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Estimating Canada's Return on Investment from an Ambitious Program to Incentivize New Antibiotics

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KEY MESSAGES

- We estimate the benefits to Canada of a new antibiotic incentive program, which would seek to generate a total of 18 new antibiotics over three decades to treat six priority pathogens.
- We assume that every country in the G7 + EU pays its "fair share" toward the total cost of $4.5 billion per drug; the Canadian contribution is 4.0%, or $179 million per new drug.
- The incentive payments would be spread over 10 years and following fulfilment Canada will be able to procure the new antibiotic for close to marginal cost.
- Over 10 years, such a program would save 2,500 lives and generate $2.1 billion in total benefits for Canada, for an ROI of 5:1.
- Over 30 years, such a program would save 48,000 lives and generate $31.5 billion in total benefits for Canada, for an ROI of 20:1.
- The global return on investment is much larger, at 27:1 over 10 years (with 518,000 lives saved); and 125:1 over 30 years (with 9.9 million lives saved).

Background and Motivation

Anti-microbial drugs form the backbone of modern medicine. Yet their lifespan is naturally limited; over time, use of these drugs selects for mutations that survive exposure those same drugs, driving "anti-microbial resistance," or AMR. Already, drug-resistant infections kill an estimated 5,400 Canadian citizens every year.[1] In the absence of sufficient research and development (R&D) investment for new antimicrobials, deaths from drug-resistant infections could increase dramatically in the coming decade.

To address this growing crisis and solve market failures that prevent the development of new antibiotics, the Government of Canada is considering a new program that would provide minimum guaranteed revenue to the successful developers of new antibiotics. In this note, we present the results of a modelling exercise to estimate the likely return on investment (ROI) from such a program, assuming it is paired with complementary and proportionate efforts from Canada's G7 partners. The results are necessarily imprecise due to several uncertain parameters, but nevertheless provide evidence of a very high expected ROI that is robust to different inputs and assumptions.

Assumptions and Methods

We construct a country-specific Excel models for each member of the G7 + EU, which we will make publicly available. We make the following assumptions across all our G7 modelling, which are explained in further detail in a companion Policy Paper:[2]

- Canada would commit to a new antibiotic incentive program, which seeks to generate a total of 18 new antibiotics over three decades to treat six priority pathogens.
- Each new drug is held in reserve for 4 years and then reduces deaths from the six priority pathogens by 5% each year; starting from year 5 onwards, effectiveness falls by 2% year on year, due to the build-up of resistance.
- Pulling one new antimicrobial to market (with full delinkage) would require global revenue guarantees of $4.5 billion USD. (For consistency, we use USD across our estimates; we assume a USD to CAD conversion rate of 1:1.30, which is average YTD for 2022 as of end-November).
- Following fulfilment of its revenue guarantee, Canada will be able to procure new antibiotics for close to marginal cost.
- We use a discount rate of 1.5% for health effects, and 3.5% for costs; and
- We assume the rate of growth of resistance is 2%. Absent new drugs, annual deaths increase by 2% each year.
- We consider only direct health gains and averted health system costs; we do not consider the broader "STEDI" benefits of new antibiotics.[3]

For Canada specifically, we make the following key assumptions:

- We assume that Canada's share of this financing will be proportionate to its current GDP share in the G7 plus EU (4.0%) with the remainder paid by other countries, which means Canada would pay $179 million per new drug. We amortize the costs over a ten-year period following market entry.
- Current annual Canadian deaths from the six priority pathogens are 3,495; each death is associated with 20 DALYs.[4]
- We use an opportunity-cost based approach to conservatively value a DALY at $50,000 CAD,[5] which translates to $38,610 USD. This implies a total DALY value per AMR death of $772,000, and $2.7 billion in annual health losses from the six priority pathogens.
- Each death is associated with health system costs of $200,200 USD; total (current) health system costs are $1.08 billion.[6]

Estimated Return on Investment

Headline results of the modelling, from Canada's perspective, are presented in Table 1. The returns are very large over 30 years, with 48,100 lives saved and benefits exceeding the costs by a factor of 20. Over 10 years, the program saves 2,500 lives; benefits exceed costs by a multiplier of around 4.5. This reflects the fact that costs are incurred throughout the program, whereas the benefits are cumulative, with many occurring decades into the future as a sustainable program is put in place.

TABLE 1 Domestic Canadian costs and benefits, over 10 years and over 30 years

	TOTAL COST (DISCOUNTED)	LIVES SAVED	DALYs SAVED	DALY VALUE (DISCOUNTED)	HEALTHCARE SAVINGS (DISCOUNTED)	DALY + HEALTHCARE SAVINGS (DISCOUNTED)	BENEFIT: COST RATIO
10-Year	$464 m	2,500	50,000	$1.71 bn	$378 m	$2.09 bn	5:1
30-Year	$1.54 bn	48,100	962,000	$26.87 bn	$4.62 bn	$31.49 bn	20:1

Global benefits are presented in Table 2, assuming that the full $4.5 billion pull incentive per antibiotic is covered in full by G7 members based on proportionate GDP. Over its full 30-year time horizon, the program averts 9.9 million deaths and 374.5 million DALYs, generating an ROI of 125 to 1. Over the shorter 10-year period, the program averts 518,000 deaths and 19.5 million DALYs, generating an ROI of 27 to 1.

