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Antimicrobial Resistance Trends in the Province of British Columbia

2013

Prepared by *the*
Do Bugs Need Drugs? Program

September 2014

Provincial Health Services Authority
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Executive Summary

This report aims to provide a comprehensive overview of antimicrobial resistance (AMR) trends in the province of British Columbia (BC). A summary of the results is presented below:

Gram Positive Organisms

- The proportion of ***Staphylococcus aureus*** isolates that were methicillin resistant (MRSA) ranged from 16.1% to 30.5% from 2007 to 2013 according to BC Biomedical data, 13.0% to 19.3% on the Island (LifeLabs) and 21.2% to 27.7% in the Mainland (LifeLabs) in 2013. In 2013, rates of resistance to clindamycin, erythromycin, and trimethoprim-sulfamethoxazole (TMP-SMX) among MRSA isolates were 4.8%, 82.8% and 1.4%, respectively (BC Biomedical data).
- ***Streptococcus pneumoniae*** isolates have demonstrated a stable rate of resistance to all antibiotics tested since 2007 according to BC Biomedical data, with Mainland data (LifeLabs) showing similar trends and Island data (LifeLabs) with lower rates. In 2013, 26.2%, 11.6% and 22.2% of all tested isolates demonstrated non-susceptibility against erythromycin, penicillin, and tetracycline according to BC Biomedical data.
- From 2007 to 2010, non-susceptibility rates to erythromycin and clindamycin decreased in ***Streptococcus pyogenes*** isolates; however, as of 2013, non-susceptibility rates had significantly increased to 18.4% and 17.9%, respectively. LifeLabs data show a similar increasing trend to both antibiotics tested (erythromycin: $p<0.001$; clindamycin: $p<0.001$). As of 2013, *S. pyogenes* isolates remain highly susceptible to penicillin and cephalothin but fully resistant to TMP-SMX and ciprofloxacin according to BC Biomedical data.
- In 2013, ***Enterococcus* spp**. isolates remained highly susceptible to ampicillin (97%) and nitrofurantoin (99.3%) according to BC Biomedical data, with LifeLabs data showing similar rates. However, one quarter of all isolates tested were non-susceptible to ciprofloxacin in 2013, a rate that has been stable over the years 2007 to 2013. A small percent of all *Enterococcus* spp. isolates (1.5%) were identified as vancomycin-resistant *Enterococcus* (VRE) in 2013 according to BC Biomedical data.

Gram Negative Organisms

- In 2013, the proportion of ***Escherichia coli*** non-susceptible to ampicillin, ciprofloxacin, and gentamicin showed a slight increasing trend and is reported to be at 47.4%, 24.9% and 8.4%, respectively (ampicillin: $p<0.01$; ciprofloxacin: $p<0.01$; gentamicin: $p<0.01$ according to BC Biomedical data). These resistance rates increase with age, being highest in those aged 70 years or more. *E. coli* isolates have demonstrated moderate levels of resistance to TMP-SMX with 25.2% of isolates demonstrating resistance in 2013, a rate that has stabilized over the time period between 2007 and 2013 ($p=0.414$). Nitrofurantoin remains a highly effective empiric treatment for uncomplicated urinary infections caused by *E. coli* with approximately 97.5% of isolates exhibiting susceptibility to this drug class. This trend is reassuring as *E. coli* is the chief causative organism for cases of uncomplicated UTI infections.
- Data from 2013 suggest that ciprofloxacin and gentamicin resistance in ***Klebsiella pneumoniae*** isolates remains low at 4.1% and 1.6%, respectively according to BC Biomedical data, with LifeLabs data showing similar rates in both Mainland and Island populations. Non-susceptibility to nitrofurantoin shows a slight decreasing trend across all data sources yet remains high in 2013 at 43.5% (BC Biomedical, $p<0.001$), 70.4% (LifeLabs- Island, $p=0.001$), and 68.1% (LifeLabs- Mainland, $p<0.001$). Additionally, resistance to TMP-SMX for *K. pneumoniae* appears to be decreasing from 10.8% in 2007 to 7.8% in 2013 ($p<0.001$) with similar rates observed in LifeLabs data.
- In 2013, 19.9% of ***Proteus mirabilis*** isolates were non-susceptible to ciprofloxacin according to BC Biomedical data, with similar rates observed on the Mainland (22.1%), but lower rates observed on the Island (4.8%). Non-susceptibility to gentamicin has stabilized during the time period 2007 to 2013 and remains low at 6.2% in 2013 with LifeLabs data showing similar rates. Additionally, the proportion of isolates non-susceptible to ampicillin has also stabilized and is reported at 20.0%, 18.7%, and 27.8% for BC Biomedical, LifeLabs-Island and LifeLabs-Mainland, respectively.
- The proportion of **SPICE** organisms non-susceptible to ciprofloxacin, gentamicin, and TMP-SMX have stabilized during the period 2008-2013 and remains low at 6.2%, 4.3% and 9.6% on the Mainland with similar rates observed on the Island (ciprofloxacin: $p=0.310$; gentamicin: $p=0.264$; TMP-SMX: $p=0.0749$).
- In 2013, 12.5% of *E.coli* isolates, 5.6% of *P. mirabilis* isolates, and 3.6% of *K. pneumoniae* isolates exhibited an **extended-spectrum β-lactamase-like (ESBL) phenotype**. Approximately half of all ESBL-like isolates (*E. coli, K. pneumoniae,* and *P. mirabilis*) demonstrated non-susceptibility to at least two of the quinolones, aminoglycosides and TMP-SMX, while approximately 20.0% of isolates demonstrated non-susceptibility to antimicrobials in all three classes.

- A slight increase is observed in the proportion of ***Pseudomonas aeruginosa*** isolates that are non-susceptible to piperacillin and ceftazidime between 2007 to 2013 and is reported at 2.9% and 2.3% in 2013 (piperacillin: p=0.004; ceftazidime: p=0.753) (BC Biomedical). Non-susceptibility to gentamicin and tobramycin remains low in 2013 at a rate of 0.4% and 3.6%, respectively, while the proportion of isolates non-susceptible to ciprofloxacin is higher at a rate of 10.3% in 2013 (BC Biomedical).
- In 2013, the proportion of ***Salmonella*** **Enteritidis** isolates non-susceptible to tetracycline, ampicillin, and chloramphenicol remains low at 3.4%, 2.3% and 1.1%, respectively. The proportion of ***Salmonella*** **Heidelberg** isolates that are non-susceptible to amoxicillin-clavulanic acid, ceftriaxone, ampicillin, and tetracycline increased substantially and is reported to be at 48.7%, 66.7%, 74.4%, and 20.8%, respectively.
- The percent of ***Haemophilus influenzae*** isolates resistant to ampicillin has remained between 14.0 and 20.0% from 2007 to 2013 and is reported to be at 19.7% in 2013.
- In 2013, the rate of non-susceptibility to erythromycin in ***Campylobacter*** remains low at 1.4% on the Island and 3.7% on the Mainland according to LifeLabs data. However, non-susceptibility rates to ciprofloxacin fluctuates substantially between 25.4% and 43.2% (2013) on the Island and between 36.9% (2013) and 50.1% during the time period 2008 to 2013 (Island: p=0.432; Mainland: p=0.059). The non-susceptibility rate to tetracycline fluctuates around 35% on both the Mainland and on the Island and is reported to be 48.9% on the Island and 42.4% on the Mainland in 2013.
- An overall decreasing trend is observed for isolates with elevated MICs to cefixime, azithromycin, and ceftriaxone in ***Neisseria gonorrhoeae*** isolates when compared to data from 2012. In 2013, 0.5% and 0.7% of isolates showed decreased susceptibility to cefixime and ceftriaxone, respectively; while 24.0% showed resistance to ciprofloxacin.
- In 2013, 4.3% of ***Neisseria meningitidis*** isolates showed resistance to ciprofloxacin. The proportion of isolates demonstrating non-susceptibility to penicillin decreased as compared to 2012 and is reported to be at 39.1% in 2013.

Other Organisms

- No cases of multi-drug and poly-drug resistance were reported in patients infected with ***Mycobacterium tuberculosis*** (MTB) in 2013. In addition, no cases of extensively drug-resistant MTB were reported during this time frame. In 2013, 8.5% of patients were infected with MTB exhibited resistance to one drug.

Data Sources

BC Biomedical Laboratories and LifeLabs Medical Laboratory Services
BC Public Health Microbiology & Reference Laboratory
Canadian Bacterial Surveillance Network
Canadian Integrated Program for Antimicrobial Resistance Surveillance

Abbreviations and Acronyms

AMR	Antimicrobial Resistance
ATC	Anatomical Therapeutic Classification
BC	British Columbia
BCAMM	British Columbia Association of Medical Microbiologists
BCCDC	British Columbia Centre for Disease Control
BCPHMRL	British Columbia Public Health Microbiology & Reference Laboratory
CA-MRSA	Community-Associated Methicillin-Resistant *Staphylococcus aureus*
CANWARD	Canadian Ward Surveillance Study
CBSN	Canadian Bacterial Surveillance Network
CIPARS	Canadian Integrated Program for Antimicrobial Resistance Surveillance
CLSI	Clinical and Laboratory Standards Institute
CNISP	Canadian Nosocomial Infection Surveillance Program
CRE	Carbapenem-resistant Enterobacteriaceae
DNA	Deoxyribonucleic acid
D-test	Double Disk Diffusion Test
ESBL	Extended-Spectrum β-lactamase
GAS	Group A Streptococcus
HA-MRSA	Hospital-Associated Methicillin-Resistant *Staphylococcus aureus*
iPHIS	Integrated Public Health Information System
MIC	Minimum Inhibitory Concentration
MRSA	Methicillin-Resistant *Staphylococcus aureus*
MSSA	Methicillin-Susceptible *Staphylococcus aureus*
NML	National Microbiology Laboratory
MTB	*Mycobacterium tuberculosis*
PHAC	Public Health Agency of Canada
SPICE	*Serratia* spp., *Providencia* spp., *Morganella* spp., *Citrobacter* spp., and *Enterobacter* spp. are collectively referred to as the SPICE organisms
TMP-SMX	Trimethoprim-Sulfamethoxazole
UTI	Urinary Tract Infection
VRE	Vancomycin-Resistant *Enterococcus*
WHO	World Health Organization

Introduction

Antimicrobial resistance (AMR) poses a serious threat to public health globally (1). Bacterial strains that develop or acquire resistance to one or more first-line antimicrobials pose numerous challenges to healthcare including: increased patient morbidity and mortality, increased drug costs, prolonged illness duration, and more expensive disease control measures (2). These antimicrobial resistant strains arise, in part, as a result of antimicrobial use that selects for resistant organisms (2). Inappropriate antimicrobial use, therefore, contributes unnecessarily to the rise in resistance. As AMR genes or plasmids can be readily transmitted between bacterial species via horizontal gene transfer (HGT), surveillance of AMR trends is critical for the rapid detection of new isolates and continuous monitoring of disease prevalence (2). This report aims to provide a comprehensive overview of antibacterial resistance trends for clinically relevant Gram positive and Gram negative bacteria in the community in the province of British Columbia (BC), for all years where data are available, as part of the *Do Bugs Need Drugs?* (DBND) program evaluation. The DBND program is a community education program for health care professionals and the public geared towards decreasing antibiotic overuse and misuse and limiting the spread of resistant organisms. DBND has been funded since its inception in BC (2005) by the Medical Beneficiary & Pharmaceutical Services Division, BC Ministry of Health. Although this report has been updated annually since 2006, data presented in this report differ from previous years due to additional information regarding changes in testing methods or number of isolates tested. The most current report should be considered the most accurate.

Methods

Data were provided by various provincial and national collaborators in either anonymized, line-listed form or aggregate form. New to the report this year is the inclusion of line-listed data provided by LifeLabs Medical Laboratory Services (LifeLabs), in addition to line-listed data provided by BC Biomedical Laboratories (now part of LifeLabs). BC Biomedical has a concentration of services in the Fraser Health Authority region whereas LifeLabs, a community-based laboratory network, provides services to Vancouver Island and the rest of the Mainland. Data from the Mainland and the Island are presented separately to provide a geographical comparison of the non-susceptibility rates. Where data from both geographical areas show similar trends, an overall statement regarding the LifeLabs data was provided. It should be noted, that LifeLabs and BC Biomedical use different susceptibility testing methodologies which may affect the estimates presented in the report. Please see Appendix B for more information.

Data analysis

Data were analyzed using SPSS 14.0 for Windows. Microsoft Excel 2007 was used in the creation of all figures and tables. Where appropriate, the trend of non-susceptibility over time was tested for significance using the two-sided non-parametric Spearman Rank test. Please note that for BC Biomedical data, the trend over time was tested for significance between 2007 and 2013 and between 2008 and 2013 for LifeLabs data. All available years were included in the analysis. The significance level for this report was set at $p<0.05$.

Updates to the report

In addition to the inclusion of LifeLabs data to this report, a short description on the new carbapenem-resistant organism (CPO) surveillance system in BC has been added within the extended-spectrum beta-lactamase (ESBL) section. Estimates from BCAMM were not included in analyses this year due to the unavailability of updated data at the time of report preparation. Several new organisms have also been added including Salmonella (non-typhoidal), Salmonella serovar Heidelberg, Campylobacter, Neisseria meningitidis, and Neisseria gonorrhoeae.

Important Notes

- Antimicrobial resistance refers to the organism's ability to survive in the presence of one or more antimicrobial agents. Organisms are tested for susceptibility to antimicrobial agents in the laboratory using the minimum inhibitory concentration (MIC) breakpoints, as set out by the Clinical and Laboratory Standards Institute (CLSI) guidelines (3). The MIC breakpoint is the lowest concentration of the drug that will inhibit growth of the bacteria (3).
- In the event that the proportion of isolates reaching the intermediate MIC breakpoint threshold is greater than 3%, intermediate and resistant isolates are presented separately. Unless otherwise indicated, all other data combine both resistant and intermediate isolates, and are referred to as the percent of isolates non-susceptible to the specified antimicrobial.
- Organism-antibiotic combinations were selected based on data availability and empiric therapy guidelines as set out in the *Bugs and Drugs* antimicrobial and infectious disease reference manual. Where applicable,

indicators from the WHO's Antimicrobial Resistance Global Surveillance report, the UK's Five Year Antimicrobial Resistance Strategy report, and DANMAP 2012 were used in reference (1;54;55).

- All resistance and non-susceptibility trends are reported on a per isolate basis with the exception of carbapenem-resistant organisms (CPOs) and *Mycobacterium tuberculosis* which are reported on a per patient basis.
- As resistance rates differed substantially between organisms, scale bars (vertical axes) on figures are not consistent between organisms. Caution should be exercised when interpreting and comparing figures across organisms.

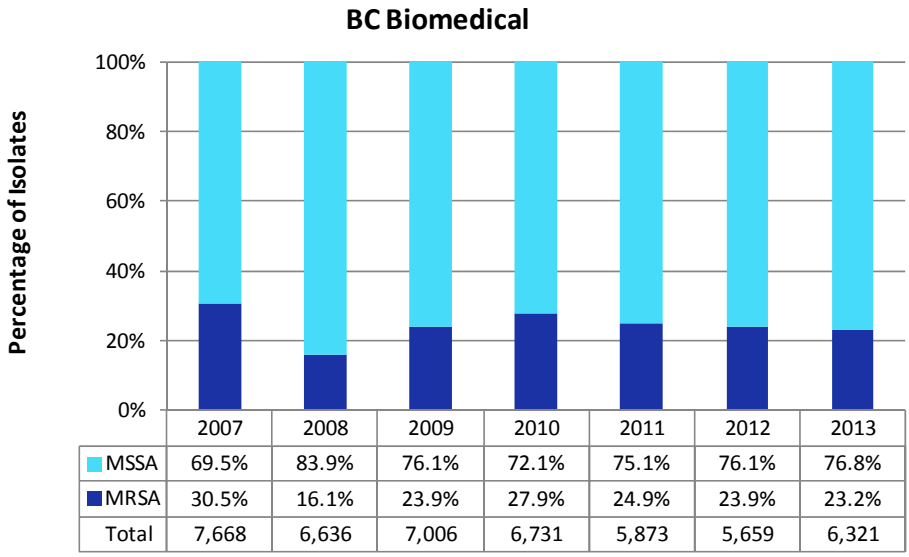
Gram-positive Organisms

1.1. *Staphylococcus aureus*

Staphylococcus aureus is a Gram positive organism that most commonly causes skin and soft tissue infections, but can also cause disease in other organ systems (e.g. pneumonia, sepsis) (4). Methicillin-resistant *Staphylococcus aureus* (MRSA) strains are the most prevalent and most clinically important form of antimicrobial resistance among the staphylococci. The existence of MRSA was first reported in 1964 in the United States and the United Kingdom, and nosocomial outbreaks were becoming common by the late 1970s (5). The first major report of MRSA in BC was an outbreak in a Vancouver teaching hospital in 1981 (5). Although MRSA infections were traditionally only acquired in the hospital setting, community-associated MRSA (CA-MRSA) strains have become prevalent both in hospitals and in the community (6). Hospital-associated MRSA (HA-MRSA) infections are typically resistant to multiple classes of antimicrobials in addition to β-lactam antimicrobials. Methicillin-susceptible *S. aureus* (MSSA) reported here, represents all strains of *S. aureus* that are susceptible to the β-lactam class of antibiotics.

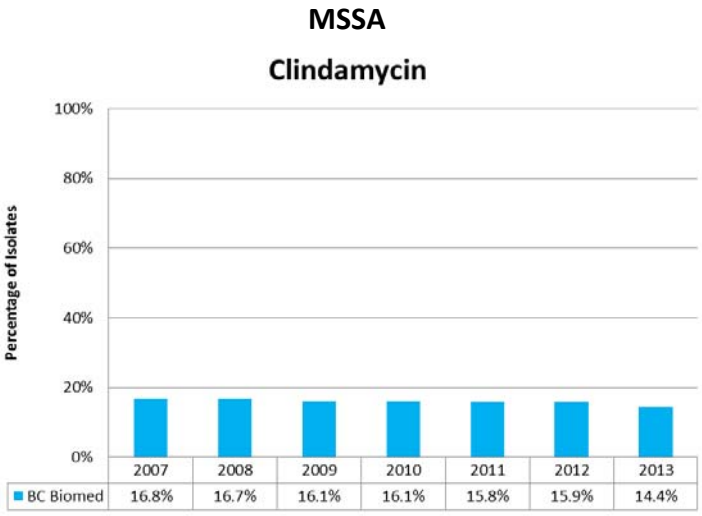
Data from BC Biomedical Laboratories indicate a higher proportion of MRSA among *S. aureus* isolates as compared to data from LifeLabs (both Mainland and Island). Vancouver Island was found to have the lowest rate of MRSA isolates at 13.0% in 2013 while the rate for BC Biomedical Laboratories and Mainland show similar rates (***Figure 1***).

BC Biomedical data shows that among MRSA isolates, resistance to erythromycin, trimethoprim-sulfamethoxazole (TMP-SMX), and tetracycline significantly declined from 2007 to 2013 (erythromycin: $p<0.01$; TMP-SMX: $p<0.01$, tetracycline: $p<0.01$), while clindamycin resistance did not change ($p=0.887$) (***Figure 2***). In 2013, more than 95% of MRSA isolates continued to be susceptible to vancomycin and mupirocin (data not shown). Among MSSA isolates, BC Biomedical data shows that resistance to erythromycin and tetracycline has remained stable from 2007 to 2013 (erythromycin: $p=0.254$; tetracycline: $p=0.303$), but resistance to TMP-SMX and clindamycin decreased during this period, reaching 0.5% and 14.4% respectively in 2013 (TMP-SMX: $p<0.01$, clindamycin: $p<0.01$) (***Figure 2***). In 2013, 99.9% of MSSA isolates were susceptible to cephalothin and all MSSA isolates were susceptible to vancomycin (data not shown). LifeLabs data show similar results (***Figure 1***).

