Internet]. University Clinical, Education & Research Associate (UCERA); 2010;69(10):232–6. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21229486

107. Turabelidze G, Lin M, Wolkoff B, Dodson D, Gladbach S, Zhu B-P. Personal hygiene and methicillin-resistant Staphylococcus aureus infection. Emerg Infect Dis [Internet]. 2006 Mar;12(3):422–7. Available from:

http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3291434&tool=pmcentrez&rendertype=abstract

108. INAC. Terminology Guide - Indian and Northern Affairs Canada [Internet]. 2000 Jun. Available from: http://www.collectionscanada.gc.ca/webarchives/20071115071752/http://www.ainc-inac.gc.ca/pr/pub/wf/trmrslt_e.asp?term=6

109. Ofner-Agostini M, Simor AE, Mulvey M, Bryce E, Loeb M, McGeer A, et al. Methicillin-resistant Staphylococcus aureus in Canadian aboriginal people. Infect Control Hosp Epidemiol Off J Soc Hosp Epidemiol Am [Internet]. 2006;27(2):204–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/16465642

110. IDSA. IDSA : IDSA Practice Guidelines [Internet]. [cited 2014 Mar 11]. Available from: http://www.idsociety.org/Templates/Landing.aspx?id=23622320151

111. Nichol K a, Adam HJ, Roscoe DL, Golding GR, Lagacé-Wiens PRS, Hoban DJ, et al. Changing epidemiology of methicillin-resistant Staphylococcus aureus in Canada. J Antimicrob Chemother [Internet]. 2013 May [cited 2014 Aug 13];68 Suppl 1:i47–55. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23587778

112. Golding GR, Levett PN, McDonald RR, Irvine J, Nsungu M, Woods S, et al. A comparison of risk factors associated with community-associated methicillin-resistant and -susceptible Staphylococcus aureus infections in remote communities. Epidemiol Infect [Internet]. 2010 May [cited 2014 Aug 13];138(5):730–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20092664

113. Pate AJ, Terribilini RG, Ghobadi F, Azhir A, Barber A, Pearson JM, et al. Antibiotics for methicillin-resistant Staphylococcus aureus skin and soft tissue infections: the challenge of outpatient therapy. Am J Emerg Med [Internet]. Elsevier Inc.; 2014 Feb [cited 2014 Aug 13];32(2):135–8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24238483

114. Wackett A, Nazdryn A, Spitzer E, Singer AJ. MRSA rates and antibiotic susceptibilities from skin and soft tissue cultures in a suburban ED. J Emerg Med [Internet]. Elsevier Ltd; 2012 Oct [cited 2014 Aug 17];43(4):754–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22494599

115. Frei CR, Miller ML, Lewis JS, Lawson K a, Hunter JM, Oramasionwu CU, et al. Trimethoprim-sulfamethoxazole or clindamycin for community-associated MRSA (CA-MRSA) skin infections. J Am Board Fam Med [Internet]. 2010 [cited 2014 Aug 17];23(6):714–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21057066

116. Miller LG, Quan C, Shay A, Mostafaie K, Bharadwa K, Tan N, et al. A Prospective Investigation of Outcomes after Hospital Discharge for Endemic, Community-Acquired Methicillin-Resistant and -Susceptible Staphylococcus aureus Skin Infection. Clin Infect Dis. 2007;44:483–92.

117. Khawcharoenporn T, Tice A. Empiric outpatient therapy with trimethoprim-sulfamethoxazole, cephalexin, or clindamycin for cellulitis. Am J Med [Internet]. Elsevier Inc.; 2010 Oct [cited 2014 Aug 17];123(10):942–50. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20920697

Appendices

Appendix A. Summary of IDSA clinical practice guidelines (FOR ADULTS) and FNIHB Clinical Practice Guidelines (FOR ADULTS)

Soft Skin Tissue Infection (SSTI)

IDSA Guidelines (73)

Impetigo: Topical mupirocin tid (for patients with limited number of lesions) or oral anti-staphylococcal or anti-streptococcal antibiotic (cloxacillin 250mg po qid, cephalexin 250mg po qid, erythromycin 250mg po qid (caution about resistance), clindamycin 300mg po tid, amoxicillin/clavulanic acid 875mg po bid, typically for 7 days

Erysipelas: Penicillin V (for GAS[21]) 300mg po qid

Cellulitis: Cephalexin 500mg po qid, or cloxacillin 500mg po qid (clindamycin 300-450mg po tid or vancomycin IV if allergy present). Duration varies by clinical severity and clinical response.

Bite wounds: 1) Amoxicillin/clavulanic acid 500mg po tid or 875mg po bid

2) Doxycycline 100mg po bid; co-trimoxazole DS 1 tab po bid; or quinolone + clindamycin

NOTE: For SSTI duration of treatment vary depending on clinical judgement and response.

