

# Pharmaceutical Regulation, Innovation, and Access to New Drugs

An International Perspective

Pre-Release Chapter



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## Executive summary

New drugs are emerging that promise improved treatments and in some cases even cures for diseases. But these drugs are expensive, and are heightening concerns from patients and insurers (particularly public insurers) about the prices that drug companies are asking for these medications.

In response, Health Canada is making changes to the way Canada's Patented Medicine Prices Review Board [PMPRB] prices drugs.

Under the current system of regulation, the issues of pharmaceutical pricing and reimbursement, though related, are distinct. Currently, the PMPRB sets maximum allowable prices for all patented drugs. The maximum allowable price for a new drug is based on a comparison, or reference, to the prices in other countries for the drug in question, as well as the highest priced drug in Canada in the same therapeutic class. At the same time, the Canada Agency for Drugs and Technology in Health (CADTH) makes non-binding recommendations for reimbursement by public insurers based on the estimated clinical benefits of a drug relative to its cost.

The proposed amendments to the PMPRB's procedures call for increasing the incorporation of CADTH's evaluation of the cost effectiveness of drugs into the determination of maximum allowable prices for patented drugs. As well, the set of countries whose prices are used as references to establish maximum allowable prices in Canada will be changed. In particular, the United States and Switzerland will be dropped from the set of reference countries and will be replaced by countries that typically have lower average prices for patented drugs.

While the Canadian government's goal of containing expenditures on patented drugs is not unique, the direction of its regulatory policy changes seems to be focusing more on controlling expenditures on pharmaceuticals than on ensuring that Canadians have access to new therapies.

Instead of this approach, public policy decision makers should be encouraging an efficient level of expenditures on pharmaceutical drugs, not simply containing expenditures on those drugs. Efficiency is achieved when the social benefits of drug expenditures, at the margin, equal their social costs. Effectively, this means that more, not less, should be spent on any drug

as long as the social benefit from its increased usage exceeds the additional expenditure.

In principle, cost-efficiency analysis is a technique for comparing the social benefits of a drug relative to its cost. In practice, the conventional application of the technique arguably leads to an underestimation of the social benefits of new drugs. There are several important potential sources of biases that are becoming especially relevant with the emergence of personalized medicine. As a consequence, the incorporation of conventional cost-efficiency analysis into the PMPRB's pricing decisions might result in the agency making pricing decisions that render new drugs increasingly less available to Canadian patients, even when those drugs promise to deliver net social benefits, either now or in the future.

Further, the proposed changes to the reference pricing procedure are likely to exacerbate the problem of reduced or delayed availability of expensive but potentially life-saving new drugs in Canada.

When a country directly or indirectly mandates lower average prices for drugs, that country becomes more attractive for other countries to include in their "country baskets" for their own reference pricing. Consequently, that country becomes a less attractive jurisdiction for pharmaceutical companies marketing new drugs. This is because the price reductions extracted by a country may lead to lower allowable prices in other countries that include that country in their reference baskets. The proposed changes to the PMPRB's reference pricing procedure might, therefore, result in Canadians having more limited or delayed access to new and highly beneficial drugs.

More generally, under reference pricing, individual governments have incentives to spend less on drugs with the expectation that their individual efforts to economize will not reduce global R&D spending on drugs. Of course, if a significant number of countries behave in this way, global R&D spending will drop to the detriment of pharmaceutical innovation. In altering its reference pricing formula to contain pharmaceutical expenditures, Canada will be indirectly exacerbating this "free-rider" problem.

Adopting a longer-run policy perspective for drug reimbursement and pricing policies is critical to the health of future generations both in Canada and internationally. The proposed changes to Canada's drug pricing procedures increase the risk that from a social benefit-cost perspective, too little rather than too much money will be spent on new drugs. Canadian policymakers need to pay careful attention to this increased risk.

