Strategies to Control Community-Associated Antimicrobial Resistance Among Enteric Bacteria and MRSA in Canada

A comprehensive review

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January 2010

National Collaborating Centre for Infectious Diseases
Centre de collaboration nationale des maladies infectieuses
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Executive Summary

Resistance to antimicrobial drugs is a concern that exists worldwide and has a significant impact on human and animal health. Knowledge and practice gaps exist around the control of antimicrobial-resistant infections in Canada, particularly in the community setting. Although much research exists on the control of hospital-acquired resistant infections, currently no comprehensive synthesis or review of the literature exists on the control of antimicrobial resistant organism infections within the community. In particular, there is little synthesis of information on those infections that represent a large component of community-level impact, namely resistant enteric bacteria and community-associated methicillin-resistant Staphylococcus aureus (CA-MRSA); these infections pose a significant health burden to Canadians.

In addition to representing a significant human health impact in the Canadian community, enteric bacteria and MRSA have similar spread and control mechanisms (e.g. hygiene and hand washing, sanitation, housing density and crowding, person-to-person spread, animal exposure), thus representing areas for common policy, intervention, and other control activities.

The objective of this work was to conduct a formal, comprehensive review of control strategies and interventions available to reduce both the development of antimicrobial resistant enteric bacteria, specifically Campylobacter spp., Salmonella spp., verocytotoxigenic Escherichia coli, Shigella spp., and CA-MRSA, and the spread of such infections within Canadian communities.

A comprehensive review was undertaken of the relevant peer-reviewed and grey English language literature from 1970 to present using a protocol based on systematic review methodology. A total of 1,467 references were identified; of these, 563 met the abstract relevancy screening criteria and of these, 203 were reviewed in detail.

In general there was reasonable scientific evidence regarding risk groups and risk factors for CA-MRSA. This information provides some insight into potential approaches to control these infections. Identified potential risk groups and risk factors include the following:

- Children
- Specific ethnic groups
- Athletes
- Drug use
- Men who have sex with men (MSM)
- Heterosexual high risk activities
- Military
- Veterinarians and animal handlers
- HIV infection
- Tattoo recipients
- Living with a carrier or case of CA-MRSA
- Emergency departments and hospitalized patients
- Antibiotic use

There was a paucity of information on risk groups and risk factors for the community-acquired antimicrobial-resistant enteric bacterial infections studied; some information exists on risk settings and risk factors for community-acquired enteric bacterial infections (without reference to resistance), but the extent to which this can be extrapolated to resistant infections
is unknown; much of this information takes the form of outbreak reports. Potential risk groups and risk factors for community–acquired antimicrobial resistant enteric infections include the following:

- Daycare centres
- Schools
- Households
- Nursing homes
- Immunocompromized individuals
- Specific sociodemographic factors (i.e. rural residents, specific ethnic groups, income, education, access to health services)
- Population density
- Season

There is a paucity of scientifically-based information (RCTs or observational studies) on interventions for CA-MRSA or for the enteric bacterial infections studied, resistant or otherwise. A number of RCTs have shown the effectiveness of handwashing in the prevention of gastrointestinal illness generally.

A limited number of intervention studies of hospital-acquired methicillin-resistant S. aureus (HA-MRSA) exist, however the extent to which the result of these studies can be extrapolated to CA-MRSA is unknown. Such extrapolation may be misleading.

There is extensive literature concerning recommendations, guidelines and suggested approaches to the control of both CA-MRSA and, to a lesser extent, for enteric bacterial infections in community settings. Although the efficacy of these approaches is plausible, it has for the most part not been formally evaluated. Proposed approaches to control of these infections include the following:

- CA-MRSA
  - Hand and personal hygiene
  - Prudent use of antibiotics
  - Decolonization
  - Early diagnosis and appropriate treatment
  - Education programs (hygiene, antibiotic use)
  - Regular cleaning and laundering in households and facilities

- Equipment disinfection
- Exclusion of those with active infection from certain high risk settings

- Community-acquired enteric bacterial infections
  - Hand, household and institutional hygiene
  - Equipment disinfection in high risk settings
  - Public and public health education
  - Early diagnosis and appropriate treatment
  - Exclusion of those with active infection from certain high risk settings

Formal evaluations of the efficacy of strategies for control of CA-MRSA and community-acquired enteric infections (resistant and otherwise) are warranted and should form the basis for public health guidelines and policy. Until such time as evaluations can be undertaken, recommendations for control of these infections must be dependent largely on historic practice, conventional wisdom, extrapolation from other contexts, consensus, and conjecture.

Potential interventions that would warrant formal evaluation in various settings and groups include the following:

- Hand and personal hygiene
- Prudent use of antibiotics
- Decolonization
- Early diagnosis and appropriate treatment
- Public education programs (hygiene, antibiotic use)
- Regular cleaning and laundering in households and facilities
- Equipment disinfection
- Exclusion of those with active infection from certain high risk settings

Ongoing collection and evaluation of information (including surveillance and epidemiologic studies) on the occurrence, settings, risk factors, and risk groups for CA-MRSA and resistant enteric infections is warranted. Such information will be useful in determining disease trends, identifying risk groups, settings and risk factors, and in identifying and evaluating potential interventions.
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Introduction

Resistance to antimicrobial drugs is a concern that exists worldwide and has a significant impact on human and animal health. Antimicrobial resistance jeopardizes the ability to treat and control infections in both animals and humans. Knowledge and practice gaps exist around the control of antimicrobial-resistant infections in Canada, particularly in the community setting. Public health practitioners are searching for appropriate actions to mitigate the effects of antimicrobial resistant pathogens in the community. Although much research exists on the control of hospital-acquired resistant infections, currently no comprehensive synthesis or review of the literature exists on the control of antimicrobial-resistant organism infections within the community. In particular, there is little synthesis of information on those infections that represent a large component of community-level impact, namely resistant enteric bacteria and community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA); these infections pose a significant health burden to Canadians (1–4).

If drug resistance continues to increase in prevalence, rising from current Canadian levels to the higher levels being reported in the United States, it is estimated that added direct expenses in Canada would rise to between $104 and $187 million annually. This is $64 to $102 million more than those infections would have cost had they been drug-susceptible. The costs of screening would remain the same, but the costs of precautions for colonized patients could rise towards $157 million; Canada reportedly spends at least $659 million annually on more than 25 million retail prescriptions for anti-infective drugs (orally administered). This is the third highest drug usage category. If drug resistance rises to endemic levels, resulting in the prescription of more potent and expensive newer drugs for all drug treatment, both in and out of hospital, drug costs could escalate to at least $1.8 billion. In addition to representing a significant human health impact in the Canadian community, enteric bacteria and MRSA have similar spread and control mechanisms (e.g. hygiene and hand washing, sanitation, housing density and crowding, person-to-person spread, animal exposure), thus representing areas for common policy, intervention, and other control activities (5).
Background

Antimicrobial Resistance

General Resistance Development

Generally, antimicrobial resistance in microorganisms can be achieved in two ways: innate or acquired. Microorganisms that have a natural resistance to a given class of antimicrobials are said to have innate resistance. Microorganisms can also develop acquired resistance by either spontaneous mutation or by horizontal transmission of extrachromosomal genes. The extra-chromosomal genes may be transferred in the form of plasmids, transposons, or integrons and may be inserted in the susceptible microbe’s chromosome or in a plasmid (6–8).

The introduction of some new antibiotics has been associated with the rapid development of resistant microorganisms. This is primarily mediated through the excessive use of antimicrobials; however, technological advances, globalization, and changes in societal behavior have also aided resistance development (7,9). The spread of AMR pathogens most often occurs because of overcrowding and poor hygienic conditions within a given population, the misuse or excess use of antimicrobials in humans and animals, and the failure of infection control programs in institutional and hospital settings (6). These factors also contribute to the dissemination of susceptible microorganisms in a given population (6). There are four major mechanisms by which antimicrobial treatments can result in the selection of resistant strains within a given population. The first is treatment failure resulting in the ability of resistant strains to propagate and spread to other hosts. The second is the elimination of susceptible strains due to treatment, thereby increasing the number of resistant strains in the population. The third is the elimination of susceptible strains from the host, increasing the risk of infection with resistant strains due to an unoccupied niche. The fourth is that resistant commensal organisms within a host may, upon treatment, propagate due to the elimination of susceptible flora, thereby increasing shedding of the resistant bacteria (10).

The overall impact of antimicrobial resistance on public health is that it can increase the burden of disease in humans by limiting antimicrobial treatment options, requiring use of more expensive or toxic drugs, delaying effective treatment, and increasing the duration or severity of infection (11,12).

Development of Resistance in Staphylococcus aureus

Staphylococcus aureus possesses the ability to readily acquire antimicrobial resistance (9). For instance, after the utilization of penicillin, resistance in S. aureus was quickly observed (13). However, unlike penicillin resistance, the development of methicillin resistance in S. aureus is less clearly defined. The mechanism responsible for resistance to methicillin is encoded by the chromosomally linked staphylococcal chromosomal cassette SCCmecA that produces a penicillin binding protein PBP2a which, if upregulated, has low affinity for beta-lactam antibiotics, including cephalosporins (0,13–15). The exact mechanism for the emergence of MRSA is unclear; however, there is evidence that the mecA gene evolved from a domestic gene possessed by S. sciuri (9,14,15). Additionally, other staphylococcal coagulase-negative strains and Enterococcus hirae are other potential sources of resistance genes (13). Therefore, the emergence of the epidemic MRSA clones is believed to have occurred due to a horizontal transfer of resistance genes from the donor microorganism into a methicillin-susceptible S. aureus (MSSA) recipient strain, which frequently encountered one another (16). The most popular theory of the initial acquisition of resistance genes in S. aureus is transduction of the SCCmecA via a phage (14). Therefore, it is unlikely that MRSA initially developed its resistance due to selective pressure of antimicrobials (14).

After nearly three decades of being exclusively associated with hospitals, MRSA emerged in various geographically distinct communities outside of health care settings, without obvious health care-associated risk factors (9,17). Despite the number of MSSA strains found to cause illness, there are only a handful of epidemic MRSA clones (16). Unlike the hospital-acquired strains in the community, the SCCmec type
IV is the dominant gene cassette which is the smallest structurally, more variable, and most mobile type of SCCmec (14). Additionally, limited resistance has been observed among CA-MRSA clones. Because of the size, mobility, and low level of resistance, there is less of an energy burden on the organism, which makes it more genetically fit for dissemination in populations (14).

**Development of Resistance in Enteric Bacteria**

Antimicrobial resistance in enteric bacteria is a growing problem. Antimicrobial resistance in enteric bacteria has been associated with the use of antimicrobial agents in food animals and can be influenced by previous antibiotic intake that affects the fecal flora in humans (18,19). The selective pressure brought about by the use of antimicrobial agents in food animals has led to the emergence and dissemination of antimicrobial-resistant bacteria, including animal pathogens, human pathogens with food animal reservoirs, and commensal bacteria (19–21).

Spread can occur through ingestion of contaminated food, direct contact with animals through colonization of resistant isolates in community settings, or through household contacts and/or intrafamilial transmission (19,22,23).

**Methicillin-Resistant Staphylococcus aureus**

Historically, *S. aureus* has been responsible for causing illness in humans ranging from uncomplicated skin lesions to septicemia. *S. aureus* is also a commensal organism that can be found on skin, nasal passages, and the perineum (24).

Methicillin, or meticillin, is a penicillinase-resistant, semisynthetic penicillin group narrow spectrum antimicrobial introduced for treatment in 1959 (25). Soon after its use in healthcare, resistance among gram-positive microorganisms was observed (25).

**Definition of MRSA**

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a coagulase-positive *S. aureus* strain that has acquired beta-lactam resistance to antimicrobials, such as methicillin and oxacillin, and is mediated by PBP2a. Resistance to methicillin was first reported in the early 1960s in the hospital environment (26). In the 1980s and 1990s, MRSA began to emerge in the community and has continued to rise in incidence. The Centers for Disease Control and Prevention (CDC) has since identified CA-MRSA as an emerging worldwide public health risk (27).

**Definition of Community-Associated MRSA and Hospital-Associated MRSA**

Since the divergence of MRSA from hospital to the community, cases and outbreaks are now described as either community-associated MRSA (CA-MRSA), or hospital-associated or health care-associated MRSA (HA-MRSA). Controversy over the definitions of the two types of MRSA has arisen; however, both the CDC and Canadian expert panels define CA-MRSA as a case with (27,28):

1. Diagnosis of MRSA was made in the outpatient setting or by a culture positive for MRSA within 48 hours after admission to the hospital
2. No medical history of MRSA infection or colonization
3. No medical history in the past year of hospitalization, admission to a nursing home, skilled nursing facility, or hospice, dialysis, or surgery
4. No permanent indwelling catheters or medical devices that pass through the skin into the body

In addition to the clinical definition of CA-MRSA, there are unique genotypic and phenotypic traits expressed by both HA-MRSA and CA-MRSA that can be used for differentiation. CA-MRSA strains typically possess the staphylococcal chromosomal cassette SCCmec type IV and less frequently type V gene, which confers resistance. It is also generally
more susceptible to antimicrobials and is associated primarily with skin and soft tissue infections (SSTI), necrotizing pneumonia, and necrotizing fasciitis (29,30). Furthermore, CA-MRSA strains have been highly associated with the presence of the virulence factor Panton-Valentine leukocidin (PVL) a cytotoxin potentially capable of causing severe tissue necrosis and leukocyte, destruction (30,31). Conversely, HA-MRSA strains do not typically have PVL and possess SCCmec types I-III, which are often multidrug-resistant and manifest by infecting wounds, ventilator-associated pneumonia, line infections and other infections involving crossing the skin barrier (29,30).

There are several strains of MRSA that have appeared in distinct geographical locations such as the United Kingdom, Holland, Germany Taiwan, Japan, Australia, Argentina, Canada, and the United States (30,31). Discrimination between hospital and community strains can be achieved using molecular typing techniques such as pulse-field gel electrophoresis and multilocus sequencing (32). Typically, in North America, USA300 (or CMRSA-10 under Canadian nomenclature) and less frequently USA400 (or CMRSA-7) strains are characteristic of MRSA strains in the community; USA100 (CMRSA-2) and 200 strains are associated with hospital-acquired strains (32,33). It is important to note that although the strain may indicate a hospital origin, the true nature of the strain is only confirmed through an epidemiological investigation.

