Combating Antimicrobial Resistance in Canada:

Listening Session with Pharmacists to Inform Public Policy Incentives

A summary report from the

Canadian Society of Hospital Pharmacists Annual Conference

February 2020

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Sponsored by:

MERCK

Canadian Anti-infective Innovation Network

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The global antimicrobial resistance (AMR) crisis is serious, yet the opportunity for Canadian leadership is extraordinary. In Canada, we have the expertise and the track record to tackle AMR and provide solutions. The Canadian Anti-Infective Innovation Network (CAIN) was created in 2016 and is currently an alliance of over 100 academic, private sector, government and not-for-profit researchers, clinicians, and advocates who are dedicated to fighting AMR from a One Health perspective[1,2]. AMR currently requires policy solutions to be multi-faceted, cut across different sectors and be suited to the local healthcare environment. In order to help inform the development of policy solutions for Canada, there is a need to understand the practice of using antibiotics in Canada's health system today, from the perspective of health providers in Canada.

Objectives

The main objectives of CAIN are to raise the profile of the AMR crisis in Canada, identify new resources to support made-in-Canada solutions, and to educate the public and public servants on the challenges we face and the opportunities we have[1]. The Pan-Canadian Framework for Action on AMR and Antibiotic Use highlights the impact of AMR on the world if we do not address the crisis, and outlines a strategy to achieve tangible goals to safeguard Canadians[3]. CAIN seeks to support the Framework by harnessing Canada's expertise, research infrastructure, and innovation to identify resources and partners.

In Canada and other jurisdictions around the world, experts and policymakers are examining public policy solutions to mitigate the impact of AMR on our health system. Canada has prepared a Pan-Canadian Framework for AMR, and Canada's corresponding Pan-Canadian Action Plan is due to be released in the coming months[3].

One set of policy solutions can be aimed at encouraging appropriate use of new antibiotics, to confront the market-related barriers that have forced the antibiotics companies to abandon the market or enter bankruptcy. Public policy incentives could relate to funding for research, regulatory guidelines and market-based incentives that address market failure surrounding the introduction of new antibiotics.

Rationale and Goals

AMR is a complex issue that requires policy solutions to be multi-faceted, cut across different sectors and be suited to the local healthcare environment. In order to help inform the development of policy solutions for Canada, there is a need to understand the practice of using antibiotics in Canada's health system today, from the perspective of health providers in Canada.

This unique listening session with Canadian hospital and community pharmacists contributes to the research and innovation pillar of the National Action Plan.

The **goals** of the listening session were to:

- Understand current "pain points" concerning the use of antimicrobials and stewardship in the hospital setting
- Discuss collaboration between pharmacists, microbiologists and infectious disease physicians
- Learn about incentive policies in other jurisdictions that involve hospital pharmacy, and obtain feedback if or how those policies would be relevant and/or helpful in Canada

The **main topics** of our listening session, including the questions posed to participating pharmacists, were:

- Best practices of hospital pharmacists when treating patients with multi-drug resistant infections
- When a patient is presented with a multidrug resistant (MDR) pathogen in the hospital:
    - How do you determine the antibiotic to be prescribed?
    - If a pathogen is known to be resistant to antibiotics in the hospital formulary, what steps are taken at that point? How would an antimicrobial strategy look?
    - What is the interaction between you, hospital administration, ID physician? Others?
    - Do you believe you have the necessary information to determine when prescribing a new antibiotic is recommended? If not, why not?
    - What challenges exist with respect to handling MDR-pathogens in a hospital setting that must be addressed to better respond to AMR as a public health issue?
- Challenges for antimicrobial stewardship pharmacists
    - What is the role of pharmacists in encouraging appropriate use/stewardship?
    - Do you feel stewardship pharmacists are supported by clinicians in decision making? Do you create institution guidelines and collect surveillance data?
    - Do you believe stewardship for older (sometimes more toxic) antibiotics should be differentiated from newer antibiotics, and if so, why/why not?
    - What are the challenges of incorporating a newer antibiotic into the stewardship protocol or formulary if the antibiotic is not yet available?
    - If you were to receive education regarding stewardship for new antibiotics, what kind of information would you be seeking? Who would be the ideal party to provide the education?
    - What data would you look for that is currently missing regarding use of new antibiotics for multi-drug resistant pathogens?
    - What are the barriers in ordering a new antibiotic to have it on your shelf?
- Implementing incentive policies in Canadian hospitals and federal/provincial/territorial government
    - How could the federal/provincial/territorial governments assist a hospital in

covering costs of optimizing the use of novel diagnostics/antibiotics?

