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Commentary

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Innovative medicines or fewer, cheaper drugs: Which way will the Trudeau government go?

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The new federal health minister and cabinet face an urgent choice: rethink the government's approach to innovation in medicines or continue on a path of increased regulation leading to cheaper but significantly fewer drugs.

Over the past four years, much concern has been expressed about the Trudeau government's changes to the regulations of the Patented Medicine Prices Review Board (PMPRB), the federal tribunal whose role is to prevent time-limited patent monopolies for new medicines from charging "excessive" prices. The new rules are expected to drastically reduce the prices of medicines (Rawson and Adams 2021a) and are already further inhibiting timely patient access to therapeutic innovations.

But what is an innovative medicine?

The European Medicines Agency's definition is "an active substance or combination of active substances that has not been authorised before" (EMA 2021). However, this characterization is broad and includes new, so-called me-too drugs. When only modestly different from a previous medicine, me-too medications are not innovative, although they still have incremental value.

Compared with the European Medicines Agency, Canada's definition is more limited. According to the Food and Drug Regulations, an innovative medicine "contains a medicinal ingredient not previously approved in a drug by the Minister and that is not a variation of a previously approved medicinal ingredient such as a salt, ester, enantiomer, solvate or polymorph" (Health Canada 2021). Thus, me-too medications are generally excluded.

Others take a narrower view of innovation. For example, only 55 (8.8 percent) of 623 drugs and vaccines newly approved by Health Canada between 1995 and 2016 were considered to be "therapeutic innovations" (Lexchin 2018) using assessments of benefit from the PMPRB, which rates few medicines each year as breakthroughs, and Prescrire, an independent French organization that is commonly critical of the biopharmaceutical industry (Prescrire 2011). In contrast, Health Canada – the regulatory agency that reviews the efficacy, safety and manufacturing quality of medicines, which should be a neutral authority – considered 159 (25.5 percent) of the 623 medicines to be of sufficient potential benefit to patients to warrant an expedited review for marketing approval.

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When the PMPRB and Prescrire assess a medicine as a breakthrough, any subsequent medicines in the class are not similarly categorized. For instance, sofosbuvir (Sovaldi), the first drug for hepatitis C, was rated as a breakthrough medicine, although it is appropriate treatment for only two of the six hepatitis C genotypes and should be used together with interferon or ribavirin delivered by painful injections. Subsequent hepatitis C medicines, including combination products, were not classified as breakthroughs, despite two combinations being able to treat all hepatitis C genotypes without need for those painful injections of interferon. The recognition of the therapeutic benefit of one combination, sofosbuvir and velpatasvir (Epclusa) which requires once daily treatment with no food restrictions, is demonstrated by it having the third highest sales value in public drug plans in Canada in 2019/20 (PMPRB 2021). Incremental improvements can add up in time to a breakthrough.

The interpretation of first-in-class as the only innovation is too narrow and bureaucratic. If the same definition was applied to human flight, it would mean that the unique innovation was the brief flights by the Wright brothers in 1903. All subsequent improvements in aviation over the following 118 years would be considered only moderate advances. This analogy illustrates the wilful ignorance of applying the unduly restrictive and arbitrary first-in-class definition to the spectrum of progress in pharmaceutical therapies.

Any medicine that is more effective and/or has fewer adverse effects than existing therapy, particularly if it is also easier to administer, can be expected

to enhance patient adherence and treatment persistence – qualities that lead to better patient outcomes. The medicine would also have societal value because taking it as prescribed is a critical factor in improving patient health and, therefore, reducing the need for ever more expensive and, in Canada, frequently difficult-to-access healthcare interventions (Moir and Barua 2021). Additions to a class of medicines often exhibit such benefits, especially when their dose size is smaller than that of the first-in-class medicine. This can result in a later addition to a drug class eventually becoming the most preferred by physicians and patients. For instance, enalapril, the second angiotensin-converting enzyme inhibitor to treat high blood pressure, and atorvastatin, the fifth statin to treat high cholesterol, are the most popular in their respective classes.