## Introduction

In her appearance before the House of Commons on May 15, 2017, former Health Minister Jane Philpott began her presentation of new regulatory amendments to the Patented Medicines Prices Review Board (PMPRB) by asking the somewhat rhetorical question: “If a new drug does not offer real health improvements, or is only slightly more effective than an existing treatment, is it fair for that drug to cost two or three times as much?” (see Kirkup, 2017). Somewhat more than a year later, Health Canada is readying changes to how drugs are priced in Canada (as discussed by Acri, 2018, and Rawson, 2018), notwithstanding concerns raised by pharmaceutical companies and patient groups. The goal of the proposed changes is to lower the cost of drugs—particularly, new drugs—to insurers and patients, and this goal is likely to be an even more prominent government imperative if Canada implements a universal single payer public prescription drug coverage program as recommended by the House of Commons Standing Committee on Health (Casey, 2018).

Under the current system of regulation in Canada, the issues of pharmaceutical pricing and reimbursement, though related, are distinct. Currently, pricing decisions in Canada are regulated by the PMPRB. The PMPRB sets maximum allowable prices that apply to all patented drugs, regardless of reimbursement decisions made by patients and insurers (public or private). Depending on the degree of therapeutic benefit they are deemed to provide relative to existing drugs on the market, the maximum allowable price for a new drug is set with reference to the prices in other countries for the drugs in question, as well as the highest priced drug in Canada in the same therapeutic class (Health Canada, 2017).<sup>1</sup> On the other hand, non-binding recommendations for reimbursement by public insurers are made by the Canada Agency for Drugs and Technology in Health (CADTH) based on the ability of pharmaceutical companies to demonstrate the value of a drug by comparing its clinical benefits in relation to its cost (Rawson, 2018).

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1. “Once a drug’s introductory ceiling price is set and it enters the market, the regulatory framework allows annual price increases in keeping with the CPI, provided these increases do not result in the Canadian price becoming greater than the highest price of the same drug among PMPRB 7 countries” (Health Canada, 2017: 7).

Arguably linked to its intention to expand the scope of drug coverage by the public insurer, the Canadian government's proposed amendments to the PMPRB call for the increasing incorporation into the PMPRB's regulatory process of criteria used in public reimbursement decisions (particularly cost-effectiveness evaluations) by agencies such as CADTH. As such, the direction of Canadian regulatory policy seems to put more emphasis on controlling expenditures on pharmaceuticals than on ensuring access for Canadians to new therapies.

As we shall discuss in the next section, Canada is not unique in implementing measures to contain expenditures on drugs. In the context of pharmaceutical care, policymakers everywhere face a challenge in balancing patient access to innovative medicines with affordability. As such, public insurers employ a mix of regulatory mechanisms to contain pharmaceutical expenditures. In particular, the use of cost-effectiveness evaluations and reference pricing to regulate the pricing and reimbursement processes is widespread. Therefore, it is important to assess the degree to which these regulatory procedures are likely to contribute to socially efficient outcomes. That is, are the procedures likely to lead regulators to choose an efficient position on the trade-off function between containing expenditures on pharmaceuticals and making new pharmaceuticals quickly and widely available to patients? In this study, we argue that these regulatory processes are likely to bias health care decision-making away from choosing the efficient position on the tradeoff function. Specifically, they are likely to be biased in ways that result in too little rather than too much being spent on pharmaceutical therapies from the perspective of balancing social benefits and social costs, at the margin.

The study proceeds as follows. The first section outlines the policy framework surrounding the regulation of drug reimbursement and pricing. It highlights the growing cost of developing new drug therapies and the emergence of "personalized medicine," which promises cures for hitherto incurable diseases.<sup>2</sup> The second section discusses the use of cost-effectiveness (or cost-efficiency) criteria for evaluating drug therapies and the potential biases in the use of such evaluation criteria to assess the value of a drug. The third section analyzes reference pricing as an instrument to establish maximum allowable prices for drugs.

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2. We outline the features of personalized medicine in later sections.



