



# Pan-Canadian Public Health Network

*Partners in Public Health*

## **Antimicrobial Stewardship**

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The Communicable and Infectious Disease Steering Committee Task Group on  
Antimicrobial Use Stewardship

Final Report to the Public Health Network Council  
April 2016

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## 1. Executive Summary

The Communicable and Infectious Disease Steering Committee (CIDSC) Task Group on Antimicrobial Use (AMU) Stewardship was mandated by the CIDSC to elaborate the stewardship component of a pan Canadian approach, identify potential sub-components and activities as well as mechanisms for promoting stewardship across jurisdictions. The Task Group contributed to and endorses this report for submission to CIDSC in fulfillment of this mandate. It broadly defines stewardship from a human health perspective in a manner that could be adopted across sectors, examines evaluated stewardship undertakings at a high level, and identifies recommendations related to the key components of stewardship which could be implemented collaboratively by jurisdictions.

Antimicrobial stewardship can be thought of as co-ordinated interventions designed to promote, improve, monitor, and evaluate the judicious use of antimicrobials in order to preserve their future effectiveness and promote and protect human health. Because stewardship encompasses activities outside the human health sector in a “One Health” approach, and involves multiple jurisdictions and regulators, a common understanding is needed, and the development of a common glossary, including shared objectives, should be considered in the development of stewardship initiatives and activities.

A review of examples of promising stewardship programs suggests that strong interdisciplinary public health action and political engagement can lead to a measurable decrease in antimicrobial resistance (AMR) and improved optimal AMU in health care settings. While more research is clearly needed to validate this and related findings in community settings, four key components of promising antimicrobial stewardship programs and initiatives emerged:

- **Leadership:** successful stewardship undertakings are grounded in accountability, appropriate and sustained resources and expertise, adequate support, and training and involve specialists in an interdisciplinary manner.
- **Interventions:** effective stewardship interventions are multi-pronged and comprehensive. They consist of awareness, education, and guidance and include diagnostic and other types of tools, providing evidence-based timely information, and engage multiple target groups for maximum effect.
- **Monitoring and Evaluation:** the literature consistently identifies the critical role of benchmarks, audit and evaluation systems to establish the appropriate use of antimicrobials.
- **Knowledge Creation, Translation and Mobilization:** expertise from across research disciplines must be leveraged in order to address information gaps, and ensure that evidence is available and applied for greatest impact.

Recommendations to the CIDSC which serve to promote stewardship across jurisdictions include:

- that a national infrastructure (e.g. governance, network, resources, etc.) be put in place to support provinces and territories in the development of stewardship programs for implementation within their jurisdictions, with further suggestions for key roles that federal, provincial and territorial partners and other stakeholders could fulfill;

- that best practices, benchmarks or standards for education and awareness activities require the engagement of multiple prescribers (including dispensers) groups, and a dual focus on prescribers and users;
- that the consistency and availability of guidance, information, tools and training for prescribing professionals and users be improved to support prescribers in their efforts to prescribe more appropriately at the local level;
- that universities, colleges and technical schools that train future prescribers incorporate mandatory stewardship education, and continuing education curricula for prescribing professionals;
- that evidence-based audit and feedback tools be developed to support prescribers in their efforts to prescribe more appropriately at the local level, and that guidance for prescribers be evaluated, adapted and implemented at regional and local levels;
- that benchmarks be established for optimal use by type of infection, and populations at greatest risk for infection, and that jurisdictions work together to establish performance targets for stewardship in hospital and other settings; and that timely evaluations of stewardship programs be conducted and publicly accessible;
- that further evidence about prescribing professions be collected, shared and mobilized so that specific interventions for these professions can be implemented; and
- that changes be made to healthcare practitioners' practice regulations and that further evidence will need to be gathered to guide and support such changes.

This report reflects literature searches, informal surveys, information available in the public domain, and references supplied by task group experts between the period of February and August 2015. Implementation of the report recommendations will need to take into account current developments in the policy and program research domains.

Finally, the Task Group suggests that the evaluation of stewardship programs and initiatives be promoted to granting agencies, and included as part of AMR/AMU priorities for funding.

## **2. Background**

This section positions the report and its recommendations within the context of Canadian federal, provincial and territorial (F/P/T) work on antimicrobial resistance and proposes a common understanding of stewardship, drivers and related factors of antimicrobial use and resistance in Canada.

Antimicrobial resistance (AMR) is recognized as an important global public health concern with impacts on health, trade, agriculture, and environment sectors. The rapid spread of multi-drug resistant bacteria is reaching a point where preventing, controlling and treating infection or diseases will be severely compromised. In Canada, the emergence of antimicrobial resistant organisms has been identified as a major concern in healthcare settings and among at-risk human populations, as well as in animals and related settings.

The Pan-Canadian Public Health Network (PHN), established in 2005, is Canada's national public health infrastructure to address such public health concerns. The PHN is the key intergovernmental mechanism used to strengthen and enhance Canada's public health capacity,

enable F/P/T governments to better work together on the day-to-day business of public health, and anticipate, prepare for, and respond to public health events and threats.

In 2014-2015, the PHN began identifying components of a pan-Canadian public health framework on AMR, focussing its attention on priority data needed to support a robust surveillance system, and the key elements of stewardship in antimicrobial use in human health. The PHN is accountable to the Conference of Federal/Provincial/Territorial (F/P/T) Deputy Ministers of Health, and this work supports one of the PHN's key objectives, the prevention and control of persistent and emerging infectious disease, through its Communicable and Infectious Disease Steering Committee (CIDSC) and its task groups.

In fall 2014, the Public Health Agency of Canada (PHAC) sought feedback from members of the CIDSC on a proposed AMR federal framework comprised of three pillars: Surveillance, Stewardship, and Innovation. All members agreed that stewardship was a priority, and that greater collaboration on this issue would be beneficial. As a result, in December 2014 the CIDSC agreed to the establishment of a Task Group composed of technical experts to elaborate the stewardship component of a framework for action on AMR and antimicrobial use (AMU), and ways to promote it across jurisdictions<sup>1</sup>. CIDSC has also established a Task Group on AMR surveillance in human health tasked with identifying key information and data about top priority organisms. This work will help inform effective AMR programs and policies in Canada and enable more systematic monitoring for specific AMR organisms.

## 2.1 Objective of Report

The report identifies key components of antimicrobial stewardship programs and initiatives in human health settings and highlights promising programs and initiatives underway in Canada and other countries. Antimicrobial stewardship initiatives and related programs typically address issues related to antimicrobial use in order to limit the spread of antimicrobial resistance and conserve the effectiveness of existing antimicrobials. The report also highlights key challenges and existing knowledge gaps and presents a series of recommendations for consideration of the CIDSC.

## 2.2 Scope of Report

The Task Group has focused specifically on the prudent use of antimicrobials in human healthcare settings (e.g., hospitals, long-term care facilities, long-term acute care facilities, ambulatory surgical centres, and private practices). Promising initiatives have been determined based on review of published and grey literature, including evaluations of programs in Canada and other countries.

While the focus of this report is on reducing and ultimately finding ways to eliminate unnecessary/inappropriate prescribing, the Task Group also acknowledges that patient safety, avoidance of unwanted side effects, and effective infection prevention and control are important factors in antimicrobial stewardship. The focus of the report is also limited to human health settings; at the same time, the Task Group recognizes that parallel action is needed in veterinary and food animal health, and in the agriculture sectors, as part of a One Health approach. In the veterinary health sector, initiatives are underway to strengthen regulation and oversight, including

control of importation of antimicrobials for personal and own-use importation, and post-market monitoring of approved antimicrobials<sup>2,3</sup>. Work is also underway to remove growth promotion claims of medically-important veterinary antimicrobial drugs<sup>4</sup>.

## 2.3 Methods and Approach of the Task Group

Search strategies were developed to identify published literature, grey literature, and relevant websites, and are outlined in Annex G. This information was reviewed, and the resulting content was organized into Annexes A-F. Annexes provided the basis for discussions concerning antimicrobial users and prescribers and dispensers of antimicrobials, as well as promising practices for stewardship programs and initiatives, while the Task Group's technical experts provided additional suggestions for content. Task Group members convened for regular meetings via teleconference to provide direction on the report and its recommendations.

## 2.4 Antimicrobial Stewardship – A Common Understanding

Antimicrobial stewardship can be broadly described as the responsible planning and management of resources in order to prevent and moderate the development of antimicrobial resistance<sup>5</sup>. For the purposes of this report, antimicrobial stewardship is defined as “*co-ordinated interventions designed to promote, improve, monitor, and evaluate the judicious use of antimicrobials in order to preserve their future effectiveness and promote and protect human health*”<sup>6</sup>.

The Task Group acknowledges that there are a variety of lenses through which antimicrobial stewardship can be viewed. Each of the following descriptions is inherently built into the above definition.

