



Antimicrobial Resistance

See also [CMA Policy Antimicrobial Resistance PD19-08](#)

OVERVIEW

The world is at the tipping point of a post-antibiotic era. “Worldwide, we are relying more heavily on antibiotics to ensure our medical, nutritional, and economic security; while simultaneously causing the decline of their usefulness with overuse and ill-advised use.”¹ It is estimated that the world’s use of antimicrobials increased by 65% between 2000 and 2015 — mainly in low- to middle-income countries.²

Dr. Margaret Chan, the former head of the World Health Organization (WHO), described antimicrobial resistance (AMR) as a slow-moving tsunami for public health. Other experts have characterized AMR as a looming “antibiotic apocalypse,” warning that all countries “will face disastrous consequences if the spread of AMR is not contained.”³ Others are now calling AMR the “climate change” of health care. According to the UK’s review on AMR, an estimated 10 million people globally will die annually by 2050, and AMR will surpass cancer to become the leading cause of death.⁴

AMR occurs when “microorganisms (such as bacteria, fungi, viruses, and parasites) change when they are exposed to antimicrobial drugs (such as antibiotics, antifungals, antivirals, antimalarials, and anthelmintics). ... As a result, the medicines become ineffective and infections persist in the body, increasing the risk of spread to others.”⁵ Microorganisms that develop antimicrobial resistance are sometimes referred to as “superbugs.” “Nightmare bacteria,” as they have been dubbed, are bacterial strains that no conventional antimicrobial can effectively treat; their incidence is on the rise.⁶

AMR represents a unique challenge for the medical profession as it is estimated that as many as 50% of current antibiotic prescriptions are either inappropriate or unnecessary.⁷ In addition, taking an antimicrobial involves potentially considerable exposure to side effects or risk. At stake are many currently routine, and lifesaving, forms of medical treatment. Critically, these include many medications for currently treatable bacterial infections, and many forms of surgery (including cesarean delivery), radiation therapy, chemotherapy and neonatal care.⁴

THE UNDERLYING DYNAMICS OF AMR

AMR is driven by a complex set of interlocking factors. These include: (1) increased global travel and medical tourism; (2) inappropriate, and unnecessarily high, use of antimicrobials in the agrifood sector; (3) poor medical prescribing practices; (4) inadequate implementation of infection prevention and control measures; (5) lack of knowledge, inappropriate expectations and misuse of antimicrobials on the part of the general public; (6) availability of poor-quality antimicrobials; (7) lack of access to rapid, affordable and accurate rapid diagnostic tools and infrastructure; (8) inadequate and underused surveillance data from AMR surveillance systems; (9) international travel rates; and (10) low commercial interest in, or support for, new antimicrobial research and development.⁸

To make progress on AMR, we need to carefully think about how to address its various drivers. Antimicrobial stewardship (AMS) is a term describing coordinated efforts, at any program level, to: (1) promote the appropriate use of antimicrobials; (2) improve patient outcomes; (3) reduce microbial resistance and preserve the effectiveness of antimicrobials; and (4) decrease the spread of infections caused by multidrug-resistant organisms.⁹ AMS efforts are based on the “One Health” approach. These include: (1) surveillance; (2) conservation of existing AM effectiveness; (3) innovation through research and development; and (4) infection prevention and control.¹⁰

Fundamentally, AMR can be thought of as a collective action problem, similar in character to the problem of climate change.^{3,11} While all stakeholders have a role to play in combatting AMR, each has very different resources, abilities and perspectives on AMR.¹² Canada and much of the developed world have the luxury of health infrastructures, finances and regulatory frameworks that can make AMR mitigation possible. But in low- to middle-income countries — places where antibiotics might be the only real health care available — the very discussion of AMS can be perceived as threatening. Simply put, this illustrates the fact that solutions to AMR need to mobilize and leverage a collective strategy that is as broad and as connected as possible. To be successful, these solutions will need to do so in a manner that acknowledges the local reality of health care delivery.¹³

