IHE Report

Investigation and Analysis of Options to Enhance Canada's Patented Medicine Price Ceiling Regulatory Regime

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Interpretation of Findings

The views expressed herein are those of the authors and do not necessarily represent the official policy or views of the Institute of Health Economics, its partners, any Alberta Government Department, or Health Canada.

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EXECUTIVE SUMMARY

Canada, like other international jurisdictions, has adopted various policies to regulate the prices of pharmaceuticals. Price regulation of patented medicines in Canada occurs at various points through the medicines supply chain and by different actors. Provincial pricing policies are typically aimed at public formulary reimbursement and allowable retail prices, including pharmacist and wholesaler markups. Ex-factory prices for patented medicines are regulated federally by a quasi-judicial authority - the Patented Medicines Price Review Board (PMPRB).

Price regulation policies are often a response to concerns about escalating costs for consumers. But these measures also directly affect consumer welfare and producer profit. Since the establishment of the PMPRB 25 years ago, there have been considerable developments in pharmaceutical and price regulation policies in other jurisdictions. In particular, there has been a move away from reference-price-based policies towards value-based pricing.

Value-based pricing policies are viewed as a potential means to resolve existing tension across competing policy objectives that have not been resolved through reference-based policies: namely, to create maximum health benefits for consumers, to pursue greater health system sustainability, and to establish incentives for producer innovation.

A growing awareness and movement toward value-based approaches to price regulation raises questions as to whether the guiding principles, regulations and guidelines of the PMPRB require re-visiting and whether current developments shed light on opportunities for improving pricing policy in Canada.

This report is an analysis of the theoretical basis for value-based pricing, relevant international developments, and areas for improvement within Canada's current patented drug pricing system. This report intends to inform future policy research, advice, and Canadian drug policy discussions regarding the feasibility and implementation of value-based pricing approaches.

Section 4 of this report provides an overview of **concepts related to pricing patented medicines**. Through an examination of current theory and empirical evidence it suggests:

- Value-based pricing must consider consumer benefit and producer profits and what the appropriate balance of these is. External price referencing is not a means of ensuring a fair balance.
- Value-based pricing *is* a means of fostering global innovation by signaling from consumers to producers what innovations are required.
- Value-based pricing *is not* a means of stimulating Canadian R&D or non-R&D investment by the pharmaceutical sector.
- Value-based pricing *is not* a mechanism to lower prices that are unaffordable; neither is it a mechanism to contain costs. It *is* a mechanism to ensure that the price paid for a drug is appropriate for the benefit it produces.

Section 5 of this report provides a review of five jurisdictions (Germany, Mexico, Sweden, UK and France) that have adopted or are considering adopting a value-based pricing approach. Several key lessons for the implementation of value-based pricing emerged from this:

- Principled approaches to value-based pricing (as seen in Sweden, Germany, and the UK) involve consistent approaches to economic evaluation and an explicit notion of opportunity cost.
- All five countries use a transparent and structured negotiation process to regulate price, allowing for diverse elements of value to be captured in prices.
- All five countries have created strong links to rules for price regulation within the reimbursement environment – even within countries that lack compulsory universal insurance or centralized purchasing regimes.

In **Sections 6 and 7**, an analysis of important components of value-based pricing is undertaken and the feasibility assessed by mapping these features onto the current Canadian environment.

Eight lessons are proposed to inform policy discussions about the desirability and feasibility of the value-based pricing of patented pharmaceuticals in Canada:

LESSON 1: *A national standard for conducting economic evaluation is the basis for informing value-based prices*

LESSON 2: *Single estimates of incremental benefits to consumers are important for supporting decisions about efficiency and compatibility with the current reimbursement environment*

LESSON 3: *Considering societal costs will require modification to existing guidance for economic evaluation. The value of information is also important to consider in pricing.*

LESSON 4: *Measuring the opportunity cost threshold for new medicines is an important avenue of future research, as an empirical measurement of impacts on life-years or quality-adjusted life-years is helpful for value-based pricing*

LESSON 5: *Systems for measuring real-world effectiveness will be required for re-assessing prices.*

LESSON 6: *Systems to support delivering and monitoring the use of medicine by indication are needed to develop menus of price-volume options based on cost-effectiveness.*

LESSON 7: *Value-based pricing requires a negotiation mechanism that is fair and transparent. This is best informed by deliberative processes that include all relevant experts and policy actors.*

LESSON 8: *Value-based pricing must involve purchasers. Current initiatives oriented to support value-based purchasing may eliminate the need for price regulation outside of purchasing arrangements.*

The paper finds that value-based pricing would require a departure from the current approach to excessive price determination within the PMPRB. Notably, value-based pricing would require a much closer relationship with public and private payers, and the institutions that support them, as prices can be further regulated in the marketplace. Any attempt to introduce value-based pricing for *ex-factory* prices would likely duplicate existing systems that attempt to affect purchase prices based on cost-effectiveness, as seen across individual provinces and in the newly-formed pan-Canadian purchasing alliance.Finally, value-based pricing cannot be simply reduced to a mathematical algorithm. Rather, it would require the full participation and consent of representative societal actors who can deliberate and negotiate with information regarding how prices will affect the health and welfare of consumers, both now and in the future.

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1 INTRODUCTION

There is a natural tension and competition across policy objectives of providing the best patient experiences and health outcomes to consumers at a minimum cost while providing the health technology industry incentives for future innovation. There has been renewed interest in the use of innovative pricing mechanisms in health care as a means to resolve this tension.

Unlike other markets, where prices are ultimately determined by consumer demand and producer supply, healthcare is an imperfect market as, among other things, it harbors the following unique combination of characteristics:

1) Most consumers do not pay directly for drugs but rather through large single payers (i.e., monopsonist payers) that use insurance schemes; and
2) The patent system provides producers with a temporary right to be sole (i.e., monopoly) suppliers as a means to recover research and development (R&D) costs and provide incentives for future innovation.[1]

In this environment, monopoly producers can set higher prices than the price that would be determined through competitive interactions between consumers and producers seen in other markets. This is especially true for those consumers who are not protected by insurance and would potentially benefit from the large-scale purchasing and negotiating power of insurance bodies. Similarly, consumers, through large single payers, can demand lower prices than producers are willing to sell at.

This means granting a temporary monopoly has a potential societal cost, as some, especially those unprotected by insurance, may be unwilling or unable to pay a monopoly price for a new drug, but would still be willing or able to pay for the same product at a lower price. This lower price may not be totally disadvantageous to the producer. That is, it is a price that would still allow the manufacturer to recoup costs. If the producer were to lower the price, however, it would forfeit revenue from those who would be willing to pay more for it. They may also forfeit opportunities to invest in future research and development which could lead to future innovation.

Like other markets with monopolies, various schemes have been proposed to improve efficiency and reduce welfare loss to consumers (i.e., by improving access) while ensuring producer profit to cover future research and development costs (and potentially, needed innovation). One approach is to use price regulation. Price regulation is "a policy response to inadequate competition in a market that includes products considered to be necessities and that has been publicly subsidised to avert under-consumption".[2] The practicality of price regulation schemes will vary according to the context in which they are implemented. Nonetheless, they have been proposed with the aim of protecting consumers through reducing the risk of under-consumption of medicines, protecting manufacturers from exploitation from monopsonist payers, ensuring monopolist gains still result in value accrued to society, and ensuring that the monopsonist does not shift costs onto uninsured consumers.

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[1] Husereau D, Cameron CG. *Value-Based Pricing of Pharmaceuticals in Canada: Opportunities to Expand the Role of Health Technology Assessment?*, Cost Drivers and Health System Efficiency 5 (Ottawa: Canadian Foundation for Healthcare Improvement, 2011). Available: www.cfhi-fcass.ca/publicationsandresources/researchreports/ArticleView/11-12-16/8eeaf655-b2b6-4c39-a909-6854acfea850.aspx

[2] Organisation for Economic Co-operation and Development. *Pharmaceutical Pricing Policies in a Global Market*, Health Policy Studies (Paris, France) (Paris: OECD, 2008)

In Canada, many health system consumers are particularly vulnerable to the 'imperfect' pharmaceutical market as insurance schemes for drug purchasing are not mandatory for consumers. Although public insurance providers and payers, such as hospitals and public drug plan formularies may develop effective systems of regulating reimbursement prices (e.g., using policy tools such as health technology assessment, formularies, and product listing agreements), they constitute a minority (40%) of the total prescription drug market.[3] Consumers without insurance can be assumed to be more sensitive to price than similar insured consumers, leading to concerns about access.

Price-taking private insurers (that pay for another 30% of Canadians) and consumers without insurance (30%) are more vulnerable to excessive prices and its unintended consequences. A report from Canada's Office of The Auditor general shows that before the establishment of current price regulation this was, in fact, the case.[4] It found annual price increases of pharmaceutical drugs were proportionally higher than annual increases in the Consumer Price Index (CPI) from 1982 to 1987. In 1987, the Patented Medicine Prices Review Board (PMPRB) was established by Parliament to "protect the interests of Canadian consumers by ensuring that the prices of patented medicines sold in Canada are not excessive."

Since the establishment of the PMPRB 25 years ago, there have been considerable international developments in pharmaceutical and price regulation policies in other jurisdictions. There have also been considerable pan-Canadian developments, particularly in the realm of public payers with the establishment of several coordinated drug review initiatives and most recently coordinated brand and generic pricing and purchasing. This raises questions as to whether the guiding principles, regulations and guidelines of the PMPRB require re-visiting and whether current developments shed light on opportunities for improving pricing policy in Canada.

1.1 Pricing and Reimbursement of Patented Medicines in Canada

Overview

Price regulation of patented medicines can occur at various points through the medicines supply chain and by different actors. As provinces are responsible for delivering care for their constituents, pricing policies are typically aimed at public formulary reimbursement and allowable retail prices, including pharmacist and wholesaler markups. Ex-factory prices for patented medicines are regulated federally by a quasi-judicial authority - the Patented Medicines Price Review Board (PMPRB).

The PMPRB was created upon an amendment to the patent act in 1987. It acts to enforce Patented Medicine Regulations (SOR/94-688)[5] that are intended to strengthen rewards and incentives for patentees while providing protection for consumers from – essentially acting as one mechanism for achieving a balance between consumer and producer interests.

The PMPRB carries two primary mandates: 1) To ensure that prices charged by patentees for patented medicines sold in Canada are not excessive; and 2) To report on pharmaceutical trends of

[3] Canadian Institute for Health Information. *Drug Expenditure in Canada, 1985 to 2011 Spending and Health Workforce* (Ottawa, Ont.: Canadian Institute for Health Information, 2011). Available: http://site.ebrary.com/lib/celtitles/docDetail.action?docID=10562849

[4] Office of the Auditor General of Canada Government of Canada. *Chapter 17—Patented Medicine Prices Review Board,* September 1, 1998. Available: www.oag-bvg.gc.ca/internet/English/parl_oag_199809_17_e_9323.html

[5] Legislative Services Branch. Consolidated Federal Laws of Canada, Patented Medicines Regulations, July 1, 2008. Available: http://laws-lois.justice.gc.ca/eng/regulations/SOR-94-688/FullText.html?term=price+review

all medicines and on R&D spending by pharmaceutical patentees. The PMPRB processes and activities seek to define a price limit or "ceiling" for ex-factory drugs for consumers as well as revenues and research and development expenditures for patentees. The operational aspects of the PMPRB are outlined through comprehensive guidelines, policies and procedures.[6] These policies, procedures and guidelines are a direct reflection of its legislative mandate outlined in the defined by the Patent Act and Patented Medicines Regulations.[7]

In brief, the PMPRB categorizes each new patented medicine sold in Canada according to a recommendation provided by an expert advisory committee (the Human Drug Advisory Panel, or HDAP). There are four distinct categories of therapeutic improvement:

> **Breakthrough:** A breakthrough drug product is the first one to be sold in Canada that treats effectively a particular illness or addresses effectively a particular indication.
>
> **Substantial Improvement:** A drug product offering substantial improvement is one that, relative to other drug products sold in Canada, provides substantial improvement in therapeutic effects.
>
> **Moderate Improvement:** A drug product offering moderate improvement is one that, relative to other drug products sold in Canada, provides moderate improvement in therapeutic effects.
>
> **Slight or No Improvement:** A drug product offering slight or no improvement is one that, relative to other drug products sold in Canada, provides slight or no improvement in therapeutic effects.
>
> (Source: [8])

If a new patented drug product has multiple approved indications or multiple uses, the category of improvement will be "based on the approved indication or use for which the drug product offers the greatest therapeutic advantage in relation to alternative therapies for the same indication/use in a significant patient population. This would exclude rare medical conditions or diseases (i.e., low incidence and prevalence in Canada)." There is no official definition of a rare medical condition in the guidelines. This is determined by the HDAP after considering the disease definition and how the drug is categorized and regulated in jurisdictions with rare disease definitions, such as the US Food and Drug Administration.[9]

The HDAP considers a submission of information provided by the producer but is able to consider any additional information it believes to be relevant. There is explicit guidance detailing to what a new drug product can be compared to. In essence, it is bound to considering therapeutic alternatives according to the World Health Organization (WHO) Collaborating Centre for Drug Statistics Methodology´s Anatomical Therapeutic Chemical (ATC) Classification System. The HDAP primarily considers factors related to patient outcomes and well-being; although it also considers factors related to caregiver burden and productivity gains. The factors considered are outlined in Box 1.