Limitations to the Definitions

Despite the above, there still remain several limitations to the definitions. For example, infected individuals may remain colonized with MRSA for extended periods of time; hence, the assignment of timelines for hospital exposure may be incorrect (13). In addition, communities such as long-term care facilities and nursing homes are inconsistently classified due to the unique nature of the population in those settings (13). Individuals with close contact to infected HA-MRSA individuals, such as health care workers or family members, who go on to become infected themselves would by CDC’s definition, be community cases despite the strain’s hospital origin. Similarly, CA-MRSA strains could move into the hospital setting and cause illness and thereby would be misclassified as a HA-MRSA (28). Therefore, the clear-cut definitions become blurred with the movement of HA-MRSA and CA-MRSA strains between the community and hospital settings. The definition of CA-MRSA thus leaves the possibility of misclassification of illness without molecular confirmation.

CA-MRSA Diagnosis

Although a suspected diagnosis may be based on patient symptoms, risk factor evaluation, and local epidemiology in the community, the presence of CA-MRSA can be confirmed through culture and/ or appropriate molecular techniques. Pustular material from the lesions should be obtained prior to incision and submitted for culture and antimicrobial susceptibility testing to ensure the correct antibiotic is prescribed (8,28). Since severe and invasive infections may also occur such as necrotizing fasciitis, necrotizing pneumonia, and bacteremia, additional samples to consider include blood, respiratory secretions, or endotracheal fluid (33).

CA-MRSA Treatment

Surgical, topical, oral, and parenteral therapies can be used to treat CA-MRSA infections. Mild skin infections do not require antimicrobial therapy; incision and drainage of subcutaneous abscesses alone is effective in many cases. Children with SSTIs showing an infected area site with a diameter < 5 cm respond well to topical therapy without antibiotics according to Popovich and Hota (34). Some infections may require both incision and drainage of the infected site and antibiotic treatment; if abscesses are difficult to drain, the patient appears systematically ill or has co-morbidities, there is a lack of response to previous treatments, or the severity of the infection is advancing, antibiotics with a follow up of forty-eight hours may be required (28,34).
Several antibiotics have been recommended to treat CA-MRSA depending on the severity, patient, and nature of the infection. These include trimethoprim-sulfamethoxazole, clindamycin, rifampin (in combination therapy), quinupristin-dalfopristin, vancomycin, linezolid, vancomycin, and tigecycline. Trimethoprim-sulfamethoxazole in combination with rifampin, and clindamycin are successful for treatment of SSTI; a susceptibility test is recommended on clinical isolates when resistance is a possibility. Quinupristin-dalfopristin and linezolid are active against almost all strains of MRSA and therefore should be used when current therapy fails; since decreased activity of vancomycin against CA-MRSA strains has been reported, use of this antimicrobial should be limited to severe sepsis such as endocarditis and septicemia. Tigecycline, approved in 2005 to treat complicated intra-abdominal infections and complicated SSTIs, should be used with caution in order to prevent the development of resistance (28,34–36).

**Resistant Enteric Bacteria**

**Definition of Enteric Bacteria**

The term ‘enteric bacteria’ generally refers to a large group of gram-negative rod-shaped bacteria found in the gut of animals and humans. Enteric pathogens are often transmitted by means of food or water (foodborne diseases) and are responsible for acute gastroenteritis; some cause systemic disease that may have chronic complications (37,38). Many enteric bacteria are commensal organisms in their primary hosts, however can be highly pathogenic if infection occurs in another species (37). This review is limited to the most common enteric bacterial pathogens of significance to public health in Canada.

**Campylobacter spp.**

*Campylobacter spp.* is the most common cause of enteric bacterial infection in humans around the world (39). *Campylobacter* species are motile, non-spore forming, comma-shaped, gram-negative rods. Fourteen species have been recognized within the genus and most reported infections of *Campylobacter* are caused by *C. jejuni* (40).

Campylobacteriosis is generally a self-limiting disease and is treated by fluid replenishment. However, in cases of severe or extraintestinal infections and in immunocompromised patients, antibiotics may be required. Erythromycin is the usual drug of choice for the treatment of *Campylobacter* infections (18). In addition to erythromycin, azithromycin is another macrolide that can be used, but macrolide resistance is spreading in many parts of the world (41,42). However, fluoroquinolones, gentamicin, and tetracycline also are clinically effective in treating *Campylobacter* infections when antimicrobial therapy is needed (13). Serious implications are associated with antimicrobial resistance in treatment situations, as *Campylobacter* isolates have demonstrated resistance to ciprofloxacin, doxycycline, ampicillin, roxithromycin, lincomycin, chloramphenicol, ceftriaxone, tetracycline, erythromycin, doxycycline, elemental quinolone, and nalidixic acid (37,44).

Fluoroquinolones used to be considered the drugs of choice for *Campylobacter* infection, but recent studies have demonstrated an increase in fluoroquinolone-resistant *Campylobacter* strains worldwide (38). Erythromycin is now considered the optimal drug for treatment of *Campylobacter* infections. Despite decades of use, the rate of resistance of *Campylobacter* to erythromycin remains low, and unlike other agents, it is not likely to damage other fecal flora (38,45).

Other reviews suggest that erythromycin resistance in developed countries, including the United States, is generally stable at less than 5% (46,47), although slightly higher resistance has been reported from Canada (48). A cluster of 11 erythromycin and ciprofloxacin resistant *C. jejuni* cases was reported from Quebec, Canada (49).

**Salmonella spp.**

*Salmonellae* are typical members of the family Enterobacteriaceae and are facultative anaerobic gram-negative bacilli that can infect or colonize a wide range of mammalian hosts. Medically important *Salmonella* organisms come from a single species, known as *Salmonella enterica*, which has
approximately 2,500 different serovars with familiar names such as *Salmonella* Typhimurium, Typhi, and Heidelberg (38,50,51).

In the 1990s, multidrug-resistant (MDR) *Salmonella* Typhimurium (MDR-ACSSuT) definitive phage type 104 (DT104), which is resistant to ampicillin, chloramphenicol, sulfonamides, streptomycin, and tetracycline, emerged and spread throughout the world (52). This strain is responsible for approximately 10% of *Salmonella* isolates in the United States today (52). Like MDR-ACSSuT *Salmonella* Typhimurium, MDR-AmpC *S. enterica* serovar Newport strains are resistant to at least ampicillin, chloramphenicol, streptomycin, sulfonamides, and tetracycline. In addition these, MDR-AmpC Newport isolates are resistant to amoxicillin/clavulanic acid and ceftiofur, and exhibit decreased susceptibility to ceftriaxone (53). Multidrug-resistant *Salmonella* strains are associated with excess bloodstream infections, hospitalizations, and death compared with pansusceptible strains (54–56). Helms and associates (56) determined that infection with quinolone-resistant *Salmonella* Typhimurium increases risk of illness or death 3.5 times (95% CI 1.4–7.1) within ninety days of initial infection, compared with that observed for infection with pan-susceptible strains.

Resistance to the extended-spectrum (third and fourth-generation) cephalosporins can occur in *Salmonella* species by means of the production of plasmid-mediated extended-spectrum ß-lactamases, as well as the acquisition of plasmids containing the AmpC ß-lactamase genes derived from the chromosomes of *Citrobacter freundii* and *Morganella morganii* (20,21).

Resistance to the commonly used antimicrobials in *Salmonella* is an important threat to public health. The patterns of resistance in the typhoidal and nontyphoidal *Salmonellae* are constantly changing (57).

**Verocytotoxigenic Escherichia coli**

*Escherichia coli* are gram-negative motile bacilli of the family Enterobacteriaceae. A primary reservoir for antibiotic-resistant *E. coli* is the gut. *Escherichia coli* O157:H7 is one of the more than thirty serotypes of *E. coli* known to produce Shigella-like toxins that are cytotoxicogenic to the intestinal vascular endothelial cells (37). Shiga-toxigenic *E. coli* have been established as a major cause of bloody diarrhea. In particular, *E. coli* O157:H7 infections can lead to hemolytic uremic syndrome with long-term chronic sequelae including renal failure (37,58).

To date resistance to ampicillin, cotrimoxazol, doxycycline, amoxicillin, co-amoxiclav, piperacillin, cefuroxime, ceftazidime, gentamicin, and ciprofloxacin has been documented in *E. coli* strains worldwide (59). Resistance has been reported in verocytotoxin-producing *Escherichia coli* (VTEC) to antimicrobial agents, including streptomycin, sulphonamides, and tetracycline (60,61).

**Shigella spp.**

*Shigella* is a genus of gram-negative bacteria closely related to *E. coli* and *Salmonella*. These bacteria invade and destroy the cells lining the large intestine causing ulceration and bloody stool. There are four species of *Shigella*: *S. dysenteriae*, *S. flexneri*, *S. boydii*, and *S. sonnei*.

More recently, shigellosis has become an increasingly significant public health problem due to development of antimicrobial susceptibility and multidrug resistance. This increased resistance frequently results in treatment failure, leading in turn to health complications and deaths (62,63).

*Shigella* strains have become progressively resistant to multiple antimicrobial agents, initially to sulfonamides, shortly after they became commercially available, then to tetracycline, chloramphenicol, and streptomycin less than ten years after each was introduced, and subsequently to ampicillin, kanamycin, and trimethoprim-sulfamethoxazole (64–67). A study by Replogle *et al.* in 2000 based in Oregon found that 59% of *Shigella* isolates were resistant to trimethoprim-sulfamethoxazole and 63% were resistant to ampicillin (66). Similar resistance patterns have been reported from England and Wales (68), Canada (69) and Germany (70).
Objectives

The objective of this work was to conduct a formal, comprehensive review of control strategies and interventions available to reduce both the development of antimicrobial resistant enteric bacteria, specifically *Campylobacter* spp., *Salmonella* spp., verocytotoxigenic *Escherichia coli*, and *Shigella* spp., and CA-MRSA, and the spread of such infections within Canadian communities. As part of this review, the current state of knowledge of such interventions and control strategies, focusing on public health, was synthesized. The following specific research question defined the scope of this review:

*Research Question*

What strategies, interventions, or other control options exist that may be used to reduce the spread of antimicrobial-resistant *Salmonella*, *Campylobacter*, verocytotoxigenic *E. coli*, *Shigella*, and CA-MRSA infections in Canadian communities, and what evidence supports these assessments?
Methods

A formal method of information retrieval, based on systematic review methodologies, was used and included the following:

- Identification of relevant databases for accessing peer-reviewed and grey literature
- Inclusion and exclusion criteria
- A clearly defined search strategy including search terms
- A method for determining the relevance of identified information
- A method for quality appraisal of the identified information

Search Strategy

Search space/locations

Databases

The following databases were searched for this review:

- PubMed/Medline
- CAB Direct
- Biosis – Web of Knowledge
- Cumulative Index to Nursing and Allied Health Literature (CINAHL)
- Cochrane Library

Websites

Websites of health technology assessment and related agencies, professional associations, and other specialized databases were also searched for relevant information. These websites were:

- Association of Medical Microbiology and Infectious Disease Canada
- Canadian Bacterial Surveillance Network
- Canadian Integrated Program for Antimicrobial Surveillance
- European Antimicrobial Surveillance System
- National Antimicrobial Resistance Monitoring System

- Alliance for the Prudent Use of Antibiotics
- Canadian Committee on Antibiotic Resistance
- Canadian Optimal Medication Prescribing and Utilization Service
- Community and Hospital Infection Control Association – Canada
- Public Health Agency of Canada
- Provincial ministries of health
- World Health Organization
- Centers for Disease Control and Prevention
- DanMAP
- Swedish Strategic Programme Against Antibiotic Resistance
- British Society for Antimicrobial Chemotherapy
- Society for Healthcare Epidemiology of America

Internet Searches

Finally, Google Scholar was searched for additional web-based material.

Search terms and techniques

First, the following key words were used for an initial search of the above search spaces:

- Antimicrobial, antibiotic, antibacterial, anti-infective
- Resistance, resistant, AMR
- Enteric disease
- Salmonella, salmonellosis, Shigella, shigellosis, E. coli, VTEC, Campylobacter
- Gastrointestinal, gastroenteritis
- MRSA, Staphylococcus aureus
- Veterinary, human public health
- Population
- Community
- Control
- Intervention
- Prevention
- Surveillance, monitoring
- Policy, policy evaluation
- Guidelines
- Best practices

The complete list of key words, phrase searches, and search strings are shown in Appendix A.
From those relevant articles identified in the above search, additional articles and references were identified by cross-referencing the reference lists in the identified articles, as well as conducting additional searches using author information from relevant identified articles.

Finally, upon the completion of the first draft, the list of identified relevant articles was reviewed by study team members (Jeff Wilson, John Conly, Tom Wong, Gayatri Jayaraman, and Andrew Papadopoulos) to identify any missing grey literature or articles in preparation or in press.

Database of Search Results
A database of identified references was created using RefWorks, an online research management program.

Data Collection and Appraisal Methods

Data Collection Timeframe
The primary search for material was conducted from February 9 to March 6, 2009. Cross-referencing articles, secondary searching by author, and expert review of the identified articles was completed by May 31, 2009.

Abstract Relevancy Screening
Abstracts were screened for relevancy in RefWorks using the Relevancy Screening Checklist (Appendix B) developed for this review.

Inclusion criteria
References that focused on strategies in the human population to control and prevent MRSA and enteric bacteria, specifically verocytotoxigenic E. coli, Shigella, Campylobacter, and Salmonella, were included. Special emphasis was given to literature focusing on the Canadian community setting. The search was restricted to the English language.

Exclusion criteria
This review does not include information on health care-associated infections or control methods relevant to health care settings unless such information (a) describes a significant risk to the community and thus represents an important control point, or (b) clearly demonstrates how such control strategies can be successfully applied in community settings.

Appraisal of Relevant Information
All documents identified as relevant through the abstract screening were reviewed as follows (Appendix B). Due to the limited availability of literature specifically describing control and prevention options for the aforementioned microorganisms at the community level, a semi-structured appraisal process was used to ensure a high sensitivity of information capture (e.g. unrelated papers or those with less rigorous study designs that suggested potential risk pathways were screened and information captured).