Global investment in antimicrobial research and development is underwhelming, a dynamic described as a “drying up” of the pharmaceutical pipeline.⁸ This is evidenced by the recent large-scale withdrawal of major pharmaceutical companies from antimicrobial research and development, reflecting the lack of profitability in this area. On the pharmaceutical side, there are clear barriers to companies investing in the development of novel antimicrobials. Underlying factors include: (1) 10-year timelines, and an estimated minimum \$1 billion price tag for development; (2) high development failure rates for new antimicrobials; (3) the inevitable emergence of resistance to any newly developed antimicrobial; (4) antimicrobials being offered at relatively cheap dosage rates over shorter durations of use; and (5) the need to preserve the efficacy of any antimicrobial’s future use, which limits their economic viability.⁸

WHAT ARE THE CANADIAN CONTEXTS?

AMR is already a major costly public health challenge in both the US¹⁴ and Canada. AMR infections are clearly linked to poorer health outcomes, longer hospital stays and higher mortality rates.³ The Public Health Agency of Canada (PHAC) estimates that roughly 18,000 hospitalized Canadians contract drug-resistant infections per year.¹⁵ The Canadian Patient Safety Institute estimates that 8,000 Canadian patients die annually with an AMR-related infection.¹⁶ It is estimated that close to 23 million antibiotic prescriptions are written annually for patients in Canada,¹⁷ the approximate equivalent to 1.6% of the population being on an antimicrobial on any given day.

An action plan in Canada is being developed by PHAC. On the surface, the action plan appears comprehensive in that it outlines a One Health approach.¹⁰ However, despite commitments to take comprehensive, measurable action on AMS, Canadian leadership on AMR has historically lagged because of a lack of concrete coordination between PHAC and the provinces and because it has been challenging to implement local initiatives systemically.¹⁸

Previous shortcomings were highlighted in the Auditor General of Canada's 2015 report¹⁹ and again in a 2017 issue brief by HealthCareCAN.¹⁸ Although efforts continue and the action plan is set for release at some point in 2019, concerns remain that: (1) the scope of coordinated efforts with the provinces and territories requires an interest in cooperation that may not exist between the two levels of government; (2) relative to the scope of the problem, sufficient and dedicated resources won't be allocated; and (3) efforts on the industrial and agricultural fronts may not be sufficiently coordinated with AMR efforts for human health.

In the spring of 2018 the House of Commons Standing Committee on Health (HESA) released a report outlining 10 recommendations for action on AMR in Canada.²⁰ Although the federal government "accepted" most of the committee's recommendations, no meaningful (and dedicated) AMR funding has been announced in advance of the action plan's launch. Indeed, the federal government's response to the HESA report sought to downplay the need for either urgent action or additional resources. This was done by pointing to nominal federal AMR efforts over the span of more than a decade.²¹

It should be noted that a small number of excellent localized AMS initiatives exist and have begun yielding promising local AMS results in Canada. AMR and AMS champions such as Choosing Wisely Canada, Do Bugs Need Drugs, and the Association of Medical Microbiology and Infectious Disease Canada have long argued that with proper resourcing, localized initiatives can be scaled up to a systemic level of application within provincial health care systems.

GLOBALLY, WHERE DOES AMR STAND?

Urgent action is required at an international level to combat AMR. Although AMR remains a complex public health challenge, the benefits of AMS are clear. The preservation of these precious resources will save lives and can positively affect both quality of care and health care

delivery costs.^{7,14} Globally, many higher income nations and, increasingly, middle-income countries have now developed AMR/AMS action plans.²² Like the situation in Canada, these emerging and existing global action strategies remain largely unimplemented. Initial cash infusions into the AM drug development pipeline are beginning to emerge.⁸

Despite this, experts warn that such investments are too short term and wholly inadequate to address the scope of the looming AMR crisis.^{8,23} This reflects the many complexities that exist in the implementation of AMR action plans, owing in large part to: (1) a general lack of resources or prioritization; (2) complacency about AMR as a pressing public health concern; (3) difficulties in generalizing local AMS efforts; (4) coordination between sectorial actors;²⁴ and (5) a lack of tangible AMR metrics and evidence.²⁵

