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RESULTS Canada:

Tuberculosis: The Heart of the Global Antimicrobial Resistance Crisis

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Tuberculosis: The heart of the global antimicrobial resistance crisis

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RESULTS Canada is a grassroots advocacy organization that works to generate the political will to end poverty. With a staff in Ottawa, a grassroots community across Canada, and membership in a global advocacy network, RESULTS Canada advocates for proven, cost effective poverty reduction strategies focusing on child health, education, nutrition, and disease eradication, including tuberculosis.

AMR and global poverty:

The link between global health concerns and global poverty are inherent in the UN Sustainable Development Goals. Insufficiently funded health systems struggle to respond and adapt to wide-ranging health threats, including infectious diseases. Though antimicrobial resistance (AMR) is developing across borders with far-reaching global impact, the diseases under the threat of developing drug resistance often disproportionately affect poorer and marginalized communities – including HIV, malaria, and tuberculosis.

RESULTS Canada was pleased to see the world come together in 2016 for the UN High Level Meeting on Antimicrobial Resistance. This was a key step in acknowledging the necessity for coordinated global action on AMR, without which could result in the loss of 10 million lives annually and could cost a cumulative 100 trillion USD by 2050.¹ More than nine million of those deaths are expected to be in developing countries. RESULTS Canada is particularly concerned with the long-term impact on the personal and economic welfare of poorer populations if global action on AMR is insufficient. In addition to the enormous loss of life, the economic fallout from AMR will fall more heavily on poorer countries, with estimates of a loss of 10% of gross domestic product in Sub-Saharan Africa by 2050.²

Tuberculosis and AMR: the global fight

RESULTS Canada acknowledges and commends the Canadian Government and Health Canada on their commitment to tackle antimicrobial resistance. Canada has demonstrated leadership in its early and proactive work on building a national framework on AMR and implementing the ONE Health Approach. This will have a lasting impact on the health and welfare of Canadians. Canada has also demonstrated global leadership through its commitment of \$9 million to the WHO Global Strategy on AMR, its chair position on the global health security agenda's AMR action package, and its partnership with the Joint Programming Initiative on AMR.

The national and global momentum to fight antimicrobial resistance is building; however, at the centre of this looming crisis is the threat of tuberculosis (TB) and the drug resistant strains that currently account for the majority of all deaths due to AMR. In fact, **Drug resistant TB currently accounts for one third of all deaths attributed to AMR.**³ As the O'Neil Review (2016) states, "tuberculosis [is] a cornerstone of the global AMR challenge."⁴

¹ O'Neil J 2016 *Tackling Drug-Resistant Infections Globally: Final report and recommendations* https://amr-review.org/sites/default/files/160525_Final%20paper_with%20cover.pdf

² Taylor J et al 2014 *Estimating the economic costs of antimicrobial resistance: Models and results* RAND https://www.rand.org/pubs/research_reports/RR911.html

³ O'Neil J 2016 *Tackling Drug-Resistant Infections Globally: Final report and recommendations* https://amr-review.org/sites/default/files/160525_Final%20paper_with%20cover.pdf

⁴ O'Neil J 2016 *Tackling Drug-Resistant Infections Globally: Final report and recommendations* https://amr-review.org/sites/default/files/160525_Final%20paper_with%20cover.pdf page 60

Tuberculosis is an ancient and complex disease that primarily attacks the lungs, and when left untreated and undiagnosed can result in death. TB bacteria are particularly prone to developing resistance to antibiotics. At a cellular level, the TB bacteria have an unusually thick, waxy cell wall, and it can survive in multiple locations in the body. These present significant challenges in developing effective treatments. The best, most widely available treatments for drug resistant TB can take up to two years to complete, include 14,000+ pills, and eight months of painful injections. In 2015 480,000 new cases of drug resistant TB were found, and it claimed 200,000 lives.⁵ Extensively drug resistant TB (resistant to four or more of the drug treatments available) has been reported in 117 WHO member states and there now exist strains of the disease that are entirely resistant to any treatments in existence.

Treating TB:

Treatment in Canada is much the same as anywhere – we are in some ways lucky that geographical distance has spared us an epidemic of drug resistant TB, and strong health care systems have permitted those cases that have arisen to be managed. But even our size and our relative affluence do not wholly protect Canada, nor does it exclude us from participating in the fight against the largest global driver of AMR deaths.

A young patient in Toronto suffering drug resistant TB is treated with the same toxic drugs as one in India, or Indonesia. The treatment in these cases is so severe, its side effects so traumatic, physically and emotionally that many struggle to complete the two year regimen.