A formal critical assessment was not conducted as the breadth of the study question and relevant literature precluded this being done in a meaningful manner. However, a qualitative evaluation of papers was performed based on critical appraisal guidelines (71). Papers that met the inclusion criteria were read and assessed based upon the following categories: risk factors, modes of transmission, sources, proposed hypothesized interventions or methods to prevent the spread of infection, and efficacy studies of intervention or prevention methods. From these papers, relevant information was extracted and used to create a comprehensive synthesis of the available literature.
Results

A total of 1,467 references were identified via the search. Of these, 563 references met the abstract relevancy screening and were thus included in the RefWorks database. Of these, 205 references met the requirements of the evaluation.

Results: Methicillin-Resistant Staphylococcus aureus

Numerous guidelines and review papers exist that describe the epidemiology and management of CA-MRSA, capturing information current to circa 2005. Since 2006, several new risk factors have been identified and several effectiveness studies have been published. Therefore, existing guidelines and review papers were summarized to provide a baseline of the known areas for the control of CA-MRSA (e.g. traditional risk groups, factors, and transmission modes), as well as recommended control options. We then summarized new literature from 2006 onwards to identify new or potential populations at-risk, risk groups, and risk factors, or new or potential transmission modes, as well as evaluated control options. For the purposes of this review, colonization is defined as the presence, growth, and multiplication of the organism without observable clinical symptoms or immune reaction. Infection refers to invasion of bacteria into tissue with replication of the organism accompanied by clinical signs of illness.

Risk Factors and Risk Groups

There are many well documented risks factors for CA-MRSA. Generally, the use of antimicrobials, skin-to-skin contact, crowded living conditions, contaminated environment, poor hand and personal hygiene, an infected or colonized housing mate/family/pet member, comorbidities, or compromised skin are all considered risk factors for CA-MRSA (72).

Several papers have illustrated risk factors for CA-MRSA. For instance, in a recent study, Beam and Buckley (73) conducted a retrospective comprehensive review to determine the prevalence rates and risk factors associated with CA-MRSA. After reviewing the available literature from 1966–2002, they concluded that individuals with health care related risk factors were more likely to become colonized with CA-MRSA than those who had no risk factors. Overall, 85% of hospitalized persons and 47.5% of healthy individuals had ≥1 health care-related risk factors for CA-MRSA such as recent hospitalization, outpatient, nursing home admission, antibiotic exposure, comorbidity, injection drug user, and close contact with an infected individual (73).

In a recent Danish study that aimed to identify risk factors for CA-MRSA, the only significant risk factor observed was non-Danish origin, likely due to close contact with non-Danish relatives or friends from countries that have a higher prevalence of MRSA (74). In another Danish study, risk factors and trends observed included a high prevalence in children from ages 1–10; travel, and/or contact with non-Danish individuals were frequently reported (75).

Specific risk groups such as children, certain ethnic groups, athletes, injection drug users, men who have sex with men (MSM), military personnel, correctional facility inmates, MRSA carriage or previous infection, chronic skin disorders, lower socio-economic groups, veterinarians, daycare, travel, and construction workers have been associated with CA-MRSA infections and colonization. Notable recent studies, which address a few select groups, are addressed in the following section. Additionally, more recently identified MRSA transmission pathways have been included in this section.

Children

Unlike in HA-MRSA, children and neonates are particularly susceptible to CA-MRSA colonization and infection. There are several review articles and case studies that provide an overview of the factors associating children and CA-MRSA, as well as the prevalence among this risk group (33,35,76–83). Healthy children can become colonized with CA-MRSA and may go on to spread the bacterium to other children, family members, and those in close contact.
A nasal colonization study found that among kindergarteners in Taiwan 9/68 (13.2%) healthy children with no reportable risk factors were colonized with CA-MRSA. All 9 strains were highly resistant to erythromycin and clindamycin and 8/9 strains were genetically related by PFGE (84). In another nasal colonization study among 123 healthy children, 73 were nasal S. aureus carriers and 4 (5.5%) were colonized with MRSA. Three of the 4 MRSA isolates were PVL positive (85). In the same study, 105 of 170 children who were patients (62%) were considered community-onset MRSA. In this study, children under the age of five years were two-fold more likely to have MRSA infection than older children (85).

Neonates are particularly susceptible to MRSA, and CA-MRSA has frequently been associated with outbreaks among neonatal intensive care units (NICU) (86–89). Transmission to and from colonized health care workers (HCWs) and family members have been identified as the source of these outbreaks (86–90). For instance, in two 2004 clusters of CA-MRSA in maternal-newborn units in Toronto, 41 babies were found to have been colonized or infected; 9 mothers and 7 of their babies were also infected or colonized (83). After several cultures, a nurse with eczema was confirmed as the likely source of transmission (83). The babies and mothers who were cared for by the nurse were 23 times more likely to be colonized or infected with MRSA (OR=22.7; 95% CI 3.3-195.9) (83).

In general, studies have identified prior use of antimicrobials and daycare exposure as a risk for CA-MRSA among children, as well as vaginal delivery and maternal smoking of tobacco or marijuana (OR=5.44; 95% CI 1.69-17.6; P=0.05) (91–93). Further risks among children include low socioeconomic status represented by Medicaid insurance program and household crowding (94). Multivariate analysis of risk factors for MRSA nasal colonization among children found that black race and previous systemic infection were significantly associated; however, race is likely to be a confounder (94). Comorbidities such as atopic dermatitis have also been associated with MRSA, although not to the same degree as S. aureus (95). Conversely, a study by Niniou et al. (91) found in children with CA-MRSA infections that intrafamilial transmission of the infection was the only significant risk factor when comparing CA-MRSA and MSSA (91). The administering of systemic antimicrobials prior to caesarean section to non-smoking mothers (CI 0.004-0.93) and endotracheal intubation (CI 0.09-1.07) appeared to be associated with health care-associated MRSA as opposed to CA-MRSA (92).

**Ethnic Groups**

As previously mentioned, certain ethnic groups are associated with CA-MRSA infection. This is likely due to differences in socioeconomic status, crowded living conditions, less access to proper health care, education level, and poor personal hygiene rather than genetic factors. More recent CA-MRSA clusters among ethnic groups, such as Pacific Islanders, Inuit, and Aboriginals have been documented. In Canada (96,97), CA-MRSA was first reported in the late 1980s in aboriginal populations in Alberta. In August of 2006 and 2007, 43 cases of CA-MRSA were reported in a remote Inuit community in Nunavut (98). Cases primarily consisted of individuals aged five to nine years and twenty to twenty-nine years. Molecular testing confirmed that the available isolates were CMRSA-7 (USA400) and CMRSA-2 (USA100). The most common risk factors among the afflicted were previous exposure to a health care worker within the last year (83%), antibiotic use within the last year (65%), household contact with a MRSA positive individual (24%), and exposure to a person with a skin infection or condition (21%). A similar increase in CA-MRSA cases, particularly among individuals under twenty years, was also reported in an outbreak of Prairies’ First Nations where socioeconomic status, crowded living conditions, and limited healthcare access were the most probable risk factors (99).

In a 2004 study, the prevalence of CA-MRSA carriage and infection among primary school children living in a small indigenous community in Queensland was assessed using nasal, throat, and skin swabs (100).
Ninety-two (57%) of 157 eligible children were included in the study. Of the 92 children tested, 27 (29%) were colonized or infected with *S. aureus*, and of those children, 14 (15% of total) harboured MRSA. Three MRSA clonal groups were observed and 8 (9%) carried classic CA-MRSA strains (100).

Between 2000 and 2002, the State of Hawaii laboratory surveillance in ambulatory settings observed a pronounced increase in cases of MRSA. As such, in 2003 a retrospective study was conducted in which clinical outcome and identification of risk factors for CA-MRSA were identified (Estivariz *et al.*, 2007). Microbiological records from four health care facilities with hospital and ambulatory clinic services in Oahu and Kauai from 2001–2003 were selected for the sample population. Overall, 1,389 patients were identified, 249 patients had insufficient information, and 389 (28%) were considered CA-MRSA cases. The study revealed that Pacific Islanders comprised the majority of CA-MRSA cases (51%), although, they represented only 24% of the total population. Sixty-three percent (148/259) of Pacific Islander adults and 24% (29/118) of children had comorbidity such as diabetes mellitus, asthma, and eczema/atomic dermatitis (101). In addition, receipt of prior antibiotics was associated with a higher risk for hospitalization. PFGE-tested isolates were 65% (26/40) USA300 strain; in addition, USA1000, USA1100, USA100 and USA800 were isolated.

**Athletes**

Athletes are a well established risk group for CA-MRSA illness and colonization. Participants of sports which are high contact, such as football, rugby, hockey, soccer, basketball, and wrestling are at risk for direct skin-to-skin contact; however, sports which are non-contact such as fencing, cross-country running, volleyball, baseball, canoeing, and weight lifting, are at risk likely due to sharing of facilities, equipment, and personal items such as towels, soap, and razors (102–106). In a recent paper by Archibald *et al.*, (107) a retrospective case-control study, an observational study and a microbiological survey of football players identified that water bottles and gloves were frequently shared among teammates, serving as a potential route of transmission. Additionally, exercise equipment and tackling equipment were not cleaned after every use (107). The findings also suggested that players were more likely to contract MRSA if they previously had a skin infection, had poor hygiene, were less aware of MRSA precautions, or were freshmen or a transfer student (107).

**Drug Use**

Injection drug use is a high risk activity for contracting bloodborne infections (108). In addition, skin and soft tissue infections (SSTI) are frequently reported among injection drug users (109). This is because of unhygienic situations in which the drugs are administered (i.e. sharing non-sterile syringes) (108). In addition, socioeconomic demographic groups, crowded housing or the use of crack houses, poor sanitation, sharing of drug paraphernalia, and unhygienic treatment of the skin have also been identified as risk factors rather than poor immune status (110). Past studies have indicated a high colonization rate of *S. aureus* among injection drug users and the ability of MSSA to colonize, which suggests drug use or shared drug paraphernalia as a potential route of transmission for MRSA (108,109).

In a matched case-control study conducted in California USA, Huang and colleagues (109) identified injection drug use as a significant risk factor for CA-MRSA as well as other potential risk factors for CA-MRSA in the community. From 127 CA-MSSA, 381 uninfected patients and 127 CA-MRSA culture positive cases, characteristics and demographic baselines were recorded. Cases were age and date matched with two control groups; randomly selected uninfected patients (glucose tested) and CA-MSSA infected patients from the same institution. The study found that 49% (AOR=2.11; 95% CI 1.1-4.3 & 4.09; 95% CI 2.2-7.5) of CA-MRSA cases had a history of injecting drug use (P<0.001), compared to only 17% and 9% of CA-MSSA and uninfected patients, respectively. The data also suggested that socioeconomic status was a risk factor for CA-MRSA.
Lower socioeconomic status was reported more frequently with CA-MRSA cases, possibly due to the relation to IDU, homelessness, or decreased hygienic conditions (109).

In another drug use case-control study conducted in Georgia, USA in 2005, risk factors (such as methamphetamine use) for MRSA SSTI among residents of a community with a large rural population were assessed (26). The study found 119 cases with SSTI infections, of which 81 (68.1%) were MRSA. Of those 81 patients, 15 were admitted methamphetamine users; 8 had MRSA SSTI, 5 were controls (non-SSTIs), and 2 had MSSA infections. All available MRSA isolates from 6 methamphetamine users and 21 non-users were USA300. MRSA cases were associated to methamphetamine usage (OR=5.10; 95% CI 1.55-16.79) in comparison to the control group. In addition, having a recent skin infection (AOR= 7.92; 95% CI 4.10-15.28), engaging in sexual acts with someone afflicted with a skin infection (AOR=5.42; 95% CI 1.68-17.50), picking of skin (AOR=2.53; 95% CI 1.22-5.23), and crowded living conditions (AOR=1.78; 95% CI 1.004-3.15) were associated with MRSA infections (26).

In a study to assess the relationship between drug abuse, length of drug use, route of administration, and CA-MRSA, 60 opiate addicts (inhalational and intravenous), 60 non-addict control patients, and 15 healthy volunteers from Cairo, Egypt were tested for MRSA colonization (108). The study found that the proportion of addicts with MRSA (colonized and/or infection) was significantly higher than that of the non-addict MRSA group (P<0.01). No MRSA was isolated from healthy volunteers. Additionally, 58 addicts (in comparison to 7 non-addict controls) reported the misuse of antibiotics as a preventive measure against infections. Both injection and inhalational drug use were associated with MRSA colonization, particularly in the nose. Thirty-one of 60 (52%; P<0.05) addicts’ nasal swabs were found to be MRSA positive in comparison to any other carriage location in both addict and non-addict groups. In addition, sputum, throat, blood, and pus were also positive swab locations and all had corresponding positive nasal swabs. Thirty-five percent (6/17) of addicts who administered drugs by injection were found to be MRSA positive, while 55% (6/11) and 59% (19/32) addicts who administered drugs by inhalation and injection/inhalation combined were MRSA-positive. Furthermore, the results showed that MRSA infections increased with the increase in length of addiction. The authors speculate that addicts are more prone to MRSA infections possibly due to impaired immune systems (excluding HIV), unhygienic syringe use and drug administration, and the altering of the nasal mucosal integrity due to drug use (108).

In another study in 2004, an outbreak of USA300 MRSA was reported in Calgary, Alberta among an urban population with histories of drug use, homelessness, or incarceration (110). Of 40 cases, 28 (70%) had a history of illicit drug use, homelessness, or incarceration; 98% of the cases suffered from SSTI infections and 14 (50%) cases had hepatitis C comorbidity (110). Incidence rates among high risk and low risk individuals were 240.2 and 169.4 per 100,000 population, respectively. The authors also found a possible relationship with crack cocaine or cocaine use as a high risk activity; of the high risk group, 71% (20/28) reported using cocaine or crack cocaine. The sharing of drug paraphernalia, syringes, unhygienic drug use, social group networks, and wound care practices could serve as a possible means of transmission for CA-MRSA (110). For example, 4/12 crack pipes tested were positive for MSSA (110).