## The policy context

There is little question that access to pharmaceuticals is a critical component of functioning modern health care systems. However, the emergence of new and expensive drugs that promise improved treatments, and in some cases even cures, is heightening concerns on the part of both public and private insurers about the prices sought by drug companies. A case in point is Sovaldi, a drug developed to treat hepatitis C. When it was initially listed in the United States in 2014, it was priced at \$84,000 for a 12-week course regime. The announced price ignited a firestorm of protest and condemnation of the manufacturer in the US Senate (Gakhole, 2016). The objections to the price charged by the manufacturer came despite the fact that Sovaldi was proven to wipe out infection in three months and without the debilitating effects of earlier treatments.

More recently, US President Trump announced his dissatisfaction with high drug prices in the US and his intention to take actions to reduce their prices (Pear, 2018a). In this regard, Alex Azar, the US Secretary of Health and Human Services, indicated that the US government might shift its coverage of expensive cancer medications from Medicare Part B to Medicare Part D to enable the U.S. government legally to negotiate prices for drugs for Medicare beneficiaries.<sup>3</sup> Importantly, as we shall discuss in a later section, he also highlighted what he described as “global free-riding” in the form of other countries “underpricing” drugs, so that American patients bear most of the costs of drug development. Indeed, in October 2018, President Trump proposed that Medicare pay for certain prescription drugs based on prices paid in other advanced industrial countries. He said that he was taking aim

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3. Medicare Part B covers payment for drugs administered in doctors’ offices or hospital outpatient departments. The US government cannot legally negotiate with drug manufacturers to obtain lower prices for Medicare Part B beneficiaries. However, under Part D, the US government contracts with private health insurance companies to manage drug benefits for the government and negotiate discounts with manufacturers for drugs that are purchased directly by beneficiaries who pay for Part D coverage. Even in the case of drugs reimbursed under Part D coverage, Secretary Azar expressed concern about the amount spent on drugs each year (Pear, 2018b).

at global free riding that forces Americans to subsidize drug prices in other countries (Pear, 2018c).

Certainly, numerous observers have remarked on an accelerated rate of introduction of expensive drugs. Some note that this reflects the rising cost of developing new drug therapies, which should legitimately include the costs of development efforts that fail to produce new approved therapies. There are varying estimates of the costs associated with developing new drug therapies. For example, DiMasi, Grabowski, and Hansen (2016) report the average pre-tax cost of 106 randomly selected new drugs obtained from a survey of 10 pharmaceutical companies. They estimate pre- and post-approval R&D costs to be about US\$2.9 billion per drug (2013 dollars). Other industry experts argue that it now costs upwards of \$5 billion, on average, to invent a new medicine (Graham, 2014). Recent and prospective cost increases associated with developing new drugs reflect, in part, the emergence of personalized medicine. The latter is defined as the receipt of care conditional on the results of a biomarker-based diagnostic test (Garrison and Towse, 2017). To date, genetic-based therapies have been expensive to develop given the costs involved in identifying genetic markers and linking them to disease processes.<sup>4</sup>

Other features of the pharmaceutical industry have been implicated as factors contributing to increasing expenditures on drugs. For example, Bach (2015) highlights the fact that expensive drugs are increasingly being introduced for conditions that affect large rather than small patient populations, thereby contributing to higher *total* costs incurred by insurers. He also mentions that the pace of conversion to generics or biosimilars (the generic version of biologic drugs) has been slowing in recent years, while the prices of many generic drugs have been increasing. A consequence is that drugs now account for upwards of 20 percent of health care expenditures (OECD, 2017).

