TRENDS IN ANTIBIOTIC UTILIZATION ASSOCIATED WITH THE “DO BUGS NEED DRUGS?” PROGRAM IN BRITISH COLUMBIA

by

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ABSTRACT

The misuse and overuse of antibiotics in the treatment of respiratory tract infections contributes to the emergence of antibiotic resistance. “Do Bugs Need Drugs” (DBND) is a multi-faceted community education program which was implemented in British Columbia (BC) in September 2005 to increase appropriate antibiotic use and prevent the spread of infections and resistant organisms. The purpose of this study was to conduct a complete descriptive analysis on the association between DBND and changes in overall, pediatric, drug-specific and indication-specific antibiotic utilization trends in BC.

Antibiotic utilization data on all oral solids classified as “antibacterials for systemic use” were obtained from the PharmaNet database for the years 1996 to 2007. These data were linked to the Medical Service Plan database. Following conversion to the defined daily dose, linear regression was used on the data to describe monthly utilization rates in each health service delivery area (HSDA) in BC. Finally, changes in antibiotic utilization trends were compared by level of program implementation to determine whether a pattern exists between differing level of public education and improvements in antibiotic use.

The monthly rate of change of all antibiotic utilization rates targeted by the program improved in association with DBND implementation in the Vancouver HSDA. Within the other HSDAs, the monthly rate of change of targeted antibiotic utilization rates improved in all areas with high DBND implementation. Inconsistent results were recorded in areas with low to medium program implementation. Declines in fluoroquinolone and newer macrolide utilization rates were not observed.

The findings of this study provide evidence that community education initiatives have the potential to improve antibiotic utilization trends in the long-term. They also demonstrate the importance of a high level of program implementation. However, as the utilization rates of commonly misused antibiotics continue to increase despite the program’s directed efforts, the results of this study suggest that education alone may not be enough to rapidly decrease current antibiotic utilization rates. Policy regulations may be required.
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<th>Description</th>
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<tr>
<td>ATC</td>
<td>Anatomical Therapeutic Chemical</td>
</tr>
<tr>
<td>BC</td>
<td>British Columbia</td>
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<tr>
<td>DDD</td>
<td>Defined daily dose</td>
</tr>
<tr>
<td>DBND</td>
<td>Do Bugs Need Drugs?</td>
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<tr>
<td>HSDA</td>
<td>Health Service Delivery Area</td>
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<tr>
<td>MSP</td>
<td>Medical Service Plan</td>
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<tr>
<td>RTI</td>
<td>Respiratory tract infection</td>
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<tr>
<td>STI</td>
<td>Sexually transmitted infection</td>
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CO-AUTHORSHIP STATEMENT

The work presented in this thesis was conducted and written by the Master’s candidate. The study provides a unique contribution to the broader evaluation of the “Do Bugs Need Drugs?” program. The candidate developed the specific study design, statistical analysis, and outcomes examined with the assistance of the thesis committee (Dr. David M. Patrick, Dr. Fawziah Marra, Dr. Bonnie Henry, and Dr. Hubert Wong). Previous work by Dr. Marra and Dr. Patrick established the collaborations between institutions which allowed access to the PharmaNet and Medical Service Plan data used in this study. Mei Chong provided the candidate with the data aggregated by health service delivery area in order to maintain the confidentiality data agreements. The thesis committee reviewed each manuscript and provided critical evaluations and suggestions for improvement; however the candidate was responsible for the writing and the final content presented.
1. BACKGROUND

1.1 Introduction

Since Alexander Fleming discovered penicillin in 1928, antibiotics have been celebrated as one of the most important discoveries in medicine. However, even then, Fleming recognized the potential limitations of this class of pharmaceuticals: “But I would like to sound a note of warning...It is not difficult to make microbes resistant to penicillin in the laboratory by exposing them to concentrations not sufficient to kill them, and the same thing has occasionally happened in the body (Fleming 1945)”. As we now enter an era where emerging resistant bacteria threaten to throw us back into a pre-antibiotic state, we must actively seek ways to maintain the effectiveness of these once hailed “magic bullets”.

The occurrence of random mutations within bacterial genomes, leading to resistant organisms, is beyond our control. However, we are in a position to limit the selective pressure placed on these genomes through the misuse and overuse of antibiotics. There is substantial ecological, observational, and experimental evidence which suggests that limiting the use of antibiotics to bacterial infections and encouraging the use of narrow rather than broad-spectrum antibiotics whenever possible may have the potential to reduce the rate of increasing bacterial resistance (Goossens, Ferech et al. 2005; Mölstad, Erntell et al. 2008; Patrick and Hutchinson 2009). By curtailing resistance, efforts promoting judicious antibiotic use will also help alleviate the pressure placed on pharmaceutical companies to rapidly develop new and effective antimicrobials (Levy and Marshall 2004).

An abundance of literature has provided valuable insight into the driving causes behind inappropriate antibiotic use (WHO 2001; Eng, Marcus et al. 2003; Cho, Hong et al. 2004; Garcia, Bouza et al. 2005; Ebert 2007). Various interventions have been designed and implemented worldwide to address one or more of these factors (Bexell, Lwando et al. 1996; Belongia, Sullivan et al. 2001; Dollman, LeBlanc et al. 2005; Gonzales, Corbett et
al. 2005; Apisarnthanarak, Danchaivijitr et al. 2006; Wutzke, Artist et al. 2006; Chazan, Turjeman et al. 2007; Blondel-Hill 2008; Mölstad, Erntell et al. 2008). A complete evaluation of these initiatives is a vital step in assessing their effectiveness and potential for improving public health.

The “Do Bugs Need Drugs?” (DBND) program is a multifaceted intervention introduced in British Columbia (BC), Canada, in September 2005. The goal of the program was to optimize antibiotic use and infection control practices (Blondel-Hill 2008). We undertook an in-depth analysis of the association between the implementation of the program and changes in antibiotic utilization trends in BC, with emphasis on the populations, drugs, and indications targeted by the initiative.

Section 1.2 presents the results of a literature review of articles on the trends and consequences of inappropriate antibiotic use, and community-based programs aimed at improving the use of antibiotics and infection control. Section 1.3 consists of an overview of the DBND program and a report of its current progress and short-term impact. The necessity and purpose of this thesis, as an evaluation of the long-term sustainable changes associated with DBND, is given in Section 1.4.

The literature review is organized so that the search strategy is provided in Subsection 1.2.1. Background information on current antibiotic utilization trends, reasons for the inappropriate use of antibiotics, and the trends and consequences of antibiotic resistance are outlined in Subsection 1.2.2. Subsection 1.2.3 consists of a discussion of the objectives, strategic approaches, limitations, and political considerations of community-based programs which aim to reduce inappropriate antibiotic use. A review of the current progress of several community-based programs is provided in Subsection 1.2.4.
1.2 Literature Review

1.2.1 Search Strategy
A strategy was developed to search the literature for articles on the implementation and evaluation of community-based interventions aimed at reducing inappropriate antibiotic use for respiratory tract infections (RTIs). Pubmed, EMBASE, Google Scholar, and the Cochrane Database of Systematic Reviews were searched for relevant articles using a combination of the basic search terms antibiotic, community, and evaluation. These terms were varied so that antibiotic was exchanged with antibacterial, consumption, utilization or use; community with program, intervention, or public health; and evaluation with process, progress, outcome, or impact. The search included all literature published in the English language from January 1990 to December 2008. The bibliographies of review articles were manually searched for relevant studies which contributed to the literature used as the basis for this review.

1.2.2 Antibiotic Use and Resistance in British Columbia
1.2.2.1. Trends in Antibiotic Utilization
In BC, the rate of overall antibiotic utilization steadily declined in the late 1990s and early 2000s, reaching its lowest level in 2002 (15.6 defined daily dose (DDD)/1000 population/day). Subsequent years showed an increase in the rate of utilization, which stabilized after a local peak in 2005 (Figure 1.1; Patrick, D.M., personal communication). Overall antibiotic utilization rates in BC were lower than the European median in 2000, but remain higher than rates of most Northern European countries with established antibiotic surveillance and control programs (Patrick, Marra et al. 2004).
Fluoroquinolones are widely used in adult patients because of their excellent tissue penetration and bactericidal activity (Gendrel, Chalumeau et al. 2003). Between 1996 and 2007, fluoroquinolone utilization rates increased from 0.95 DDD/1000 population/day to 1.64 DDD/1000 population/day (Figure 1.2; Patrick, D.M., personal communication). A large increase in fluoroquinolone-resistant urinary isolates of *Escherichia coli*, many of which are multi-drug resistant (Karlowsky, Hoban et al. 2006), has raised significant concerns regarding the frequent use of these antibiotics (Urbanek, Kolar et al. 2005; Karlowsky, Hoban et al. 2006; Rasool, Fuertes et al. 2008). The utilization rates of newer macrolides (azithromycin and clarithromycin) have also increased (from 0.84 DDD/1000 population/day in 1996 to 3.02 DDD/1000 population/day in 2007; Figure 1.2; Patrick, D.M., personal communication). Newer macrolides are of particular interest as there is some evidence to suggest that these drugs may be more effective at selecting for resistance due to their low $C_{\text{max}}$ and longer-half-lives (Drusano and Craig 2000; Kastner and Guggenbichler 2001).
FIGURE 1.2: Average daily fluoroquinolone and newer macrolide utilization rates by year.

Since the 1990s, the rates of antibiotic prescriptions written for children have been decreasing in Canada (Marra, Patrick et al. 2006), the United States (McCaig, Besser et al. 2002; Finkelstein, Huang et al. 2008) and Europe (Marra, Monnet et al. 2007). In Canada, pediatric prescription rates dropped by one third between 1996 and 2003, primarily due to a large reduction in the use of penicillins and cephalosporins (Marra, Patrick et al. 2006). However, similar to the trends observed among adults, the use of newer macrolides among children has increased in recent years (Marra, Patrick et al. 2006). This increase is especially prominent among children in preschool and/or from low-income families (Kozyrskyj, Carrie et al. 2004). Thus, although significant improvements in pediatric prescription rates have been observed, the continued high use of certain antibiotic classes highlights the need for persistent efforts promoting appropriate antibiotic use.

1.2.2.2 Drivers of Inappropriate Antibiotic Use

Despite the fact that many healthcare providers recognize inappropriate antibiotic use and emerging bacterial resistance as serious national problems (Palmer and Bauchner 1997; Wester, Durairaj et al. 2002; Cho, Hong et al. 2004), the misuse of antibiotics is common-place in both industrialized (Schwartz 1999) and developing countries (Isturiz
and Carbon 2000; Sirinavin and Dowell 2004). Currently, the majority of antibiotics prescribed in community practice and primary care settings are for RTIs, especially among children (Kozyrskyj, Carrie et al. 2004; Marra, Patrick et al. 2006). Many of these prescriptions provide little clinical benefit as RTIs are predominantly of viral origin (Gonzales, Steiner et al. 1997; Butler, Kinnersley et al. 2001; Briel, Christ-Crain et al. 2005; Gerber 2005).

In recognition of this inappropriate use of antibiotics, several studies have identified key individual-level factors driving the misuse and overuse of these pharmaceuticals (WHO 2001; Eng, Marcus et al. 2003; Cho, Hong et al. 2004; Ebert 2007). These factors can be broadly categorized as originating from prescribers, patients, or both (Table 1.1).

**TABLE 1.1: Factors contributing to inappropriate antibiotic use for the treatment of respiratory tract infections.**

<table>
<thead>
<tr>
<th>Factor</th>
<th>Prescriber Driven</th>
<th>Patient Driven</th>
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<tbody>
<tr>
<td>Physician misconceptions (beliefs, attitudes, knowledge)</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Unfamiliarity with local resistance trends</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Common, habitual (overuse)</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Diagnostic uncertainty (underuse of laboratory testing)</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Patient pressure (from patient, parents, or daycares)</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Patient misconceptions (e.g. regarded as cure-all)</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Inappropriate use (e.g. not completing prescriptions)</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Socioeconomic and cultural factors</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Time pressure, convenience</td>
<td>X</td>
<td>X</td>
</tr>
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</table>

When faced with a decision, prescribers are influenced by their personal beliefs, attitudes, knowledge, specialty, and past experiences (Cho, Hong et al. 2004; Kozyrskyj, Dahl et al. 2004). Unfortunately, the information which they use to make their decisions does not always correspond to the current recommended treatment regimes, especially if diagnostic uncertainty exists (Arnold, Teresa et al. 2005). Prescribers may also be unfamiliar with current local antibiotic resistant trends, which otherwise would promote a more judicious approach towards antibiotic use (Wester, Durairaj et al. 2002).
ongoing study by Brehaut and Poses et al. will quantify the extent to which inappropriate utilization stems from biased clinical judgments (Brehaut, Poses et al. 2007).

“Patient pressure” is strongly associated with receiving an antibiotic prescription for RTIs (Mangione-Smith, McGlynn et al. 1999; Coco and Mainous 2005; Ebert 2007). This type of pressure frequently stems from patients who expect an antibiotic when they visit a doctor (Mangione-Smith, McGlynn et al. 2001; Arnold, Teresa et al. 2005), parents who request antibiotics for their child (Palmer and Bauchner 1997; Mangione-Smith, McGlynn et al. 2001), or from daycare policies which require proof of antibiotic treatment before allowing a child to return to school (Kuzujanakis, Kleinman et al. 2003; Ebert 2007). Patient demands are often based on past experiences or misconceptions, such as the assumption that antibiotics are “cure-alls” which work on both viral and bacterial infections, or that a prescription can be stopped when symptoms improve (Palmer and Bauchner 1997; Fuertes, Vrbova et al. 2008).

Socioeconomic factors also play a role in the level of “patient pressure” expressed, with higher rates of antibiotic use documented among children of low education and low income mothers (Thrane, Olsen et al. 2003; Kozyrskyj, Dahl et al. 2004). These trends may suggest that parents with high income or those with more education may be better informed about appropriate antibiotic therapy (Pichichero 1999), or may have more flexibility with work and are thus able to bring their child back to the physician if symptoms worsen (Belongia, Naimi et al. 2002).

Time pressure is attributable to the combination of patients seeking immediate relief, prescribers trying to stay on schedule, and also prescribers erring on the side of caution when an important bacterial infection is suspected, especially with young children. Treatment should be started as soon as possible if the infection is truly bacterial, typically through the use of a broad-spectrum antibiotic. Ideally, the prescription should be changed to a narrow-spectrum antibiotic once susceptibility and culture testing results are received. Unfortunately, because of lack of time, culture and susceptibility testing is now always conducted. Treatment regimes are thus not optimized, a process which would
otherwise prevent many unnecessary prescriptions of broad-spectrum antibiotics (Ebert 2007). Finally, under strict time restraints, prescribers sometimes find it simpler to supply unnecessary antibiotics rather than to explain to patients why symptomatic treatment would suffice.

1.2.2.3 Trends and Consequences of Antibiotic Resistance

Antibiotic resistance arises via random mutations occurring through natural selection, but also through the evolutionary pressure placed on bacterial genomes by the overuse and misuse of antibiotics within a population (Neu 1992; Kastner and Guggenbichler 2001; Bronzwaer, Cars et al. 2002; Urbanek, Kolar et al. 2005; Malhotra-Kumar, Lammens et al. 2007; Riedel, Beekmann et al. 2007). The complex mechanisms by which random mutations lead to resistance remain somewhat elusive, although advances in the field are providing some insight (Perfeito 2007). Nevertheless, there is very little doubt that the rapid increase in resistance can be slowed and controlled through the appropriate use of antibiotics in people and animals, and efficient infection control practices (WHO 2001(2)).