In 2005, Gilbert et al. (111) conducted a cross-sectional prevalence study in the same demographic groups to measure the prevalence of colonization or infection with USA300 strain of MRSA, as well as to identify the factors associated with USA300 colonization or infection (111). From 271 study participants, the overall prevalence was estimated to be 5.5% (95% CI 3.1%-9.0%); colonization and infection with USA300 strain were 4.8% and 1.8%, respectively (111). Interestingly, 2 of 4 crackpipes sampled were positive for the USA300 strain, of which 1 crack pipe owner tested negative for MRSA.
Of the 271 study participants, 55% (149) reported a history of homelessness and 95.2% (258) reported a history of illicit drug use. Living in crowded residence facilities, cocaine or crack cocaine use, borrowing crack pipes, using drugs at crack houses, or injection-related behaviours were not found to be associated with colonization or infection with USA300 strain. Other significant risk factors reported in the study were allowing others to manipulate skin infections, drug use with either a sex trade worker (STW) or with a client, with a casual sex partner, or with a regular sex partner. Cases were also more likely to have a greater number of binges, binges lasting five days or more, and used drugs multiple times during the day. In addition, cases were more likely to have had recent skin infections, self-administer old antibiotics, and seek medical attention.

**Men who have Sex with Men**

Men who have sex with men (MSM) are a well-known risk group for CA-MRSA infections often due to the close person-to-person intimate contact, fecal carriage, and high risk sexual activities. Little information regarding CA-MRSA colonization and the potential for dissemination in the community has been gathered. Most studies reflect MSMs who are HIV-positive; however, more recent literature has shown that MSM behaviour, independent of HIV status, is a risk factor for CA-MRSA (112). A cross-sectional study in Toronto, Ontario was conducted by Antoniou et al. (112) to determine the prevalence of CA-MRSA colonization in MSM cohorts. Of the 500 participants, 8 (1.6%; 95% CI 0.6-2.6%) were CA-MRSA positive from nasal or rectal or both swabs, of which 4 were from HIV-positive individuals. The prevalence was lower than expected and therefore it is likely that the true prevalence is low in that particular sampling area. There were no observable differences between the CA-MRSA positive and negative groups for variables within the previous three months for high risk sexual behaviours, antimicrobial use or treatment for a sexually transmitted infection.

Another recent Canadian study, which assessed and described the clinical characteristics and management of CA-MRSA infections in a MSM cohort, reported that 17 patients (out of approximately 12,000 patients in the practice) were positive for MRSA, of which 12 were HIV-positive. The overall relevant results showed that antibiotic exposure within the previous six months was the most important risk factor for infection among the study participants (113)

Multidrug resistance among USA300 has been reported among certain risk groups such as MSM. In an attempt to investigate a multidrug-resistant USA300 cluster of infections in the San Francisco and Boston areas, Diep et al. (114) reported the incidence and risk factors of multidrug-resistant USA300 in San Francisco and Boston among MSM. This was accomplished by conducting four studies: a population-based study to determine the incidence and spatial clustering of multidrug-resistant USA300; two clinic-based cross-sectional surveys to identify risk factors; and a post hoc analysis of multidrug-resistant USA300 isolates obtained from emergency departments. The researchers reported from the population-based survey that the MRSA incidence was 275 cases per 100,000 persons (95% CI 256-295/100000), with an annual incidence of multidrug-resistant USA300 (containing the conjugative pUSA03 plasmid) of 26 cases per 100,000 persons (95% CI 16-36/100000). In the HIV clinic-based study, 183 consecutive MRSA patients treated were selected and of those, 170 (93%) were USA300 and 30 of those were multidrug-resistant (16% of total MRSA cases). In comparison, the general population in San Francisco General Hospital had only 2% of cases that were MDR. Bivariate and multivariate analyses indicated male-male sex as a significant risk factor for multidrug-resistant USA300 infections (AOR=13.2; 95% CI 1.7-101.6; P<0.001) 95%. In addition, the use of antimicrobials and prior MRSA infections also showed a strong association with multidrug-resistant infections. In the community health clinic-based study, similar results were observed among MRSA patients. Of 130 MRSA patients, 126 (97%) had USA300 and 60 of those were multidrug-resistant (46% of total MRSA). All of the patients with multidrug-resistant MRSA were MSM and the information
available suggested that although HIV infection is a risk factor for multidrug-resistant USA300 infections, male-male sex is also an independent significant risk factor. Finally, in the emergency department study, 212 USA300 isolates from ER departments in 11 US cities identified only 2 multidrug-resistant isolates that carried the pUSA03 plasmid, of which 1 patient was MSM (114).

Heterosexual High Risk Activities

High risk sexual activities are not restricted to MSM populations, but also involve those with heterosexual partners. Although not typically recognized as a risk factor for MRSA, direct person-to-person contact can serve as a means of transmission of the bacterium. The definition of high risk individuals in this instance is those who do not exercise proper precautions between infectious and non-infectious individuals and as a result allow for the transmission between partners. Cook et al. (115) conducted a prospective community-based study of the prevalence of CA-MRSA over a two-year period. Of interest, they examined three households in which heterosexual transmission of CA-MRSA likely occurred. In one household, a child contracted the CA-MRSA from her mother who had multiple partners and who reported that her husband and one partner had pimples. Although not isolated in nasal swabs, vaginal and groin swabs were positive for CA-MRSA and had identical PFGE patterns, suggesting sexual transmission. In the second household, a husband and wife both became infected multiple times. Nasal swabs from both persons were negative; however, groin and vaginal swabs were both positive and identical. The third household involved a woman who had recurrent MRSA abscesses which were linked by association to her boyfriend who suffered from infections while in the military. The woman consistently had negative nasal swabs but was positive on groin swabs (115). Overall, 10/345 (2.9%) of the index cases identified through the clinical microbiology database were positive for infection in the genital area, although, it is likely these numbers are underestimated.

Additional instances of genital CA-MRSA have been documented. For instance, in one case study, a man who had unprotected intercourse with an infected prostitute contracted a genital CA-MRSA infection, suggesting sexual transmission. He had no other risk factors for MRSA (116). In another case study documented by the same author, a healthy immunocompetent woman was also reported to have contracted MRSA from her sexual partner. A subsequent retrospective chart review of all patients presenting genital infections consistent with MRSA infections to the emergency department found that 18% of infections were confined to the genital region. Sexually transmitted CA-MRSA infections are likely to be underreported and more likely than previously believed (116).

Military

Although CA-MRSA clusters among those serving in the military are well documented in the literature, few reports have been published since 2006. Those serving in the military are particularly susceptible to becoming colonized or infected due to crowded living conditions, the sharing of barracks and personal items, use of contaminated equipment, poor access to laundering and bathing facilities, and unhygienic conditions (117). Military aviators may be at an even higher risk as there is an increase in shared life-support equipment, which is often not sanitized between uses (117). Overall, the prevalence of CA-MRSA is likely higher than reported as skin lesions are often misdiagnosed, for example, as spider bites (72).

Veterinarians and Animal Handlers

Veterinarians and other individuals who work closely with animals have previously been identified as a risk group for CA-MRSA. Close contact with infected or colonized animals is the most significant high risk behaviour among this risk group. Hence, occupational health risk among veterinarians is well documented (118,119). For instance, one survey found that veterinarians were significantly more likely to be colonized with MRSA in comparison to those without animal exposure (3.9% vs. 0.7%; P=0.02) (120).
The length of time spent with animals was also found to be associated with MRSA acquisition; however, exposure to pigs was not significant (120). In another survey which assessed the prevalence of MRSA nasal colonization and risk factors it was found that 6.5% (27 of 417) attendees at an international veterinary conference were colonized (119). The only significant variable for colonization was large animal practice (OR=2.9; 95% CI 1.2-6.6). Interestingly, only two MRSA clones were isolated from the nasal swabs – CMRSA-5 and CMRSA-2. CMRSA-5 (USA500) were only isolated from large animal personnel while CMRSA-2 were associated primarily with small-animal clinic personnel.

In another survey of veterinarians at an international swine conference, 12.5% (34/272) of participants were found to carry a meca-positive S. aureus strain (121). Of these, 31 participants carried non-typeable strains but after spa-typing were classified as variants of ST398, a MRSA strain known to pass between pigs and humans (121). Diversity among the clones was found among the veterinarians; SCCmecV (n=24), IVa (n=3) and Ill (n=2). Univariate analysis found that MRSA carriage was associated with frequent (daily or a minimum of five hours per week) pig contact, while contact with cows, country of origin, and use of protective measures did not prove significant (121).

Frequent contact with colonized horses is also a source of MRSA infection among veterinarians and animal handlers. Among 257 survey participants at an equine conference, 26 (10.1%) were positive for MRSA (118). After multivariate analysis, four factors associated with MRSA acquisition were identified as having an MRSA positive equine patient, previous MRSA infection, hand washing between infectious cases, and hand washing between farms (118). The most common clones were equine clone USA500 (n=14), USA100 (n=9), and USA300 (n=1) (118).

Overall, these studies show the possibility of human MRSA colonization and infection due to close contact with colonized animals. Although it has previously been established that animals can become colonized with MRSA, putting veterinarians, technicians and those with close contact to animals at risk, it is important to note that the transmission pathway between animals is bi-directional and the identification of identical MRSA in both humans and animals simultaneously is not necessarily indicative of zoonotic transmission (122).

A cluster of MRSA cases among family members of a pig farmer, his pigs and co-workers was investigated in 2004 in Denmark (123). After unsuccessful treatment of a young mother with mastitis, her family was screened for MRSA. Her baby daughter and husband were also found to be colonized six months later. In an attempt to find the reservoir of the MRSA, pigs and farming co-workers on the farm were also screened. In total, ten pigs were randomly selected from the holdings closest to the home and swabbed. Family members and co-workers received throat and nasal swabs. The results showed that 3 family members, 3 co-workers, and 8/10 pigs were colonized with MRSA. Only the mother and child were affected clinically. All pig MRSA isolates were non-typeable by PFGE and were identical to the human MRSA isolates. The results indicated that this cluster of cases was not only zoonotic in origin but also transmitted person-to-person (123).

**HIV Infection**

In a recent study, CA-MRSA infections among HIV positive individuals from 1993 to 2005 were analyzed for trends, infection rates, and risk factors. In total, 435 HIV-positive individuals were assessed, of which, 31 were positive for MRSA. Twenty-nine of those were considered CA-MRSA-positive, and 26 were reportedly SSTI. There were no significant differences in demographic characteristics of HIV-positive and uninfected individuals. Risk factors observed in this study after multivariate analysis were the recent use of beta-lactams (OR=2.46 for the receipt of 1 prescription, P<0.001), low current CD4 counts (OR per 100 CD4 cells=0.84, P=0.03), a higher HIV maximum log10 HIV viral load (OR=4.54, P<0.001), and a history of syphilis/high risk sexual activity (OR=4.55, P=0.01). Overall, the HIV-positive population in the study had an 18-fold higher infection rate than the general public (124).
**Tattoo Recipients**

Between 2004 and 2005, six unrelated clusters of SSTI caused by CA-MRSA were reported among 44 tattoo recipients from 13 unlicensed tattoo artists in Ohio, Kentucky, and Vermont (89). There were 34 primary and 10 secondary USA300 cases who were otherwise healthy reported during the outbreaks; one Ohio patient reportedly suffered from hepatitis C. Although gloves were often worn during tattooing, other hygienic infection control measures were frequently not observed and gloves were often not changed between clients. Furthermore, lesions were also observed on the hands of tattooists. Secondary cases were likely to have occurred through person-to-person contact. These clusters of CA-MRSA illustrate the importance of personal protective equipment and infection control procedures in preventing transmission of the bacterium.

**Living with a Carrier or Case of CA-MRSA (Familial Transmission)**

Close contact and shared environment/fomites with a carrier or an infected individual is a known risk for contracting CA-MRSA. Zafar and associates (125) designed a study to assess the frequency of nasal colonization with CA-MRSA among CA-MRSA patients and members of their households over an eighteen-month period. In total, 51 patients were enrolled into the study, 18 of which did not have household members. High colonization rates in patients and high MRSA and MSSA rates among household members were observed. Of the 51 enrolled patients, 21 (41%) were colonized with MRSA. In addition, 10/49 (20%) household members were colonized and carried the same PFGE pattern as the corresponding patient. The risk for MRSA colonization among household members was highest for parents of the patient. Although household associations were not found to be significant, it is worthwhile to note that the sample size was small and likely to have insufficient power to detect real differences were they to exist. From 76 isolates obtained from both infective and colonized cases, 68 were deemed related and only 4 possessed unique PFGE patterns (125).

In another study conducted in Hong Kong in 2004–2005, patients presenting with CA-MRSA infections who were reported to a monitoring system were recruited for a study to screen household members prospectively (126). Through the reporting system, 24 episodes of SSTI and 1 case of meningitis caused by CA-MRSA were identified among 23 patients. The 23 patients belonged to 21 unrelated families, of which 12 families (46 members) participated. In total, 2 infections and 4 carriers (13%) of CA-MRSA were identified amongst 2 families through nasal, axillary skin, and cutaneous wounds. Interfamilial transmission was confirmed through PFGE analysis (126).

Multiple occurrences of familial transmission of CA-MRSA were also documented in a two year Dutch study (123). During the study period, 10 PVL- MRSA familial transmissions were observed; 7/10 had skin infections and 6 families had a link with a foreign country (123). Twenty-seven MRSA isolates were assessed using PFGE, spa-typing, and multilocus sequence typing; members within a household carried the same strains, indicating familial transmission. The most common transmission involved parent to child or vice versa, although multiple transmissions between siblings and parents were also observed. Of note, one family had both PVL-negative and PVL-positive strains within the same household. Similar strains were found between families and it was later discovered that those families lived within the same neighbourhood. Overall, 7/10 families carried USA300 strains of MRSA, while the remaining 3 families carried the ST59 strain (123).

**Emergency Department and Hospitalized Patients**

It has been previously believed that certain MRSA clones were exclusively confined to either the hospital or community environments. However, more recent research has identified the encroachment of CA-MRSA strains into the hospital setting and in some instances causing outbreaks (127). According to the 2006-2007 Canadian Nosocomial Infection Surveillance Program (CNISP) results, there was an
overall minor increase in MRSA cases (1%) from 2006 to 2007; however, among those cases reported by CNISP hospitals, there was a CA-MRSA increase of 6% (128). This raises concerns as CA-MRSA which appears to be more virulent is now among a population of compromised patients (127). The following studies validate the movement of CA-MRSA into the hospital environment and the replacement of classic HA-MRSA clones.