Whatever the precise causes, growing expenditures on drugs have focused increased attention on whether it is cost-effective to reimburse drug manufacturers for specific new medications given the budget constraints under which public insurers operate. The goal is to spend money wisely and foster the “right” type of innovation. To this end, policymakers are using evidence-based decision making to ensure that the prices paid for new therapies reflect their real-world health benefits compared to alternatives, as well as to adjust the price based on evidence about their actual impacts (OECD, 2017). The reliance on cost-effectiveness analysis, where data is regularly updated, reflects a growing concern among policymakers that prices of drugs for cancer and rare diseases are increasing, sometimes without commensurate increases

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4. Some critics of the industry argue that drug companies spend too much on marketing new drugs and too little on basic research, See, for example, Light and Lexchin (2012). However, Philipson (2016) discusses how marketing expenditures by pharmaceutical companies improves patients’ welfare.

in health benefits for patients (Bach, 2015). It is, therefore, perhaps unsurprising that an increasing number of new drugs targeting severe diseases are not meeting cost-effectiveness thresholds. For example, the proportion of oncology drugs not recommended for reimbursement by the National Institute for Health and Care Excellence (NICE) in England has increased over the years.<sup>5</sup> Nearly 60 percent of new indications approved after 2007 based on safety were not recommended for reimbursement, while the figure was 31 percent for the whole period from 2000 to 2016 (OECD, 2017). This shows less willingness to reimburse in recent years.

Even in the case of many specialty drugs that offer considerable therapeutic value to patients and represent significant improvements over alternative treatment options, the higher prices of those drugs threaten the sustainability of government funding models. For example, in the case of new hepatitis C drugs such as Sovaldi, the budget impact of treating the entire population affected proved to be “unaffordable” for many OECD countries and rationing access to the most severely affected patients was implemented (OECD, 2017). The presence of budget constraints in the drug funding models of insurers means that those insurers will make widespread access contingent on negotiating lower prices from manufacturers. Reference pricing is one instrument for constraining expenditures. Negotiating discounts and rebates to public payers, public tendering, and price freezes are related instruments.

It is beyond the scope of this essay to go into detail about how specific countries utilize cost-effectiveness or cost-utility decision rules for making reimbursement and pricing decisions. There are numerous differences in how evaluation criteria are applied and how pricing decisions are made.<sup>6</sup> However, authorized drugs are evaluated for reimbursement at a predetermined price set either by the manufacturer or after negotiations between the relevant public authority and the manufacturer, in the absence of a predetermined price.<sup>7</sup> The evaluation criterion typically relies upon a version of cost-effectiveness analysis. Furthermore, most European countries (as well as Canada) employ external reference pricing, either as the main pricing criterion or to augment cost-effectiveness analysis. Given the ubiquity of these procedures in reimbursement and pricing decisions, typically for new pharmaceuticals

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5. NICE is an independent public body that develops quality standards and performance metrics for those providing and commissioning health, public health, and social care services.

6. For a detailed discussion of regulatory procedures in individual European countries, see Panteli et al. (2016).

7. As a rule, marketing authorization is required before medicines can be made available and any decisions are made on reimbursement or price. The authorization process aims to verify the quality, safety, and efficacy of a candidate drug. Safety is the main criterion for authorization. See Panteli et al. (2016).

used in the publicly financed (statutory) health care system, it is relevant to consider how they affect the tradeoff insurers see themselves facing between controlling expenditures on prescription drugs and ensuring that the insured have access to quality health care.<sup>8</sup> In the next two sections, we evaluate the potential for insurers to err on the side of being too restrictive in their decisions regarding reimbursement and pricing, to the detriment of those they are insuring.

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**8.** Price regulation is more typical of ambulatory care. For the inpatient sector, direct negotiations between hospitals and manufacturers are often possible. However, health authorities often put limits on inpatient pharmaceutical budgets.