Governance (FPT) - how governments and other social organizations interact, how they relate to citizens and how they make decisions<sup>7</sup>. The governance perspective addresses stewardship in terms of “*a national coordinated legislative or regulatory approach designed to optimize use of antimicrobial therapy*”<sup>8</sup>. Government agencies across jurisdictions (local, provincial/territorial, national, international) focus on policy development, coordination and collaboration on a variety of strategies and initiatives that can be implemented across sectors.

Systems - defined in terms of key stakeholders who map and measure health systems, identify where some of the key blockages and challenges lie, and design sound, synergistic and system-ready interventions targeting those weaknesses<sup>9</sup>. Health systems involve all stakeholders – government, non-governmental organizations (NGOs), healthcare organizations, academic institutions, professional institutions, and the general public. Coordinated interventions are part of a systems-based approach, in that they are designed to improve and measure the appropriate use of antimicrobials by promoting the selection of the optimal antimicrobial drug regimen, dose, duration of therapy, and route of administration<sup>10</sup>.

Public health - defined as the organized efforts of society to keep people healthy and prevent injury, illness and premature death and disability, improving health and well-being and reducing inequalities in health. It focuses on preventing disease and optimizing the health of the population rather than addressing the illnesses of individuals, and is the combination of programs, services

and policies that protect and promote health<sup>11</sup>.

Clinical - defined within the context of care and treatment of an individual/patient as: “*the optimal use of antimicrobials (including selection, dose, and duration of use) for the treatment or prevention of infection in order to achieve the best clinical outcomes with minimal patient toxicity and minimal adverse events*”<sup>12</sup>. It is also “*the commitment to always use antibiotics appropriately and safely—to use the right antibiotic at the right time, at the right dose, and for the right duration*”<sup>13</sup>. It may also include the commitment to use an antibiotic for the right reason<sup>14</sup>.

## 2.5 Current Environment – Antimicrobial Resistance

This section discusses antimicrobial resistance in human healthcare settings and at-risk populations, potential impacts of travel and human and financial costs.

The emergence of antimicrobial-resistant organisms is a major public health concern in Canada, particularly in health care settings and in vulnerable populations<sup>15</sup>. The Public Health Agency of Canada’s surveillance programs have identified that these organisms appear to be thriving in both health care and community settings and are capable of causing severe, life-threatening infections that may be more difficult to manage because of limited treatment options<sup>16</sup>. This leads to the use of more expensive, last-recourse antimicrobials. Because AMR may emerge in bacteria as a response to selective antimicrobial pressure, there is a potential risk that fewer and fewer antimicrobials will remain effective in the future<sup>17</sup>. The use of last-recourse antimicrobials to treat serious infections (after all other treatment options have failed) is becoming more common in both health care and community settings<sup>18</sup>.

Unnecessary antibiotic treatment, such as for asymptomatic urinary tract infections (UTIs) and in viral infections in children has been shown to account for a substantial burden of inappropriate antimicrobial use and unnecessary drug/treatment regimens in Canadian long-term and acute care settings<sup>19, 20, 21, 22</sup>. Organisms in health care settings that cause infections acquired during hospitalization or as the result of health care provided in hospitals or alternate settings such as outpatient clinics, physician/dental offices and long-term care facilities can cause severe, life-threatening infections, especially in the elderly, young infants and patients who have weakened immune systems due to other diseases, such as cancers and heart or kidney disease<sup>23</sup>.

AMR is particularly significant in these settings as the organisms spread easily from person-to-person within or between health care facilities and have been linked to large hospital outbreaks. In addition, patients are prescribed antimicrobial agents for other infections or for prevention of infection, which may lead to the emergence of novel AMR. Many of these organisms are now emerging in community settings as well as in individuals with no recent exposure to health care settings<sup>24</sup>.

Resistance among common pathogens causing community and hospital-associated infections is increasing worldwide, though regional patterns of resistance vary<sup>25</sup>. Significantly, resistance to last-resort antibiotics has led to an epidemic of hard-to-treat infections, such as MRSA, ESBL-producing Enterobacteriaceae, CRE, NDM-1, VRE, and gonorrhoeal infections<sup>26</sup>. These infections have the potential to spread quickly through international trade and travel. *C. difficile*, an infection

that can occur following antibiotic treatment, is another serious threat to human health related to antibiotic use<sup>27</sup>.

Certain antibiotics used in high doses or over a prolonged period of time will increase the chance of developing resistant infections<sup>28</sup>. The presence of *C. difficile* bacteria, together with a large number of patients receiving antibiotics in healthcare settings, can lead to frequent *C. difficile* outbreaks. In healthcare settings, *C. difficile* infections can be limited through careful use of antibiotics and strict adherence to infection prevention and control measures<sup>29</sup>.

*Clostridium difficile*, multi-drug-resistant *Enterobacteriaceae* (including Extended spectrum beta-lactamases (ESBL) and Carbapenem-resistant *Enterobacteriaceae* (CRE), methicillin resistant *Staphylococcus aureus* (MRSA, and vancomycin-resistant *Enterococci* (VRE)) are all organisms of clinical significance in Canadian hospitals<sup>30</sup>. These organisms are also responsible for hospital outbreaks and contribute to the overall burden in Canada's publicly-funded healthcare system. Incidents of many of these organisms are decreasing or remaining stable<sup>31</sup>. However, continued monitoring is essential to identify changes or emerging trends.

Gonorrhea infections are also of particular concern. The World Health Organization announced in 2012 that millions of people with gonorrhea may be at risk of running out of treatment options unless urgent action is taken<sup>32</sup>. Global surveillance has led to the detection of extensively drug resistant strains of gonorrhea in Australia, France, Japan, Norway, Sweden, and the United Kingdom.

In Canada, gonorrhea infections have doubled since 1997. The infection particularly affects youth and adults from both sexes and is particularly high in Nunavut, the Northwest Territories, Yukon, and the Prairie provinces<sup>33</sup>.

The risk of untreatable gonorrhea emerging in Canada remains high with treatment failures being observed across the country. As a result, the Public Health Agency of Canada has updated its treatment guidance for gonorrhea to recommend combination therapy, specifically stating that monotherapy should be avoided. In particular it states that quinolones such as ciprofloxacin and ofloxacin are no longer recommended for the treatment of gonococcal infections in Canada, and should only be given as an alternative treatment if antimicrobial susceptibility testing is available and quinolone susceptibility is demonstrated; or if local quinolone resistance is under 5% and a test of cure can be performed<sup>34</sup>.

Since 2009, overall infection rates for MRSA in Canada have been decreasing, especially in hospital settings; however, current MRSA case numbers still exceed those in the early 2000's, suggesting that further effort to reduce rates is warranted. The annual number of cases of infections resistant to Carbapenem antimicrobials, a class of last line antimicrobials, has tripled since surveillance began in 2010<sup>35</sup>.

Multi-drug resistant (MDR)-TB is of significant concern because it is difficult to treat. The prevalence of TB in vulnerable populations is high and the introduction of MDR-TB in community groups such as those living on First Nation reserves and incarcerated individuals can lead to significantly increased morbidity and mortality.

In December 2014 the United Kingdom Review on Antimicrobial Resistance reported that unless action is taken to address global AMR, it could cost the world at least an additional 10 million lives a year by 2050, more than the number of people who currently die from cancer. Research, development, and commercialization of antimicrobials are costly, and investment in development of new antimicrobials is decreasing. Resistance would have a cumulative cost of at least \$100 trillion USD, more than one and a half times annual world GDP today<sup>36</sup>.

In conclusion, AMR poses a high risk to human health, including at risk populations. AMR related morbidity and mortality places an increased burden on the public healthcare system and on the economy.

## **2.6 International and Government of Canada Activities to Reduce Antimicrobial Resistance**

This section presents common themes from reports, conferences, strategies, and plans which address AMU stewardship in Canada and elsewhere. More detail about these reports and activities can be found in Annexes B and C.

### **2.6.1 National Level Conferences and Strategies**

Over the past two decades, antimicrobial stewardship has been recognized in Canada as a key component of a multifaceted approach in preventing the spread and emergence of AMR. The term “antimicrobial stewardship” was formally used in 1997 at the first Canadian Consensus Conference on Antimicrobial Resistance, jointly sponsored by Health Canada and the Canadian Infectious Disease Society (now Association of Medical Microbiology and Infectious Disease Canada). Recommendations were made regarding AMU in healthcare settings, improving public perception of the risks/benefits of antimicrobials, the need for timely surveillance data to detect AMR in healthcare settings, and mobilizing leadership mechanisms. An action plan for public and health professionals was developed with plans to measure its effectiveness, identify obstacles, and provide suggestions for ways to overcome them<sup>37</sup>. A series of one day seminars on AMU stewardship across Canada followed with the objective of developing strategies to optimize antimicrobial prescribing in the acute care settings.