An update on antibiotic resistance in BC is compiled in a yearly report entitled “Antimicrobial Resistance Trends in the Province of British Columbia” (Rasool, Fuertes et al. 2008). In its most recent version, published in August 2008, the following important trends were identified. The percent of Staphylococcus aureus isolates that are methicillin-resistant has significantly increased between the years 1999 to 2008 (p-value <0.05). Over the last two to three years, this increase has been primarily driven by community-associated isolates. Streptococcus pneumoniae continues to demonstrate increasing resistance to erythromycin. Streptococcus pyogenes and Staphylococcus aureus resistance to erythromycin has remained stable from 2006 to 2007. Gram negative organisms, most notably the urinary tract pathogens such as Escherichia coli, Proteus mirabilis and Klebsiella pneumoniae, have demonstrated increasing resistance to ciprofloxacin (Figure 1.3).
There are several patient, healthcare, and economic costs associated with antibiotic resistance. The failure of first-line agents is associated with increased patient morbidity and mortality, longer hospital stays, and higher rates of re-admission and return visits (Cosgrove, Sakoulas et al. 2003; Cosgrove 2006). These and other associated adverse events place a heavy burden on our already strained healthcare facilities. Enormous economic burdens are also associated with antibiotic resistance. Recent Canadian studies estimated the total cost (hospitalization, treatment, control measures, and laboratory investigations) to care for one patient with a methicillin-resistant Staphylococcus aureus infection averaged over 12,000 CAD (Kim, Oh et al. 2001; Goetghebeur, Landry et al. 2006). Studies in the United States quote much higher figures (Cosgrove 2006; Klevens, Morrison et al. 2007).

1.2.3 Community-Based Interventions and Appropriate Antibiotic Use
The growing popularity of community-based interventions in health promotion and preventative medicine represents a shift in emphasis from individual-level explanations of health to one that also encompasses social and environmental influences (Merzel and D'Afflitti 2003). This type of population-level approach has proven effective in several
well designed community-based educational interventions addressing issues such as cigarette smoking, seat-belt and bicycle helmet use, and HIV prevention (Rietmeijer, Kane et al. 1996; Klassen, MacKay et al. 2000; Lumley, Oliver et al. 2006). The method of improving health from a population perspective was adapted by many hospital and community-based interventions addressing inappropriate antibiotic use and emerging resistance (Bexell, Lwando et al. 1996; Belongia, Sullivan et al. 2001; Dollman, LeBlanc et al. 2005; Gonzales, Corbett et al. 2005; Apisarnthanarak, Danchaivijitr et al. 2006; Wutzke, Artist et al. 2006; Chazan, Turjeman et al. 2007; Blondel-Hill 2008; Mölstedt, Erntell et al. 2008).

Evaluation of such programs and their impacts has allowed the identification of components that, when used in combination with one another, appear to be closely linked to program success. These components include clear and measurable objectives integrated into a comprehensive evaluation scheme set prior to implementation, a dynamic multidimensional approach culturally appropriate for unique target audiences, and an understanding of the limitations of a program and its evaluation. This chapter will elaborate on each of these components, placing a particular emphasis on their applicability to community-based interventions. The importance of obtaining political support will also be outlined.

1.2.3.1 Objectives
A well-designed community-based intervention must be a dynamic entity which can be easily evaluated so that its weaknesses and strengths can be identified and addressed in future developments (Dwyer and Makin 1997). Relevant, meaningful, and measurable objectives must be integrated into the implementation and evaluation of a program during the planning stage. These objectives should encompass all aspects of the program, such as its efficiency and effectiveness, the interest of people delivering and receiving the initiatives, as well as any unanticipated effects, beneficial or otherwise (Rychetnik, Frommer et al. 2002).
This text will follow the suggestions and definitions of Judd et al., and classify program objectives as either contributing to one of three main aspects of evaluation: process, impact, or outcome (Figure 1.4; Judd, Frankish et al. 2001).

![Figure 1.4: Components of a complete health promotion program evaluation.](image)

**1.2.3.1.1 Process Evaluation**
Process evaluation entails spatial and temporal reporting of the number of people who have been reached by the intervention, and the number and types of components which have been deployed (e.g. number of pamphlets mailed). This type of reporting allows the differentiation between interventions which failed to show a measurable effect because they were indeed ineffective, from those that failed due to poor implementation. In the latter case, a detailed process evaluation can drill downwards and establish which components of an intervention were the least effective and why (i.e. poor uptake, lack of co-operation or perceived benefit, politics, funding, etc.). Process evaluation is essential for assessing the internal and external validity of community-based interventions (Durlak and DuPre 2008).

**1.2.3.1.2 Impact Evaluation**
Impact evaluation requires the assessment of proximal, short-term changes in knowledge and behaviour. A variety of impact measures are used as surrogates for changes in attitude or actions towards antibiotic use or resistance. Subjective measures include self-reported behaviour change (Stille, Rifas-Shiman et al. 2008) and pre-post questionnaires/assessments (Parsons, Morrow et al. 2004). Objective measures commonly used are changes in retail sales of antimicrobial drugs (Belongia, Knobloch et al. 2005), decreases in utilization/prescription rates (Belongia, Knobloch et al. 2005;
Finkelstein, Huang et al. 2008), and reductions in morbidity, mortality, length of hospital stay, duration of therapy, or the occurrence of clinical or non-clinical adverse events (Cosgrove 2006).

1.2.3.1.3 Outcome Evaluation
Outcome evaluation assesses long-term sustainable changes in policy or the health status of the population attributable to an intervention. In order to achieve such changes, short-term improvements identified in an impact evaluation must be maintained, so that good habits are developed and conscious decision making is no longer required (Glasgow, Vogt et al. 1999).

The desired outcome of any intervention targeting antibiotic use should not be the elimination of these pharmaceuticals from the medical treatment regime, as antibiotics are vital to modern medicine. Rather, these interventions should aim to develop good antibiotic stewardship strategies, which would ultimately lead to a reduction in our antibiotic “resistance footprint” (Patrick and Hutchinson 2009). Such stewardship should not only include selection of the appropriate drug when indicated, but also adherence to pharmacodynamic principles when deciding on dose and duration, and consideration of adverse side effects as identified by pharmacovigilance research (WHO 2002). In addition, it is imperative that any bacterial treatment regime be based on a population rather than a solely individualistic approach. Treatment should be selected to minimize the advantage it provides to resistant organisms in the community or the hospital, while ensuring effective treatment for the patient (Shales, Gerding et al. 1997; Polk 1999; Ball, Cars et al. 2002; Fishman 2006). This ecological approach is essential as, although certain antibiotic treatment regimes may be beneficial to an individual, they may be detrimental to the community as a whole (Lipsitch and Samore 2002; Patrick, Purych et al. 2008).

Assessing the relationship between the implementation of an intervention and a long-term change in behaviour is quite challenging due to the impact of secular trends and small effect sizes (Fishbein 1996; Merzel and D'Afflitti 2003). Nevertheless, when studies
have attempted to do so, outcome measures which have been used include sustainable improvements in utilization patterns and the stabilization of, or decrease in, the trends of antibiotic resistance. Mainous et al. comprehensively addressed the former outcome measure by evaluating changes in utilization rates as well as variations in the rate of change of these antibiotic utilization rates over time (Mainous, Hueston et al. 2000). Assessing variations in the rate of change of utilization rates (the slope) is extremely valuable, as even if the intervention produces minimal change in the absolute rate of utilization, it may have significant impact in the long-term if the sustained rate of increase is reduced (Figure 1.5; MacDougall and Polk 2005).

![Diagram](image)

**FIGURE 1.5:** Change in the slope of antibiotic utilization rates, from expected rates (a) to observed rates (b), associated with the implementation of an intervention.

### 1.2.3.2 Multidimensional Approach

Promoting behavioural change is a complex process affected by personal beliefs, expectations, motivations, psychosocial environments, and social and contextual factors (Belongia and Schwartz 1998; Finch, Metlay et al. 2002). As of yet, no single type of intervention has emerged as being sufficient to address all of these relevant issues. Rather, it is generally agreed that a multidimensional approach, tailored to respond to the unique needs of a community or institution, is required to attend to the various reasons driving inappropriate antibiotic use and the barriers to change (Gonzales, Steiner et al. 1999; Arnold and Straus 2005; Paskovaty, Pflomm et al. 2005; Wutzke, Artist et al. 2006;
Ranji, Steinman et al. 2008). As Gerald Nadler’s Uniqueness Principle states: “No two problems are the same” (Nadler and Hibino 1995). Why then, would we expect two identical solutions?

1.2.3.2.1 Strategies

Many studies have identified a broad range of effective communication strategies which can be used in community health promotion. These methods include, but are not limited to, education in schools, mass media campaigns, and the distribution of written information (Finch, Metlay et al. 2002; Stille, Rifas-Shiman et al. 2008).

Most community-based interventions take advantage of preschool and elementary school settings to promote their initiatives. Interventions are most effective when they are incorporated into the school curriculum and appropriate policies are developed (Mukoma and Fisher 2004). Strengths of this type of health promotion include the ability to reach a large proportion of a well-defined population at a low cost, and the opportunity to educate children in a familiar environment which is conducive to learning.

Multiple types of media have been used effectively in population health interventions, and continue to be improved (Randolph and Viswanath 2004). Public transit, print media, radio, and television are among the most commonly used media. Television is considered one of the most effective methods for promoting public messages, but also among the most expensive (Finch, Metlay et al. 2002; Goossens, Guillemot et al. 2006; Stille, Rifas-Shiman et al. 2008). Depending on budgetary restrictions, a balance must be achieved between the medium selected, the quality of the advertisements (time of day, type transit vehicle, station), and the frequency with which they are played or posted.

Written health promotion material can take several forms including posters, pamphlets/brochures, parent guides, newspaper articles, magazine inserts, etc. The spread of this material can also vary substantially. Mass mailouts, distribution at health clinics, hospitals, community centers, or more recently, on websites, are all commonly used media. Although valuable on its own, the distribution of written material should
compliment other initiatives or be linked to recognizable health organizations or government entities to optimize its effectiveness (Finch, Metlay et al. 2002).

1.2.3.2.2 Target Populations
Interventions which include audience-specific components targeted to relevant populations tend to report good results (Gonzales, Steiner et al. 1999; Belongia, Sullivan et al. 2001; Finkelstein, Davis et al. 2001; Finch, Metlay et al. 2002; Perz, Craig et al. 2002). Literature has shown that parents and children harbour misconceptions about bacteria and antibiotic resistance (Palmer and Bauchner 1997; Kuzujanakis, Kleinman et al. 2003; Saunders, Tennis et al. 2003; Milandri 2004). These misconceptions can be corrected through public education (Trepka, Belongia et al. 2001; Finkelstein, Stille et al. 2005), thereby alleviating the “patient pressure” placed on doctors by parents, and educating both populations about the differences between bacteria and virus and the proper use of medications. Healthcare professionals (doctors, nurses, pharmacists, pharmacy technicians) are another audience group which is heavily targeted by programs promoting the judicious use of antibiotics. Often, healthcare professionals receive targeted education within academic or hospital-settings, in addition to being exposed to general public health messaging efforts.

1.2.3.2.3 Messaging
Regardless of the communication method or target population selected, health information should be promoted via brief, clear and consistent messaging to multiple stakeholders on a regular basis, in order to maximize the likelihood of retention (Finch, Metlay et al. 2002; Stille, Rifas-Shiman et al. 2008). With respect to reducing the misuse and overuse of antibiotics in the community, the context of the messaging should elicit the differences between bacteria and viruses, the importance of proper antibiotic use, the consequences of misuse, and the benefits of symptomatic treatment and infection control (Sirinavin and Dowell 2004; Paskovaty, Pflomm et al. 2005).
1.2.3.3 Limitations

Community-based programs are subject to various limitations which, according to Merzel et al., can be categorized into 5 areas: 1) methodological issues, 2) the influence of secular trends, 3) smaller-than-expected effect sizes, 4) limitations of the interventions, and 5) limitations of theory (Merzel and D'Afflitti 2003). The following discussion will focus on some methodological issues and how they relate to antibiotic stewardship efforts.

1.2.3.3.1 Study Design

The selection of an appropriate study design to evaluate the impact of an intervention must be addressed before program implementation. Depending on the circumstances, any experimental or observational study design will produce accurate and useful results (Concato, Shah et al. 2000). What is important when selecting an approach, is to consider the research question of interest, how the data will be (or was) collected, the fundamental limitations to each technique, and any feasibility constraints.

A case-control study which randomizes at the community-level or higher is an experimental study design commonly used in program evaluations (Bexell, Lwando et al. 1996; Trepka, Belongia et al. 2001; Flottorp, Oxman et al. 2002; Doyne, Alfaro et al. 2004; Taylor, Kwan-Gett et al. 2005; Finkelstein, Huang et al. 2008). However, this study design is plagued by low statistical power, especially since the effect sizes expected are typically quite small (Fishbein 1996; Merzel and D'Afflitti 2003). In addition, it is often very difficult to find an appropriate control group (Farquhar 1978; Nebot 2006).

In light of these difficulties, most studies follow a quasi-experimental design (i.e. matched comparison communities), although this type of study is not without limitations (Merzel and D'Afflitti 2003). Selection bias can alter the results as antibiotic utilization rates vary significantly with respect to percent urbanization, demographic structure (Garcia, Bouza et al. 2005), access to health care, and cultural differences (Sirinavin and Dowell 2004). In addition, all (quasi)experimental designs suffer from the possibility of cross contamination bias, or the effect of possible confounders such as formulary
changes, independent initiatives aimed at the same goal, major changes in professional practice guidelines, and co-morbid illnesses.

Another approach to evaluating the impact of interventions is to use observational (i.e. comparing the state of the objects of interest before and after the intervention) rather than experimental techniques. This requires conducting descriptive statistics and renders it impossible to separate potential causal impacts of program implementation from natural secular trends. Nevertheless, descriptive statistics can provide an ecological perspective of changes in population utilization trends associated with public education, as will be shown throughout this thesis.

1.2.3.3.2 Inconsistent Measures and Definitions

The use of prescription data (and not consumption data) in reporting, coupled with the lack of a long-term consistent definition of measurement for antibiotic use, has rendered it difficult to directly compare the results of different study designs and program strategies (Marra, Monnet et al. 2007). However, an increase in the use of the defined daily dose (DDD), the international standard unit of measurement recommended by the World Health Organization, has led to improvements in recent years. The DDD is a measure of the “average maintenance dose per day for a drug used in its main indication in adults” (WHO 2008).

Finally, a common language as to what is “inappropriate prescribing” must be established in order to evaluate program effectiveness (Nathwani and Davey 1999). Universal guidelines for first-line treatment of common indications must be readily available and frequently updated. Information on local antibiotic utilization and resistance trends and global strategies for containing resistance must also be accessible. Resources have been and continue to be developed in order to alleviate this problem (WHO 2001(2); WHO 2001(3); Gyssens 2005; Blondel-Hill and Fryters 2006; Rasool, Fuertes et al. 2008).
1.2.3.4 Political Considerations

Community-based programs can have a substantial impact on antibiotic utilization trends when they work in conjunction with regulations. As such, these programs must go beyond the individual and seek political support to advocate for change on a policy level (Belongia and Schwartz 1998). An example of a powerful regulation is the documented impact that formulary restriction has on controlling the utilization rate of an antibiotic and its costs (Marra 2004; Martin, Ofotokun et al. 2005; Parrino 2005; Paskovaty, Pflomm et al. 2005). The task of obtaining political support is facilitated by studies which demonstrate that antibiotic management programs are likely to be cost-effective over the long term with respect to antibiotic costs (John and Fisherman 1997; Carling, Fung et al. 2003).