## Overview of cost-effectiveness analysis

The cost-effectiveness assessment of the value of a given prescription drug is typically based on epidemiological and cost projections for a specific disease. The assessment provides an estimate of what the insured population should be willing to pay for the drug being considered in the form of an incremental insurance premium. The so-called incremental cost-effectiveness ratio (ICER) is estimated by comparing the cost of the new technology to the cost of the current standard of care (SOC) in the numerator of the ICER and the benefits of the new technology to the benefits of the SOC in the denominator. Benefits are measured by the estimated quality-adjusted life years (QALYs) associated with the new technology over and above the QALYs associated with the SOC.<sup>9</sup> A QALY represents the estimated value of a quality-adjusted life year averaged across the insured population.

$$\text{ICER} = (\text{Cost}_{\text{new technology}} - \text{Cost}_{\text{SOC}}) / (\text{QALYs}_{\text{new technology}} - \text{QALYs}_{\text{SOC}})$$

If this ratio is less than the insurer's ceiling willingness to pay, then the new technology represents good value for money to the health insurer.<sup>10</sup> The amount that public insurers are willing to pay for an additional QALY apparently varies across insured individuals and diseases, as well as across political jurisdictions. For example, Garrison and Towse (2017) state that in the UK, the threshold used on behalf of the National Health Service ranges from £20,000 per QALY to £50,000 per QALY for life threatening conditions. In the US, the ratio varies from \$50,000 per QALY to \$150,000 or more per QALY depending upon the individuals using the new technology or the disease being addressed.

In principle, the value of a QALY in the calculation should represent the monetary value of an extra quality-adjusted life year to the insured users of the new technology. This is obviously difficult to measure, since insured users are typically not asked to pay the full cost of new drugs or other treatments

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9. An extensive discussion of the ICER is found in Garrison and Towse (2017).

10. See Lakdawalla et al. (2012).

at the point of care.<sup>11</sup> However, it is possible that there are systematic biases in evaluating the cost-effectiveness of new therapies, and that the net effect of the biases is to understate the benefits of new therapies or, equivalently, to underestimate the cost-effectiveness of those therapies.

### **Possible biases in cost-effectiveness assessments**

One important potential source of bias in conventional cost-effectiveness analysis is what researchers have identified as the “value of hope” (see Lakdawalla et al., 2012). The value of hope denotes an improved psychological state enjoyed by patients because those patients anticipate an improved health status from a specific medical intervention. This bias is particularly relevant in the case of personalized medicine, which has the potential to benefit dramatically some patients with specific genetic makeups. While not all patients may benefit from the medical intervention if the likely beneficiaries are not precisely known before the intervention is undertaken, all patients receiving the intervention can enjoy increased hope. In this regard, patients may place more hope in a therapy with a wider “spread” of outcomes that include the potential for a longer period of survival. This increased hope would presumably be manifested in an increased willingness to pay for the intervention on the part of patients if the patients did pay for the therapy at the point of delivery.

It should be noted that increased hope is a real psychological benefit, even if individual patients overestimate their odds of being significantly benefited by treatment. Furthermore, a more optimistic subjective prognosis might improve the patient’s health status by, among other things, encouraging the patient to pursue treatment and make healthier lifestyle decisions. However, to the extent that increased hope is not incorporated into the QALY estimate for a new technology, the cost-effectiveness evaluation of that technology will be biased downward. Lakdawalla et al. (2012) argue that assessments of medical technologies should either incorporate hope into the value of therapies or set a higher threshold for an acceptable cost-effectiveness ratio, particularly when the technologies are applied in an “end-of-life” context.

Another potential source of bias in cost-effectiveness assessments is the existence of option value. Researchers have noted that the therapeutic benefits of a medical intervention are conditioned by the potential for additional therapies to emerge over time that are complementary to earlier interventions. Hence, if an earlier intervention can extend the life of a patient so that the patient can benefit from later innovations with significantly improved

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11. Cost sharing arrangements vary across countries and patient groups. For an overview, see Gliberman (2016).

therapeutic values, the earlier innovation creates what economists call option value. That is, the original innovation creates opportunities (or options) for patients to try newer therapies that have improved therapeutic value. If only the original therapeutic value of a medical intervention is considered when assessing its cost-effectiveness, the assessment might understate the value of that intervention to the patient when even a small expected extension of life might enable the patient to benefit from a newer and more effective therapy.