Subsequent conferences, meetings, and seminars have been held over the years in Canada, each one aiming to raise awareness, promote discussion on AMR and AMU, and “kick start” action on stewardship. Key recommendations called for stronger leadership in the area of AMR surveillance and stewardship, a coordinated and integrated AMR and AMU surveillance system, more timely reporting, improved AMR data from the community, and education for healthcare professionals.

A National Policy Conference in 2002 provided recommendations related to antibiotic use in human and animal health, and the need for national standards for antibiotic use in humans and practice specific guidelines on prudent use of antimicrobials in animals<sup>38</sup>. In 2004, the Canadian Committee on Antimicrobial Resistance (CCAR) made recommendations on antibiotic prescribing practices, surveillance, appropriate interventions and improved communication<sup>39</sup>.

In 2009, the Report from the Pan-Canadian Stakeholder Consultations on Antimicrobial Resistance discussed improper use of antibiotics and antivirals in humans and animals. Specific antimicrobial stewardship recommendations identified the need for a lead steward to provide easy access to antimicrobial usage guidelines and surveillance data on antimicrobial utilization and antimicrobial resistant organisms for/to stakeholders; build on education and training, then combine with regulations, and; increase collaboration between schools and institutions<sup>40</sup>.

Although the consultations noted that progress had been made over the preceding decade, considerable work was still required, particularly in developing a universally agreed to definition of stewardship, understanding stewardship across the continuum of care, and developing a coordinated and integrated interdisciplinary pan-Canadian approach to antimicrobial stewardship. Consultations also highlighted the need to develop and promote public and professional awareness of AMU stewardship responsibilities, ensure that AMU is based on best available evidence, and develop a comprehensive way of measuring AMU that is consistent across Canada, across the continuum of care, and across sectors. A number of solutions were also suggested, including setting standard guidelines through the creation of a National AMR Stewardship Working Group, and addressing communication, education and enforcement, and surveillance approaches<sup>41</sup>.

Another important development in Canada took place in 2012 when Accreditation Canada released the Antimicrobial Stewardship “Required Organizational Practice” (ROP) for assessment on-site beginning in January 2013 for organizations providing inpatient acute care. To comply with this ROP, organizations must implement an antimicrobial stewardship program to optimize antimicrobial use<sup>42</sup>.

In 2014, the NCCID/AMMI report on surveillance of AMR and AMU in Canada included two recommendations pertaining to AM stewardship. The first one focused on the development of methods that would collect data on indications for prescribing in human and animal health AMU surveillance systems, to support the development of methods for prescriber audit and feedback for education and AMR control. The second recommendation focussed on the development and dissemination of AMR and AMU education materials for medical and veterinary health professions and the public<sup>43</sup>.

Some common themes from the work of Canadian stakeholders to reduce AMR emerge:

- Leadership and collaboration for optimal antimicrobial use requires multi-sectoral engagement across human, animal health and food production industry, as well as collaboration across all levels of government (FPT), professional organizations, non-governmental organizations serving the human health sector, and the private sector. Good communication among all stakeholders is also important.
- Leadership, accountability, and oversight in healthcare settings require a sufficient number of qualified human resources. Specific expertise is needed in order to achieve the successful establishment of coordinated, integrated, and interdisciplinary stewardship teams to address AMR, and to provide feedback to prescribers and users of antimicrobials.

- Stewardship undertakings should be formalized through policy and regulatory mechanisms. Canada began to formalise its commitment to stewardship through policy and regulatory mechanisms in its 2015 Federal Action Plan on Antimicrobial Resistance and Use in Canada: Building on the Federal Framework for Action, which included milestones for specific work with F/P/T partners and other stakeholders in human and animal health.
- Investment in population-based surveillance programs and electronic tools coordinated at the national and FPT level are required to capture necessary data and information on emerging trends and regional variances. Timely information and data from all settings (including the community) are important.
- Data from surveillance programs can be used to monitor and evaluate stewardship program outcomes, including impact on infection prevention and control, appropriateness of AMU, clinical outcomes, and prescribing practices. This can be done across healthcare settings.
- Promotion of education and awareness for both prescribers and the general public (e.g. provide antimicrobial stewardship training for prescribers as part of the formal education curriculum, including post-graduation and continuing education credit programs; provide awareness and educational campaigns for the general public). The use of evidence-based, practice-specific guidelines is also recommended.

In conclusion, the last two decades of consensus-based and multi-stakeholder activities in Canada have resulted in recommendations with implications for future antimicrobial stewardship programs and initiatives. Key themes that emerge are: the need for strong leadership, appropriate levels of qualified human resources as well as material resources (i.e. databases), investment in surveillance programs, monitoring and evaluation of stewardship activities, education and awareness for prescribers and users, evidence-based, practice specific-guidance, and further formalization through policy, legislative and regulatory mechanisms.

These are consistent with themes emerging from recent recommendations concerning the implementation of stewardship activities to reduce antimicrobial resistance, as outlined in the United Kingdom's Five Year Antimicrobial Resistance Strategy 2013 to 2018, and in the United States' 2014 National Strategy for Combating Antimicrobial Resistant Bacteria.

## **2.6.2 International strategies and plans from other countries**

The World Health Organization (WHO) serves as the key global entity to raise awareness about AMR in healthcare settings, and successfully sought the adoption of the World Health Assembly Resolution to Combat AMR in May 2014. The WHO is currently working with key partners to develop the draft Global Action Plan (GAP), approved by its Member States at the World Health Assembly (WHA) in May 2015, whose goal is to ensure the continuity of successful treatment and prevention of infectious diseases with effective and safe medicines. The Global Action Plan identifies a set of principles, and five strategic objectives, two of which focus on key stewardship concepts: to improve awareness and understanding of antimicrobial resistance; and optimizing the use of antimicrobial agents. Member countries are being urged to implement the global action

plan and adapt it to meet national priorities and specific contexts, and to mobilize additional resources for its implementation.

Since 2008, countries have identified varying degrees of progress in response to global dialogues and calls for action. Through the adoption of the global action plan, governments all committed to have in place by May 2017 a national action plan on AMR that is aligned with the global action plan. Governments and global health institutions have supported coordinated action across sectors and countries to promote AMU stewardship. The United Kingdom (UK), United States (U.S.), and European Commission (EC) have developed detailed plans with significant financial investments.

- The *UK 5 Year Antimicrobial Resistance Strategy 2013 to 2018* includes actions specific to stewardship such as optimisation of prescribing practices through good antibiotic stewardship, promoting better use of antibiotics and new diagnostics; improving professional education, training, and public engagement to improve practice and increase understanding<sup>44</sup>.
- The *U.S. National Action Plan for Combating Antimicrobial Resistant Bacteria* focuses on slowing the overuse and misuse of antimicrobials in health and agricultural settings, dissemination of information to the public, control of infection transmission across community and healthcare settings, and improving international collaboration and capacity for AMR prevention, surveillance, control, and research and development<sup>45</sup>.
- The *EU Action Plan against the Rising Threats from Antimicrobial Resistance* includes national mechanisms for coordination, national guidelines on prudent use of antimicrobials, public awareness, and surveillance of antibiotic consumption<sup>46</sup>.

Common themes of these strategies include:

- Political engagement;
- Jurisdictional securement of resource allocations; and
- Coordinated, comprehensive, multi-year action plans to address AMR/AMU.

National advisory councils of leaders and experts have been established to guide the development of action plans with targets and commitments to report progress.

Countries also agree that the optimization of the use of antimicrobial medicines in human health involves better understanding the evidence concerning the increasing use of antimicrobial agents, better data about antimicrobial use at point of care, strengthened regulation and research into the distribution and use of antimicrobials, effective and evidence-based diagnostic tools, including at point of care, that are easily integrated into clinical and pharmacological practice, and better regulation of over the counter and internet sales of antimicrobial agents<sup>47</sup>.

And finally, countries, including Canada, support the principle of sustainability, wherein country action plans on antimicrobial resistance include an assessment of resource needs. The implementation of these plans will require long-term investment in surveillance, operational research, laboratories, human and animal systems, competent regulatory capacities, and

professional education, training, and feedback on prescribing profiles, in both the human and animal health sectors.

By signing on to the WHO Global Action Plan, countries agree that the improved use of antimicrobials means: committing resources to ensure sustainability; effective communication, training and education for prescribers in the form of professional education and certification; raising awareness of AMU-related issues; and surveillance and research to strengthen knowledge and evidence bases for effective action. The U.S., U.K., and EC have developed national strategies with identified investments, targets and mechanisms for reporting on related action plans.

## 2.7 Stewardship – A Shared Responsibility

This section outlines the roles and responsibilities of various organizations and stakeholders regarding antimicrobial stewardship.

Stewardship is an ethic that organizations and individuals alike can adopt, and adopting this ethic means committing to the responsible use of resources, as well as conserving and ensuring that those resources or better are available to future generations.

