



Rx

HANDLE WITH CARE:

Preserving Antibiotics Now and Into the Future

Chief Public Health Officer of Canada's 2019 Spotlight Report



Également disponible en français sous le titre :
Pleins feux de l'administratrice en chef de la santé publique du Canada,
2019 : Manipuler avec soin: préserver les antibiotiques aujourd'hui
et demain

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Minister of Health, 2019

Publication date: June 2019

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Cat: HP2-18E-PDF
ISSN: 2562-6280
Pub: 190081

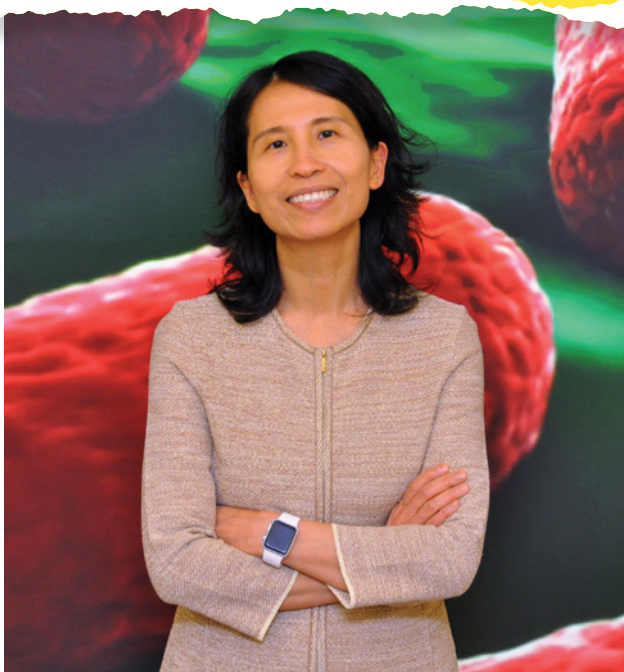


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A Message from Canada's Chief Public Health Officer



Antibiotics are precious medicines that are critically important for curing serious infections. Taking them unnecessarily can encourage the tide of antibiotic-resistant bacteria and could also disrupt the balance of microbes that live naturally in your body. These resistant superbugs can go on to infect others and can increase the risk of complications from essential medical procedures, such as C-sections, hip replacements, and chemotherapy.

The more and more we use antibiotics unnecessarily, the less effective they will become. Many Canadians have already experienced serious infections with antibiotic-resistant bacteria or know someone who has. A world without effective antibiotics is not one we would wish on future generations.

Why are antibiotics sometimes prescribed and taken when they aren't needed? It turns out the decision to prescribe and use antibiotics is more than just a medical one. It is shaped by relationships with our healthcare providers, pressures within the medical clinic and health system, and the misperception that antibiotics are magic bullet solutions.

Through this report, I examine why people may be prescribed antibiotics unnecessarily and what we can do about it.

While different ways of reducing unnecessary antibiotic use are being implemented in different areas of Canada, we lack evidence on how effective they are and we have not adequately spread best practices across the country. We need to get practical tools into the hands of prescribers and monitor their impact on prescribing patterns.

As Canada's federal champion for antimicrobial resistance, I hope that by reading this report, we can all examine our own reasons for wanting or prescribing antibiotics, ask more questions, and think twice about their use.

By changing our prescribing behaviours, it is possible for us to preserve antibiotics now and into the future.



Introduction

It is hard to imagine that our grandparents and great-grandparents lived in a world without antibiotics. This was a time when many people died from now-curable infectious diseases. That is not a world we would wish on our children or grandchildren.

And yet, antibiotics are becoming ever less effective, because bacteria can evolve to withstand their effects—a process called antibiotic resistance. Left unchecked, there is risk of losing these medications as an essential life-saving treatment. Although the future is hard to predict, it is estimated that antibiotic-resistant infections could cause 10 million deaths a year globally by 2050, which is more than the current annual worldwide deaths from cancer.²

Antibiotic use is an issue not only in human health care but also in animal health as well. Leaders in Canada and around the world are actively joining forces across health and agricultural sectors to tackle antibiotic resistance. For example, Canada's Pan-Canadian Framework for Action on Antimicrobial Resistance, and the soon-to-be released action plan, aims to strengthen Canada's ability to combat the risks of antimicrobial resistance.

This report focuses on antibiotic use and prescribing practices in our communities (or non-hospital settings). This is where 92% of antibiotics prescriptions are written and filled by doctors, nurses, dentists and pharmacists.³

What are antimicrobials?

Antimicrobials are a group of four types of medicines that kill microbes or stop their growth¹:

- Antibiotics are used to treat bacterial infections (such as strep throat and urinary tract infections);
- Antivirals are used against illnesses caused by viruses (such as influenza and HIV);
- Antifungals are used against infections caused by fungi (such as yeast infections); and
- Antiparasitics are used against parasites (such as pinworms).

This report focuses on unnecessary antibiotic use, how it contributes to the problem of antibiotic resistance, and what we can do about it.

The goal of this report is to describe why unnecessary antibiotic use sometimes happens and what we can do about it.

What is considered unnecessary use of antibiotics?⁴

- Taking or being prescribed antibiotics for infections caused by a virus
- Being prescribed the wrong type, dose or duration of antibiotics
- Taking antibiotics in ways other than how they were prescribed
- Taking leftover antibiotics without a prescription or using someone else's antibiotics

Microbes, good and bad

Every one of us is home to trillions of microscopic organisms that live naturally in our gut, on our skin, and in other areas of our body. This ecosystem of microbes, called the microbiome, helps with digestion, immunity, heart health, and more.⁵ The microbiome is passed down at birth from mother to infant and then changes over time, becoming unique to each person based on diet and environment.⁶ Science is only beginning to discover the multiple effects the microbiome has on human health.

Most of the time we exist in harmony with our microbiome. Our immune system is active all the time, preventing potentially harmful microbes from causing illness and keeping our microbiome in balance. For example, *Staphylococcus aureus*, a bacterium well known to infect humans, normally lives in the noses of about 20% of the population but rarely causes serious illness.⁷ Sometimes infections do happen, however, caused by foreign bacteria passed on from other people, animals, contaminated food or water, or by the bacteria that already co-exist in our bodies finding an opportunity to breach our immune defenses.

The immune system usually recognizes and fights off harmful microbes in just a few days. Other times, a bacterial infection might require antibiotics. Some people are at higher risk for serious illness, and even death from infections, especially the very young, the

elderly, or people who have a chronic disease or serious injury. For people receiving cancer therapy or who have a weakened immune system, it is crucial that antibiotics remain effective. Before the discovery of antibiotics, people who suffered from serious bacterial infections often died and many medical procedures were unsafe to perform. The discovery of antibiotics and other antimicrobial drugs is considered one of the most important achievements in medical history.⁸ The “Golden Age” of antibiotics between 1938 and 1952 saw the biggest declines in deaths from infectious diseases.



Saving lives with antibiotics – Vinesha's battle with childhood cancer
<https://www.youtube.com/watch?v=1E0tDPTULuM>

The way antibiotics kill or stop the growth of bacteria depends on the drug⁹. While no antibiotic can cure every infection, many antibiotics are multi-purpose (or ‘broad spectrum’) and can cure infections caused by many different bacteria, in contrast to more selective (or ‘narrow spectrum’) antibiotics. Some antibiotics, like penicillin and amoxicillin, break down bacterial cell walls so the bacteria burst and die. Other antibiotics, like erythromycin, prevent bacteria from building essential proteins. Certain antibiotics, like daptomycin, are reserved as last-resort options and are used only when other antibiotics have failed to stop an infection. The best type of antibiotic to prescribe depends on the type of bacteria causing the infection, the site and the severity of that infection.

Magic bullet or double-edged sword?