Results of a sensitivity analysis are shown in Table 3, demonstrating robustness of the high ROI to many different assumptions and scenarios. From both the Canadian and global perspectives, the biggest sensitivity is related to the efficacy of drugs that result from this initiative against AMR-related deaths. Another significant sensitivity is number of deaths at baseline; our base case uses numbers

TABLE 2 Global costs and benefits, over 10 years and over 30 years

	TOTAL COST (DISCOUNTED)	LIVES SAVED	DALYS SAVED	VALUE OF DALYS SAVED	BENEFIT: COST RATIO
10-Year	$11.7 bn	518,000	19.5 m	310.6 bn	27:1
30-Year	$38.9 bn	9,933,000	374.5 m	4,874.2 bn	125:1

TABLE 3 Sensitivity analysis of ROI estimates under different scenarios (benefit to cost ratio)

SCENARIO	10-YEAR, CANADA[a]	30-YEAR, CANADA[a]	10-YEAR, GLOBAL[b]	30-YEAR, GLOBAL[b]
Base Case	5:1	20:1	27:1	125:1
GRAM #s on Canada Baseline Deaths (1,877/year)	2:1	11:1	27:1	125:1
No Growth in AMR Deaths (0 % Per Year)	4:1	13:1	23:1	82:1
Fast Growth in AMR Deaths (5% Per Year)	6:1	39:1	34:1	237:1
Slower Resistance Growth to New Antimicrobi-als (1% Per Year)	5:1	22:1	27:1	136:1
Faster Resistance Growth to New Antimicrobials (5% Per Year)	4:1	16:1	25:1	100:1
Lower Drug Efficacy Scenario (2% Death Reduc-tion Per Drug at Peak Efficacy)	2:1	8:1	11:1	50:1

a. Includes health benefits and averted healthcare costs
b. Includes health benefits only

derived from Council of Canadian Academics (2019); as these figures are substantially higher than the estimates presented in the GRAM study (2019), use of the latter estimates would reduce the expected ROI, though it would remain positive in both the short- and long-term. The program remains highly beneficial even if there is no counterfactual growth in AMR deaths over the next 30 years.

Technical Appendix

This technical appendix details the construction for Canada-specific parameters that are input into the modelling. The rationale for all other input parameters, and complete model design, are detailed in a companion working paper (Towse and Silverman Bonnifield, 2022).

GDP fair share calculation

Each country's "fair share" was calculated as proportionate to their respective GDPs within the G7 + EU using World Bank data for 2021 (Appendix Table 1).

Exchange rates

All figures were converted into USD for consistency, using the year-to-date average exchange rate for 2022 as of November 30, 2022. For Canada, the exchange rate used was 1.30 CAN to 1 USD.

Deaths and DALYs at baseline

Across all G7 members, we consider six priority pathogens. For Canada, we used the figure presented in Council of Canadian Academies (2019) on total number of deaths per year at baseline (5,400).

We used data associated with the GRAM study, available here derive, to derive estimates on (1) proportion of deaths attributable to the six priority pathogens (65%); and the number of DALYs associated with each AMR death from the six priority pathogens (20).

Health system costs

We calculate total national health system costs associated with each death – that is, total health system costs for AMR divided by the number of deaths, not the direct costs incurred by each patient who dies of AMR.

For Canada, health system costs are derived from Council of Canadian Academies (2019), which specifies $1.4 billion CAD in health system costs associated with AMR per year in Canada, or $259,000 CAD in healthcare spending associated with each of the 5,400 deaths. This converts to $200,200 USD given the YTD exchange rate.

APPENDIX TABLE 1 GDP fair share calculation

	GDP (TRILLION)	PERCENT	CONTRIBUTION PER NEW DRUG
USA	23,00	45,8%	2.061.342.362
Japan	4,94	9,8%	442.740.490
United Kingdom	3,19	6,4%	285.899.223
Canada	1,99	4,0%	178.350.926
European Union	17,09	34,0%	1.531.666.999
Total	50,21	100,0%	4.500.000.000

Endnotes

1 Council of Canadian Academies, 2019. When Antibiotics Fail. Ottawa (ON): The Expert Panel on the Potential Socio-Economic Impacts of Antimicrobial Resistance in Canada, Council of Canadian Academies. Available at: https://cca-reports.ca/wp-content/uploads/2018/10/When-Antibiotics-Fail-1.pdf

2 Towse and Silverman Bonnifield, 2022. "An Ambitious USG Advanced Commitment for Subscription-Based Purchasing of Novel Antimicrobials and Its Expected Return on Investment." CGD Policy Paper 277. Washington, DC: Center for Global Development. https://www.cgdev.org/publication/ ambitious-usg-advanced-commitment-subscription-based-purchasing-novel-antimicrobials

3 See Outterson and Rex (2020) and broader discussion in the Towse and Silverman Bonnifield (2022).

4 We use the total death number estimated by Council of Canadian Academies, 2019. We derive the proportion of deaths from the six priority pathogens (65%) and number of DALYs lost per AMR death (20) from GRAM-study data, available here.

5 This is the lower end of the threshold range used by Canada's HTA agency; see here, for example.

6 Figure is derived from the total costs of $1.4 billion CAD cited in Council of Canadian Academies, 2019, divided by the total number of deaths and converted to USD.

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