To investigate the shift in CA-MRSA to the health care setting, Popovich et al. (129) conducted a study to describe the epidemiology of seven years of MRSA bloodstream infections by using phenotypic and genotypic analysis and by reviewing charts and collecting patient-level information to determine risk factors for MRSA (129). The study identified an increase of 24-49% in community-genotypes over the time span of Jan 2000 to June 2003 and July 2003 to Dec 2006. In contrast, hospital-onset MRSA occurrences remained stable throughout the study period. The risk for hospital MRSA bloodstream infection due to a community strain increased in comparison to hospital strains causing hospital-onset illnesses. Moreover, there was a significant decrease in clindamycin, gentamicin, and ciprofloxacin resistance which corresponded to the increase in CA-MRSA strains (129). Upon multivariate analysis there were no significant risk factors for infection caused by CA-MRSA in comparison to HA-MRSA. It is important to note that although CA-MRSA and HA-MRSA strains were identified, the authors did not determine if the patients were actually colonized prior to hospital-onset.

In a similar study in Taiwan, researchers examined the distribution of SCCmec types among 382 HA-MRSA and 26 CA-MRSA isolates obtained over a 7 year study period. While SCCmec IV was predominately associated with CA-MRSA, 3-20% of HA-MRSA were SCCmec IV isolates from 1999-2004. However, a substantial shift was noted in 2005 where the prevalence increased to 43%. Overall, CA-MRSA patients were observed to be younger than HA-MRSA patients. Additionally, CA-MRSA strains (including hospital-associated SCCmec IV) were found to be susceptible to antimicrobials. Molecular testing of the isolates found three major clusters that accounted for 77% of the isolates. From those clusters it was found that the pulsotypes B and C, which contained SCCmec types IV and V, had spread between the community and the hospital environments (130).

A retrospective study in Alabama examined MRSA isolates from 2000–2004 to determine when CA-MRSA first emerged in both outpatients and inpatients, as well as to determine the overall MRSA population dynamics (131). Two hundred and fifty-three study isolates were selected at random from the surveillance isolate bank based upon source location. Patient medical records were also concurrently reviewed to establish the isolates as HA-MRSA or CA-MRSA. Molecular analysis of the isolates found that the USA300 genotype was first isolated in the outpatient population in 2001 (2/15) and in 2003 (1/36) for the inpatient population. In 2004, the highest prevalence of USA300 was observed in both inpatient (14/35) and outpatient populations (8/14). Overall, USA300 was the second most common (8.4%) pulsotype found among HA-MRSA isolates (131). CA-MRSA strain USA300 was not only strongly associated to CA-MRSA patients but also found among hospitalized patients suggesting the shift of dominance in traditional hospital strains (131).

The University Hospital Basel in Switzerland, which has an overall low MRSA prevalence, tested inpatient strains from 2000–2004 (excluding epidemic and outpatient isolates) to determine if the presence of SCCmec IV and PVL corresponded with the epidemiological information obtained from patients (132). In total, 77 isolates from sporadic cases were analyzed; 14.3% (11) were classified CA-MRSA and 85.7% (66) were classified HA-MRSA. The majority of the analyzed strains originated from colonized patients (75.8%), while only 24.2% were came from infections. Among those, SCCmec IV/Va was the most frequently isolated (42.9%) from patients; the rate of SCCmec IV/Va also increased from 33.3% to 57.9% from 2000 to 2004 and the rate of SCCmec IV/Va from HA-MRSA strains also increased from 33.3% to 66.7% (132). Overall, sporadic cases of...
CA-MRSA have increased in the hospital environment and consequently are replacing well-known hospital strains of MRSA (132).

Finally, Huang et al. (133) in a retrospective case study described and compared the characteristics associated with CA-MRSA and HA-MRSA infections in patients at UC-Davis Medical Center from December 2003 to May 2004 (133). The study identified 283 MRSA patients; 127 (44.9%) met CA-MRSA classification and 156 (55.1%) were classified as HA-MRSA. USA300 was found significantly more often among CA-MRSA isolates (87%, 108/124), although it was also found among HA-MRSA isolates (33%, 48 of 147 P<0.001. Similar to the previously mentioned Taiwan study, HA-MRSA USA300 strains were significantly (P<0.01) less resistant to antimicrobials in comparison to other HA-MRSA strains; however, USA300 from CA-MRSA sources were significantly less resistant to ciprofloxacin than HA-MRSA strains.

What can be taken from these studies is that overall, classic HA-MRSA clones which have dominated the hospital environment appear to be becoming replaced by less resistant CA-MRSA clones. CA-MRSA could have a lower cost of fitness (or increased energy efficiency) due to the lack of resistance genes, allowing it to out-compete HA-MRSA (127). In addition, the apparent increased growth rate may also be beneficial for CA-MRSA strains. Alternatively, increased colonization in the community could be responsible for the influx of patients into the hospital. To prevent the further development of antimicrobial resistance, three control approaches were proposed by Wenzel et al. (127): limit the introduction of the microorganism into the community and healthcare settings, establish effective antibiotic stewardship, and promote infection control policies and procedures to prevent the transmission of the microorganism (127).

Potential for Waterborne Transmission

The survival dynamics of fourteen HA- and two CA-MRSA strains were examined by Tolba and colleagues (134) in samples of aquatic (river), marine (sea), and recreational (pool) water (134). No significant differences between HA-MRSA and CA-MRSA strains were observed in survival dynamics; however, both river and seawater samples survived longer than recreational water. Enumeration of MRSA strains in pool water samples was not able to detect viable organisms after two days. Both river and seawater sustained MRSA for up to fourteen days post-inoculation; however, seawater had significantly higher (P=0.02) bacterial counts than river water (134). These results demonstrate the potential for waterborne transmission of MRSA and particularly for the need of proper recreational water chlorination. However, it is hypothesized that given the dilution factor and large inoculation dose needed to reach critical counts to elicit a human infection, the likelihood of infection is quite low (134).

Routes for Indirect Person-to-Person Transmission

Potential indirect person-to-person transmission routes have also been identified. In these cases, a contaminated fomite or environmental source could serve as the means of transmission. These previously unrecognized sources should be considered when examining methods for infection control or prevention.

Scuba diving equipment

Although previously not considered a risk factor, the improper cleaning or sharing of scuba diving equipment may be a possible transmission route for MRSA (135). Two instances of CA-MRSA infections, both males from Switzerland with unremarkable medical histories, were reported among scuba divers in the Philippines. The strains isolated from the two divers were clonally related and consistent with the Philippines strain. Although the exact source of the infections could not be isolated, it was hypothesized that the use of rented scuba gear was
the source (135). Because scuba gear is infrequently cleaned between uses, this poses a likely source of transmission between gear and users (135).

**Coins**

It has been previously established that currency (banknotes and coins) may harbour a plethora of microorganisms which in turn can be transmitted person-to-person through money exchange (136). Because *S. aureus* has been isolated previously from currency, the survival dynamics of MRSA was examined on coins (136). Using two strains of CA-MRSA and twelve strains of HA-MRSA, coins were inoculated both directly and with organic matter (pus and blood). Lengths of survival time and enumeration counts on the various mediums were measured. This study found MRSA was not detectable on coins inoculated directly with MRSA after twenty-four hours; however, coins which were inoculated with an organic substrate (pus and blood) and MRSA had survival times up to thirteen days. A 1 log and 2 log cfu/coin reduction in counts for blood and pus, respectively, was observed. Overall, there was no significant difference between the survival of CA-MRSA and HA-MRSA strains. These findings are particularly important given the association between contaminated hands and MRSA and the potential for cross-contamination between coins and hands (136).

**Dentures**

Prior studies have identified the oral cavity and dentures as harbouring MSSA and MRSA and that they may as a result serve as a reservoir and a source of re-infection (137). A study to identify the survival dynamics of planktonic HA- and CA-MRSA strains in five popular denture cleaning solutions was conducted. Quantitative enumeration of the solutions post-inoculation showed that the denture cleaning products were able to eliminate the strains after ten minutes. No statistical significance was observed in difference between survival of HA-MRSA and CA-MRSA strains (137). Further study is needed to identify the survival dynamics of these strains under biofilm conditions on dentures.

Overall, waterborne and indirect person-to-person transmission present previously unidentified routes for possible CA-MRSA infection. It is worthwhile to note, however, that these routes have received limited appraisal and are limited to laboratory and case study information, therefore further study is warranted to examine the likelihood and validity of these claims.

**Proposed Control Options**

There are a number of excellent guidelines published within the past decade that have outlined suggested control and prevention methods for general and specific populations (28,138–145). While some of these guidelines are focused on nosocomial MRSA and the hospital setting, others present the best-available information on CA-MRSA control and prevention. Due to the relative lack of specific literature on the efficacy of approaches to control and prevention of CA-MRSA, selected relevant HA-MRSA inventions were included to provide the reader with the available information on approaches that may be effective. In some instances, HA-MRSA guidelines may be used as a supplement to the available knowledge and extrapolated to the community setting (34).

Based on the epidemiology of CA-MRSA, the following control measures have been proposed as biologically plausible (though, as yet, largely unproven) ways to control the spread of the microorganism:

- Hand and personal hygiene
- Prudent use of antibiotics
- Decolonization
- Early diagnosis and appropriate treatment
- Public education programs (hygiene, antibiotic use)
- Regular cleaning and laundering in households and facilities
- Equipment disinfection
- Exclusion of those with open lesions from certain settings

We present here an overview of recent literature which addresses these proposed approaches.
According to the Centers for Disease Control and Prevention, CA-MRSA can be controlled by limiting transmission through the 5Cs: crowding, frequent skin contact, compromised skin, sharing contaminated personal items, and lack of cleanliness (3). Certain groups are more greatly affected by CA-MRSA possibly because there is less control over these factors (3).

**Hand and Personal Hygiene**

Hands can become contaminated with a multitude of microorganisms by interactions with fomites/environmental sources, personal interaction, diagnostic procedures, administration of food or medicines, and manipulation of indwelling devices (146). In general, hand hygiene is a critical infection control method for both resistant and susceptible microorganisms. Proper hand hygiene practices are commonly cited in papers as a means to control the dissemination of microorganisms. For example, studies on hand hygiene over the past decade of research reported a decrease in MRSA incidence in the hospital which correlated with the introduction of alcohol-based hand rub campaigns (147). Most hand hygiene practices are based upon national standards for the control of the spread of microorganisms (148). In most instances, the “social hand wash” is performed, which is meant to remove transient microorganisms and debris (148). However, according to a systematic review of hand washing techniques in primary care and the community, there is a lack of well-designed studies to assess the effectiveness of hand washing hygiene (148). Factors such as water quality, natural hand flora, hand scrubbing time, hand position, and water direction may also play a role in the elimination of pathogens on hands (148). Additionally, increased compliance with hand hygiene often corresponds to the ease and time efficiency of hand sanitization pumps (149). A survey on hand hygiene in hospitals noted that compliance to hand hygiene campaigns was at best 66% (147). Most common reasons for non-compliance were poor accessibility to sinks, towels or hand rubs, lack of training/education and leadership, and personal lack of recognition of the importance of good hand hygiene (147). To the best of our knowledge, CA-MRSA hand washing efficacy studies have not been reported. Further study at the community level is needed to properly describe the most effective method of hand washing. On the whole, proper hand hygiene and strict compliance to standard precautions could prevent most cases of cross-transmission without the need of identification of human reservoirs (149).

As previously mentioned, CA-MRSA is transmitted most often through person-to-person contact. Therefore, in addition to good hand hygiene, overall personal hygiene is important to maintain (34,150,151). Proper hygiene is of particular importance to athletes due to the close contact. For instance, it is important for all athletes to shower immediately following all practices and games and before entering the athletic training room. They should always wash with liquid soap (not bars of soap), and antimicrobial soaps, such as 4% chlorhexidine, should be intermittently used during the athletic season (Rogers, 2008). The CDC in 2002 also reported that the use of alcohol-based hand rubs is more effective than 3% chlorhexidine soaps (Benjamin et al., 2007). Because of the rise of MRSA in the community, there is a need to re-emphasize the role of personal hygiene and other prevention methods which limit the transmission of MRSA between household members, communities, and hospitals (Humphreys, 2009).

**Prudent Use of Antibiotics**

There is some literature on the effects of antimicrobial use, and CA-MRSA and resistance in HA-MRSA has been frequently reported in the literature as having an association with antimicrobial use. Many papers have examined the relationship between beta-lactam, fluoroquinolone and macrolide use and the increase in resistance amongst MSSA and MRSA (154–156). A significant association between the use of fluoroquinolones and colonization with MRSA has been observed (154,155).

In the hospital it is suggested that antibiotic selection pressure greatly facilitates the acquisition and
colonization with MRSA by decreasing competitive commensal flora (149). A recent systematic review found a significant association for fluoroquinolones (RR=3; 95% CI 1.7-1.9; P<0.001), cefalosporins (RR=2.2; 95% CI 1.7-2.9), glycopeptides (RR=2.9; 95% CI 2.4-3.5), and beta-lactams (RR=1.9; 95% CI 1.7-2.2) with MRSA isolation (156). Generally, the use of antimicrobials can have several negative ecological effects on MRSA transmission and survival such as: decreasing susceptible skin microflora thereby increasing the risk of MRSA colonization; increased transmission due to the selection of MRSA through antimicrobial use; antimicrobial selection pressure may cause levels of MRSA shedding to increase; indirect elimination of competitive susceptible organisms (MSSA) could inadvertently increase MRSA within the population (157). Specifically, fluoroquinolones most likely allow for colonization because they disrupt the microflora and allow resistant strains to occupy the available niche and increase bacterial adhesion with fibronectin (154,156). Consequently, the restricted use of fluoroquinolones may decrease MRSA rates (149). This observation was noted in one study in which, upon the removal of selection pressure, MRSA isolation rates decreased (155). A multitude of observational studies have concluded that antimicrobial usage results in a parallel change in the incidence of MRSA; however, there are relatively few intervention studies examining the relationship between antimicrobial use and MRSA incidence (157). Harbarth and Samore (157) have suggested that the use of a time-series analysis which uses aggregate ecological level data could help eliminate confounding which has been found among traditional epidemiological studies. Overall, there is a significant gap in knowledge of what actually happens to MRSA incidence when an antibiotic intervention is implemented (157).