- If the federal/provincial/territory governments provided a pocket of funding to cover costs of optimizing the use of novel antibiotics, how could that work in your pharmacy?
- Would a subscription based model work for your hospital to ensure products were kept on the shelf?
- Are there any policies that would not have a cost component to them that will enhance innovation?

Antimicrobial resistance crisis in Canada

Antimicrobial resistance (AMR) is an increasing worldwide public health threat that can lead to an economic disaster in Canada. In 2018, there were approximately 250,000 antibiotic resistant infections and 5,400 Canadians with these infections died[4]. It is estimated that by 2050, if resistance to first-line antimicrobials remains constant at the present rate, AMR could be attributed to 7,000 deaths, reduce Canada's gross domestic product by $13 million per year, and Canada's healthcare costs would increase to $6 billion per year. This crisis may be aggrevated by the ongoing Coronvavirus Disease 2019 (COVID-19) pandemic. Azithromycin, a commonly used antibiotic to treat bacterial infections, is being increasingly prescribed and studies in randomized trials in an effort to improve clinical outcomes in COVID-19 patients and identify effective treatment against COVID-19, respectively. We may find that reductions in COVID-19 mortality may lead to increases in AMR mortality, beyond those currently estimated by 2050. More than ever before, there is a need for antimicrobial stewardship programs and policies to reduce infection rates and improve antimicrobial use, which will require support from physicians, nurses, hospital management, and pharmacists.

Infectious disease consultant, antimicrobial stewardship, community, and student pharmacists in Canada

Hospital pharmacists (HPs) are an essential and valuable resource in the fight against AMR. HPs can specialize as infectious diseases consultants and antimicrobial stewardship pharmacists who are responsible for interacting with patients, therapy decision making, developing antibiograms, collection of antimicrobial metrics, and antimicrobial drug-use evaluations within the hospital setting. Public Health Ontario has published antimicrobial stewardship strategies, programs, and tools mostly for hospitals and corporations[5]. While most antibiotic resistant infections appear in the hospital setting, a majority of antibiotics are administered in outpatient/community settings. In fact, in 2016, 92% of the defined daily dose of antimicrobials were dispensed through community pharmacies, compared to 8% dispensed through hospital pharmacies[4]. Therefore, there is a need for community pharmacists (CPs) to develop antimicrobial stewardship programs in outpatient settings[6].

To understand the best practices and challenges of pharmacists in Canada, this listening session included infectious disease consultant, antimicrobial stewardship, community, and student pharmacists employed in Ontario.

BEST PRACTICES AND CHALLENGES OF PHARMACISTS

Approval processes drive inaccessibility of antibiotics

Universal access to effective antibiotics is essential for fighting antimicrobial resistance[7]. One of the main challenges is the fragmentation and administrative burden of antibiotic approval leading to the inaccessibility of novel antibiotic use. In Canada, the Special Access Programme (SAP) considers access to antimicrobials that are unavailable for sale in Canada. The SAP approval requires the pharmacist to identify the known risks of the product, marketed alternatives, manufacturing standards, product information provided by the manufacturer, the drug's stage of development, and level of evidence for use in a condition[8]. However, pharmacists find it very difficult and time consuming to identify the information required for SAP approval as is not in their realm of expertise and much of this information, e.g., manufacturers of drugs, is subject to change. Ontario pharmacists' challenges are heightened with the additional need to obtain Exceptional Access Program (EAP) approval to facilitate patient access to antimicrobials that are not funded by the Ontario Drug Benefit program formulary. While the EAP has published approval criteria and listed frequently requested drugs that have patient-centric templates, the SAP does not have a list of previously approved drugs, nor is the process patient-centric or easy to understand[9]. Furthermore, the narrow scope of the programs' eligible indications for antibiotic treatment can limit approved use. Above all, obtaining SAP and EAP approval is a lengthy process while their patients' health are limited by time.