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[6] PMPRB. *Compendium of Policies, Guidelines and Procedures -Updated June 2012,* March 1, 2013. Available: www.pmprb-cepmb.gc.ca/english/view.asp?x=1733&mid=1636
[7] PMPRB. *Legislation, Regulations and Guidelines*, February 14, 2003. Available: www.pmprb-cepmb.gc.ca/english/view.asp?x=73
[8] PMPRB. *Compendium of Policies, Guidelines and Procedures -Updated June 2012*
[9] Personal Communication, PMPRB, 16th April 2013

The HDAP is intended to be a structured deliberative process that seeks to find a consensus based on evidence through the critical interaction of individuals with varying values and perspectives.[10] Therapeutic categorization, then, is not an algorithm; it is a matter of judgment by experts considering a free-range of information and evidence about the factors used to recommend a therapeutic category. Experts are given flexibility to imagine the level of improvement that will occur in the real world, when factors beyond those in randomized controlled trials will lead to realized outcomes.

Box 1: Factors Considered by PMPRB HDAP When Recommending Therapeutic Category

Primary Factors

- Increased efficacy
- Reduction in incidence or grade of important adverse reactions

Secondary Factors

- Route of administration
- Patient convenience
- Compliance improvements leading to improved therapeutic efficacy
- Caregiver convenience
- Time required to achieve the optimal therapeutic effect
- Duration of usual treatment course
- Success rate
- Percentage of affected population treated effectively
- Disability avoidance/savings

Factors not considered (unless the impact of these factors results in either increased efficacy and/or a reduction in the incidence or grade of important adverse reactions):

- The mechanism of action
- A new chemical entity
- A different pharmacokinetic profile

(Source, 11)

Price testing

Along with the recommendation, comparators are identified by the HDAP for purposes of future price testing by the PMPRB. The intent of price testing is to determine whether the new drug is being sold at an excessive price. The type of price test performed varies according to the therapeutic category the patented drug falls into. The test to see if the price of the drug sold is excessive will usually involve external reference pricing, unless the drug is deemed to be of "Slight or No Improvement" in which external reference pricing will only be applied when therapeutic reference pricing is not feasible. External reference pricing involves a comparison to publicly available ex-factory prices from France, Germany, Italy, Sweden, Switzerland, the United Kingdom, and the

[10] Culyer A. *Deliberative Processes in Decisions About Health Care Technologies: Combining Different Types of Evidence, Values, Algorithms and People.* (Office of Health Economics, June 2009). Available: www.ohe.org/publications/recent-publications/list-by-title-20/detail/date////deliberative-processes-in-decisions-about-health-care-technologies.html
[11] PMPRB. *Compendium of Policies, Guidelines and Procedures -Updated June 2012*

United States. Prices are also tested to ensure they do not exceed the highest price sold internationally. A depiction of price tests is shown in Table 1 below.

Table 1: Price tests employed by the PMPRB

Therapeutic Category	Price Test	
Slight or No Improvement	Therapeutic Class Comparison	Highest International Price Comparison Test
Moderate Improvement	Midpoint of Median International Price Comparison Test and Therapeutic Class Comparison Test	
Substantial Improvement	Highest of Median International Price Comparison Test and Therapeutic Class Comparison Test	
Breakthrough	Median International Price Comparison Test	

The PMPRB has conducted periodic reviews of its policies, guidelines, and procedures. These reviews involve consultation from stakeholders, primarily pharmaceutical producers and academics. The last update was occurred in June 2012 and reflected concerns from stakeholders around transparency, consistent terminology, and price-adjustment and accounting procedures. These revisions were based on a number of consultations that occurred between 2005 and 2009. The consultations also focused on current methods to test prices, and whether therapeutic categorization is adequate or should be revisited.

Through these consultations, and in other international jurisdictions, concerns have emerged that reference-based approaches to pharmaceutical pricing regulation may be suboptimal, as it may still offer insufficient protection for consumers and provide suboptimal incentives for producers.[12] A number of key international jurisdictions, including Germany and the UK, who led price regulatory reforms in the late 1980s are currently re-visiting or implementing new policies, in an attempt to provide a pricing scheme that more closely reflects price and demand in a perfect market, optimizing the share of value between consumers and producers. In the UK, the promised implementation of a scheme for pricing pharmaceuticals in January 2014, and which is still in development, has been labeled "value-based pricing".[13]

Value-based pricing policies are viewed as a potential means to resolve existing tension across competing policy objectives that have not been resolved through reference-based policies; namely, to create maximum health benefits for consumers, opportunities for health system sustainability and clear incentives for future producer innovation.

[12] Dylst P, Vulto A, Simoens S. The Impact of Reference-pricing Systems in Europe: a Literature Review and Case Studies. *Expert Review of Pharmacoeconomics & Outcomes Research* 2011;11(6):729–37; Brekke KR, Grasdal AL, Holmås TH. Regulation and Pricing of Pharmaceuticals: Reference Pricing or Price Cap Regulation?. *European Economic Review* 2009;53(2):170–85, doi:10.1016/j.euroecorev.2008.03.004; Miraldo M. Reference Pricing and Firms' Pricing Strategies. *Journal of Health Economics* 2009;28(1):176–97, doi:10.1016/j.jhealeco.2008.09.006; Lopez-Casasnovas G and Puig-Junoy J. Review of the Literature on Reference Pricing. *Health Policy* 2000;54(2):87–123

[13] Claxton K. OFT, VBP: QED? *Health Economics* 2007;16(6):545–58

2 OBJECTIVES

The Office of Pharmaceutical Management Strategies (OPMS) at Health Canada has a mandate to examine ongoing issues related to the pharmaceutical sector. This includes the societal consequences of different policies related to drug pricing, health technology assessment and reimbursement.

The intent of this report is to examine current policies and explore the feasibility of a value-based approach to pricing. This report is an analysis of the theoretical basis for value-based pricing, relevant international developments, and areas for improvement within Canada's current patented drug pricing system. By providing key considerations regarding the potential benefit, harm and feasibility of implementing value-based pricing for patented medicines in Canada, this report intends to inform future policy research, advice, and Canadian drug policy discussions.

3 METHODS

3.1 General Approach

The approach to this research follows a conventional academic style of descriptive content analysis[14] with some formal evaluation. In short, outputs were established in an analysis plan, a thorough literature search and informal survey of key organizations and individuals was conducted, and a list of "lessons learned" about the value-based pricing of patented pharmaceuticals from international trends which could be mapped against the Canadian environment was developed. Subsequently, we identified areas for changes in the interface between drug cost reimbursement and Canada's policy approach, patented drug regulations, and guidelines. The feasibility of the various policy options was determined, based on analysis and discussions with key informants.

3.2 Specific Approach

a. Consultation and analysis plan

The final content of the key metrics and information sources were developed through informal discussion with experts and a face-to-face meeting with representatives from OPMS. The sample frame used to describe the pricing systems in select OECD countries was also established.

b. Identification of relevant literature for international analysis

A search of grey literature sources and relevant political-economic social sciences databases was conducted in consultation with a professional research librarian. Databases searched from 1998-Feb,2013 included: Medline, Embase, International Pharmaceutical Abstracts, DARE, NHS EED, HTA, EconLit, Academic Search Complete, Business Source Elite, Health Business Elite, Health Policy Reference Center, Web of Science, RePec, and SSRN. An informal survey of key academic and public policy informants was also conducted. The search strategy is shown in Appendix B.

c. Data synthesis and lessons learned

We identified reimbursement and pricing policy along with other relevant events in the last 5 years. A narrative discussion highlighting key trends and emerging themes across jurisdictions and a list of facilitators, barriers and lessons learned appears in the next section.

[14] Howlett M, Lindquist E. Beyond Formal Policy Analysis: Governance Context and Analytic Styles in Canada. In: *Policy Analysis in Canada: The State of the Art.* (Toronto: University of Toronto Press, 2006)

A description of current patented medicine pricing and reimbursement environment was conducted and compared to the key features, emerging themes and lessons learned across select OECD jurisdictions. What exists and what will need to be improved or developed is highlighted. Finally, some lessons for Canada are drawn from these comparisons.

4 Overview of Concepts Relevant to Pricing of Patented Medicines

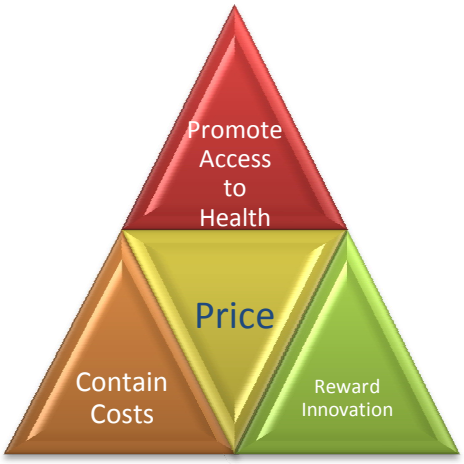
4.1 Pricing of Patented Medicines

4.1.1 Overview of current pricing approaches for patented medicines

All OECD countries have implemented measures to regulate market access of new drugs and to grant temporary monopoly rights to producers.[15] These measures have been implemented as a policy response to the need for promoting societal health, through ensuring product supply, quality and associated claims of safety and potential benefits to consumers; and promoting economic opportunities for manufacturers, by providing assurances re-investment into future R&D and future innovation through assured profits.

Price regulation policies (price 'controls') are often a response to concerns about escalating costs. However, these measures also affect consumer welfare and producer profit. Price controls can be applied to manufacturer ex-factory prices or subsequent wholesale and retail prices. They can also be linked to reimbursement with mechanisms to publicly negotiate price or through confidential rebates given back to insurers from manufacturers.

Figure 1: Pricing policies and competing policy goals



The vast majority of OECD countries have universal coverage schemes that allow for price regulation connected to reimbursement and purchasing of patented medicines. Only three countries - Canada, Mexico, and the US -- do not have compulsory insurance schemes that can be used to universally regulate the prices of pharmaceuticals. Both Canada and Mexico have adopted policies to

[15] Organisation for Economic Co-operation and Development. *Pharmaceutical Pricing Policies in a Global Market*

ensure that patented medicines sold to uninsured consumers are not priced excessively.[16,17] Similar to Canada, price regulation applies to on-patent drugs and is based on retail sales. Unlike Canada, participation by manufacturers is voluntary. An international reference price is used as a basis for determining whether prices are excessive.

Price regulation mechanisms across international jurisdictions can be cost-based, reference-based, profit-based or value-based. Price regulation schemes across jurisdictions may use one or a combination of internal and external reference pricing mechanisms (see Table 2).

Table 2: Price regulation schemes and their application internationally

Scheme	Jurisdiction(s) , e.g.
Free pricing – Prices are not subject to regulation; producer charges what market will bear.	**USA**
Cost-based pricing – Prices are based on marginal costs of production (costs of research, production, promotion, and distribution).	**India (prior to 2013)**
Reference pricing – Prices are set through comparison to an existing standard. An ***internal*** reference price generally involves comparing the price of the drug to another drug with similar chemical, pharmacologic, or therapeutic properties.[18] An ***external*** reference price involves comparing the price of a drug to prices in other jurisdictions selected according to some notion of comparability, usually economic or geographic.[19]	**Most European Countries (not UK, Germany, Cyprus, Malta, Bulgaria)**
Profit-based pricing – Prices may be set freely but rebates paid to regulator based on profits.	**UK**
Value-based pricing – Prices are negotiated based on perceived or realized benefits; nominally a pre-determined balance of benefits to both consumers and producers.	**Sweden**

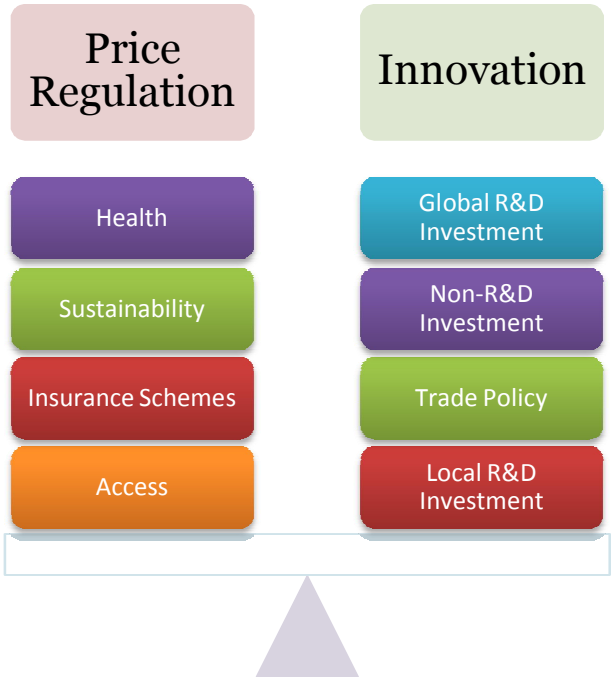
(Source: Adapted from [20])

Pricing policies are appealing as they are intended to create social benefits by improving the affordability of a product. However, in a perfect market, any policy that attempts to regulate market forces will often have unintended consequences. For example, setting a maximum allowable price for a good can increase demand, or encourage parallel importation and lead to product shortages. It may also provide incentives to producers to circumvent controls, requiring additional (and resource-intensive) bureaucracy to monitor compliance. It may also have other effects such as deterioration in product quality by producers trying to recoup lost revenue through cost-cutting measures.