Abscesses:

Cutaneous – Incision & Drainage (I&D) procedure is sufficient unless cellulitis present, abscess > than 5cm, or involving face

Furuncle/carbuncle – moist heat, I&D

FNIHB CPG (78)

Impetigo:

1) Mupirocin ointment tid x 7-10 days
2) Cloxacillin 500mg po qid x 7-10 days (for multiple infected lesions)
3) Cephalexin 500mg po qid x 7-10 days (for multiple infected lesions)
4) Erythromycin 1000mg divided by bid, tid, or qid x 7 to 10 days

Erysipelas: No specific guidelines

Cellulitis:

Mild cellulitis:

1) Cephalexin 500mg po qid x 10 days
2) Cloxacillin 500mg po qid x 10 days
3) Azithromycin 500mg po x 1 day, then 250mg po daily x 4 days

Moderate to severe cellulitis (only under MD direction):

1) Cefazolin 1g iv/im q8h or Cefazolin 2g iv q24h PLUS Probenecid 1g po daily
2) Clindamycin 600mg iv/im q8h. Duration not specified.

Bite Wounds:

1) Amoxicillin/clavulanic acid 875mg/125mg po bid x 7-10 days

2) Cefuroxime or doxycycline (no dosage, frequency, duration specified)

Abbreviations:

od: once daily

bid: twice daily

tid: three times daily

qid: four times daily

po: per os (orally administered)

IV: intravenously

IM: intra-muscular

DS: double strength

Appendix B. IDSA and SHEA guidelines for antimicrobial stewardship

IDSA and SHEA Guidelines for Antimicrobial Stewardship

- Have a multidisciplinary antimicrobial stewardship team composed of an infectious diseases physician, a clinical pharmacist, a clinical microbiologist, an information system specialist, an infection control professional, and hospital epidemiologist.
- Collaborate with the hospital infection control and pharmacy and therapeutics committees.
- Obtain support and collaboration from the hospital administration, medical staff leadership.
- Negotiate with hospital administration to obtain authority, compensation, and expected outcomes for the program.
- Have hospital administrative support to measure and track antimicrobial use on an ongoing basis.
- Adopt one of the two core strategies:
    - A: Prospective audit with intervention and feedback
    - B: Formulary restriction and preauthorization
- Consider following elements and prioritize as supplements:
    - A: Education
    - B: Guidelines and clinical pathways
    - C: Antimicrobial cycling
    - D: Antimicrobial order forms
    - E: Combination therapy
    - F: Streamlining or de-escalation of therapy
    - G: Dose optimization
    - H: Parenteral to oral conversion
- Have healthcare information technology in the form of electronic medical records, computer physician order entry, and clinical decision support.
- Computer-based surveillance system.
- Engage a clinical microbiology laboratory.
- Gather data on both process and outcome measures

Appendix C. Antibiotic Tracking Case Report Form

ANTIBIOTIC TRACKING Case Report Form (CRF)

***Instructions:** Please use this form to track all antibiotics that have been prescribed to a patient. Please note that this sheet represents all antibiotics that have been prescribed to **ONE** specific patient, per occurrence.

Location : Assigned Chart number:

HC-RN / Agency RN / NP / MD / Dentist (Circle ONE) Date of prescribed antibiotic: (DD/MM/YY) _____

Patient: Gender____ Age____(years) Weight_____(kg) Ht (cm)____ Creatinine_____mmol/L or Clcr _____mL/min Allergy:_____
(Date correlating with Antibiotic treatment)

OTHER MEDICAL CONDITIONS (please check all that apply)	Yes
COPD	
DIABETES	
PREGNANCY	
CARDIAC (please specify):	
IMMUNOCOMPROMISED	
ALCOHOLISM	
ASPLENIA	
LIVER DISEASE	
RENAL DISEASE	
OTHER (please specify):	

INDICATIONS FOR USE (please check all that apply)	Yes or No
FEVER	
URINARY TRACT SYMPTOMS	
RESPIRATORY SYMPTOMS	
DIARRHEA	
SKIN/WOUND INFECTION	
SEXUALLY TRANSMITTED INFECTION	
EYES	
Other (please specify):	
IS PATIENT COLONIZED WITH RESISTANT ORGANISM?	
	Unknown

DIAGNOSTIC TESTS (please check all test that were performed)	Yes or No	RESULTS (ATTTACH C&S WITHOUT PT'S ID)
BLOOD CULTURE		
URINE CULTURE		
URINALYSIS		
SPUTUM CULTURE		
THROAT CULTURE		
STOOL CULTURE/TEST		
CHEST X-RAY		
CBC		
WOUND CULTURE		
VAGINAL		
OTHER (Please specify)		

DOES PATIENT HAVE ANY OF THE FOLLOWING DEVICES?

Y	N	
		URINARY CATHETER
Y	N	CENTRAL LINE
Y	N	OTHER (please specify):

Antibiotic prescribed (dose/route/frequency/duration)

COMMENTS:

CLINICAL OUTCOMES: ☐ CURE ☐ FAILURE ☐ Unknown
☐ IMPROVEMENT ☐ D/C because of adverse events (See below)

ADVERSE EVENTS: ☐ Allergic Reaction: _____
☐ Drug Interaction: _____
☐ Others: _____

ADJUNCTIVE THERAPY: _____ ☐ I&D PROCEDURE DATE (if done): _____

DISPOSITION:
☐ Medivac ☐ Other _____
☐ Schedivac ☐ Unknown
☐ Home

☐ WOUND CARE