One possible solution to optimize the use, and facilitate access to novel antibiotics, is to harmonize the SAP and EAP approval at the federal level to ensure adequate access to antibiotics. Hospital pharmacists believe a top-down approach is the most suitable for implementing antibiotic access policies because it allows for a governance structure that each institution can adopt. It would be difficult for each institution to develop their own approach to accessing antibiotics as this would not be sustainable across institutions, since funding mechanisms differ at each institution, within each ward, and pharmacy. An example of an initiative that can be paralleled as a potential solution to barriers in accessing antibiotics is the development of the Canadian Antidote Registry[10]. In this model, there is a national web-based registry where each hospital is required to report their inventories of antidotes, and there are provincial and local coordinators appointed for each province/territory and hospital/health institute, respectively, who are hospital pharmacists that will lead the initiative. The Canadian Antidote Registry is a top-down approach to solving the previously inadequate stocking of antidotes, which hospital pharmacists feel is an appropriate solution to their current, locally coordinated, grassroots initiatives to accessing antibiotics that are not available in Canada. Lessons can also be drawn from the system established for streamlined access to artesunate or quinine for the treatment of severe malaria. The Canadian Malaria Network (CMN) was created in collaboration with Health Canada and the Public Health Agency of Canada because of adverse outcomes associated with the delay in acquiring parenteral malaria therapy. Whereas severe malaria is not common in Canada (14 cases on average per year), AMR is an ever-increasing threat to public health, with 5,400 directly attributable deaths in 2018 and estimated to rise to 13,700 in 2050. With citizens and AMR widespread across Canada, the need for rapid access and distribution of novel antibiotics is imperative. A Canadian model for

antibiotic reimbursement paralleling the CMN is promising as it streamlines the administrative burden to access new antibiotics and dissociates the financial burden of using new antibiotics from the hospital payer. Details of how such a program might look across federal, provincial, territorial and hospital levels based on the CMN are outlined in **Feature 1**. Overall, it is recommended that a national program or policy should be developed to ensure consistency and sustainability across provincial, local, and institutional levels. This would allow for easier surveillance and tracking of antibiotic use, revealing opportunities to integrate stewardship principles into use of these novel antibiotics.

Feature 1

Organizational Level	Framework for a National Network based on the Canadian Malaria Network (CMN)
Federal	Antimicrobial approval for access and funding facilitated due to centralization at the federal level. Leadership provided by a 1) national program coordinator and 2) national pharmacy coordinator. All antibiotics could be made available solely by Health Canada's Special Access Program, like the malaria drugs. Criteria for novel antibiotic use established.
Provincial / Territorial	Distribution executed by varying depot hospital pharmacies required to stock a given type and quantity of novel antibiotic. Standard stock of novel antibiotics can be set by local leaders (e.g. clinical pharmacists, clinical microbiologists, infectious disease specialists, epidemiologists) across depot pharmacies and tailored to local AMR epidemiology. Each participating center can have a designated physician with experience in treating AMR infection (e.g. infectious disease specialist) who is appointed to guide in the management of AMR infections. Each centre provides surveillance data to Health Canada on all malaria cases treated with these antibiotics. • The CMN is established in 13 medical centres across Canada • The AMR program equivalent will likely need more participating centres given the burden and widespread of AMR in Canada, relative to malaria. • Designated physician and pharmacy contacts (by province)
Hospital	To obtain the new antibiotic, the listed pharmacy for your area can be contacted. The designated participating centre physician can serve as a resource for any questions related to antibiotic treatment. Prescribing physicians, within or outside a depot hospital, will have the following minimum reporting requirements to the network and Health Canada: adverse events, patient characteristics and drug usage. The treatment can be delivered from depot centres via courier to prescribing physicians.