The effectiveness of antibiotics has led many to view them as “magic bullets”—medicines that could treat any infection while leaving the rest of the body unharmed.¹⁰ As our understanding of these medicines and the complex nature of our microbiome have grown, antibiotics have instead proven to be double-edged swords, because they not only kill the bacteria causing the infection but also destroy the innocent bystanders of the bacterial world. This can change the balance of the microbiome, and allow foreign microbes to invade or cause an over-growth of native microbes that is harmful. For example, yeast infections from the *Candida* fungi or diarrhea and bowel ulcers from the bacterium *C. difficile*, can be unintended consequences of antibiotic use.¹¹ Antibiotics are just like any other medication and while they offer tremendous benefits, they also carry a small risk of allergic reactions, negative interactions with other drugs, and other side effects.¹² For example, a recognized side effect of amoxicillin is a body rash that occurs if this antibiotic is given to someone who has a viral infection, such as mononucleosis or “mono”.¹³

For people with a serious infection, the benefits can far outweigh the risks of antibiotics. It is this low risk that sometimes encourages healthcare providers to prescribe antibiotics when an antibiotic treatment is not needed. Using antibiotics to fight infectious diseases is an important driver of the development of antibiotic resistance, and limiting unnecessary use can help to counter it.

The emergence of antibiotic resistance

Like all living things on earth, bacteria are constantly and quickly evolving in order to survive. Some strains of bacteria have natural genetic traits that protect them against the antimicrobial substances produced by other bacteria and fungi, with which they compete for survival (such as the mold *Penicillium* from which penicillin was discovered).¹⁸ We learned how to isolate these substances, make our own, and use them as antibiotics. As we started using more and more antibiotics to fight bacterial infections in people and animals, the problem of antibiotic resistance became apparent. Any time an antibiotic is

Discovery and the dawn of the “Golden Age” of antibiotics

The “Golden Age” of antibiotics followed the chance discovery of penicillin by Dr. Alexander Fleming. In 1928, Dr. Fleming discovered that one of his experiments with the bacterium *Staphylococcus* had become contaminated with a “white, fluffy growth”—the mold *Penicillium*.¹⁴ To his surprise, he discovered through the microscope that many of the bacteria had died as a result of the mold.¹⁴ This unexpected observation eventually led to synthesis and manufacture of the antibiotic penicillin in the 1940s.^{8, 15}

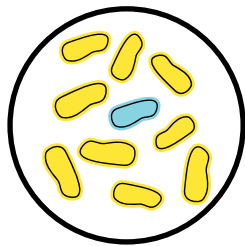
Although Dr. Fleming is widely viewed as the discoverer of antibiotics, many early 20th-century scientists were finding ways to tackle the germs infecting the population at that time.⁸ More than a decade before Fleming, German physician Dr. Paul Ehrlich coined the term *Zauberkegel* (German for “magic bullet”) during the development of Salvarsan, an arsenic-based dye designed to target syphilis like a gun’s bullet hitting a target.¹⁶ This discovery was followed by the development of sulfonamides that entered the market by 1935 and dramatically lowered deaths from pneumonia, meningitis, and other infections after childbirth.⁸ Penicillin became available in 1941 for treatment of a wide range of bacterial infections. Further research and development eventually led to the availability of semi-synthetic penicillins, cephalosporins, and carbapenems.

The discovery and development of new antibiotics has slowed considerably over recent decades.¹⁷ Today fewer than 10 of the 50 leading pharmaceutical companies have active antibiotic development programs, as most new developments are led by specialized small- and medium-sized pharmaceutical companies.¹⁷

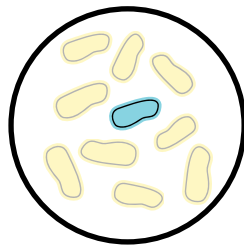
used, the bacteria with the genetic traits that protect them against the antibiotic will survive and multiply, while those without those genes die.¹⁹ The surviving bacteria multiply very quickly, in as little as 20 minutes in the case of *E. coli* bacteria. The next generation of bacteria will now also carry these resistance genes and will also be able to withstand the effect of the antibiotic. Bacteria can even share resistance genes with other bacteria, through a process called horizontal gene transfer.²⁰ Over time, as populations of bacteria are continually exposed to different antibiotics, they become increasingly resistant to ever more antibiotics until eventually, very few or no effective antibiotic treatments will be left.

The emergence of antibiotic resistance is not new. As early as 1924, four years before the discovery of penicillin, researchers had already identified a strain of syphilis that was resistant to Salvarsan, the drug used to treat the disease at that time.^{21, 22} In the years following, many forewarned of the emergence of antibiotic resistance, including Dr. Alexander Fleming, the discoverer of penicillin. True to these warnings, the first cases of penicillin-resistant bacterial infections were observed in 1945.⁸ By the mid-1950s, 90% of tested strains of *Staphylococcus aureus* were resistant to penicillin.²³

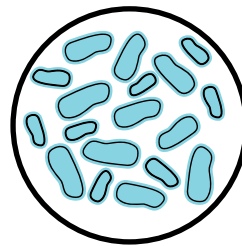
HOW ANTIBIOTIC RESISTANCE HAPPENS



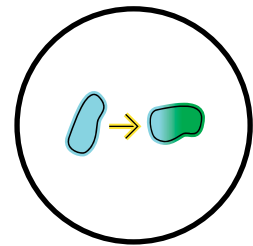
Our body is **home to countless microbes**. Some may be resistant to antibiotics



Antibiotics kill the bacteria causing the infections as well as the good bacteria



The antibiotic-**resistant bacteria** are now able to **grow and take over**



Some bacteria may **give** their antibiotic **resistance to other bacteria**



Normal bacterium



Resistant bacterium



Dead bacterium

Antibiotic resistance today

Many Canadians know someone who has been impacted by antibiotic-resistant infections. Antibiotic resistance makes it harder to fight infections, leading to more and longer hospital stays, which increase health care costs. It is estimated that 1 in 16 Canadians admitted to hospital will develop an infection from a resistant superbug²⁴ and that 7 in 10 Canadians worry about the risk of infection at hospitals and healthcare facilities.²⁵ Progress has been made in Canada and rates of antibiotic resistance are lower than in many other countries in the world. For example, worldwide, the rate of infections caused by Enterobacteriaceae resistant to a last line of defence class of antibiotics called carbapenems has increased over time, but in Canada

it has remained low and relatively stable.³ That said, there has been a five-fold increase in bacteria resistant to carbapenems found in people who do not have an infection, suggesting that these bacteria are becoming more common in Canada. The rate of methicillin-resistant *Staphylococcus aureus* infections (often called MRSA) acquired in hospital decreased slightly between 2012 and 2017, but the rate of MRSA infection acquired in the community increased over that time period. Similarly, while hospital associated *C. difficile* infection rates declined in previous years, *C. difficile* infection rates acquired in the community remained stable since 2015. Rates of resistant gonorrhoea infections, one of the most commonly sexually transmitted diseases in Canada, have also risen over the past decade: now more than 50% of gonorrhoea infections are due to bacteria that are resistant to at least one antibiotic.²⁶