**Decolonization**

Carriage of MRSA is an important risk factor for infection and also may aid in dissemination of the microorganism (149). Mupirocin nasal ointment is often used to eradicate carriage because of its effectiveness, safety, and economical feasibility; however, there is debate over its true success rate for long-term eradication (149). It is commonly stated that decolonization should not be conducted in patients with active infections. The use of topical treatments should be used first before the use of systemic medications, and in the case of CA-MRSA, cleaning of the environment and household screening for MRSA should be conducted (146). In addition, the possibility of mupirocin resistance should be considered when using as a decolonization treatment (146).

**Early Diagnosis and Appropriate Treatment**

Unknown MRSA carriers constitute the main reservoir for MRSA and are therefore key for further transmission. Thus the screening and identification of carriers, specifically among high risk groups, is very important in cases of outbreaks or in the hospital environment (149). In the hospital, infection control methods such as active surveillance screening of patients to detect MRSA have proven to be effective particularly in outbreak situations (3). At the community level, early identification and diagnosis of CA-MRSA infections is critical to the management of disease, as well as the prevention of spread to household members and others in the community (158). Rapid screening using molecular methods would decrease the waiting period and allow for faster diagnosis and assignment of proper treatment thereby decreasing the possibility of transmission in the interim (149). The effectiveness of costly nasal surveillance has not been demonstrated in the general community (3). Additionally, because CA-MRSA is likely to colonize sites other than the nares, there is a possibility for a proportion of colonized individuals to be missed (34). To identify trends of CA-MRSA in the community and hospitals, health officials could make CA-MRSA a reportable disease (158).

Risk factors and community levels of resistance should be considered when prescribing antibiotics for
CA-MRSA (150). Empiric therapy should be aimed to avoid adding selective pressure for the development of antimicrobial resistance (150).

**Public Education Programs**

Education of basic proper preventative measures and identification of CA-MRSA should be implemented in both the community and healthcare settings. In addition, the education of high-risk groups such as athletes, trainers, physiotherapists, coaches, teachers, and school nurses should be enforced to help in the early identification and management of CA-MRSA infections (152,153). The use of posters, handouts, presentations, and other means of training should be used as teaching tools (152).

**Regular Cleaning and Laundering in Households and Facilities**

Towels, sleepwear, and underwear should be laundered daily to reduce the possibility of re-infection or cross-contamination within a household (158). Standard laundering guidelines for towels and uniforms state that they must be washed using standard detergent in water that is at least 140F (60°C) and clothing must be dried on a hot setting or hung to completely dry (152). Clothing that has become contaminated with wound exudates should be laundered immediately with hot water and laundry detergent to avoid cross-contamination (34). In addition, personal items such as razors or items which come in close contact with the body should never be shared (34).

**Environmental Cleaning**

Environmental cleaning is essential to prevent cross-contamination and re-infection of individuals.

In addition to commonly shared surfaces in households, stethoscopes, locker rooms, artificial turf, workout rooms and equipment, shoes, and uniforms should also be considered for cleaning to prevent transmission of CA-MRSA among certain risk groups (152,158,159). Approved detergents and disinfectants and cleaning top-down should be used on all surfaces that come in contact with secretions or wound drainage (34,147). Depending on the situation, decontamination methods may be chosen based upon the level of environmental contamination and the risk posed for other individuals and patients for re-infection (146). Frequently touched surfaces should be thoroughly cleaned to prevent cross-contamination (146). Although the impact of environmental cleanliness is not as critical as hand hygiene in the prevention of transmission, when combined with proper infection control procedures, environmental control proves beneficial by decreasing microbial counts for a given period of time (146,147,149).

**Exclusion of Those with Open Lesions from Certain Settings**

Because of the frequent skin-to-skin contact in sports, particularly in contact sports in which skin may become compromised during the game, CA-MRSA infections can easily spread between team members if there is a lack of preventative measures in place. In general, athletes, according to the NCAA standards, may be excluded from play if there are wounds that cannot be covered with appropriate bandages. In addition, wrestlers specifically are only allowed to return to play if they do not present new lesions within forty-eight hours of a meet and confirmed cases of CA-MRSA have to complete seventy-two hours of antibiotic therapy and have no active lesions at the time of the meet (152).

**Specific Evaluation Studies of Control Options**

As previously mentioned, there is limited information that specifically evaluates CA-MRSA interventions. To our knowledge, there is only one intervention study (160) which specifically evaluated the efficacy of CA-MRSA interventions in the community. However, intervention studies based on body washes, environmental decontamination, decolonization, and other methods relating to hospital environments have been documented. These interventions may be of relevance to CA-MRSA although this remains largely unproven.
Decolonization

Mupirocin is an antimicrobial that is used for topical decolonization treatment of the anterior nares to reduce/eliminate *S. aureus* (160). Mupirocin-resistant strains are reported among MRSA and can result from indiscriminate use or overuse of mupirocin. Although still under debate, the elimination of MRSA carriage may greatly reduce the risk of infection (161). Decolonization of MRSA in the hospital outbreak setting has variable results with respect to efficacy, although many studies have shown that targeted decolonization in outbreak situations was effective (161,162). Long-term eradication of MRSA has not been reliably shown in the literature, although some short-term success has been cited.

Ellis and associates (160) carried out a cluster randomized, double-blind, placebo-controlled trial to determine if prompt, targeted use of intranasal mupirocin in CA-MRSA colonized soldiers would not only reduce the risk of infection in the colonized individual but also deter new colonization within the unaffected surrounding population and reduce the risk of infection within the study group. United States Army personnel enrolled in the 16-week Health Care Specialist Course from January to Dec 2005 were eligible for recruitment. Of the eligible participants, 3,447 were cultured and randomized to groups; 7 classes representing 1,669 and 1,779 individuals were randomly assigned to the placebo and treatment groups, respectively. Initially, CA-MRSA carriage was found in 3.9% (134) participants; 66 were randomized into the placebo group and 68 in the mupirocin group. Treatment of 2% intranasal mupirocin and a placebo were administered to the CA-MRSA positive participants. The groups were re-screened at eight to ten weeks and placed under observation for sixteen weeks. Five of 65 (7.7%; 95% CI 4.0-11.4%) and 7 of 66 (10.6%; 95% CI 7.9-13.3%) mupirocin and placebo group, respectively, developed CA-MRSA infections during the course of the study. Among individuals not initially colonized by CA-MRSA, 56/1607 (3.5%; 95% CI 2.6-5.2%) of the treatment group and 63/1,459 (4.3%; 95% CI 2.7-5.9%) of the placebo group became infected. At the eight to ten week re-screening, CA-MRSA colonization decreased from 4.0% (95% CI 1.1-6.9%) to 3.2% (95% CI 1.0-5.5%) in the placebo group and from 3.8% (95% CI 1.9-5.7%) to 1.9% (95% CI 1.1-2.8%) in the mupirocin group. New CA-MRSA colonization was reported in 24/1459 (1.6%; 95% CI 0.05-2.8%) and 23/1607 (1.4%; 95% CI 0.05-2.3%) of placebo and mupirocin groups, respectively. The most common type of CA-MRSA was USA300 (54%) followed by USA800 (40%); only 1 case of USA100 was identified. No mupirocin resistance was detected during the course of the study. In conclusion, the authors found no significant reduction in CA-MRSA infections or colonization in the mupirocin group.

Environmental Decontamination

The failure of decolonization/reoccurrence of MRSA in an individual has often been attributed to re-infection through environmental contamination, such as in the work place (hospital environment) and the home (163). Previous studies have identified MRSA survival in dust and on surfaces for up to five weeks (163). Household environments present an increased difficulty when considering appropriate cleaning agents in comparison to hospital environments. Typically, porous materials and surfaces cannot be as easily cleaned and, in addition, certain industrial strength cleaners are not appropriate for household furniture (163).

In the home environment, pets, family members, and fomites/surfaces can act as reservoirs causing re-infection (163). To evaluate the effectiveness of home environmental decontamination using gaseous ozone, the household of a repeatedly infected nurse with eczema was decontaminated. In December 2001, the nurse who suffered from eczema was involved in a hospital cluster of MRSA cases involving two patients and two additional nurses. Although the patients and nursing staff recovered, the index nurse continually became re-infected with MRSA despite several antimicrobial treatment interventions. Environmental screening of her household was conducted and 11/32 (34%)
household swabs were MRSA-positive; however, her children and cat were MRSA-negative. Her house was then decontaminated by first discarding carpet, couches and curtains and then sealing each room and using gaseous ozone (estimated to be 12 ppm) for a ten to twenty-four hour period. The household was sampled two days later and found to be free of MRSA. After decontamination of the household, the nurse and her family/pet remained MRSA-negative for the duration of the study period (September 2005). This study indicates a possible alternative to previously established household cleaning methods (steam, cleaning of all hard furnishing with detergent, damp dusted, vacuumed, replacement of furniture). The study cited the cost savings of using the ozone technique compared with that of other approaches.

It is worthwhile to note that although environmental contamination appears to be a likely source for reinfection, limited, targeted community-based studies have been conducted on environmental contamination control methods.

**Hand Washing and Hand Hygiene**

Because contaminated hands are one of the most important methods of MRSA transmission, hand washing and hand hygiene are critical in preventing MRSA colonization or infection. Compounding the hand hygiene issue, poor hand washing compliance between patients is often observed in hospitals in health care workers (HCW) and physicians. This could be extrapolated back to the community for households that have a family member who is MRSA-positive. It should be noted that information regarding *S. aureus* hand hygiene was not included in this review.

An observational study was conducted to determine the efficacy of a 2% chlorhexidine gluconate solution against five MRSA strains (USA300, USA400, USA500, USA600, USA700) and two *Acinetobacter baumannii* strains (164). This was accomplished by observing the bacterial time-kill and the corresponding minimum inhibitory concentration (MIC) value for each microorganism. More specifically, the MIC was determined using a broth macrodilution procedure and the time-kill analysis was determined based on the exposure of the culture suspension to 2% chlorhexidine for 15 seconds and 1, 3, 6, 9, 12, and 15 minutes (164). The results of the experiment demonstrated that 2% chlorhexidine was able to reduce bacterial counts by 99.9% within 3 minutes. MIC values for the test strains were 1:2,048 and 1:8,192 prepared from the stock 2% chlorhexidine solution. Chlorhexidine gluconate treatment is an effective alternative to ionophores, which may become deactivated by bodily fluids, and is safer than flammable alcohol (164).

**Education of Health Care Workers**

CA-MRSA typically manifests as SSTI infections and as such dermatologists may be among the clinicians who encounter many cases (165). Eighteen non-cosmetic dermatologists forming three focus groups participated in discussions regarding the awareness and perceptions of CA-MRSA, the number of CA-MRSA infections treated in the previous year, the relevant clinical practice, and the best content and format for educational materials (165). The results of the case scenario from the focus groups indicated that the participants only initially identified CA-MRSA in 3% of skin lesions presented to the dermatologist. When asked about diagnosis and treatment options for a patient presenting with a skin lesion, culturing the lesion was conducted in 31% of cases. When given further clinical information on the lesion case, participants described that they would perform incision and drainage on the abscess (46%). The most frequent method for managing the patient presenting with the skin lesion was the prescribing of antimicrobials (33%). Only 38% of the participants discussed transmission and contagiousness of the wound with their patients. Despite standardized guidelines for the identification of and treatment protocols, there was a notable disparity in treatment approaches and identification ability. Although the participants acknowledged that CA-MRSA was a significant problem, only half reported it being a problem in their practice and 94% of the participants reported treating a CA-MRSA positive patient within the previous twelve months. When a suspected case
of CA-MRSA was observed, 90% of participants reported always obtaining a culture, 42% performed incision and drainage, and most reported giving instructions to the patients on personal hygiene, wound care, and general management of the illness. Most participants felt journal articles were the best way to convey CA-MRSA information, while the most effective method of conveying information to patients was felt to be pamphlets or tear-off information sheets. Understanding the awareness and treatment strategies of dermatologists for CA-MRSA is critical for the development of effective infection control guidelines and educational materials for infected/colonized individuals.

Infected or colonized HCWs can spread pathogenic microorganisms, such as MRSA, throughout the work environment. In Norway, half of the reported MRSA cases originated outside of the hospitals and 108/603 were in long-term care facilities; 10% of the MRSA cases were with HCWs. Because patients in nursing homes often require extensive close contact for assistance, the duration of patient care is strongly associated with the amount of bacterial contamination on HCWs’ hands (166). A study evaluating the infection control procedures, particularly focusing on MRSA, in nursing homes in Oslo, Norway was conducted (166). In total, 42/55 (76.4%) of nursing homes in Oslo were included in the study; 388/528 questionnaires were retrieved. Overall, only 17% of the caregivers had experienced MRSA within their wards. Notable findings in the study were: 70% of the personnel had no specific training in health care; of the educated individuals, 52% were nurses and 45% were enrolled nurses. According to the Norwegian national policy, personnel should be tested before entering work in an institution if they have possible exposure to MRSA in Norway or other counties. Although most managers, caregivers, and nursing staff reported written policies for infection control in their facilities, approximately 30% of facilities had written policies for screening and control of personnel before beginning work. Screening guidelines of patients during outbreaks were reported in 89–96% of respondents; only 80% of the caregivers and managers reported testing all personnel and all patients in the ward in outbreaks. A hand hygiene program was instituted in 2004; however, there has been limited evaluation of its effectiveness in nursing homes. Because hand hygiene is so integral to MRSA transmission, further study is needed of this issue.
**Results: Resistant Enteric Bacteria**

Unlike for CA-MRSA, there are no guidelines or review papers on the epidemiology, microbiology, or control of resistant enteric organisms in community settings. Rather, literature exists in two areas, the development and spread of resistance within enteric bacteria, and the risks, transmission, and control options for enteric bacteria (regardless of resistance status). Therefore, information was summarized for *Salmonella* spp., *Campylobacter* spp., verocytotoxigenic *E. coli*, and *Shigella* spp. generally, and then combined with existing knowledge on the development and spread of resistance for extrapolation to resistant enteric organisms. The literature search encompassed material from 1970 to present.