Better managing antimicrobial use is a shared responsibility among multiple stakeholders including public health and healthcare professionals, healthcare organizations, local, provincial, territorial, national, the research community, and others who provide and use antimicrobials and who care for the people who use them. The development, promotion, and implementation of initiatives to promote optimal use of antimicrobials across Canada will require collaboration among all of these stakeholders, helping to create synergies in order to effectively combat antimicrobial resistance.

**The general public** - individual users of antimicrobials and their care providers are responsible for decisions affecting their own health, and the health of children and others they may be entrusted with. At the same time, they are users of antimicrobials, including those prescribed by regulated healthcare providers, and consumers of both healthcare services and health information.

**Regulated healthcare providers** such as physicians are required by law to deliver competent, ethical and professional services, and are accountable to the public through their respective colleges. Responsibilities for AMR/AMU include investment in building/maintaining professional capacity and demonstrating leadership to address AMR/AMU through oversight, training, capacity building (e.g. prescription practices, patient counseling on AMU), and systematic education/accreditation/ standards concerning AMR/AMU targeted for their professionals.

**Healthcare delivery organizations** engage multi-disciplinary teams to deliver healthcare services and provide a measure of leadership and oversight by informing and developing guidance (e.g. clinical pathways); developing policies and procedures, outbreak response coordination and technical expertise; monitoring and reporting; and oversight of professional accreditation, education and auditing. Specific responsibilities concerning AMR/AMU focus on: clinical elements, including prudent prescription practices, infection prevention and control practices, and patient counselling on antimicrobial use.

**Local public health authorities** can have roles in outbreak response coordination, the administration of health promotion and disease prevention programs, immunization, food premises inspection, healthy growth and development including parenting education, health education for all age groups and selected screening services.

**Community-care settings** play a role in patient and public awareness of AMR/AMU issues, oversight of practices and protocols in terms of administration and operations concerning transfer, care and treatment, adherence to care and access to services, accommodations, hygiene and food practices and response to AMR occurrences.

**Health professional organizations** are mandated with oversight of professional healthcare providers, including professional regulation, licensing and accreditation, education and auditing. Responsibilities for AMR/AMU include the provision of leadership regarding formal and continuing education, professional standards, practitioner competencies and certification, other learning opportunities, and research, with the overall goals to ensure a high quality healthcare system and provide high-quality healthcare for patients and their communities.

**Provincial/Territorial governments** play a key role by virtue of their responsibility for the delivery of healthcare, public health programs and services, and approval of medical coverage for antimicrobials. P/T governments develop policy and share promising practices through a range of methods, including webinars and guidance tools for public health and healthcare professionals, and awareness initiatives targeted for the public.

The **Public Health Agency of Canada** is responsible for providing leadership on the public health aspects of antimicrobial resistance and antimicrobial use, and engaging with other federal organizations in food, agricultural, and health sectors to regulate, develop policy, and invest in research. The Public Health Agency of Canada works with domestic and international partners in laboratory services, surveillance, public awareness and guidance development.

The **Pan-Canadian Public Health Network (PHN)** is Canada's key intergovernmental mechanism to strengthen and enhance Canada's public health capacity, enable F/P/T governments to better work together and anticipate, prepare for, and respond to public health events and threats. It has a role in developing components of the pan-Canadian framework antimicrobial resistance.

In conclusion, antimicrobial stewardship is a shared responsibility among many stakeholders including governments, health professional organizations, community care providers, clinics and hospitals, regulated healthcare providers, prescribers and users. Government, private and civil society organizations, and individuals can all have active roles in antimicrobial stewardship.

### **3. Users and Prescribers of Antimicrobials in Canada**

This section discusses populations groups in Canada that are being dispensed higher levels of antimicrobials, populations where the risk of outbreak of antimicrobial resistant infections is higher, and Canadian prescribers of antimicrobials. It also outlines evidence about prescribers who dispense high numbers of antimicrobials, and settings where dispensing rates are highest.

Suggestions are made where future stewardship undertakings may be developed, and targets may be set for greater impact.

### 3.1 Users of Antimicrobials

Antimicrobials are prescribed to all age groups among the general population. There are certain groups within the population that use antimicrobials more frequently than others. In 2013, evidence indicates that antimicrobials were dispensed at higher levels among the youngest (0-5 years old) and oldest (65+ years old) age groups across Canada<sup>48</sup>, as well as the elderly, pregnant women, patients with concurrent conditions/comorbidities, or those in certain institutional environments (i.e., burn units, long-term care facilities, intensive care units)<sup>49</sup>.

The social determinants of health also play a role in higher rates of AMU. Evidence shows that factors linked to high AMU include low-income, high unemployment, and lower socioeconomic standing<sup>50</sup>. There is also a higher risk of outbreak of resistant infections among at-risk populations when environmental factors and hygienic conditions play a role.

This was the case in First Nations communities in northern Saskatchewan when low-quality running water resulted in an onset of community-acquired MRSA (CA-MRSA) in 2002<sup>51</sup>. In 2004, another CA-MRSA outbreak in Calgary, Alberta specifically affected individuals with a history of illicit drug use, homelessness, or recent incarceration<sup>52</sup>. Outbreaks of antimicrobial resistant infections in at-risk populations can be difficult to control, and may become endemic.

In conclusion, evidence shows that certain population groups have a higher risk for AMU and contracting antimicrobial resistant infections. Tailoring stewardship initiatives to the needs of these populations may lead to greater gains than more generalized activities. Consideration of specific, targeted interventions to meet AMR infection prevention objectives could be warranted, as they are for other interventions to prevent and control infectious diseases. Finally, education directed to parents would be beneficial, as they are a key intermediary group between young children and seniors, populations with high rates of AMU<sup>53</sup>.

### 3.2 Prescribers of Antimicrobials

Prescribers of antimicrobials work in various human health settings. In hospital settings, the key prescribers are general practitioners, specialist physicians, pharmacists, and nurse practitioners. In the community setting, many more professionals prescribe antimicrobials, such as physician assistants, pharmacists, midwives, optometrists, clinical nurses, nurse practitioners, dentists, dental surgeons, dental hygienists, naturopaths and podiatrists.

Of these prescribing professionals, some prescribers may play a key role in stewardship<sup>54</sup>. For instance, physicians often establish a diagnosis, provide treatment, and educate their patients on taking medication. General practitioners and specialist physicians in hospital settings generally prescribe AMs on a more consistent basis than other health professionals<sup>55</sup>. Pharmacists also play a key role by dispensing medications, providing follow-up education to patients, and providing alternatives to antimicrobials, and often overseeing hospital stewardship programs.

There is evidence of potentially inappropriate prescribing practices in some professional groups. Between 1966 and 2013, British Columbia observed a 62% increase in rate of prescribing by dentists by population<sup>56</sup>, leading some experts to suspect that dentists and dental surgeons are high prescribers. A linkage was also made between prescribing and resistance in Prince Edward Island, with dental prescribing being linked to community-based *C. difficile*<sup>57</sup>. Prescribing practices of naturopaths in British Columbia are highlighted as potentially problematic, with more than 3 times the average number of days of therapy per prescription than that of any other profession<sup>58</sup>. Since the average prescription from a naturopathic doctor is for a much longer course of therapy, there is concern whether their prescribing is guideline concordant. Canadian public opinion research on antibiotics in 2008 suggested that physicians were also overprescribing, while more recent analysis of human antimicrobial drug use in Canada suggest guidance and other stewardship activities continue to be relevant for this prescribing group.

Consistent overprescribing of antimicrobials may be a concern in particular settings. For example, in an ambulatory care centre in Southwestern Ontario, older patients (66+ years old) with chronic kidney disease were prescribed doses of antimicrobials that were higher than the recommended amount listed in the guidelines<sup>59</sup>. It appears that overprescribing antibiotics for chronic kidney disease may be common<sup>60</sup>.

In conclusion, certain prescribing professions may benefit from tailored stewardship education, especially if they have been identified as key sources of health information for Canadians, and if they have been identified as overprescribing. Stewardship interventions could include tools that would enable those who commonly overprescribe to both use antimicrobials more judiciously and to resist patient or consumer pressure for antimicrobials. In order to mitigate overprescribing in setting-specific situations, it is important that consistent information be available and accessible for all prescribing professionals to ensure that there is a common understanding about AMU.

#### **4. Promising Stewardship Initiatives and Programs from Canada and Other Countries**

This section outlines common components of evaluated stewardship initiatives and programs in Canada and other countries, in hospital and community settings. It is not a complete list. Key components drawn from promising stewardship initiatives both within Canada and from other countries are summarized, and the information can be used to inform future stewardship strategies as well as recommendations. Details can be found in Annex F.

It is important to note that antimicrobial stewardship programs and infection prevention and control programs can be mutually beneficial. Actions such as identifying reported trends and outbreaks of epidemiologically significant organisms can provide relevant information to both programs. Healthcare providers can also be educated about infection prevention policies in the course of interaction with stewardship approaches<sup>61</sup>.