ANTIBIOTIC RESISTANCE IN CANADIAN COMMUNITIES

Methicillin-resistant
Staphylococcus aureus infections

INCREASED BY
60%

since 2012

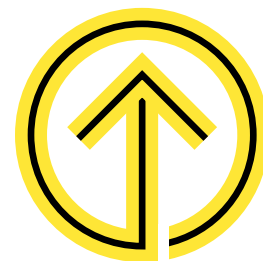


MORE THAN
50%

of all gonorrhoea
infections are

RESISTANT

to at least one antibiotic



C. difficile infections

REMAINED
stable

since 2015



5x INCREASE

in people carrying the

BACTERIA RESISTANT

to carbapenems which are
amongst the most powerful
antibiotics that exist





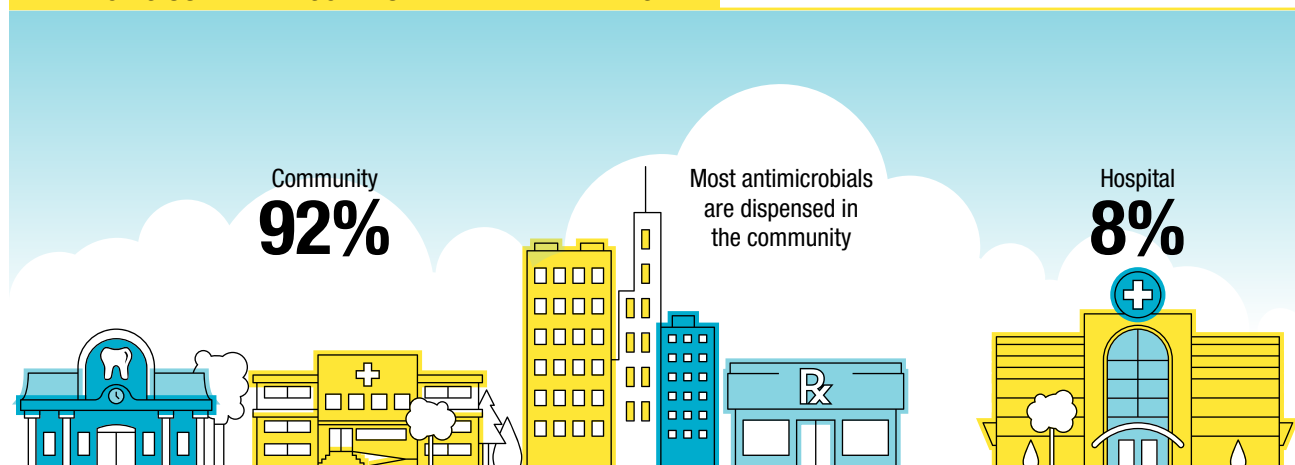
Antibiotic use in Canada

Healthcare providers recommend an antibiotic prescription most often for common illnesses, such as respiratory and urinary tract infections in adults or for ear infections in children.³ In 2017 alone, Canadians filled over 24 million antibiotic prescriptions, primarily in community pharmacies.³ However, we do not know how many of these prescriptions in Canada are provided unnecessarily for illnesses such as the common cold, flu (influenza), or viral sore throat.²⁶ In the United States, national data suggest that 30% of oral antibiotics are unnecessary.²⁷

General and family practitioners prescribe about 65% of antibiotics in the community; dentists, nurses and pharmacists prescribe about 22%; and other medical specialists prescribe the rest.²⁶ More antibiotics are prescribed to Canadians over age 60 than to younger people.³ Antibiotic use varies across Canada, with the highest prescription rates being observed in Prince Edward Island and Newfoundland and Labrador combined, and the lowest in the territories, followed by Quebec and British Columbia in 2017.³



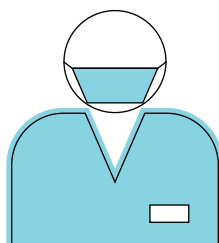
ANTIBIOTIC USE IN THE COMMUNITY AND PRIMARY CARE



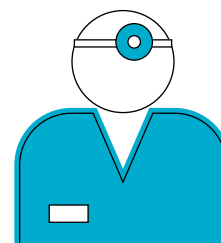
TYPES OF ANTIBIOTIC PRESCRIBERS IN THE COMMUNITY



65% prescribed by
general practitioners
and doctors

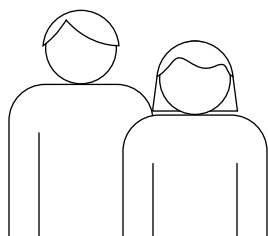


22% prescribed by
dentists, nurses and
pharmacists

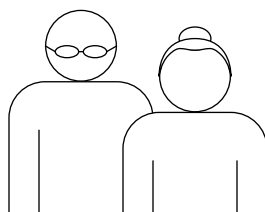


13% prescribed
by other specialists
(e.g. dermatologists
and pediatricians)

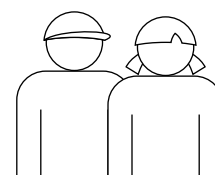
MOST COMMON INFECTIONS TREATED WITH ANTIBIOTICS



Respiratory tract infections



Urinary tract infections



Ear infections



Antibiotic prescription: the cultural ingredients

Why do people take antibiotics when they might not need them? Like many aspects of health care, the decision is more than just a medical one. As described in detail below, prescription and use of antibiotics is driven by many factors. The trusting relationship between patients and healthcare providers is particularly important to prevent unnecessary use of antibiotics. This relationship can be influenced by organizational factors, such as how busy the medical clinic is, the medical culture in the clinic, and the availability of guidelines and tools. At the broader level, how we view antibiotics as a society and our public expectations about how they work and when they should be used also play a part in unnecessary antibiotic use. Together these factors create a culture that can influence antibiotic prescribing.

Most of the research on how these social factors influence antibiotic prescribing comes from other countries. There is a lack of information on what is driving Canadians to use antibiotics unnecessarily. Here we describe what is happening in countries similar to Canada, starting with the relationship between patients and their healthcare provider, then to factors within the medical system, and then finally, to societal views about antibiotics.



Patient & provider relationships

The relationship that nurses, doctors, and other healthcare providers build with their patients is one of the most important predictors of antibiotic use.

CLEAR COMMUNICATION

Patients and healthcare providers who trust each other and have a good relationship generally have better communication on health issues. Patients who ask questions and listen to options take antibiotics less often. Similarly, providers who know their patient, listen to their patient, and are able to explain a course of action in an understandable way are less likely to prescribe unnecessary antibiotics.²⁸⁻³¹



MISUNDERSTANDINGS

Misunderstandings can lead to unnecessary antibiotic use.^{32–35} Healthcare providers sometimes think that their patients expect an antibiotic prescription, when in reality they seek advice and reassurance.³⁶ For example, parents of young children might want to make sure their child's illness isn't serious or want advice on how to help their child feel better, instead of specifically seeking antibiotics. At times, providers may also prescribe an antibiotic to maintain positive relationships with their patients or

believe that a patient's satisfaction is associated with leaving the medical visit with a prescription.^{37–39}

Organizational factors

When healthcare providers prescribe antibiotics, they do so within a medical practice and within the broader healthcare system. Certain factors in this system can influence the relationship between patients and providers and affect the likelihood of unnecessary prescription of an antibiotic.

TIME PRESSURES AND QUICK FIXES

Saving time can be a motivating factor for both patients and healthcare providers. In busy clinics, healthcare providers may have little time for each patient and writing a prescription can be a fast way to conclude a doctor's office visit.^{32, 40, 41} This time pressure can affect the relationship, as there may be less time for healthcare providers to share information and for patients to ask questions.

Outside the clinic, time pressures can also be a motivating factor for a patient who is sick and not attending work or school.²⁸ In this case, receiving a prescription can help justify the person's need to stay

Seeking reassurance for a child's ear infection in a busy medical clinic: Amanda's story



"It was a few years back when the incident happened. My daughter was two and a half years old. It was in the middle of the night and she had been up a few times. She barely had a fever yet was upset and crying. The next morning, a Saturday, I did not know if I should seek care since our family doctor's office was closed. I had heard about a walk-in clinic that was open on the weekend and decided to go there because I did not want to wait until Monday for her family doctor.

I went mostly because I wanted to know what she had. I thought she had an ear infection but wasn't 100% sure and if it was something more serious, I wanted to make sure. You hear of people who do not seek care in these situations, thinking that it is nothing serious, and then it turns out to be meningitis. This is why it is important to get these issues documented and recorded.

After we arrived at the clinic, my daughter was seen fairly quickly by a doctor and a medical student. Almost immediately, I was told that my daughter had an ear infection, that kids get these all the time, and then received a prescription for an antibiotic called amoxicillin. The doctor and the medical student left the room immediately after. The whole encounter lasted less than five minutes and I felt very rushed and unimportant. There was no opportunity to discuss alternative options. I did not feel comfortable to voice my concerns to the doctor because I did not want to make her look bad in front of her medical student. I took the prescription but did not get it filled. Instead, I went home, gave my daughter a Tylenol, and had her rest. A day or two later, she was feeling better."