**Risk Factors and Risk Groups (Both Non-Resistant and Resistant Cases)**

**Day care Centres**

Day care centres are a high risk environment for the spread of enteric bacteria, given the age of the children and the potential for person-to-person transmission. Opportunities for transmission of bacteria include non-toilet trained children, staff both preparing food and changing diapers, low staff-to-child ratio, poor hygiene, and the likelihood that children will have oral contact with contaminated hands and objects (167,168). Typically, children under three years of age have a higher incidence of diarrheal illness than older children (169). Hiruta *et al.* (170) found a significant increase in diarrheal incidence in one year olds compared with the rest of the age groups (up to six years old). Day care centres in which staff prepared and served food and changed diapers were reported to have a 3.3 times higher incidence of diarrheal illnesses than centres in which staff did not combine these activities. These results illustrate the role day care staff may play in transmission of disease and the importance of good hand hygiene practices (169).

Much of the published literature related to the epidemiology of enteric illness in day care centers has focused on outbreaks, and these studies are reviewed here. Such studies have investigated the source, transmission pathways, and identified control points to stop further spread of infection (171).

Common enteric bacteria that cause outbreaks in day care centres include *Shigella sonnei* (171–174), *Salmonella typhimurium* (174,175), and *E. coli* O157:H7 (176,177). Hiruta *et al.* (170) reported that all isolates tested from children involved in an *E. coli* O26:H11 outbreak were found to be resistant to multiple antimicrobials.

To manage day care centre outbreaks, intervention and control measures have been implemented, including exclusion criteria, isolation in the day care centre, and education. Many of the day care centres excluded children and staff who had symptoms of or stool samples that tested positive for enteric bacteria. The majority of the day care centres required two consecutive negative stool cultures or symptoms to have ceased for at least twenty-four hours before returning (170,171,177,178). Some day care centres were able to provide an isolation room for infected staff and children (171,175,178). Children were typically moved to the infection-free room after two consecutive stool samples were culture-negative (175). In one outbreak, a licensed centre for 92 children allowed children and staff to return following antimicrobial therapy and cessation of diarrhea, but before cultures were negative. These children and staff were isolated in a separate room with a bathroom, sink, and playground until two consecutive stool cultures were negative. By providing an isolation unit, this centre prevented the need for parents to seek alternative care, and risk spreading the disease further. This strategy was also well received by parents of non-affected children, knowing that affected children were isolated and the public health department was providing surveillance (178).

As part of outbreak management and prevention of future outbreaks, day care centres have provided education on proper hand hygiene, diaper-changing...
procedures, and disinfection of the diaper-changing area, toys and other environmental surfaces (175,178). In some cases, the closing of day care centre kitchens was warranted (170). Initiating appropriate action has prevented many day care centre outbreaks from spreading to the surrounding community. Following the implementation of interventions, outbreaks within day care centres have been contained, ranging from after two days (178) to three weeks (171) after the intervention. Successful interventions included education on hand hygiene and diarrhea surveillance for families, day care centres, summer camps, and schools. Furthermore, people with diarrhea were referred to a diarrhea clinic in some cases for diagnosis and treatment (171). Gilbert et al. (178) noted the need for education and increased awareness of disease transmission for parents and staff, and called for clear definitions and policies to control outbreak situations.

Studies of shigellosis outbreaks illustrate the potential for an illness to extend from a day care center into the general population. From June 2001 to March 2003, the incidence of shigellosis increased five to forty-fold in six states in the USA, with illness originating in day care centres and spreading to the community (173). The affected facilities took appropriate intervention measures. Specifically, infected children were excluded from the centre and public health departments provided hand hygiene education to the community to control the outbreak (173). An outbreak of *S. sonnei* was identified in one neighbourhood (pop 60,000) affecting mostly children under five years of age. It was determined that children attending day care were the main risk factor for transmission of the illness into households. Secondary transmission within households was common. *Shigella sonnei* outbreaks in this community tend to be cyclic in nature, recurring every five to six years. This may indicate a low-level endemic transmission, with outbreaks occurring when a new group of young children enters the day care centres without previous *Shigella* exposure (172). In the report of six statewide outbreaks of *Shigella sonnei* in the United States, health department treatment suggestions varied; some recommended antibiotic treatment for all stool-confirmed cases, while some did not recommend antibiotic treatment except in severe cases. All health departments suggested referring to the antimicrobial resistance data to guide treatment agent selection (173).

**Schools**

Similar to the information on enteric illness in daycares, the literature has focused on outbreaks when discussing enteric illness in schools. Of particular relevance to this review, Maguire et al., (179) investigated a *Shigella sonnei* outbreak that occurred in a primary school, affecting 42% of the students and staff. Children aged four to eight years had the highest incidence of diarrhea, at 33% and the incidence was 8% for children aged eight to twelve years. Isolates of *Shigella sonnei* were found to be resistant to sulphonamides, streptomycin, and ampicillin.

Outbreak management methods included excluding children and staff from the school until diarrhea ceased. Food hygiene and cleaning practices at the school were examined and found to be adequate. However, infected food handlers with diarrhea were excluded for forty-eight hours after symptoms ceased and all uncooked food was excluded from the menu until the end of the outbreak. Reminders of the importance of hand hygiene, especially following bathroom use and before eating, were issued to staff, children, and parents.

**Households**

The home is a central hub of activity and the place from which we all go into the community, and thus can facilitate spread of disease (180). The household is a complex environment that may contain members of varied ages and house pets, and where daily activities such as food preparation and personal hygiene practices occur. Household members vary in risk level of infectious disease, depending on age and health status. More high risk people are being cared for at home (including neonates, elderly, immunocompromised), requiring additional care in household cleanliness and decontamination (181).
As such, the home environment has been the subject of in-depth epidemiological studies related to spread of infectious disease.

Numerous studies investigating the domestic environment have shed light on how infectious diseases are spread through the home, with many infections being due to inadequate hygiene. Hygiene within the home includes many aspects such as general cleaning, food preparation, and personal hygiene. Proper hygiene during food preparation in the home is essential in preventing cross contamination from raw meats and fruits and vegetables and also from household members carrying an infectious disease (182). The goal for applying proper hygienic procedures in the home is not to attain sterility, but rather to decrease the number of microorganisms to levels that will not adversely affect health (183). Routine cleaning of the house is often sufficient to reduce contamination, but when a member is ill with an infectious disease, heightened awareness of cleaning and decontamination is necessary. This can be achieved by recognizing the areas of the home that are most likely to be in contact with pathogens.

Sites and surfaces in the home can be categorized into 4 groups: reservoir sites, reservoir-disseminators, hand and food contact surfaces, and other surfaces. Reservoir sites include toilets, which have a high contamination probability, but where the chance of transfer is limited. Reservoir-disseminator sites are highly contaminated areas and high risk transfer sites, such as taps, handles or dish cloths, which can easily spread bacteria. Food handling hygiene is imperative, including proper storage, preparation, cooking temperature, and serving. Hand hygiene during food preparation is essential to reduce person-to-person transmission and avoid cross-contamination by other surfaces (180,182,183). In general, contact surfaces such as kitchen counters, taps, handles, and contaminated cloths have lower bacterial levels because they tend to be drier, but these items still have potential for contact transfer (180). Cleaning of surfaces can be attained either by removal or inactivating the organism. If removal of bacteria with soap and water is not possible, such as on a fixed surface which cannot be washed in a sink or exposed to mechanical action, inactivation with a disinfectant is ideal (180,183). Disinfectants can provide a margin of safety by ensuring that bacteria are inactivated at specific points in the house, but these products are not necessary in all situations. Generally, reservoirs of high contamination with low transfer risk under normal conditions (e.g. toilets, drains) do not need to be disinfected. However, if there is an infectious disease outbreak, disinfection to kill pathogens is recommended to reduce the risk of transfer (180).

Much of the infectious disease within the home is associated with secondary transmission through person-to-person contact. Parry and Salmon (167) quantified and characterized household transmission of shiga toxin-producing Escherichia coli O157 (STEC O157) following sporadic infections in the community. Secondary household transmission was calculated at 4–15%. Household members most likely to contract STEC O157 from case-patients are children aged one to four years and adults under thirty-five years. Children are more likely to put contaminated hands and objects in their mouths and persons fifteen to thirty-five years are more likely to be caring for children with diarrhea. Werber et al. (184) found that household transmission occurred mainly from children under the age of ten years old to younger siblings. A combination of the case-patient being under the age of five years and the presence of a sibling independently increased the risk of secondary transmission within the household (184).

Nursing Homes and Long-Term Care Facilities

Nursing home and long-term care facility (LTCF) residents are at high risk of acquiring infectious disease. Nursing homes and LTCFs provide an ideal setting for the transmission of disease with elderly residents sharing air, food, water, and health care in an institutional setting. Typically, elderly residents are predisposed to infections due to multiple chronic diseases and physical impairments (185). Bacteria may be more likely to cause disease due to low
inoculum levels required to produce clinical infections in elderly people.

Due to other chronic disease conditions in elderly patients, enteric bacterial infections may be overlooked or misdiagnosed, even at times of an outbreak. Additionally, patients may not be able to report symptoms due to confusion or dementia (186). Furthermore, visitors and staff may carry pathogens from the community into the nursing home. Geriatric patients are at higher risk for complications or death when infected with enteric bacteria compared to other population groups (187). The most common causes of gastrointestinal infection outbreaks are *Salmonella* and *Escherichia coli* O157:H7 and less commonly *Campylobacter jejuni* and *Shigella* (185).

The use of antibiotics in LTCFs for the elderly population is a growing concern. O’Fallon, *et al.* (188) conducted a survey with licensed LTCFs assessing methods, frequency, content, and dissemination of information used to track infections and antibiotic use. Most facilities used paper charting for tracking infections and antibiotic use, which limits the ability to provide trends, disseminate data and analyze, or to combine data with medical records. Current United States federal guidelines require that LTCFs conduct infection control programs and recommend practices to track infections and antibiotic resistance. However, there is no set instruction for facilities on how to achieve these requirements and as a result, LTCFs are not consistent with respect to infection tracking. Specific guidelines are needed for LTCFs in infection tracking and antibiotic use.

**Immunocompromised Individuals**

Immunocompromised individuals are a group that includes newborn infants, the elderly, patients recently discharged from the hospital, persons with chronic immune system impairment such as those with HIV infection, or patients undergoing immunosuppressive drug therapy (182). People may be immunocompromised temporarily due to pregnancy or development stage (e.g. infants). Long-term or permanent immunocompromise may be due to immunosuppressive treatment (e.g. cancer or organ transplant) or from an infectious disease such as HIV/AIDS. For this population, likely routes of exposure to enteric bacteria arise in the home environment, such as through food preparation, pet care and gardening. Immunocompromised people are at increased risk of infection, complications and death due to a lower dose of bacteria being required to initiate infection (189). It is important for immunocompromised people to recognize areas of higher risk for transmission and reservoirs (189). For example, food preparation is an area of concern for immunocompromised individuals. Safe food-handling guidelines should be followed, including practicing hand hygiene when handling raw meat and eggs, and thorough washing of cutting boards and counters to avoid cross-contamination (189).

**Sociodemographic Factors**

Examining sociodemographic and economic factors in relation to the incidence of enteric bacteria may provide insight into the dynamics of community transmission of infectious diseases and opportunities for control and prevention.

Chang and colleagues (190) investigated how sociodemographic and economic factors may be associated with enteric illness at the county level. With the rise in day care centres and nursing home facilities to accommodate the increasing number of children and elderly people requiring this type of care, the potential risk for pathogen exposure and transmission in the community has also increased. Salmonellosis incidence has been found to be higher in communities with a higher percentage of children less than five years and people over sixty-five years. A higher salmonellosis incidence was also reported in communities with higher percentage of black or Hispanic residents, which may be contributed to by socioeconomic and cultural differences, knowledge and food safety practices and personal hygiene practices (190).

Salmonellosis and shigellosis were positively associated with numerous sociodemographic and economic factors, such as population distribution.
by selected age groups, race, ethnicity, urbanization, poverty level, crime rate, and physician population ratio in a study by Chang et al. (190). However, all of these factors were negatively associated with E. coli O157:H7 infection. Inconsistent associations for salmonellosis, shigellosis, and E. coli O157:H7 infections included population distribution by education level, population living on a farm, local per capita expenditures for education, and Medicare enrolment rates. The differences in disease incidence was concluded to be partly due to sociodemographic and economic factors, demonstrating the complex relationship between community characteristics and dynamics of disease transmission. Identifying these county-level factors associated with enteric illness will assist in developing specific interventions for outbreak management and prevention (190).

**Population Density**

The influence of population density and its association with antibiotic resistance is also an area of recent research. Bruinsma et al. (191) examined the prevalence of antibiotic resistance of three cities in three countries, specifically Athens, Greece; Groningen, Netherlands; and St. John’s, Newfoundland. Prevalence of antibiotic-resistant E. coli was measured in healthy people in relation to antibiotic consumption and population density as a measure of crowding in each community. Levels of antibiotic-resistant E. coli to various antibiotics (amoxicillin, cefazolin, nalidixic acid, ciprofloxacin, chloramphenicol, gentamicin, nitrofurantoin, oxytetracycline, and trimethoprim) were found to be associated with population density, with the highest resistance and density in Athens, followed by Groningen, and St. Johns. The results of this study indicate that population density is a factor in antibiotic resistance, suggesting that the opportunity of a susceptible host acquiring resistant bacteria from a resistant carrier is greater in areas of higher population density.

MacDougall et al. (192) conducted a study examining hospital and community fluoroquinolone use and resistance in S. aureus and E. coli in hospitals. Results indicated a significant association between E. coli resistant to fluoroquinolones in hospitals and fluoroquinolone use in the community surrounding hospitals within a sixteen kilometre radius. It was concluded that population density of the community surrounding the hospitals was significantly related to resistance in E. coli and S. aureus reported in hospital antibiograms, with hospitals in dense populations having a greater burden of ill patients who are more likely to develop infections with a resistant pathogen. A possible explanation for this is that density affects the circulation of antimicrobial resistance in the community through a higher rate of cross-transmission among people living in close proximity.

**Regional and Seasonal Variation**

Some studies have found that the incidence of enteric illness may vary between urban and rural regions. Chang et al. (190) found in all regions investigated, salmonellosis and shigellosis had higher incidence rates in counties where > 50% of the population lived in urban areas. E. coli O157:H7 incidence was higher in counties where > 50% of the population lived in rural areas (190). Campylobacter incidence was detected to be lower in rural areas compared with urban areas (193). In a contrasting study conducted in Manitoba, Canada, the incidence of Campylobacter was significantly higher in rural and farming populations. The highest incidence rates were detected in populations living in proximity to high densities of farm animals (194). Antibiotic resistance rates were found to have increased with growing urbanization, with the majority of resistance to fluoroquinolones (193).