Infection prevention practitioners and hospital epidemiologists play a joint role in benefiting antimicrobial stewardship programs by providing support and guidance in surveillance for organisms of interest, implementing interventions to guide the delivery of evidence-based

practices, and translating and communicating data and infection rates to healthcare providers and prescribers, including hospital administrators.

This section highlights only programs that have been evaluated. It should be noted that of the stewardship undertakings reviewed, evaluations are often not conducted, or are not publicly available. Therefore, this section may not capture the full landscape of promising stewardship components.

## 4.1 Canada

### 4.1.1 Do Bugs Need Drugs? (Scope: provincial)

The community-based education program Do Bugs Need Drugs? (DBND) began in Grande Prairie, Alberta, with the objective of raising awareness of AMR issues, including appropriate prescribing practices and optimal AMU. The program has a dual focus: 1) to provide educational resources to physicians, nurses, and pharmacists in community hospitals and long-term care facilities; and 2) to provide public education on AMR risk and AMU to the general public, such as students of all ages, parents, caregivers, teachers, employers, and employees<sup>62,63</sup>. DBND uses a multimedia approach, encompassing print materials, awareness campaigns, public and continuing education<sup>64</sup>.

Evaluations of DBND have shown a reduction in the rate of community prescribing, especially for respiratory tract infection in children in British Columbia, and in long-term care centres in Alberta. This was achieved by educating staff and providing feedback on antibiotic prescription rates. The awareness campaign evaluations demonstrated increased public knowledge that viral infections do not require antibiotics; increased awareness and practice of hand washing; and increased awareness of AMR.

Evaluations conclude that based on the success of DBND, a multimedia approach using print materials, advertising campaigns, and continuing education and awareness for all ages and a variety of health professionals results in a positive reach to many target audiences.

### 4.1.2 Pilot Antimicrobial Resistance Awareness Campaign (Scope: national)

The Public Health Agency of Canada's *Antimicrobial Resistance Awareness Campaign* pilot took place in November 2014. The objective was to improve knowledge and awareness of prudent and responsible AMU in the Canadian public (parents, children, and seniors), as well as in Canadian general physicians<sup>65</sup>.

Various knowledge products, including webinars, campaign and health promotion materials (i.e., brochures, posters, and infographics), and web tools were disseminated through various promotion mediums, including social media, news outlets, online, radio, and print. An evaluation survey was conducted in February 2014 to assess the campaign's impact to physicians and the public.

Results showed that the majority of physicians are aware and knowledgeable about AMU and AMR, and can regularly and confidently address these topics with patients; however, physicians were also less likely to counsel patients on topics related to infection prevention and control, and

some had false knowledge regarding causes of resistance. Post-campaign surveys indicate that 47% (n = 354) of surveyed physicians recalled receiving messages from the Government of Canada during the campaign period. Physicians and the Canadian public had good uptake of campaign materials beyond Antibiotic Awareness Week<sup>66</sup>.

Overall, evaluations concluded that using various methods of dissemination targeted specifically at particular audiences is effective. To better communicate with Canadian physicians, information should be disseminated at conferences, in scientific literature, and online.

#### **4.1.3 Hospital-based initiatives (Scope: site-specific)**

There are a number of examples of hospital-based stewardship programs. This report highlights three due to the availability of their evaluations: Mount Sinai Hospital-University Hospital Network (MSH-UHN)<sup>67</sup>, Toronto East General Hospital (TEGH)<sup>68</sup>, and Niagara Health Services Antimicrobial Stewardship Program (NHS)<sup>69</sup>. These three programs have the shared objectives of reducing AMU, especially broad-spectrum antimicrobials, while MSH-UHN and TEGH also aims to reduce *C. Difficile* infection rates. The target audiences are hospital prescribing professionals.

The main intervention techniques are prospective audit and feedback in the ICUs and the use of an infectious disease physician or pharmacist leader. Both MSH and TEGH distributed educational materials to relevant in-hospital healthcare professionals prior to implementing the stewardship program.

Evaluations of MSH and TEGH show a reduction in antimicrobial drug costs (\$27,917 less than the same period in the previous year) and reduction in the use of broad-spectrum pseudomonal antimicrobial agents by 38.9%. During the pilot, there were no cases of *C. Difficile*, and only one case post-pilot, as well as no differences in mortality or illness severity. The NHS program also saw a decrease in broad-spectrum antibiotic use by 21.2% and reduction in antipseudomonal use by 20.6%.

Overall, creators of these stewardship programs highlight the importance of appropriate human resources for effective leadership, the value of prospective audit and feedback in reducing AMU, as well as knowledge exchange, peer-to-peer communication, and decision support as key factors in success.

#### **4.1.4 Multipronged Educational Strategy on Antibiotic Prescribing (Scope: provincial)**

The program “Multipronged educational strategy on antibiotic prescribing” was implemented following a significant rise of *C. difficile* infection in the province of Québec<sup>70</sup>. The focus of this strategy was on education, particularly on implementing user-friendly guidelines targeted to outpatient physicians and community pharmacists.

Guidelines were disseminated using a multidisciplinary and mostly web-based strategy, including having downloadable versions on a dedicated website, and promotion by professionals and experts during educational events. They also had strong acceptance by the pharmaceutical industry. The guidelines themselves emphasized proper antimicrobial regimens, not prescribing antimicrobials when a viral infection was suspected, and prescribing the shortest treatment duration possible.

After guideline dissemination, evaluations found that antimicrobial use in the rest of Canada was 23.3% higher per capita than in Québec<sup>71</sup>. Antibiotic costs also fell by \$134.5/1000 Québec inhabitants, compared to the rest of Canada<sup>72</sup>.

These results show that user-friendly guidelines that are based on scientific content, concise, prepared by credible organizations, endorsed by professional organizations, and actively promoted have a significant impact on reducing inappropriate antimicrobial prescribing practices in the community, as well as reducing costs.

#### **4.1.5 Pilot study for appropriate anti-infective community therapy: Effect of a guideline-based strategy to optimize use of antibiotics (Scope: provincial)**

A community-wide, multidisciplinary educational strategy was used in Ontario with the objectives of enhancing adoption of clinical guidelines and improving AMU<sup>73</sup>. Target audiences were health professionals, pharmaceutical representatives, and the general public.

Educational strategies included a public educational campaign (such as town halls, pamphlets distributed by local pharmacists, and presentations to schools and community groups) for the general public. Health professionals also received continuing medical education, including educational packages containing guidelines, relevant scientific literature, and materials from pharmaceutical companies. Physicians also received a “non-drug prescription pad” to use during patient visits. The two main messages disseminated were to not use antibiotic for viral respiratory infections, and to use drugs recommended in the “Anti-infective Guidelines for Community-Acquired Infections”.

Evaluations show that the total number of antibiotic claims decreased by 9.4% during intervention time, with the most significant decrease occurring with upper respiratory tract viral infections (especially bronchitis)<sup>73</sup>. Physicians were found to be 29% less likely to prescribe second-line antibiotics, and more than twice as likely to prescribe first-line antibiotics after receiving education<sup>73</sup>. Participating physicians were also more likely to follow drug recommendations outlined in published guidelines, and patients were more willing to accept viral diagnoses.

The authors of the evaluation concluded that synchronizing educational efforts to the public and professionals are important in facilitating improved AMU. Innovative elements of the intervention also included leadership by motivated local health professionals in coordinating educational elements, support for these leaders, and using user-friendly and credible materials<sup>73</sup>.

## **4.2 Other Countries**

### **4.2.1 European Antibiotic Awareness Day (Scope: multi-national)**

European Antibiotic Awareness Day (EAAD), held since 2008, raises awareness regarding AMR and appropriate prescribing<sup>74</sup>. The target audience for this campaign is health professionals and the general public, including school-aged children and parents. Key messages, logos, slogans, a media and education toolkit, as well as a multimedia campaign (using webpages, booklets, and pamphlets) were all mechanisms used to reach target audiences.

Evaluations show that repeated campaigns can lead to greater involvement of professional organizations. For instance, the 2011 campaign saw an increase of more than 25% and 50% in

orders for leaflets and posters respectively, compared to 2010<sup>75</sup>. In addition, 20 countries reported experiencing a positive change attributed to EAAD, including greater AMR awareness, more prudent AMU, more political support, decrease in antimicrobial consumption, and creation of national plans against AMR<sup>76</sup>.

Overall, evaluations of EAAD have also shown these initiatives to be cost-effective and successful in raising awareness of AMR and AMU issues, and in driving behavioural changes.

#### **4.2.2 Get Smart: Know When Antibiotics Work (Scope: national)**

The United States Center for Disease Control's campaign *Get Smart: Know When Antibiotics Work* had the objectives of reducing the rates of AMR by promoting appropriate prescribing guidelines, decreasing antibiotic demand for viral upper respiratory infections, and increasing adherence to prescribed antibiotics for upper respiratory infections<sup>77</sup>.