[16] Ibid.; Moïse P, Docteur E. *Pharmaceutical Pricing and Reimbursement Policies in Mexico*. Health Working Papers 25 (Paris: OECD, 2007). Available: *www.oecd.org/dataoecd/39/36/38097348.pdf*
[17] These mechanisms also lead to price-setting which theoretically benefits insured consumers
[18] Lopez-Casasnovas and Puig-Junoy. Review of the Literature on Reference Pricing
[19] Organisation for Economic Co-operation and Development. *Pharmaceutical Pricing Policies in a Global Market*
[20] Madrid I, Velázquez G, Fefer E. *Pharmaceuticals and Health Sector Reform in the Americas: An Economic Perspective* (Washington, D.C.: Action Programme on Essential Drugs, World Health Organization: Regional Program on Essential Drugs and Technology, Division of Health Systems and Services Development, Pan American Health Organization, 1998)

As previously mentioned, pharmaceutical markets of patented medicines are not perfect markets for a variety of reasons including the unique nature of buyers and sellers (i.e., monopsonists and monopolists). While regulating prices could make medicines more affordable and have positive effects on consumer demand, it will also have an effect on producer profit, R&D investment and future innovation. There may also be other important policy factors, such as trade policy, that will affect these relationships. In the next section, we will attempt to map out what is known about these relationships (see Figure 2)

Figure 2: Relationships to be considered in pricing policy intended to foster innovation



4.1.2 Price, quantity, investment and innovation

Price and quantity and research and development

The economic effects of setting drug prices must consider **the quantity of drugs sold**. The quantity of drugs sold and the rate of diffusion will depend on a number of factors aside from price, including cultural factors, access to insurance, population prevalence and incidence for the licensed indication, promotional activity, clinical awareness, supply chain mechanisms and reimbursement processes. Price and volume (which together make budget impact) are a major consideration for reimbursement by public insurers, who act as the primary consumers of drug products. Indeed, high prices, and not economic value, have been shown to be a more significant factor in recommendations not to list drugs within the Common Drug Review process.[21]

Various mechanisms have been employed to restrict quantity as a means of reducing budget impact including limited-use criteria on a formulary or negotiating confidential price-volume limits along with the associated rebates with producers. The Common Drug Review has recently increased the number of reasons for recommending restrictions as a possible means of improving patient access

[21] Rocchi A, et al. Common Drug Review Recommendations An Evidence Base for Expectations?. *Pharmacoeconomics* 2012;30(3):229–46

by reducing the numbers of do not list recommendations.[22] This is in line with other international assessment processes.[23] It is understandable that public drug plans would focus on price and quantity given the limited incentives that they are given to consider reductions in costs outside their budgets. These include recovered costs from improved productivity or reductions in costs due to reduced caregiver burden or hospitalization.

For producers, price and volume are components of sales. Revenue from sales generates low-cost capital available for research and development (R&D) and is the primary source of private R&D for larger companies.[24] Because of the relatively low marginal costs of production for any new medicine, anticipated sales are also seen as an important indicator of return on investment (i.e., marginal rate of return) for any drug being developed for global markets. Sales are highly correlated with company profitability, stock prices and expenditures on development R&D.[25] Globally, there is considerable investment on R&D in the pharmaceutical sector. In 2010, the industry dedicated approximately 15% of net sales to R&D with a total investment of USD 135 billion in 2011.[26] Investment in R&D has seen a compound annual growth rate of 6.5% since 2005 but there has been slower growth in the last few years.[27] Increasingly, the pharmaceutical industry must also consider the effect of fourth-hurdle HTA processes on sales that will affect return on investment and subsequently R&D decisions.[28]

Although concerns have been raised regarding delays in innovation as a consequence of the reduced growth in R&D investments (called R&D intensity) that have been observed in the past few years, true innovation is determined by a number of factors and related to the choices regarding how R&D expenses are made, as well as R&D intensity. For example, pricing systems that always set prices of new medicines similarly for similar drugs incent producers to make R&D choices to develop non-innovative "me-too" agents rather than new medicines for unmet needs.[29] Current systems of pricing and reimbursement may foster spending on R&D but still lead to new medicines that are not innovative or required. A summary of issues related to innovation are seen in Box 2.

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[22] Available: *www.cadth.ca/media/cdr/cdr-pdf/CDEC_Deliberative_Framework_e.pdf*

[23] Clement FM, et al. Using Effectiveness and Cost-effectiveness to Make Drug Coverage Decisions: a Comparison of Britain, Australia, and Canada. *JAMA* 2009;302(13):1437–43

[24] Organisation for Economic Co-operation and Development. *Pharmaceutical Pricing Policies in a Global Market*

[25] Golec J, Vernon J. Measuring US Pharmaceutical Industry R&D Spending. *PharmacoEconomics* 2008;12:1005–17; Organisation for Economic Co-operation and Development, *Pharmaceutical Pricing Policies in a Global Market*

[26] *The 2012 EU Industrial R&D Investment SCOREBOARD* (Spain: European Commission Joint Research Centre Institute for Prospective Technological Studies, 2013). Available: http://iri.jrc.ec.europa.eu/docs/scoreboard/2012/SB2012.pdf

[27] *Strength & Opportunity 2012: The Landscape of the Medical Technology, Medical Biotechnology, Industrial Biotechnology and Pharmaceutical Sectors in the UK. Annual Update - December 2012.* Annual Report 4 (London: HM Government, 2012); *The 2012 EU Industrial R&D Investment SCOREBOARD*

[28] Miller P. Role of Pharmacoeconomic Analysis in R&D Decision Making - When, Where, How? *Pharmacoeconomics* 2005;23(1):1–12

[29] Pattikawa L, Commandeur HR. Innovation And Market Value Performance: Does Product Innovation Matter? (n.d.). Available: http://pattivali.com/files/Innovation-and-market-value-performance. Lenny.pdf; Organisation for Economic Co-operation and Development, *Pharmaceutical Pricing Policies in a Global Market*

Box 2: *How can we define innovation from R&D?*

Definitions of the concept innovation in health technology can be grouped into four separate themes. While "innovation" can be used to refer to something that is new (i.e., invention), value-based innovation will tend to have important therapeutic effects, usually improved benefit and reduced harm compared to existing alternatives. Innovation in medicine can be categorized as science-, marketing-, health- or social change-based definitions of innovation and may be used differently by different policy actors.

Table 1: Types of Innovation in Health Technology

Theme	Description	Metrics	Descriptions of Small and Large Innovation, By Theme		Uses
			Small	Large	
Science	New Process or Product	Patents, Papers	Invention	New Chemical Entity	Government (R&D Intensity or Productivity) and Industry (Productivity)
Marketing	Quality Ladder - Management	Revenue, Growth, Balance of Trade	Enhancement	Blockbuster, Radical, Wide Diffusion	Industry (Productivity)
Health	Therapeutic Advance - Medicine	Health Outcomes, Measures of Health Equity	Convenient	New population, Large Disease Burden	Government (Health Policy), Clinical (Policy and Practice)
Social Change	Interaction with Environment	Societal Acceptance, Diffusion	"New" Idea	Transformative	Government (Policy), Industry

(Adapted from [30])

R&D investment

Before discussing the effect of pricing policy on local and global R&D investment, it is important to acknowledge that what constitutes pharmaceutical R&D investment is controversial, with no clear definition of what activities and costs are clearly defined by R&D. Some have suggested R&D activities should be more-narrowly defined as those activities required for invention (i.e., laboratory-based discovery research, and subsequent clinical research in humans) while others have included research related to manufacturing and promotion (such as a market access focus groups). PMPRB's current system for reporting expenses on R&D in Canada specifically excludes "market research, sales promotions, quality control or routine testing of materials, devices or products and routine data collection … not eligible for an investment tax credit".[31]

There are numerous legitimate economic activities outside of research supporting invention and product development that a firm may be engaged with including manufacturing, promotion, sales, distribution, legal and administrative activities (such as market access). These other expenditures have been estimated to far outweigh those on basic R&D. A study by Gagnon suggests promotional

[30] CADTH. The Economic Value of Innovative Health Technologies Discussion Paper [Unpublished]
[31] PMPRB. *Annual Report 2011*, June 13, 2012. Available:www.pmprb-cepmb.gc.ca/english/view.asp?x=1625&mid=1552

activities alone may account for two times the expenditure of basic R&D.[32] Nonetheless, investment in these activities is understandable given constant threats to the company profitability and the limited time frame in which to recoup costs.[33] Additionally, investment in non-R&D activities would be expected to vary according to legal and policy environments.

Regional investment and regional sales

Despite this controversy in definitions, we can assume that estimates of R&D investment represent required investment by the pharmaceutical sector to bring innovation to the market. In this section, we examine the theoretical and known effects of pricing policies and sales on local (regional) investment.

Although sales are correlated significantly with R&D expenditures, it is important to note that local sales are not necessarily related to local R&D investment. In 2011, Canada accounted for 2.6%of the global market of pharmaceutical sales[34] but for only 0.7% of global R&D investment.[35] Like other industries, decisions to invest regionally largely depend on factors such as the availability of specialized resources, available capital, academic environments, and intellectual property rights.[36] Currently, investment in R&D and non-R&D activities by the pharmaceutical industry sector primarily occurs in the US, UK, Japan, Germany, and France.[37]

The factors that *most importantly* contribute to foreign direct investment by multinational pharmaceutical companies have been a matter of academic investigation.[38] One particular issue is the wide variety of price control mechanisms employed by different countries, but price control is not always related to regional R&D or investment. For example, the UK exercises significant price (and profit) control but has continued to enjoy significant investment in pharmaceutical and biotechnology investment.[39] In the Office of Fair Trading report that first proposed value-based pricing, the authors concluded, "We find that there is very little evidence to link the price of pharmaceuticals in the UK with the overall attractiveness of the UK as a location for pharmaceutical R&D investment. This does not mean that overall pharmaceutical prices should be pushed down as low as possible."[40]

Explanations for this may relate to other causes, although creating valid comparisons requires controlling for a myriad of structural and co-existing policy differences across countries. For

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[32] Gagnon MA, Lexchin L. The Cost of Pushing Pills: A New Estimate of Pharmaceutical Promotion Expenditures in the United States. *PLoS Medicine* 2008;5(1):e1, doi:10.1371/journal.pmed.0050001

[33] Grootendorst P. *How Should We Support Pharmaceutical Innovation?* SEDAP Research Paper 246 (Hamilton: McMaster, 2009)

[34] MIDAS©, 2005-2011, IMS Health Incorporated: cited by Boudreau 4th Annual Market Access Summit November 21, 2012

35 Based on $USD 135bn for 2011 in OECD (2011), *Key Biotechnology Indicators*. OECD Publishing: cited in Strength & opportunity 2012: the landscape of the medical technology, medical biotechnology, industrial biotechnology and pharmaceutical sectors in the UK. Annual update - December 2012. London: HM Government; 2012

[36] Koenig P, MacGarvie M. Regulatory Policy and the Location of Bio-pharmaceutical Foreign Direct Investment in Europe. *Journal of Health Economics* 2011;30(5):950–65, doi:10.1016/j.jhealeco.2011.07.005

[37] *Strength & Opportunity 2012: The Landscape of the Medical Technology, Medical Biotechnology, Industrial Biotechnology and Pharmaceutical Sectors in the UK.* Annual Update - December 2012

[38] NERA Economic Consulting, *Key Factors in Attracting Internationally Mobile Investments by the Research-Based Pharmaceutical Industry* (London: NERA Economic Consulting, 2007)

[39] *Strength & Opportunity 2012: The Landscape of the Medical Technology, Medical Biotechnology, Industrial Biotechnology and Pharmaceutical Sectors in the UK.* Annual Update - December 2012

[40] Office of Fair Trading, *The Pharmaceutical Price Regulation Scheme* (London: Crown Business, 2007)

example, in Canada, shortly after the inception of Canada's PMPRB, Bill C-91 was passed and allowed for a number of policies to encourage regional investment. The act abolished compulsory licensing, extended patent protection length, prohibited stockpiling ingredients for generic manufacturing, allowed for strategies of evergreening (i.e., mechanisms to directly or indirectly extend monopoly privileges), and provided tax credits for R&D expenditure. Yet the impact of these policies on regional investment is questionable.[41] While some have suggested policies directed at price control may lead to differences in regional investment, others have suggested economic factors, such as access to low cost facilities, specialized resources, and access to markets play a more predominant role.[42] There is no clear consensus regarding how and whether 'economic' or 'strategic' factors play a more important role but several recent examples highlight the importance of economic factors in local investment decisions:

- The European Federation of Pharmaceutical Industries and Associations has reported rapid growth in investment in emerging economies such as Brazil, China and India, which has led to a migration of economic and research activities outside of Europe. They report that in 2011 "the Brazilian and Chinese markets grew by more than 20% (20.0% and 21.9% respectively) compared with an average market growth of 2.6% for the five major European markets and 3.6% for the US market".[43]
- In a more recent examination across Western European countries, the location of foreign non-manufacturing investments was found to be less concentrated in countries with explicit price controls than countries with reference pricing regimes or no price regulation.[44] Despite this, European countries from 2002 to 2009 who adopted more stringent price regulation measures saw "only weakly significant [negative] effects for R&D, and no effect for manufacturing investments".
- The province of Quebec saw considerable losses in pharmaceutical industry investment with reported declines in jobs from 10,422 to 7,549 (28%) in the pharmaceutical and medical manufacturing sector between 2007 and 2012 despite strategic policies intended to provide manufacturers the best available price and extended reimbursement eligibility for brand name pharmaceuticals (BAP-15).