Political efforts are also required to monitor current and future trends in antibiotic utilization and resistance on a global scale. Several national and international surveillance systems have already been established, but Monnet concluded that there are only six international antimicrobial surveillance networks that meet the US CDC definition of public health surveillance (Monnet 2000). Jones and Masterton argue that only three of these systems are true global surveillance programs: the Meropenem Yearly Susceptibility Test Information Collection, The Alexander Project, and The SENTRY Antimicrobial Surveillance Program (Jones and Masterton 2001). Canada itself hosts several surveillance programs such as the Canadian Nosocomial Infection Surveillance Program, the Canadian Bacterial Surveillance Network, and the Canadian Integrated Program for Antimicrobial Resistance Surveillance. Unfortunately, due to differences in program objectives, variations in methodology and expectations for performance, relatively unsophisticated monitoring data, and a lack of coordination between programs, it is not possible to create a comprehensive multinational report card at this time (Stephen, Dawson-Coates et al. 2005). This pressing issue must be addressed soon, especially as history has proven that resistant bacteria are not constrained by political boundaries (Isturiz and Carbon 2000).
1.2.4 Review of Current Progress of Community-Based Programs

A systematic review and quantitative analysis assessing the effectiveness of various strategies to reduce inappropriate antibiotic use was recently conducted (Ranji, Steinman et al. 2008). Of the 38 interventions targeting acute RTIs, 15 included a component of patient education and/or community outreach and are thus relevant for discussion.

Among these 15 community-based trials, the mean reduction in the percentage of patients who received antibiotics was 11%. Public education strategies used included group educational sessions, written materials, educational videos, acute RTIs self-management guides, paper or computer-based decision support systems, and mass media campaigns. Overall, patient education proved effective in reducing antibiotic use, especially when coupled with active clinician education. This is consistent with the health promotion literature which states that providing information is unlikely to result in meaningful behaviour change unless it is linked with a more expansive and participatory component (Belongia and Schwartz 1998; Arnold and Straus 2005). The review also emphasized the importance of addressing several RTIs (rather than single conditions) in order to maximize the reduction in inappropriate antibiotic use.

In addition to reporting the level of change in antibiotic use, other important observations were identified in the review and through a manual search of the source articles. First, there was no increase in clinical or non-clinical adverse events associated with a reduction in antibiotic prescribing for RTIs. One case-control study reported significantly higher rates of return visits among patients who received antibiotics compared to those who did not (2.5% vs. 1.0%; p-value <0.001; Hickman, Stebbins et al. 2003). The rationale provided for this latter observation was that patients who received antibiotics often required a subsequent prescription or had an adverse reaction to the antibiotic prescribed. It was also suggested that reducing antibiotic use may actually decrease the overall occurrence of adverse events in patients due to a reduction in antibiotic usage-associated events (i.e. allergic reaction or pseudomembranous colitis), although there is currently no data to support this theory (Hennessy, Petersen et al. 2002).
Second, several studies demonstrated that patient satisfaction is not correlated with receipt of antibiotics (Hamm, Hicks et al. 1996; Mangione-Smith, McGlynn et al. 1999; Welschen, Kuyvenhoven et al. 2004). Rather, a correlation exists between patient satisfaction and time spent with the physician (p-value <0.01) and with the level of understanding of the selected treatment (p-value =0.02; Hamm, Hicks et al. 1996). Additionally, one study showed that prescribing antibiotics for children with upper RTIs is not associated with a reduction in time spent with a patient (odds ratio =1.60, 95% confidence interval: 0.76 – 3.35; Coco and Mainous 2005).

Finally, most studies reported no positive changes in the rate of colonization by resistant-bacteria or in trends of antibiotic resistance. Only one of the 15 community studies reported a significant reduction in the rate of penicillin G-nonsusceptible Streptococcus pneumoniae colonization for a prescription-reduction intervention compared to a control group (34.5% vs. 46.2%, p-value = 0.05; Guillemot, Varon et al. 2005). This observation is not entirely surprising as changing trends in resistance may take several years to follow changes in antibiotic utilization patterns. As such, interventions need to be maintained over long periods in order to lead to significant changes in resistance (Belongia, Sullivan et al. 2001; Perz, Craig et al. 2002).

Similar literature reviews looking at hospital-based interventions and interventions for healthcare professionals have been conducted (Owens, Fraser et al. 2004; Arnold and Straus 2005; MacDougall and Polk 2005). These reviews echo the observation that active and participatory strategies are most effective at altering behaviour. Specifically, small group continuing education sessions, including outreach visits and academic detailing (one-on-one sessions between local experts and prescribers), have emerged as some of the most efficient means to educate prescribers (Belongia and Schwartz 1998; O'Brien, Freemantle et al. 2001; Finch, Metlay et al. 2002). Audit and feedback on physician prescribing practices (Belongia and Schwartz 1998; Parrino 2005), antibiotic cycling programs (Merz, Warren et al. 2004), computer-assisted software programs (Fishman 2006), and printed prescription pads (Rubin, Bateman et al. 2005) have also shown some success, especially when used in combination with other types of strategic interventions.
Mass mail-outs of printed educational material appear the least successful at inducing behavioral change.

1.3 “Do Bugs Need Drugs?”

1.3.1 Overview
The DBND program <www.dobugsneeddrugs.org> was implemented in BC in September 2005 with funding provided by the PharmaCare division of the BC Ministry of Health. The goal of the program was to address inappropriate antibiotic use and increasing resistance rates in BC. Using active education as its primary tool, DBND promotes proper infection control measures (e.g. handwashing), provides education to the public and healthcare professionals on appropriate antibiotic use for RTIs, and raises awareness of the scope and implications of resistance via several program components (Table 1.2) and three key messages:

1. Handwashing is the best way to stop the spread of infections.
2. Not all bugs are equal. Both viruses and bacteria cause infections but antibiotics only work against bacteria.
3. Use antibiotics wisely to prevent antibiotic resistance.

The public education arm of the program consists of an extensive media campaign, educational sessions for target populations, and the distribution of several types of printed material. One of the major strengths of the public education offered is that several components are tailored to specific audiences in order to enhance knowledge uptake.

Healthcare professional education includes Train-the-Trainer workshops, continuing education sessions (Canadian Council on Continuing Education for Pharmacists, Mainpro M1 and Mainpro C), and the distribution of the “Bugs and Drugs” antimicrobial reference guide. Additionally, a variety of presentations are given at provincial, national, and international conferences and academic meetings. During all healthcare education initiatives, emphasis is placed on the appropriate utilization of fluoroquinolones and
newer macrolides due to their frequent and common misuse, and the rapidly growing resistance to these pharmaceuticals (Cizman, Pokorn et al. 2001; Linder, Huang et al. 2005; Rasool, Fuertes et al. 2008).

TABLE 1.2: “Do Bugs Need Drugs?” program components.

<table>
<thead>
<tr>
<th>Component</th>
<th>Target Audience</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Public Education</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mass media campaign</td>
<td>General public</td>
<td>Transit, radio, and television advertisements</td>
</tr>
<tr>
<td>Grade 2 and Daycare Program</td>
<td>Children and their families</td>
<td>Sessions delivered within schools and daycares. Emphasis placed on three key messages.</td>
</tr>
<tr>
<td>Assisted Living Program*</td>
<td>The elderly</td>
<td>Sessions delivered within assisted living facilities. Emphasis placed on three key messages.</td>
</tr>
<tr>
<td>Distribution of printed materials</td>
<td>General public</td>
<td>Distribution of signs, posters, pamphlets, parent guides, inserts in parent magazines, activity placemats and stickers for children</td>
</tr>
<tr>
<td><strong>Healthcare Education</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Train-the-Trainer</td>
<td>Pharmacists, pharmacy technicians, medical students, nurses, and early childhood educators</td>
<td>Instructional workshop on how to teach the Grade 2, Daycare, and Assisted Living components of the DBND program.</td>
</tr>
<tr>
<td>Canadian Council on Continuing Education for Pharmacists</td>
<td>Pharmacists and pharmacy technicians</td>
<td>Five hour sessions which focuses on appropriate antibiotic treatment, reasons for misuse, and the scope and implications of antibiotic resistance</td>
</tr>
<tr>
<td>Mainpro M1</td>
<td>Physicians and medical students</td>
<td>One hour session which aims to improve the accuracy of diagnosis and optimize prescribing for common RTIs.</td>
</tr>
<tr>
<td>Mainpro C</td>
<td>Physicians and medical students</td>
<td>Extensive educational course followed by an assessment of knowledge uptake. Prescription information is collected, analyzed, and used to provide personalized feedback on individual and aggregated prescribing practices.</td>
</tr>
<tr>
<td>“Bugs and Drugs” book</td>
<td>All healthcare professionals</td>
<td>Recommendations for appropriate antibiotic use and care of patients with infectious diseases</td>
</tr>
</tbody>
</table>

*The Assisted Living Program began in 2008.*
1.3.2 Process and Impact Evaluation
A process and impact evaluation of the DBND program was conducted in the Spring of 2008, and measured the level of implementation and the program’s current impact on several short-term objectives (Fuertes, Vrbova et al. 2008). The main observations recorded in this evaluation are as follows:

1. The overall consumption of antibiotics for systemic use remained stable from 2005-2007, arresting the upward trend seen from 2003-2005. Encouraging declines in pediatric prescription rates were observed.
2. Antibiotic costs covered by the provincial insurance (PharmaCare) decreased from 2005 to 2006. This reduction is believed to be attributable to a reduction in costs of some drug targets of the DBND program.
3. There was some stabilization of previously increasing trends of resistance among gram positive pathogens. However, alarming trends of increasing resistance among uropathogens were documented.
4. Since the inception of the program, 24,557 grade 2 children, 4,645 children in daycare, and 6,027 health care professionals were taught components of the DBND program.

The level of implementation (process) and short-term changes (impact) associated with each of the components of the DBND program was assessed individually, and is briefly described below. A Program Logic Model depicting the link between these components and the measures evaluated is provided in Appendix A.

1.3.2.1 Media Campaign
Several types of media were explored during the first year of DBND implementation (television ads, cinema slides, inserts in parent magazines). The television campaign was repeated in the majority of the province in January 2007 for four consecutive weeks, whereas radio advertisements were used in the northern parts of BC. In 2006, between 80-85% of the primary audience of women with children were reached an average of 6.0-9.3 times. The 2007 campaign achieved similar numbers: between 70-95% of the target audience was reached an average of 6.0-12.0 times.
The public transit campaign was launched for four consecutive weeks in October 2007. In total, 710 advertisements were posted on various types of transit through the Greater Vancouver Regional District, Kelowna, and Victoria. Estimates provided by Translink, the South Coast BC Transportation Authority, suggest that greater than 42% of all Greater Vancouver Regional District residents took at least one type of public transportation during October 2007, and thus had the opportunity to see the DBND advertisements.

**1.3.2.2 Grade 2 Program**
The Grade 2 Program was implemented and maintained to various degrees in all five health authorities in BC. The number and percentage of students reached each scholarly year are depicted in Figures 1.6-1.8.

![FIGURE 1.6: Number (left) and percentage (right) of grade 2 students who participated in the Grade 2 Program during the 2005 to 2006 school year per health authority.](image)
FIGURE 1.7: Number (left) and percentage (right) of grade 2 students who participated in the Grade 2 Program during the 2006 to 2007 school year per health authority.

Pre and post surveys were used to assess the impact of the Grade 2 Program on the knowledge of parents whose children participated. Analysis of the survey results indicated a statistically significant increase in the proportion of correct responses for five out of the six questions regarding the importance of proper handwashing, the differences
between viruses and bacteria, the appropriate use of antibiotics, and the potential consequences of misusing these pharmaceuticals (p-value <0.05). Importantly, these results demonstrated that the Grade 2 Program not only educates children, but also contributes to the knowledge of their parents and other family members.

1.3.2.3 Daycare Program
Although slower in its inception, the Daycare Program was successful in recent years. The number of children in daycare reached each year since September 2006 is illustrated by health authority in Figure 1.9.

![Figure 1.9: Number of children who participated in the Daycare Program during the 2006 to 2007 (left) and 2007 to 2008 (right) school years per health authority.](image)

1.3.2.4 Health Care Education Program
Over 5000 healthcare professionals have participated in educational workshops and lectures (Table 1.3). Several of these sessions were centered on introducing the DBND program and reporting on its progress. Other sessions focused on teaching healthcare professionals how to enhance public knowledge (Train-the-Trainer sessions), improve adherence to antibiotic treatment regimes for RTIs, and increase awareness of local antibiotic resistance trends (Continuing Education).
TABLE 1.3: Summary of the audiences attending each type of healthcare education session (September 2005 to December 2007).

<table>
<thead>
<tr>
<th>Target Audience</th>
<th>Type of Session</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Continuing Education*</td>
<td></td>
</tr>
<tr>
<td>Early Childhood Educators/Providers</td>
<td>150 54</td>
<td>260</td>
</tr>
<tr>
<td>Infection Control Practitioners</td>
<td>100 90 2</td>
<td>192</td>
</tr>
<tr>
<td>Medical Students</td>
<td>150 -</td>
<td>150</td>
</tr>
<tr>
<td>Nurses</td>
<td>- 350 189 20</td>
<td>168</td>
</tr>
<tr>
<td>Nursing Students</td>
<td>- - 10</td>
<td>536</td>
</tr>
<tr>
<td>Other Health Professionals</td>
<td>152 30 -</td>
<td>10</td>
</tr>
<tr>
<td>Pharmacists/Pharmacy Technicians</td>
<td>159 - 12</td>
<td>89</td>
</tr>
<tr>
<td>Physicians</td>
<td>2331 200 16 17</td>
<td>2564</td>
</tr>
<tr>
<td>Public</td>
<td>- 155 60 -</td>
<td>296</td>
</tr>
<tr>
<td>Total</td>
<td>2892 945 361 37 93</td>
<td>1063</td>
</tr>
</tbody>
</table>

*Participants of the Canadian Council on Continuing Education for Pharmacists, Mainpro M1, and Mainpro C sessions were included under the heading of Continuing Education.
Short-term changes in knowledge and behaviour were assessed following all Train-the-Trainer sessions and Continuing Education courses. There was a significant increase in the knowledge of all three DBND messages for nursing students and pharmacists/pharmacy technicians (p-value <0.05), pre and post the Train-the-Trainer workshops. Both types of healthcare professionals showed a significant increase in knowledge regarding the types of antimicrobial-containing products currently on the market, as well as the extent of their wide-spread distribution. There was also an increase, post-course, in the percentage of participants who agreed that antibiotic resistance is a very serious problem, with 100.0% of them rightfully indicating that the best way to stop the spread of infections is through proper and frequent handwashing.

The Continuing Education sessions also showed very encouraging results. The proportion of pharmacists who were aware of all three DBND messages was significantly higher following the Canadian Council on Continuing Education for Pharmacists Program (40.0% pre, 95.0% post, p-value <0.05), as was their knowledge of the scope and implications of antibiotic resistance. The Mainpro M1 presentation was rated very positively, with an overall score of 4.6 out of 5 for questions referring to the relevance and usefulness of the presentation. The most intensive component of the DBND program, the Mainpro C course, yielded excellent results with respect to diagnosis and treatment regimes for common RTIs (bronchitis, otitis media, pharyngitis, and sinusitis) and current trends in antibiotic resistance. The results of the Mainpro C course also helped identify current misconceptions and knowledge gaps among physicians and medical students, most of which concerned signs of colonization of specific organisms and the appropriate duration of antibiotic therapies. Finally, during the Mainpro C course, prescription patterns were collected and analyzed, allowing for inter-provincial comparisons.

1.3.2.5 Public Print Material
Public print material was widely distributed, either in conjunction within different DBND components or through mass mailouts and distribution to several health institutions. Various types of print material were tailored to appeal to specific audiences, but all of them emphasized the key DBND messages. The “Bugs and Drugs” antimicrobial
reference guide provides recommendations for appropriate antibiotic use. In 2006, every healthcare professional in BC received a copy via a large provincial-level distribution. Subsequent yearly mailouts to first-year students ensures the continued use of this reference guide. Table 1.4 provides a summary of the yearly distribution of public and healthcare professional education print material.