The campaign led to the generation of materials and strategies for key partners (state and local health departments) to assist them in running local stewardship campaigns. Products include guidelines for healthcare professionals in both outpatient and inpatient settings; information for patients and pharmacists; continuing education and curriculum opportunities such as free online courses for healthcare professionals, medical students, and pharmacists; and awareness initiatives, such as Get Smart about Antibiotics Week.

Evaluations from "Get Smart Colorado" conclude that these interventions have shown a 3.8% decrease in retail pharmacy antibiotic dispenses per 1000 people, an 8.8% decrease in managed care-associated antibiotic dispenses (per 1000 people), with the highest decline occurring with pediatric members, with an associated decline in pediatric office visit rates<sup>78</sup>. Overall, the media campaign was associated with a reduction in community AMU, a decrease in office visit rates for pediatric patients; the campaign also appeared to be cost-saving<sup>79</sup>.

#### **4.2.3 Belgian Antibiotic Policy Coordination Committee (Scope: national)**

The Belgian Antibiotic Policy Coordination Committee (BAPCOC) has the overall objective of promoting judicious use of antimicrobials in humans and animals, and to promoting infection control and hospital hygiene to reduce AMR rates. Prescribers and users in both community and hospital settings are targeted<sup>80</sup>.

In the hospital setting, national campaign actions include promotion of hand hygiene in hospitals, publication of clinical practice guidelines, and staffing and technical support for all antimicrobial management teams in all Belgian hospitals. Community setting activities include multimedia campaigns to promote proper community AMU, such as the use of media, booklets, handouts, posters, prime-time television, radio, websites, and personalised letters to physicians. BAPCOC also promotes research and surveillance programmes on AMR-AMU in humans.

Evaluations have shown that public awareness campaigns led to a 36% decrease in AMU during the winter seasons, with macrolide resistance decreasing from 17% in 2001 to 2% in 2007. Hand hygiene compliance increased from 53% to 69% between the first and second campaigns. Ninety percent of Belgian hospitals have the infrastructure in place for proper antibiotic management and

infection control, and since 2004 there has been a 35% reduction of nosocomial MRSA infections in acute care patients<sup>81</sup>.

Overall, BAPCOC initiatives have resulted in a measurable decrease in AMR and AMU in the community and hospitals. It can be concluded that strong interdisciplinary public health, scientific, and political engagement will lead to evidence-based interventions, resulting in a decrease in AMR-AMU in the community and hospitals.

#### **4.2.4 Swedish Strategic Program for the Rational Use of Antimicrobial Agents and Surveillance of Resistance Program (Scope: national)**

The Swedish Strategic Program for the Rational Use of Antimicrobial Agents and Surveillance of Resistance Program (Strama) was created to address increasing use of antibiotics and the spread of resistant pneumococcal clones in the early 1990s. Strama is a multidisciplinary and multisectoral program which has developed into a coordinated national effort. Initial activities targeted penicillin resistance in *S.Pneumoniae* in the community, and initiatives have since expanded to include primary care, hospital care, nursing homes, day-care centres, as well as clinical trials<sup>82</sup>.

Local Strama groups are independent networks, coordinated by each county department for communicable disease control. They are comprised of specialists in various fields including infectious diseases, microbiology, infection control, general medicine, and pharmacy. These local groups are the drivers of Strama programs, which typically focus on providing prescribers with feedback on local or individual data for comparison with other prescribers and prevailing therapy recommendations.

A national office supports local groups, coordinates different initiatives, supplies national data, and manages a national website. Strama also has regular collaboration with news media, brochures, mobile applications, posters, on websites, and television spots, as well as education in children's health centers and schools. Other aspects of Strama include therapeutic guidelines, quality diagnostic procedures with quick turnaround, stewardship programs specific to ICU, and continuing education for prescribers<sup>83</sup>.

Evaluations have shown increased awareness as a result of Strama, and a continuous decrease in total antibiotic sales in general practice in Sweden from the 1990s until 2004. Strama's multidisciplinary program has contributed to a decrease in antibiotic use without measurable negative consequences<sup>84</sup>.

Overall, the evaluation concludes that factors of success include the use and early involvement of pre-existing structures and resources (such as communicable disease officers), using a multidisciplinary approach, collaboration with local drug and therapeutics committees and microbiology laboratories, and political support at a national level.

In conclusion, based on a review of promising and evaluated stewardship programs and initiatives, it appears that multidisciplinary programs, including those that target multiple audiences, use multiple methods of information dissemination, and that incorporate a number of approaches, appear to be most effective. More specifically, stewardship programs with appropriate expertise and clear leadership, and multiple interventions such as audit and feedback, evidence-based and

user-friendly guidelines, and parallel educational and awareness initiatives for both users and prescribers, have shown positive outcomes. Interventions should be targeted to specific target audiences as necessary (for instance, high risk users and/or high prescribers). As seen in Annex F, stewardship programs with evaluations represent only a small portion of overall existing programs. Therefore, systematic evaluations of stewardship programs need to be conducted regularly.

## **5. Challenges and Knowledge Gaps**

This chapter identifies important challenges and knowledge gaps emerging from the review of promising stewardship programs and initiatives and discussion with Task Group members.

### **5.1 Appropriate expertise**

The success and sustainability of stewardship undertakings requires appropriate and sustained resourcing, particularly, appropriate expertise, something which may not always be possible in a given setting or jurisdiction.

### **5.2 Prescriber Resources**

Most evidence-based treatment guidelines include when and how much to prescribe, without focusing on which pharmaceutical drugs to prescribe. Most treatment guidance does not focus on when not to prescribe antibiotics, as this function has generally been led by awareness campaigns. More research is required to determine if this type of guidance exists, whether producing prescriber guidance on when not to prescribe antibiotics will be beneficial, and how to implement it.

Accessibility of guidelines is another challenge. Canadian physicians have reported having difficulty locating relevant resources regarding AMR in general and regarding testing protocols<sup>85</sup>. Different guideline documents are available for different prescribing professionals. It would be important to have one or more specific sources for treatment guidelines to ensure these are standard across the country and align with the needs of provinces and territories, and the state of AMR at a local level.

Experts have expressed concern that treatment guidelines are not being used consistently across Canada. Guidance is produced at national, provincial/territorial, regional, and local level. Various guidelines can cause confusion at the prescriber level on how to treat an infection, possibly leading to suboptimal treatment. For example, physician level data shows that current antimicrobial treatment practices for gonorrhea do not follow the revised national guidelines from the Agency<sup>86</sup>.

Gaps in counselling activities of general practitioners on AMR topics may be due to their belief that other healthcare professionals, such as pharmacists or nurses, are addressing these issues with their patients<sup>87</sup>. Educational and training initiatives regarding stewardship should therefore be targeted at all prescribing professionals to help address this gap.

A scan of professional colleges and associations' websites for prescribing professionals (Annex C) showed that the majority do not have information on their public-facing websites regarding AMR or AMU stewardship. A challenge lies in determining the most effective way to engage colleges and associations within their mandates, and in clarifying their roles in promoting issues related to AMR and AMU stewardship to prescribing professionals.

Therefore, further work is needed to increase the consistency and availability of guidance on when, how and why to prescribe antimicrobials. Evidence is needed to support the development of effective guidance on when not to prescribe. Finally, information about antimicrobial prescribing and effective uptake for more categories of prescribing professionals is needed in order to support awareness, education and training among a greater number of professionals prescribers of antimicrobials.

### **5.3 Evaluation of Diagnostic Technologies**

According to the WHO March 2015 Draft Global Action Plan, rapid diagnostic tools that distinguish bacterial from viral infections and identify and characterize resistant bacteria are needed to help guide appropriate use of antimicrobials in human medicine. Evidence-based prescribing and dispensing is also recommended as the standard of care. In order for rapid diagnostic tools to be effectively and efficiently incorporated into stewardship initiatives, guidance and further research on implementation of new technologies is needed.

Integration of test-of-cure (re-culturing at the site of infection to determine if infection is still present) into guidance documents may help to increase awareness in physicians and shift prescribing practices over time. Physician-level data from the community has shown that individuals diagnosed with sinusitis and bronchitis has the highest percentage of antimicrobial recommendations provided for treatment, even though these infections are caused by viruses.

This signals a misuse of antimicrobials requiring further review, and a need to promote appropriate diagnostics, leading to more appropriate AMU. Innovation in diagnostic testing is evolving in Canada and other countries. Ideally, primary care physicians would be equipped with rapid diagnostic tools which allowed for definitive diagnosis between bacterial and viral infections, and detection of drug resistance in a timely manner, allowing for correct prescriptions to be provided to patients. Such tests have been successfully incorporated into some stewardship programs and may become important additions to future stewardship efforts. There is some evidence suggesting they are of particular value in low-resource settings. The UK national strategy on AMR allocates resources for AMR research, including clinical research infrastructure and collaboration between relevant stakeholders, while the US national strategy calls for the relevant stakeholders to be provided with the clinical isolates and technical tools needed to address test development, validation, review, and reimbursement of rapid diagnostic tools.