Price discrimination, parallel imports and trade agreements

Other policy factors play an important role in pricing policy and may play an even-more-important role in a *value-based* pricing system. First, in order to increase their profitability, manufacturers must be given the ability to charge different prices (i.e., "price-discriminate") for the same product across different jurisdictions. Price discrimination allows producers to maximize their profits by selling at a price that reflects consumer purchasing power in each jurisdiction. If a consumer who is prepared to pay more for a product in a relatively-wealthy jurisdiction is allowed to purchase a product from a poorer jurisdiction at a lower price (called parallel importation), the producer forfeits profit. In a situation where products are sold freely across borders, producers would have to lower their price to

[41] Gagnon MA, Hébert G. *The Economic Case for Universal Pharmacare* (Ottawa: Canadian Centre for Policy Alternatives, 2010). Available: www.policyalternatives.ca/publications/reports/economic-case-universal-pharmacare
[42] Koenig and MacGarvie. *Regulatory Policy and the Location of Bio-pharmaceutical Foreign Direct Investment in Europe*
[43] European Federation of Pharmaceutical Industries and Associations. *The Pharmaceutical Industry in Figures* (Belgium: EFPIA, 2012).
[44] Koenig and MacGarvie. *Regulatory Policy and the Location of Bio-pharmaceutical Foreign Direct Investment in Europe*

compete with re-sold products, or they might refuse to sell, or make it difficult to obtain the product (or not develop the product to begin with). Policies that support price discrimination allow producers to receive the profit that would otherwise be lost if this were to happen.

To effectively price discriminate, manufacturers must be sufficiently protected from parallel imports. Parallel imports reduce the share of the producer's profits that are influenced by the price of the product. Parallel imports may ultimately lead to consumer losses as producers employ additional tactics (such as price increases where possible or delays in innovation from reduced R&D) to compensate for the losses that result from this additional competition.

Similarly external reference pricing may significantly affect prices and producer profits. Dubbed a "free-rider" problem, jurisdictions that externally reference prices in countries with less ability to pay (or less activity related to the pharmaceutical sector) may be detracting from the producer's profitability. Conversely, countries that externally reference prices in jurisdictions with more pharmaceutical sector-related economic activity (and, therefore, a greater ability to pay) may be insufficiently rewarding consumers, as higher prices result in lower consumer use.

More recently, trade agreements have become a factor in pricing policy. Trade agreements have traditionally been used as a tool to protect economic interests of foreign companies from unfair discrimination from price subsidies. However, pricing policy became a subject of provisions in the 2004 Australia-United States Free Trade Agreement (AUSFTA).[45] Although a senior negotiator for AUSFTA suggested that the agreement would not dismantle listing and pricing mechanisms of Australia's National drug insurance program (the Pharmaceutical Benefits Scheme), others suggested that the agreement led to significant political pressures to provide price premiums for product listing decisions that would have otherwise not occurred.[46] Nonetheless, trade agreements which have no formal boundaries for provisions may invite provisions **that have the opposite effect of parallel imports** – transferring consumer benefits to producer benefits through the enforcement of higher prices.

More recently, drug producer Eli Lilly has launched a case against the government of Canada citing trade agreements. In particular, the company has alleged a doctrine of Canada's patent laws is inconsistent with an article in the North American Free Trade Agreement (NAFTA) suggesting the doctrine unfairly affects patent validity and "is inconsistent with Canada's commitments under NAFTA". A notice of intent to challenge the patent law seeks $100 million in damages and may set a precedent for future decisions.[47] Although not a challenge to Canada's pricing policy, the effect that this may have on current and future patent terms will have an indirect effect on drug costs due to extended monopoly pricing.

4.2 Value-based Pricing

4.2.1 What is value-based pricing?

The term "value-based pricing" that is now widely used to describe pricing of medicines was first promoted in a report from the UK Office of Fair Trading (OFT) that examined then-current

[45] Faunce TA. Challenges for Australia's Bio/nanopharma Policies: Trade Deals, Public Goods and Reference Pricing in Sustainable Industrial Renewal. *Australia and New Zealand Health Policy* 2007;4(1). Article Number: 9.
[46] Ibid.
[47] "Eli Lilly CEO Warns Canadian Court Rulings Put Jobs at Risk. *The Globe and Mail.* Available: www.theglobeandmail.com/report-on-business/industry-news/the-law-page/eli-lilly-ceo-warns-canadian-court-rulings-put-jobs-at-risk/article8645925/ (accessed 12 April 2013)

practices of price and profit controls and options for improvement. Value, in this report, referred to therapeutic value. Three value-based pricing designs were identified in the report[48]:

1. **Therapeutic group reference pricing.** This can mean setting a flat reimbursement price for all drugs with a similar chemical action, including drugs with differing relative efficacy. Germany has such an approach in some drug classes.
2. **Therapeutic tendering.** Bids are invited to supply the public health service in a list of therapeutic areas. In each area one or two bids are accepted, according to an analysis of the efficacy, costs and logistics of each product. New Zealand is an example of a country that has experimented with therapeutic tendering.
3. **Cost effectiveness pricing.** This method, used in Australia and elsewhere, involves setting the maximum price of a product at a level that ensures it does not exceed a given ICER relative to a substitute (typically a cost per incremental [quality-adjusted life-year (QALY)]).

   (Source: OFT Annex L, p.28)

The report subsequently suggested a preference for the third option (cost-effectiveness pricing) as unlike option 1, it would be feasible to implement as it would not rely on consumers (or their physicians, acting as consumer agents) to understand all of the available choices and prices that could be paid. It would also avoid the potential exploitation of producers by single payers that could happen with option 2.

In many respects, option 3 - cost-effectiveness pricing, is what loosely occurs with public payers through Canada's Common Drug Review process. A new drug submitted to CDR may lead to a "Do not list at the submitted price" recommendation as it is perceived to be not cost-effective at a given price; producers then have an opportunity to resubmit at a lower, confidential price or accept the recommendation and negotiate price with the provinces individually. More recently, drug plan managers may also receive direction to list with the condition of a lower negotiated price.[49]

In making the recommendation, the UK OFT report alludes to the concept of "static efficiency," which is about good value for money in the short-term, i.e., health benefits at the current price. Static efficiency aligns with the goal of health payers and the policy objective of fiscal responsibility within the health system. Health systems that are statically efficient are maximizing the use of dollars within their budgets.

The report also alludes to a second type of efficiency, called "dynamic efficiency," which additionally concerns itself with good value for money in the long-term, and includes the benefits from R&D.[50] A dynamically efficient system will allow producers to obtain sufficient profits to generate longer term benefits, while also allowing for benefits to the consumers in the short term. The concern with any use of value in making price determinations is that if price is only based on short-run (static) health measures, long-run (dynamic) measures of social value realized from R&D efforts may be missed.

[48] Office of Fair Trading. *The Pharmaceutical Price Regulation Scheme*
[49] Available: www.cadth.ca/media/cdr/cdr-pdf/CDEC_Deliberative_Framework_e.pdf
[50] Philipson T,Jena A. *Surplus Appropriation from R&D and Health Care Technology Assessment Procedures* (National Bureau of Economic Research Cambridge, Mass., USA, 2006)

Box 3: Economic Efficiency

Economics concerns itself with the consumption and production of goods and services. *Health economics* may look at how consumers use the service of health care or the production of health or states of health as a "good" from this service.

Economic *efficiency* is more specifically concerned with how resources (anything that is used to produce goods and services) can be best used. For example, consider the different types of questions that a health system administrator may have regarding how best to spend money on the prevention or treatment of human infection with human immunodeficiency virus (HIV). Questions related to expenditure illustrate the various forms of efficiency that must be considered:

Type of Efficiency	Definition	Illustrative Question	Analysis Required
Technical efficiency	Producing the maximum output from the minimum number of inputs	Which is better, using 10mg of drug A twice daily or 10 mg five times daily?	Effectiveness analysis
Productive efficiency	Producing the maximum possible output at the minimum cost	Which is more cost-effective, drug regimen A or drug regimen B?	Cost-effectiveness analysis (economic evaluation)
Allocative efficiency	Producing the maximum possible output for a given budget	How much money should be allocated to early prevention versus treatment of HIV?	Program budgeting and marginal analysis

Static efficiency considers itself with these types of efficiency in the short term. For example, the administrator may decide that all of the budget be allocated to a treatment program versus a prevention program, as there will be much more benefit in terms of reduced suffering and death from HIV infection (using the most cost-effective treatments) than from the most cost-effective prevention programs, which will still produce much less benefit for the same investment. This is a question of allocative efficiency in the short-term.

Dynamic efficiency considers the effect of time on any of these types of efficiency. For example, the administrator may not have considered that the lack of prevention programs will lead to much greater infection rates and need for treatment in the future. He may also not have considered that the cost of treatment may fall considerably in the future, as monopoly producers lose their patent protection (balanced against paying them now for future innovation). Investing more in prevention currently may be the best overall use of resources if future costs and benefits are considered. He may also need to consider the delay in potential innovation if immediate investment in treatment is delayed.

Adapted from Palmer [51]

Like any examination of efficiency, health economics does not tell us what that the optimal balance between consumers and producers should be. It can only provide insight into what the effect of price will be on short and long-term costs and outcomes. Recommendations from the OFT commissioners are as follows:

[51] Palmer S, Torgerson DJ. Definitions of Efficiency. *BMJ* 1999;318(7191):1136

> *In our view, pricing according to cost effectiveness offers the best potential for the right balance to be struck between long and short run efficiency. It does so by setting the maximum price in relation to an assessment of the incremental value of the therapeutic benefits of the drug ... The key question in conducting relative assessments that optimally recognise the short- and long-term value of new medicines is what type of products to compare them to.*
>
> (OFT, p29)

Since the release of the report, the UK government responded, suggesting it would agree to the recommendations and that these should be discussed as part of a re-negotiation of the Pharmaceutical Price Regulation Scheme (PPRS) used to regulate prices. The UK Department of Health has committed to re-negotiation of PPRS by January 2014, which is anticipated to incorporate some aspects of value-based pricing.

The term value-based pricing is now being used to describe systems of price regulation based on health technology assessment – even by those that have not been previously referred to using that term. Health technology assessment is a policy tool that attempts to "capture value" through a thorough examination of available evidence to inform decision-making. For example, Sweden, Australia, and even Canada have all been recently identified as having value-based pricing systems. This is presumably because they use economic evaluation or therapeutic referencing to determine price. In some cases, value-based pricing is used in reference to reimbursement schemes; some have suggested the more appropriate term in these cases would be *value-based purchasing*.

The distinction between price-setting as an activity and price-setting within the context of reimbursement (generally, negotiation) is an important one; prices for reimbursement can consider multiple additional factors including co-payments for consumers, product bundling, current formulary status, and other local factors. Value-based pricing not linked to reimbursement must assume one price for all and must consider factors specific to individual payers in aggregate.