## Personalized medicine

As noted above, personalized medicine involves the receipt of care conditional on the results of a biomarker-based diagnostic test. In effect, personalized medicine involves tailoring medical treatments (particularly drugs) to the patient's genetics. This new health care technology is producing more expensive drugs but with potentially greater health care benefits than "conventional" drugs. The higher cost of personalized medicine is posing a financial challenge to health insurers, so that the existing tradeoff between affordability and access to state-of-the-art health care is becoming even more acute.<sup>12</sup>

The value of hope and the option value for personalized drug therapies may be even greater than they are in the case of conventional therapies. Therefore, conventional cost-effectiveness criteria for evaluating new drugs may underestimate the value of personalized drugs to insured populations and therefore result in inefficiently low levels of spending by insurers on new biopharmaceuticals.

A potential source of bias that might be particularly, albeit not exclusively, related to personalized medicine is linked to assessing the value of diagnostic tests underlying the development of personalized pharmaceuticals. Public insurers typically compensate drug developers for diagnostic testing based on the costs of such testing. Garrison and Towse (2017), among others, note that cost-based compensation is likely to understate the value of testing to patients, since the knowledge gained from any diagnostic test can potentially be used in future drug development activities, including combining two or more existing medicines to enhance the clinical benefits of each individual drug. In this context, clinical tests linking genetic characteristics to the therapeutic value of drug therapies create "knowledge externalities." Specifically, future developers of personalized health care applications learn from the successes and failures of earlier development efforts to identify genetic characteristics that leverage the therapeutic benefits of specific therapies. The existence of knowledge externalities implies that the social benefits of

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12. The implications of new health care technologies, including genetically targeted biopharmaceuticals, for health care policy are discussed in OECD (2017).

any individual diagnostic testing activity is likely to exceed the private costs of carrying out such testing. Therefore, if insurers establish the amount that they are willing to pay for a drug using conventional estimates of cost-effectiveness, they will likely set their reservation prices below socially efficient levels. This is especially the case to the extent that drug developers receive no government subsidies for clinical testing and development.

The value of diagnostic testing may also be underestimated if cost-effectiveness assessments do not recognize that by helping to identify which patients are most likely to benefit from a new drug therapy, diagnostic testing contributes to higher QALYs associated with specific therapies. That is, the QALY increases associated with targeted use of a therapy are likely to be larger per dollar of drug development cost than the QALY increases estimated from the use of any new drug by the population of all insured that have the disease targeted by that drug. This efficiency gain is sometimes referred to as the “medical value of knowing.” The Office of Health Economics (2016) explains this phenomenon as follows: Diagnostics can provide valuable information that helps guide medical decisions. Greater information generally means a reduction in uncertainty that can improve patient well-being and health care decision making. Patient well-being is improved because of improved adherence to the prescribed drug regime by those likely to be “responders” and by helping “non-responders” find their best alternative treatment more quickly. While these benefits of targeted personal medicine can also be produced by “trial-and-error” medicine, the precision associated with personalized medicine is likely to produce more substantial gains in medical knowledge and improved treatment efficacy compared to trial-and-error medicine.

Diagnostic testing also helps inform patients about their future health status, which can assist patients to make better decisions in non-medical areas of their lives including how long they should plan to work, whether they should buy long-term care insurance, how to structure their finances and so forth.<sup>13</sup> Even in the absence of formal tests, counselors may use their knowledge of genetics and epidemiology to help concerned families gauge their chances of contracting a disease in order to plan their lives accordingly.

Finally, diagnostic testing creates knowledge for a patient that can generate what has been called “psychic value.” Lee, Neumann, and Rizzo (2010) offer the example of an individual who has a family history of Huntington’s disease or some other disease for which there is no clinical treatment. A genetic test might inform the patient that he or she is not likely to develop the disease, which would obviously bring substantial emotional relief to that patient. To be sure, learning that one has a genetic predisposition to a fatal disease would likely cause emotional distress, which is why many individuals

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13. This phenomenon is typically referred to in the literature as the “value of planning.” For a more detailed discussion, see Lee, Neumann, and Rizzo (2010).



choose not to have genetic testing for health conditions that run in their families. Hence, while the psychic value of genetic testing will vary across patients and disease conditions, ignoring psychic value might well contribute to under-estimating the benefits of diagnostic tests.