## 5.4 Monitoring and Evaluation

### 5.4.1 Monitoring of Prescribing Practices

Antimicrobial stewardship programs are most effective when there is a surveillance system or audit feedback in place. Audit or surveillance systems are crucial for the success of a program as they can provide retrospective or prospective data on antimicrobial use<sup>88,89</sup>.

In the community setting, little is known about some professions in which the use of antimicrobials has been increasing over time, such as pharmacists or dentists<sup>90</sup>. There is also limited data around AMU correlations categorized by prescriber category. There is a need for research to gather evidence of prescribing habits of various health professionals.

Available information on indication and antimicrobial recommendations has shown that diseases that are more likely to be caused by viruses, such as bronchitis or sinusitis, have high levels of antimicrobials being recommended for treatment. In addition, AMU varies significantly across long-term care facilities, indicating that there is no standardized approach to treatment in these settings<sup>91</sup>. It is estimated that about half of long-term care facility prescriptions for antimicrobials are unnecessary or inappropriate<sup>92,93</sup>. Many gaps still exist in the surveillance of AMR among different healthcare settings, with the biggest current gap being AMR surveillance in the community. Antimicrobial resistant organisms in the community are of particular concern as these can be common and easily transmitted. Improved monitoring of AMU in these settings may therefore be useful, in order to develop stewardship programs effective in long-term care and other community settings.

### 5.4.2 Need for Standardized Data

Information and data regarding AMR and AMU in Canada is obtained through surveillance and monitoring. Challenges exist in obtaining the data that is necessary to provide an accurate picture of the issue. Although various groups at different levels (i.e. local, regional, provincial, federal) are carrying out collection and integration of resistance data, the challenge lies in the absence of standardized methodology and definitions for resistant strains. This makes it difficult to compile and analyze information from various locations. The types of data collected and the settings in which surveillance is conducted can impact public health decision-making on AMR issues, which in turn will influence public health actions and activities.

### 5.4.3 Benchmarks for Optimal Use

Benchmarking optimal, appropriate, or judicious use of antimicrobials is difficult, because it depends on the patient's diagnosis, the antimicrobial used, and resistance. Optimal use should not be measured as a whole (i.e. total prescriptions) but instead at the individual drug type level; for instance, changes may not be observed in total use but this could be masking large changes in the use of individual drugs which might be of concern. Since each patient case is looked at individually to determine the best course of action, there is currently no standardized benchmark for optimal use. Consideration should be given to establishing optimal use and guidance by type

of infection, and by other factors, such as those associated with populations at particular risk of infection with AMR organisms.

## **5.5 Knowledge Creation and Future Research**

### **5.5.1 Prescribing Professionals**

Antimicrobial stewardship programs generally require a multidisciplinary team including infectious disease specialists, pharmacists, physicians, and nurses. Future research, educational initiatives, and guidance products should focus on all prescribing professionals. Since administering antimicrobials and patient education falls into the scope of practice of each prescribing professional, it is important that each professional group is knowledgeable about antimicrobial stewardship programs. Further information about professional groups prescribing antimicrobials is warranted, in order to appropriately target guidance products and other resources.

### **5.5.2 Regulatory Changes in Healthcare Practice**

Further research is needed to determine whether changes are required to the regulation of healthcare practices.

### **5.5.3 Assessing Effectiveness of Public Awareness Campaigns**

Awareness campaigns focussing on educating the public and health professionals about AMR and AMU have been undertaken in Canada and internationally. However, the lack of standardized indicators makes it difficult to determine the effectiveness of the campaigns<sup>94</sup>. Behaviour change related to outcome is usually difficult to measure. The most common indicators to determine the actual effectiveness of AMR campaigns are those that measure campaign reach, as defined by various web analytics measures, uptake of KTE tools, awareness of campaigns, number of knowledge products distributed, and prescription rates. Campaigns are most effective when using staged and increasingly targeted approaches, to build awareness and support behaviour change over a number of years (e.g. smoking cessation, impaired driving); Overall, further research into standardized indicators for awareness and behavior change campaigns in the context of antimicrobial stewardship, and the need for more rigorous stewardship program evaluations in general, should be considered.

## **6. Conclusion**

Leadership, appropriate interventions, monitoring and evaluation, the need for more knowledge about effective stewardship, and the evidence-base that will advance it - knowledge creation, translation and mobilization, have been identified in this report as key components of promising antimicrobial stewardship programs and initiatives. Key challenges and existing knowledge gaps have also been determined, along with a series of recommendations for consideration of the CIDSC.

While an intersectoral approach is needed, and characterized by the “One Health” approach, a common understanding or lexicon could be helpful to jurisdictions and other stakeholders to support common understanding of key components and objectives for stewardship going forward.

On an international level, in signing on to the WHO Global Action Plan, Canada and other countries agree that the improved use of antimicrobials means committing resources to ensure sustainability; effective communication, training and education for prescribers in the form of professional education and certification; raising awareness of AMU-related issues; and surveillance and research to strengthen knowledge and evidence bases for effective action<sup>95</sup>.

Countries also agree that the optimization of the use of antimicrobial medicines in human health involves better understanding the evidence concerning the increasing use of antimicrobial agents, better data about antimicrobial use at point of care, strengthened regulation and research into the distribution and use of antimicrobials, effective and evidence-based diagnostic tools for guiding use that are easily integrated into clinical and pharmacological practice, and better regulation of over the counter and internet sales of antimicrobial agents.

The provisions of these agreements align well with the findings of this report. Antimicrobial stewardship programs that are grounded in strong leadership and appropriate expertise can lead to successful and sustainable outcomes. Programs in health care settings require accountability, appropriate human resource capacity and expertise, adequate support, training, and appropriate level of compensation.

At a systemic level, a multipronged approach that incorporates a number of program elements has been shown to be promising. Programs that include a variety of interventions such as education and awareness, and the use of knowledge products such as evidence-based guidance and reference tools have demonstrated positive outcomes.

Expert and peer-led programs appear among the most promising of those evaluated. Experts in a broad range of disciplines including epidemiology, infection prevention and control, information technology, and microbiology will help to strengthen these programs. As in the case of the Belgian Antibiotic Policy Coordination Committee initiative, strong interdisciplinary public health, scientific, and political engagement can lead to a measurable decrease in AMR and improved AMU in the community and hospitals.

Promotion of education and awareness for both prescribers and the general public, and provision of antimicrobial stewardship training for prescribers as part of the formal education curriculum, including post-graduation and continuing education credit programs, can lead to more successful outcomes and greater sustainability. Education efforts targeted towards the public and professionals need to be synchronized, consistent and accessible in terms of information provided so that users and prescribers are working towards common objectives. The development of innovative knowledge-based interventions can also be led by health professionals who can recommend how to make these types of tools accessible, and how to support their use.

Multimedia approaches using print materials, advertising campaigns, and continuing education and awareness for all ages and a variety of health professionals have been shown to reach many target audiences. Finally, using various methods of dissemination targeted specifically at

particular audiences has been shown to be effective. To better communicate with Canadian prescribers, information should also be disseminated at conferences, in scientific literature, and online.

Certain prescribing professions may also benefit from targeted interventions, especially if they have been identified as providers of health information for Canadians, and where there is evidence of overprescribing<sup>96</sup>. In order to mitigate overprescribing in setting-specific situations, it is important that consistent information be available and accessible for all prescribing professionals to promote a common understanding about when to use antimicrobials. Stewardship interventions could include tools that include information on judicious use of antimicrobials and information on how to deal with patient pressure to receive antimicrobials.

Certain population groups are prescribed more antibiotics and are at greater risk of contracting AM resistant infections. Therefore stewardship initiatives may have greater impact if they include population-specific focusses. Education programs directed to parents may be beneficial because parents are key intermediaries between young children and seniors.

New and improved interventions such as rapid diagnostic tools need to be made available to professional prescribers and effectively and efficiently incorporated into stewardship initiatives. Guidance and further research on implementation of these technologies is needed in order to facilitate and improve prescribing practices.

It is important to point out that few existing stewardship programs have been systematically monitored or evaluated. This is therefore a clear area for further research. As a result, it is difficult to determine whether policies and guidelines are being used as expected, and it is equally challenging to determine whether interventions have resulted in improved antibiotic use and reduced resistance in important organisms. The last two decades of consensus-based and multi-stakeholder activities in Canada have resulted in recommendations with implications for monitoring and evaluation of stewardship activities, consistent with international strategies and activities. Monitoring and evaluation are critical in order to identify opportunities for improvement and assess the impact of improvement efforts.

The hospital-based stewardship program evaluations demonstrated a number of successful outcomes in this regard. The creators of these programs highlight the value and importance of appropriate human resources for effective leadership, the value of prospective audit and feedback in reducing AMU, as well as knowledge exchange, peer-to-peer communication, and decision support as key factors in success. It can be concluded that sharing of best practices and lessons learned both internally and publicly are important factors that can lead to more successful stewardship programs.