We need to use the right antibiotic at the right time <https://www.youtube.com/watch?v=YqgRmcblFbc>

home and rest¹⁰ or, in other cases, may be perceived as a way to get back to work more quickly.^{28, 42, 43} A person's ability to take time off from work due to illness depends on where they work, the type of work they do, and their financial situation. Organizations with sick-leave policies make it easier for employees to rest at home, which also prevents the spread of infection and keeps the rest of an organization's workforce healthy. But when a parent needs to return to work and bring their children back to daycare or school, they often feel pressure to ask for an antibiotic prescription.²⁸

MEDICAL CULTURE

Like all people, healthcare providers can be influenced by their peers' beliefs and actions. In medical clinics where antibiotics are over-prescribed, it can become the accepted practice or norm for all the providers. In these clinics there is limited feedback from colleagues that can caution against inappropriate prescribing.^{44–46}

DIAGNOSTIC UNCERTAINTY

Some healthcare providers may be less comfortable with not knowing the cause of an infection, when dealing with ambiguous patient symptoms such as a sore throat or cough. This diagnostic uncertainty is one of the most commonly cited causes of inappropriate antibiotic prescribing.^{29, 47} More than two thirds of family

doctors who prescribed antibiotics unnecessarily in the United Kingdom said that they did so because they did not know whether an infection was viral or bacterial.⁴⁸ To avoid this feeling of “not knowing” and to minimize the unlikely possibility of missing a serious bacterial infection, healthcare providers sometimes prescribe, and patients sometimes request, antibiotics when these may not be needed.^{28–30, 49, 50}

MEDICAL GUIDELINES AND ANTIBIOTIC PRESCRIBING POLICIES

Healthcare providers often receive guidance (called clinical practice guidelines) to help them make medical decisions. Few guidelines around the world consider antibiotic resistance in their recommendations.⁵¹ Roughly two out of three medical guidelines for common infectious illnesses (pneumonia, urinary tract infections, ear infection, sinus infection, and sore throat) used in mainly high-income countries do not consider antibiotic resistance in their recommendations.⁵¹ That said, it is unclear from the available evidence to what extent medical guidelines have an impact on healthcare providers' decisions to prescribe antibiotics.³⁸ For example, one Canadian study reported that providing physicians and pharmacists with user-friendly, web-based guidelines targeting the most common infectious conditions resulted in an immediate decrease in antibiotic use that lasted for at least three years.⁵² However, another study suggested

that passive guideline circulation alone is not enough to ensure that physicians are aware of, and follow, new and updated guidelines.⁵³

Societal factors

PUBLIC EXPECTATIONS

Between 1950 and 2012, the death rate from infectious diseases in Canada declined by 62% for men and 57% for women.⁵⁴ While most of the improvement was the result of public health efforts such as routine childhood vaccination, improvements in food safety, access to potable water and improved sanitation measures, Canadians also benefitted immensely from the use of antibiotics.⁵⁴ The societal benefit of antibiotics in reducing deaths from infectious disease has shaped our expectations that antibiotics can be widely used to quickly treat all infections, a practice that in turn reduces their effectiveness.¹⁰

Antibiotic prescriptions are so routine that patients sometimes expect a prescription as a regular part of their medical visit. A patient might specifically request an antibiotic believing that it will help get rid of a cold or influenza, or help a child who is ill.^{48, 55} In the United Kingdom, almost 1 in 10 adults who visit a medical clinic expected to have antibiotics prescribed every time or most times they visit.⁴⁸

PUBLIC KNOWLEDGE

Antibiotic resistance is complex, and many people do not fully understand the role of antibiotics in the development of antibiotic-resistant bacteria. About one in three people in the United Kingdom have not heard of “antibiotic resistance” and about one in four people do not believe it is due to unnecessary antibiotic use.⁵⁹ Research also suggests that most people believe antibiotic resistance is developed by the human body, rather than by bacteria, and believe that minimizing antibiotic resistance is beyond their control.⁵⁹ Patients may need information from their healthcare provider on how antibiotics work, the types of infections they are used for, as well as a warning that they should not be saved for future use.^{60, 61}

Urinary tract infections in seniors

Antibiotics are frequently prescribed for urinary tract infections when they are not always necessary. This can in part be driven by family members’ expectations for antibiotics for elderly relatives.⁵⁶ As in other parts of the body, the urinary tract is populated by microbes that change over time and presence of bacteria does not always indicate an infection that requires treatment.⁵⁷ The need for antibiotics depends on symptoms of urinary tract infection, which can be difficult to determine for elderly patients, especially those with dementia.⁵⁸ Caregivers seeking medical care for elderly family members may need advice and reassurance in particular when a patient can’t advocate for him/herself.

Healthcare access challenges in rural and remote communities: Dr. Peter Daley’s story



“In my experience working in Newfoundland, community context matters and access to health care can impact antibiotic use. We hear from some patients that they stockpile antibiotics at home for use and sharing when needed. We also hear about physicians giving antibiotics by phone without examining patients. There are some incredibly remote areas, where a physician is not regularly available. This lack of access may lead to stockpiling of antibiotics in anticipation.”



What can be done to reduce unnecessary antibiotics?

There are a number of ways that patients, healthcare providers, and health system leaders can help reduce unnecessary use of antibiotics.

What patients can do

The public can help prevent the problem of antibiotic resistance by trying to avoid infections and using antibiotics appropriately when infections occur.

Protect yourself from infection. An easy way to reduce your risk of catching an infection is to wash your hands before eating or preparing food, after using the washroom, and after coughing or blowing your nose. Also, when you are sick, stay home, if possible, to avoid spreading germs, and avoid close contact with other people until you feel better. Cough and sneeze into your arm, not your hands. Maintaining a healthy lifestyle, including healthy diet and physical activity, can help keep you well. You can also use condoms to protect yourself and others from infections that can spread through sexual contact, including antibiotic-resistant gonorrhea.

Keep vaccinations up to date. These can protect you and your family members from various bacterial infections. For example, the DTaP vaccine protects against the bacteria that cause diphtheria, tetanus,

and whooping cough, while the meningococcal vaccine prevents infection by bacteria that can cause meningitis.⁶² Of note, research has shown that young children who receive a pneumococcal vaccine need fewer antibiotics for ear infections than children who are not vaccinated.⁶³

Antibiotics are often unnecessarily prescribed for symptoms of influenza, a viral respiratory infection. If you catch influenza, antibiotics will not help with symptoms. Getting the yearly influenza vaccine may help you avoid influenza and avoid spreading it to others. The introduction of the universal influenza immunization program in Ontario has been shown to reduce the number of influenza-associated antibiotic prescriptions in the province.⁶⁴ In addition, the influenza vaccine is associated with reductions in middle ear infections and less use of antibiotics in children.⁶⁵

If you do get sick, **always speak with a healthcare provider before using antibiotics.** Antibiotics work through various mechanisms and not all antibiotics work for all infections. To avoid contributing to the development and spread of antibiotic resistance, you should always follow the treatment directions given to you by a healthcare provider and not take leftover antibiotics, or antibiotics that have not been prescribed for you.

Talk to your provider and ask questions. You can ask whether an antibiotic prescription is really necessary and talk about your expectations around antibiotics. Nurses, doctors, and other healthcare professionals sometimes assume that their patients want an antibiotic and feel obliged to prescribe one, when what patients are really seeking is reassurance about the seriousness of their health problem and clear communication.³⁶ Having an open conversation with your provider about your views and concerns can help avoid these misunderstandings. While one unnecessary dose of antibiotics might seem like a small concern, a study from the United States suggests that one in four antibiotics are prescribed in situations where they are definitely not needed, and another one in three are prescribed for conditions where they may not be needed.⁶⁶

Remember your immune system and your microbiome. Your body has a built in defense mechanism to fight off infection and antibiotics are not always necessary. Antibiotics only work against infections caused by bacteria; antibiotics can't make you feel better when you have a cold, influenza or other viral illness. Oftentimes, infections caused by bacteria or viruses will go away on their own; in fact, 7 out of 10 people feel better within a week, whether or not they use antibiotics for bronchitis⁶⁸ and 9 out of 10 people feel better within one to two weeks, whether or not they use antibiotics for sinus infections.⁶⁹ Antibiotics also have side effects and can destroy the normal bacteria that make up your microbiome and help keep you healthy.