Even when SAP and EAP approvals are obtained, the clinical microbiology lab within the hospital / health institution must develop appropriate antibiotic susceptibility tests to determine if the antimicrobial will be effective in treating a patient's infection. Institutions can have automatic or manual methods of antibiotic susceptibility testing and this newly approved antibiotic must pass the same standards as the institution's current formulary. One possible solution is for public health laboratories to take the lead in developing and validating antibiotic susceptibility tests for commonly SAP/EAP approved antibiotics.

A patient's challenging transition between the hospital and community

When hospital pharmacists decide on the antibiotic therapy to treat an infection, they also have to consider the patient's transition into the community. HPs often treat complicated and severe infections starting with intravenous (IV) antibiotic therapy. While some patients are clinically indicated to convert from IV to oral antibiotic therapy[11], others require long-term IV therapy to treat their infection, even if they are otherwise healthy and stable. While there are some outpatient IV antibiotic clinics in Canada, they are not uniformly nor easily accessible, especially when some therapies require daily visits[12,13]. Therefore, if the HP decides to start IV antibiotic therapy, the patient could stay in the hospital for weeks to months because of the lack of alternatives in the community to finish treatment[14]. A prolonged hospital stay reduces hospital bed efficiency, in turn increasing hospital costs and resources. While access to community IV care is different in each province and territory, British Columbia has a robust model for outpatient IV therapy that could be realized in other provinces and territories. British Columbia offers many home and community IV programs to help with discharged patients' transition to safe and effective IV antibiotic therapy. They are also home to the Community Transitional Care Team which offers residence, food, and long-term antibiotic therapy for patients with chronic and acute addiction issues[14,15]. Long term care homes in British Columbia offer IV therapy to residents[16], while in Ontario, long term care home residents can be transferred to the hospital to access IV therapy[17] because of the poorly coordinated services among healthcare providers[18]. Even though Public Health Ontario has established an antibiotic stewardship recommendations long term care facilities, they do not cover improving access to intravenous antibiotic therapy when indicated[19] . Thus, a potential soluation to improving an Ontario patient's transition from hospital to community is to develop a provincially connected and sustainable program for IV hospital access.

Lack of collaborative practice in the community

Community pharmacists struggle with deciding whether or not to dispense antimicrobials to patients, who in their opinion, have no clinical indications of requiring antimicrobial, for example, treating a viral, fungi, or parasite infection with an antibiotic. Disagreeing with, and even, contacting the prescribing physician is difficult and often does not lead to a consensus decision[20]. If the community pharmacist refuses to fill the prescription, the patient will likely fill their prescription elsewhere and foster a poor relationship with the patient. There have been efforts to lead practice changes to bolster antimicrobial stewardship in community health care settings, however community-based prescribers need to be motivated to adopt these practices[21]. It is clear that attitude and behavioural changes in all antibiotic therapy decision makers must be met for antimicrobial stewardship programs to be effective.

There exists a lag time and pure disconnect in the information flow between hospital and community pharmacists. HPs, especially those working in an academic / teaching institution, feel that information about new antibiotics, e.g., newly published scientific articles, are easy to access since there is much discussion with colleagues. However, CPs feel it is their own independent effort in staying updated with the latest science on new antibiotics. In addition to

information about new antibiotics, patient information is siloed. While hospital pharmacists use ConnectingOntario ClinicalViewer to view microbiology lab results and patient data, CPs have limited access to patient and hospital data, thus they often rely on the patient themselves to reveal their personal history, symptoms, and diagnoses. A solution would be to allow community pharmacists to have access to ConnectingOntario ClinicalViewer, or even a centralized database that contains epidemiological data for antibiotic susceptibility testing results for their community. Each year the British Columbia Centre for Disease Control (BCCDC) monitors trends in antibiotic resistance and antibiotic utilization in BC[22]. In particular, BCCDC partners with BCBiomed and LifeLabs to show community antibiotic susceptibility testing result trends, organism and antibiotic combinations. Other provinces could also develop similar programs, and this would be easier if there was a national framework in place to ease data tracking and dissemination.