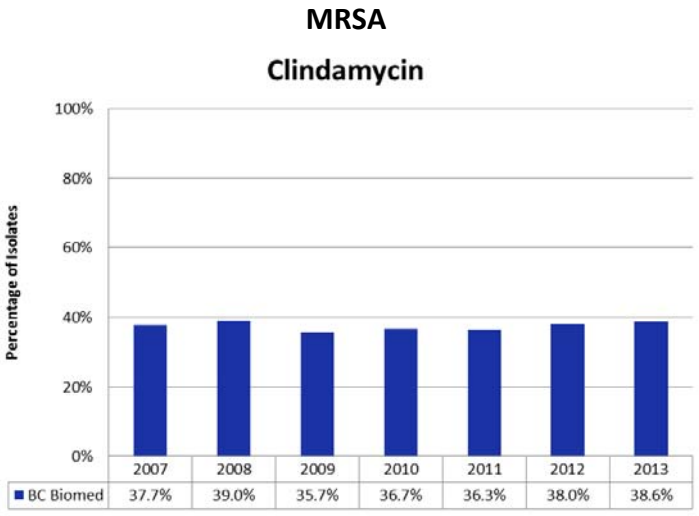


	2007	2008	2009	2010	2011	2012	2013
MSSA	69.5%	83.9%	76.1%	72.1%	75.1%	76.1%	76.8%
MRSA	30.5%	16.1%	23.9%	27.9%	24.9%	23.9%	23.2%
Total	7,668	6,636	7,006	6,731	5,873	5,659	6,321

Figure 1- Proportion of *Staphylococcus aureus isolates* methicillin-sensitive (MSSA) and methicillin-resistant (MRSA) (2007-2013)
Source: BC Biomedical Laboratories



	2007	2008	2009	2010	2011	2012	2013
BC Biomed	16.8%	16.7%	16.1%	16.1%	15.8%	15.9%	14.4%



	2007	2008	2009	2010	2011	2012	2013
BC Biomed	37.7%	39.0%	35.7%	36.7%	36.3%	38.0%	38.6%

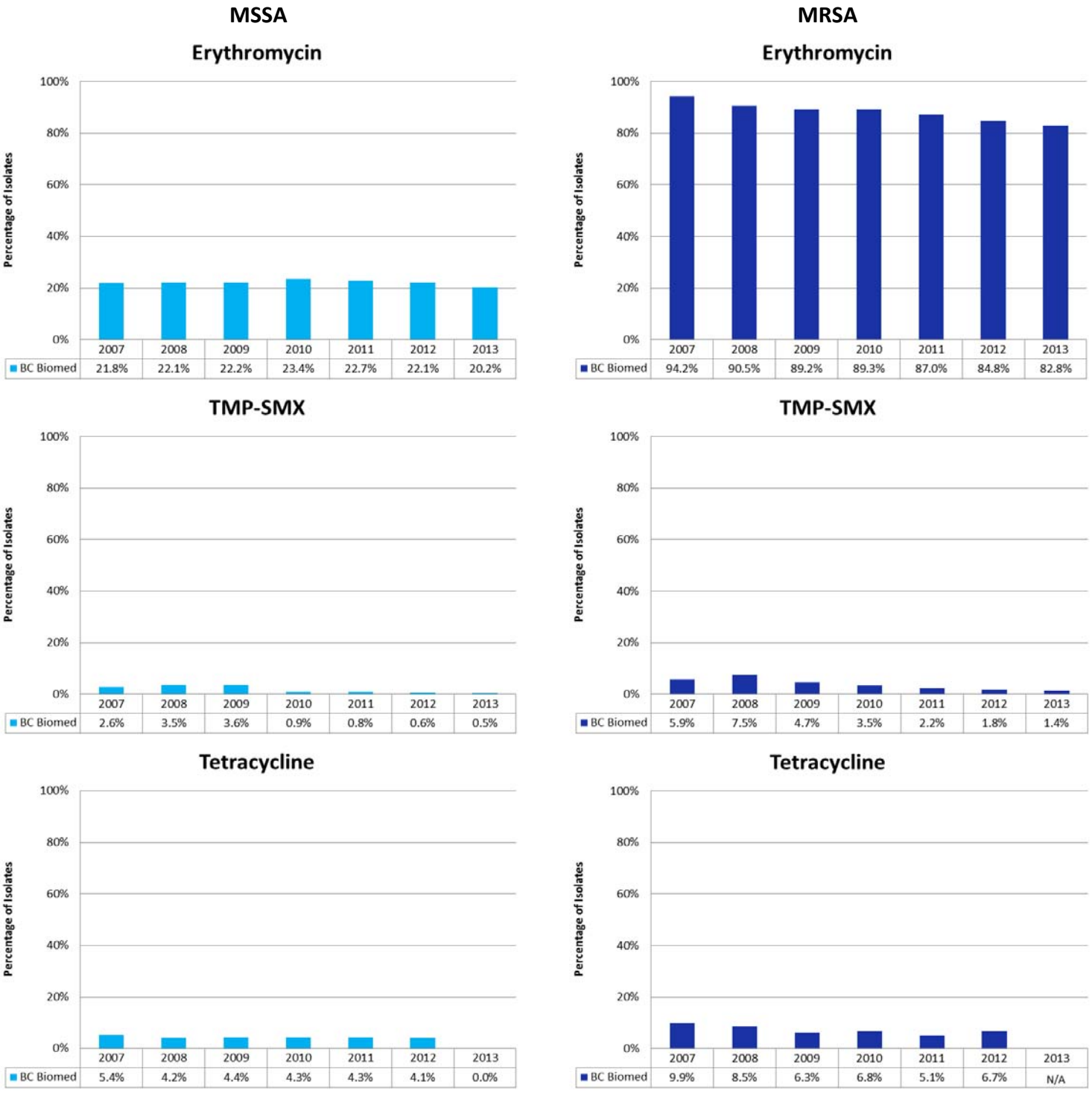


Figure 2- Proportion of MSSA and MRSA isolates non-susceptible to clindamycin, erythromycin , TMP-SMX, and tetracycline (2007-2013).
Source: BC Biomedical Laboratories

Please note: Resistance data to tetracycline was not available for BC Biomedical Laboratories in 2013.

1.2. ***Streptococcus pneumoniae***

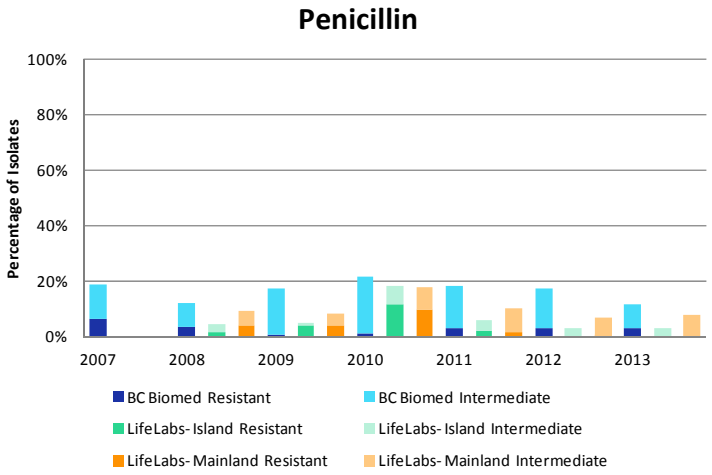
Streptococcus pneumoniae (pneumococcus) is the leading cause of community-acquired pneumonia (CAP), but is also commonly found to be the predominant cause in acute otitis media, bacteraemia, and meningitis (7). All diseases associated with pneumococcal infection follows colonization of the mucosal surface of the upper respiratory tract. Although colonization at this site is asymptomatic, further spread of pneumococci into sections of the airway that are typically sterile will trigger the inflammatory response which results in disease (7). The major virulence factor of pneumococcus is its polysaccharide capsule, of which 91 serotypes differing both structurally and antigenically, has been identified thus far (7;8). Competition exists, not only amongst the various pneumococcal strains, but also among the 700 other microbial species estimated to reside within the human pharynx (7). This highly populated microbial environment presents an excellent opportunity for *S. pneumonia* to take up exogenous DNA from closely related oral streptococcal species and co-colonizing pneumococci thus increasing its overall fitness (7). First-line treatment for pneumococcal infections typically includes β-lactams, macrolides, and tetracycline (see Bugs & Drugs 2012 edition for the full list of recommended therapies) (9). However, uptake of genes by *S. pneumonia* that encode altered penicillin-binding proteins has contributed to the resistance of β-lactams which severely impacts the effective treatment of pneumococcal infections (7). The first *S. pneumonia* isolate described to be non-susceptible to penicillin was identified in Australia in 1967. Resistance to penicillin emerged and spread rapidly to other part parts of the world in 1990s and was associated with increased antibiotic consumption (10). The first case of a penicillin-resistant isolate in BC was reported in 1993 (8). Since the advent of antibiotics, outbreaks of invasive *S. pneumonia* have been relatively rare. However, during the period 2005-2009, an epidemic of invasive pneumococcal disease caused by *S. pneumonia* serotype 5 was observed in Canada, with 33% of cases (343 cases) reported in British Columbia (8). A heptavalent pneumococcal vaccine (PCV7) was introduced in BC since 2003 and covers 80% of serotypes causing invasive disease in children younger than five (11).

According to BC Biomedical Laboratories data, 11.6% of *S. pneumoniae* were non-susceptible to penicillin in 2013, the majority of which showed intermediate resistance (***Figure 3***).The proportion of *S. pneumoniae* non-susceptible to erythromycin remained stable around 30% from 2007 to 2013 (p=0.810) and is at 26.2% in 2013 14.3% (***Figure 3***). Similarly, non-susceptibility towards TMP-SMX has appeared to remain stable at approximately 20% of isolates from 2007 to 2013 (p=0.435). Tetracycline non-susceptibility has exhibited similar trends, with non-susceptibility rates fluctuating between 15% and 20% from 2007 to 2013 (p=0.380) (***Figure 3***). Levofloxacin non-susceptibility has remained less than 5% of isolates since 2007 and currently sits at 2.2% (data not shown). All isolates were susceptible to ceftriaxone and vancomycin in 2013 and all isolates were fully resistant to cefixime (data not shown).

Data from the CBSN suggest a general increase in the percent of isolates non-susceptible to erythromycin, clindamycin, and ciprofloxacin between 1994 and 2013 (erythromycin: p<0.01, clindamycin: p<0.01 and ciprofloxacin: p<0.01), a trend not observed in the BC Biomedical data (***Figure 4***). Due to changes in methodology of testing (changes in MIC breakpoints), only resistance data was used for analysis of *S. pneumoniae* to tetracycline which is at a rate of 10.2% in 2013. Penicillin non-susceptibility has fluctuated quite drastically between less than 5% to more than 20% for the period of 1994 to 2013 (p=0.473). From 2009 to 2011, it appeared as though the rate of isolates non-susceptible to penicillin was decreasing from 20.0% to 8.2%; however, non-susceptibility increased again in 2012 and is reported to be at 20.3% in 2013 (***Figure 4***). TMP-SMX non-susceptibility had remained stable, just above 20.0%, from 207 to 2011 but decreased by more than ten percent in 2012 and is reported to be at 15.3% in 2013 (p=0.270) (***Figure 4***). Ceftriaxone non-susceptibility remains low in 2013 at a rate of 6.4%, with a peak noted in 2010 (10.6%) (***Figure 4***). Additionally 100% of *S. pneumoniae* isolates remained sensitive to moxifloxacin and levofloxacin in 2013 (***Figure 4***).

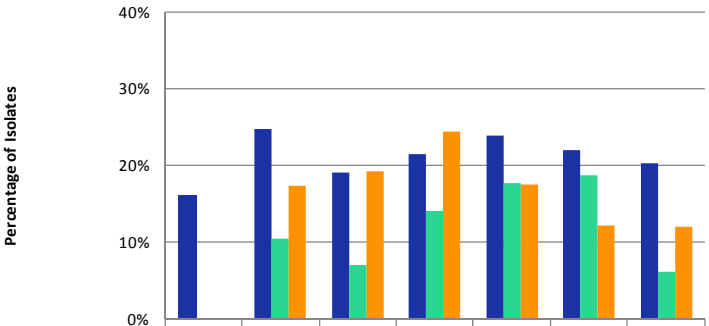
LifeLabs data suggest that higher non-susceptibility rates across all tested antibiotics exist on the Mainland when compared to Vancouver Island among *S. pneumoniae* isolates. Analyses for resistance against penicillin were restricted to oral-penicillin susceptibility results for non-meningitis *S. pneumoniae* isolates. A decreasing trend is observed in non-susceptibility towards penicillin and is at a rate of 3.1% on Vancouver Island and 7.9% in 2013, which is lower than BC Biomedical rate (11.6%) (***Figure 3***). In 2013, non-susceptibility data to TMP-SMX was 11.9% for Mainland isolates and 6.0% for Island isolates, which is much lower than BC Biomedical data (20.2%) (***Figure 3***). The rate of erythromycin non-susceptibility in 2013 was higher among isolates from the mainland (24.5%) when compared to isolates from the island (12.1%) with the rate from mainland closely mirroring the trend observed from BC Biomedical (***Figure 3***). The rate of tetracycline non-susceptibility has remained above 20% since 2008 and is much higher for the Mainland (20.9%) when compared to Island (6.0%) in 2013 (***Figure 3***).

Discrepancies between the data sources may be due to the differences in the site of data collection. BC Biomedical Laboratories collect isolates from community sources throughout the Fraser Health region, LifeLabs Medical Laboratory Services collects isolates from community sources from Lower Mainland as well as Vancouver Island while CBSN obtains isolates from several hospitals in BC; for 2010 to 2013, susceptibility results from two hospitals were available at time of publication.



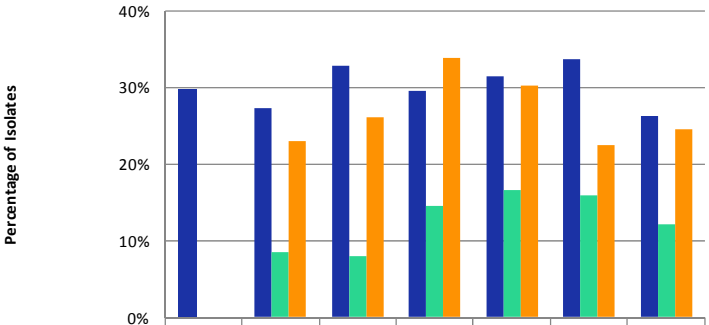
		Year						
Data Source	Susceptibility	2007	2008	2009	2010	2011	2012	2013
BC Biomed	I[a.]	12.3%	8.8%	16.3%	20.7%	15.0%	14.5%	8.4%
	R[b.]	6.5%	3.4%	0.8%	0.9%	3.0%	2.7%	3.2%
LifeLabs- Island	I	N/A	2.8%	0.8%	6.5%	3.9%	2.9%	3.1%
	R	N/A	1.4%	4.1%	11.6%	1.9%	0.0%	0.0%
LifeLabs- Mainland	I	N/A	5.0%	4.2%	7.9%	8.5%	6.6%	7.9%
	R	N/A	8.5%	4.0%	9.6%	1.4%	0.2%	0.0%

TMP-SMX



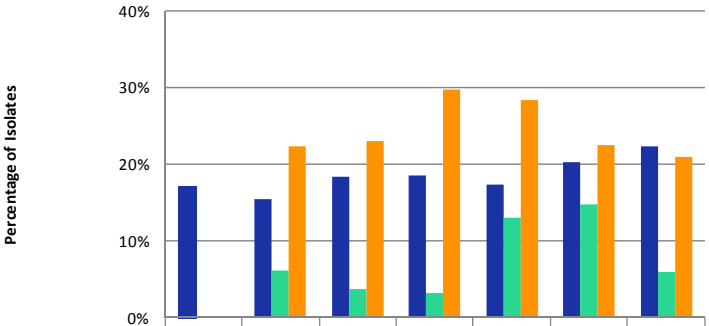
	2007	2008	2009	2010	2011	2012	2013
BC Biomed	16.13%	24.68%	18.94%	21.37%	23.88%	21.93%	20.20%
LifeLabs- Island	N/A	10.5%	6.9%	14.0%	17.7%	18.8%	6.0%
LifeLabs- Mainland	N/A	17.3%	19.2%	24.3%	17.5%	12.2%	11.9%

Erythromycin



	2007	2008	2009	2010	2011	2012	2013
BC Biomed	29.7%	27.3%	32.8%	29.5%	31.4%	33.7%	26.2%
LifeLabs- Island	N/A	8.5%	8.0%	14.6%	16.6%	16.0%	12.1%
LifeLabs- Mainland	N/A	22.9%	26.1%	33.8%	30.2%	22.4%	24.5%

Tetracycline



	2007	2008	2009	2010	2011	2012	2013
BC Biomed	17.1%	15.4%	18.3%	18.4%	17.4%	20.2%	22.2%
LifeLabs- Island	N/A	6.0%	3.7%	3.2%	13.1%	14.6%	6.0%
LifeLabs- Mainland	N/A	22.4%	23.1%	29.6%	28.2%	22.5%	20.9%

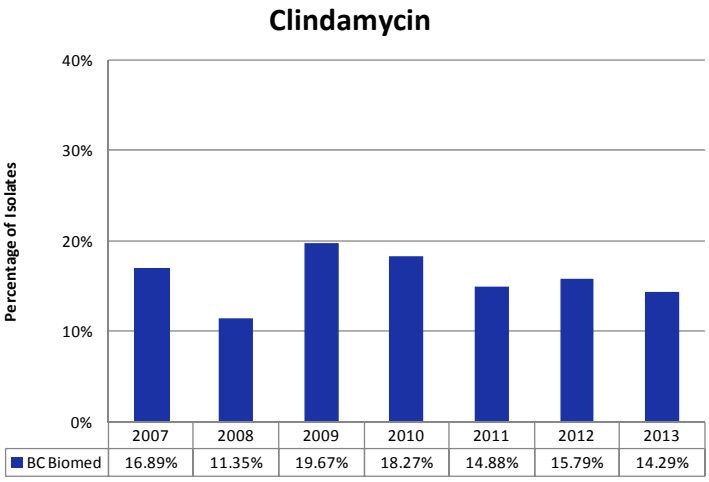
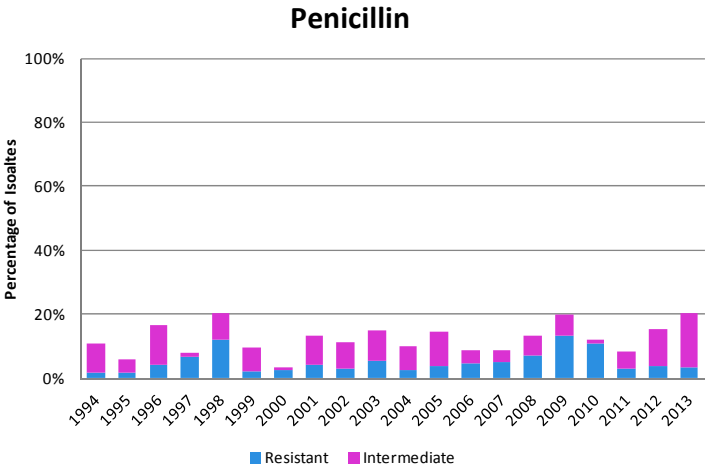
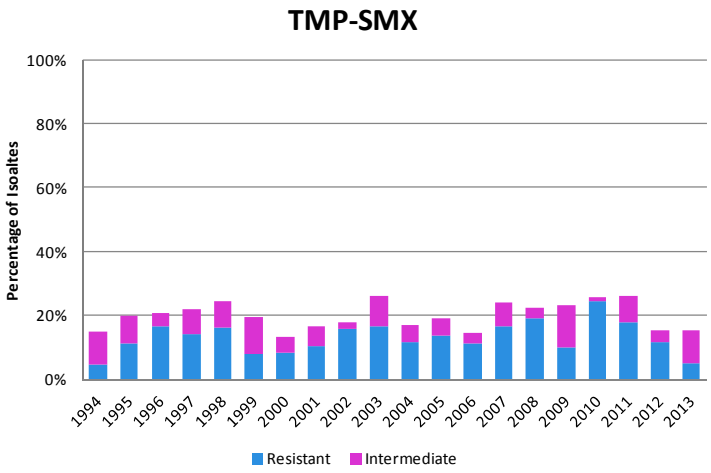
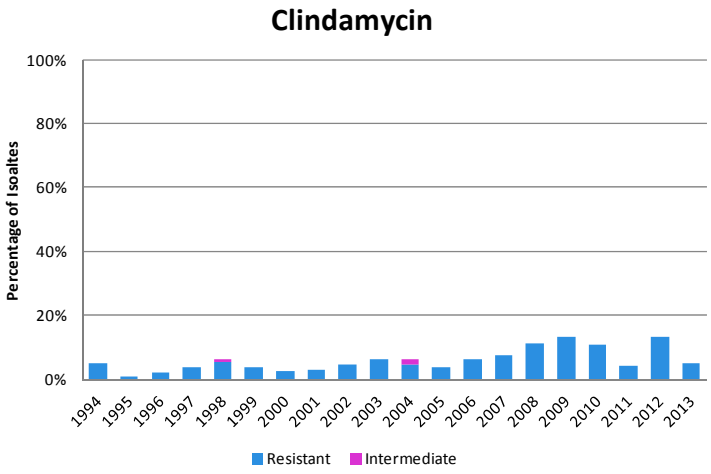


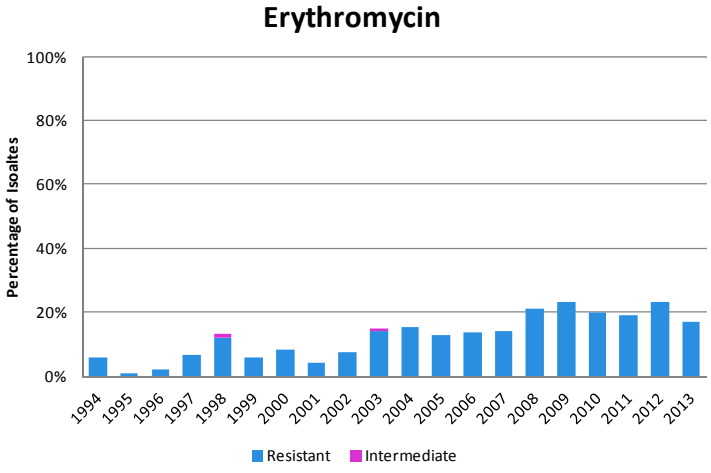
Figure 3- Proportion of *Streptococcus pneumoniae* isolates non-susceptible to penicillin, TMP-SMX, erythromycin, tetracycline, and clindamycin (2007-2013)
Source: BC Biomedical Laboratories and LifeLabs Medical Laboratory Services
[a]I= Isolates classified as having intermediate resistance based on MIC breakpoints and CLSI guidelines
[b]R= Isolates classified as resistant based on MIC breakpoints and CLSI guidelines

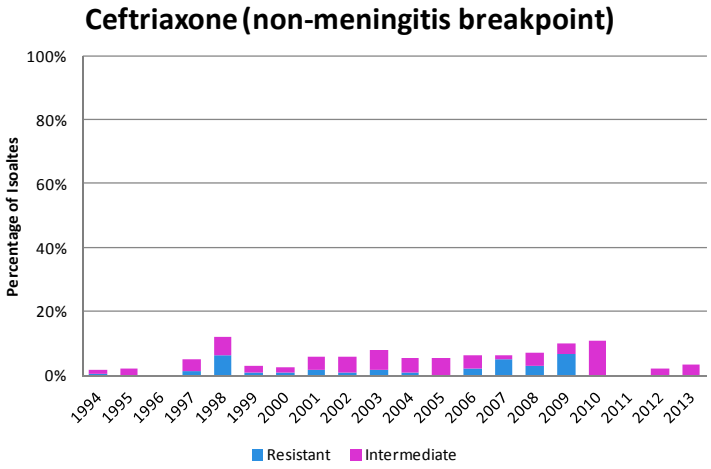
Please note: LifeLabs data for resistance to clindamycin was limited (n<30); hence, data were not included in the analysis.