The value of monitoring and evaluation is highlighted in the example of the Belgian Antibiotic Policy Coordination Committee (BAPCOC). Its overall objective is to promote judicious use of antimicrobials in humans and animals, and to promoting infection control and hospital hygiene to reduce AMR rates. Overall, BAPCOC initiatives have resulted in a measurable decrease in AMR and AMU in the community and hospitals. Strong interdisciplinary public health, scientific, and

political engagement can lead to evidence-based interventions, and can result in a decrease in AMR, and more appropriate AMU in the community and hospitals.

Monitoring and evaluation of guidelines is essential in order to determine how they can be improved and whether they are being used consistently and effectively. Evaluations would help to increase the consistency and availability of guidance on when, how and why to prescribe antimicrobials. Evidence is needed to support the development of effective guidance on when not to prescribe. A good example of how evaluation can serve to inform the development of strong guidelines can be found in the Quebec based program “Multipronged educational strategy on antibiotic prescribing” that implemented user-friendly guidelines targeted to outpatient physicians and community pharmacists across the province. Evaluation of the guidelines showed that user-friendly guidelines that are based on scientific content, concise, prepared by credible organizations, endorsed by professional organizations, and actively promoted have a significant impact on reducing inappropriate antimicrobial prescribing practices in the community, as well as reducing costs.

Standardized benchmarks for optimal use currently do not exist. It can be concluded that the establishment of optimal use and guidance by type of infection, and by other factors, such as those associated with populations at particular risk of infection with AMR organisms would help prescribers determine the best course of action.

Federal, provincial and territorial governments play a key role in the collection of data and the monitoring of stewardship initiatives, and can provide support for carrying out intervention monitoring and evaluation. Surveillance data should be used to monitor and evaluate stewardship initiatives, including monitoring processes and outcome measures of hospital and community stewardship programs in order to assess their impact. Appropriate targets and indicators are required for this activity, and the activity would need to involve individuals with expertise in these data systems/analyses. Surveillance data would therefore help target stewardship interventions towards identified outliers and problem areas.

In conclusion, a successful and sustainable antimicrobial stewardship program should be based on a multi-sectoral / multi-pronged approach involving a wide range of stakeholders at the national, provincial/territorial, and healthcare organizational level. Findings of this report are based on the review of promising initiatives in human health settings in order to identify components of stewardship that could be promoted across sectors, enabling a more systematic approach to addressing antimicrobial stewardship in Canada. These findings have informed specific recommendations for the consideration of the Communicable and Infectious Disease Steering Committee and are provided in Section 7.

## **7. Recommendations**

This section presents recommendations for future antimicrobial stewardship initiatives and programs for consideration by CIDSC, drawing on common themes from reports and consensus statements from Canada and other countries, reviews of promising stewardship undertakings and challenges and gaps emerging from the literature and identified by experts from the Task Group.

## 7.1 Recommendations for Core Components of a Stewardship Program or Initiative

### 7.1.1 Leadership

Leadership has been identified as a key component of stewardship programs and interventions themselves. Stewardship programs should be grounded in strong leadership, accountability, appropriate human resource capacity, adequate support, training, and compensation and involve a variety of specialists across departments in an interdisciplinary manner at all stakeholder levels including national, provincial/territorial, and at the health care organization level. Investments by all jurisdictions will be needed.

- 1. It is recommended that a national infrastructure be put in place to support provinces and territories in their efforts to develop effective antimicrobial stewardship programs for implementation in healthcare settings and in communities within their jurisdiction.**

A national infrastructure could include, for example, the establishment of networks, governance mechanisms, and/or platforms with appropriate sustainable resources in order to communicate and share information, identify and implement promising practices/tools across health jurisdictions in Canada. The Public Health Network should play a key role in the establishment of such an infrastructure. Federal, provincial, and territorial governments, as well as national healthcare and professional associations would also play key roles.

Accountability for outcomes, and for reporting on progress towards outcomes, in the development of this infrastructure, should be assigned to a specific entity or jurisdiction.

While an intersectoral approach is needed, and characterized by the “One Health” approach, a common understanding or lexicon could be helpful to jurisdictions and other stakeholders and support a common understanding of key components and objectives for stewardship going forward.

### 7.1.2 Interventions: Education, Awareness and Tools for Prescribers and Users

Facility-specific institutions (e.g., hospitals, long-term care facilities, ambulatory surgical centres, and private practices) could benefit from stewardship program leaders who are responsible for program outcomes. A physician champion as lead with a pharmacist co-lead has been shown to be especially effective. If in-house experts are unavailable, an external consultant could be used to assist with implementation. Provincial and territorial healthcare associations could play key roles in implementation.

Less information is available about leadership for successful stewardship programs in community settings, and additional information is required to identify promising practices in this area.

- 2. It is recommended that best practices for leading the successful implementation of stewardship programs in facilities and in communities be developed and shared, as part of a national infrastructure to support provinces and territories.**

Education and awareness activities should target multiple prescriber groups, across both hospital and community settings. This will help ensure that individuals receive consistent messaging about appropriate use of antimicrobials from all prescribing professionals (i.e. from the prescriber as well as the dispenser of the antimicrobial). Education initiatives should also have a dual focus of both prescribers and users, both in hospital and community settings, to ensure that the same message is being received by both groups.

- 3. It is recommended that best practices, benchmarks or standards for education and awareness activities within the context of stewardship programs require 1) the targeting of multiple prescriber groups and 2) a dual focus on users and prescribers.**

Guidelines should be made more easily accessible and available in a timely manner to all prescribers and dispensers. Professional organizations, colleges, and associations, can play a key role in the dissemination of these resources and information through various media techniques (i.e. websites, conferences). General public awareness initiatives should also use various media techniques to reach the widest audience possible. For example, an algorithm with the most common inappropriate prescribing practices for viral infections could support prescribers in their decision making.

Health care workers (health professionals, staff in health care settings) should be given baseline training in infection prevention and control practices as part of antimicrobial stewardship programs, and this knowledge should be maintained at provincial and regional levels to significantly improve the overall situation in health care settings. Professional colleges can play a key role in this initiative since they have a role in establishing best practices.

- 4. It is recommended that the consistency and accessibility of materials, training in infectious disease prevention and control, and related tools for prescribing professionals and users be improved, to facilitate appropriate prescribing practices.**

These products must be developed on the basis of evidence from surveillance and related activities.

- 5. It is recommended that universities, colleges, and technical schools that train future prescribers incorporate mandatory antimicrobial stewardship education as part of their training for students and residents, as well as continuing education curriculums for all prescribing professionals.**

### 7.1.3 Monitoring and Evaluation

Federal, provincial and territorial governments play a key role in collection of data and the monitoring of stewardship initiatives, and can provide support for carrying out intervention monitoring and evaluation.

Surveillance data should be used to monitor and evaluate stewardship initiatives, including monitoring processes and outcome measures of hospital and community stewardship programs in order to assess their impact. Appropriate targets and indicators are required for this activity, and the activity would need to involve individuals with expertise in these data systems/analyses. Surveillance data would therefore help target stewardship interventions towards identified outliers and problem areas.

Individual healthcare facilities can include surveillance of AROs in their mandates, based on their capacity for data collection and access to hospital laboratory services. AMR and AMU data should be used to inform population-specific stewardship approaches, such as programs targeted at those at highest risk for acquiring antimicrobial resistant organisms.

- 6. It is recommended that evidence-based audit and feedback tools and mechanisms be developed to support prescribers in their efforts to judiciously prescribe at the local level, including recommending alternatives to antimicrobials to their patients.**
- 7. It is recommended that guidelines for prescribers be evaluated, adapted and implemented at provincial and regional levels. Provinces, territories and regional jurisdictions should be responsible for ongoing monitoring and evaluation of the guidance once implemented.**

Tools such as audit forms and drug use evaluations and feedback will help to standardize evaluations of stewardship programs. The jurisdiction responsible for the stewardship program should be responsible for conducting evaluations.

- 8. It is recommended that benchmarks be established for optimal use by type of infections, and populations at greater risk for infection.**
- 9. It is recommended that federal, provincial and territorial governments work together to establish performance measurement targets in hospital and community settings for consideration by jurisdictions.**
- 10. It is recommended that timely evaluations of stewardship programs be conducted and that the results be made publicly accessible so that best practices can be shared.**

Consideration should be given to the federal role in recommending to granting agencies that evaluation of stewardship projects be included as a priority for funding.

#### **7.1.4 Future Research: Knowledge creation, translation and mobilization**

**11. It is recommended that further evidence be gathered on the prescription profiles of all prescribing professionals. This would help determine the need and type of stewardship interventions for these professions, such as guidance or education. Federal, provincial, and territorial jurisdictions governments should be responsible for collection, analysis and mobilization of this information.**

**12. Finally, changes to healthcare practitioners' practice regulations are recommended; however further evidence should be gathered to support such a change.**

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