## Reference pricing and other initiatives to reduce drug prices

One frequently employed strategy in price regulation is the use of external (or international) reference pricing. This strategy has been established in almost all European countries (as well as Canada) either as the main or secondary criterion for determining drug prices. As a rule, external reference pricing is applied to reimbursable patent medicines.<sup>14</sup> Specific attributes of reference pricing vary across countries. For example, the number of countries used as references range from three in Portugal to thirty in Poland (Panteli et al., 2016). In most cases, an average of a basket of external prices is used as a pricing benchmark, but some countries such as Spain use the lowest external price as a benchmark.

To the extent that reference pricing schemes do not include US prices in the relevant basket, external reference pricing will result in lower government-approved drug prices, since US drug prices are substantially higher than in other countries.<sup>15</sup> Panteli et al. (2016) summarize evidence showing that the development of drug prices in a reference pricing environment can drive down drug prices by as much as 15 percent in a ten-year period. However, other cost-containment actions by government regulators also make a significant contribution to lowering prices over time. These actions include discounts and rebates to public payers, public tendering, and price freezes.

Initiatives to reduce drug prices will increase the consumer surplus captured by purchasers of pharmaceuticals in the short run, while reducing the profits of producers. Philipson (2017) discusses how cost-containment

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<sup>14</sup>. In the case of Canada, external reference pricing applies to all patented medicines. Many European countries also use internal reference pricing (IRP), where the prices of therapeutic equivalents within the country are used as references. IRP is most commonly used in the pricing of generic drugs. See Panteli et al. (2016).

<sup>15</sup>. Proposed reforms to the regulatory process in Canada call for the PMPRB to drop the US and Switzerland as external reference countries in Canada's reference basket. Both countries typically have higher drug prices than the countries that will be included in the reference basket. For a discussion, see Aciri (2018).

strategies of public health care schemes are equivalent to rate-of-return regulation, with adverse implications for dynamic efficiency. Specifically, such strategies reduce the incentives of producers to innovate. There is empirical evidence to support Philipson's concern. For example, Giacotto, Santerra, and Vernon (2005) show pharmaceutical R&D spending increases with real drug prices after holding constant other determinants of R&D. Specifically, their estimated elasticity coefficient for the United States suggests that a 10 percent increase in the growth of real drug prices is associated with a nearly 6 percent increase in the growth of R&D intensity.<sup>16</sup>

Empirical evidence also identifies the adverse impact of price regulation regimes on how quickly new drugs become available to prescribers. For example, Danzon and Epstein (2012) examine drug launch experiences in 15 countries from 1992 to 2003 for drugs in 12 major therapeutic categories. They conclude that to the extent that price regulation reduces price levels, such regulation directly contributes to launch delay in the regulating country. In a similar vein, Cockburn, Lanjouw, and Schankerman (2016) analyze the timing of launches of 642 new drugs in 76 countries during 1983–2002. They show that patent and price regulation regimes strongly affect how quickly new drugs become commercially available in different countries. Price regulation delays launch, while longer and more extensive patent rights accelerate it. Panteli et al. (2016) note that a 2011 study of 20 European countries found that the time frame between market entry and the end of the post-marketing evaluation ranged between 116 and 550 days. This does not account for additional delays if the health authorities and the manufacturer cannot agree upon a price, and the manufacturer chooses not to supply the market until it is profitable to do so.<sup>17</sup> Barua and Esmail (2013) also found considerable delays in access to new medicines in Canada in comparison with access in the United States and Europe. Delays in access to drugs in Canada were not only a result of longer approval processes for market authorization but were primarily due to differences in the dates on which manufacturers submitted new drugs to agencies for regulatory approval.