Interim solutions to challenges in achieving best practices of hospital and community pharmacists can temporarily facilitate the day-to-day responsibilities of hospital and community pharmacists, however implementing appropriate incentive policies in Canada is required for the sustainable fight against AMR.

IMPLEMENTING INCENTIVE POLICIES IN CANADA

Antibiotic research and innovation is limited by difficulties experienced in the discovery science, regulatory, and commercialization stages[23]. Surveillance, stewardship, and infection prevention and control are all effective measures to delay the development of AMR; however, when faced with an antibiotic resistant organism to save a patient's life, our healthcare workers (HCWs) — doctors, pharmacists, laboratory technicians — rely on an arsenal of antibiotics assembled over the last century — starting with Alexander Fleming's accidental discovery of penicillin in 1928 — to fight infection[23,24]. The development of AMR is inevitable, and we will run out of antibiotics if no immediate action is taken. We need to reinvigorate the antibiotic pipeline by implementing incentive polices for novel antibiotics to ensure they are available when we need them[25]. In this section, we will discuss funding structures of novel antibiotics and will draw on existing policy responses that could be adapted for the Canadian AMR setting.

1. How could the federal/provincial/territorial governments assist a hospital in covering the cost of optimizing the use of novel antibiotics?

*By implementing policies to **centralize funding** of novel antibiotics.*

Antibiotic costs are covered largely by hospital pharmacy budgets, which vary by hospital and hospital unit[26]. Unlike oncology drugs which are orders of magnitude more expensive, antibiotics are not a large proportion of the hospital pharmacy budget and changes to their funding model may have lesser impact on provincial funding allocations to hospitals if removed.

Opportunities for further exploration:

- Separation of antibiotics from the hospital budget and direct integration into an AMR only government funding model

- Lessons can be drawn from the provincial funding mechanism for extracorporeal membrane oxygenation (ECMO), where cost of treatment is covered directly by the province[27]. This strategy has several advantages which include 1) bypassing hospital formularies and pressure to return funding into the hospital budget, and 2) preventing risk of diluting funds for novel antibiotics amongst other expenses covered by the hospital budget. The extent of the coverage is based on hospital volume and epidemiological data of prior use. Similar strategies can be applied for patients with antibiotic resistant infections, in which cost of treatment with antibiotics for resistant infection would be reimbursed for a set number of patients determined from prior AMR hospital epidemiological data (e.g. annual number Carbapenemase Producing *Enterobacteriaceae* cases). These 'buckets of funding' would be dedicated to treating antibiotic resistant infections and would mitigate financial pressure to use cheaper, less effective antibiotics because the funding for novel antibiotic use would not be leveraged against competing drugs in the total hospital budget. This strategy could also encourage appropriate decision making in hospital formularies for novel antibiotics and could be pathogen-specific. It could be informed by the World Health Organization's priority pathogens list to not only reimburse a set number of patients, but a set number of infection types, particularly carbapenem resistant organisms which are a critical priority.

2. How can the federal/provincial/territorial governments reinvigorate research and innovation of novel antibiotics?

*With **financial incentive policies** for novel antibiotics.*

Stewardship programs promote the prudent use of novel antibiotics — a limited resource — and reserve their use until alternative antibiotics have proved ineffective. This effort to delay the development of resistance in novel antibiotics, along with the short duration of treatment, translates to limited use of novel antibiotics and precludes the return of investment for pharmaceutical companies, so much so many have gone bankrupt after market access (e.g. Achaogen filed for bankruptcy 10 months after plazomicin was approved by the FDA)[26,28].
The financial woes of antibiotic research and development begin long before market access. Over the years, many Big Pharma companies have abandoned antibiotic research, leaving small pharmaceutical companies to undertake the overwhelming financial burden to bring an antibiotic to market and may lack infrastructure for commercialization. The current state of the antibiotic pipeline is inadequate because of this, with only 41 in clinical development, of which 18 are addressing critical threats. It is expected that only 20% will make it to regulatory stages. Immediate action to reinvigorate the antibiotic pipeline is needed. Incentives can help mitigate the financial burden for small pharmaceuticals pre- and post- market access, and attract 'big pharma' back into antibiotic research and development. Perpetual payments for every successful antibiotic brought to market is unsustainable[29]. Perhaps a fundamental shift in antibiotic research innovation is overdue, in which for-profit interests in antibiotic research and development are replaced with a publicly funded payment model?