Innovation clearly has more than one dimension, not just whether the active ingredient is novel or the drug is the first-in-class. Deciding whether a medicine is innovative can be a subjective assessment. Nevertheless, innovative medicines should include those with a new mechanism of action that expands the possible beneficial outcomes for a disorder while maintaining patient safety, or those that treat diseases where limited or no treatment options exist. Thus, drugs that are life-extending by a good margin would be in this category. This would include all recent anti-viral medicines for hepatitis C (not just Sovaldi), precision therapies such as chimeric antigen receptor (CAR) T-cell medications that are now standard treatments for many cancers, and gene-specific therapies for cancers and rare disorders.

Medicines that significantly improve a person's quality of life must also be considered innovative. Therapies, such as voretigene neparvovec (Luxturna) that prevents vision loss from inherited retinal dystrophy, nusinersen (Spinraza) that can prevent physical deterioration and premature death from spinal muscular atrophy, and other drugs that allow cystic fibrosis sufferers to breathe, individuals with sickle cell disease to experience less pain and require fewer emergency department visits, hospitalizations and blood transfusions, and rare disorder sufferers to live relatively normal lives, should be regarded as innovative. Vaccines against COVID-19 are also innovative medicines, not just the first one nor even just the first mRNA version.

Many of these new therapies are costly because they require many millions (Wouters, McKee, and Luyten 2020), if not billions, of dollars and years to develop, test in animals and then in humans, and satisfy regulatory processes and standards as being safe and efficacious before making them available to patients. As examples, the first research (Daley 2021) on retinal disease that led to Luxturna's approval in the United States in 2017 was initiated in 1991, and research that resulted in the approval of Spinraza in the United States in 2016 began in the late 1990s.

Although the mRNA vaccines may appear to the public to have been produced within a short time frame, initial research began in 1987 (Dolgin 2021). The rapid development of these vaccines was only possible with the vast resources

and scientific know-how of major multinational biopharmaceutical companies and, in some cases, strategic investments by American and British governments but not by Canada's federal government. One has only to consider the ineffectual efforts made by our government to realize the truth of this statement (Rawson, Koester, and Adams 2021). The development of one of the mRNA vaccines depends upon licensing a delivery technology developed by a Vancouver-based company, but only a tiny number of Canadians participated in a couple of domestic trials and none of the COVID-19 vaccines approved so far were developed or manufactured in this country, demonstrating the also-ran status of Canada when delivering therapeutic innovation to patients.

Innovation is inherent in the evolution of humankind – a society that doesn't innovate stagnates or, worse, fails. It is multi-dimensional, difficult to measure and can be elusive and challenging to measure (Cross 2020) but it is essential. Canadians with unmet health needs, such as effective treatments for cancer and rare disorders, particularly need innovative advancements. To create and commercialize such medicines requires specialized expertise and significant financial resources that must be recovered by their developers if they are to continue to advance therapeutics.

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For a drug or vaccine that will be used by millions or billions of individuals, the investment in its development might be recouped with a relatively low price per treatment or patient, as is the case with COVID-19 vaccines. Most governments, Canada's included, are willing to pay for these types of medicines – in fact, it would be politically inadvisable not to do so. However, if a medicine, which required millions of dollars and years to develop, is only likely to be appropriate therapy for a relatively small group of patients, its cost will be high on a per patient basis, although the total cost is affordable when the principles of insurance are applied to spread the risk.

Canada's governments frequently react negatively to "sticker shock" and complain about high asking prices for medicines, but they fail to acknowledge the practice of extensive discounts obtained through negotiations with developers. This response occurs even if the drug provides life-changing outcomes in terms of longer survival and/or significant improvements in quality of life that allow individuals to participate more effectively in society and require fewer hospitalizations and other expensive healthcare interventions. Governments should recognize the social value of innovation (Conti, Frank, and Gruber 2021) and pay for them at prices that encourage developers to make them available in Canada.

The Trudeau government's reaction to the costs of innovative medicines has been to introduce regulations to severely reduce their prices. The federal emphasis appears to be on health system sustainability and is not aligned with patient values. The regulations are already deterring biopharmaceutical developers from launching new medicines in Canada resulting in longer waits for access to therapies. Without doubt, global companies will prioritize the launch of their products in other countries with more collaborative policies (Rawson and Adams 2021b). Instead of introducing antagonistic policies, the federal government should learn from programs in other jurisdictions, such as the Innovative Medicines Initiative partnership between the European Union and the European biopharmaceutical industry (Laverty and Meulien 2019), which encourages the development and accessibility of new medicines that address unmet health needs.