**TABLE 1.4: Distribution of print material by year (September 2005 to December 2007).**

<table>
<thead>
<tr>
<th>Material</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Activity Placemat</td>
<td>48</td>
<td>18,306</td>
<td>4,661</td>
<td>23,015</td>
</tr>
<tr>
<td>Stickers</td>
<td>245</td>
<td>36,905</td>
<td>24,026</td>
<td>61,176</td>
</tr>
<tr>
<td>Signs and posters</td>
<td>847</td>
<td>18,490</td>
<td>6,038</td>
<td>25,375</td>
</tr>
<tr>
<td>Parent guides: English</td>
<td>22,441</td>
<td>239,010</td>
<td>24,129</td>
<td>285,580</td>
</tr>
<tr>
<td>Parent guides: other languages</td>
<td>-</td>
<td>14,617</td>
<td>4,591</td>
<td>19,208</td>
</tr>
<tr>
<td>Pamphlet</td>
<td>5,591</td>
<td>230,094</td>
<td>24,563</td>
<td>260,248</td>
</tr>
<tr>
<td>“Bugs and Drugs” guide</td>
<td>18,162</td>
<td>777</td>
<td>628</td>
<td>19,567</td>
</tr>
<tr>
<td>Total</td>
<td>76,506</td>
<td>1,115,621</td>
<td>176,644</td>
<td>1,368,771</td>
</tr>
</tbody>
</table>

**1.4 Rationale for Current Work**

Given the large monetary and human resources devoted to the development and implementation of this large community-based program, there is a need to fully evaluate the relationship between the DBND program and antibiotic utilization trends in BC. The 2008 DBND evaluation demonstrated excellent progress in audience and geographic reach and significant short-term changes in public and healthcare professional knowledge and behaviour. What remains to be seen is whether these short-term changes developed into meaningful improvements in antibiotic use, and whether these improvements are most significant among the main targets of the program.

The setting for this evaluation is unique as the province of BC is the only political jurisdiction in North America with a comprehensive central prescription network system. This secure pharmacy network links all retail pharmacies into a central set of data.
systems, providing a complete listing of all individual ambulatory care prescriptions dispensed to all BC residents, regardless of formulary status. As such, information on antibiotic utilization for the entire population of BC is available, rather than just a sample. Thus, the strengths of this study lie in the fact that there is no error or bias introduced into the results via a sampling technique and no need to conduct inferential statistics. Ecological factors which may affect the results were accounted for as best as possible in the analyses.

To our knowledge, no other study has fully evaluated the long-term effects of a large-scale multifaceted community-based program on antibiotic utilization rates in a Canadian context. The specific objective of this study was to evaluate the association between the DBND program and changes in overall, pediatric, drug-specific, and indication-specific antibiotic utilization trends. This objective was addressed via the following two research questions and associated hypotheses:

1.4.1 Research Questions
1. How has the monthly rate of change of antibiotic utilization rates varied in the Vancouver Health Service Delivery Area (HSDA) following the implementation of the DBND program, specifically with respect to
   a. overall antibiotic utilization?
   b. overall pediatric prescriptions (<15 years old)?
   c. antibiotics which are specific targets of the program, specifically fluoroquinolones and newer macrolides (azithromycin and clarithromycin)?
   d. antibiotics which are presently commonly misused, as measured by pediatric prescription patterns for acute bronchitis, acute pharyngitis, and otitis media?

2. Can a pattern be identified between increasing program implementation and larger improvements in the monthly rate of change of overall and target-specific utilization rates, pre and post program implementation?
1.4.2 Hypotheses

1. The monthly rate of change of antibiotic utilization rates in the Vancouver HSDA will improve after program implementation (M₂) compared to before (M₁). This improvement will be greatest among specific targets of the program (pediatric, fluoroquinolones, newer macrolides, and pediatric prescriptions for acute bronchitis, acute pharyngitis, and otitis media). Mathematically, this hypothesis can be defined M₂ – M₁ < 0.

2. Differing levels of program implementation within HSDAs will be positively correlated with larger improvements in the monthly rate of change of antibiotic utilization rates (overall and target-specific), pre and post program implementation. Mathematically, this hypothesis can be defined as M₂ – M₁ for a HSDA with high implementation < M₂ – M₁ for a HSDA with low implementation.

The abovementioned research questions were addressed using two data sources and the DBND Program Evaluation Report (Fuertes, Vrbova et al. 2008). Drug utilization data was obtained from PharmaNet, a secure province-wide network administered by the BC Ministry of Health and the College of Pharmacists of BC. The Medical Service Plan (MSP) database was used to obtain information on patient age and sex, date of visit, physician reimbursement claims, physician specialty and geographic location of the physician’s office. The linkage of the PharmaNet and MSP databases allowed the analysis of indication specific-changes in prescription patterns. Detailed information on each of these data sources is provided in Appendix B. The DBND Program Evaluation Report (2008) provided information on the geographical and audience reach of the program’s initiatives, granting insight as to the varying levels of program deployment in the 16 HSDAs in BC.
1.5 References


2. TRENDS IN ANTIBIOTIC UTILIZATION IN VANCOUVER ASSOCIATED WITH A COMMUNITY EDUCATION PROGRAM ON ANTIBIOTIC USE

2.1 Introduction

Despite the well-established notion that inappropriate antibiotic use facilitates the emergence of resistant bacteria, the misuse and overuse of these pharmaceuticals remains a serious problem worldwide. In BC, alarming trends in resistance continue to be recorded. For example, increased resistance to erythromycin was documented in gram-positive organisms, such as *Streptococcus pneumoniae*, *Streptococcus pyogenes*, and *Streptococcus aureus*, correlated to the utilization of newer macrolides (Rasool, Fuertes et al. 2008). Current estimates also show that the majority of antibiotics prescribed are for RTIs which are predominantly of viral origin (Gonzales, Steiner et al. 1997; Gerber 2005; Marra, Patrick et al. 2006). It is expected that the prevalence of resistant bacteria can be slowed by alleviating the selective pressure placed on bacteria using proper antibiotic stewardship strategies (Ball, Cars et al. 2002; Paskovaty, Pflomm et al. 2005; Fishman 2006).

Literature has identified several factors which contribute to the inappropriate use of antibiotics. Frequently reported are time pressure and “patient pressure”, the latter of which refers to the pressure felt by prescribers when patients demand antibiotics for themselves or their children (Palmer and Bauchner 1997; Mangione-Smith, McGlynn et al. 2001; Kuzujanakis, Kleinman et al. 2003). Additionally, although it is crucial to treat bacterial infections rapidly, especially among young children, the under-use of culture and susceptibility testing to confirm the origin of the infection and to subsequently optimize the initial prescription (typically a broad-spectrum antibiotic) also contributes to inappropriate antibiotic use (Arnold, Teresa et al. 2005; Ebert 2007). The problem is

1 A version of this chapter will be submitted for publication. Fuertes, E., Henry, B., Marra, F., Wong, H. and Patrick, D.M. Trends in Antibiotic Utilization Associated with a Community Education Program on Antibiotic Use.
further amplified by prescribers’ harbouring misconceptions or inadequate knowledge regarding current guidelines and local antibiotic resistance trends (Wester, Durairaj et al. 2002; Kozyrskyj, Dahl et al. 2004).

In order to address these factors, various interventions were developed. Historically, their focus was on improving healthcare professional education and hospital infection control practices, as resistant bacteria were typically found within the hospital setting. However, the identification of unique strains of resistant organisms in the community, which are selected for by a set of population-level factors (household contacts, schools, jails, etc.), has highlighted the importance of public education and community-involvement (Fey, Said-Salim et al. 2003; Furuya and Lowy 2006). Literature now suggests that the greatest successes with regards to improving appropriate antibiotic use have stemmed from programs which include both public and healthcare professional education, allowing for a multifaceted approach to the complex issue of antibiotic use and resistance (Gonzales, Steiner et al. 1999; Arnold and Straus 2005; Paskovaty, Pflomm et al. 2005; Ranji, Steinman et al. 2008).

The DBND program is one such initiative which was implemented in BC, in September 2005 (Blondel-Hill 2008). DBND was designed to capitalize on what is currently known about efficient health promotion and antibiotic use: knowledge uptake and behaviour change is maximized through the use of clear messaging to relevant audiences, using active rather then passive participation strategies (Finch, Metlay et al. 2002; Arnold and Straus 2005; Ranji, Steinman et al. 2008). The overall objective of DBND is to use education as a tool for decreasing inappropriate antibiotic use and preventing the spread of infections and resistant organisms. The specific aim of the community arm of this program is to emphasize the importance of proper handwashing, explain the difference between viruses and bacteria, and alert the public to the emergence and consequences of resistant bacteria.

In the summer of 2008, the audience and geographic reach of the program as well as its impact on short-term knowledge and behaviour was evaluated (Fuertes, Vrbova et al. ...
The current study is an extension of this evaluation, and aims to investigate the relationship between the DBND program and population-level changes in antibiotic utilization patterns in Vancouver, BC.

2.2 Methods

2.2.1 Intervention
The inception of the DBND program took place in September 2005. However, January 2006 is considered the first post-intervention month in this analysis for two reasons. First, by selecting the first month of the year as the marker for the beginning of a new trend, one can compare yearly trends, pre and post program implementation, without seasonal bias affecting the results. Second, the first television campaign took place in January 2006. This component is considered the effective beginning of the program, especially as television is the most efficient method of advertising in terms of both geographical and target audience reach (Finch, Metlay et al. 2002; Goossens, Guillemot et al. 2006; Stille, Rifas-Shiman et al. 2008).

Although the DBND program was introduced across all of BC, there are regional differences in the level of program implementation. The program was deployed to its fullest in the Vancouver HSDA during its first two years of existence (Table 2.1). As such, in order to assess the true potential of the program, this study limited the characterization of antibiotic utilization patterns to those in the Vancouver HSDA.
TABLE 2.1: “Do Bugs Need Drugs?” program components delivered in Vancouver from September 2005 to December 2007

<table>
<thead>
<tr>
<th>Public Education</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Component</td>
<td>Audience Reached</td>
<td>Description</td>
</tr>
<tr>
<td>Mass media campaign</td>
<td>General public</td>
<td>556 transit ads (buses, skytrains, express trains) posted in 2007, and a yearly 4-week television campaign in January 2006 and 2007</td>
</tr>
<tr>
<td>Grade 2 and Daycare Program</td>
<td>4836 grade 2 children 550 daycare children</td>
<td>Sessions delivered within schools and daycares. Emphasis placed on key DBND messages.</td>
</tr>
<tr>
<td>Distribution of printed materials</td>
<td>General public</td>
<td>Distribution of over 12,000 signs, posters, pamphlets, parent guides, inserts in parent magazines, activity placemats and stickers for children</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Healthcare Education</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Component</td>
<td>Audience Reached</td>
<td>Description</td>
</tr>
<tr>
<td>Train-the-Trainer</td>
<td>325 pharmacists, pharmacy technicians, medical students, nurses, and early childhood educators</td>
<td>Instructional workshop on how to teach the Grade 2, Daycare, and Assisted Living components of the DBND program.</td>
</tr>
<tr>
<td>Canadian Council on Continuing Education for Pharmacists</td>
<td>Pharmacists and pharmacy technicians</td>
<td>Five hour session focused on appropriate antibiotic treatment, reasons for misuse, and the scope and implications of antibiotic resistance</td>
</tr>
<tr>
<td>Mainpro M1</td>
<td>Over 400 physicians and medical students</td>
<td>One-hour session which aims to improve the accuracy of diagnosis and optimize prescribing for common RTIs.</td>
</tr>
<tr>
<td>Mainpro C</td>
<td>20 physicians</td>
<td>Extensive educational course followed by an assessment of knowledge uptake. Prescription information is collected, analyzed, and used to provide personalized feedback on individual and aggregated prescribing practices.</td>
</tr>
<tr>
<td>“Bugs and Drugs” book</td>
<td>All healthcare professionals</td>
<td>Recommendations for appropriate antibiotic use and care of patients with infectious diseases</td>
</tr>
</tbody>
</table>

2.2.2 Data Sources
Drug utilization data from January 1996 to December 2007 were obtained from the PharmaNet database. This database collects information on all antibiotics dispensed through community pharmacies in BC. All oral solid antibiotics which fall under the heading of “antibacterials for systemic use”, as classified by the Anatomical Therapeutic
Chemical (ATC) classification system, were included in the dataset. Information on patient age and sex, geographical location (HSDA) of the pharmacy, antimicrobial agent prescribed, and the date, dose, and quantity dispensed was available. Underreporting and misclassification in this type of administrative database is minimal (Levy, O’Brien et al. 2003).

All antibiotic utilization rates were expressed in DDD per 1000 population per day. The DDD is the international standard unit of measurement developed by the World Health Organization and is a measure of the “average maintenance dose per day for a drug used in its main indication in adults” (WHO 2008). All data pertaining to children less than 15 years of age were expressed as prescriptions per 1000 population per day, as the DDD is not accurate for children whose antibiotic dosing is dependent on weight. Population statistics were obtained from BC Stats (BC STATS 2008).

The MSP database contains information on patient age and sex, date of visit, physician reimbursement claims (Doves 1997), physician specialty, and geographic location of the physician’s office. The MSP and PharmaNet databases were linked by a third party. Specifically, antibiotic prescriptions were linked to the most recent physician visit during the 5 days preceding the date of dispensing of the prescription, as previously described (Marra, Patrick et al. 2006). Any prescriptions that could not be linked to a visit were removed from the analysis (overall linkage success rate for all indications was 67.9 %). All personal identifiers were removed prior to receipt of the final dataset.

2.2.3 Choice of Populations, Drugs, and Indications of Interest
Overall antibiotic utilization rates represent the population-level utilization patterns, and were thus of interest. Particular attention was paid to the utilization patterns of fluoroquinolones and newer macrolides (azithromycin and clarithromycin), as these drug classes are specific targets of several components of the DBND program. Similarly, changes in overall and indication-specific prescribing patterns among children (<15 years) were analyzed, as several DBND initiatives are geared towards children or their parents. Pediatric prescribing patterns for acute bronchitis, otitis media, and acute
pharyngitis were investigated as antibiotics are commonly prescribed for these predominantly viral upper RTIs.

2.2.4 Statistical Analysis
Using the multiplicative Holt-Winters exponentially smoothed trend method, which takes into account monthly fluctuations, a relatively consistent seasonal pattern over time, and a long-term trend in the data (Kalekar 2004), we predicted daily antibiotic utilization rates on a monthly basis from January 2006 to December 2007. These predicted rates correspond to what would have been expected in the absence of the DBND program, and are based on the repeating seasonal pattern and long-term trend seen from December 1996 to December 2005. The daily utilization rates predicted by the model were graphically overlaid with those actually observed for the 24 months after DBND implementation (January 2006 – December 2007). The difference between expected and observed rates was calculated

Linear regression was used to assess changes in overall, class-specific, and indication-specific daily antibiotic utilization rates over time. The regression equation was composed of a “time” variable, as the main predictor, and a “program” variable (Eq. 1). The latter term accounted for the presence of the DBND program, as of January 2006 (t₀), and allowed for the comparison of the monthly rate of change (slope) of daily antibiotic utilization rates before (Eq. 2) and after (Eq. 3) DBND implementation.

\[
\text{Daily antibiotic utilization rate} = \beta_0 + \beta_1 \text{(time)} + \beta_2 \text{(time-}t_0\text{)(program)} \quad (\text{Eq. 1})
\]

\[
\text{Slope of utilization rates before DBND} = \beta_1 \quad (\text{Eq. 2})
\]

\[
\text{Slope of utilization rates after DBND} = \beta_1 + \beta_2 \quad (\text{Eq. 3})
\]

\[
\text{Difference in the slope of utilization rates} = \text{slope after} - \text{slope before} = (\beta_1 + \beta_2) - \beta_1 = \beta_2 \quad (\text{Eq. 4})
\]

The difference in the monthly rate of change of antibiotic utilization rates, pre and post DBND implementation (Eq. 4), was the main outcome of interest. This difference was of
particular importance as even if the intervention produced minimal change in antibiotic utilization rates themselves, it may have had a significant impact if the rate of change of utilization rates was improved long-term. A negative difference indicates an improvement in the monthly rate of change of utilization rates, whereas a positive difference indicates a worsening in utilization trends. Through the use of examples, Table 2.2 summarizes the possible scenarios in which a negative and positive difference in the monthly rate of change of antibiotic utilization rates could occur. All statistical analyses were conducted in SAS, version 9.1 for Windows.