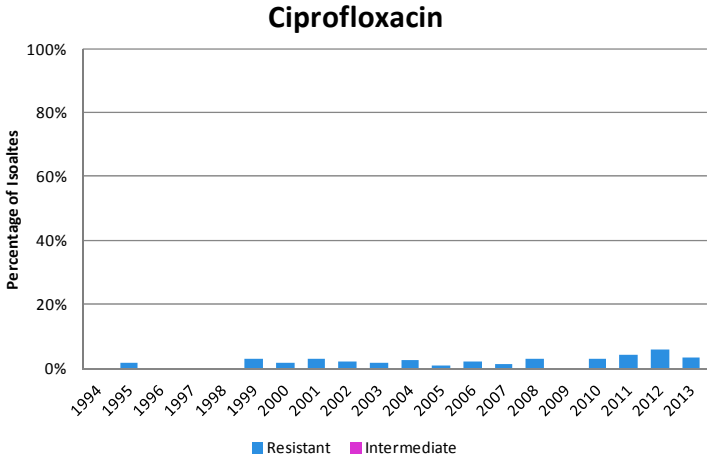


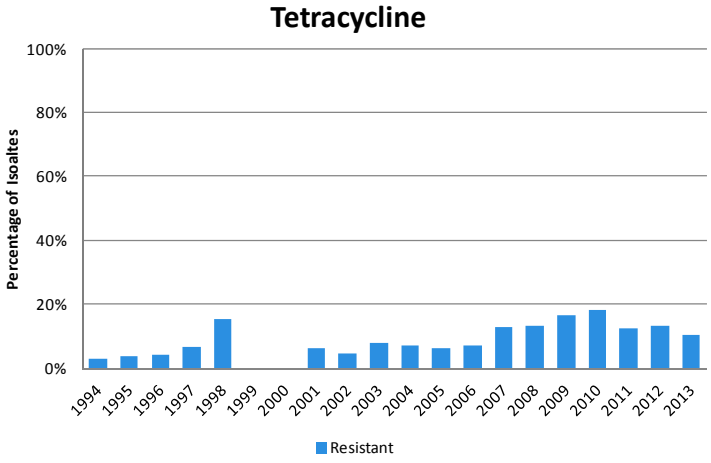

TMP-SMX
100%
80%
60%
40%
20%
0%
Percentage of Isoaltes
1994 1995 1996 1997 1998 1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013
Resistant
Intermediate


Clindamycin
100%
80%
60%
40%
20%
0%
Percentage of Isoaltes
1994 1995 1996 1997 1998 1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013
Resistant
Intermediate


Erythromycin
100%
80%
60%
40%
20%
0%
Percentage of Isoaltes
1994 1995 1996 1997 1998 1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013
Resistant
Intermediate


Ceftriaxone (non-meningitis breakpoint)
100%
80%
60%
40%
20%
0%
Percentage of Isoaltes
1994 1995 1996 1997 1998 1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013
Resistant
Intermediate


Ciprofloxacin
100%
80%
60%
40%
20%
0%
Percentage of Isoaltes
1994 1995 1996 1997 1998 1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013
Resistant
Intermediate


Tetracycline
100%
80%
60%
40%
20%
0%
Percentage of Isoaltes
1994 1995 1996 1997 1998 1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013
Resistant

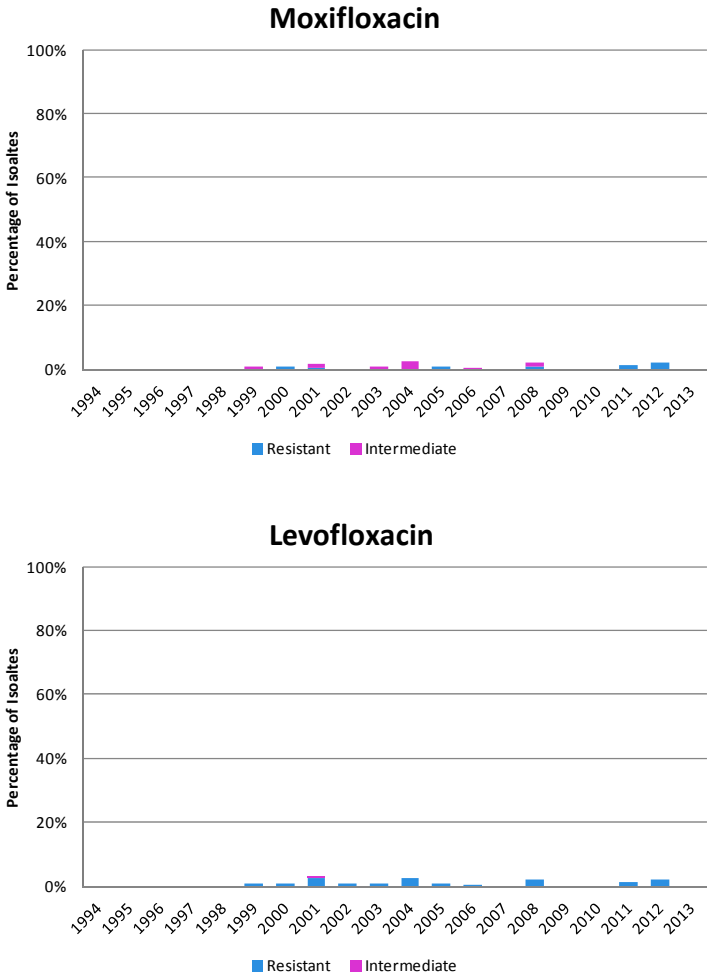


Figure 4- Proportion of *Streptococcus pneumoniae* isolates non-susceptible to penicillin, TMP-SMX, clindamycin, erythromycin, ceftriaxone, ciprofloxacin, tetracycline, moxifloxacin, and levofloxacin (1994-2013).
Source: CBSN

1.3. *Streptococcus pyogenes*

Streptococcus pyogenes, also known as β-hemolytic Group A Streptococci (GAS), typically presents as a relatively mild, non-invasive throat infection ("Strep throat"), but can also cause more serious invasive infections including necrotizing fasciitis and toxic shock syndrome (12). Recommended therapies for GAS infections include penicillin, clindamycin, azithromycin, clarithromycin, and cephalexin (9). Erythromycin-resistant isolates of *S. pyogenes* were first documented in the United Kingdom during the 1950s, consequently, erythromycin is no longer a recommended empiric therapy following BC provincial guidelines.

Two main mechanisms of resistance against macrolides (e.g. azithromycin, clarithromycin, erythromycin) are utilized by *S. pyogenes*. The first mechanism is the methylation of bacterial ribosome by a protein (encoded by *erm*), which reduces the affinity of the antimicrobial drug for the ribosome (13). This is referred to as the MLS_B phenotype (13). Another mechanism contributing to the macrolide resistance involves an efflux pump specific for macrolides coded by the *mefA* gene, which pumps macrolides out of the cell thus reducing the antimicrobial effect (13). The presence of this efflux system in a macrolide resistant strain is referred to as the M phenotype (13). There are variations in the types of M/*emm* in GAS (14). Until the mid 2000s, M1 was the most prevalent M type, however, from 2006-2009, Western Canada observed the emergence of M/*emm* 59 type GAS (14).

BC Biomedical Laboratories data include both invasive and non-invasive GAS isolates for all years available. All isolates remained susceptible to penicillin, amoxicillin-clavulanate, and cephalothin as of 2013 (data not shown). The percent of isolates non-susceptible to erythromycin had appeared to be decreasing from 2007 to 2010 but have since increased, peaking at 22.7% non-susceptibility in 2012 (p=0.002) but has decreased slightly and was reported at 18.4% in 2013 (***Figure 5***). Non-susceptibility patterns to clindamycin show a similar trend to erythromycin non-susceptibility for all years (2007-2013), peaking at a non-susceptibility rate of 22.3% in 2012 (p=0.032) and decreasing to 17.9% in 2013 (***Figure 5***). The non-susceptibility rate to clindamycin observed in BC is much higher than national rates as reported by the CANWARD study which showed 100% susceptibility (15). The difference may be attributed to the difference in source of isolates, as isolates tested in the CANWARD study are hospital-based. All isolates were fully susceptible to penicillin and cephalothin, but fully resistant to ciprofloxacin and TMP-SMX in 2013 (data not shown) (15).

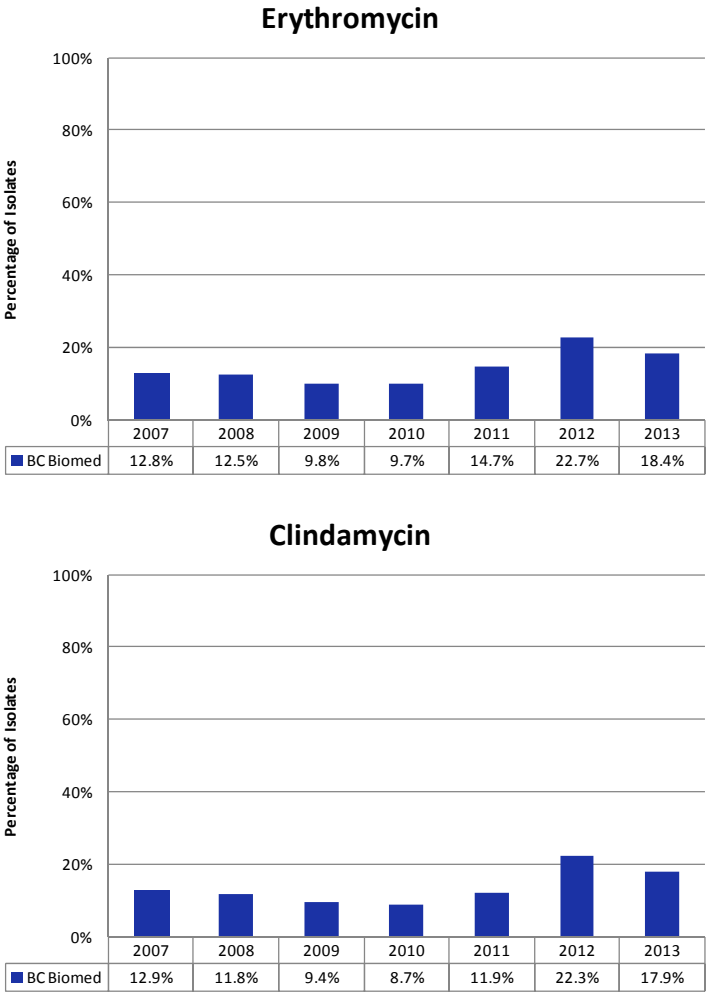


Figure 5- Proportion of *Streptococcus pyogenes* isolates non-susceptible to erythromycin and with inducible clindamycin non-susceptibility (as determined by the D-test in the presence of erythromycin) (2007-2013)
Source: BC Biomedical Laboratories

Please note: LifeLabs does not routinely test for susceptibility in GAS isolates; data was not included in the analysis for this report.

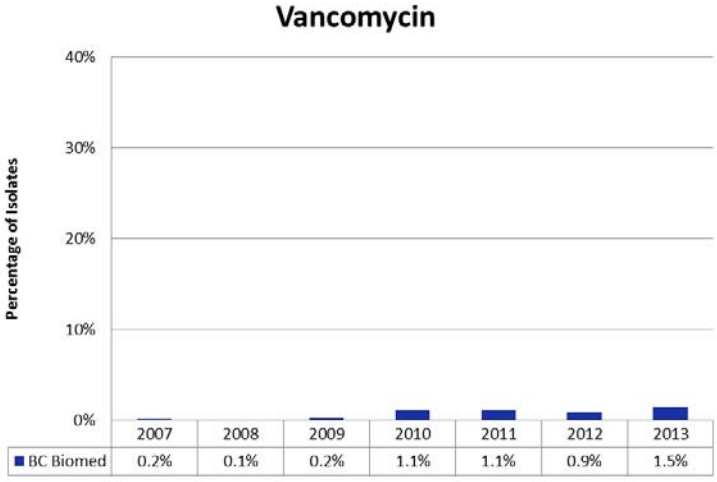
1.4. *Enterococcus* spp.

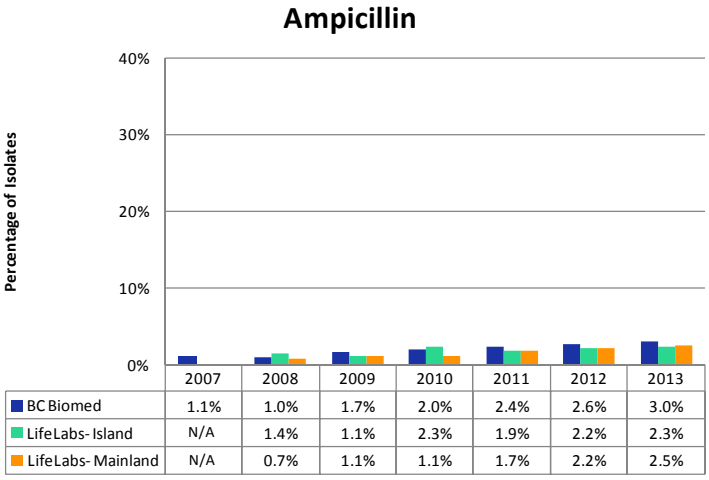
A prominent nosocomial pathogen, enterococci, specifically *Enterococcus faecalis* and *Enterococcus faecium*, are normal enteric flora bacteria that may cause urinary tract infections (UTIs), intra-abdominal infections, and bacteremia. Most enterococcus strains are intrinsically resistant to macrolides, lincosamides, TMP-SMX, and β-lactams including cephalosporins and some penicillins (16).

Vancomycin-resistant *Enterococci* (VRE) typically present as nosocomial infections often affecting patients that are immunocompromised, previously treated with antibiotics for an extensive period, have undergone surgical procedures and those with medical devices such as a urinary catheter (17). Transmission of VRE can occur by direct person to person contact or contact with contaminated surfaces such as hands of care-givers during hospitalization and toilet seats (17). The Public Health Agency of Canada collects data on VREs in acute-care hospitals through the Canadian Nosocomial Infection Surveillance Program (CNISP) (17). The first case of VRE was first reported in Canada in the early 1990s, with the first outbreak of VRE occurring in an Ontario hospital in 1995 (18). Surveillance data generated from CNISP shows that although the rate remains low, a significant increase in nosocomial VRE infections since 2008 exists, mainly affecting the older population with previous hospitalization (17).

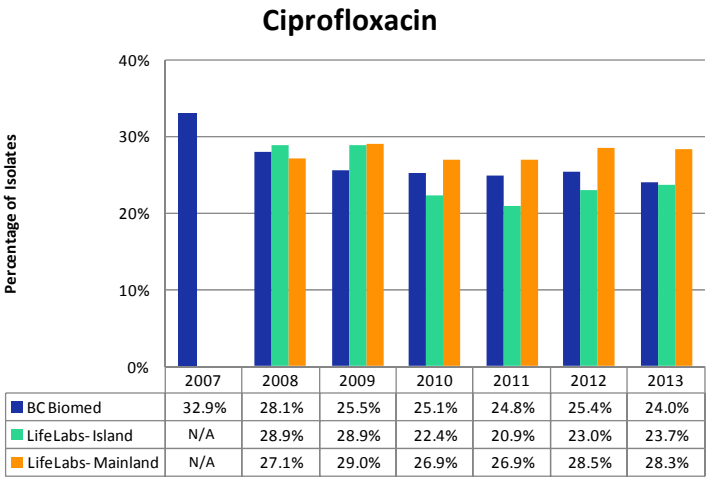
Resistance in *Enterococcus* spp. isolates to ampicillin shows an increasing trend during the period 2007 to 2013 and is reported to be at 3.0% (BC Biomedical, $p<0.001$), 2.3% (LifeLabs-Island, $p=0.004$) and 2.5% (LifeLabs-Mainland, $p<0.001$) (***Figure 6***). According to BC Biomedical Laboratories data, the proportion of *Enterococcus* spp. isolates resistant to nitrofurantoin and vancomycin remained under 2% since 2007 and is reported to be at 0.7% and 1.5% respectively (***Figure 6***). LifeLabs data show slightly higher non-susceptibility rates to nitrofurantoin with an increasing trend since 2008 and is reported to be at 4.6% on the Island and 4.0% on the Mainland in 2013 (***Figure 6***). A slight increase in non-susceptibility to vancomycin resistance, according to BC Biomedical Laboratories data, was observed in 2013 (***Figure 6***).

Ciprofloxacin non-susceptibility shows a declining trend from 2007 to 2013 using data from BC Biomedical and LifeLabs; yet, approximately one fourth of isolates showed non-susceptibility in 2013 across all three data sources. In 2013, non-susceptibility rates was reported at 23.7% for LifeLabs isolates from Vancouver Island, 28.3% for LifeLabs isolates from Mainland, and 24.0% for BC Biomedical isolates. Additionally, a decreasing trend was observed over time from 2007 to 2013 within the BC Biomedical data ($p<0.01$) (***Figure 6***). When resistance to ciprofloxacin of urinary *Enterococcus* isolates is broken down into ten-year age groups, an increase in the proportion of isolates resistant to ciprofloxacin is observed among older individuals, particularly those aged 70 and older (***Figure 7***). A similar trend is observed in the data from BC Biomedical Laboratories for *E. coli* isolates (**Figure 9**). The higher rates of resistance among older adults may be explained by the greater lifetime cumulative exposure to ciprofloxacin and other antibiotics and, consequently a greater selection for resistance (19).

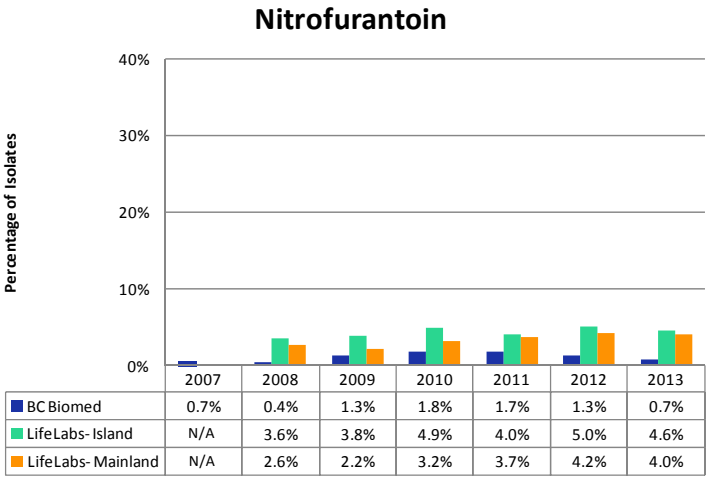




	2007	2008	2009	2010	2011	2012	2013
BC Biomed	1.1%	1.0%	1.7%	2.0%	2.4%	2.6%	3.0%
LifeLabs- Island	N/A	1.4%	1.1%	2.3%	1.9%	2.2%	2.3%
LifeLabs- Mainland	N/A	0.7%	1.1%	1.1%	1.7%	2.2%	2.5%

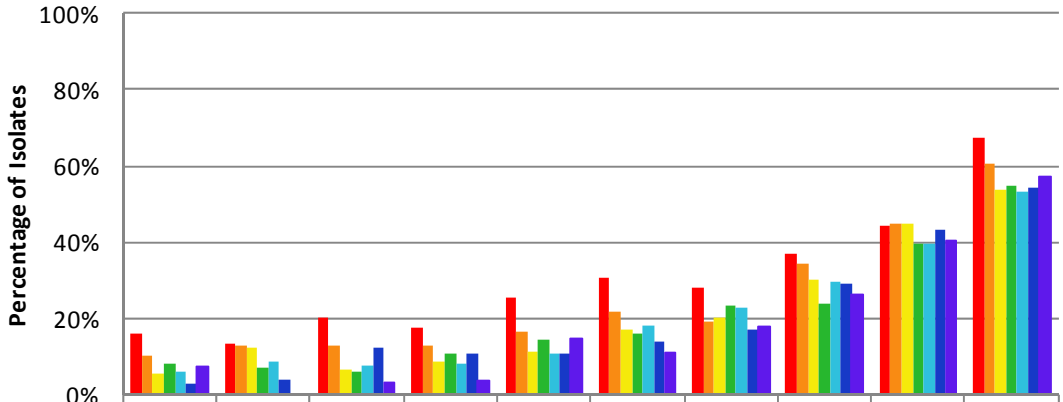


	2007	2008	2009	2010	2011	2012	2013
BC Biomed	32.9%	28.1%	25.5%	25.1%	24.8%	25.4%	24.0%
LifeLabs- Island	N/A	28.9%	28.9%	22.4%	20.9%	23.0%	23.7%
LifeLabs- Mainland	N/A	27.1%	29.0%	26.9%	26.9%	28.5%	28.3%



	2007	2008	2009	2010	2011	2012	2013
BC Biomed	0.7%	0.4%	1.3%	1.8%	1.7%	1.3%	0.7%
LifeLabs- Island	N/A	3.6%	3.8%	4.9%	4.0%	5.0%	4.6%
LifeLabs- Mainland	N/A	2.6%	2.2%	3.2%	3.7%	4.2%	4.0%

Figure 6- Proportion of *Enterococcus* spp. isolates non-susceptible to vancomycin, ampicillin, nitrofurantoin, and ciprofloxacin (2007-2013)
Source: BC Biomedical Laboratories and LifeLabs Medical Laboratory Services



	<10	10-19	20-29	30-39	40-49	50-59	60-69	70-79	80-89	>90
2007	15.8%	13.3%	20.1%	17.6%	25.3%	30.4%	27.9%	37.0%	44.5%	67.4%
2008	10.3%	12.9%	12.8%	13.0%	16.3%	21.8%	19.2%	34.4%	44.9%	60.5%
2009	5.4%	12.0%	6.3%	8.8%	11.1%	17.1%	20.1%	30.0%	44.8%	53.7%
2010	7.9%	6.8%	5.9%	10.5%	14.5%	16.0%	23.4%	23.7%	39.5%	54.6%
2011	5.8%	8.5%	7.8%	8.3%	10.8%	18.0%	22.8%	29.8%	39.4%	53.2%
2012	2.7%	4.1%	12.2%	10.7%	10.6%	14.0%	16.9%	29.0%	43.4%	54.1%
2013	7.3%	0.0%	3.3%	3.5%	14.4%	11.0%	17.7%	26.3%	40.5%	57.1%

Figure 7 - Proportion of *Enterococcus* spp. urinary isolates non-susceptible to ciprofloxacin by age of patient (2007-2013)
Source: BC Biomedical Laboratories

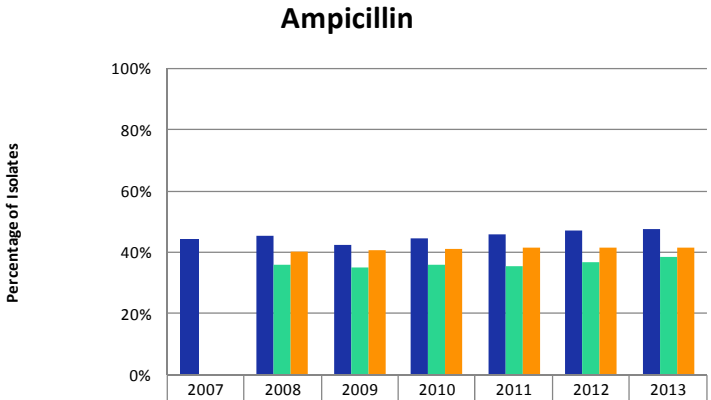
Gram-negative Organisms

1.5. *Escherichia coli*

Escherichia coli typically exist as a commensal bacteria colonizing the gastrointestinal tract of human, rarely causing disease other than in immunocompromised individuals or when the barriers between gastrointestinal epithelial cells is disrupted (20). However, there now exists several strains of *E.coli* that have acquired specific virulence factors that allow them to colonize new niches causing a variety of disease including enteric/diarrhoeal disease, urinary tract infections (approximately 85-90%), and sepsis/meningitis (21;20). A wide genetic diversity exists in pathogenic *E.*coli due to the possession of a variety of specialized virulence genes encoded on pathogenicity islands (mobile genetic elements) which is acquired via HGT (22;20). Antibiotic therapy for *E.coli* varies depending on the infection, however, therapy generally includes fluoroquinolones, trimethoprim/sulfamethoxazole, and cephalosporins, for which resistance is rapidly rising (20).