Five questions to discuss with your healthcare provider⁶⁷

1. What are you most worried about?
2. What are you expecting from today's visit?
3. What are your treatment options?
4. What are the benefits and harms of antibiotics?
5. What do you think about the options?

What healthcare providers can do

Take the time to talk with patients about their health and foster good relationships. This can go a long way to preventing overuse of antibiotics. Share your knowledge about antibiotics, how they work, and ways to feel better when the infection is likely caused by a virus. You can also counsel your patients not to save antibiotics for future infections. Given that 600 million medical prescriptions are dispensed in community pharmacies in Canada every year and pharmacists already play an important role during the quality check of prescriptions⁷⁰, pharmacists are well positioned to engage patients at the time of purchasing an antibiotic, and to assist practitioners in determining the optimal treatment.⁷¹

Shared decision making is recognized as an effective strategy for reducing overuse of treatments in general and reducing decisional conflict around treatment options.⁷² In shared decision making, providers help their patients make informed decisions about treatment by discussing benefits and harms, and taking time to understand their values and preferences. Evidence shows that passive sharing of information with patients through posters and leaflets is not enough to reduce antibiotic use.^{73, 74}





Taking time to discuss treatment options with patients: A nurse's story in a wound clinic

"Mr. S, an older patient, arrived at our wound clinic after suffering from leg ulcers for two years. During that time he was repeatedly treated with antibiotics. He said that the antibiotics he was taking were ending that day and he desperately needed a prescription renewal because he continued to experience burning pain and itching.

Upon examination, it became evident that he was actually suffering from a skin reaction caused by water retention in his legs. It was clear that he required compression and steroids instead of antibiotics. However, Mr. S was very skeptical when we told him of our treatment plan—he was so worried...he said that if we did not give him antibiotics he would go to a local emergency department to ask for them. Ordinarily we would see a patient like Mr. S three to four weeks after his initial visit but we negotiated with him. If he stayed off the antibiotics, we would see him much sooner, after a week. We also told him to contact our office if his symptoms worsened. At his one-week follow-up, Mr. S walked into our clinic all smiles and hugged every member of our staff. He mentioned that within 24 hours his burning pain had subsided. Now he is receiving daily nursing visits and we anticipate that within one month, his wounds will heal and he will be ready for home care."

Promote appropriate antibiotic use. Several organizations have developed tools that may help in this effort, including delayed prescriptions and viral prescriptions. A delayed prescription for antibiotics is intended to be filled in a few days if symptoms do not improve, allowing time for lab tests to come back or for a person's body to fight the infection on its own. In a similar manner, "viral prescriptions" explain why an antibiotic isn't being prescribed and provide instruction on things the patient can do to feel better (such as rest, drink plenty of fluids, take over-the-counter pain relief medication, etc.). While more research is needed to determine their effectiveness in the Canadian context, evidence from outside Canada suggests they are good tools to manage risks and reduce unnecessary

antibiotic use.^{75–78} Working with a researcher or research team to rigorously test these interventions in your practice is another way you can help determine whether such strategies are effective.

As healthcare conditions can influence antibiotic prescribing behaviours, healthcare providers could benefit from innovative solutions to help them tackle organizational or structural challenges, such as time-pressure or access-to-care issues. For example, telemedicine (providing medical care from a distance using information and/or telecommunications technology) may help remove barriers by offering an alternative way for patients to access health care in remote Canadian regions.⁷⁹

Stay up to date on antibiotic prescription guidelines and best practices, along with local antibiotic resistance patterns. This can help you make informed choices about which antibiotics to use. Appropriate prescribing is about more than just knowing when to prescribe and when not to prescribe an antibiotic. It is also about making a decision to provide the right drug, in the right dose, at the right time, for the right duration. For example, it is important not to use a broad spectrum antibiotic for an infection where a narrow spectrum antibiotic would be effective. How long to advise patients to take antibiotics has also evolved. It used to be common to tell patients to finish the whole course of antibiotics, due to concerns about ineffectiveness of shorter treatment periods and increased risk of antibiotic resistance. However, neither of these concerns is supported by scientific evidence.^{80, 81} When discussing the duration of treatment with patients, healthcare providers can take a more tailored approach that considers the patient, the reason for antibiotics and duration compared with the best available evidence.^{80, 81}

To improve prescribing, providers can take advantage of opportunities to engage in continuing professional education around antibiotic prescribing and antibiotic resistance. Research suggests that giving healthcare providers access to in-person educational seminars on appropriate prescribing can reduce unnecessary antibiotic prescribing.^{82–84}

What health system leaders can do

Health system leaders working in medical associations, government, medical accreditation bodies, and other groups, can work collectively to address antibiotic use. More judicious use of antibiotics has the potential to benefit health care systems in multiple ways, such as by reducing costs and improving quality of care.^{85, 86}

Promote positive antibiotic prescribing practices.

There is strong evidence in other countries that providing feedback to healthcare providers on their prescribing habits is an effective way to improve appropriate antibiotic use.^{73, 87, 88} Given that healthcare providers are influenced by their peers, providing information that compares

them with their top-performing colleagues is particularly effective, especially when combined with a “nudge” or alert to provide a justification when entering a prescription into an electronic medical record.⁸⁹ Of note, while the availability of some rapid diagnostic tools may help healthcare providers manage the issue of diagnostic uncertainty and to optimize the antibiotic treatment duration^{90, 91}, their impact on antibiotic prescribing practices in community and primary care environments remains poorly understood.⁹² It is important to rigorously assess these actions to determine their effectiveness in the Canadian context.

Share knowledge, skills, and training. It takes a village of providers to guide appropriate use of antibiotics. Inter-professional organizations for nurses, doctors, dentists and pharmacists, all guided by different standards and protocols, can be brought together to develop and implement core competencies on appropriate prescribing, patient communication and shared decision making. These can also be included in medical and health curricula and continuing education programs.

At the same time, educational campaigns using a variety of formats geared to different populations such as parents and seniors can help promote appropriate antibiotic use.^{90, 93} Educational campaigns in medical clinics for parents of young children have shown effectiveness in reducing overall antibiotic use.⁹⁰ Nationwide and community-level communication campaigns have also been shown to result in fewer unnecessary antibiotic prescriptions, especially for viral respiratory tract infections. Primarily tested in the United States and Europe, these types of campaigns use a variety of formats geared toward specific populations (like parents and older adults) and healthcare providers. A prominent and promising Canadian example is the “Do Bugs Need Drugs?” program in British Columbia that is not only targeting healthcare providers but also other groups such as children, teachers and seniors. There was also a 13% decrease in antibiotic prescription rates during the time of this initiative (2005–2018).⁹⁴ Campaigns alone without other providers and organizational interventions are not as effective as those linked with other actions.⁹³

Finally, patient-focused posters and brochures alone are ineffective at decreasing antibiotic use.^{73, 95}

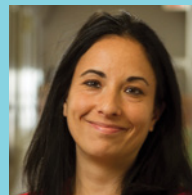
Continue investing in research and surveillance.

There are no or limited data in Canada to show how many antibiotics are prescribed appropriately.²⁶ This type of data, along with other information, can provide a way to measure how well actions are working to improve appropriate antibiotic use. Across the country, we see regional differences in overall antibiotic use, but there is insufficient information to understand why these differences exist and how much of these differences is due to unnecessary use.

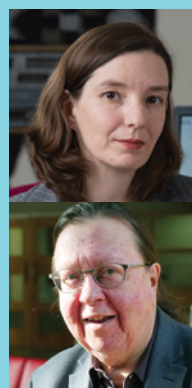
There is very little social science research in Canada that focuses on patient-provider relationships, expectations and beliefs around antibiotics, and how various social factors shape unnecessary use. Among the studies that exist in peer countries, it is unclear whether findings can be applied to the Canadian context.^{49, 96} More information is needed to understand how community contexts (such as geography, infection patterns, public health activities, etc.) vary and influence healthcare providers' decisions around antibiotic prescription. In Canada and abroad, research on antibiotic use tends to focus on the knowledge and attitudes of patients and providers, with much less focus on the health system and societal factors that may be at play.