Opportunities for further exploration:

- **Push incentives** reduce the up front cost of research and development. They include grants and public-private partnerships and attract venture capitalists, but are riskier given that only 1/5 antibiotics will make it to market. In contrast, **pull incentives** focus on reimbursement for cost per sale post-market access[26,28,29].

- Lessons can be drawn from the Developing an Innovative Strategy for Antimicrobial Resistant Microorganisms (DISARM) act introduced in the US in 2019. The DISARM act permits for greater reimbursement of novel antibiotics from Medicare, but requires participating hospitals to conduct surveillance of antibiotic use, report findings to the US Centers for Disease Control and Prevention (CDC) and establish antibiotic stewardship programs[30].
- **Market entry awards and advance market commitments** are types of pull incentives that would support the transition from research to market by rewarding market access and subsidising the cost of novel antibiotics over a predefined time frame, respectfully. They aim to support commercialization in an effort to stabilize the antibiotic market and prevent bankruptcy post-market access[26,28].
- **Subscription payment models**, which are a derivative of advance market commitments, aim to decouple cost from the volume of antibiotics sold. Applied to novel antibiotics, they would award pharmaceutical companies having brought novel antibiotics to market with structured payments based on their estimated value to society. The United Kingdom launched the world's first subscription payment model incentive for novel antibiotics in July 2019 and has the potential to generate a sustainable market for antibiotics, especially if expanded to other high-income countries with large pharmaceutical markets like the US[23,31]. Potential unification of target antibiotics, prioritizing those classified as critical and high priority by the WHO (e.g. CROs, extremely drug-resistant (XDR) Gram-negative Bacilli and Mycobacterial infections), and funding between countries, similar to what the Vaccine Alliance (Gavi) has done with vaccines, can be implemented for the antibiotic pipeline and AMR[28].
- **A publicly funded payment model** for novel antibiotics would fundamentally shift the antibiotic market, which has historically been for-profit and founded in entrepreneurship[28]. A key advantage to a non-for-profit model would be the freedom to address unmet needs due to lack of pressure to generate profit for shareholders and increase antibiotic prices. Antibiotics with low sales would be economically feasible. The TB Alliance and the Medicines for Malaria Venture demonstrate the potential for successful nonprofit models for the research and development of essential medicines[28]. An estimated $1 billion to $2 billion in market entry awards is required for every antibiotic post-regulatory approval[32]. Experts have called for the serious consideration of a non-profit payment model for novel antibiotics, in which one-time seed capital to establish this not-for-profit organization can be reallocated from a single market entry award[28].

Changes to the funding models of antibiotic research, development and commercialization need to be accompanied by changes to antibiotic stewardship programs. The Canadian Antimicrobial Resistance Surveillance System (CARSS) is Canada's national system for reportable antimicrobial resistance and use, but captures data from a limited number of bacteria, physicians and hospitals[33]. These changes may provide an opportunity for CARSS to create a more integrated and informative network of AMR surveillance and epidemiology with participating hospitals — how US hospitals participating in the DISARM act are accountable for reporting to the CDC[30]. New funding models may encourage the addition of new antibiotics to hospital formularies and lessen the pressure to use less effective, existing antibiotics because they are cheaper. This may help stewardship programs accurately balance effectiveness with judicious use of antibiotics, independent of cost.

3. Are there policies that would not have a cost component to them that will enhance innovation and optimize use of novel antibiotics?