For anyone that has completed this exhausting two-year treatment regimen for drug resistant TB – it is a full time job – trips to the hospital every day, and in many cases, these last an entire day. The treatment is life-saving, but it is toxic with dangerous and life altering side effects. The most common side effects – nausea, numbness, and dizzy spells sound manageable – for a short time – but they last days, weeks, months, years. Imagine being bedridden from fatigue, or because you have lost all sensitivity in your legs and you can no longer walk. Not to mention those who experience the more severe effects, including permanent deafness, blindness, and depression. In the words of one patient in Canada, “the drugs pushed me to the brink of depression by the second month of isolation”. She still had three months of isolation and 22 months of treatment left to go.

Economic impact:

As a key driver of antimicrobial resistance across the world, tackling drug resistant tuberculosis presents an opportunity to make significant progress against the catastrophic human costs of the AMR pandemic. There is, of course, also an economic impact, given the long hospital stays, costs for medication, and lost wages and participation in the economy. **In the G20 alone, it is estimated that by 2050 drug resistant tuberculosis may cause a lost economic output of US\$10.5 trillion**, and an additional US\$6.2 trillion outside the G20 states.⁶

The solution:

Global leadership and action on tuberculosis is a necessary complement to the strategic shift of the ONE Health approach and the national framework Canada has taken such extraordinary leadership on. However guidelines and surveillance to improve antimicrobial use are as essential as the need to invest in the

⁵ 2015 WHO *Global Tuberculosis Report 2015*

⁶ Extracted from a report prepared by KPMG LLP in the UK, derived from research commissioned by the Wellcome Trust, as part of an independent review into antimicrobial resistance supported by the Department of Health and the Wellcome Trust.

research and development of better ways to diagnose and treat infections. Without more and better investment in R&D for resistant-prone diseases, we will end up in a post-antibiotic era.

R&D into diseases that predominantly affect the poor (including drug-resistant strains) is woefully underfunded, and there are substantial gaps in the innovation model for novel drugs and vaccines. There is a significant role for both Canadian researchers and the federal government to play in addressing these challenges. Funding in Canada into R&D products for neglected diseases totaled only USD \$79 million from 2010-2015. This is extremely low when we compare to countries during the same time frame such as the UK (USD \$231 million) and US (USD \$2.1 billion). Canada has a collection of world class researchers and facilities, particularly in its universities and educational institutions. Prioritizing R&D into global health and neglected diseases could have a phenomenal Canadian-led impact on the burden of AMR globally.

Additionally, antimicrobial resistant diseases flourish under the current system in which new health products are brought to market. New and necessary ways to treat, diagnose, and prevent the spread of these infectious diseases are stymied by a market failure – this is particularly true for those diseases that predominantly affect poorer populations, such as tuberculosis. Pharmaceutical companies are rarely prepared to commit the necessary resources to bring a product to market, and in many cases have all but abandoned the development of antibiotics. Given the current market system, pharmaceutical companies and private sector investors find other health investments more financially rewarding than antimicrobials – a large part of why the AMR crisis is as dire as it currently is.

Tuberculosis, having had such little investment for so long, and given its unique biological makeup, is doubly affected by this market failure. The current model is geared towards individual investment in a drug, while TB requires a cocktail of drugs. Developing one drug at a time is not only too slow, it is dangerous. Each new drug brought to market is then used with a regimen of drugs that are already experiencing resistance globally. Given the significant public health threat posed by antimicrobial resistance, and the failure of the market to offer a solution, it falls to public and philanthropic funders to build models that create the right incentives to unlock new drug development. This will require a global commitment, but will make a truly global impact. A new incentive mechanism that encourages investment into the R&D of tuberculosis and focuses on regimen-wide drug development would make an unprecedented impact on the economic and human costs of the global AMR pandemic.

RESULTS Canada recommends that:

Canada match its national commitments to its global ones, and by so doing, commit to the global fight against drug-resistant tuberculosis as a component of its antimicrobial resistance strategy, demonstrating leadership and accountability for the global movement against TB, and progress towards meeting the WHO End TB Strategy, ending TB by 2030.

This may include:

- Supporting a global mechanism that addresses the market failure for the development of essential new drug regimens for tuberculosis.
- Enhancing Canada's investment in global health R&D, particularly for neglected diseases, such as tuberculosis.

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RESULTS Canada is a partner of ACTION, a global partnership of independent organizations working to influence policy and mobilize resources to fight diseases of poverty and achieve equitable access to health.