More research is needed on actions to promote appropriate antibiotic use in Canada, particularly around whether existing programs, policies, and stewardship initiatives work, which elements are most effective, and how they work to improve antibiotic prescribing in the community. Given the size of Canada and variation across the country, in terms of cultures and contexts, more rigorous assessments are needed to inform our current efforts. To plan effective strategies, it is important to know why and how something works to encourage appropriate antibiotic prescribing.

Examples of research underway in Canada to better understand the social and cultural factors influencing antibiotic use in specific populations:



Dr. Dubé is conducting a new population-based study looking at anti-microbial resistance knowledge, attitudes, beliefs and practices of people in Quebec.



Dr. Hindmarch and Dr. King, in collaboration with Indigenous researchers, are conducting research to understand Indigenous people's perspectives around antimicrobial resistance.



Preserving antibiotics now and into the future

The decision to prescribe and use antibiotics is shaped by more than medical needs. Unnecessary antibiotic use is also influenced by our relationship with our healthcare providers, the culture of medicine and the health system, and our collective expectations about how antibiotics work.

Taking a clear and stepped approach can help us reduce unnecessary use of antibiotics. It is important to take action by implementing and evaluating promising behavioural interventions, while at the same time building the collaborations necessary within and across communities. Pharmacists, nurses and doctors can all work together to implement common protocols and to support more social science research and surveillance.

As patients, ask your provider if you really need an antibiotic. Explore other options and other potential causes of your illness and/or discomfort. If you need an antibiotic, take it as indicated and return any unused medication to a pharmacy. Also, we can all practice infection prevention through simple measures like hand washing, avoiding spreading illness to others and keeping vaccinations up to date.

For providers and your member associations, you can collaboratively explore opportunities to share competencies, protocols, training and feedback opportunities. Additionally, there are tools and initiatives underway across Canada that you can implement in your practice and measure what works. In these ways, we can each personally contribute to ongoing coordinated efforts taking place across the country to tackle antibiotic resistance.

Public health and health system leaders can strengthen and sharpen the evidence base by better understanding antibiotic use in Canada and what works to decrease unnecessary use. This clearly requires partnerships between health and social scientists.

While research from peer countries is helpful and informative, we need to better understand Canadian decisions to take antibiotics and healthcare provider decisions to prescribe them. We need to understand how living in poverty, living in rural regions, or having inadequate access to healthcare may be affecting antibiotic use across the country, so we can work to enable all Canadians to enjoy good health regardless of their social circumstances and where they live. Likewise, we can build partnerships across the country to develop, adopt, test, and scale actions that show promise in promoting appropriate antibiotic use in Canada.

Recognizing that reducing unnecessary antibiotic prescribing in community settings is but a small cog in the bigger articulation of work to combat antimicrobial resistance, I look forward to using the findings from this Spotlight Report and the forthcoming Pan-Canadian Action Plan to work with leaders across the country. Together, we can take action to preserve the infection-fighting ability of antibiotics now and into the future.

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Acknowledgements

Many individuals and organizations have contributed to the development of Handle with Care: Preserving Antibiotics Now and Into the Future: The Chief Public Health Officer of Canada's Spotlight Report 2019.

I would like to express my appreciation to the committee of public health and antibiotic resistance experts who provided invaluable advice and expertise in reviewing many drafts:

- **Dr. Peter Daley**
Associate Professor of Medicine,
Infectious Diseases, Memorial University
- **Dr. Ève Dubé**
Medical Anthropologist, Institut national
de la santé publique du Québec
- **Dr. Yoav Keynan**
Scientific Lead, National Collaborating Centre
on Infectious Disease, and Associate Professor,
Microbiology and Infectious diseases,
University of Manitoba
- **Prof. Helen Lambert**
Medical Anthropologist, Bristol Medical School,
University of Bristol, United Kingdom
- **Dr. David Mowat**
Former Medical Health Officer,
Peel Health Region, Ontario
- **Dr. Cory Neudorf**
Professor, Department of Community Health and
Epidemiology, College of Medicine, University
of Saskatchewan and, Medical Director,
Health Surveillance & Reporting,
Saskatchewan Health Authority
- **Dr. David Patrick**
Interim Executive Director, British Columbia Centre
for Disease Control

- **Dr. Michael Routledge**
Medical Officer of Health, Manitoba Health,
Seniors and Active Living Medical Officer
of Health, Manitoba
- **Dr. James Brooks**
AMR Surveillance Lead, Public Health Agency
of Canada and Assistant Professor of Medicine,
University of Ottawa.

In addition, I would also like to recognize the assistance and report contributions made by partners and stakeholders, including:

- Expert Advisory Group on Antimicrobial Resistance to the CPHO ([link to membership](#));
- CPHO Health Professional Forum ([link to membership](#));
- Michael G. DeGroote Cochrane Canada and GRADE Centres (McMaster University);
- Canadian Nurses Association;
- Canadian Patient Safety Institute; and
- Association of Medical Microbiology and Infectious Disease Canada.

I would also like to extend sincere thanks to the many experts and staff within the Public Health Agency of Canada and Health Canada for review of and input into the report.

I appreciate the excellence and dedication of my CPHO Reports Unit throughout the development of this report: Éline Chatigny, Bonnie Hostrawser, Dr. Marie Chia, Dr. David Grote, Dr. Marianne Gee, Debjani Mitra, Elyse Fortier, Susan Rogers Van Katwyk, Edrich Richards and Rhonda Fraser.



References

- 1 <https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance>.
- 2 O'Neill, J. Antimicrobial resistance: Tackling a crisis for the health and wealth of nations. The Review on Antimicrobial Resistance. (2014).
- 3 <https://www.canada.ca/en/public-health/services/publications/drugs-health-products/canadian-antimicrobial-resistance-surveillance-system-2018-report-executive-summary.html>.
- 4 <https://www.canada.ca/en/public-health/services/antibiotic-antimicrobial-resistance/about-antibiotic-resistance.html>.
- 5 Blum, H. E. The human microbiome. *Adv. Med. Sci.* **62**, 414-420 (2017).
- 6 Ursell, L. K., Metcalf, J. L., Parfrey, L. W. & Knight, R. Defining the human microbiome. *Nutr. Rev.* **70 Suppl 1**, S38-44 (2012).
- 7 Brown, A. F., Leech, J. M., Rogers, T. R. & McLoughlin, R. M. Staphylococcus aureus Colonization: Modulation of Host Immune Response and Impact on Human Vaccine Design. *Front. Immunol.* **4**, 507 (2014).
- 8 Mohr, K. I. History of Antibiotics Research. *Curr. Top. Microbiol. Immunol.* **398**, 237-272 (2016).
- 9 Kohanski, M. A., Dwyer, D. J. & Collins, J. J. How antibiotics kill bacteria: from targets to networks. *Nat. Rev. Microbiol.* **8**, 423-435 (2010).
- 10 Chandler, C., Hutchinson, E. & Hutchison, C. Addressing Antimicrobial Resistance through Social Theory. (2016).
- 11 Keeney, K. M., Yurist-Doutsch, S., Arrieta, M. C. & Finlay, B. B. Effects of antibiotics on human microbiota and subsequent disease. *Annu. Rev. Microbiol.* **68**, 217-235 (2014).
- 12 Cunha, B. A. Antibiotic side effects. *Med. Clin. North Am.* **85**, 149-185 (2001).
- 13 Chew, C. & Goenka, A. QUESTION 2: Does amoxicillin exposure increase the risk of rash in children with acute Epstein-Barr virus infection? *Arch. Dis. Child.* **101**, 500-502 (2016).
- 14 Fleming, A. On the Antibacterial Action of Cultures of a Penicillium, with Special Reference to their Use in the Isolation of B. influenzae. *Br. J. Exp. Pathol.* **10**, 226-236 (1929).
- 15 Aminov, R. History of antimicrobial drug discovery: Major classes and health impact. *Biochem. Pharmacol.* **133**, 4-19 (2017).
- 16 Heynick, F. The original 'magic bullet' is 100 years old – extra. *Br. J. Psychiatry* **195**, 456 (2009).
- 17 Hesterkamp, T. Antibiotics Clinical Development and Pipeline. *Curr. Top. Microbiol. Immunol.* **398**, 447-474 (2016).
- 18 Nesme, J. & Simonet, P. The soil resistome: a critical review on antibiotic resistance origins, ecology and dissemination potential in telluric bacteria. *Environ. Microbiol.* **17**, 913-930 (2015).
- 19 Andersson, D. I. & Hughes, D. Selection and Transmission of Antibiotic-Resistant Bacteria. *Microbiol. Spectr.* **5**, 10.1128/microbiolspec.MTBP-0013-2016 (2017).
- 20 Juhas, M. Horizontal gene transfer in human pathogens. *Crit. Rev. Microbiol.* **41**, 101-108 (2015).
- 21 Stekel, D. First report of antimicrobial resistance pre-dates penicillin. *Nature* **562**, 192-018-06983-0 (2018).
- 22 Silberstein, S. Zur Frage der salvarsanresistenten Lues. *Archiv für Dermatologie und Syphilis* **147**, 116 (1924).
- 23 Munch-Petersen, E. & Boundy, C. Yearly incidence of penicillin-resistant staphylococci in man since 1942. *Bull. World Health Organ.* **26**, 241-252 (1962).
- 24 Martin, P. *et al.* Prevalence of antibiotic-resistant organisms in Canadian Hospitals. Comparison of point-prevalence survey results from 2010, 2012, and 2016. *Infect. Control Hosp. Epidemiol.* **40**, 53-59 (2019).
- 25 www.nhlc-cnls.ca/assets/2016%20Ottawa/NHLCIpsosReportJune1.pdf.
- 26 <https://www.canada.ca/en/public-health/services/publications/drugs-health-products/canadian-antimicrobial-resistance-surveillance-system-2017-report-executive-summary.html>.
- 27 Fleming-Dutra, K. E. *et al.* Prevalence of Inappropriate Antibiotic Prescriptions Among US Ambulatory Care Visits, 2010-2011. *JAMA* **315**, 1864-1873 (2016).
- 28 Harbarth, S. & Monnet, D. L. in *Antibiotic Policies: Fighting Resistance* (eds Gould, I. M. & van der Meer, J. W.) 29-40 (Springer US, Boston, MA, 2008).