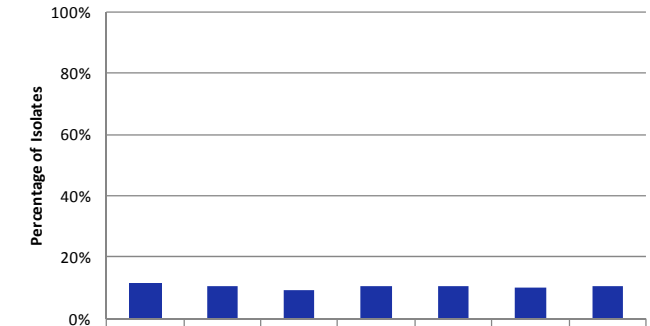
The highest proportion of non-susceptible isolates occurred for ampicillin, with 47.4% of isolates showing non-susceptibility in 2013 according to BC Biomedical data (***Figure 8***). Approximately one-fourth of isolates were non-susceptible to TMP-SMX (25.2%) and ciprofloxacin (24.9%) in 2013 (***Figure 8***). The proportion of E. coli isolates non-susceptible to ampicillin, ciprofloxacin, and gentamicin significantly increased between the years 2007 and 2013 (ampicillin: $p<0.01$; ciprofloxacin: $p<0.01$; gentamicin: $p<0.01$), while nitrofurantoin and cefotaxime showed a decreasing change in non-susceptibility since 2007 (nitrofurantoin: $p<0.01$; cefotaxime: $p<0.01$) (***Figure 8***). The non-susceptibility rate was relatively stable for TMP-SMX ($p=0.414$). Trends noted of *E.coli* non-susceptibility from LifeLabs data for ampicillin, ciprofloxacin, nitrofurantoin, TMP-SMX and gentamicin were similar to those observed in BC Biomedical data (***Figure 8***).

When resistance to ciprofloxacin of urinary *E. coli* isolates is broken down by ten-year age groups, the proportion of resistance increases with increasing patient age, particularly after age 50 (***Figure 9***). This is similar to the trend observed in *Enterococcus* isolates (***Figure 7***), and could be explained by the general tendency for greater cumulative lifetime exposure to ciprofloxacin and other antibiotics among older adults, and greater selection for resistance (19). An American study by Sanchez et al. found that resistance to ciprofloxacin increased at a faster rate over a ten year period for geriatric outpatients when compared with non-geriatric adults (23). The increasing likelihood of UTIs in the geriatric population was attributed to changing physiology, while increases in the number and duration of antibiotic therapy prescriptions in this population likely lead to selective pressures for resistant *E. coli* strains (23).



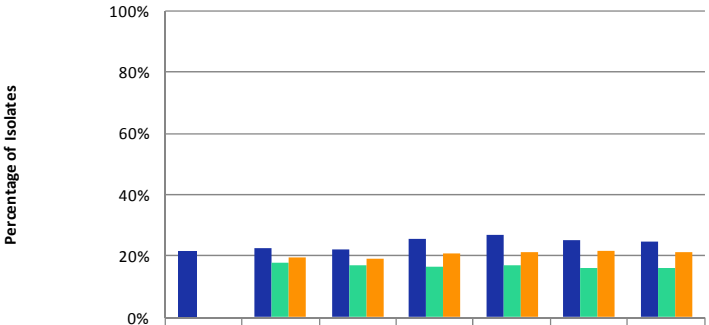
	2007	2008	2009	2010	2011	2012	2013
BC Biomed	44.1%	45.2%	42.3%	44.6%	45.8%	47.1%	47.4%
LifeLabs- Island	N/A	35.9%	35.0%	35.8%	35.7%	36.9%	38.3%
LifeLabs- Mainland	N/A	40.2%	40.6%	41.2%	41.4%	41.3%	41.7%

Cefotaxime



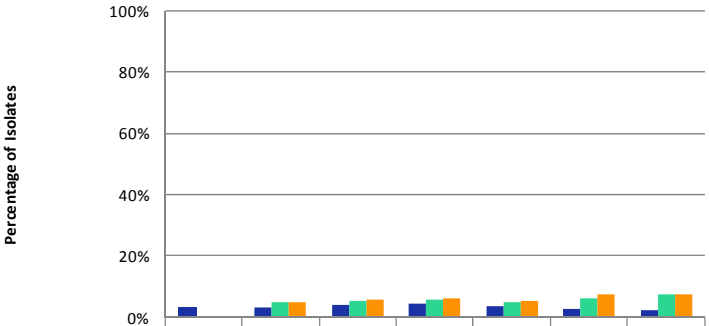
	2007	2008	2009	2010	2011	2012	2013
BC Biomed	11.5%	10.6%	9.1%	10.4%	10.4%	10.0%	10.4%

Ciprofloxacin

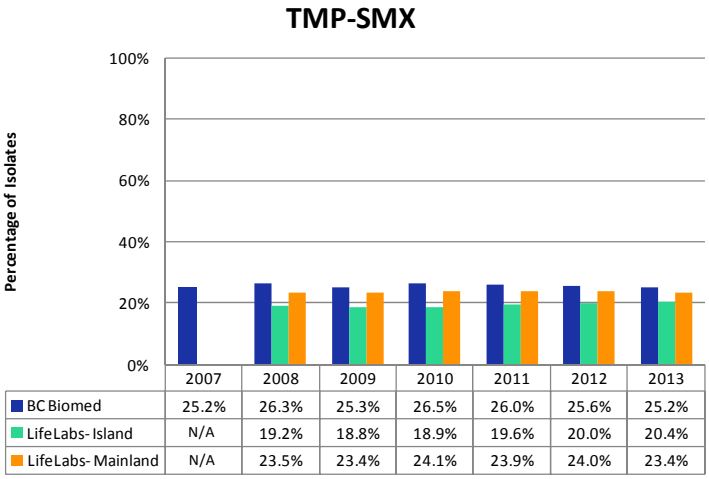


	2007	2008	2009	2010	2011	2012	2013
BC Biomed	21.8%	22.5%	22.3%	25.7%	26.8%	25.3%	24.9%
LifeLabs- Island	N/A	17.8%	16.8%	16.7%	16.9%	15.9%	16.0%
LifeLabs- Mainland	N/A	19.4%	19.0%	21.0%	21.4%	21.7%	21.5%

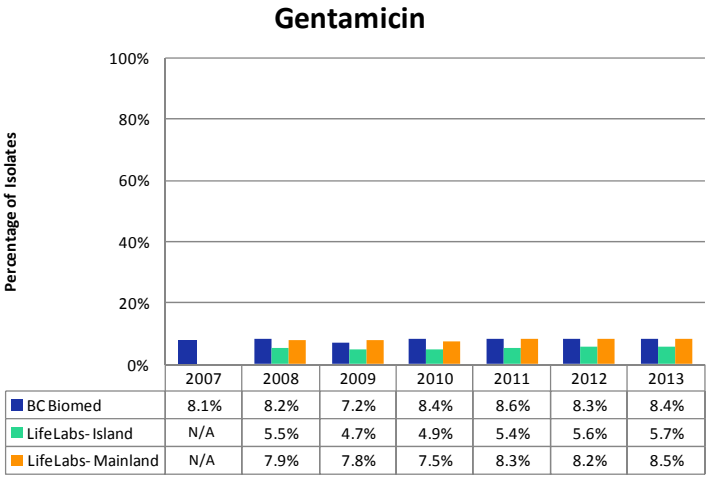
Nitrofurantoin



	2007	2008	2009	2010	2011	2012	2013
BC Biomed	3.1%	3.1%	3.9%	4.3%	3.8%	2.9%	2.5%
LifeLabs- Island	N/A	4.7%	5.3%	5.7%	5.1%	6.2%	7.7%
LifeLabs- Mainland	N/A	4.8%	6.0%	6.3%	5.3%	7.4%	7.7%



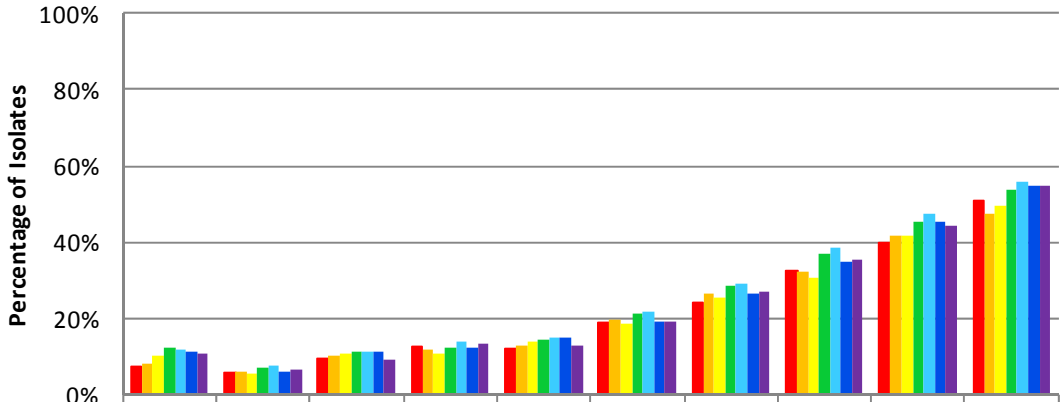
	2007	2008	2009	2010	2011	2012	2013
BC Biomed	25.2%	26.3%	25.3%	26.5%	26.0%	25.6%	25.2%
LifeLabs- Island	N/A	19.2%	18.8%	18.9%	19.6%	20.0%	20.4%
LifeLabs- Mainland	N/A	23.5%	23.4%	24.1%	23.9%	24.0%	23.4%



	2007	2008	2009	2010	2011	2012	2013
BC Biomed	8.1%	8.2%	7.2%	8.4%	8.6%	8.3%	8.4%
LifeLabs- Island	N/A	5.5%	4.7%	4.9%	5.4%	5.6%	5.7%
LifeLabs- Mainland	N/A	7.9%	7.8%	7.5%	8.3%	8.2%	8.5%

Figure 8- Proportion of *Escherichia coli* isolates non-susceptible to ampicillin, cefotaxime, ciprofloxacin, nitrofurantoin, TMP-SMX and gentamicin (2007-2013).
Source: BC Biomedical Laboratories and LifeLabs Medical Laboratory Services

Please note: LifeLabs data for resistance to cefotaxime was limited (data provided for 2008 and 2009 only); hence, data was not included in the analysis.



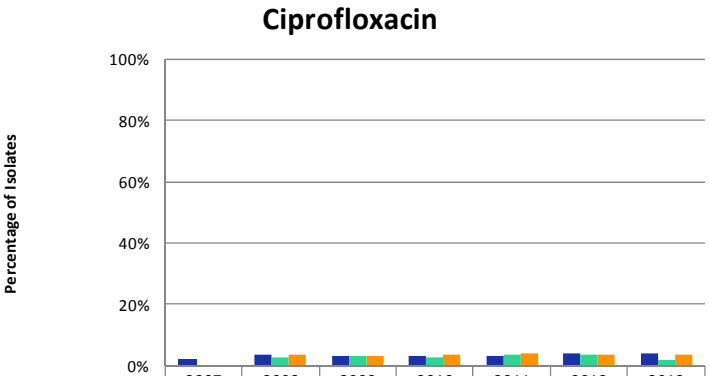
	<10	10-19	20-29	30-39	40-49	50-59	60-69	70-79	80-89	>90
2007	7.1%	5.8%	9.6%	12.5%	12.2%	18.8%	24.0%	32.3%	39.7%	50.8%
2008	8.2%	6.2%	10.4%	11.7%	12.5%	19.6%	26.7%	32.0%	41.6%	47.7%
2009	10.2%	5.2%	10.4%	10.5%	13.6%	18.4%	25.3%	30.5%	41.8%	49.4%
2010	12.0%	7.1%	11.4%	12.5%	14.5%	21.1%	28.8%	36.7%	45.4%	53.9%
2011	11.6%	7.5%	11.4%	13.6%	14.7%	21.6%	28.9%	38.5%	47.4%	55.7%
2012	11.1%	5.9%	11.4%	12.3%	14.9%	19.1%	26.5%	34.9%	45.4%	54.5%
2013	10.8%	6.4%	9.3%	13.4%	12.7%	19.1%	26.9%	35.2%	44.0%	54.6%

Figure 9- Proportion of *Escherichia coli* urinary isolates non-susceptible to ciprofloxacin by age of patient (2007-2013)
Source: BC Biomedical Laboratories

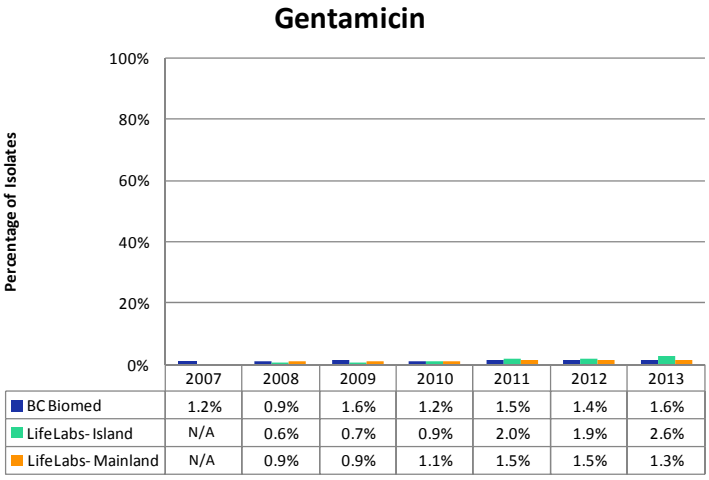
1.6. *Klebsiella pneumoniae*

Klebsiella pneumoniae is a gram-negative bacteria commonly found in both the environment (soil, water … etc) and on the mucosal surface of mammals including humans. Although *K. pneumonia* is widely known to be the cause of community-acquired pneumonia, the vast majority occurs as nosocomial infections, presenting primarily as an opportunistic infection targeting patients that are immunocompromised during hospitalization. Studies have shown that the degree of *K.pneumoniae* colonization is found to be directly proportional to the length of hospitalization, and the nosocomial colonization is significantly associated with the use of antibiotics (particularly multiple antibiotics or use of broad-spectrum antibiotics) rather than factors associated with delivery of care during hospitalization. The urinary tract is a common site of infection in *K. pneumoniae*, contributing to 6-17% of all nosocomial UTI cases. Moreover, *K .pneumoniae* is also a cause of gram-negative bacteraemia, second only to *E.coli,* and is the most frequently identified carbapenemase-producing Enterobacteriaceae (Please refer to section 1.8 for more information on carbapenemase-producing organisms) (24).

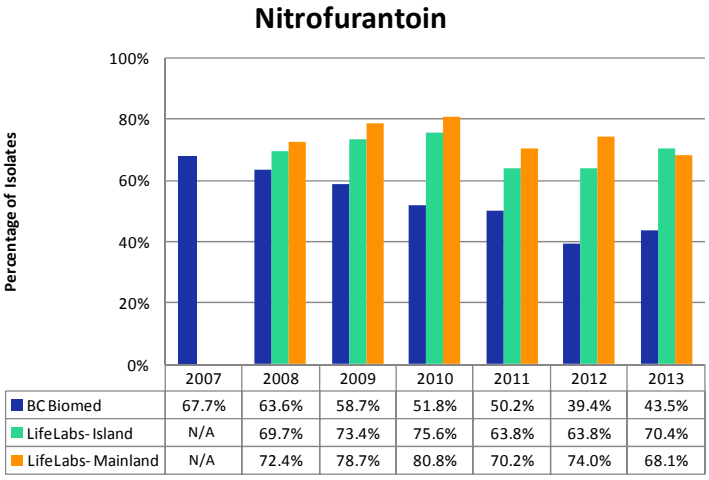
BC Biomedical data show an increasing trend in non-susceptibility rates to ciprofloxacin, yet rates remains low and is reported to be 4.1% in 2013 (p=0.007) (***Figure 10***). Similar rates are observed in LifeLabs data both on the Island and in the Mainland, however, the overall trend from 2008 to 2013 has not changed significantly (Mainland: p=0.487; Island: p=0.860) (***Figure 10***). This is slightly higher than the rate of non-susceptibility reported nationally in the CANWARD study in 2012 (2.4%) (15). A slight increasing trend in the non-susceptibility to gentamicin is observed in both data sources, and remains low at a rate of 1.6% (BC Biomedical), 2.6% (LifeLabs-Island), and 1.3% (LifeLabs- Mainland); however, the change is non-significant in the BC Biomedical data (BC Biomedical: p=0.117; LifeLabs-Island: p<0.001; LifeLabs-Mainland: p=0.0314) (***Figure 10***). These rates are similar to that reported nationally in the CANWARD study (1.8%) (15). Contrastingly, non-susceptibility rates to nitrofurantoin show a significant decreasing trend for BC Biomed data; in 2013, the BC Biomedical rate is much lower (43.5%) when compared to LifeLabs rates (Mainland: 68.1%; Island: 70.4%) (BC Biomedical: p<0.001; LifeLabs-Island: p<0.001; LifeLabs-Mainland: p<0.001) (***Figure 10***). The proportion of *K. pneumoniae* isolates non-susceptible to TMP-SMX has continued to decrease from 12.0% in 2008 to 7.8% in 2013 according to BC Biomedical data (p<0.001) (***Figure 10***).



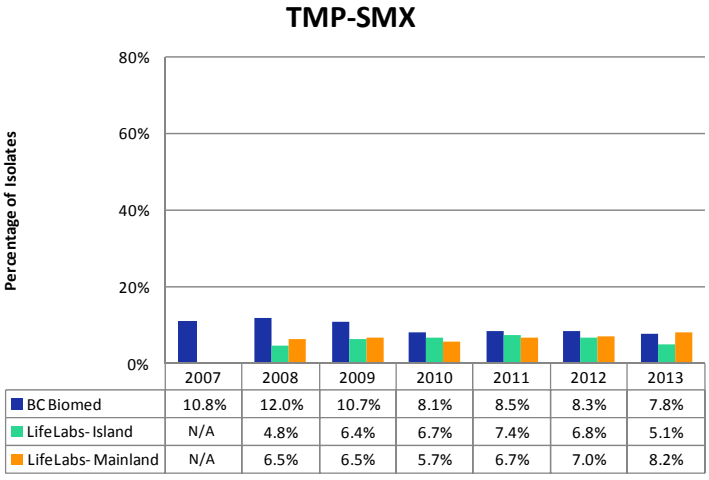
	2007	2008	2009	2010	2011	2012	2013
BC Biomed	2.4%	3.7%	3.0%	3.4%	3.0%	3.9%	4.1%
LifeLabs- Island	N/A	3.0%	3.3%	3.0%	3.7%	3.7%	2.1%
LifeLabs- Mainland	N/A	3.8%	3.2%	3.6%	4.2%	3.5%	3.5%



	2007	2008	2009	2010	2011	2012	2013
BC Biomed	1.2%	0.9%	1.6%	1.2%	1.5%	1.4%	1.6%
LifeLabs- Island	N/A	0.6%	0.7%	0.9%	2.0%	1.9%	2.6%
LifeLabs- Mainland	N/A	0.9%	0.9%	1.1%	1.5%	1.5%	1.3%



	2007	2008	2009	2010	2011	2012	2013
BC Biomed	67.7%	63.6%	58.7%	51.8%	50.2%	39.4%	43.5%
LifeLabs- Island	N/A	69.7%	73.4%	75.6%	63.8%	63.8%	70.4%
LifeLabs- Mainland	N/A	72.4%	78.7%	80.8%	70.2%	74.0%	68.1%



	2007	2008	2009	2010	2011	2012	2013
BC Biomed	10.8%	12.0%	10.7%	8.1%	8.5%	8.3%	7.8%
LifeLabs- Island	N/A	4.8%	6.4%	6.7%	7.4%	6.8%	5.1%
LifeLabs- Mainland	N/A	6.5%	6.5%	5.7%	6.7%	7.0%	8.2%

Figure 10- Proportion of *Klebsiella pneumoniae* isolates non-susceptible to ciprofloxacin, gentamicin, nitrofurantoin, and TMP-SMX (2007-2013)
Source: BC Biomedical Laboratories and LifeLabs Medical Laboratory Services

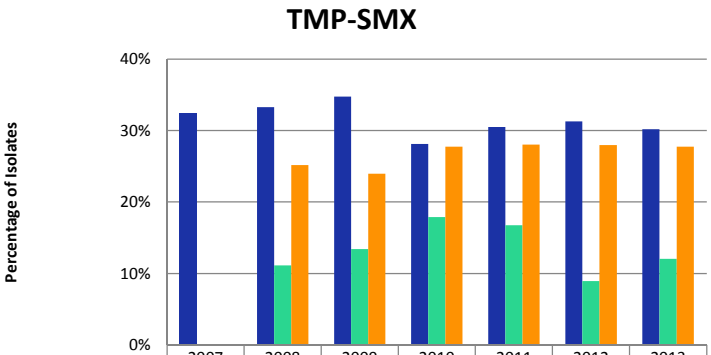
1.7. *Proteus mirabilis*

Proteus mirabilis is an enteric bacterium that causes approximately 2% of UTIs (21). In the past, TMP-SMX was the first-line treatment for UTIs; however, use of fluoroquinolones (e.g. ciprofloxacin) and aminoglycosides (e.g. gentamicin) has become more common over the years (9;25). In Canada, the percent of P. mirabilis isolates producing ESBLs is considerably less than other countries (26).