Seasonal variation in the incidence of enteric bacteria is well-recognized. Van Hees et al. (193) investigated seasonal differences of Campylobacter infections and antibiotic resistance patterns and found that infection incidence rates were higher in the summer than in winter; however, resistance rates were opposite, being higher in the winter and lower in the summer.
Reservoirs and Transmission of Enteric Bacteria

Only those studies pertaining to antibiotic-resistant enteric bacteria are reviewed here.

Waterborne Transmission

Water is an ideal vehicle for transmission of enteric bacteria throughout the community. Many enteric illness outbreaks are due to a contaminated community water source.

Alamanos et al. (195) reported a community outbreak of *Shigella sonnei* affecting 288 of 2,213 residents (>10% of the population). People from zero to fourteen years had the highest incidence of infection and the risk decreased significantly with age and, interestingly, was lowest in the people over sixty-five years. However, the likelihood of hospitalization was highest in affected people over sixty-five years. *Shigella sonnei* strains isolated from cases were resistant to antibiotics (ampicillin, co-trimoxazole and tetracycline) and the same resistance profile was detected in isolates from water samples. (195).

Person-to-Person Transmission

Hands are extremely important as a person-to-person transmission route because they come into contact with known entry points for pathogens, such as the nose, eyes, and mouth (182). Seto et al. (196) examined the effectiveness of promoting prevention of secondary transmission during an enteric bacteria outbreak. The model used in this study suggests that preventing secondary transmission could result in 5–11% reduction of symptomatic cases.

A community-based study was undertaken to assess the prevalence and determinants of antibiotic resistance of *E. coli* of a large population consisting of *E. coli*-infected and uninfected children. Information and stool samples were collected from household members of the study children to investigate the role of family transmission in comparison to other risk factors. The study demonstrated that the prevalence of resistant *E. coli* is relatively low and there was no difference in prevalence between parents and children (197).

Lietzau et al. (197) investigated the role of conjugal transmission of resistant *E. coli* in comparison with other risk factors such as recent antibiotic therapy or hospital stay. The prevalence of resistant *E. coli* to various antibiotics was similar between husband and wife: for ampicillin resistance, prevalences were 18.9% for men and 15.7% for their spouses; 10% and 9.2% for men and their spouses respectively for cotrimoxazole and 13.1% and 14.9%, for men and spouses, respectively were resistant to doxycycline; cephalosporin, gentamicin, and quinolones resistance prevalences were 3% or less. Strong associations with resistance were found among partners; if the spouse carried resistant *E. coli*, the prevalence of resistance in men was 50%, 25% and 20.6% for ampicillin, cotrimoxazole, and doxycycline, respectively, compared with 11.9%, 8.1% and 11.6% otherwise. Recent antibiotic use and hospital stay or visit within the last twelve months were not associated with antibiotic resistance. No associations were found between resistance and various sociodemographic factors such as patient age, education level, occupation, number of household members, square metre per person in the household, elderly household members, and whether there was a household pet.

Proposed Control Options for Enteric Bacteria

A variety of measures have been proposed as biologically plausible ways to control the transmission of enteric infections, although these are for the most part unstudied, with the exception of hand hygiene. We present here an overview of the literature which addresses these proposed approaches.

Hand Hygiene

Thorough hand washing and hand sanitizer continues to be among the best defense against transmission of enteric illness. Numerous studies have investigated the effectiveness of hand hygiene (182,198–200). Good hand hygiene is instructed in many day care...
and nursing home facilities, and is also promoted through postings in health care and public areas (173,200-202).

**Household Hygiene**

The house environment should be approached with a holistic view, as there are many opportunities to prevent transmission of gastrointestinal illness within the home. Household areas of risk, and therefore potential points of control, are personal hygiene, environmental hygiene (toilets, bath sinks, surfaces), care of domestic pets, and care of family members at increased risk. Hand hygiene is the central component for prevention of transmission in all household areas.

To control secondary transmission, Werber et al. (184) suggests immediately separating siblings in the household if one is infected with enteric bacteria. The presence of a sibling (RR 3.8; 95% CI 0.99-14.6) and children under five years old being the primary case patient (RR 2.03; 95% CI 0.99-41.6) were independent predictors for secondary transmission in the household. Secondary cases could be reduced by up to 50% if the infected child was immediately isolated following laboratory confirmation of the diagnosis.

**Equipment Disinfection**

An ideal method to control spread of enteric illness is through disinfection of equipment that may be shared among people. Kotch et al. (200) examined equipment used in day care centres. The main areas of concern were diaper-changing, hand-washing, and food preparation equipment. Day care centres were provided with unique cast polymer tabletops with impermeable, seamless surfacing for diaper-changing, hand-washing, and food-preparation. Other features included automatic faucets and foot-activated roll out diaper disposal bins to minimize contact by hands. The intervention centres had significantly reduced diarrheal illnesses (0.90 vs. 1.58 illnesses per 100 child-days in control centres), number of days ill due to diarrhea in children in treatment compared to control centres (4.0% vs. 5.0% of days ill per 100 child-days), and days ill among teaching staff due to any illness (0.77% vs. 1.73% in control centres). High-quality day care equipment combined with hygiene education can significantly reduce diarrheal illnesses among children and sick days among staff (200).

**Public Health Education**

Public health departments have the potential opportunity to play a large role in the control and prevention of enteric illnesses. Delivery of public health messages through a variety of media such as the Internet, television, radio, and newspapers can be an effective way to educate the general population (196).

Public health departments can also make recommendations on control methods to prevent secondary transmission within the household and community. Recommendations include frequent hand washing, avoiding contact with feces, minimizing contact with infected persons, proper food preparation and consumption, and staying home from work or school if having diarrhea during outbreaks (196).

Public health officials can assist in stopping and controlling outbreaks at day care centres. Control options often recommended include isolating or excluding children with enteric illness symptoms or confirmed diagnosis; education on hand hygiene and washing, diaper-changing procedures and disinfection of the diaper-changing area, toys, and other environmental surfaces (173,175,178).

**Specific Evaluation Studies of Control Options**

There are very few published studies that evaluate the effectiveness of specific control strategies relevant to community-based settings for enteric pathogens (resistant or non-resistant), and those few published studies all focus on washing/hand hygiene.
**Hand Washing**

Aiello *et al.* (199) preformed a meta-analysis of four databases for hand hygiene trials published between January 1960 and May 2007, collecting a total of thirty qualifying studies. The meta-analysis found that for all hand hygiene interventions, gastrointestinal illness was reduced by 31% (95% CI=19%, 42%). The most effective interventions for reducing gastrointestinal illness was a combination of using non-antibacterial soap along with hand hygiene education, decreasing gastrointestinal illness by 39% (95% CI=12%, 57%). No evidence was found to support the use of alcohol-based hand sanitizers or antibacterial soap being more effective than non-antibacterial soap against the prevention of gastrointestinal illnesses. This finding was also supported by a systematic review by Aiello *et al.*, (199), who found no difference in gastrointestinal illness symptoms when using non-antibacterial soap compared with antimicrobial soap. Regardless, the use of nonantibacterial soap, antimicrobial soap, or hand sanitizers will reduce the amount of bacteria on hands and impact transmission of illness in home and community (182).

Bloomfield *et al.* (182) conducted a review of the impact of hand hygiene in reducing transmission of infectious diseases in the home and community, as well as evaluating the use of alcohol-based hygiene procedures alone or combined with hand washing. Hands are a significant factor in the transmission of enteric infection because they come into direct contact with areas of pathogen entry such as the nose, mouth, and eyes. Yet, hands are also the last measure of defense against disease transmission. The authors found that overall good hygiene, but especially good hand hygiene, in both the home and community has a significant benefit in decreasing the incidence, ranging from 48–57%, of gastrointestinal illnesses. Public education of the effectiveness of hand hygiene and the proper application of hand hygiene can impact gastrointestinal illnesses, by reducing transmission.
Conclusion

Similarities between CA-MRSA and resistant enteric bacteria

CA-MRSA and community-acquired antimicrobial resistant enteric bacteria share features which suggest opportunities for common approaches to their control:

- Modes of transmission: CA-MRSA and resistant enteric bacteria may by spread by direct person-to-person transmission and fomites
- Risk Groups: These organisms share some high risk groups including children, the elderly, immunocompromised individuals, those with pre-existing medical conditions, familial groups and animal handlers
- Prevention: Proposed methods of control of these infections share some common features including: hand and personal hygiene, prudent use of antimicrobials, early diagnosis and appropriate treatment, public education programs (hygiene, antibiotic use), regular cleaning and laundering in households and facilities, equipment disinfection, and exclusion of those with active infections from certain settings

Limitations to the information on strategies to control community-associated antimicrobial resistant Staphylococcus aureus and enteric bacterial infections

- In general there is reasonable scientific evidence regarding risk groups and risk factors for CA-MRSA. This information provides some insight into potential approaches to control these infections.
- There is a paucity of information on risk groups and risk factors for the community-acquired antimicrobial resistant enteric bacterial infections studied; some information exists on risk settings and risk factors for community acquired enteric bacterial infections, but the extent to which this can be extrapolated to resistant infections is unknown; much of this information takes the form of outbreak reports
- There is a paucity of scientifically-based information (RCTs or observational studies) on interventions for CA-MRSA or for the enteric bacterial infections studied—resistant or otherwise. A number of RCTs have shown the effectiveness of handwashing in the prevention of gastrointestinal illness generally.
- A limited number of intervention studies of HA-MRSA exist, however the extent to which the result of these studies can be extrapolated to CA-MRSA is unknown; such extrapolation may be misleading
- There is an extensive literature concerning recommendations, guidelines, and suggested approaches to the control of both CA-MRSA and, to a lesser extent, enteric bacterial infections in community settings. Although the efficacy of these approaches is plausible, it has for the most part not been formally evaluated

Recommendations

- Formal evaluations of the efficacy of strategies for control of CA-MRSA and community-acquired enteric infections (resistant and otherwise) are warranted and should form the basis for public health guidelines and policy
- Until such time as such evaluations can be undertaken, recommendations for control of these infections must be dependent largely on historic practice, conventional wisdom, extrapolation from other contexts, consensus and conjecture
Potential interventions that would warrant formal evaluation in various settings and groups include the following:

- Hand and personal hygiene
- Prudent use of antibiotics
- Decolonization
- Early diagnosis and appropriate treatment
- Public education programs (hygiene, antibiotic use)
- Regular cleaning and laundering in households and facilities
- Equipment disinfection
- Exclusion of those with active infection from certain settings

Ongoing collection and evaluation of information (including surveillance and epidemiologic studies) on the occurrence, settings, risk factors, and risk groups for CA-MRSA and resistant enteric infections is warranted. Such information will be useful in determining disease trends, identifying risk groups, settings and risk factors, and identifying and evaluating potential interventions.
References


# Appendices

## Appendix A: Key Words and Search Strings

### Enteric Disease
- Gastrointestinal
- Gastroenteritis
- GI illness
- GI discomfort
- GI distress
- GI symptoms
- Emesis
- Vomiting
- Diarrhea*
- Abdominal cramp
- Abdominal pain
- Transmissible

### Community
- Community acquired
- Community associated
- Population
- Nursing homes
- Long-term care facilities
- Assisted living
- Group-homes
- Day care facilities
- Educational institutions
- Dormitories
- Sports arenas
- Sports equipments
- Gymnasiums
- Gyms
- Prisons
- Children
- Elderly
- Aboriginal
- First Nations
- Athletes
- Military
- Schools

### Enteric Bacteria
- Salmonell*
- Shigell*
- *Escherichia coli* 0157:H7
- *E. coli* 0157:H7
- VTEC
- Verotoxin-producing *E. coli*
- Verotoxin-producing *Escherichia coli*
- Verocytotoxin-producing *E. coli*
- Verocytotoxin-producing *Escherichia coli*
- STEC
- Shiga toxin-producing *E. coli*
- Shiga toxin-producing *Escherichia coli*
- SLTEC
- Shiga-like toxin-producing *E. coli*
- Shiga-like toxin-producing *Escherichia coli*
- Campylobac*
- Transmissible

### Staphylococcus aureus
- Methicillin-resistant *staphylococcus aureus*
- MRSA
- Community-acquired methicillin resistant *staphylococcus aureus*
- CA-MRSA
- Transmissible

### Control
- Intervention*
- Prevention
- Surveillance
- Monitoring
- Polic*
- Policy Evaluation
- Best Practices
- Guidelines

### Health Practices
- Veterinary
- Animal workers
- Personal support workers
- Immunocompromised individuals

### Antimicrobial
- Antibiotic
- Antibacterial
- Anti-infective
- Antiseptic

### Resistance
- Antimicrobial
- AMR
- Resistance
- Resistant

### Search Strings
- Antimicrobial AND Enteric Disease AND Enteric Bacteria AND Antibiotic
- Antimicrobial AND Resistance AND Enteric Disease AND Enteric Bacteria AND Community AND Health practices
- Antimicrobial AND Resistance AND Enteric Disease AND Enteric Bacteria AND Community AND Control
Appendix B: Abstract Relevancy Screening Checklist

1. Does the abstract investigate/discuss any of the following keywords (check all that apply):
   - [ ] Control
   - [ ] Intervention
   - [ ] Prevention
   - [ ] Surveillance
   - [ ] Monitoring
   - [ ] Policy
   - [ ] Policy evaluation
   - [ ] Best practices
   - [ ] Guidelines

2. Does the abstract investigate community-acquired illness (versus hospital-acquired)? Y / N

3. Does the abstract discuss any of the following populations specifically? Y / N
   - [ ] LTC
   - [ ] Nursing homes
   - [ ] Assisted living
   - [ ] Group homes
   - [ ] Daycares
   - [ ] Schools
   - [ ] Dormitories
   - [ ] Sports arenas, teams, athletes, gyms
   - [ ] Prisons
   - [ ] Children
   - [ ] Elderly
   - [ ] Immunocompromised
   - [ ] First Nations, aboriginals

4. Does the abstract discuss any of the following pathogens? Y / N
   - [ ] MRSA
   - [ ] Salmonella
   - [ ] E. coli (VTEC/STEC/SLTEC)
   - [ ] Shigella
   - [ ] Campylobacter

5. Does the abstract material refer to human cases of AMR, enteric bacteria, or MRSA? Y / N