**TABLE 2.2: Examples summarizing all possible changes in the monthly rate of change of antibiotic utilization rates**

<table>
<thead>
<tr>
<th>Change in Slope</th>
<th>Slope before</th>
<th>Slope after</th>
<th>Difference in slopes</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slope Improved</td>
<td>+ 0.4</td>
<td>+ 0.3</td>
<td>-0.1</td>
<td>Monthly rate of increase of utilization rates has slowed.</td>
</tr>
<tr>
<td>Slope Improved</td>
<td>+ 0.4</td>
<td>- 0.3</td>
<td>-0.7</td>
<td>Monthly rate of change of utilization rates is now decreasing, rather than increasing.</td>
</tr>
<tr>
<td>Slope Improved</td>
<td>- 0.4</td>
<td>- 0.6</td>
<td>-0.2</td>
<td>Monthly rate of decrease of utilization rates has accelerated.</td>
</tr>
<tr>
<td>Slope Worsened</td>
<td>+ 0.4</td>
<td>+ 0.5</td>
<td>+0.1</td>
<td>Monthly rate of increase of utilization rates has accelerated.</td>
</tr>
<tr>
<td>Slope Worsened</td>
<td>- 0.3</td>
<td>+ 0.1</td>
<td>+0.4</td>
<td>Monthly rate of change of utilization rates is now increasing rather than decreasing.</td>
</tr>
<tr>
<td>Slope Worsened</td>
<td>- 0.3</td>
<td>- 0.2</td>
<td>+0.1</td>
<td>Monthly rate of decrease of utilization rates has slowed by.</td>
</tr>
</tbody>
</table>

*Slopes are measured in DDD/1000 population/day over a one month period.

2.3 Results

2.3.1 Trends in Yearly Antibiotic Utilization Rates

**2.3.1.1 Overall and Class-Specific Trends**

In Vancouver during the late 1990s, utilization of all antibiotics for oral systemic use steadily declined, reaching its lowest level in 2004 (15.4 DDD/1000 population/day). Subsequent years showed an increase in utilization rates until 2005, after which antibiotic use remained relatively stable (Figure 2.1). From 1996 to 2007, fluoroquinolone and macrolide utilization rates increased, most notably since 2002. The increase in
fluoroquinolone utilization was driven by elevated ciprofloxacin use (0.8 to 1.2 DDD/1000 population/day between 1996 and 2007). The increase in macrolide utilization was primary due to increasing use of newer macrolides (clarithromycin and azithromycin; 1.1 to 2.6 DDD/1000 population/day between 2002 and 2007), as erythromycin use has steadily declined since 1996 (Figure 2.2). Table 2.3 summarizes the changes in utilization rates in Vancouver by ATC class, between 1996 and 2007.

FIGURE 2.1: Average daily utilization rates for all oral solid antibiotics for systemic use in Vancouver. The implementation of the program is indicated by the vertical line.
FIGURE 2.2: Average daily macrolide utilization rates in Vancouver. The implementation of the program is indicated by the vertical line.
The table shows average daily antibiotic utilization rates in Vancouver by year.

<table>
<thead>
<tr>
<th></th>
<th></th>
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<th></th>
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<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibacterials for systemic use (J01)</td>
<td>20.6</td>
<td>19.4</td>
<td>18.6</td>
<td>18.4</td>
<td>17.2</td>
<td>17.0</td>
<td>16.2</td>
<td>16.1</td>
<td>15.4</td>
<td>16.4</td>
<td>16.0</td>
<td>16.3</td>
</tr>
<tr>
<td>Tetracyclines (J01A)</td>
<td>3.6</td>
<td>3.5</td>
<td>3.5</td>
<td>3.4</td>
<td>3.2</td>
<td>3.1</td>
<td>2.8</td>
<td>2.7</td>
<td>2.6</td>
<td>2.7</td>
<td>2.7</td>
<td>2.7</td>
</tr>
<tr>
<td>Penicillins (J01C)</td>
<td>7.8</td>
<td>7.2</td>
<td>6.6</td>
<td>6.5</td>
<td>5.7</td>
<td>5.7</td>
<td>5.4</td>
<td>5.3</td>
<td>4.9</td>
<td>5.2</td>
<td>4.9</td>
<td>5.0</td>
</tr>
<tr>
<td>extended spectrum (J01CA)</td>
<td>6.3</td>
<td>5.7</td>
<td>5.3</td>
<td>5.2</td>
<td>4.6</td>
<td>4.6</td>
<td>4.3</td>
<td>4.2</td>
<td>3.9</td>
<td>4.1</td>
<td>3.9</td>
<td>4.0</td>
</tr>
<tr>
<td>β-lactamase sensitive (J01CE)</td>
<td>0.7</td>
<td>0.6</td>
<td>0.6</td>
<td>0.5</td>
<td>0.5</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
</tr>
<tr>
<td>β-lactamase resistant (J01CF)</td>
<td>0.6</td>
<td>0.6</td>
<td>0.5</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
</tr>
<tr>
<td>combinations, β-lactamase inhibitors (J01CR)</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
</tr>
<tr>
<td>Other β-lactams (J01D)</td>
<td>1.2</td>
<td>1.0</td>
<td>1.1</td>
<td>1.0</td>
<td>0.9</td>
<td>0.8</td>
<td>0.8</td>
<td>0.7</td>
<td>0.7</td>
<td>0.7</td>
<td>0.6</td>
<td>0.6</td>
</tr>
<tr>
<td>cephalosporins (J01DC)</td>
<td>1.9</td>
<td>1.8</td>
<td>1.8</td>
<td>1.7</td>
<td>1.7</td>
<td>1.7</td>
<td>1.7</td>
<td>1.7</td>
<td>1.7</td>
<td>1.7</td>
<td>1.7</td>
<td>1.7</td>
</tr>
<tr>
<td>Sulfonamides and trimethoprim (J01E)</td>
<td>2.2</td>
<td>2.0</td>
<td>1.9</td>
<td>1.8</td>
<td>1.6</td>
<td>1.4</td>
<td>1.3</td>
<td>1.1</td>
<td>1.1</td>
<td>1.0</td>
<td>1.0</td>
<td>1.1</td>
</tr>
<tr>
<td>trimethoprim and derivatives (J01EA)</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>short-acting sulfonamides (J01EB)</td>
<td>&lt;0.1</td>
<td>&lt;0.1</td>
<td>&lt;0.1</td>
<td>&lt;0.1</td>
<td>&lt;0.1</td>
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* Rates expressed in DDD/1000 population/day
Changes in the average daily overall utilization rates in January and February were of particular interest, as the larger DBND initiatives (i.e. televisions/radio and public transit campaigns) typically occur at the beginning of each year. Currently, there is no evidence to indicate a pattern of decreasing antibiotic use over time since DBND implementation, when considering only these two months. Overall antibiotic utilization rates for both months reached their lowest in 2004 (16.9 and 16.0 DDD/1000 population/day in January and February, respectively) and have since increased (19.1 and 19.0 DDD/1000 population/day in January and February, respectively, in 2007).

2.3.1.2 Pediatric Overall and Indication-Specific Prescribing Trends
Overall prescription rates for children decreased by 1.96 prescriptions/1000 population/day between 1996 and 2007. Prescription rates for the indication of acute bronchitis, acute pharyngitis, and otitis media decreased by 0.15, 0.13, and 0.25 prescriptions/1000 population/day, respectively, between 1996 and 2007 (Figure 2.3).

FIGURE 2.3: Average daily prescription rates for otitis media, acute pharyngitis, and acute bronchitis among children. The implementation of the program is indicated by the vertical line.
2.3.2 Expected vs. Observed Utilization Rates

Observed antibiotic utilization rates among the Vancouver population and prescription rates among children, from January 2004 to December 2007, are depicted in Figures 2.4 and 2.5, respectively. The expected rates following DBND implementation, as forecasted by the multiplicative Holt-Winters exponentially smoothed trend method are also presented. During the 24 months following program implementation, the observed total antibiotic use was 4.6% lower than expected, whereas the observed total number of prescriptions dispensed among children was 8.3% lower than expected.

FIGURE 2.4: Observed and expected average daily overall antibiotic utilization rates in Vancouver. The implementation of the program is indicated by the vertical line.
2.3.3 Monthly Rate of Change of Utilization Rates
2.3.3.1 Overall and Class-Specific Trends

The monthly rate of decrease of overall antibiotic utilization rates slowed by 0.0986 DDD/1000 population/day, when comparing 10 years pre (1996-2005) and two years post (2006-2007) DBND. This reduction in improvement is a consequence of the large historical decline in utilization rates observed in the late 1990s. When comparing only two years pre (2004-2005) and post (2006-2007) program implementation, the monthly rate of decrease of overall antibiotic utilization rates accelerated by 0.0748 DDD/1000 population/day, which corresponds to a 153% improvement in the rate at which overall antibiotic use is reduced. Assessing variations in the monthly rate of change (slope) of utilization rates over the last four years (rather than since 1996) is more relevant to this evaluation, as the DBND program was implemented to arrest the upward trend seen in drug-specific utilization rates in recent years. Encouraging changes in the slope of fluoroquinolone and newer macrolide daily utilization rates were also observed after the initiation of DBND (Table 2.4).
TABLE 2.4: Monthly rate of change (slope) of daily antibiotic utilization rates in Vancouver*

<table>
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<td>Overall</td>
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<td>-0.0748</td>
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<td>Fluoroquinolones</td>
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<td>-0.0022</td>
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<td>Newer Macrolides</td>
<td>0.0257</td>
<td>-0.0059</td>
<td>-0.0316</td>
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*Slopes are measured in DDD/1000 population/day over a one month period.

2.3.3.2 Pediatric Overall and Indication-Specific Prescribing Trends
Among children, the monthly rate of change of daily overall prescription rates slowed by 0.0197 prescriptions/1000 population/day. With respect to specific diagnoses, the monthly rate of change of daily pediatric prescription rates for the indication of acute bronchitis, acute pharyngitis, and otitis media slowed by 0.0027, 0.0023, and 0.0006 prescriptions/1000 population/day, respectively (Table 2.4). Similar indication-specific trends were seen among adults: the monthly rate of change of utilization rates improved by 0.0111, 0.0022, and 0.0015 DDD/1000 population/day for the indications of acute bronchitis, acute pharyngitis, and otitis media, respectively.

TABLE 2.5: Monthly rate of change (slope) of daily prescription rates among children in Vancouver†

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<td>Pharyngitis</td>
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</tr>
<tr>
<td>Otitis Media</td>
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<td>-0.0013</td>
<td>-0.0006</td>
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</tbody>
</table>

†Slopes are measured in prescriptions/1000 population/day over a one month period.

2.4 Discussion
The overall consumption of antibacterials for systemic use has remained stable over the last two years, arresting the upward trend seen since 2002. Unfortunately, the use of specific classes of antibiotics, namely the fluoroquinolones and newer macrolides,
continues to increase. This observation is of particular concern as there is some evidence which suggests that these antibiotics may be more efficient at inducing resistance (Drusano and Craig 2000; Kastner and Guggenbichler 2001), and multidrug resistant organisms (Karlowsky, Hoban et al. 2006).

Among children, encouraging declines in prescription rates were observed. The drop in overall prescription rates (from 1996 to 2007) was primarily driven by a decline in amoxicillin use (0.95 prescriptions/1000 population/day), and to some extent erythromycin use (0.47 prescriptions/1000 population/day). However, it is important to note that in recent years, the use of clarithromycin and azithromycin has increased slightly among children. This trend could have important detrimental consequences with respect to antibiotic resistance (Kastner and Guggenbichler 2001; Kozyrskyj, Carrie et al. 2004; Marra, Patrick et al. 2006). A drop in amoxicillin was responsible for the largest decrease in utilization for all three indications investigated (0.07 prescriptions/1000 population/day for both acute bronchitis and acute pharyngitis, and 0.13 prescriptions/1000 population/day for otitis media, from 1996 to 2007).

The decreases in utilization and prescription rates observed over the last two years are not in large excess of what would be expected based on past secular trends, although small reductions in expected utilization rates were documented. These results indicate that the DBND program did not lead to significant short-term changes in utilization rates during its first two years of implementation in Vancouver. However, what this study does provide is evidence that DBND has the potential to lead to long-term sustainable changes in the current course of utilization patterns. The results of this study demonstrate that the rate of change of utilization rates among all populations, drugs, and indications targeted by DBND improved after January 2006.

Often, a reduction in overall antibiotic utilization is viewed as a success (Wutzke, Artist et al. 2006; Finkelstein, Huang et al. 2008; Ranji, Steinman et al. 2008). However, improving prescribing practices may, in-fact, require an increase in utilization rates of certain classes of antibiotics. What is most important when evaluating appropriate
antibiotic stewardship is to assess whether 1st line antibiotic treatment options are being used whenever possible. This study has attempted to achieve this by reporting on antibiotics which are commonly misused (i.e. fluoroquinolones and newer macrolides), and by assessing prescription patterns by indication.

Although unique in its methodology, this study joins several others which have evaluated community-based programs aimed at improving antibiotic use (Belongia, Knobloch et al. 2005; Gonzales, Corbett et al. 2005; Wutzke, Artist et al. 2006; Finkelstein, Huang et al. 2008). However, because these interventions vary substantially with respect to objectives, measures of outcome, target populations, and type of initiatives used, it is difficult to draw meaningful comparisons between their levels of success. Nevertheless, the results obtained in this evaluation are in-line with what was anticipated from a previous process and impact evaluation of the DBND program, which demonstrated significant improvements in public and healthcare professional knowledge and short-term behaviour (Fuertes, Vrbova et al. 2008). Increased concerted effort and a longer period of program duration may be required in order for the program to be associated with a lowering of antibiotic utilization rates, themselves. In addition, policy regulations may be considered, such as formulary restrictions which have shown to be effective at reducing drug use (Marra 2004).

The setting for this evaluation is unique as BC is one of the only existing political jurisdictions in North America with a comprehensive central prescription network system. As such, a complete listing of all individual ambulatory care prescriptions dispensed to all Vancouver residents, either through a community pharmacy or a hospital outpatient pharmacy for patient use at home, regardless of formulary status, was used in this study. Consequently, there is no error or bias introduced into the results via a sampling technique or chance. As the purpose of this study was to perform extensive descriptive analysis of changing antibiotic utilization trends in Vancouver, but not to make inference on these trends nor to generalize to any population other then the one included in the study, reporting statistical significance using p-values was not relevant.
Our study has several limitations. First, due to the ecological nature of this project, we are unable to comment conclusively on a causal pathway between the implementation of the DBND program and changes in antibiotic utilization patterns. This limitation is common among population-level interventions which lack an appropriate control group (Nebot 2006). Second, PharmaNet does not collect information on prescriptions dispensed within hospital facilities or through internet pharmacies. It is also currently not mandatory for physicians to record medications provided to patients during an office, clinic, or emergency department visit, although this practice is encouraged. Medications used for treatment of sexually transmitted infections (STIs) are also not recorded in the PharmaNet database. Consequently, reported antibiotic utilization rates may be slightly underestimated. However, the researchers do not believe that these factors have significantly changed pre and post the intervention, and thus will not affect the main conclusions of this study. Further, STIs were not a main target of DBND, nor have they been shown to heavily impact utilization at a population level.

A review of the recent medical literature and discussions with practicing physicians indicated that no major changes in professional practice guidelines impacting antimicrobial use occurred simultaneously to DBND implementation, although there were some improvements in the standard of care of patients. There was also no change in the formulary status of any important antimicrobials agent during the life-span of DBND, thus removing the listing or de-listing of drugs from insurance plans as a potential confounder of this study. However, the impact of independent initiatives aimed at similar goals as DBND, such as “Clean Hands, Dirty Hands”, may have affected antibiotic utilization rates.