According to BC Biomedical data, the percent of isolates non-susceptible to ampicillin and gentamicin has remained relatively stable since 2007, and is reported at 20.0% and 6.2% respectively in 2013 (ampicillin: p=0.52; gentamicin: p=0.44) (***Figure 11***). The percent of P. mirabilis isolates resistant to TMP-SMX has fluctuated around 30% with a slight decrease from 32.4% in 2007 to 30.2% in 2013 (p=0.024) (***Figure 11***). Non-susceptibility rates to ciprofloxacin has stabilized over the years from 2007 and is reported to be at 19.9% in 2013 (p=0.121) (***Figure 11***).

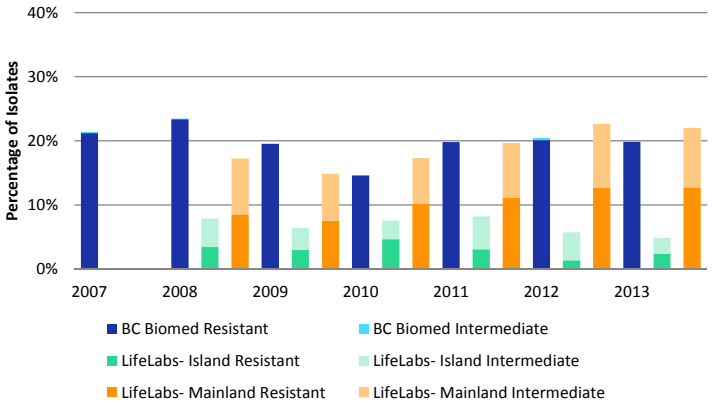
LifeLabs data show similar stabilizing trends in non-susceptibility patterns to gentamicin and ampicillin since 2007 and is reported to be at 3.7% (Island), 6.1% (Mainland) and 18.7% (Island), 27.8% (Mainland), respectively, d in 2013 (***Figure 11***). Non-susceptibility to ciprofloxacin remains relatively stable on the Island and is reported to be at 4.8% in 2013 while an increasing trend exists on the Mainland from 17.3% in 2008 to 22.1% in 2013 (Island: p=0.061; Mainland: p<0.001) (***Figure 11***). Similar to trends seen in ciprofloxacin, non-susceptibility to TMP-SMX has increased from 25.2% in 2007 to 27.7% in 2013 on the Mainland, while a non-significant decreasing trend is observed on the Island and is reported to be at 12.0% in 2013 (Mainland: p=0.011; Island: p=0.372) (***Figure 11***).

Nationally, hospital isolates as reported by the CANWARD study in 2012, appear to have lower non-susceptibility to TMP-SMX (15.4%) and ciprofloxacin (7.7%) when compared with community isolates from BC Biomedical data and LifeLabs data for the Mainland (***Figure 11***) (15). In contrast, the CANWARD study reported 10.3% of hospital isolates nationally to be non-susceptible to gentamicin, which is slightly higher than rates observed in BC (***Figure 11***) (15). All isolates are considered inherently resistant to nitrofurantoin (data not shown).



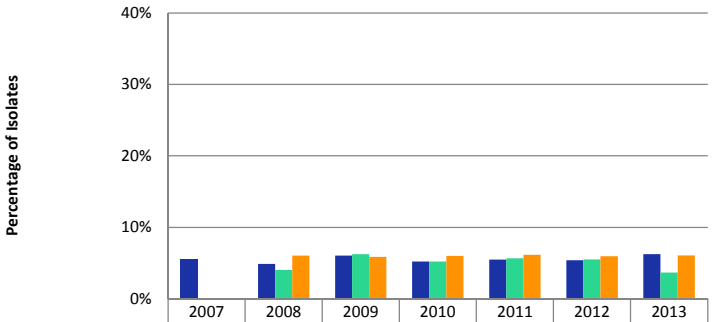
	2007	2008	2009	2010	2011	2012	2013
BC Biomed	32.4%	33.3%	34.7%	28.1%	30.5%	31.3%	30.2%
LifeLabs- Island	N/A	11.2%	13.4%	17.9%	16.7%	8.9%	12.0%
LifeLabs- Mainland	N/A	25.2%	24.0%	27.7%	28.0%	28.0%	27.7%

Ciprofloxacin

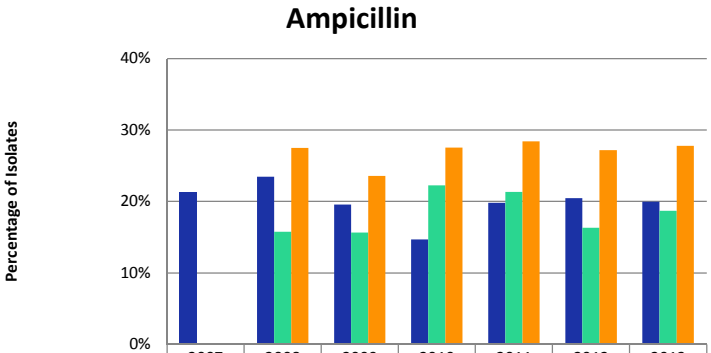


		Year						
Data Source	Susceptibility	2007	2008	2009	2010	2011	2012	2013
BC Biomed	I[a]	0.1%	0.1%	0.1%	0.1%	0.0%	0.4%	0.1%
	R[b]	21.2%	23.4%	19.5%	14.6%	19.8%	20.1%	19.8%
LifeLabs- Island	I	N/A	4.4%	3.4%	2.9%	5.1%	4.4%	2.4%
	R	N/A	3.4%	3.0%	4.7%	3.1%	1.4%	2.4%
LifeLabs- Mainland	I	N/A	8.8%	7.3%	7.2%	8.5%	10.0%	9.3%
	R	N/A	8.5%	7.6%	10.1%	11.1%	12.6%	12.8%

Gentamicin



	2007	2008	2009	2010	2011	2012	2013
BC Biomed	5.6%	4.9%	6.0%	5.2%	5.5%	5.4%	6.2%
LifeLabs- Island	N/A	4.0%	6.2%	5.2%	5.7%	5.5%	3.7%
LifeLabs- Mainland	N/A	6.0%	5.9%	6.0%	6.2%	6.0%	6.1%



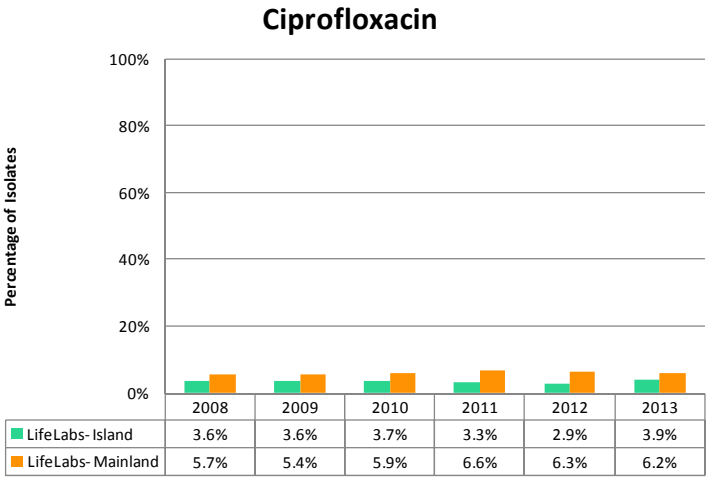
	2007	2008	2009	2010	2011	2012	2013
BC Biomed	21.4%	23.5%	19.6%	14.7%	19.8%	20.5%	20.0%
LifeLabs- Island	N/A	15.8%	15.7%	22.3%	21.3%	16.3%	18.7%
LifeLabs- Mainland	N/A	27.5%	23.6%	27.5%	28.4%	27.2%	27.8%

Figure 11- Proportion of *Proteus mirabilis* isolates non-susceptible to ciprofloxacin, TMP-SMX, gentamicin, and ampicillin (2007-2013)
Source: BC Biomedical Laboratories and LifeLabs Medical Laboratory Services

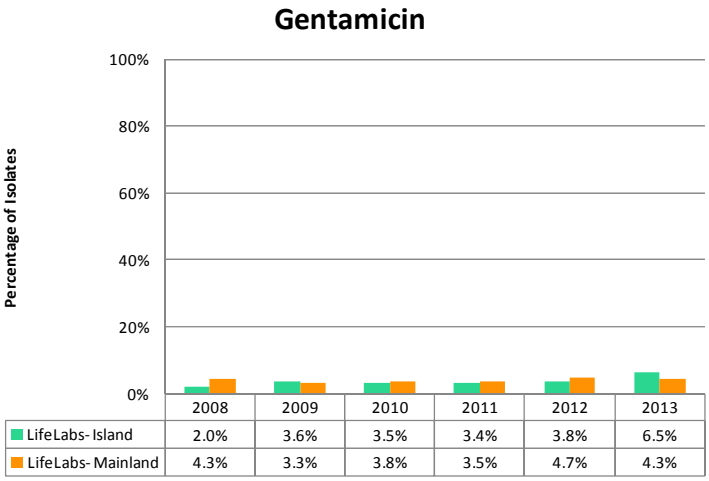
[a]I= Isolates classified as having intermediate resistance based on MIC breakpoints and CLSI guidelines
[b]R= Isolates classified as resistant based on MIC breakpoints and CLSI guidelines

1.8. *Serratia, Providencia, Morganella, Citrobacter*, and *Enterobacter* spp.

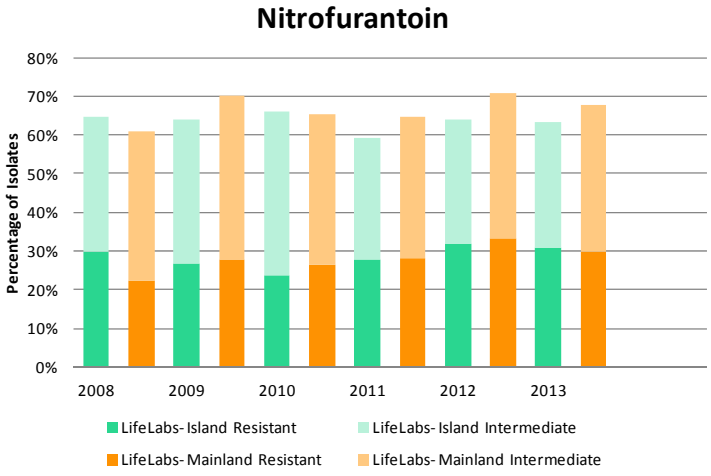
Serratia spp., *Providencia* spp., *Morganella* spp., *Citrobacter* spp., and *Enterobacter* spp. are collectively referred to as the SPICE organisms or 'ESCPM' group (27). Most SPICE organisms are opportunistic nosocomial pathogens that commonly cause urinary tract or respiratory infections and have the ability to produce inducible β-lactamases (28;29). The number of SPICE organism isolates non-susceptible to the tested antimicrobials with the exception of nitrofurantoin, have remained relatively low during the testing period from 2007 to 2013 (i.e., less than 10%) (***Figure 12***). Non-susceptibility to nitrofurantoin remains high across all years since 2007 and was reported to be at 63.5% on the Island and 67.7% on the Mainland in 2013 (***Figure 12***). SPICE organisms remain highly susceptible to ciprofloxacin and gentamicin with less than 7% of isolates exhibiting non-susceptibility.



	2008	2009	2010	2011	2012	2013
LifeLabs- Island	3.6%	3.6%	3.7%	3.3%	2.9%	3.9%
LifeLabs- Mainland	5.7%	5.4%	5.9%	6.6%	6.3%	6.2%



	2008	2009	2010	2011	2012	2013
LifeLabs- Island	2.0%	3.6%	3.5%	3.4%	3.8%	6.5%
LifeLabs- Mainland	4.3%	3.3%	3.8%	3.5%	4.7%	4.3%



		Year					
Data Source	Susceptibility	2008	2009	2010	2011	2012	2013
LifeLabs- Island	I[a]	35.0%	37.4%	42.1%	31.5%	31.9%	32.8%
	R[b]	29.7%	26.6%	23.8%	27.7%	32.0%	30.7%
LifeLabs- Mainland	I	38.7%	42.4%	39.0%	36.6%	37.6%	37.9%
	R	22.3%	27.8%	26.4%	28.1%	33.2%	29.8%

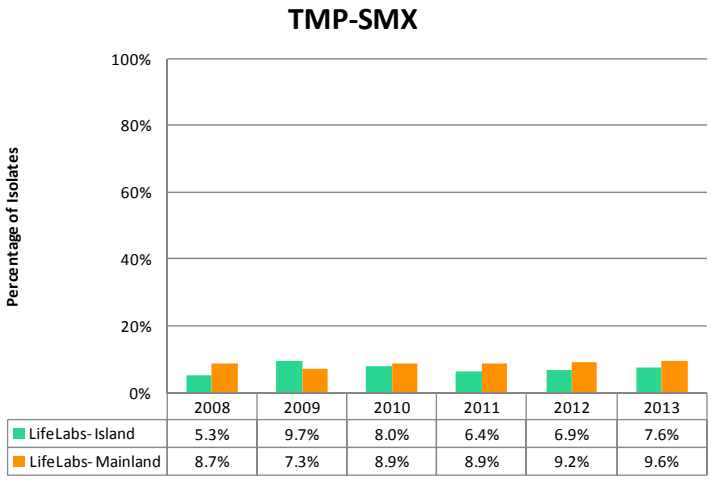


Figure 12- Proportion of SPICE (*Serratia* spp., *Providencia* spp., *Morganella* spp., *Citrobacter* spp., and *Enterobacter* spp.) isolates non-susceptible to ciprofloxacin, nitrofurantoin, gentamicin, and TMP-SMX (2008-2013)
Source: LifeLabs Medical Laboratory Services

[a]I= Isolates classified as having intermediate resistance based on MIC breakpoints and CLSI guidelines
[b]R= Isolates classified as resistant based on MIC breakpoints and CLSI guidelines

1.9. **Extended spectrum β-lactamase producing Enterobacteriaceae**

Extended spectrum β-lactamases (ESBLs) are enzymes often associated with bacteria within the *Enterobacteriaceae* family that hydrolyze antibiotics belonging to the penicillin and cephalosporin classes (30). Laboratories detect the presence of ESBLs by evaluating the organism's phenotypic resistance patterns to different antibiotics (31). An ESBL-producing organism must demonstrate resistance to a third generation cephalosporin (e.g. cefotaxime, ceftriaxone or ceftazidime) but not cephamycins (e.g. cefoxitin) or carbapenems (e.g. imipenem, meropenem or ertapenem) (31). In addition, it must also demonstrate a change in susceptibility to third generation cephalosporin in the presence of a β-lactamase inhibitor (e.g. clavulanic acid, tazobactam or sulbactam) (31).

ESBL-producing organisms were first described in 1983, and have since been a major cause of hospital-acquired infections. Although a variety of bacteria have been found to produce ESBLs, they are most often identified in *Klebsiella pneumonia* and *Escherichia coli (32).* Genes encoding ESBL are usually located on large plasmids containing resistance genes to many other antibiotics such as aminoglycosides, trimethoprim, sulphonamides, tetracycline, and chloramphenicol; thus, accumulation of multiple resistance genes due to the plasmid-mediated transmission of ESBL genes result in strains that are multi-resistant to a variety of antibiotics limiting the choice of effective therapy (32). In Canada, the first case of ESBL-producing *E.coli* strains occurred in Ontario in 2000 (33).

The CLSI does not recommend confirming ESBLs and consequently, BC Biomedical Laboratories does not directly confirm potential ESBL isolates. BC Biomedical Laboratories refers to isolates exhibiting cephalosporin resistance as broad-spectrum beta-lactamase producers. Consequently, data from BC Biomedical Laboratories were used to estimate extended spectrum β-lactamase-like (ESBL-like) producers, determined through resistance to third generation cephalosporins (e.g. ceftriaxone, cefotaxime, ceftazidime, or cefixime). This method is likely to overestimate the proportion of isolates that are ESBL-like producers. Although data from BC Biomedical Laboratories would represent an overestimation of true ESBL numbers, the data are still useful as they will include all possible ESBL-producing *E. coli, K. pneumonia,* and *P. mirabilis* isolates. Thus, it is still meaningful to represent the data in this report in order to use this denominator to identify multi-drug resistance patterns associated with *E. coli, K. pneumonia,* and *P. mirabilis* isolates with phenotype compatible with ESBLs, and to monitor for any changing trends.

In BC, laboratory testing for ESBL-producing *E. coli* and *K. pneumoniae* is done routinely by phenotypic methods. BCAMM reports estimates of ESBL-producing *E. coli* and *K. pneumoniae* observed in all community laboratories, and 23 health organizations' hospital laboratories across BC (34). The results are presented for both community and hospital settings, in order to reflect the potential differences in prevalence within the respective settings.

Data from BC Biomedical Laboratories suggest that the majority of ESBL-like isolates were *E. coli*, while *K. pneumoniae* and *P. mirabilis* made up similar but substantially lower proportions of all ESBL-like isolates in 2013 (***Figure 14***). Approximately 12.5% of *E. coli* isolates exhibit an ESBL-like phenotype, a rate which has not changed drastically over the past six years (p=0.052) (***Figure 14***). The percent of *K. pneumonia* and *P. mirabilis* isolates demonstrating an ESBL-like phenotype decreased significantly from 8.5% in 2007 to 3.6% and from 12.5% to 5.6% in 2013 respectively (*K. pneumonia*: p=0.023 and *P. mirabilis*: p=0.023) (***Figure 14***).

Data for *E. coli, K. pneumonia,* and *P. mirabilis* isolates with phenotypes compatible with ESBLs were analyzed for their resistance to quinolones (e.g. ciprofloxacin, levofloxacin), aminglycosides (e.g. gentamicin, amikacin, tobramycin) and TMP-SMX, as well as combinations of these drugs (i.e. 2 classes or all 3 classes) (***Figure 15***).

Non-susceptibility rates for ESBL-like *E. coli* isolates have remained relatively stable over the past seven years for quinolones, aminoglycoside and TMP-SMX. In 2013, 71.4% of ESBL-like *E. coli* isolates were non-susceptible to quinolones; a non-significant increase of nearly 6% from 2007 to 2013 (p=0.180) (***Figure 15***). Aminoglycoside and TMP-SMX non-susceptibility rates were estimated at 27.9% and 53.0%, respectively for ESBL-like *E. coli* isolates in 2013 (***Figure 15***).

Non-susceptibility to quinolones in ESBL-like *K. pneumoniae* isolates showed a upward trend from 2007 to 2012, however decreased again to 49.3% in 2013 (p<0.01) (***Figure 15***). Similarly, a strong positive trend was also observed for aminoglycosides non-susceptibility with nearly a four-fold increase in the non-susceptibility rate from 2007 to 2013 and is reported to be 32.6% in 2013 (p=0014) (***Figure 15***). In 2013, non-susceptibility rates to TMP-SMX for ESBL-like *K. pneumoniae* isolates remained high at 62.92% (p=0.939) (***Figure 15***).

Although *P. mirabilis* isolates with an ESBL-like phenotype exhibited a slight increase in non-susceptibility to quinolones from 2011 to 2012, there is an overall decreasing trend from 53.2% in 2007 to 32.6% in 2013 (p=0.036) (***Figure 15***). The non-susceptibilty rates of *P. mirabilis* isolates with an ESBL-like phenotype exhibited a decreasing trend from 65.32% in 2007 to 38.37% in 2013 (p=0.036) (***Figure 15***). Contrastingly, aminoglycoside non-susceptibility has increased approximately five-fold since 2007 to 44.2% of ESBL-like *P. mirabilis* isolates in 2013 (p=0.003) (***Figure 15***).

When looking at multi-drug non-susceptibility, the proportion of ESBL-like *E. coli* and *P. mirabilis* isolates non-susceptible to more than one class of antimicrobial has remained relatively stable from 2007 to 2013, while the proportion of ESBL-like *K. pneumoniae* isolates non-susceptible to two or more classes appears to be increasing (*E. coli*: p=0.180; *P. mirabilis*: p=0.071; *K. pneumoniae*: p=0.014) (***Figure 15***). The proportion of ESBL-like *P. mirabilis* isolates that are non-susceptible to all three classes of antibiotics (i.e. aminoglycosides, quinolones and TMP-SMX) has increased more than 10-fold from 1.7% in 2007 to 21.4% in 2013 (p=0.023) (***Figure 15***). Contrastingly, the proportion of ESBL-like *E. coli* isolates that are non-susceptible to all three classes of antibiotics has decreased from 24.9% in 2007 to 16.5% in 2013 (p=0.014) (***Figure 15***).