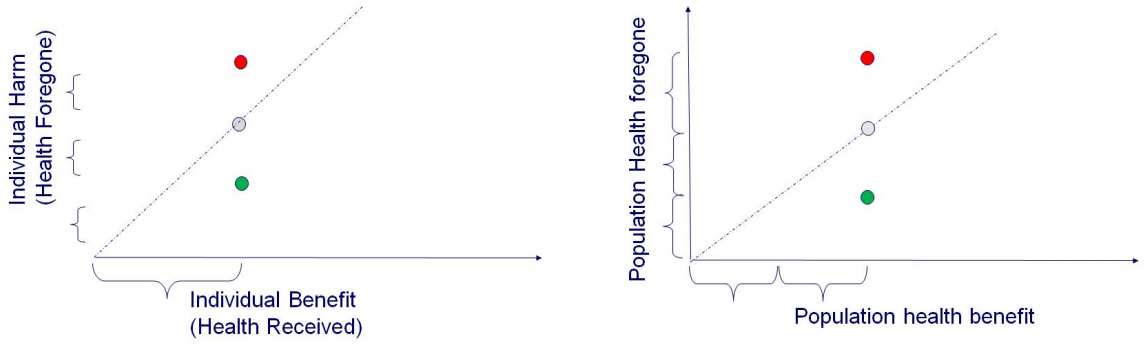
4.2.2 Whose values?

The value of individual clinical decisions generally relies on weighing some measure of benefit (such as avoiding a heart attack) against some measure of harm (like an adverse effect). When examining the value to a society, we must further consider the population health effects. When policy makers face a constrained budget, value is determined by considering how much overall health we are willing to give up (by using available resources) compared to how much health we have to gain. Any use of *new* resources can be considered an "opportunity cost" in order to recognize that the resources that are new to health must be coming from somewhere else. Opportunity cost can be expressed in terms of either health or dollars, as these are exchangeable. The concept of opportunity costs in population-based decisions is illustrated in Figure 2.

Value is technically defined as what consumers individually would be willing to pay or to give up for an additional good or service. In social terms, value is a population-based, rather than individual, which recognizes that we must consider both what is gained and what is lost – and not always by the same people. This perspective may be difficult to comprehend for *individual* consumers of technology or producers of technology. For a consumer, a new medicine might be perceived to provide individual rewards despite the fact that there might be high opportunity costs (experienced

by others) from its use. For a manufacturer, developing a new technology might be profitable despite a low (or negative) net benefit to society.[52]

Figure 2: The value of individual versus population decisions for health



Each circle represents a decision taken by an individual or an average of decisions based on a population. Decisions depicted by red circles have a negative net health benefit while those in green have a positive net health benefit. Grey circles depict no net health benefit. In individual decisions, potential benefit is weighed up against potential harm. In population-based decisions, benefit is a result of health outcomes from dedicating resources to a new intervention and harm is health foregone from using resources from somewhere else within the health system.

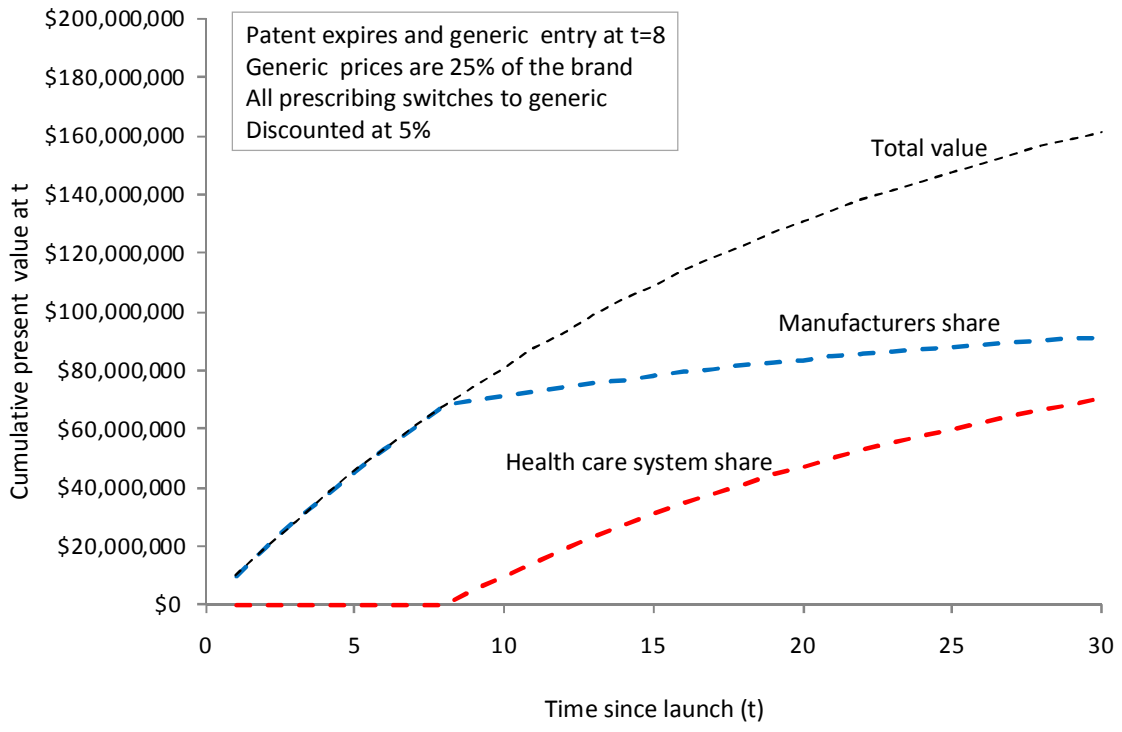
For a new medicine to be *statically* efficient, what is gained must be no less than what is given up in the short term, not taking into account R&D investment and its long term impacts. Dynamic efficiency further concerns itself with how much is given up currently in order to enhance the health of present *and future* generations. There is widespread debate about how much *should* be given up (i.e., how much to reward to manufacturers in terms of profits) to lead to long-term efficiency. The prices that are set by pricing policies will determine this balance implicitly. Some have suggested that using cost-effectiveness analysis to determine price will lead to profits that will be inadequate for optimal R&D investment – i.e., that producers should be allowed maximal profits.[53] Others have suggested that like other markets, consumers should retain some of the benefits.[54]

To illustrate the share of value between consumers and producers, Husereau adapted an analysis by Claxton for the Canadian context.[55] In this example, a new product that has no short term net benefit is adopted. The cumulative value of an innovation (discounted at a rate of 5%) is shown to be shared between the manufacturer and the Canadian health care system. During patent protection, the price is assumed to be the maximum the health system is willing to give up (that is, net health benefits are equal to zero) and all value is appropriated by the manufacturer.

[52] Drummond M, Tarricone R, Torbica A. Assessing the Added Value of Health Technologies: Reconciling Different Perspectives. *Value in Health* 2013;16(Suppl 1):S7–S13, doi:10.1016/j.jval.2012.10.007
[53] Danzon PM, Towse AK, Mestre-Ferrandiz J. *Value-based Differential Pricing: Efficient Prices for Drugs in a Global Context* (National Bureau of Economic Research, Inc, December 2012). Available: http://EconPapers.repec.org/RePEc:nbr:nberwo:18593
[54] Claxton K, Sculpher M, Carroll S. Value Based Pricing for Pharmaceuticals: Its Role, Specification and Prospects in a Newly Devolved NHS. *CHE Working Papers* (2011)
[55] Husereau and Cameron. *Value-Based Pricing of Pharmaceuticals in Canada: Opportunities to Expand the Role of Health Technology Asessment?*

At 8 years, the patent expires and competitive generics enter the market. After this time, manufacturers will appropriate 57% of the value after 30 years and retain 49% of the share under simplified scenario where the innovation is forever relevant (see Figure 3).

Figure 3: Share of value from health technology between the manufacturer and the Canadian healthcare system



Share of consumer and producer benefits (i.e., the social surplus). This example assumes that: i) competitive generic entry occurs, reducing prices to 25% of the brand; and either ii) all prescribing is switched to generics; or iii) any new patented drugs are priced relative to the generic version of the old. If the three assumptions do not hold and none can be taken for granted, then the manufacturers share would be higher.

4.2.3 Elements of value

Until now, we have presented value as a single measure of health. Universal units of health that allow comparability across health programs have been developed, and include metrics of mortality (e.g., life-years) or mortality adjusted for measures of preferences for health (e.g., quality-adjusted life years, disability adjusted life-years, healthy year equivalents).

It is increasingly recognized that potential benefits may go beyond the health system. Investment in new medicines (and removing resources from other health programs) may lead to measurable changes in measures of justice (adequacy and equity in access); income protection; freedom of choice for consumers; and appropriate autonomy for providers. A recent synthesis of elements of value is shown in Box 4.

Box 4: Examples of Elements of Value

Health outcomes (population and individual health outcomes)
- Increased effectiveness
- Increased safety

Other patient, caregiver and/or population health benefits
- Reduction of uncertainty (e.g., following diagnosis)
- Reduced caregiver burden
- Unmet needs
- More treatment choice
- Improved access to services
- Greater equity

Health system benefits
- Decreased net costs of delivery per patient
- Lower budget impact
- Fewer sunk and other costs (operating costs)
- Greater economies of scale or scope
- Greater ease of incorporating technology into current system (and ease of future disinvestment)
- Improved administration/delivery/supply chain

Benefits beyond health system
- Costs to other areas of government (e.g., education, justice system)
- Political acceptability
- Social impact (e.g., environmentally friendly)

(Adapted from HTAi 2013 Policy Forum Document, Table 1, pg 7)

4.2.4 Implementing value-based pricing

Whatever the chosen measure(s) of value, the same principles of shared value (between consumers and producers) and opportunity cost will need to be considered in determination of price. For each new market entrant, opportunity costs still represent the marginal value of forfeited resources for the new investment. Although more than one value measure may be desirable, some (e.g., equity in access AND health) will require more sophisticated approaches to assessment and may be more difficult to implement in practice. In Canada, where per capita spending on health care varies across provinces and different structures exist to deliver care, deciding on a single metric of value may prove difficult.

Sussex and colleagues have suggested that any value-based pricing approach will require considerations of: 1) What units of value should be employed (as per above); 2) How to measure and value these elements; 3) How to combine these element into a single common measure; 4) How to link comparisons of value measures and costs to price.[56] In the UK, measures of value currently being considered include disease severity, unmet need and other measures of innovativeness, and impacts beyond the health system.

[56] Sussex J, Towse A, Devlin N. Operationalizing Value-based Pricing of Medicines: a Taxonomy of Approaches. *Pharmacoeconomics* 2013;31(1):1–10

There is also some debate as to whether decisions about price should assume a fixed or flexible health budget.[57] With a fixed health budget, opportunity costs are thought of in terms of consequences of re-allocating resources within a health system whose available resources have already been determined (through a legitimate political process). With a flexible health budget, the consequences of allocating additional resources to the health system away from another sector such as education must be considered. As with using multiple measures of value, measures of value that consider opportunity costs across all governmental sectors become more difficult to assess in practice due to the increased need for information. Regardless of the value measure adopted, consistent approaches to technology assessment and economic evaluation will be required to assess the value of new patented medicines.

There are additional issues of concern for implementing a value-based pricing system. Because price cannot be considered separately from volume, value-based prices must be assigned to products intended for specific patient populations for which there may not be good measures. Although public drug insurance plans may have some ability to limit use according to the patient's indication, this will be more challenging when applied to private and uninsured consumers. This means that a value-based price is prone to error from information about sales. This error in price based on poor information about patient populations may unfairly reward consumers while penalizing producers (or the opposite). Since physicians prescribing medicines do not currently document indications for use (and are usually given clinical autonomy to do so), implementing a system of pricing that relies on patient characteristics might prove infeasible.

Value-based pricing also poses other challenges. In its simplest manifestation, (a fixed health budget and a single unit of health representing value), the threshold beyond which decisions impose a negative net health benefit to the system (i.e., cost-effectiveness threshold) must be established. In Canada, as with most other international jurisdictions, the opportunity costs of making decisions about new medicines have not been measured. An attempt to measure opportunity costs from actual resource allocation decisions in the UK has recently been completed, through a detailed examination of investment and disinvestment decisions taken by local UK commissioners and providers. A 'best' threshold was estimated to be £18,317 per QALY.[58] Of course, a threshold can be "assumed," though it may not be consistent with the "true" opportunity cost of actual decisions.