2.5 Conclusions

Our study reported an improvement in the rate of change of utilization rates among antibiotic targets of a community-based program. While we did not find a lowering of the utilization rates of all program targets, we hypothesize that this can be achieved through consistent and repeated implementation of current initiatives. Expansion of the DBND
program to include educational sessions focused on other indications for which antibiotics are commonly misused, such as urology infections, should also increase the program-associated improvements in antibiotic use. Future studies are required to assess additional long-term impacts of the DBND program, including the stabilization of, or decrease in, bacterial resistance rates. Finally, whether the results presented in this study are consistent with utilization patterns in other areas where the DBND program was implemented remains to be explored.
2.6 References


3. EVALUATION OF THE “DO BUGS NEED DRUGS?” PROGRAM IN 16 HEALTH SERVICE DELIVERY AREAS IN BRITISH COLUMBIA

3.1 Introduction

Several bacterial organisms have demonstrated alarming rates of antibiotic resistance, often correlated to the use of specific antibiotics (Kastner and Guggenbichler 2001; Bronzwaer, Cars et al. 2002; Urbanek, Kolar et al. 2005; Malhotra-Kumar, Lammens et al. 2007; Riedel, Beekmann et al. 2007; Rasool, Fuertes et al. 2008). To address this issue, governments and institutions worldwide have established community-based programs promoting a judicious approach to antibiotic use and improved infection control (Bexell, Lwando et al. 1996; Belongia, Sullivan et al. 2001; Dollman, LeBlanc et al. 2005; Gonzales, Corbett et al. 2005; Apisarnthanarak, Danchaivijitr et al. 2006; Wutzke, Artist et al. 2006; Chazan, Turjeman et al. 2007; Blondel-Hill 2008; Mölstad, Erntell et al. 2008). However, evaluation of these programs have yielded inconsistent results as to their effectiveness for improving antibiotic prescribing practices (Ranji, Steinman et al. 2008). Moreover, determining whether successful interventions are generalizable to other populations and settings is often a question left unanswered.

Some researchers have attempted to address the issue of generalizability by implementing the same community-based program in several areas and evaluating the outcomes per distinct region (Farquhar, Maccoby et al. 1977; Fortmann, Flora et al. 1995; Finkelstein, Huang et al. 2008). This type of program delivery can threaten the internal validity of an intervention if it is tailored to the demographic, geographic, and cultural context of each unique population and setting, as is usually recommended (Arnold and Straus 2005; Paskovaty, Pflomm et al. 2005). Those responsible for delivering programs in various areas are thus placed in the difficult situation of achieving a balance between adaptation and fidelity (Castro, Barrera et al. 2004; Durlak and DuPre 2008). Nevertheless,

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A version of this chapter will be submitted for publication. Fuertes, E., Henry, B., Marra, F., Wong, H. and Patrick, D.M. Evaluation of the “Do Bugs Need Drugs?” Program in 16 Health Service Delivery Areas in British Columbia.
repeatedly evaluating the effectiveness of a program using a standardized framework informed by well-developed criteria (Glasgow, Vogt et al. 1999; Judd, Frankish et al. 2001; Rychetnik, Frommer et al. 2002) provides valuable insight as to whether a program will remain effective when it is widely distributed in different community settings by busy, understaffed, large health administrations.

The DBND program is a multifaceted community education initiative which was implemented in the sixteen HSDAs in BC (Blondel-Hill 2008). Because of variation in the level of program implementation, primarily driven by differences in the proportion of children reached by the program during its first two years of existence (Figure 3.1), a unique opportunity to investigate inter-regional changes in utilization patterns associated with level of program implementation was created. In addition to differences in the delivery of the children components, the extent of the media campaign also varied across the province. The television campaign was implemented in all HSDAs, except for Northwest and Northern Interior in 2006, and Northwest, Northern Interior and Northeast in 2007. Radio was used in these regions instead. A transit campaign was delivered in Fraser North, Fraser South, Vancouver, Richmond, South Vancouver Island, and parts of the Okanagan in 2007. The other public education components (distribution of print material) were approximately equally distributed across the province.
A previous study identified an association between DBND and improvements in the monthly rate of change of utilization rates in the Vancouver HSDA, where the deployment of the program was longest and most intense (Section 2). The purpose of this study was to examine whether the trends observed in Vancouver were consistent with those in other areas in which DBND was implemented, and whether a pattern exists between level of program implementation and change in antibiotic utilization trends. In addition, differences in antibiotic utilization rates between urban and rural areas in BC were explored.

### 3.2 Methods

#### 3.2.1 Data Sources
Drug utilization data from January 1996 to December 2007 were obtained from the PharmaNet database in BC. These data were linked to the MSP database, as previously described (Marra, Patrick et al. 2006). All utilization rates were expressed in DDD per 1000 population per day (WHO 2008). All data pertaining to children less than 15 years of age were expressed as prescriptions per 1000 population per day, as the DDD is not an
accurate measure for children whose antibiotic dosing is dependent on weight. Population statistics were obtained from BC Stats (BC STATS 2008).

Antibiotic utilization trends were investigated by HSDA. This level of aggregation was selected as higher levels of grouping (i.e. health authorities) would have resulted in a very low number of units per implementation category. In contrast, smaller units of analysis (i.e. local health areas) could not be used in this study as this would breach the data confidentiality agreement, which states that no personal identification should be made possible in this evaluation. In addition, it would have been difficult to reliably assess the differences in the degree of program penetration at the local health area level.

3.2.2 Implementation Ranking of the Health Service Delivery Areas
Each HSDA was ranked by level of DBND implementation (low, medium, or high). As it is impossible to combine all of the different DBND public education components into a meaningful overall measure of program delivery, the proportion of children who participated in either the Grade 2 or Daycare Program was used as a surrogate for the level of DBND implementation. Additional public initiatives that took place (e.g. media campaign) were taken into consideration during the ranking. These initiatives are fully described in Section 1.3.1.

Any activity delivered at an international, national, or provincial level (e.g. conference presentations, publications, distribution of the Bugs and Drugs book), and all healthcare professional initiatives (Continuing Education and Train-the-Trainer sessions) were not considered during the ranking. This later omission was necessary because individuals come from all over the province to participate in the healthcare components. As such, if these participants were not eliminated, the implementation level of HSDAs in which professional sessions are most likely to be held (i.e. Vancouver) would be overestimated.

3.2.3 Statistical Analysis
Changes in daily antibiotic utilization rates over time were assessed using linear regression, as previously discussed in Section 2.2.4. The regression was conducted for
overall, class-specific, and indication-specific utilization rates within each HSDA. Utilization trends from 2004 to 2007 were of specific interest, as DBND was put in place to arrest the upward trend in antibiotic utilization rates observed in recent years.

The main outcome of interest was the difference between the monthly rate of change of daily antibiotic utilization rates, pre and post DBND. Specifically, the difference was calculated by subtracting the slope of daily utilization rates post DBND (2006-2007) from the slope of daily utilization rates pre DBND (2004-2005). As such, a negative difference indicates that the monthly rate of change of utilization rates improved in association with DBND implementation, whereas a positive difference indicates that the rate at which antibiotic utilization rates change worsened after the program was put in place. The range and mean differences within each program implementation category were calculated. Because the data used in this study included all ambulatory prescriptions dispensed in BC, the measures reported are precise accounts of changes in antibiotic utilization. As such, reporting statistical significance using p-values and confidence intervals is irrelevant, as sampling and statistical inference do not apply to the measured outcomes.

Variations in the monthly rate of change of utilization rates were also compared between urban and rural areas. In this study, Vancouver, Richmond, and Fraser South were considered urban areas, as defined by Statistics Canada (Statistics Canada 2001). The other HSDAs were classified as rural. All statistical analyses were conducted in SAS, version 9.1 for Windows.

3.3 Results

3.3.1 Implementation Ranking of the Health Service Delivery Areas
The uptake of the DBND program was highest in Vancouver, North Shore Coast Garibaldi, Fraser East, and Fraser North. In contrast, Kootenay Boundary, Northeast, Okanagan, and Thompson Cariboo Shuswap received a low level of program implementation. The eight remaining HSDAs were considered areas of medium program
implementation (East Kootenay, Fraser South, Richmond, South Vancouver Island, Central Vancouver Island, North Vancouver Island, Northwest, and Northern Interior; Figure 3.2). All high implementation HSDAs (and some in the medium category) coincided with areas which received good transit and television advertising. It is important to note that although a low proportion of children in Fraser South participated in the program, this HSDA was included in the medium implementation category due to the likelihood of contamination from highly ranked surrounding areas.

![Map showing categorization of health service delivery areas in British Columbia by level of “Do Bugs Need Drugs?” implementation.](image)

**FIGURE 3.2: Categorization of the 16 health service delivery areas in British Columbia by level of “Do Bugs Need Drugs?” implementation.**

### 3.3.2 Trends in Yearly Antibiotic Utilization Rates

#### 3.3.2.1 Overall and Class-Specific Trends

Trends in overall antibiotic utilization rates vary substantially between HSDAs (Table 3.1). Antibiotic utilization rates in Vancouver have steadily decreased over the last decade. From 1999 to 2007, Northwest consistently recorded the highest antibiotic utilization rate (22.5 DDD/1000 population/day in 2007). In 2007, Northwest was followed by Fraser South, North Shore Coast Garibaldi, and Northern Interior (18.2, 18.1,
18.0 DDD/1000 population/day, respectively). Since 2000, Richmond has documented the lowest antibiotic utilization rate among all HSDAs in BC (14.1 DDD/1000 population/day in 2007; Figure 3.3).
### TABLE 3.1: Average daily antibiotic utilization rates for the 16 health service delivery areas in British Columbia.

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</tr>
<tr>
<td>South Vancouver Island</td>
<td>17.5</td>
<td>16.6</td>
<td>16.6</td>
<td>16.6</td>
<td>17.1</td>
<td>17.1</td>
<td>16.3</td>
<td>16.6</td>
<td>16.1</td>
<td>16.5</td>
<td>16.3</td>
<td>16.6</td>
</tr>
<tr>
<td>East Kootenay</td>
<td>18.9</td>
<td>17.3</td>
<td>16.4</td>
<td>16.7</td>
<td>15.6</td>
<td>16.0</td>
<td>15.3</td>
<td>15.9</td>
<td>15.8</td>
<td>16.4</td>
<td>15.8</td>
<td>16.5</td>
</tr>
<tr>
<td>Central Vancouver Island</td>
<td>18.7</td>
<td>17.8</td>
<td>16.6</td>
<td>16.6</td>
<td>16.0</td>
<td>16.1</td>
<td>15.1</td>
<td>16.2</td>
<td>16.0</td>
<td>16.8</td>
<td>15.9</td>
<td>16.4</td>
</tr>
<tr>
<td>Vancouver</td>
<td>20.6</td>
<td>19.4</td>
<td>18.6</td>
<td>18.4</td>
<td>17.2</td>
<td>17.0</td>
<td>16.2</td>
<td>16.1</td>
<td>15.4</td>
<td>16.4</td>
<td>16.0</td>
<td>16.3</td>
</tr>
<tr>
<td>Okanagan</td>
<td>17.9</td>
<td>16.2</td>
<td>14.8</td>
<td>14.8</td>
<td>14.3</td>
<td>14.5</td>
<td>13.4</td>
<td>14.9</td>
<td>14.9</td>
<td>15.7</td>
<td>15.5</td>
<td>15.8</td>
</tr>
<tr>
<td>Kootenay Boundary</td>
<td>17.7</td>
<td>18.2</td>
<td>17.0</td>
<td>16.7</td>
<td>15.7</td>
<td>15.7</td>
<td>14.0</td>
<td>14.4</td>
<td>14.4</td>
<td>15.1</td>
<td>14.9</td>
<td>14.3</td>
</tr>
<tr>
<td>Richmond</td>
<td>17.5</td>
<td>16.1</td>
<td>15.7</td>
<td>15.2</td>
<td>14.2</td>
<td>14.1</td>
<td>13.4</td>
<td>13.6</td>
<td>13.2</td>
<td>14.1</td>
<td>13.8</td>
<td>14.1</td>
</tr>
</tbody>
</table>

*Rates expressed in DDD/1000 population/day
FIGURE 3.3: Average daily antibiotic utilization rates for all solid antibiotics for systemic use by year and health service delivery area. The utilization rates in Northwest, Vancouver, and Richmond have been emphasized. The implementation of the program is indicated by the vertical line.

The elevated antibiotic utilization rates observed in Northwest are driven by a high consumption of fluoroquinolones (increase of 1.3 DDD/1000 population/day from 1996 to 2007; Figure 3.4). The use of this pharmaceutical has also increased in all other HSDAs, but to a lesser extent. Newer macrolide (azithromycin and clarithromycin) utilization rates have also risen over the last decade in all HSDAs. Fluoroquinolone and newer macrolide utilization rates from 1996 to 2007 are summarized in Appendix C for all HSDAs.
3.3.2.2 Pediatric Overall and Indication-Specific Prescribing Trends

Among children, prescription rates steadily declined from 1996 to 2007 in all HSDAs. This decrease was most notable in Vancouver (decrease of 1.96 prescriptions/1000 population/day between 1996 and 2007; Figure 3.5). In 2007, prescription rates were highest in Northwest followed by Fraser South and Fraser East (2.09, 1.85, and 1.81 prescriptions/1000 population/day, respectively). For the last seven years, Kootenay Boundary has recorded the lowest prescription rates (1.13 prescriptions/1000 population/day in 2007).
Pediatric prescription rates for the indications of acute bronchitis, acute pharyngitis, and otitis media declined in all HSDAs from 1996 to 2007. The greatest reduction in the use of antibiotics for acute bronchitis and acute pharyngitis occurred in Vancouver (0.15 and 0.13 prescriptions/1000 population/day, respectively, from 1996 to 2007). Prescribing rates for the indication of otitis media decreased most significantly in South Vancouver Island (0.42 prescriptions/1000 population/day from 1996 to 2007).

Among adults, antibiotic utilization rates for the indication of acute bronchitis, acute pharyngitis, and otitis media decreased within 11, 10, and 15 HSDAs, respectively, between 1996 and 2007. During this time frame, the largest decline in antibiotic use for acute bronchitis, acute pharyngitis, and otitis media among adults was recorded in Central Vancouver Island (0.41 DDD/1000 population/day), Vancouver (0.25 DDD/1000 population/day), and Thompson Cariboo Shuswap (0.02 DDD/1000 population/day), respectively.
3.3.3 Monthly Rate of Change of Antibiotic Utilization Rates by Level of Program Implementation

3.3.3.1 Overall and Class-Specific Trends

The monthly rate of change of overall antibiotic utilization rates improved in association with the implementation of the program in all HSDAs (range: -0.0012 to -0.1765 DDD/1000 population/day, mean: -0.0933 DDD/1000 population/day). The smallest and largest differences in the monthly rate of change both occurred in HSDAs with medium DBND implementation (East Kootenay and Northwest, respectively).

The monthly rate of change of fluoroquinolone utilization rates improved in association with DBND in all HSDAs with high program implementation (range: -0.0031 to -0.0076 DDD/1000 population/day, mean: -0.0056 DDD/1000 population/day). Unfortunately, the monthly rate of change of fluoroquinolone utilization rates accelerated within two HSDAs with medium program implementation (0.0071 DDD/1000 population/day in East Kootenay and 0.0030 DDD/1000 population/day in South Vancouver Island), and one HSDA in which DBND uptake was low (0.0002 DDD/1000 population/day in Northeast).

The monthly rate of change of newer macrolide utilization rates improved within all HSDAs, regardless of the level of program implementation (range: -0.0064 to -0.0882 DDD/1000 population/day, mean: -0.0407 DDD/1000 population/day). Dotplots depicting the difference in the monthly rate of change of daily overall, fluoroquinolone, and newer macrolide utilization rates, pre and post DBND, by level of program implementation are presented in Figure 3.6.
FIGURE 3.6: Difference in the monthly rate of change of overall, fluoroquinolone, and newer macrolide daily antibiotic utilization rates, pre (2004-2005) and post (2006-2007) “Do Bugs Need Drugs?”, by level of program implementation. All differences are measured in DDD/1000 population/day over a one month period. Each circle represents one health service delivery area with the diameter of the circle proportional to the population size.