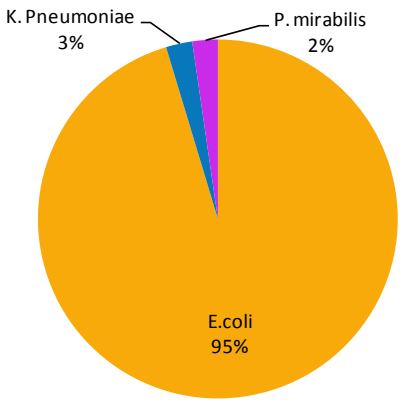
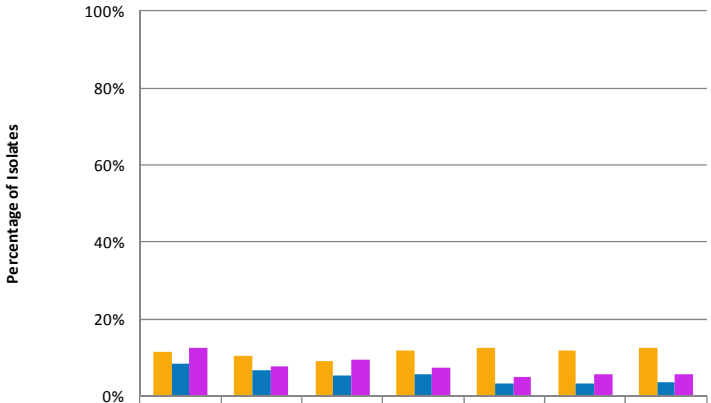
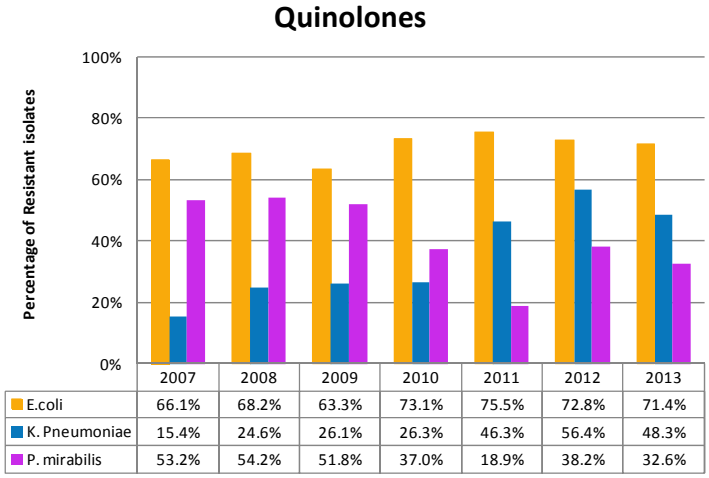


Figure 13- Distribution of ESBL- like phenotypes in *Escherichia coli, Klebsiella pneumoniae,* and *Proteus mirabilis (*2013)
Source: BC Biomedical Laboratories

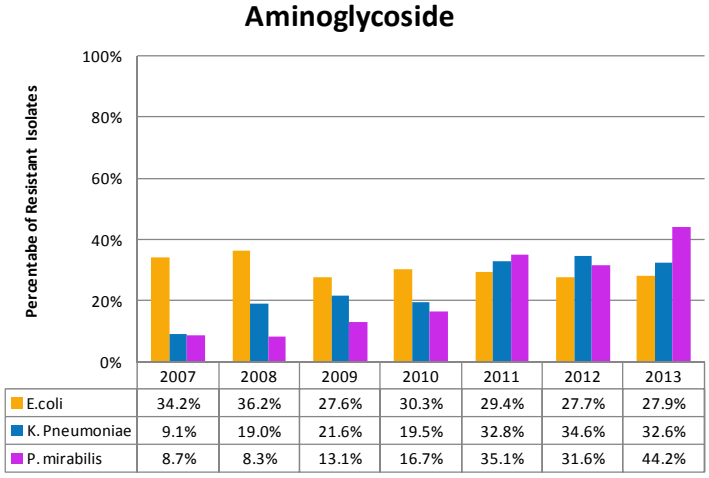


	2007	2008	2009	2010	2011	2012	2013
E.coli	11.5%	10.6%	9.1%	11.8%	12.4%	11.7%	12.5%
K. Pneumoniae	8.5%	6.7%	5.3%	5.6%	3.3%	3.3%	3.6%
P. mirabilis	12.5%	7.7%	9.5%	7.3%	5.0%	5.5%	5.6%

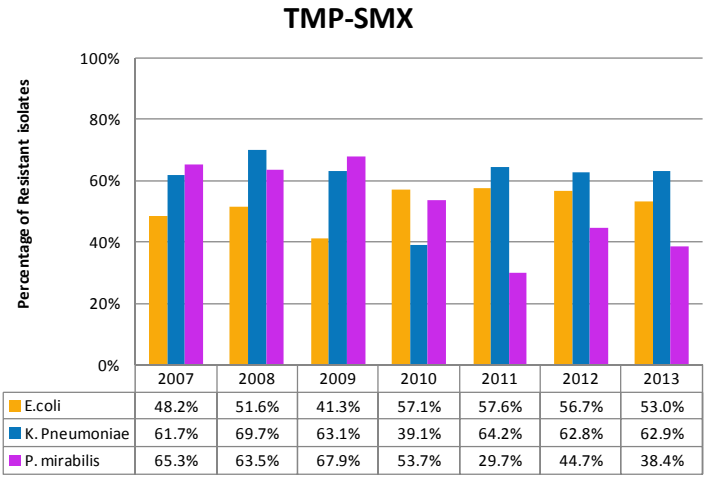
Figure 14- Proportion of *Escherichia coli, Klebsiella pneumoniae* and *Proteus mirabilis* isolates demonstrating ESBL-compatible phenotype (2007-2013)
Source: BC Biomedical Laboratories



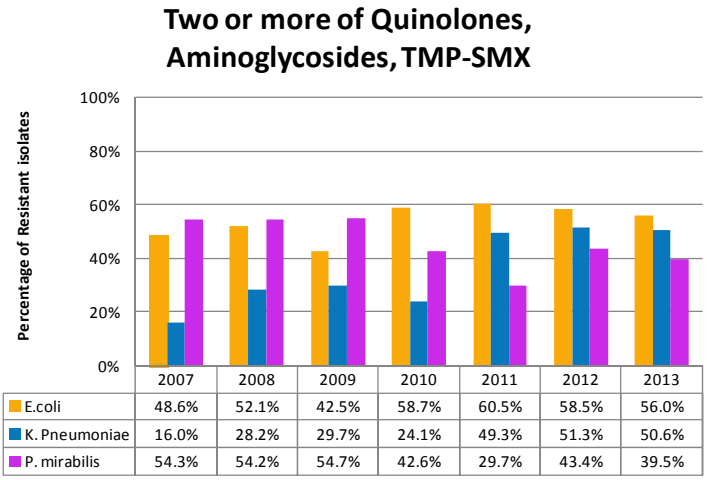
	2007	2008	2009	2010	2011	2012	2013
E.coli	66.1%	68.2%	63.3%	73.1%	75.5%	72.8%	71.4%
K. Pneumoniae	15.4%	24.6%	26.1%	26.3%	46.3%	56.4%	48.3%
P. mirabilis	53.2%	54.2%	51.8%	37.0%	18.9%	38.2%	32.6%



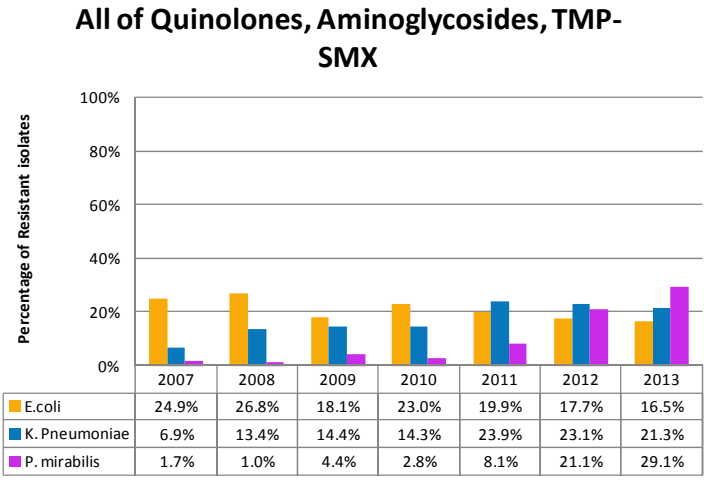
	2007	2008	2009	2010	2011	2012	2013
E.coli	34.2%	36.2%	27.6%	30.3%	29.4%	27.7%	27.9%
K. Pneumoniae	9.1%	19.0%	21.6%	19.5%	32.8%	34.6%	32.6%
P. mirabilis	8.7%	8.3%	13.1%	16.7%	35.1%	31.6%	44.2%



	2007	2008	2009	2010	2011	2012	2013
E.coli	48.2%	51.6%	41.3%	57.1%	57.6%	56.7%	53.0%
K. Pneumoniae	61.7%	69.7%	63.1%	39.1%	64.2%	62.8%	62.9%
P. mirabilis	65.3%	63.5%	67.9%	53.7%	29.7%	44.7%	38.4%



	2007	2008	2009	2010	2011	2012	2013
E.coli	48.6%	52.1%	42.5%	58.7%	60.5%	58.5%	56.0%
K. Pneumoniae	16.0%	28.2%	29.7%	24.1%	49.3%	51.3%	50.6%
P. mirabilis	54.3%	54.2%	54.7%	42.6%	29.7%	43.4%	39.5%



	2007	2008	2009	2010	2011	2012	2013
E.coli	24.9%	26.8%	18.1%	23.0%	19.9%	17.7%	16.5%
K. Pneumoniae	6.9%	13.4%	14.4%	14.3%	23.9%	23.1%	21.3%
P. mirabilis	1.7%	1.0%	4.4%	2.8%	8.1%	21.1%	29.1%

Figure 15- Proportion of *ESBL-like Escherichia coli, Klebsiella pneumonia,* and *Proteus mirabilis* isolates demonstrating non-susceptibility to quinolones, aminoglycosides or TMP-SMX, two or more, and three of quinolones, aminoglycosides, and TMP-SMX (2007-2013)
Source: BC Biomedical Laboratories

Carbapenemase-Producing Organisms (CPOs)

In response to the emergence of CPOs as an infectious disease concern in BC, the British Columbia Public Health Microbiology and Reference Laboratory (BCPHMRL) and Provincial Infection Control Network (PICNet) collaborated with representatives from each health authority to produce a BC CPO Surveillance System that will be implemented in acute care facilities in BC (35). The purpose of the system is to identify and monitor incidence of CPOs among patients and to synthesize epidemiological and laboratory data to inform best practice and management of patients with CPO infections (35). The population under surveillance consists of patients admitted to acute care facilities, haemodialysis patients visiting renal clinics and patients deemed to be at high risk for CPO infection (35). Organisms that harbour a carbapenemase gene included in the surveillance are Enterobacteriaceae, *P. aeruginosa*, and *Acinetobacter spp*, isolates identified to be resistant to carbapenems undergo phenotypic or molecular screening for CPO (35).

According to the BCPHMRL *Laboratory Trends* report, 156 patients with CPO have been identified since 2008: 93 harboured the New Delhi Metallo-β-lactamase-1-gene (NDM-1), 28 cases harboured the *Serratia marcescens* enzyme (SME) resistance genes, 23 cases with OXA-48 carbapenemase and 11 cases with the *Klebsiella pneumoniae* carbapenems (KPC) β-lactamase gene overall {BC Public Health Microbiology and Reference Laboratory, 2014 121 /id}. Prior to 2010, only one patient in 2008 and 2009 were identified to carry CPO; however, an increasing number of cases are being identified each year. In 2013, the majority of patients infected with CPOs carried NDM-1 (64.9%), followed by 16.9% of patients infected with organisms carrying the SME gene.

Table 1- Gene harboured in identified cases of carbapenemase-producing organisms (CPO) from 2008 to March of 2014.

	Collection Year							
Gene	**2008**	**2009**	**2010**	**2011**	**2012**	**2013**	**2014**	**Total**
NDM-1	1	1	3	8	14[b.]	50[c.]	16	93
KPC	0	0	1[a.]	1	1	6	2	11
VIM	0	0	1[a.]	0	0	0	0	1
OXA-48	0	0	0	1	9[b.]	8	5	23
SME	0	0	1	4	8	13	2	28
Total	1	1	6	14	32	77	25	156

Source: BCPHMRL and National Microbiology Laboratory

a. Counts include 1 patient with KPC and VIM.
b. Counts include 2 patients with NDM-1 and OXA-48
c. Counts include 1 patient with NDM-1 and KPC

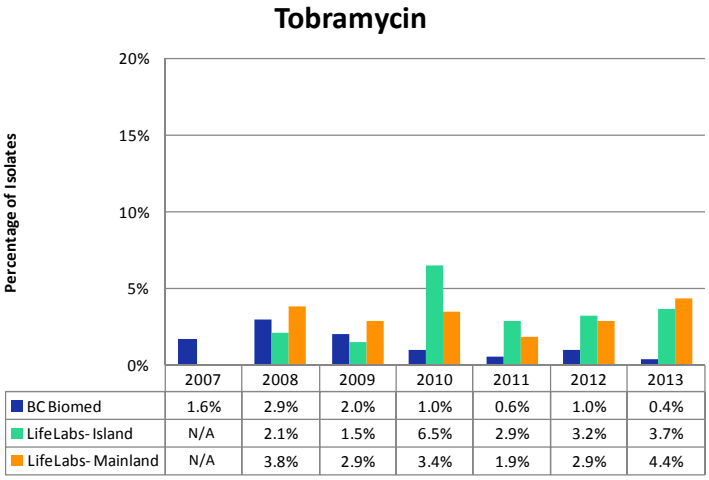
AmpC

AmpC genes are inducible genes that are triggered in response to the presence of a β-lactam. These genes can also be found on transmissible plasmids, allowing the gene to be transferred between bacteria (3). The gene codes for the production of β-lactamase enzymes, allowing the organism to break down penicillins, cephalosporins and other β-lactam drugs (36). Data for 2012 and 2013 were not available at the time of report completion.

1.10. *Pseudomonas aeruginosa*

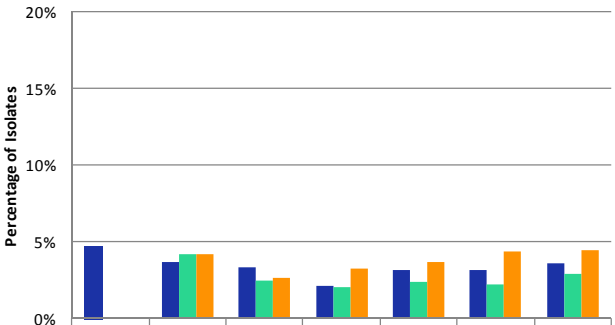
Pseudomonas aeruginosa are prominent nosocomial pathogens that infect numerous sites including the respiratory tract, urinary tract, blood, skin, and soft tissue. The main virulence factor is its low permeability in the outer membrane, which reduces the uptake of antibacterial agents into the cell (37). Treatment for *P. aeruginosa* infections typically includes piperacillin, tobramycin, ceftazidime, carbapenems, fluoroquinolones, and aminoglycosides (9).

The percent of P. aeruginosa isolates that are non-susceptible to tobramycin show a decreasing trend according to BC Biomedical data from 1.6% in 2007 to 0.4% in 2013 ($p<0.001$) (***Figure 16***). Data from LifeLabs show much higher rates of non-susceptibility to tobramycin and is reported to be at 3.7% on the Island and 4.4% in the Mainland (***Figure 16***). Rates of non-susceptibility reported in LifeLabs is similar to national data reported in the CANWARD study (4.9%) (15). The proportion of *P.aeruginosa* that is non-susceptible to gentamicin remains stable and was reported at 3.6% (BC Biomedical) and 2.9% (LifeLabs- Island) (BC Biomedical: $p=0.116$; LifeLabs: $p=0.113$) (***Figure 16***). This is lower than the national non-susceptibility rate reported in the CANWARD study (9.5%) (15). Non-susceptibility rates to ciprofloxacin show a slightly decreasing trend since 2007 and is reported at 10.2% in 2013 ($p=0.034$) (***Figure 16***). A similar trend is observed in LifeLabs on the Mainland with a slightly higher rate of 12.0% reported in 2013 ($p=0.048$) (***Figure 16***). This non-susceptibility rate of *P.aeruginosa* to ciprofloxacin is lower than the national rate reported in the CANWARD study (16.6%) (15). According to BC Biomedical, over the testing period (2007 to 2013), not more than 3% of isolates in any year (2.3% in 2013) were non-susceptible to ceftazidime and less than to 3% (2.9% in 2013) for piperacillin (***Figure 16***). Non-susceptibility rates for piperacillin shows a slight increasing trend from 2007 to 2013 ($p=0.001$) (***Figure 16***). Ceftazidime non-susceptibility, as reported by LifeLabs has increased from 2.6% in 2009 to 4.5% in 2013 for Mainland, which remains lower than national rates reported in the CANWARD study (15.0%) (***Figure 16***) (15).



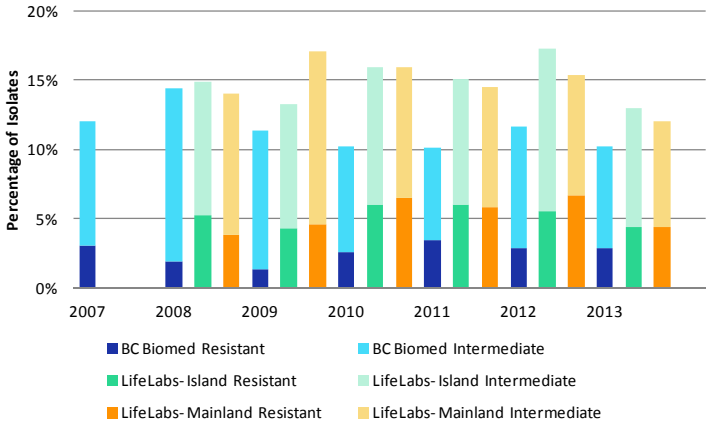
	2007	2008	2009	2010	2011	2012	2013
BC Biomed	1.6%	2.9%	2.0%	1.0%	0.6%	1.0%	0.4%
LifeLabs- Island	N/A	2.1%	1.5%	6.5%	2.9%	3.2%	3.7%
LifeLabs- Mainland	N/A	3.8%	2.9%	3.4%	1.9%	2.9%	4.4%

Gentamicin

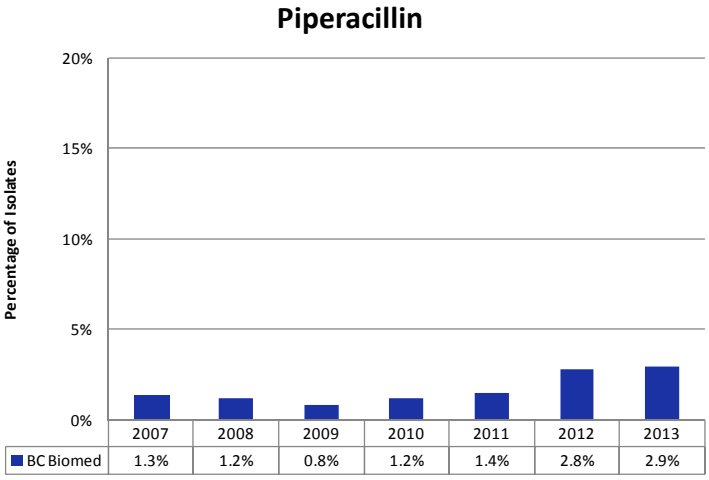


	2007	2008	2009	2010	2011	2012	2013
BC Biomed	4.7%	3.7%	3.4%	2.2%	3.2%	3.2%	3.6%
LifeLabs- Island	N/A	4.2%	2.4%	2.1%	2.4%	2.3%	2.9%
LifeLabs- Mainland	N/A	4.2%	2.6%	3.2%	3.7%	4.4%	4.5%

Ciprofloxacin



		Year						
Data Source	Susceptibility	2007	2008	2009	2010	2011	2012	2013
BC Biomed	I[a]	9.0%	12.5%	10.0%	7.7%	6.6%	8.8%	7.3%
	R[b]	3.1%	1.9%	1.3%	2.6%	3.5%	2.9%	2.9%
LifeLabs- Island	I	N/A	9.6%	9.0%	10.0%	9.0%	11.7%	8.5%
	R	N/A	5.3%	4.3%	6.0%	6.0%	5.5%	4.4%
LifeLabs- Mainland	I	N/A	10.2%	12.5%	9.4%	8.7%	8.7%	7.6%
	R	N/A	3.9%	4.6%	6.4%	5.8%	6.7%	4.4%



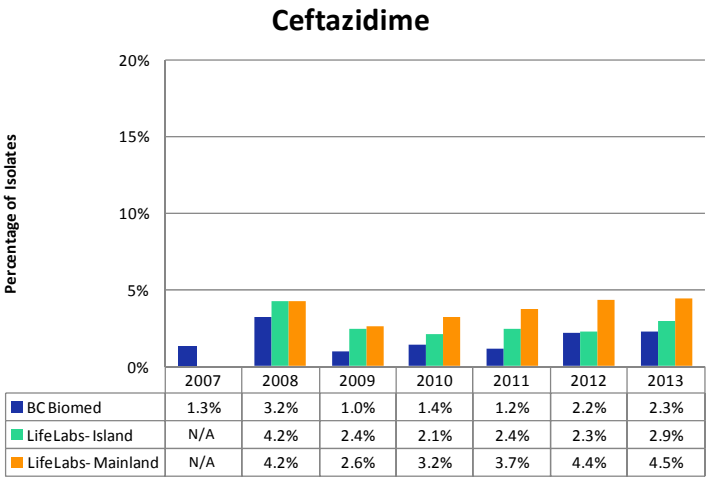


Figure 16- Proportion of *Pseudomonas aeruginosa* isolates non-susceptible to tobramycin, gentamicin, ciprofloxacin, piperacillin, and ceftazidime (2007-2013)
Source: BC Biomedical Laboratories and LifeLabs Medical Laboratory Services

Please note: LifeLabs data for resistance to piperacillin was limited (data provided for 2008 and 2009 only); hence, data was not included in the analysis.