- 29 Deschepper, R. *et al.* Are cultural dimensions relevant for explaining cross-national differences in antibiotic use in Europe? *BMC Health Serv. Res.* **8**, 123 (2008).
- 30 Pechere, J. C. Patients' interviews and misuse of antibiotics. *Clin. Infect. Dis.* **33 Suppl 3**, S170-3 (2001).
- 31 Rosman, S. in *Les pratiques de prescription des antibiotiques en médecine générale en France et aux Pays-Bas* 81-99, (2010).
- 32 Cadieux, G., Tamblyn, R., Dauphinee, D. & Libman, M. Predictors of inappropriate antibiotic prescribing among primary care physicians. *Canadian Medical Association journal* **177**, 877 (2007).
- 33 McNulty, C. A. M., Nichols, T., French, D. P., Joshi, P. & Butler, C. C. Expectations for consultations and antibiotics for respiratory tract infection in primary care: the RTI clinical iceberg. *Br. J. Gen. Pract.* **63**, e429-36 (2013).
- 34 Rowan, M. & Thompson, C. Building Canada's Antimicrobial Stewardship Action Plan: Issues and insights from interviews with key informants. (2016).
- 35 Avorn, J. & Solomon, D. H. Cultural and economic factors that (mis) shape antibiotic use: the nonpharmacologic basis of therapeutics. *Ann. Intern. Med.* **133**, 128-135 (2000).
- 36 Bosley, H., Henshall, C., Appleton, J. V. & Jackson, D. A systematic review to explore influences on parental attitudes towards antibiotic prescribing in children. *J. Clin. Nurs.* **27**, 892-905 (2018).
- 37 Ternhag, A., Grunewald, M., Naucier, P. & Wisell, K. T. Antibiotic consumption in relation to socio-demographic factors, co-morbidity, and accessibility of primary health care. *Scand. J. Infect. Dis.* **46**, 888-96 (2014).
- 38 Teixeira Rodrigues, A., Roque, F., Falcao, A., Figueiras, A. & Herdeiro, M. T. Understanding physician antibiotic prescribing behaviour: a systematic review of qualitative studies. *Int. J. Antimicrob. Agents* **41**, 203-212 (2013).
- 39 Coenen, S. *et al.* Appropriate international measures for outpatient antibiotic prescribing and consumption: recommendations from a national data comparison of different measures. *Jac* **69**, 529-534 (2013).
- 40 Daneman, N. *et al.* Influences on the start, selection and duration of treatment with antibiotics in long-term care facilities. *CMAJ* **189**, E851-E860 (2017).
- 41 Fleming-Dutra, K. E., Bartoces, M., Roberts, R. M. & Hicks, L. A. Characteristics of Primary Care Physicians Associated With High Outpatient Antibiotic Prescribing Volume. *Open Forum. Infect. Dis.* **5**, ofx279 (2018).
- 42 Touboul Lundgren, P., Khouri, P. & Pradier, C. [How to raise awareness about antibiotics and vaccination among French teenagers?]. *Sante Publique* **29**, 167-177 (2017).
- 43 Borg, M. A. National cultural dimensions as drivers of inappropriate ambulatory care consumption of antibiotics in Europe and their relevance to awareness campaigns. *J. Antimicrob. Chemother.* **67**, 763-7 (2012).
- 44 Daneman, N. *et al.* Influences on the start, selection and duration of treatment with antibiotics in long-term care facilities. *CMAJ* **189**, E851-60 (2017).
- 45 Doyon, S. *et al.* Quantitative evaluation of a clinical intervention aimed at changing prescriber behaviour in response to new guidelines. *J. Eval. Clin. Pract.* **15**, 1111-7 (2009).
- 46 Livorsi, D. J. *et al.* Setting the Research Agenda for Preventing Infections From Multidrug-Resistant Organisms in the Veterans Health Administration. *Infect. Control Hosp. Epidemiol.* **39**, 186-188 (2018).
- 47 Gaygisiz, U., Lajunen, T. & Gaygisiz, E. Socio-economic factors, cultural values, national personality and antibiotics use: A cross-cultural study among European countries. *J Infect Public Health* **10**, 755-760 (2017).
- 48 Cole, A. GPs feel pressurised to prescribe unnecessary antibiotics, survey finds. *BMJ* **349**, g5238 (2014).
- 49 van Duijn, H. *et al.* Patients' views on respiratory tract symptoms and antibiotics. *Br. J. Gen. Pract.* **53**, 491-492 (2003).
- 50 Deschepper, R., Vander Stichele, R. H. & Haaijer-Ruskamp, F. M. Cross-cultural differences in lay attitudes and utilisation of antibiotics in a Belgian and a Dutch city. *Patient Educ. Couns.* **48**, 161-169 (2002).
- 51 Elias, C. *et al.* Guideline recommendations and antimicrobial resistance: the need for a change. *BMJ Open* **7**, e016264-2017-016264 (2017).
- 52 Weiss, K., Blais, R., Fortin, A., Lantin, S. & Gaudet, M. Impact of a multipronged education strategy on antibiotic prescribing in Quebec, Canada. *Clin. Infect. Dis.* **53**, 433-9 (2011).
- 53 Dickson, C. *et al.* The antibiotic management of gonorrhoea in Ontario, Canada following multiple changes in guidelines: an interrupted time-series analysis. *Sex. Transm. Infect.* **93**, 561-565 (2017).
- 54 <https://www150.statcan.gc.ca/n1/pub/11-630-x/11-630-x2016003-eng.htm#def1>.
- 55 Grigoryan, L. *et al.* Determinants of self-medication with antibiotics in Europe: the impact of beliefs, country wealth and the healthcare system. *J. Antimicrob. Chemother.* **61**, 1172-9 (2008).
- 56 Fleming, A., Bradley, C., Cullinan, S. & Byrne, S. Antibiotic prescribing in long-term care facilities: a meta-synthesis of qualitative research. *Drugs Aging* **32**, 295-303 (2015).
- 57 Detweiler, K., Mayers, D. & Fletcher, S. G. Bacteruria and Urinary Tract Infections in the Elderly. *Urol. Clin. North Am.* **42**, 561-568 (2015).