Other challenges that may also be applicable to Canada are outlined in papers by Claxton[59], Persson[60], Kanavos[61], and Hughes[62]. These include: non-linear pricing of drugs, the effect on international reference pricing, the need for *ex post* assessments and consideration of price changes of medicines, the need for rules for subsequent price negotiation between reimbursement bodies and producers, opportunities for gaming through artificial product differentiation, how comparators are chosen, and whether innovation itself should be a value metric. It should be emphasized that

[57] Danzon, Towse, Mestre-Ferrandiz. *Value-based Differential Pricing: Efficient Prices for Drugs in a Global Context*
[58] Claxton K, et al. Methods for the Estimation of the NICE Cost Effectiveness Threshold (2012). Available: *www.york.ac.uk/media/che/documents/reports/Methods%20for%20the%20Estimation%20of%20the%20NICE%20Cost%20Effectiveness%20Threshold%20(Draft%20Final%20Report)%20(1).pdf*
[59] Claxton, Sculpher, Carroll. *Value Based Pricing for Pharmaceuticals: Its Role, Specification and Prospects in a Newly Devolved NHS.*
[60] Persson U, Svensson J, PetterssonB. A New Reimbursement System for Innovative Pharmaceuticals Combining Value-Based and Free Market Pricing. *Applied Health Economics and Health Policy* 2012;10(4):217–25
[61] Kanavos P, et al. *Short- and Long-Term Effects of Value-Based Pricing Vs. External Price Referencing.* (London: European Commission, Directorate-General Enterprise, 2011)
[62] Hughes DA. Value-based Pricing: Incentive for Innovation or Zero Net Benefit?. *Pharmacoeconomics* 2011;29(9):731–35

value-based pricing is not necessarily an instrument of cost control – its effect on expenditures (prices and volume) will solely depend on the degree to which what is produced is perceived as valuable.

4.2.5 Value-based pricing in universal vs. self-pay environments

As previously mentioned, the presence of an insurance scheme must be also be considered when discussing price, as the out-of-pocket price-lowering effect for individual patients will lead to increased (and perhaps excessive) prescription volumes. Uninsured patients lack the financial protection of insurance but are also less likely to consume medicines. Creating different value-based prices for insured and uninsured consumers may prove difficult to implement.[63]

4.3 Conclusions

The value of something must ultimately be defined by what we are willing to give up in order acquire it. The goals of all health systems are to provide health through adequacy and equity in access; and choice for consumers and their physician agents so that they may achieve their health goals now and in the future. The goals of all producers are to profit from new medicines, so that they meet immediate and long-term business goals.

In many markets, prices are ultimately determined through competitive interactions between consumers and producers. The unique nature of pharmaceutical markets means prices cannot be easily determined this way. If a price is determined through regulation rather than market forces, it defines the balance of short- and long-term benefits for consumers and producers.

Unlike external reference pricing, value-based prices are intended to find a best balance between consumer and producer goals. Even a new medicine with proven individual benefits with a price fairly reflecting other markets can lead to profound societal losses (in terms of health and dollars) for Canadians. If prices are too low, however, the loss of profit to producers will lead to reduced global R&D investment and may ultimately reduce immediate (through refusal to sell) or future (through reduced R&D investment) benefits from innovation.

Value-based pricing is *not* a cost-containment measure or mechanism to lower prices that are unaffordable; under value-based pricing, costs paid for pharmaceuticals will ultimately reflect benefits to society. Value-based pricing *is* a means of fostering global innovation by signaling from consumers to producers what innovations are required but it *is not* a means of stimulating Canadian R&D or non-R&D investment by the pharmaceutical sector.

Value-based pricing may also be a means of supporting more efficient health care spending but will depend on how value is defined, and what other behaviours consumers and producers are allowed to engage in. The next section of this report will explore this further along with a review of international developments in moving toward value-based pricing models. It will endeavour to outline lessons that could be learned for implementing value-based pricing for patented medicines in Canada.

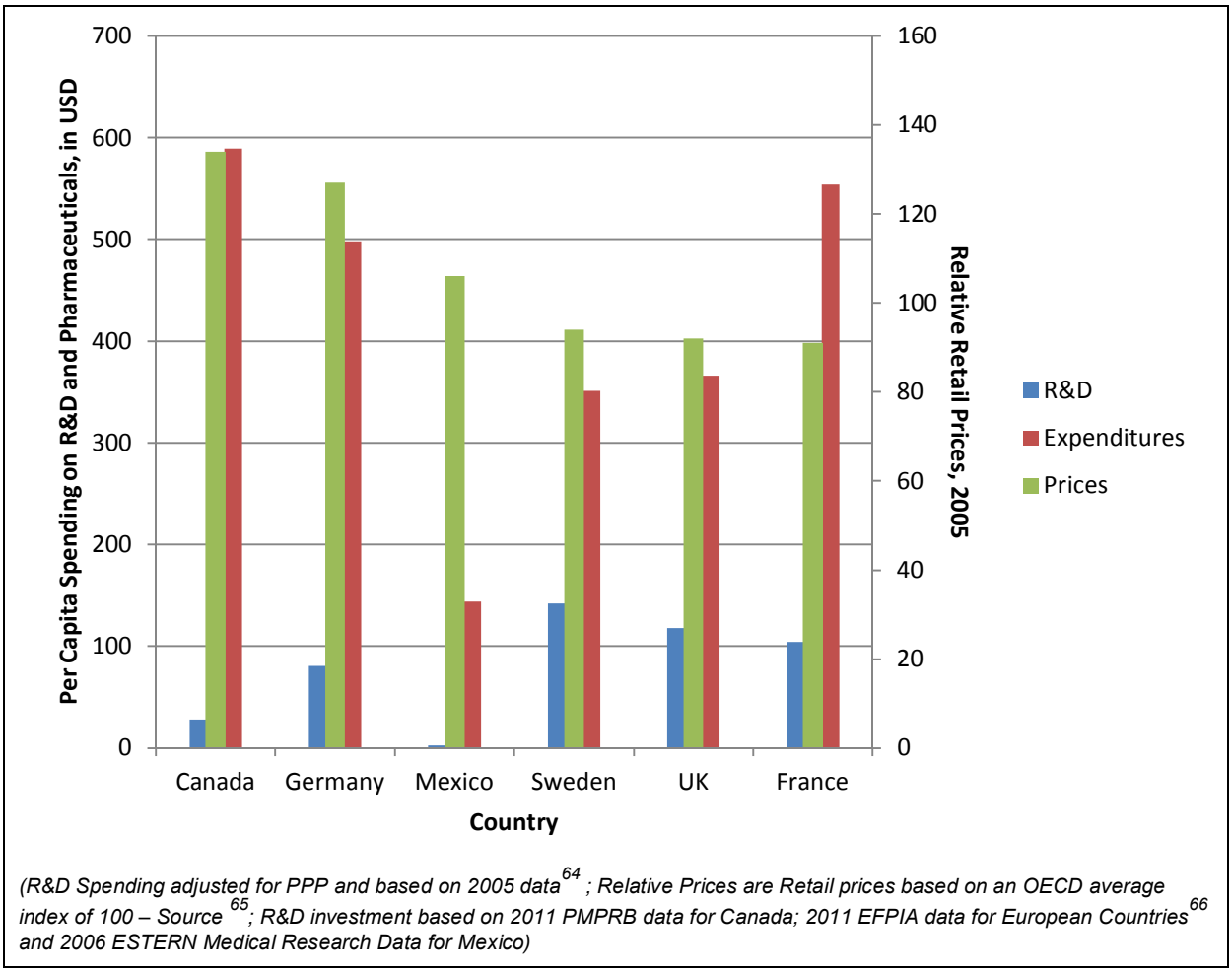
[63] Danzon, Towse, and Mestre-Ferrandiz. *Value-based Differential Pricing: Efficient Prices for Drugs in a Global Context*

5 INTERNATIONAL PERSPECTIVES

5.1 Current Trends

A sample of countries that have used or are considering value-based pricing approaches that may have lessons for Canada are described in this section. Current differences between the prices paid for pharmaceuticals, per capita spending on pharmaceuticals, and per capita R&D investment by the pharmaceutical industry are shown in Figure 4. The (lack of a positive) relationship between local R&D, prices and expenditures (sales) can be seen from the figure. Despite having pricing policies that lead to the highest relative prices and consumption that leads to the highest sales across six countries, Canada has the lowest regional R&D investment next to Mexico.

Figure 4: Relative price, per capita spending and per capita R&D investment across Canada, Mexico, Germany, Sweden, UK and France



(R&D Spending adjusted for PPP and based on 2005 data[64] ; Relative Prices are Retail prices based on an OECD average index of 100 – Source [65]; R&D investment based on 2011 PMPRB data for Canada; 2011 EFPIA data for European Countries[66] and 2006 ESTERN Medical Research Data for Mexico)

[64] Organisation for Economic Co-operation and Development, *Pharmaceutical Pricing Policies in a Global Market*
[65] Ibid
[66] European Federation of Pharmaceutical Industries and Associations, *The Pharmaceutical Industry in Figures*

Varied approaches to both drug pricing across these countries is shown in Table 2 below. Key features of price regulation include whether prices are evaluated before or after launch (called *ex ante* and *ex post* assessment) and whether there is a reliance on therapeutic reference pricing, international reference pricing, or price negotiation through reimbursement, called product listing agreements.

Table 2: Price regulation mechanisms across selected OECD countries

	Ex Ante				Ex Post			
	Free pricing	TRP	IRP	PLAs	Price cuts	Profit Controls	TRP	IRP
Canada		✓	✓	✓			✓	✓
Germany		✓		✓			✓	
Mexico	✓	✓	✓	✓			✓	✓
Sweden		✓		✓			✓	
UK	✓			✓	✓	✓		
France	✓	✓	✓	✓			✓	

TRP=Therapeutic reference pricing; IRP=International reference pricing; PLAs=Product Listing Agreements

5.2 Overview of specific countries

5.2.1 UK

The UK has used a combination of price and profit control, called the Pharmaceutical Price Regulation Scheme (PPRS), which is set to expire at the end of 2013. In response to the original OFT document, a series of more flexible pricing options within the PPRS scheme were introduced in 2009. In 2010, the UK Department of Health released an outline of the newly proposed value-based pricing system for public consultation. At the basis of the proposal was a price structure based on evaluations of cost-effectiveness for new drugs and a basic UK threshold, "reflecting the benefits displaced elsewhere in the NHS when funds are allocated to new medicines".[67] Thresholds would then be adjusted where a medicine was marketed for "diseases with unmet need or which are particularly severe", "medicines that can demonstrate greater therapeutic innovation and improvements compared with other products"; and "medicines that can demonstrate wider societal benefits."[68]

A wide majority of responses to the consultation indicated support for the principles of value-based pricing. In a response to the consultation, the government noted:

[67] Department of Health, Medicines, Pharmacy & Industry Group16, *A New Value-based Approach to the Pricing of Branded Medicines: a Consultation* (London: Department of Health, UK, 2010)
[68] Ibid

> *There are questions about the impact of medicines' prices on companies' decisions on where to locate investments or conduct research. As highlighted in the 2007 NERA study Key Factors in Attracting Internationally Mobile Investments by the Research-Based Pharmaceutical Industry[69], this is a global market, and companies locate where they can find the best science base at reasonable cost, taking into account other factors such as tax, flexible labour markets and economic stability.*
>
> (Source, Government Response, p13[70])

In response, the government initiated other R&D-focused initiatives to strengthen local investment, including "actions to improve the UK's competitiveness as a location for clinical trials by reducing the regulatory burden; actions to encourage collaboration and innovation in the life sciences sector". Other initiatives to promote innovation with the life sciences sector included the creation of Academic Health Science Networks, the establishment of specialized commissions and networks with industry and innovation Challenge Prizes that attempt to provide direct rewards for innovation.

As the threshold would serve as a basis for making pricing decisions, a large study was commissioned to accurately measure it, and to set up a system for ongoing monitoring.[71] Additional ongoing research is attempting to examine how to capture and aggregate wider benefits, how to account for therapeutic improvements, and how the threshold should relate to price. Although currently in negotiation between the government and industry, it is widely anticipated that some value-based pricing linked to reimbursement will serve the basis of price regulation starting in January 2014.

UK - Lessons for Canada

- **Measuring an Opportunity Cost Threshold -** The UK experience to date highlights the need for a grounded approach to value-based pricing and purchasing. Unlike Canada, the UK has the benefit of basing prices on performance within a single health system. It is able to accurately estimate a threshold for opportunity costs and budget and population impacts. Like Canada, concerns have been raised about the difficulty of measuring sales from one or more indications, which is critical for making assertions about a value-based price.
- **Using a Principled Approach -** The UK is also carefully considering additional issues related to implementation, including what medicines should be subject to a value-based price (e.g., all new entrants after implementation or all medicines). In a joint statement issued by the Department of Health and the Association of the British Pharmaceutical Industry (ABPI), the parties declared that value-based pricing would be "introduced in a planned and progressive way. It will focus primarily on new medicines (new active substances) placed on the market from January 2014. There is the possibility that a small number of existing medicines might also be assessed and – potential candidates might include some of those which are currently being funded through the Cancer Drugs Fund." [72] The statement also suggested that manufacturers would be free to price their products at launch.

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[69] NERA Economic Consulting, *Key Factors in Attracting Internationally Mobile Investments by the Research-Based Pharmaceutical Industry*. Cited by Medicines, Pharmacy & Industry Group. Government response to consultation. London: UK DoH; 2011

[70] Medicines, Pharmacy & Industry Group. *Government Response to Consultation* (London: UK DoH, 2011).