[a]I= Isolates classified as having intermediate resistance based on MIC breakpoints and CLSI guidelines
[b]R= Isolates classified as resistant based on MIC breakpoints and CLSI guidelines

1.11. *Salmonella*

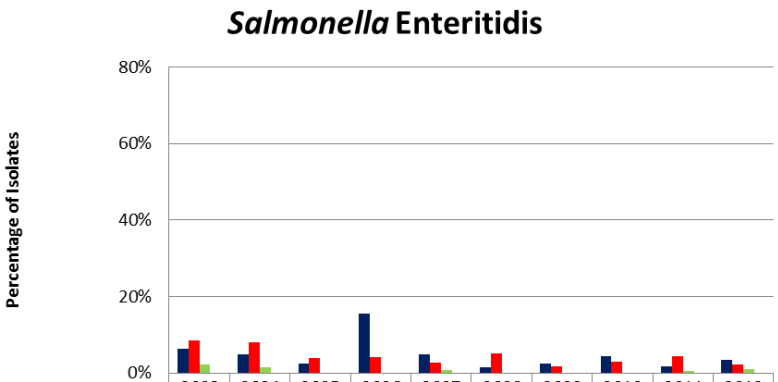
Nontyphoidal salmonellosis is one of the most prevalent and widely distributed foodborne diseases and is caused by *Salmonella enteric* serovars Typhimurium, Enteritidis, Newport, and Heidelberg (38). As a common cause of gastroenteritis in Canada, although it is typically self-limiting, it may cause serious complications in immunocompromised individuals, the elderly, and infants (38). *Salmonella* can be found in both domestic and wild animals and is find widely distributed in food animals such as poultry, pigs and cattle (1). It is predominantly transmitted through human consumption of contaminated food that originated from animals including eggs, meat, poultry and milk; however person-to-person transmission is possible through the fecal-oral route as well (1).

Salmonella enteric serovar Enteritidis (SE) is a rod shaped bacterium that is facultative anaerobic and non spore-forming (39). SE first became one of the leading causes of salmonellosis in humans in the late 1970s and continues to be the chief cause of salmonellosis (25.7% of cases) in Canada as shown through data collected in 2007 (39). SE is an especially resilient organism and was reported to have survived in animal feeds and feces for more than two years (39). Studies have shown that the most likely source of SE infections in humans is from eggs, as SE is able to persist on the shell surface potentially cross-contaminating the liquid portion of the egg when it is cracked for consumption (39).

Of the antimicrobials tested in 2012, SE isolates demonstrated 100% susceptibility to ceftriaxone and azithromycin (data not shown). Resistance to ampicillin was reported at 2.25% in 2012, which remains lower than rates seen in 2003 and 2004 (approximately 8%) (***Figure 17***). Following a large increase from 2.6% in 2005 to 15.5% in 2006, tetracycline resistance rates returned to rates seen prior to 2006 and was reported at 3.4% in 2012 (***Figure 17***). Resistance to chloramphenicol remained below 2.0% from 2004 to 2011 and was at 1.1% in 2012 with 5 isolates identified (***Figure 17***).

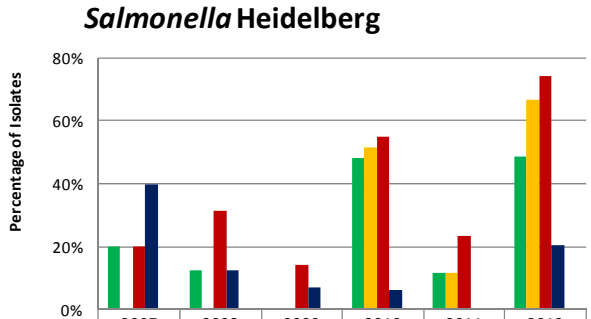
Salmonella serotype Heidelberg (SH) is among the top 3 serovars isolated from patients infected with *Salmonella* in Canada and the most common source is from consumption of contaminated poultry or eggs (40). Most infections lead to mild to moderate infections; however, severe illness such as septicemia, myocarditis, extraintestinal infections, and death can also occur (40). The wide usage of ceftiofur, a third generation cephalosporin, in animal husbandry is becoming a major public health concern as this practice will lead to resistance to other cephalosporins used to treat a variety of human infections (40).

In BC, the resistance of SH to ceftriaxone was over 50% in both 2010 and 2012, and reported to be at 66.7% in 2012, which is at its highest since 2007 (***Figure 18***). Resistance to amoxicillin-clavulanic acid has fluctuated largely and peaked in 2013 at 48.7% (***Figure 18***). Resistance to ampicillin has fluctuated around 20% during the period from 2007 to 2012 except for the increase observed in 2010 and 2012, and is reported to be at its peak with a rate of 74.4% in 2012 (***Figure 18***). Resistance to tetracycline showed a decreasing trend from 40.0% in 2007 20.5% in 2012 (***Figure 18***). Data was collected from both hospital and community *Salmonella* isolates.



	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Tetracycline	6.4%	4.8%	2.6%	15.5%	4.9%	1.4%	2.5%	4.4%	1.7%	3.4%
Ampicillin	8.5%	8.1%	3.8%	4.2%	2.8%	5.2%	1.7%	3.0%	4.5%	2.3%
Chloramphenicol	2.1%	1.6%	0.0%	0.0%	0.7%	0.0%	0.0%	0.0%	0.6%	1.1%
Total	47	62	78	71	144	211	118	135	155	178

Figure 17- Proportion of *Salmonella* Enteritidis isolates resistant to ampicillin, tetracycline, and chloramphenicol in British Columbia (2003-2012).
Source: CIPARS



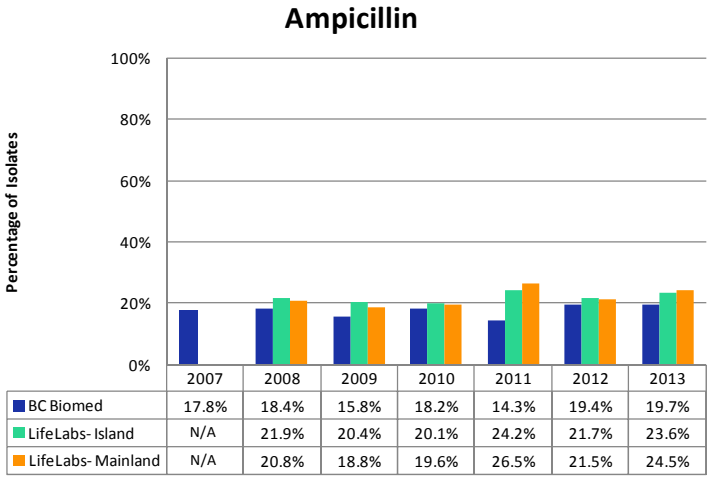
	2007	2008	2009	2010	2011	2012
Amoxicillin-clavulanic acid	20.0%	12.5%	0.0%	48.4%	11.8%	48.7%
Ceftriaxone	0.0%	0.0%	0.0%	51.6%	11.8%	66.7%
Ampicillin	20.0%	31.3%	14.3%	54.8%	23.5%	74.4%
Tetracycline	40.0%	12.5%	7.1%	6.5%	0.0%	20.5%
Total	5	16	14	31	17	39

Figure 18 - Proportion of *Salmonella* Heidelberg isolates resistant to amoxicillin-clavulanic acid, ceftriaxone, ampicillin, and tetracycline in British Columbia (2007-2012)
Source: CIPARS

1.12. *Haemophilus influenzae*

Haemophilus influenzae is a respiratory tract bacterium that causes numerous invasive diseases including bacterial meningitis, bacterial pneumonia, epiglottitis, septic arthritis, cellulitis, and pericarditis.

According to BC Biomedical Laboratories data, ampicillin resistance fluctuated around 18.0% from 2007 to 2013 with the exception of a temporary drop to 15.8% in 2009 and 14.3% in 2011 (***Figure 19***). In 2013, resistance to ampicillin was reported at 19.7% among all *H. influenzae* isolates (***Figure 19***). LifeLabs data for *H. influenzae* isolates from Vancouver Island and the Mainland regions showed that non-susceptibility rates have stabilized over the period from 2008-2013 and is reported to be at 23.6% and 24.5% of isolates on the Island and in the Mainland, respectively, in 2013 (***Figure 19***).



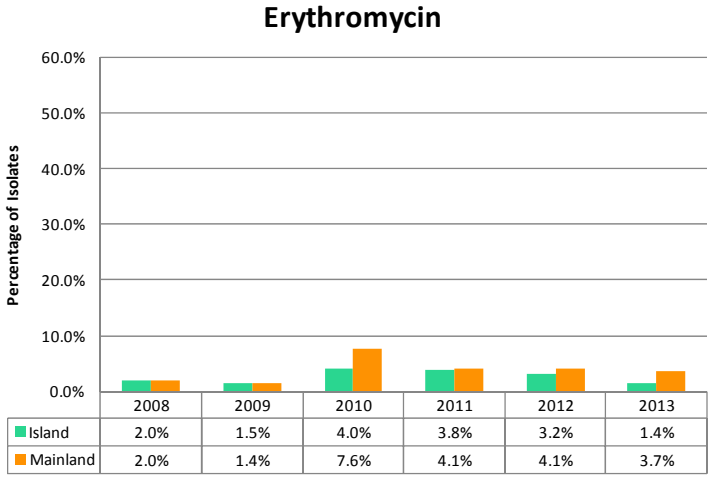
	2007	2008	2009	2010	2011	2012	2013
BC Biomed	17.8%	18.4%	15.8%	18.2%	14.3%	19.4%	19.7%
LifeLabs- Island	N/A	21.9%	20.4%	20.1%	24.2%	21.7%	23.6%
LifeLabs- Mainland	N/A	20.8%	18.8%	19.6%	26.5%	21.5%	24.5%

Figure 19 - Proportion of *Haemophilus influenzae* isolates resistant to ampicillin (2007-2013)
Source: BC Biomedical Laboratories and LifeLabs Medical Laboratory Services

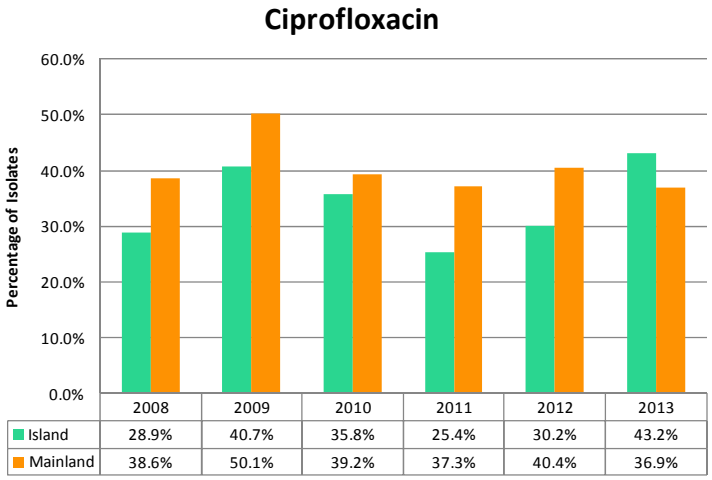
1.13. *Campylobacter*

Campylobacter are spiral shaped bacteria that are a major cause of campylobacteriosis, a foodborne diarrhoeal illness (41). In a report on burden of foodborne illness published by the BCCDC, it was found that *Campylobacter* spp. is the leading cause of foodborne illness by bacteria, contributing to 24,603 cases during the period 2000-2010 (41). Campylobacteriosis is mostly reported as single, sporadic cases in Canada; however, outbreaks where two or more cases are linked to a common exposure do occur (42). Transmission of this bacterium in humans is mostly through consumption of contaminated poultry, water, produce, and unpasteurized dairy products, but can also directly transmit from the primary source (such as chicken) to contaminate other food products or surfaces (42). Although most infections caused by *Campylobacte*r are self-limiting, serious complications can occur in the young, the elderly, and immune-compromised individuals (43). Erythromycin is considered the drug of choice for campylobacteriosis, however, due to its broad spectrum of activity against enteric pathogens, fluoroquinolones are also used (43). Tetracycline and gentamicin are also considered in cases of systemic infections (43). Similarly, it is recommended in the Bugs and Drugs guide that macrolides (azithromycin and erythromycin) be used as empiric therapy only when infection is severe or prolonged or when the patient is immunocompromised (9).

Non-susceptibility rates to erythromycin on the Island and in the Mainland show similar trends, peaking in 2010 at a rate of 4.0% (Island) and 7.6% (Mainland) (***Figure 20***). The reported rate of non-susceptibility to erythromycin for 2013 is 1.4% and 3.7% for Island and Mainland, respectively (***Figure 20***). Non-susceptibility rates to ciprofloxacin was consistently higher for Mainland (fluctuating around 40%) when compared to the Island (fluctuating around 30%) except for the year 2013, which was reported to be 43.2% on the Island and 36.9% on the Mainland (***Figure 20***). Non-susceptibility rates to tetracycline exhibit similar trends between data from the Mainland and the Island with the rate higher on the Island (43.2%) when compared to the Mainland (36.9%) in 2013 (***Figure 20***).



	2008	2009	2010	2011	2012	2013
Island	2.0%	1.5%	4.0%	3.8%	3.2%	1.4%
Mainland	2.0%	1.4%	7.6%	4.1%	4.1%	3.7%



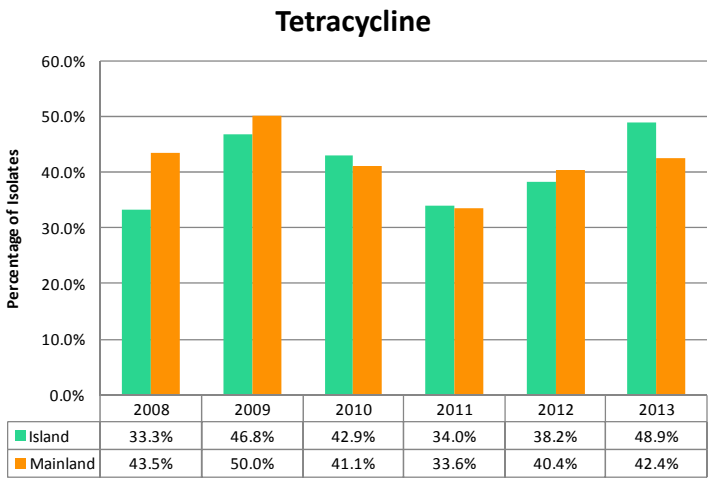
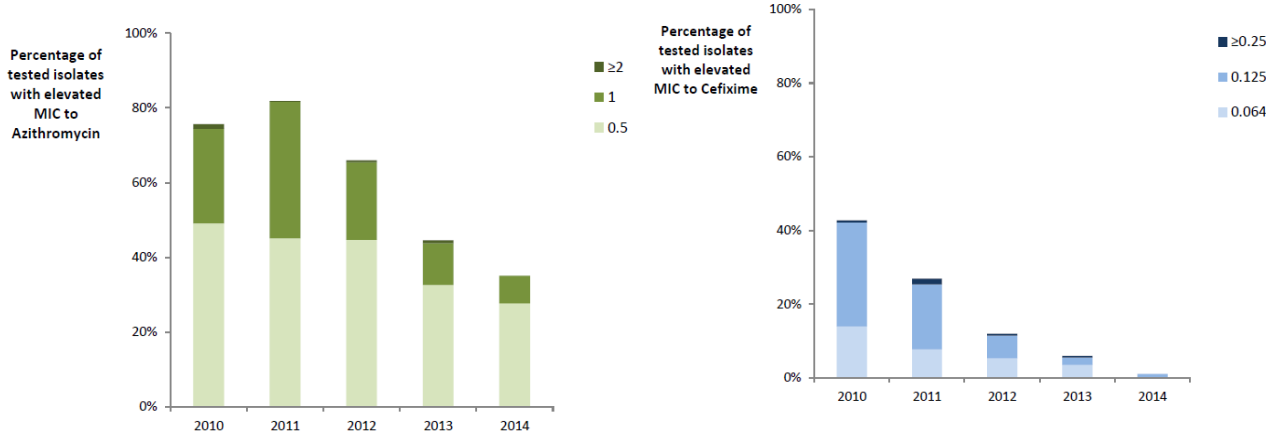


Figure 20- Proportion of *Campylobacter* spp. non-susceptible to ciprofloxacin, erythromycin, and tetracycline (2008-2013). Source: LifeLabs Medical Laboratory Services

1.14. *Neisseria gonorrhoeae*

Neisseria gonorrhoeae is a, non-spore forming, non-motile bacteria that produces β-lactamase (44). It is the causative agent of gonorrhoea (gonococci) and is most often found in the urethra in males and the cervix in females, but could also be transmitted sexually to the rectum and the pharynx (45). The emergence of resistance to penicillin and tetracycline was first described in Asia in the 1970s and by the mid-1990s, resistance to fluoroquinolones also emerged and began to spread internationally (1). Due to the resistance of *N. gonorrhoeae* to all standard first-line antimicrobial agents, third-generation cephalosporins became the last remaining option for empiric monotherapy (1). Currently in BC, the recommended empiric therapy of *N. gonorrhoeae* as outlined in the Bugs and Drugs guide is cefixime and ceftriaxone, with azithromycin recommended as the alternative therapy (9). However, an increase in resistance to oral cephalosporin (e.g. cefixime) has led to several countries reporting treatment failure (1).

In BC, the BC Public Health Microbiology and Reference Laboratory (BCPHMRL) routinely tests *N. gonorrhoeae* antimicrobial susceptibility to a panel of antibiotics including cefixime, ceftriaxone, and azithromycin (46). An overall decreasing trend is observed among isolates with elevated MICs to cefixime, azithromycin, and ceftriaxone (***Figure 21***). In 2013, 0.5% of isolates demonstrated decreased susceptibility (MIC ≥ 0.25 µg/mL) to cefixime, 0.7% of isolates demonstrated decreased susceptibility (MIC ≥ 2 µg/mL) to ceftriaxone, 0.7% of isolates showed resistance to azithromycin, and 24.0% of isolates showed resistance to ciprofloxacin (***Figure 21***). To further understand resistance patterns in the population, resistant isolates were sent to the National Microbiology Laboratory for multi-antigen sequence typing (46). The two most common sequence types were ST-1407 and ST-3158, each representing around a quarter of all tested strains in 2010, with decreasing trends over the year with only 1-2 isolates identified in 2013 (46). However, in 2013, over 54% of all resistant isolates is were of ST-5985 sequence type, which is associated with tetracycline resistance (46).



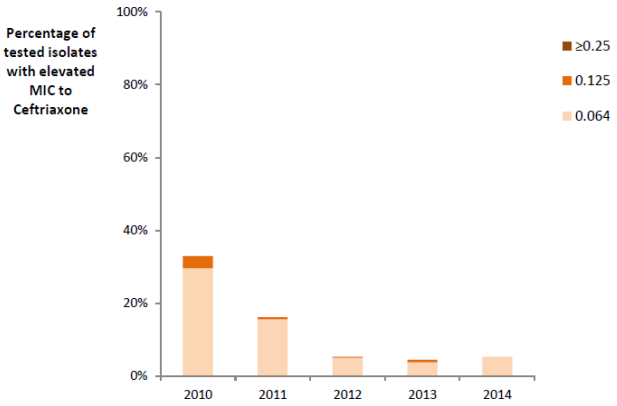


Figure 21- Percentage of tested *N. gonorrhoeae* isolates with elevated MICs to azithromycin, cefixime and ceftriaxone from 2010 – April 30th, 2014. MIC units are in µg/mL.
Source: BCPHMRL, Public Health Advanced Bacteriology & Mycology Program

1.15. *Neisseria meningitidis*

Neisseria meningitidis is an aerobic bacterium that normally colonizes the mucosa of the upper respiratory tract (46). It has a wide range of clinical manifestations, from transient fever and sore throat to fatal meningitis and fulminant septicemia (47). Thirteen serotypes based on differences in the polysaccharide capsule of *Neisseria meningitidis* have been identified to date with 90% of meningococcal diseases worldwide caused by serogroups A, B, and C (48;46). In Canada, serogroups B and C have been largely responsible for most of the cases since 1993 (incidence rates ranging from 0.2 – 0.44 per 100,000 population and 0.13 to 0.65 per 100,000 population for B and C respectively) (48). In BC, serogroup B (12%- 43%) and serogroup Y (4% - 26%) were predominant during the time period from 2008 to 2013 (46). Meningococcal infections is highly contagious and is transmitted between human-to-human through direct contact with infectious respiratory droplets or oral secretions (48). Meningitis is a most fatal illness caused by *N. meningitidis* and requires immediate management with effective antibiotics once illness is suspected (49). Penicillin G is the recommended empiric therapy for invasive meningococcal disease (including Canada), however, resistance due to alterations in the penicillin binding proteins first reported in the 1980s has led to use of third-generation cephalosporins such as ceftriaxone for initial treatment (49)(9). Intermediate resistance to quinolones was reported a 2008 ago with a slowly increasing trend over the years, however, the trend is not accompanied by an increase in the MICs (49).

According to data from BCPHMRL, non-susceptibility rates to ciprofloxacin remains low at 4.3% out of the 420 tested isolates in 2013 (data not shown). Although the proportion of tested isolates non-susceptible to penicillin remains high in 2013 at a rate of 39.1%, it has decreased from a rate of 52.0% in 2012 (data not shown).