The range and mean differences in the monthly rate of change of daily overall, fluoroquinolone, and newer macrolide utilization rates, pre and post DBND, by level of program implementation are summarized in Table 3.2.
TABLE 3.2: Range and mean differences in the monthly rate of change of daily overall, fluoroquinolone, and newer macrolide utilization rates, pre and post “Do Bugs Need Drugs?”, by implementation category*

<table>
<thead>
<tr>
<th>Antibiotics of Interest</th>
<th>Implementation Category</th>
<th>Low</th>
<th>Medium</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Range of Differences</td>
<td>Mean Difference</td>
<td>Range of Differences</td>
<td>Mean Difference</td>
</tr>
<tr>
<td>Overall</td>
<td>[-0.0635, -0.1384]</td>
<td>-0.1080</td>
<td>[-0.0012, -0.1765]</td>
<td>-0.0797</td>
</tr>
<tr>
<td>Fluoroquinolone</td>
<td>[0.0002, -0.0132]</td>
<td>-0.0052</td>
<td>[0.0071, -0.0164]</td>
<td>-0.00394</td>
</tr>
<tr>
<td>Newer Macrolide</td>
<td>[-0.0144, -0.0838]</td>
<td>-0.0379</td>
<td>[-0.0064, -0.0882]</td>
<td>-0.03823</td>
</tr>
</tbody>
</table>

*Differences are measured in DDD/1000 population/day over a one month period.

3.3.3.2 Pediatric Overall and Indication-Specific Prescribing Trends

Among children, the monthly rate of change of overall prescription rates improved in all HSDAs in association with DBND implementation (range: -0.0012 to -0.0386 prescriptions/1000 population/day, mean: -0.0170 prescriptions/1000 population/day; Figure 3.7). For the indication of acute bronchitis, the monthly rate of change of daily prescription rates improved within all HSDAs, except in one with medium implementation. In this HSDA, the prescription rates continued to decrease after program implementation, but at a slightly lower rate than before the program was put in place (0.0001 prescriptions/1000 population/day in Central Vancouver Island). Similarly, the monthly rate of change of daily prescription rates for acute pharyngitis improved within all HSDAs, except one with low implementation (0.0002 prescriptions/1000 population/day in Kootenay Boundary). For the indication of otitis media, the monthly rate of change of daily prescription rates improved for 77% of HSDAs with low or medium program uptake, and for 100% of HSDAs with high DBND implementation, pre and post DBND. Dotplots depicting the difference in the monthly rate of change of daily overall and indication-specific pediatric prescription rates, pre and post DBND, by level of program implementation are depicted in Figures 3.7 and 3.8, respectively.
FIGURE 3.7: Difference in the monthly rate of change of daily overall pediatric prescriptions rates, pre (2004-2005) and post (2006-2007) “Do Bugs Need Drugs?”, by level of program implementation. All differences are measured in prescriptions/1000 population/day over a one month period. Each circle represents one health service delivery area with the diameter of the circle proportional to the population size.
FIGURE 3.8: Difference in the monthly rate of change of daily pediatric prescriptions rates by indication and level of program implementation, pre (2004-2005) and post (2006-2007) “Do Bugs Need Drugs?”. All differences are measured in prescriptions/1000 population/day over a one month period. Each circle represents one health service delivery area with the diameter of the circle proportional to the population size.

The range and mean difference in the monthly rate of change of daily prescription rates among children by indication and level of program implementation are summarized in Table 3.3.
### Table 3.3: Range and mean differences in the monthly rate of change of daily overall and indication-specific pediatric prescriptions rates, pre and post “Do Bugs Need Drugs?”, by implementation category.

<table>
<thead>
<tr>
<th>Indication of Interest</th>
<th>Implementation Category</th>
<th>Low</th>
<th>Medium</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Range of Differences</td>
<td>Mean Difference</td>
<td>Range of Differences</td>
<td>Mean Difference</td>
</tr>
<tr>
<td>Overall</td>
<td>[-0.00117, -0.0244]</td>
<td>-0.0131</td>
<td>[-0.0049, -0.0386]</td>
<td>-0.0181</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>[-0.0003, -0.00283]</td>
<td>-0.0015</td>
<td>[0.00006, -0.0042]</td>
<td>-0.0018</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>[0.000174, -0.0002]</td>
<td>-0.0009</td>
<td>[-0.0009, -0.0069]</td>
<td>-0.0032</td>
</tr>
<tr>
<td>Otitis Media</td>
<td>[-0.00062, -0.00422]</td>
<td>-0.0007</td>
<td>[0.00191, -0.0083]</td>
<td>-0.0021</td>
</tr>
</tbody>
</table>

† Differences are measured in prescriptions/1000 population/day over a one month period.

### 3.3.4 Utilization Patterns in Urban and Rural Health Service Delivery Areas

Historically, urban areas have reported higher overall antibiotic utilization rates compared to rural areas. However, since 2003, the rate of overall antibiotic utilization has been nearly identical across these two categories (16.9 and 16.8 DDD/1000 population/day in urban and rural areas, respectively, in 2007). Interestingly, from 1996 to 2007, rural areas have consistently reported higher fluoroquinolone utilization rates, whereas urban areas have documented higher newer macrolide utilization rates (Figure 3.9). Prescription rates among children are consistently higher in urban areas (1.63 and 1.48 prescriptions/1000 population/day in urban and rural areas, respectively, in 2007).
FIGURE 3.9: Urban and rural average daily fluoroquinolone and newer macrolide utilization rates by year. The implementation of the program is indicated by the vertical line.

In association with the implementation of DBND, the monthly rate of change of fluoroquinolone utilization rates improved to a greater extent in urban areas compared to rural areas, as did the rate of change of pediatric prescription rates for all indications and for the indications of acute bronchitis and acute pharyngitis. The monthly rate of change of overall and newer macrolide utilization rates and pediatric prescription rates for the indication of otitis media did not follow this trend (Table 3.4)
TABLE 3.4: Range and mean differences in the monthly rate of change of the utilization rates of all program targets, pre and post “Do Bugs Need Drugs?”, by implementation category

<table>
<thead>
<tr>
<th>DBND Targets</th>
<th>Urban</th>
<th>Rural</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Range of Differences</td>
<td>Mean Difference</td>
</tr>
<tr>
<td>Overall</td>
<td>[-0.0692, -0.1204]</td>
<td>-0.0881</td>
</tr>
<tr>
<td>Fluoroquinolone</td>
<td>[-0.0062, -0.0115]</td>
<td>-0.0082</td>
</tr>
<tr>
<td>Newer Macrolide</td>
<td>[-0.0288, -0.0522]</td>
<td>-0.0375</td>
</tr>
<tr>
<td>Overall</td>
<td>[-0.0167, -0.0209]</td>
<td>-0.0191</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>[-0.0019, -0.0027]</td>
<td>-0.0023</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>[-0.0023, -0.0069]</td>
<td>-0.0042</td>
</tr>
<tr>
<td>Otitis Media</td>
<td>[0.0011, -0.00010]</td>
<td>-0.0002</td>
</tr>
</tbody>
</table>

*Differences are measured in DDD/1000 population/day over a one month period.
† Differences are measured in prescriptions/1000 population/day over a one month period.

3.4 Discussion

Stratification of antibiotic utilization rates by HSDA demonstrated that considerable variation in antibiotic use exists across the different health jurisdictions in BC. Overall antibiotic utilization rates are highest in the North and in the Fraser Valley, and lowest in Richmond. The areas with the highest utilization rates also report the greatest use of fluoroquinolones and newer macrolides. Encouraging declines in prescription rates among children have occurred in all HSDAs, primarily due to a drop in the use of amoxicillin.

The results obtained in this study provide some evidence of a pattern between the level of DBND implementation and the amount of improvement in the monthly rate of change of utilization rates. The monthly rate of change of newer macrolide utilization rates slowed the most within HSDAs with high DBND implementation and the least within HSDAs with low program implementation. This trend was not evident among fluoroquinolone
utilization rates or when considering overall antibiotic use. A large drop in fluoroquinolone use was not anticipated, as this class of antibiotics is primarily used for treatment of urinary tract infections, which were not a target of the program. Among children, a pattern between increasing level of DBND implementation and larger improvements in the monthly rate of change of prescription rates was identified when considering overall pediatric prescriptions and those for acute bronchitis. This result was expected as several of the DBND initiatives are targeted towards antibiotic use in children.

Importantly, the results of this study indicate that the monthly rate of change of overall, class-specific, and indication-specific utilization rates improved in all areas with high DBND implementation. In addition, the level of improvement per category of interest was very consistent within these high implementation HSDAs. As such, these results suggest that although more encouraging results were sometimes observed within HSDAs with low and medium program implementation, a consistent level of improvement was always observed in HSDAs which received a high level of public education.

Examination of utilization patterns by population density (urban vs. rural) demonstrated that the monthly rate of change of most pediatric prescription rates of interest improved to a greater extent in urban areas compared to rural ones, in association with the DBND program. Because several of the large public education components were centered in urban HSDAs, many of which specifically targeted children, these results are not unexpected. The historical difference in fluoroquinolone and newer macrolide utilization rates between urban and rural areas identified in this study provides insight as to which key messages should be emphasized in these regions.

The delivery of the DBND program will be improved using the results of this study. HSDAs which currently record the highest utilization rates will be targeted by future initiatives. In order to optimize improvements in utilization rates, effort will be dedicated towards ensuring that the program is delivered to a high degree in all areas, thereby justifying the use of economic and human resources. Finally, because this evaluation
provides some evidence as to the effectiveness of the program among different British Columbian populations, expansion of the DBND program to other jurisdictions in Canada through collaborations will be considered.

The conclusions drawn in this study contribute to the growing body of implementation science literature which states that the level and quality of program implementation affects the outcomes of promotion and prevention programs (Durlak and DuPre 2008). It is important to provide evidence to this relationship, as it is not uncommon for potentially good programs to be deemed ineffective and therefore rejected, without any consideration of whether the program was properly designed, implemented, and supported (Durlak 1998). In the literature, this failure to consider all program implementation aspects has been coined a Type III error (Scanlon, Horst et al. 1997). The authors recognize that audience reach, which was used to rank the HSDAs by level of implementation in this study, is only one of several factors which affect the implementation level of a program (Durlak and DuPre 2008). However, the DBND Evaluation Committee deemed that the proportion of children taught is the most representative and quantifiable measure of program implementation. As this committee has extensive experience with the program, their suggestions and approval was highly regarded.

The major strengths of this study lay in the data available for use. As PharmaNet provides a comprehensive list of all prescriptions dispensed through community pharmacies in BC, a detailed inter-regional comparison of changes in utilization trends in all 16 HSDAs was possible. The exhaustive account of all DBND activities (location, audience, and type) was also vital to this study. Without such meticulous information, the association between the program and changes in utilization patterns would have to be examined at a provincial level. This type of analysis would bias the association to the null, and mask the important observation that proper program implementation matters.

This study has several limitations. The planned staggered delivery of the various program components across the 16 HSDAs was not achieved during the first two years of program implementation. Rather, due to human resource limitations and variations in the level of
interest by administrative bodies, a delivery tactic which aimed to maximize geographical
and audience reach in areas readily interested and ready to accommodate the program
was adopted. As such, it is currently not feasible to consider the important effect of the
inevitable time-lag between knowledge uptake leading to response and health promotion
(Nutbeam 1999; McMichael and Butler 2006). Second, baseline antibiotic utilization
rates were not the same among all HSDAs. One could therefore hypothesize that larger
improvements would be expected in areas with higher baseline rates, independent of the
level of DBND implementation. However, as the mean difference in the monthly rate of
change of utilization rates, pre and post DBND, within an implementation category was
used to generate the major conclusions of this study, the potential effect of any outliers
should be minimized (Daniel 2005). Calculation of the median difference in the monthly
rate of change of utilization rates, pre and post DBND, per implementation category was
not informative due to the small number of HSDAs in the low and high program
implementation categories.

Third, as the majority of the DBND program components are delivered in English, there
is the potential for language differences to impede the effective delivery of the program’s
messages. However, because several of the DBND public education components are
visual, and some of the material has undergone multiple linguistic translations, the
authors do not consider this a major limitation of this study. Fourth, although the
classification of the HSDAs by level of urbanization was conducted according to
Canadian standards (BC STATS 2008), the authors recognize that variation in level of
urbanization exists within each of these large geographical areas. In addition, because
only three HSDAs were classified as urban, a small sample size was used to calculate the
estimates for this group. The use of administrative data and the inability to draw causal
associations in an ecological study also remain limitations of this study. The reader is
asked to refer to the discussion in Section 2.4 for a comprehensive review of these issues.

Finally, although encouraging, it is important to recognize the preliminary and modest
nature of the results documented in this evaluation. Further efforts are required to fully
assess the association between DBND and improvements in knowledge of antibiotics and
their use. Continuous yearly program evaluations will assist in building an evidence base of the program’s potential and in identifying any additional effects, beneficial or otherwise, which may have been missed in this study.

3.5 Conclusions

Our study highlighted the potential of the DBND program to improve long-term utilization patterns when the program is effectively delivered. Our results also provide some evidence as to the relationship between level of program implementation and improvements in program outcomes. Future investigations should address the current uncertainty regarding the time-lag between public education, knowledge uptake, and behaviour change. In addition, further stratification as to the types of initiatives delivered in various areas would yield insight as to the effectiveness of the different DBND health promotion strategies. Finally, the use of more rigorous administrative controls should be considered as an option for promoting more significant changes in utilization patterns.
3.6 References


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4. FINAL DISCUSSION

4.1 Summary

The relationship between the DBND program and changes in antibiotic utilization trends in BC was fully described in this thesis. Specifically, population-level antibiotic utilization trends from 1996 to 2007 were examined by ATC class, geographical location, and select indications. The results generated compliment previous DBND evaluations which assessed knowledge uptake and short-term behaviour change.

Prior to initiating this study, it was hypothesized that the rate at which antibiotic utilization rates increased would slow in association with DBND, and that this outcome would be most prominent among program targets. The utilization trends of fluoroquinolones and newer macrolides (azithromycin and clarithromycin), as well as the prescription patterns for predominantly viral upper respiratory tract infections (acute bronchitis, acute pharyngitis, and otitis media) were selected for evaluation as several of the DBND initiatives directly target these pharmaceuticals and indications. Overall utilization rates were also of interest as they represent population-level antibiotic use.

During the first study (Chapter 2), the investigation of the relationship between DBND and changes in antibiotic utilization patterns was limited to the Vancouver HSDA. This location was selected as DBND was first implemented in this health jurisdiction, and a large proportion of DBND activities have since then taken place there. As such, a possible association between changes in antibiotic use and the program would be most detectable in Vancouver. The results of this preliminary study indicated that although overall antibiotic utilization rates remained stable in 2006 and 2007, the use of fluoroquinolones and newer macrolides continued to increase in Vancouver despite the program’s efforts. However, the monthly rate of change of these pharmaceuticals improved in association with the DBND program. Additionally, encouraging declines in overall prescription rates and those for the indication of acute bronchitis, acute pharyngitis, and otitis media were observed among children.
The second paper (Chapter 3) assessed whether the trends observed in the Vancouver HSDA were consistent with antibiotic utilization trends observed in other areas in BC in which DBND was implemented, and whether a pattern exists between level of program implementation and change in antibiotic use. Stratification of utilization patterns by HSDA demonstrated that substantial differences in antibiotic use exist across these regions. Some evidence of a pattern between increasing program implementation and improvements in antibiotic use was documented, especially among certain program targets (newer macrolides, overall pediatric prescription rates and those for acute bronchitis). However, the most important observation drawn from this study was that the rate of increase of overall, class-specific, and indication-specific utilization rates slowed in all areas with high DBND implementation. This result highlights the important fact that the level of program implementation affects the outcomes obtained in health promotion programs (Durlak and DuPre 2008).