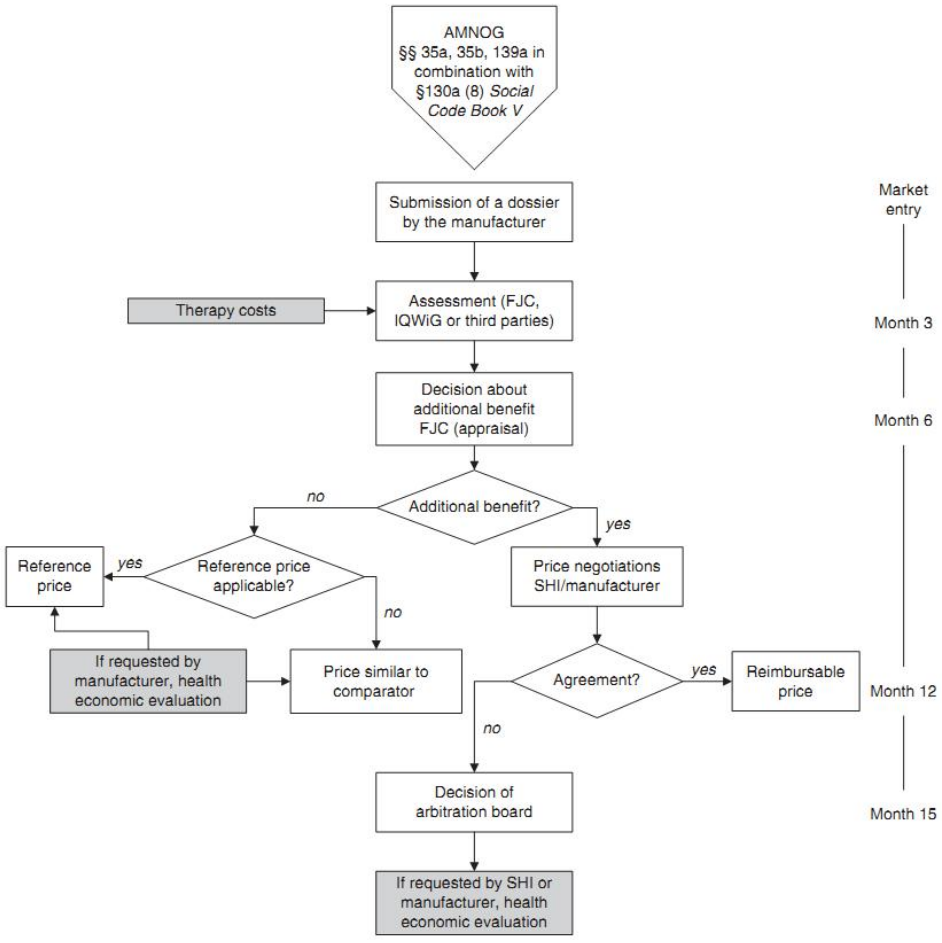
[71] Claxton et al. Methods for the Estimation of the NICE Cost Effectiveness Threshold.

[72] Department of Health. ABPI and DH Publish Statement on Arrangements for Pricing Branded Medicines from 2014. Article available at: www.dh.gov.uk/health/2012/08/abpi-dh-statement/ (accessed 1 March 2013)

5.2.2 Germany

In Germany, where pre-reimbursement price controls did not previously exist, concerns about unsustainable pharmaceutical expenditures led to the formal adoption of economic evaluation methods to inform negotiations for prices of new or relevant drugs within the Statutory Health Insurance System.[73] Despite these efforts, legislation was passed to freeze current prices of patented medicines and reorganized insured prices in 2010. Subsequently, the "Act to Reorganize the Pharmaceuticals' Market in the Statutory Health Insurance System" (Gesetz zur Neuordnung des Arzneimittelmarktes in der gesetzlichen Kranken-versicherung [AMNOG]) came into effect January 2011 (Figure 5) The new legislation outlines a system that combines rapid, therapeutic benefit assessment with therapeutic reference pricing and negotiation.[74]

Figure 5: Process for Price Negotiation in the Era of AMNOG



[73] Gerber A, Stock S, Dintsios CM. Reflections on the Changing Face of German Pharmaceutical Policy: How Far Is Germany from Value-based Pricing? *Pharmacoeconomics* 2011;29(7): 549–53; Gissel C. Pharmaceutical Pricing Based on Early Benefit Assessments. *Value in Health.* Conference: 17th Annual International Meeting of the International Society for Pharmacoeconomics and Outcomes Research, ISPOR 2012 Washington, DC United States (2012); Gandjour A. Germany's Decision Rule for Setting Ceiling Prices of Drugs: a Comparative Analysis with Other Decision Rules. *Applied Health Economics & Health Policy* 2011;9(2):65–71

[74] Gerber, Stock, Dintsios. Reflections on the Changing Face of German Pharmaceutical Policy: How Far Is Germany from Value-based Pricing?"

Germany - Lessons for Canada

- **Transparently Negotiated Prices Linked to Reimbursement-** The German value-based approach to price setting works within a larger drug insurance system framework. It is similar to Canada only in that responsibility for health care is decentralized - the system requires one body to negotiate prices on behalf of all of the approximately 300 SHI sickness funds. Unlike Canada's current system of province-by-province negotiation, prices, even in the form of rebates become part of a public record. The system requires that negotiated prices are binding for all SHI funds and private health funds; individual funds, which constitute a minority, are allowed to create separate arrangements.
- **Incorporating Considerations of Equity-** The German approach could be called value-based, although it has adopted a disease-specific approach – additional costs and benefits of any new medicine are compared to other drugs used to treat similar patients (e.g., patients with colon cancer) that reduce the emphasis from efficiency to equity. From a pure economic efficiency standpoint, this approach only makes sense if the resources available to that program are not available to other health programs. This means nurses, operating room time, molecular and genetic diagnostic services, etc. must be resources only available to delivering cancer care and those same operating rooms, nurses, etc. cannot be deployed for other purposes (e.g., operating room time for vascular surgery, nurses for intensive care). Similarly, the budget for cancer must be the budget for cancer and not available to other health programs.

5.2.3 Sweden

Until 2002 Sweden used a therapeutic reference pricing system linked to its public drug insurance reimbursement system for determining the price of new drugs. In 2002, this system was replaced by a system which considered economic evidence and an explicit payer threshold. The process, which is linked to reimbursement, is called the Dental and Pharmaceutical Benefits Board (Tandvårds- och läkemedelsförmånsverket), or TLV. The TLV sets both the pharmacy purchase price level and the pharmacy margin for reimbursed drugs and has no responsibility for the drug budget, which is decentralized to regional (city-based) councils. There are no restrictions on prices for non-reimbursed drugs and, like Canada, the price paid for medicines in hospitals can be negotiated.

Like the German system, decisions about price are governed by legislation, but unlike the German system, these prices cannot be further negotiated at a regional level. Other demand-side policy measures (e.g., formularies, guidelines) can be used to control costs through affecting quantities of drug consumed. Like Germany, Sweden uses a disease-specific approach to assessments of value.

Sweden, like Canada, employs a transfer payment system to equalize wealth across have and have-not regions and like Canada, sees differences in uptake in health care priority programs across regions not explained by regional need. For example, Persson describes an almost two-fold difference in the use of (presumably cost-effective) tissue necrosis factor inhibitors for rheumatoid arthritis across two regions with similar disease prevalence.[75]

[75] Persson, Svensson, Pettersson. *A New Reimbursement System for Innovative Pharmaceuticals Combining Value-Based and Free Market Pricing*

Sweden - Lessons for Canada

- **Pricing in a De-Centralized Environment is Possible -** Sweden's system of transfer payments and decentralized decision-making provides some insight for value-based pricing in Canada. A recent industry proposal co-authored by Persson suggests that a Federal desire for research and development investment linked to a regional desire for fiscal constraint should inform the payment scheme[76] – the producer surplus for innovation could be financed from federal coffers and through the transfer payment system. However, unlike Canada, drug insurance is a compulsory measure of the federal contribution. This proposal reflects similar proposals that suggest co-payments could be linked to therapeutic benefit.
- **Implementing Real-World Re-Assessment -** Sweden has also created a system of ex-post monitoring of therapeutic value, although it is not widely implemented.[77] Ongoing monitoring through pharmacovigilance is an important component of any value-based pricing system, and the challenges faced with this approach highlight important lessons for Canada.

5.2.4 France

In France, considerable attempts have been made in the last few years to strengthen approaches to economic evaluation of new drugs. This includes an additional onus on manufacturers to demonstrate evidence of cost-effectiveness compared to existing alternatives.

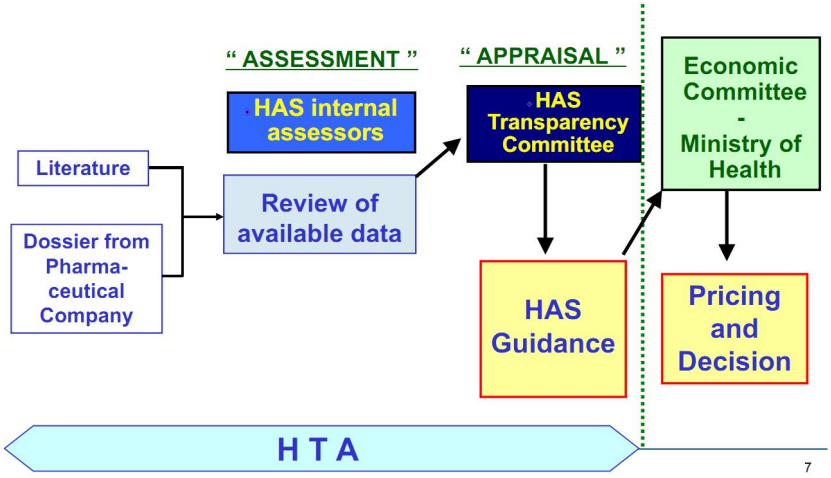
Pricing for drugs reimbursed through public drug insurance are determined by examining the relative benefit of a drug compared to alternatives. Six measures of therapeutic benefit are used to determine price: 1) innovative product of significant therapeutic benefit; 2) product of therapeutic benefit, in terms of efficacy and/or reduction in side effect profile; 3) already existing product, where equivalent pharmaceuticals exist; moderate improvement in terms of efficacy and/or reduction in side effect profile; 4) minor improvement in terms of efficacy and/or utility; 5) no improvement but still granted recommendations to be listed; 6) negative opinion regarding inclusion on the reimbursement list. Guidance on additional benefit also informs how to deal with uncertainty about clinical performance (e.g., product listing agreements).

An external price referencing mechanism is used for proposing prices of innovative drugs by manufacturers. The price is then negotiated between the manufacturer and government and becomes public knowledge and is used to determine prices sold to consumers through compulsory universal insurance. Prices are subject to re-evaluation. There are no regulations regarding price for non-reimbursable drugs.

[76] Ibid

[77] Persson U, Levin LA, Pettersson B. Important to Keep the Principle of Value-based Pricing of Drugs. *Lakartidningen* 2009;106(44):2862–64

Figure 6: Process for price negotiation in France



ASMR: Amélioration du Service Médical Rendu / Improvement of the Medical Benefit; LDMI : Liste des Dispositifs Medicaux Implantables (Source Harrousseau, HTAi 2011, Brazil)

France – Lessons for Canada

- **Distinguishing between a "Me-Too" and an Unknowns -** Not unlike Canada, France has expanded and refined its categorical approach to assessing therapeutic benefit. However, France has also adopted a more flexible system for using therapeutic comparators and has strengthened the application of cost-effectiveness analysis. In Canada's current system, a drug that lacks significant information to determine whether it will have incremental benefit in the real world (e.g., due to surrogate endpoints or narrow populations studied) will be in the same therapeutic category as a drug with an overabundance of good information firmly demonstrating it is similar to other drugs in its class. This provides a producer with an incentive for increased uncertainty from incomplete or reduced research information.[78] In France, an additional category of a "negative" opinion (albeit linked to reimbursement) provides a disincentive for drugs where the incremental value is uncertain. France also uses negotiation rather than a strict formula for setting drug prices. Negotiation allows a more informal approach to considering regional investment and other economic factors. Expanded therapeutic categories coupled with the use of economic evaluation and negotiation allow a much more nuanced approach to pricing pharmaceuticals that provide little or no benefit.
- **Implementing Real-World Re-Assessment -** France has placed much emphasis on *ex post* assessment granting term limited reimbursement and promoting drug class re-evaluation and pharmacovigilance efforts. Beyond safety signals observed at market access, considerations of uncertainty during pricing and reimbursement decisions become a primary factor in considerations about what drugs to re-assess.