Other organisms

1.16. *Mycobacterium tuberculosis*

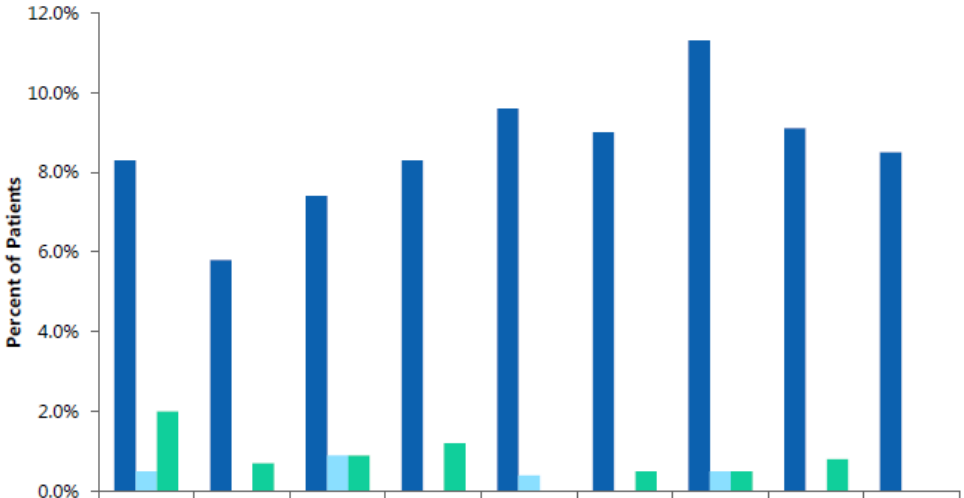
Mycobacterium tuberculosis (MTB) is a slow-growing, aerobic, acid-fast bacterium that is the causative agent for tuberculosis (TB) (50). The infection usually causes disease in the lungs (pulmonary TB), but the bacteria can travel through the bloodstream to other parts of the body (extrapulmonary TB) (50). In British Columbia, there were about 300 cases of TB disease reported over the last decade with an average incidence rate of 7.0 cases per 100,000 people, which is higher than the national level (51).

Mono-resistant TB (MTB) is defined as resistance to one of the first-line drugs, isoniazid (INH), rifampin (RMP), ethambutol (EMB), or pyrazinamide (PZA) (52). Poly-resistant TB is defined as resistance to two or more first-line drugs not including INH and RMP combination (52). Multi-drug resistant TB (MDR-TB) is defined as TB that is resistant to at least the two best first-line drugs, INH and RMP, but does not meet the definition of extensively drug-resistant TB (XDR-TB) (52). XDR-TB is defined as a form of TB that is resistant to INH and rifampin (i.e. MDR-TB), as well as resistance to second-line drugs fluoroquinolone and to any one of the three injectable second-line anti-TB drugs (amikacin, kanamycin or capreomycin) (52).

Susceptibility data for TB is presented as per patient rather than per isolate in order to maintain consistency with reporting to the Public Health Agency of Canada. A total of 2075 patients with culture-confirmed TB strains and drug susceptibility testing (DST) results were reported between 2005 and 2013 by the BCPHMRL (***Figure 22***). In BC, MTB was on the rise from 5.8% in 2006 to 11.3% in 2011 but has since decreased and was reported to be at 8.5% in 2013 (***Figure 22***). Proportions of poly-resistance TB has varied between 0.0% and 0.9% while proportions of MDR-TB have fluctuated between 0% and 2% throughout the same period (***Figure 22***).

Rates in BC are comparable to national rates for 2012 (data not shown). BC had the second highest number of TB cases in Canada in 2012, following Ontario (52). For more information on TB, the most recent BCCDC report can be found online at:

http://www.bccdc.ca/NR/rdonlyres/C43269A4-2140-44AB-9CC6-D0B956FE0151/0/TB_Annual_Report_2011_20131007.pdf.



	2005	2006	2007	2008	2009	2010	2011	2012	2013
Mono-resistant	8.3%	5.8%	7.4%	8.3%	9.6%	9.0%	11.3%	9.1%	8.5%
Poly-resistant	0.5%	0.0%	0.9%	0.0%	0.4%	0.0%	0.5%	0.0%	0.0%
Multi-resistant	2.0%	0.7%	0.9%	1.2%	0.0%	0.5%	0.5%	0.8%	0.0%
Number of Mono-resistant strains	17	16	17	21	23	18	22	21	19
Number of Poly-resistant strains	1	0	2	0	1	0	1	0	0
Number of Multi-resistant strains	4	2	2	3	0	1	1	2	0
Total Number of Tested Patients	204	275	231	254	239	201	194	254	223

Figure 22 - Proportion and number of *M. tuberculosis* complex patients that are mono-resistant, poly-resistant and multi-drug resistant in British Columbia, Canada (2005-2013)
Source: BCPHMRL

Please note: Data provided by the BCPHMRL represent patients with tuberculosis caused by species within the *Mycobacterium tuberculosis* complex including, but not limited to, *Mycobacterium tuberculosis.*

Acknowledgement

This report was prepared by Sophie Wang for the *Do Bugs Need Drugs?* program under the supervision of Dr. David Patrick and Diana George at the BC Centre for Disease Control. Sophie Wang is a Master of Public Health (MPH) student at Simon Fraser University. Dr. David Patrick is the Medical Epidemiology Lead for Antimicrobial Resistance at the BCCDC and the Director of the School of Population and Public Health at UBC. Diana George is the epidemiologist for the *Do Bugs Need Drugs?* program. The *Do Bugs Need Drugs?* program has been funded since its inception in BC in 2005 by Pharmaceutical Services, BC Ministry of Health. The authors thank Pharmaceutical Services for their continued support, and would like to acknowledge the following organizations and individuals for their provision of data and collaboration on this project:

BC Association of Medical Microbiologists (BCAMM)

Dr. Sylvie Champagne
Dr. Diane Roscoe

BC Centre for Disease Control (BCCDC)

BC Public Health Microbiology and Reference Laboratory (BCPHMRL)
Dr. Linda Hoang
Dr. Miguel Imperial
Dr. Judy Isaac-Renton
Dr. Patrick Tang
Dr. Mabel Rodrigues
Yin Chang

Communicable Disease Prevention and Control Services (CDPACS)
Dr. Mark Tyndall
Dr. David Patrick
Mei Chong
Diana George
Kim Dreher
Diana Serban

Canadian Antimicrobial Resistance Alliance

Dr. George Zhanel

Canadian Bacterial Surveillance Network (CBSN)

Karen Green

Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS)

Rita Finley

Canadian Nosocomial Infection Surveillance Program

Dr. Elizabeth Bryce

Do Bugs Need Drugs? (DBND)

Dr. Edith Blondel-Hill
Dr. Fawziah Marra
Dr. David Patrick
Dr. Dale Purych
Kim Dreher
Diana George
Diana Serban
Sophie Wang

LifeLabs Medical Laboratory Services

Michael Kelly
Dr. Romina Reyes
Dr. Dale Purych (BC Biomedical Laboratories)
Dr.Miguel Imperial
Derrick Kan

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Appendix A: Supplemental Tables

Table A.1 -Total number of isolates tested for antimicrobial susceptibility from the various data sources

	MRSA			MSSA			*Streptococcus pneumoniae*		
Year	**BB**	**LL-M**	**LL-I**	**BB**	**LL-M**	**LL-I**	**BB**	**LL-M**	**LL-I**
2007	5332	N/A	N/A	5325	N/A	N/A	156	N/A	N/A
2008	5566	3007	1077	5562	7839	4498	154	520	291
2009	5330	2531	896	5330	7820	4319	132	475	375
2010	4851	2392	711	4850	7464	4051	118	403	182
2011	4409	2136	720	4407	7647	4107	137	462	164
2012	4309	2103	654	4307	7809	4022	114	436	144
2013	4856	1953	563	4855	7253	3754	99	415	168

	Streptococcus pyogenes			*Enterococcus* spp.			*Escherichia coli*		
Year	**BB**	**LL-M**	**LL-I**	**BB**	**LL-M**	**LL-I**	**BB**	**LL-M**	**LL-I**
2007	873	N/A	N/A	3466	N/A	N/A	24365	N/A	N/A
2008	949	242	64	3238	3290	1718	24569	23315	11845
2009	619	165	29	3302	3339	1873	24851	24415	12346
2010	490	185	34	3648	3026	1810	27514	24727	12601
2011	449	171	60	2945	3234	1823	24448	26323	12872
2012	432	147	39	3058	3624	1912	26289	28334	13021
2013	454	117	38	3335	3393	1731	29473	27122	13344

	Klebsiella pneumoniae			*Proteus mirabilis*			SPICE		
Year	**BB**	**LL-M**	**LL-I**	**BB**	**LL-M**	**LL-I**	**BB**	**LL-M**	**LL-I**
2007	2059	N/A	N/A	1381	N/A	N/A	N/A	N/A	N/A
2008	2121	2075	1271	1251	1307	520	N/A	1470	753
2009	2108	2021	1363	1442	1418	530	N/A	1470	807
2010	2358	2047	1280	1480	1414	482	N/A	1521	755
2011	2016	2288	1273	1468	1484	515	N/A	1673	864
2012	2343	2555	1304	1370	1728	527	N/A	1855	850
2013	2551	2497	1381	1538	1588	573	N/A	1798	925

Year	ESBL			*Pseudomonas aeruginosa*			*Haemophilus influenzae*		
	ECOL[a.]	KPNE[b.]	PMIR[c.]	BB	LL-M	LL-I	BB	LL-M	LL-I
2007	24365	2059	1381	921	N/A	N/A	587	N/A	N/A
2008	24569	2121	1251	852	1066	736	522	1078	554
2009	24851	2108	1442	893	1117	780	408	1050	480
2010	27514	2358	1480	783	1115	672	392	1037	428
2011	24448	2016	1468	696	1159	624	307	1008	468
2012	26289	2343	1370	687	1312	712	252	748	335
2013	28778	2490	1538	758	1186	684	259	846	351

Year	*Campylobacter*		
	BB	LL-M	LL-I
2007	N/A	N/A	N/A
2008	N/A	496	203
2009	N/A	500	200
2010	N/A	465	149
2011	N/A	488	159
2012	N/A	541	190
2013	N/A	463	141

Note: BB= BC Biomedical Laboratories; LL-I= LifeLabs-Island; LL-M: LifeLabs-Mainland

[a.] ECOL= *E.coli*
[b.] KPNE= *K. pneumoniae*
[c.] PMIR= *P.mirabilis*
[*.] Data provided by BC Biomedical Laboratories

Table A.2- Summary of antimicrobial modes of action and bacterial mechanisms of resistance.

Antimicrobial Class Example(s)	Action	Antimicrobial Mechanism	Resistance Mechanism	Common bacteria exhibiting resistance mechanism
B-lactams Ampicillin Amoxicillin Penicillin Cephalosporins	Bactericidal	*Inhibit cell wall synthesis*; Bind to penicillin-binding proteins (PBPs) and prevent transpeptidation of bacterial cell wall	1. Alter composition of PBPs and prevent β-lactam binding 2. Production of β-lactamases	1. *S. aureus* (MRSA), *S. pneumoniae* 2. *Enterococcus* spp., *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *H. influenzae*, *N. gonorrhoeae*
Glycopeptides Vancomycin	Bactericidal	*Inhibit cell wall synthesis*; Bind to D-Ala-D-Ala dipeptide precursor and prevent peptidoglycan synthesis	1. Acquisition of *van* gene cassette, which encodes an alternate dipeptide precursor, D-Ala-D-Lac, with reduced affinity for glycopeptides	1. *Enterococcus* spp. (VRE), *S. aureus* (VRSA)
Aminoglycosides Streptomycin Gentamicin Amikacin	Bactericidal	*Inhibit protein synthesis*; Bind to the 30S ribosomal subunit and prevent peptide elongation	1. Mutation in the ribosome binding site 2. Increased efflux or decreased uptake 3. Enzymatic modification via phosphorylation, adenylation, or acetylation	1. *Enterococcus* spp., *Salmonella* 2. *P. aeruginosa* 3. Gram-negative bacteria
Macrolides Erythromycin Clarithromycin Azithromycin	Bacteriostatic	*Inhibit protein synthesis*; Bind to 23S rRNA in the 50S ribosomal subunit and prevent peptide elongation	1. Increased efflux due to acquisition of *mef* gene, which encodes the efflux system (M phenotype) 2. Methylation of the 23S rRNA due to acquisition of the *erm* gene, which encodes a ribosomal methylase (MLS_B phenotype)	1. *S. pneumoniae*, *S. pyogenes* 2. *S. aureus*, *S. pneumoniae*, *S. pyogenes*
Lincosamides Clindamycin	Bacteriostatic	*Inhibit protein synthesis*; Bind to 23S rRNA in the 50S ribosomal subunit and prevent peptide elongation	1. Methylation of the 23S rRNA (MLS_B phenotype)	1. *S. aureus*, *S. pneumoniae*, *S. pyogenes*
Tetracyclines Tetracycline Doxycycline Minocycline	Bacteriostatic	*Inhibits protein synthesis*; Bind to 30S ribosomal subunit and prevent binding of incoming aminoacyl-tRNA	1. Mutation in the 30S ribosomal subunit 2. Increased efflux	1. Gram-negative and Gram-positive bacteria 2. Gram-negative and Gram-positive bacteria
Quinolones Ciprofloxacin Levofloxacin Moxifloxacin	Bactericidal	*Inhibit DNA and RNA synthesis*; Inhibit supercoiling enzymes, DNA gyrase A and topoisomerase IV	1. Mutation in supercoiling enzymes causing reduced affinity for quinolones 2. Increased efflux	1. *S. aureus*, *S. pneumoniae*, Gram-negative bacteria 2. *S. aureus*
Sulfonamides and Trimethoprim TMP-SMX	Bactericidal	*Prevent synthesis of folic acid*; Sulfonamides - compete with *p*-amino-benzoic acid by binding dihydropteroate synthase Trimethoprim – bind dihydrofolate reductase and prevent production of folic acid	1. Mutations in folic acid synthesis enzymes causing reduced affinity for sulfonamides and trimethoprim 2. Overproduction of enzymes	1. *S. aureus*, *S. pneumoniae*, Gram-negative bacteria 2. *E. coli*
Nitrofurans Nitrofurantoin	Bactericidal	Thought to prevent protein synthesis by damaging ribosomal proteins	1. Diminished nitroreductase activity causing less electrophilic conversion of nitrofurantoin	1. Urinary tract infection pathogens

Appendix B: Data Sources

The data sources used for the compilation of this report are outlined below. The specific bacterial species provided by each data source are indicated. Organisms are tested for susceptibility to antimicrobial agents in the laboratory using the minimum inhibitory concentration (MIC) breakpoints, as set out by the Clinical and Laboratory Standards Institute (CLSI) guidelines (3).

BC Association of Medical Microbiologists (BCAMM)
Extended spectrum β-lactamase-producing Enterobacteriaceae (ESBL producing Enterobacteriaceae)

The BC Association of Medical Microbiologists (BCAMM) collects data from a representative sample of community-based and hospital-based laboratories in BC. Refer to the BCAMM 2011 Report for a complete list of all participating laboratories (34). Data for 2012 and 2013 were not available at the time of this report, thus no new data from this source was included in the 2013 report. Note that the participating community-based laboratories include BC Biomedical Laboratories and LifeLabs, which provide most of the out-patient coverage for the province and are also included in this report. Limitations of the BCAMM data include the possibility of more than one isolate from the same patient being tested and included by different participating sites, re-testing of isolates at certain sites, the lack of denominator data for *Enterococci* as they are part of normal enteric flora and often non-pathogenic, and the inability to differentiate community-acquired and hospital-acquired infections.

BC Biomedical Laboratories and LifeLabs Medical Laboratory Services
Methicillin-resistant *Staphylococcus aureus* (MRSA), *methicillin-sensitive Staphylococcus aureus* (MSSA), *Streptococcus pneumoniae, Streptococcus pyogenes, Enterococcus* spp., *Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Serratia* spp., *Providencia* spp., *Morganella* spp., *Citrobacter* spp., *Enterobacter* spp., *E. coli, K. pneumoniae,* and *P. mirabilis* isolates with phenotype compatible with ESBLs, *Pseudomonas aeruginosa, Salmonella (non-typhoidal), Haemophilus influenza* and *Campylobacter* spp.

As of April 2, 2013, LifeLabs Medical Laboratory Services completed the purchase of BC Biomedical Laboratories following approvals from the Federal Competition Bureau and the Provincial government (53). The laboratories implement different methods for susceptibility testing (e.g. Vitek versus replicator) and their information systems have not yet been merged, thus, the data provided independently from both constituents were analyzed separately for this report.

BC Biomedical Laboratories collected isolates from 45 community-based patient service centres located throughout the Lower Mainland of BC. Clustering of patient services is found in the Fraser Health Authority. Since 2007, BC Biomed provided anonymous monthly line-listed datasets, which were analysed in collaboration with the *Do Bugs Need Drugs?* (DBND) program in BC.

The data shown for *E. coli, K. pneumoniae,* and *P. mirabilis* isolates with a phenotype compatible with ESBLs in the present report were not provided directly from the BC Biomedical Laboratories. Instead, these isolates were identified based on resistance to third generation cephalosporins (e.g. ceftriaxone, cefotaxime, ceftazidime, or cefixime). However, because cephamycin results were not available, true identification of ESBL producing *E. coli*, *K. pneumoniae,* and *P. mirabilis* isolates was not possible and an overestimation is expected. Without direct confirmation, these isolated will be identified as extended spectrum beta-lactamase-like (ESBL) producers or "isolates with phenotype compatible with ESBLs."

As a new addition the 2013 report, LifeLabs has provided anonymous, monthly, line-listed susceptibility data from 2008 to November of 2013. LifeLabs collects isolates from 80 community-based patient service centres located throughout Vancouver Island and the Mainland of BC. Due to the clustering of patient services in the Vancouver Island and Vancouver Coastal Health Authorities, isolates may not be representative of the entire province, however, in combination with BC Biomedical Laboratories data, a larger geographical representation can be attained. An indicator of the testing area of the LifeLabs laboratory associated with a given isolate has also been provided in the data (e.g. Mainland versus Island), and has allowed for analysis of these regions separately.

BC Public Health Microbiology & Reference Laboratory (BCPHMRL)
Carbapenase-producing organisms (CPO), Extended spectrum β-lactamase producing Enterobacteriaceae (ESBL-producing Enterobacteriaceae), *Neisseria gonorrhoeae, Neisseria meningitidis, Mycobacterium tuberculosis*

Since the fall of 2010, the BCPHMRL implemented genotypic methods for testing Enterobacteriaceae isolates in order to confirm antibiotic susceptibility profiles for isolates with unusual phenotypic profiles submitted from front-line

microbiology laboratories. In particular, the BCPHMRL looks for gene targets associated with ESBL (SHV, TEM, CTX-M and OXA-1), AmpC (CMY-2, CMY-1/MOX, CMY-2/LAT, DHA, ACC, MIR/ACT and FOX) and carbapenem (KPC, NDM, IMP and VIM) resistance. These data are reported in the BCAMM report. Additionally, updated carbapenase-producing organism (CRO) trends are included in the *Lab Trends* report (46).

Since 2010, the BCPHMRL has been monitoring the resistance patterns of *N.gonorrhoeae* to a panel of antimicrobials using E test® on culture positive isolates. Antibiotics included in the panel include azithromycin, ceftriazone, cefixime, ciprofloxacin, penicillin, spectinomycin, and tetracycline (46). Antimicrobial susceptibility testing has also been performed on *N.meningitidis* since 2012; E test® susceptibility results include ceftriaxone, ciprofloxacin, penicillin, rifampin, and nalidixic acid.

Tuberculosis data from 2005 to 2013 were provided directly from the BCPHMRL. The BCCDC is informed of tuberculosis cases directly from providers and laboratories throughout the province. All new cases of TB with confirmatory testing in BC and bacterial isolate available (approximately 80% of all cases) are tested for susceptibility against anti-tuberculosis agents. Data used for analysis are extracted from iPHIS (Integrated Public Health Information System). Please note that data on TB is now displayed on a per patient basis, rather than a per isolate basis for consistency with Public Health Agency of Canada (PHAC) reporting. Drug resistance is noted for patients with isolates that were mono-resistant, multi-drug resistant (MDR-TB) and poly-resistant.

Canadian Bacterial Surveillance Network (CBSN)

Streptococcus pneumoniae

The Canadian Bacterial Surveillance Network (CBSN) receives isolates from one or more hospitals located in BC each year (nine different hospitals in total since 1994). From participating hospitals, CBSN collects a set of consecutive clinically relevant *Streptococcus pneumoniae* isolates (from any site) as well as isolates from a sterile site. Limitations that may affect the data are the collection method being from any site, and isolate submission being voluntary with only two hospitals having submitted isolates for 2010, 2012, and 2013 and only one for 2011. Aggregated data for *Streptococcus pneumoniae* were available for years 1994 to 2009 and line-listed data was provided for years 2010 to 2013. Please note that the oral penicillin and non-meningitis ceftriaxone CLSI breakpoints are used in this report.

Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS)

Salmonella Enteritidis and *Salmonella* Heidelberg

Salmonella isolates from the BC Public Health Microbiology and Reference Laboratory (BCPHMRL) were forwarded to the National Microbiology Laboratory (NML) in Winnipeg, Manitoba for susceptibility testing. Only isolates from the first fifteen days of each month were sent to CIPARS with the exception of *Salmonella* Typhi and *Salmonella* Newport, for which all isolates are submitted. For *Salmonella* Enteriditis, due to the large number of isolates submitted by the larger Canadian provinces (British Columbia, Alberta, Ontario and Québec), only half of the isolates received during the first 15 days of the month were tested for antimicrobial susceptibility. The remaining isolates were stored and tested as resources were available. Consequently, the tested isolates represent approximately half of all non-typhoidal *Salmonella* cases in BC. The twelfth edition of the Performance Standards for Antimicrobial Resistance Testing from the CLSI was used to classify MIC breakpoints for resistance (4). Aggregated data were available for years 2003 to 2011.