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16. As we discuss in the next section, medical R&D spending is driven by world returns to R&D. Since the United States is such a large consumer of pharmaceuticals, its spending alone can influence R&D activities of drug companies.

17. Manufacturers may also delay marketing drugs in specific markets if “low prices” in those markets will be used for reference pricing elsewhere.

## Conclusion

The Canadian government's proposed amendments to the PMPRB call for the increasing incorporation into the PMPRB's regulatory process of criteria used in public reimbursement decisions (particularly cost-effectiveness evaluations) by agencies such as CADTH. As such, the direction of Canadian regulatory policy seems to put more emphasis on controlling expenditures on pharmaceuticals than on ensuring access of Canadians to new therapies. Canada is not unique in implementing measures to contain expenditures on drugs. In fact, policymakers around the world face a similar challenge in balancing patient access to effective medicines with affordability. As such, governments and public insurers employ a mix of regulatory mechanisms to contain pharmaceutical expenditures. In particular, the use of cost-effectiveness analysis and reference pricing to regulate pricing and reimbursement of drugs is widespread.

Our discussion highlights the potential for conventional cost-effectiveness analysis, as well as other efforts by governments to contain the costs of new medical technologies, including pharmaceuticals, to discourage technological change. They can also delay access to new and effective therapies. These concerns augment a more general phenomenon that Philipson (2016) discusses in detail. Namely, national health care authorities have incentives to "free-ride" on the research and development (R&D) activities carried out in other countries. The basis of Philipson's argument is that medical R&D is driven by world returns to R&D undertaken by pharmaceutical companies and not by the returns from individual domestic markets. Therefore, taxation to fund the reimbursements and profits to the health care industry involves a private (country-specific) cost with a worldwide benefit through stimulating innovation. It follows that if medical innovation benefits all countries, any individual country has an incentive to reimburse manufacturers at less than the socially efficient rate from a multi-country perspective. As a result, there will be too little medical innovation from a global perspective given the public goods characteristic of pharmaceutical R&D.

New and innovative therapies, particularly personalized medicine, offer the potential for major improvements in the therapeutic effectiveness

of new drug therapies.<sup>18</sup> A growing emphasis of public (or statutory) insurers on cost containment, including in the United States, could undermine what might be a revolutionary technological regime that will bring major gains in longevity and health status. In essence, there is a large multinational option value to encouraging ongoing drug development activities. Policymakers in developed countries especially need to address the existence of “gains from cooperating” in bearing the (admittedly high) near-term costs of new drug development. As noted earlier, the potential is growing for stronger cost containment efforts to be imposed on drug expenditures by the US government under Medicare. Since the US accounts for around 40 percent of world pharmaceutical expenditures (Philipson, 2016), new cost containment actions by the US could severely threaten spending by drug companies on developing new therapies unless other countries loosen their own cost controls.

In rethinking existing and prospective cost containment strategies, policymakers should also implement procedures that recognize the “life-cycle” benefits of new drugs, including the knowledge externalities that new drugs provide future research efforts. While difficult to do, it is clearly inappropriate to adjust prices downward if new drugs fail to provide their anticipated benefits, while not retroactively rewarding manufacturers that produce breakthrough therapies offering therapeutic benefits and knowledge externalities that were not perfectly anticipated. As well, once a new drug is developed, the incremental cost of treating patients with that drug is relatively low. So while a new drug might create financing problems from a short-run perspective, the problem becomes much less relevant in the longer run.

Adopting a longer-run policy perspective for drug reimbursement and pricing policies is critical to the health of future generations. As Garrison and Towse (2017) conclude, if pricing and reimbursement policies within and across countries, as well as across distinct diagnostic and treatment developments, do not efficiently share costs and reward value appropriately, the global rate of innovation will be sub-optimal, with a long-run adverse impact on public health.

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<sup>18</sup> The OECD (2017) highlights the growth of personalized medicines in recent years. Such treatments accounted for more than 25 percent of drugs approved by the US regulator in 2015.

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