Reduce barriers to regulatory approval *for novel antibiotics.*

Regulatory review of novel antibiotics by Health Canada is costly and timely, ranging from 6 months to 2 years. This delay to market access is in addition to the 10 plus years dedicated to drug discovery and clinical trial research to demonstrate efficacy and safety[34]. Opportunities for expedited review and approval, especially for antibiotics indicated for difficult to treat infections like hospital acquired pneumonia, could help motivate the antibiotic pipeline. The Generating Antibiotic Incentives Now (GAIN) act introduced in the US in 2012 is one such opportunity. It offers quicker registration and approval, 5 additional years of market exclusivity and special designation for use in a limited population with unmet needs; however, use and return on investment are based on post-market activities, which are associated with their own unique barriers[35].

Greater emphasis on AMR in formulary decisions *for novel antibiotics.*

The Canadian Agency for Drugs and Technologies in Health (CADTH) employs a pan-Canadian approach in formulating drug reimbursement recommendations for federal, provincial and territorial public drug plans, with the exception of Quebec, after regulatory approval by Health Canada[36]. In their consolidation of studies that report on clinical effectiveness, safety and cost-effectiveness, the health and economic burden of AMR could be stressed. Accounting for AMR epidemiology and cost in their analyses, relative to the cost of a novel antibiotic, would better inform decision makers at all levels of government and allow for adaptation of formularies to a province's, city's or hospital's AMR landscape.

Audit and feedback *to guage use of novel antibiotics.*

A recently published study found that US hospitals waited a median of 398 days to prescribe any one of the 6 new antibiotics approved by the US Food and Drug Administration in the last 5 years, with some hospitals waiting more than 4 years[37]. Audit and feedback provides an opportunity to understand the prescribing and dispensing patterns of novel antibiotics (e.g. delay of use of a newly approved antibiotic). This exercise could also inform hospital formularies and clinical decision support tools that would help identify a subset of patients that would benefit most from these novel antibiotics, without compromising on antibiotic stewardship.

KEY TAKEAWAYS

- Best practices, including acces to novel or non-marketed anitbioics of hospital and community pharmacists are limited by:
    - The lengthy turnaround time and administrative burden of obtaining Special Access Programme and Exceptional Access Program approval to use antibiotics Canada or fund antibiotics in Ontario that are not covered by the provincial formulary.
    - The inability of a patient to transition to the community with intravenous antibiotic therapy in Ontario due to poor coordination of services among health care workers, driving the sparsity of outpatient IV clinics in Ontario.
    - The siloed communication and lack of collaborative practice between health care workers in the hospital and the community.
- The cost of novel antibiotics discourages their appropriate clinical use; however, centralizing funding at the federal level by removing the financial burden from hospitals may mitigate pressure to use cheaper, less effective antibiotics. Centralized funding may come with a call for increased surveillance of novel antibiotic use and AMR, which could reveal opportunities to integrate stewardship principles into the use of these novel antibiotics.
- The current state of the antibiotic pipeline is inadequate and challenges in commercialization further threaten novel antibiotic research and innovation; however, Canada is well positioned to provide incentive policies.
    - Push incentives reduce the up front cost of research and development, whereas pull incentives focus on reimbursement for cost per sale post-market access to in an effort to create a viable antibiotic market.
    - A subscription payment model, one type of pull incentive, could award pharmaceutical companies having brought a novel antibiotic to market with structured payments based on their estimated value to society.
    - A publicly funded payment model would fundamentally shift the structure and operation of the antibiotic market, which has historically been for-profit and founded in entrepreneurship. A key advantage to a not-for-profit model would be the freedom to address unmet needs from lack of pressure to generate profit for shareholders and increase antibiotic prices. Antibiotics with low sales would be economically feasible.
- Reducing barriers in regulatory approval, actively considering AMR in formulating drug reimbursement recommendations, and audit and feedback of novel antibiotic use are all strategies without a cost component that could also help optimize use and innovation of novel antibiotics.

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