- 58 Cortes-Penfield, N. W., Trautner, B. W. & Jump, R. L. P. Urinary Tract Infection and Asymptomatic Bacteriuria in Older Adults. *Infect. Dis. Clin. North Am.* **31**, 673-688 (2017).
- 59 McCullough, A. R., Parekh, S., Rathbone, J., Del Mar, C. B. & Hoffmann, T. C. A systematic review of the public's knowledge and beliefs about antibiotic resistance. *J. Antimicrob. Chemother.* **71**, 27-33 (2016).
- 60 Rennert-May E. & Conly J. Antimicrobial stewardship: A Canadian perspective. *Int. J. Health Gov.* **21**, 165-179 (2016).
- 61 Cabral, C. *et al.* Influence of Clinical Communication on Parents' Antibiotic Expectations for Children With Respiratory Tract Infections. *Ann Fam Med* **14**, 141-7 (2016).
- 62 <https://www.canada.ca/en/public-health/services/diseases.html?vaccine-preventable>.
- 63 Eythorsson, Elias *et al.* Impact of the 10-valent pneumococcal conjugate vaccine on antimicrobial prescriptions in young children: a whole population study.
- 64 Kwong, J. C., Maaten, S., Upshur, R. E., Patrick, D. M. & Marra, F. The effect of universal influenza immunization on antibiotic prescriptions: an ecological study. *Clin. Infect. Dis.* **49**, 750-756 (2009).
- 65 Norhayati, M. N., Ho, J. J. & Azman, M. Y. Influenza vaccines for preventing acute otitis media in infants and children. *Cochrane Database Syst. Rev.* **10**, CD010089 (2017).
- 66 Chua, K. P., Fischer, M. A. & Linder, J. A. Appropriateness of outpatient antibiotic prescribing among privately insured US patients: ICD-10-CM based cross sectional study. *BMJ* **364**, k5092 (2019).
- 67 <https://www.publichealthontario.ca/-/media/documents/infographic-lets-talk-do-you-think.pdf?la=en>.
- 68 Smith, S. M., Fahey, T., Smucny, J. & Becker, L. A. Antibiotics for acute bronchitis. *Cochrane Database of Systematic Reviews* (2017).
- 69 Ahovuo-Saloranta, A. *et al.* Antibiotics for acute maxillary sinusitis in adults. *Cochrane Database of Systematic Reviews* (2014).
- 70 Boucher, A. *et al.* Quality-related events reported by community pharmacies in Nova Scotia over a 7-year period: a descriptive analysis. *CMAJ Open* **6**, E651-E656 (2018).
- 71 <https://www.pharmacists.ca/advocacy/antimicrobial-resistance/>.
- 72 Legare F. *et al.* Training family physicians in shared decision-making to reduce the overuse of antibiotics in acute respiratory infections: A cluster randomized trial. *CMAJ* **184**, E726-E734 (2012).
- 73 Hallsworth, M. *et al.* Provision of social norm feedback to high prescribers of antibiotics in general practice: A pragmatic national randomised controlled trial. *The Lancet* **387**, 1743-1752 (2016).
- 74 NICE. Antimicrobial stewardship: systems and processes for effective antimicrobial medicine use. (2015).
- 75 Hoyer, S., Frich, J. C. & Lindbaek, M. Use and feasibility of delayed prescribing for respiratory tract infections: a questionnaire survey. *BMC Fam. Pract.* **12**, 34 (2011).
- 76 McNulty, C. A. M., Lecky, D. M., Hawking, M. K. D., Quigley, A. & Butler, C. C. Delayed/back up antibiotic prescriptions: what do the public think? *BMJ Open* **5**, e009748 (2015).
- 77 Raft, C. F., Bjerrum, L., Arpi, M., Jarlov, J. O. & Jensen, J. N. Delayed antibiotic prescription for upper respiratory tract infections in children under primary care: Physicians' views. *Eur J Gen Pract* **23**, 190-195 (2017).
- 78 Ryves, R. *et al.* Understanding the delayed prescribing of antibiotics for respiratory tract infection in primary care: a qualitative analysis. *BMJ Open* **6**, e011882 (2016).
- 79 Owens, B. Telemedicine on the rise but lagging in Canada. *CMAJ* **190**, E1149-E1150 (2018).
- 80 Langford, B. J. & Morris, A. M. Is it time to stop counselling patients to "finish the course of antibiotics"? *Can. Pharm. J. (Ott)* **150**, 349-350 (2017).
- 81 Spellberg, B. The New Antibiotic Mantra-"Shorter Is Better". *JAMA Intern. Med.* **176**, 1254-1255 (2016).
- 82 Butler, C. C. *et al.* Effectiveness of multifaceted educational programme to reduce antibiotic dispensing in primary care: practice based randomised controlled trial. *BMJ* **344**, d8173 (2012).
- 83 Ferrat, E. *et al.* Effects 4.5 years after an interactive GP educational seminar on antibiotic therapy for respiratory tract infections: A randomized controlled trial. *Fam. Pract.* **33**, 192-199 (2016).
- 84 Le Corvoisier, P. *et al.* Long-term effects of an educational seminar on antibiotic prescribing by GPs: a randomised controlled trial. *Br. J. Gen. Pract.* **63**, e455-64 (2013).
- 85 <https://www.ourcommons.ca/DocumentViewer/en/42-1/HESA/report-16/>.
- 86 O'Neill, J. Tackling drug-resistant infections globally: the review on antimicrobial resistance. (2016).
- 87 Gulliford, M. C. *et al.* Effectiveness and safety of electronically delivered prescribing feedback and decision support on antibiotic use for respiratory illness in primary care: REDUCE cluster randomised trial. *BMJ* **364**, l236 (2019).
- 88 Naughton, C., Feely, J. & Bennett, K. A RCT evaluating the effectiveness and cost-effectiveness of academic detailing versus postal prescribing feedback in changing GP antibiotic prescribing. *J. Eval. Clin. Pract.* **15**, 807-812 (2009).

- 89 Meeker, D. *et al.* Effect of Behavioral Interventions on Inappropriate Antibiotic Prescribing Among Primary Care Practices: A Randomized Clinical Trial Behavioral Interventions and Inappropriate Antibiotic Prescribing Behavioral Interventions and Inappropriate Antibiotic Prescribing. *JAMA* **315**, 562-570 (2016).
- 90 McDonagh, M. S. *et al.* Interventions to reduce inappropriate prescribing of antibiotics for acute respiratory tract infections: summary and update of a systematic review. *J. Int. Med. Res.* **46**, 3337-3357 (2018).
- 91 Stover, K. R., Kenney, R. M., King, S. T. & Gross, A. E. Evaluation of the Use of Novel Biomarkers to Augment Antimicrobial Stewardship Program Activities. *Pharmacotherapy* **38**, 271-283 (2018).
- 92 Tonkin-Crine, S. *et al.* Clinician-targeted interventions to influence antibiotic prescribing behaviour for acute respiratory infections in primary care: an overview of systematic reviews. *Cochrane Database of Systematic Reviews* (2017).
- 93 Cross, E. L., Tolfree, R. & Kipping, R. Systematic review of public-targeted communication interventions to improve antibiotic use. *J. Antimicrob. Chemother.* **72**, 975-987 (2017).
- 94 <http://www.bccdc.ca/our-services/programs/community-antimicrobial-stewardship>.
- 95 de Bont, E., G.P.M., Alink, M., Falkenberg, F. C. J., Dinant, G. & Cals, J. W. L. Patient information leaflets to reduce antibiotic use and reconsultation rates in general practice: a systematic review. *BMJ open* **5**, e007612; e007612-e007612 (2015).
- 96 Rosman, S. *et al.* Prescribing patterns for upper respiratory tract infections in general practice in France and in the Netherlands. *Eur. J. Public Health* **18**, 312-316 (2008).