Innovative medicines satisfying previously unmet health needs should be made available expeditiously to all Canadians that require them in a sustainable access program. Access to medicines in Canada is already restricted or prevented by existing rigid and often hostile health technology assessments (Rawson 2021) and/or non-transparent price negotiation processes, which are inadequate for properly assessing the holistic health value of drugs for precision medicine or fairly negotiating prices. It is vital that access to innovative medicines is not further limited or denied as a result of actions or non-actions in Ottawa. The new pricing regulations are expected to take effect on January 1, 2022. It is critical that the new federal government, Cabinet and Health Minister take a sober second look at the unintended consequences and engage in meaningful collaboration (Fralick 2021) to ensure timely access to medicines that can save, transform or extend lives.

Canadians deserve nothing less!

About the authors

Dr. Nigel Rawson is a pharmacoepidemiologist and pharmaceutical policy researcher based in Saskatoon, Saskatchewan. He is also a Senior Fellow with the Fraser Institute and an Affiliate Scholar at the Canadian Health Policy Institute. He holds an MSc in statistics and a PhD in pharmacoepidemiology. Dr. Rawson has performed epidemiologic studies of the use of drugs and their outcomes and pharmaceutical policy issues for over 40 years, and published more than 140 articles in peer-reviewed journals and book chapters. He is also the author of the monograph "Drug Safety: Problems, Pitfalls and Solutions in Identifying and Evaluating Risk." He has held academic positions in the United Kingdom and Canada, been a senior researcher in an independent research centre in one of the United States' largest health insurers collaborating with the Food and Drug Administration on drug safety studies, and GlaxoSmithKline's only epidemiologist in Canada. Between 2012 and 2020, Dr. Rawson was President of Eastlake Research Group whose mission was to create data-driven responses to pharmaceutical policy issues. He continues this work as an independent researcher.

John Adams is a seasoned management consultant with a current focus on advocacy for unmet patient health needs. He has extensive experience in public policy, governance and senior management.

He volunteers as the Board Chair of the Best Medicines Coalition (BMC), a national non-profit of 29 patient organizations, which together represent millions of Canadian patients. The mission of BMC is to help ensure timely access to medicines that meet patient needs and that are safe and effective. BMC is engaged in current issues of national pharmacare, drug supplies and shortages, COVID-19 issues including therapeutic scams, price controls on medicines, health technologies assessment and regulatory reform.

Previously he served ten years on the board of the Canadian Organization for Rare Disorders. He has a son with a rare genetic disorder phenylketonuria (PKU) which is a brain-threatening disorder and is co-founder and President of both a Canadian non-profit and a global charity for that rare disease. That son participated in a clinical trial for the first drug to treat PKU, and is an example of a person outside the USA who benefits from the US Orphan Drug Act.

Olaf Koester is the Managing Partner, OHWK Business Management Advisory. Olaf is a strategic thinker and seasoned pharmaceutical policy and market access expert with a passion for innovation, collaboration, delivery, and results. He leverages extensive senior level drug plan management leadership, health technology assessment, pricing, reimbursement, and health system experience to provide pharmaceutical industry-leading advisory services to global pharmaceutical manufacturers to develop and enhance commercial and market access strategies and to facilitate resolution of complex regulatory, access, reimbursement, and policy challenges in the Canadian market. Olaf's practice focus is in the functional areas of Canadian health technology assessment, price negotiations, market access, marketing, pricing, health outcome program development and product utilization strategy development.

Prior to taking on the leadership for OHWK Business Management Advisory, Olaf enjoyed an extensive and successful public service career. Senior leadership roles at Manitoba Health included Acting Assistant Deputy Minister, Director Provincial Drug Programs, and Director Blood Programs. In his responsibilities at Manitoba Health, Olaf provided expertise, advice, and briefings to the most senior levels of government, including the Premier and the Minister of Health, on all aspects of drug and ancillary benefit program design and management, provincial policies, directives, and legislation including utilization management strategies, licensing provisions and practice standards for professionals, product selection, pricing, and reimbursement strategies.

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Endnotes

1 The views expressed are the authors' own and do not necessarily represent those of the organizations with which they collaborate.

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