Together, these papers indicate that DBND was unsuccessful in lowering fluoroquinolone and newer macrolide utilization rates, despite the fact that these pharmaceuticals were prime program targets for two years. However, the potential for DBND to improve long-term antibiotic utilization trends using public education was demonstrated among all program targets investigated in this evaluation. Moreover, as positive changes in utilization trends were seen in all health jurisdictions in which DBND was highly implemented, the program appears to be generalizable to different British Columbian populations.

### 4.2 Contributions to Research

It is important to recognize that the goal of this thesis was not to draw a causal association between DBND and improvements in antibiotic use in BC. Rather, this study aimed to conduct a comprehensive descriptive analysis of past and current antibiotic utilization trends, and any changes in these trends which occurred simultaneously to the delivery of a province-wide public education campaign. As such, the results presented in this thesis contribute to the growing body of ecological evidence regarding the
effectiveness of community-based programs aimed at improving antibiotic use. This evidence-base acts as the foundation of more conclusive hypothesis-testing randomized control, cohort, or case-control studies, some of which have already been attempted (Perz, Craig et al. 2002; Doyne, Alfaro et al. 2004; Welschen, Kuyvenhoven et al. 2004).

This evaluation followed a unique approach when assessing the potential of DBND to influence antibiotic use in the long-term. The novel methods employed allowed for the identification of improvements in the rate of change of utilization rates, as well as reductions in the utilization rates themselves. To our knowledge, the former outcome has only been measured in one other evaluation of a community-based program targeting antibiotic knowledge and use (Mainous, Hueston et al. 2000). The conclusions of this study also have several local and practical applications.

The change in antibiotic utilization trends documented will act as baseline information on which to compare future analyses. As the DBND program has been funded until 2012 by the PharmaCare division of the BC Ministry of Health, and will be subject to yearly evaluations, this baseline information will be essential for developing a longitudinal view of the program’s effect on antibiotic utilization patterns. In addition, if the program is expanded to other parts of Canada (or internationally), the baseline trends documented in BC will be compared to those in newly targeted regions. This scenario is highly feasible given that DBND is a transportable program with several of its educational materials having already undergone translation into many languages. At a minimum, these types of comparisons will contribute to the assessment of the generalizability of DBND to populations outside of BC. On a broader scope, the expansion of the program will foster strong collaborations with outside governments and institutions. These collaborations could lead to meaningful inter-provincial and international descriptions of antibiotic utilization trends, and how these trends change in association with community education initiatives.

Because PharmaNet is the only comprehensive central prescription network in North America, our study is unique in reporting population-level antibiotic utilization trends.
Other studies describing antibiotic use are typically conducted at a provincial or national-level using a sample of the population. These studies are thus subject to methodological issues relating to sampling and inferential statistics (Merzel and D'Afflitti 2003). The inclusion of geographical information in the dataset used in this study also provided valuable insight as to the considerable variation in utilization patterns that exist in different areas within BC. Finally, as the data was available for the last twelve years, a comparison between historical and current trends was also possible.

A key aspect of this study was the ability to assess changes in utilization patterns by indication through the linkage of the PharmaNet and MSP databases. Although rarely available at a population-level, this information allowed researchers to identify the indications driving utilization rates and to examine the difficult question as to whether DBND decreased inappropriate antibiotic use, and not just overall antibiotic use. Specifically, the analysis of indication-specific utilization trends allowed investigation as to whether doctors in BC selected first-line agents for treatment more frequently after the implementation of DBND, compared to before.

The data linkage mentioned above, pioneered by the work of Dr. M. Fawziah and Dr. D. M. Patrick (Marra, Patrick et al. 2006), is an excellent example of the benefits of strong institutional collaborations. The working relationship that exists between the College of Pharmacists and the BC Center for Disease Control allowed researchers to take advantage of updated and detailed provincial-level antibiotic utilization data linked to reason for prescribing, and create one of the most comprehensive descriptions of antibiotic use in BC. In addition, this data provided the outcome measures necessary for an objective evaluation of the long-term effects of a large multifaceted community-education program.

4.3 Study Limitations

The conclusions drawn in this thesis were limited by experimental design and the use of administrative data. We were unable to establish a causal association between DBND and
changes in utilization patterns due to the ecological approach used. This limitation is common among population-level interventions which lack an appropriate control group (Nebot 2006). In addition, it is important to acknowledge the preliminary and modest nature of the results documented in this thesis. Future evaluations are required to fully assess the relationship between changes in utilization patterns and the DBND program over time.

It is also important to acknowledge that the true potential of the intervention may have been attenuated as a consequence of incomplete program delivery attributable to languages concerns among the highly multicultural population living in BC. However, the authors do not believe that language significantly affected the results as several of the public education components have undergone multiple linguistic translations. The simultaneous delivery of independent initiatives aimed at the similar goals as DBND (i.e. Clean Hands, Dirty Hands) or changes in infection control practices remain potential confounders of this study.

Although the use of the PharmaNet data is likely the largest asset of this study, this administrative dataset is not without limitations. First, prescriptions dispensed within hospital facilities or through internet pharmacies, by physicians during an office, clinic, or emergency department visit, or for the treatment of STIs are not captured by PharmaNet. However, the authors do not believe that these factors have significantly changed pre and post DBND, and thus, should not have affected the major conclusions of this study. Finally, it is important to note that PharmaNet only records the purchase of antibiotics, but not their actual consumption. Nevertheless, as the program aims to improve knowledge about the use of antibiotics, tracking physician prescribing and consumer purchasing patterns remains a valid means of monitoring antibiotic use. In addition, the authors anticipate that a strong correlation exists between the purchase of antibiotics and their consumption.
4.4 Knowledge Translation

Several strategies will be used to ensure a complete dissemination and efficient uptake of the findings of this evaluation to healthcare professionals, the public, policy makers, and researchers. The DBND program circulates brief reports to healthcare professionals who participate in the program, in which the results from this study will be incorporated. Program performance updates are also distributed to family physicians using a regular BC Centre for Disease Control contribution to the BC Medical Journal. The important trends observed in this analysis will also be incorporated into future knowledge translation products tailored to healthcare professionals and the public, as has been done for previous program evaluations (Fuertes, Vrbova et al. 2008). These products are designed to provide feedback to those who have participated in the program, and to encourage others to take part. Whenever possible, the main conclusions drawn in this study will also be built into current and future DBND initiatives and highlighted during press releases.

Policy makers will be informed of these results through direct briefings with the government on the impact of the program, and through a yearly comprehensive program evaluation report submitted to the BC Ministry of Health. All reports produced will be shared with the regional health authorities in BC to help them decide on local priorities. Finally, the results of this study were presented to researchers and policy makers in the form of a poster at the 26th International Congress of Chemotherapy in June, 2009. Furthermore, publication in reputable professional journals will be sought.

4.5 Implications for Policy and the “Do Bugs Need Drugs?” Program

The results of this evaluation have important political implications towards the development of regulations regarding antibiotic use in BC. During its first two years of implementation, the DBND program was shown to be associated with an improvement in the monthly rate of change of antibiotic utilization rates. However, what was not observed was a lowering of the utilization rates, themselves. As DBND was a well-
received program which targeted all relevant audiences using several uniquely tailored initiatives, these results may suggest that healthcare and public education alone are not enough to rapidly achieve significant improvements in antibiotic use. Policy regulations may be required, especially with regards to frequently and commonly misused antibiotics which may possess traits prone to inducing bacterial resistance, such as the fluoroquinolones and newer macrolides (Drusano and Craig 2000; Cizman, Pokorn et al. 2001; Kastner and Guggenbichler 2001; Urbanek, Kolar et al. 2005; Karlowsky, Hoban et al. 2006). Such regulations could include formulary restrictions which have shown to be highly effective at reducing drug use (Marra 2004), or administrative controls which limit the use of certain antibiotics to severe or resistant infections. Because this analysis included antibiotic utilization patterns from all BC residents, and the DBND program is a large and diverse program implemented in all health jurisdictions in the province, the conclusions drawn in this study will weight heavily in the minds of policy makers.

The results of this analysis are also valuable to the health service providers in BC. The Provincial Health Services Authority and the five regional health authorities can examine the trends outlined in this thesis and consider how antibiotic use has changed over time in each HSDA, and how it differs between HSDAs. In order to facilitate this comparison and allow health providers to focus on their geographical area of interest, HSDA-specific overall antibiotic utilization trends are summarized by health authority in Appendix D. Finally, the results of this analysis also provide justification for the use of valuable and limited healthcare and economic resources dedicated to the fight against inappropriate antibiotic use and emerging resistance.

In addition to informing policy decisions regarding antibiotic use, the results of this study will also be used when deciding on local DBND priorities for next fall, and will provide direction for future program initiatives. For example, HSDAs with the highest rates of misuse or overuse will be heavily targeted with education tailored to their unique needs. An influx of new messages and focused attention will be delivered towards classes of antibiotics which are currently overused, and indications for which second and third line antibiotics are still frequently selected over first line agents. The comprehensive
description of utilization patterns by indication provides some evidence as to the important health messages which need to be promoted at provincial and national academic meetings.

4.6 Future Directions

This project has left important questions unanswered. In the future, it will be essential to identify which DBND initiatives are most effective at improving antibiotic knowledge and use, and whether they are optimally effective when used in combination with one another. This type of knowledge will allow the program coordinators to prioritize the delivery of the components. Second, as the program continues to be delivered and evaluated over the next three years, the potential to address the complex issue of a time-lag between health promotion, knowledge uptake, and behaviour change will be created. A more detailed inter-regional comparison of changes in utilization trends will also be possible.

Third, the DBND program is currently looking at expanding its focus to incorporate messaging on proper prescribing practices for urinary tract infections. Evaluating the impact of these new initiatives, and whether they can be designed to further improve appropriate prescribing for RTIs remains to be seen. Additionally, a proposed project which will provide physicians in BC with personalized feedback regarding their prescribing patterns, and how these compare with they’re peers, is being considered. The aim of this project would be to further the improvements in utilization patterns documented in this thesis. Finally, although we were in an excellent position to explore antibiotic utilization trends, this study did not investigate whether any changes in patterns of bacterial resistance occurred in association with DBND. This outcome will be explored in future studies, as changing trends in antibiotic resistance may take up to a year or two to follow any changes in patterns of antibiotic utilization.
4.7 References


APPENDIX A: Program Logic Model

**Resources**
- Funds and endorsement from the Ministry of Health
- Media and technical materials from Alberta Health
- DBND program and evaluation coordinators and committee
- Contribution from nurses, students and pharmacists
- Administrative and technical support

**Strategies**
- Television & radio advertisement campaign
- Transit advertisement campaign
- Train individuals who will subsequently teach daycare and grade 2 children, and those in assisted living
- 1. Bugs and Drugs book
   2. Parent guide, pamphlets, posters, & stickers
- 1. Continuing Medical Education
   2. Continuing Education for Pharmacists
   3. Train-the-Trainer Education

**Process Evaluation**
- Number, date, & location of TV, radio, and transit ads
- Number of trainers, daycare and grade 2 children, and older adults taught, date & location of teaching
- 1) Number of books distributed to each type of physician & location.
   2) Type of material, date & location
- Date & location of course, number of participants & the location of their practice, knowledge surveys
- Prescription pad data

**Impact Evaluation**
- Increased public knowledge that viral RTIs do not require antibiotics
- Decrease in requests for antibiotics by the public
- Increased awareness of the importance of proper handwashing
- Decrease in physician's prescribing antibiotics for suspected viral infections
- Increased use of first line antibiotic agents
- Change in prescription patterns for antibiotics

**Outcome Evaluation**
- Decrease in antimicrobial resistance in BC
- Quality Assurance
- Increased in overall use of antibiotics by 1 DDD per 1000 population per day in BC
- Healthcare professional knowledge and attitude change surveys
- Decrease in the use of newer macrolides & fluoroquinolones by 20% in BC
- Reduction in prescriptions for bronchitis and otitis media by 15% in BC

PharmaNet data analysis
Linked PharmaNet and MSP data analysis
APPENDIX B: Data Sources

PharmaNet

PharmaNet is a province-wide network administered by the BC Ministry of Health and the College of Pharmacists of BC. This secure pharmacy network links all retail pharmacies into a central set of data systems, providing a complete listing of all individual ambulatory care prescriptions dispensed to all BC residents through a community pharmacy in BC or through a hospital outpatient pharmacy for patient use at home, regardless of formulary status. However, PharmaNet does not collect information on prescriptions dispensed within hospital facilities or through internet pharmacies. It is also currently not mandatory for physicians to record medications provided to patients during an office, clinic, or emergency department visit, although this practice is encouraged. Medications used for treatment of STIs are not recorded in the PharmaNet database.

Medical Service Plan

The MSP provides insurance for medically required services and requires the enrollment of all residents of BC. The MSP database contains information on patient age and sex, date of visit, physician reimbursement claims, physician specialty, and geographic location of the physician’s office.
APPENDIX C: Fluoroquinolone and Newer Macrolide Utilization Rates by Health Service Delivery Area

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*Rates expressed in DDD/1000 population/day
### TABLE C.2: Newer macrolide utilization rates by health service delivery area*

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*Rates expressed in DDD/1000 population/day
APPENDIX D: Antibiotic Utilization Rates by Health Authority

FIGURE D.1: Antibiotic utilization rates by health service delivery areas that make up the Northern Health Authority. NW = Northwest; NI = Northern Interior, NE = Northeast.

FIGURE D.2: Antibiotic utilization rates by health service delivery areas that make up the Interior Health Authority. TCS = Thompson Cariboo Shuswap; EK = East Kootenay; OK = Okanagan; KB = Kootenay Boundary.
FIGURE D.3: Antibiotic utilization rates by health service delivery areas that make up the Vancouver Island Health Authority. NVI = North Vancouver Island; SVI = South Vancouver Island; CVI = Central Vancouver Island.

FIGURE D.4: Antibiotic utilization rates by health service delivery areas that make up the Vancouver Coastal Health Authority. NSCG = North Shore Coast Garibaldi; VAN = Vancouver; RMD = Richmond.
FIGURE D.5: Antibiotic utilization rates by health service delivery areas that make up the Fraser Health Authority. FRS = Fraser South; FRE = Fraser East; FNR = Fraser North.
APPENDIX E: The University of British Columbia Behavioural Research Ethics Board Approval Certificate

The University of British Columbia
Office of Research Services
Behavioural Research Ethics Board
Suite 102, 6190 Agronomy Road, Vancouver, B.C. V6T 1Z3

CERTIFICATE OF APPROVAL - MINIMAL RISK

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<tbody>
<tr>
<td>Elaine Fuerjes</td>
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<th>SPONSORING AGENCIES:</th>
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<td>Michael Smith Foundation for Health Research</td>
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<th>PROJECT TITLE:</th>
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<tr>
<td>An Investigation of Antibiotic Utilization Within Populations and the Effectiveness of Educational and Administrative Programs Designed to Promote Changes in the Use of these Pharmaceuticals.</td>
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<th>CERTIFICATE EXPIRY DATE:</th>
<th>September 29, 2009</th>
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<th>DOCUMENTS INCLUDED IN THIS APPROVAL:</th>
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<tr>
<td>Protocol:</td>
<td>September 29, 2008</td>
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<tr>
<td>Research Proposal</td>
<td>N/A September 15, 2008</td>
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<td>Other:</td>
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The research is being conducted on the impact of the "Do Bugs Need Drugs?" < www.dobugsneeddrugs.org> program on antibiotic utilization in BC. The website for this health initiative is provided to allow interested reviewers to become more familiar with the goals of the program.

The application for ethical review and the document(s) listed above have been reviewed and the procedures were found to be acceptable on ethical grounds for research involving human subjects.

Approval is issued on behalf of the Behavioural Research Ethics Board and signed electronically by one of the following:

Dr. M. Judith Lynam, Chair
Dr. Ken Craig, Chair
Dr. Jim Rupert, Associate Chair
Dr. Laurie Ford, Associate Chair
Dr. Daniel Salhani, Associate Chair
Dr. Anita Ho, Associate Chair