If AMS gains are to be made in low- and middle-income countries, the impact of limited resources in those settings will need to be considered.¹³ Realistically these countries will require various forms of monetary incentives and assistance to be able to effectively adopt AMR programs. If such support is not provided, human health rights will be affected and global AMS efforts will be undermined. Finally, there are now well-established calls for an international model, even a treaty, to be implemented on AMR/AMS.^{12,26}

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² Klein EY, Van Boeckel TP, Martinez EM, et al. Global increase & geographic convergence in antibiotic consumption between 2000 & 2015. *PNAS* 2018;115(15):E3463–E3470. Available: <http://www.pnas.org/content/pnas/early/2018/03/20/1717295115.full.pdf> (accessed 2018 Aug 15).

³ OECD, WHO, FAO, OIE. *Tackling antimicrobial resistance: ensuring sustainable R&D. Final note*. Paris: OECD, WHO, FAO, OIE; 2017. Available: <http://www.oecd.org/g20/summits/hamburg/Tackling-Antimicrobial-Resistance-Ensuring-Sustainable-RD.pdf> (accessed 2018 Aug 15).

⁴ Wellcome Trust, UK Department of Health. *Tackling drug-resistant infections globally: final report & recommendations. The review on antimicrobial resistance (governmental report)*. Chaired by O’Neil J. London (UK): Wellcome Trust; 2016. Available: https://amr-review.org/sites/default/files/160518_Final%20paper_with%20cover.pdf (accessed 2018 Aug 15).

⁵ World Health Organization (WHO). *Antimicrobial resistance*. Geneva: WHO; 2018. Available: <http://www.who.int/mediacentre/factsheets/fs194/en/> (accessed 2018 Aug 15).

⁶ Woodworth K, Walters M, Weiner L, et al. Vital signs: containment of novel multidrug-resistant organisms and resistance mechanisms – United States, 2006–2017. *MMWR* 2018;67(13):396–401. Available: <https://www.cdc.gov/mmwr/volumes/67/wr/mm6713e1.htm> (accessed 2018 Aug 15).

⁷ Cecchini M, Lee S. *Low-value health care with high stakes: promoting the rational use of antimicrobials*. Paris: Organisation for Economic Co-operation and Development; 2017. Available: <http://apps.who.int/medicinedocs/documents/s23152en/s23152en.pdf> (accessed 2018 Aug 15).

⁸ Stern S, Chorzelski S, Franken L, et al. *Breaking through the wall: a call for concerted action on antibiotic research & development*. Berlin: German Federal Ministry of Health; 2017 Feb. Available: https://www.bundesgesundheitsministerium.de/fileadmin/Dateien/5_Publikationen/Gesundheit/Berichte/GUARD_Follow_Up_Report_Full_Report_final.pdf (accessed 2018 Aug 15).

⁹ Association for Professionals in Infection Control and Epidemiology (APIC). *Antimicrobial stewardship*. Arlington (VA): APIC; 2012. Available: <https://apic.org/Professional-Practice/Practice-Resources/Antimicrobial-Stewardship> (accessed 2018 Aug 15).

¹⁰ Public Health Agency of Canada. *Tackling antimicrobial resistance and antimicrobial use: a pan-Canadian framework for action*. Ottawa: Public Health Agency of Canada; 2017. Available: <https://www.canada.ca/content/dam/hc-sc/documents/services/publications/drugs-health-products/tackling-antimicrobial-resistance-use-pan-canadian-framework-action/tackling-antimicrobial-resistance-use-pan-canadian-framework-action.pdf> (accessed 2018 Aug 15).

¹¹ World Bank Working Group. *Drug-resistant infections: a threat to our economic future. Final report*. Washington (DC): The World Bank; 2017. Available: <http://documents.worldbank.org/curated/en/323311493396993758/pdf/114679-REVISED-v2-Drug-Resistant-Infections-Final-Report.pdf> (accessed 2018 Aug 15).

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