[78] This missing information has a societal cost which could be borne by consumers as will be explained in the Section 6.2.1 Value of Information

5.2.5 Mexico

Although Mexico spends relatively little per capita on pharmaceuticals compared to other OECD countries, it has adopted similar policies to Canada in response to the management of pharmaceutical expenditures. First, Mexico, like Canada, relies on a relatively high proportion of private/out-of-pocket financing of pharmaceutical expenditures compared to other OECD countries. This means Mexico, like Canada, must either allow free pricing prior to reimbursement or find separate mechanisms to regulate the price of medicines. Mexico has also seen similar or greater increases on public expenditure on pharmaceuticals, mostly due to an effort to increase access to medicines through expansion of the existing subsidized public insurance system.[79]

Until 2007, all public institutions and insurance plans in Mexico negotiated prices individually with producers. Pricing of patented medicines loosely resembled Canada's system of pricing by therapeutic category and then relying on reference prices. Although unlike Canada's system of pricing, participation by pharmaceutical companies was voluntary.[80]

In February 2007, based on studies revealing a fragmented system of price negotiation and previous data indicating a preponderance of excessive retail prices, a new agreement between federal and provincial governments, industry, wholesalers, pharmacies, and the medical profession was signed.[81] Out of this commitment, labeled the *Compromiso para garantizar la suficiencia, disponibilidad y precio justo de medicamentos* (Commitment to guarantee supply, access and fair price of medicines), a new commission responsible for negotiating a public price on behalf of all institutions was created, the *Coordinating Commission for Negotiating Prices of Medicines and Other Health Interventions* (Comisión Coordinadora para la Negociación de Precios de Medicamentos y Otros Insumos para la Salud, CCNPMIS).[82]

In addition to annual negotiation of public procurement prices for patented medicines, the CCPNM has also been tasked with 1) preparing technical information necessary to conduct negotiations, including economic evaluation information, prices of patented medicines; and 2) implement appropriate negotiation strategies to improve the public procurement of patented medicines. Since its inception, the CCPNM has led to significant reductions in costs paid for patented medicines, which are a considerable driver of expenditure growth.[83]

Mexico – Lessons for Canada

- **The Need for Negotiation -** Mexico has gone away from a system of therapeutic categorization and reference pricing toward a coordinated system of public negotiation for prices based on economic evaluation. Like Canada, Mexico is a federation of regional governments with multiple public and private insurance systems along with uninsured consumers. Unlike Canada, Mexico has a federally funded public insurance program that formed the impetus for coordination across institutions. Nonetheless, Mexico has demonstrated that a "suggested" value-based price can be determined through coordinated processes prior to reimbursement.

[79] Moïse and Docteur. *Pharmaceutical Pricing and Reimbursement Policies in Mexico*
[80] Ibid
[81] Gómez-Dantés O., et al. A New Entity for the Negotiation of Public Procurement Prices for Patented Medicines in Mexico. *Bulletin of the World Health Organization* 2012;90(10):788–92, doi:10.2471/BLT.12.106633.
[82] Ibid
[83] Ibid

- **Cost-Savings are Possible -** Price regulation based on value and coordinated negotiation appears to have met policy objectives of improving access while containing expenditures. Mexico has managed to coordinate price regulation across federal-provincial boundaries with accompanying rules around price negotiation across institutions. However, Mexico has a lower R&D intensity than Canada and many OECD countries. R&D as a percentage of GDP in 2005 was 0.32% (OECD average of 2.26%).[84].

5.3 Summary of International Systems and Lessons for Canada

A summary of the various features relevant to value-based pricing from international jurisdictions is presented in Table 3. All use an assessment of benefits and costs as a basis for price negotiation. Despite some jurisdictions having decentralized purchasing authority, all countries have linked price-setting mechanisms to reimbursement directly or created a memorandum of understanding regarding prices (as in Mexico). Only Mexico exclusively concerns itself with patented medicines.

Table 3: Characteristics of value-based pricing schemes internationally

	Patented Medicines Only	Link to Reimbursement	Centralized Pricing	Use of Economic Evaluation	Opportunity Cost Threshold	Mechanism For Negotiation	After Launch Monitoring
Germany		✓		✓	✓	✓	
Mexico	✓	✓		✓		✓	
Sweden		✓	✓	✓	✓	✓	✓
UK*		✓	✓	✓	✓	✓	✓
France		✓	✓	✓		✓	✓

* proposed

5.4 Conclusions

An examination of different health systems reveals the importance of the connection between value-based pricing and value-based purchasing. Value-based pricing has been successfully adopted in systems similar to the Canadian system with decentralized purchasing authority. However, pricing rules in these systems requires extensive coordination, incentives, and in many cases legislation of rules around negotiation and purchasing after price determinations are made.

All systems highlight the need for a principled approach which involves a consistent approach to economic evaluation to inform a deliberative process of negotiation. A measure of opportunity cost has been defined to inform assessments of value in each instance, in most cases based on therapeutic benefit. Deliberation and negotiation involving purchasers allows additional context-specific factors to be considered in price determination.

The importance of revisiting prices and monitoring value after launch (ex post) by monitoring utilization, health outcomes, and associated costs is a consistent theme. It is clear that the approaches to price regulation are continuing to evolve and there are no universal solutions.

[84] Moïse and Docteur. *Pharmaceutical Pricing and Reimbursement Policies in Mexico*

In the next section, we will visit important components of value-based pricing highlighted here (approach to economic evaluation, measure of opportunity costs, ex post assessment) and how they are currently realized in the Canadian policy environment.

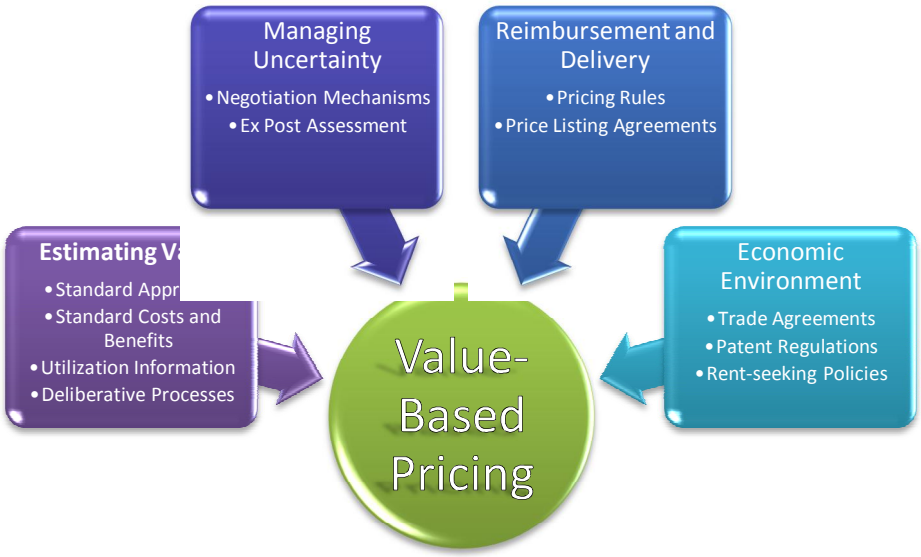
6 ANALYSIS OF MECHANISMS NEEDED FOR VALUE-BASED PRICING

As previously discussed, the value of new medicines can be characterized by analyzing the effects of adoption of new interventions using one or more important elements/measures of value. The opportunity cost of adoption is the total value of benefits foregone or displaced by shifting resources to acquiring the new medicine. The approach to examining value differs across countries but all attempt to use a consistent approach that is tied to negotiation. In most countries, value-based pricing can be tied to mechanisms of reimbursement.

The anatomy of value-based pricing and the various mechanisms required to make it effective have been revealed in the previous sections. This includes a principled approach to estimating the value of new medicines that uses clearly-defined measures of benefit and costs and relates this to a clearly-defined estimate of opportunity cost. Estimation of value may involve metrics beyond health outcomes (e.g., such as equity or the value of a new medicine with no therapeutic benefit) and capturing these are better served by transparent and deliberative processes. Health systems must also consider how to deal with the uncertain value of new medicines; uncertainty, which has an economic cost, can be managed by price negotiation and re-assessment after launch. Finally, as highlighted in previous sections, implementing value-based pricing must also consider factors important in any price regulation scheme, including the structure of health delivery and reimbursement and other relevant factors outside of health, such as patent law and the impact of trade agreements. This is depicted in Figure 7 below.

The next sections will discuss current approaches to these mechanisms in Canada and examine how these approaches might need to change to support value-based pricing.

Figure 7: Mechanisms needed for value-based pricing



6.1. Current Approaches to Estimating Value of New Medicines

6.1.1 Assessment of benefits

Although frameworks for the value assessment of drugs between reimbursement authorities and the PMPRB appear to be very different, they both rely heavily on an initial assessment of therapeutic benefit to inform discussion. Therapeutic benefits are determined by a thorough assessment of literature, clinical and epidemiologic judgment, and expert deliberation. It appears "Canadian" value assessment relies heavily on clinical metrics of relative benefit, similar to France and Germany.

Current guidance for evaluating the economic impact of adopting new medicines is produced by the Canadian Agency for Drugs and Technologies in Health[85]. Generally consistent with Treasury Board Guidance for assessing the health impact of new federal regulatory proposals, CADTH guidelines suggest costs be compared against non-monetized health benefits.[86] This is also generally consistent with international approaches, as there are significant challenges with arriving at market values for human health and welfare, and there are social and ethical implications of making decisions based on these values. It is even further complicated when the value of potential benefits may accrue to small and identifiable populations of individuals.[87]

The CADTH guidelines further suggest a standard approach whereby new medicines are valued according to outcomes that are the most relevant to patients. Where improvements to health-related quality of life is expected, the guidelines suggest comparing costs to a single measure of effectiveness that incorporates health-related quality of life, preferably (but not necessarily) a quality adjusted life year (QALY).[88] A QALY compared to its associated incremental cost (called an incremental cost-effectiveness ratio, or ICER) then allows for comparisons "across different conditions and interventions" within the health system.

Guidance for new drug submissions to CDR similarly recommends that a primary analysis be *either* an examination of cost per life-year gained or cost per QALY gained. The use of other outcomes is allowable only if they do not rely on patient perception (e.g., they should be objective measures, such as a laboratory measure) and cannot be easily extrapolated to life-years or QALYs.

For example, a new active substance (boceprivir, priced at $25-50K/course of treatment) for treating patients with chronic hepatitis C used a $CAD/QALY in its economic submission; in contrast, another submission to the CDR for a first-in-class drug indicated for patients with phenylketonuria, (priced at between $24- $180K/course of treatment, depending on dose) relied on a measure of CAD/[change in 6-week blood phenylalanine level], a measure with an uncertain effect on patient mortality *or* health-related quality of life.

6.1.2 Assessment of costs

Considerable effort has gone into developing systems to accurately measure and value resources associated with delivering various programs. An important concept in economic evaluation is that costs are not simply charges or expenditures. Costs must represent the true opportunity costs of

[85] CADTH. *Guidelines for the Economic Evaluation of Health Technologies: Canada* (Canadian Agency for Drugs and Technologies in Health, 2006)
[86] Treasury Board of Canada Government of Canada. Canadian Cost-Benefit Analysis Guide: Regulatory Proposals. Guide, September 26, 2007. Available: www.tbs-sct.gc.ca/rtrap-parfa/analys/analys07-eng.asp#Toc178397867
[87] Broome J. Trying to Value a Life. *Journal of Public Economics* 1978;9(1):91–100, doi:10.1016/0047-2727(78)90029-4
[88] CADTH. *Guidelines for the Economic Evaluation of Health Technologies* (Canadian Agency for Drugs and Technologies in Health, 2006)

services provided. In some cases, this means a shadow price must be used that adjusts prices that do not accurately approximate costs.[89] There is no current comprehensive set of unit costs for health system resources in Canada as these would be expected to vary by province.[90] Instead, province specific cost lists and databases for costing programs have been developed.[91]

The types and relevant range of costs considered are currently based on national guidance for technology assessment.[92] Currently, national guidelines for the economic evaluation of new medicines suggest that costs to the publicly funded health system, including direct costs to the system, and costs to patients (out-of-pocket costs, travel costs caregiver costs, lost time for unpaid work) should be included and other costs (such as costs outside the health sector and productivity losses) should only be considered in a secondary analysis if felt to be important.[93] This approach appears to be consistent with the notion that a wider societal perspective will only be relevant in the minority of cases[94].

Claxton and colleagues have suggested that *regularly* accounting for a wider perspective may be impractical as these costs will only have an impact under rare circumstances: where the external benefits associated with the health gains are likely to be substantially greater or substantially less than the external benefits associated with health forgone elsewhere in the health system.[95] Additionally, properly applied, technologies with low benefits from a societal standpoint will have to be identified and re-assessed. Rather than a regular application of a wider perspective, the authors suggest a triaging approach to screen for these exceptional circumstances.

It has also been suggested that larger economic benefits as a result of local or global R&D investment could be incorporated into a value assessment.[96] This has been additionally suggested by Garrison, who observed that most analyses conducted from a societal perspective fail to account for dynamic efficiency.[97] This means even if analyses are conducted using a "societal" perspective and according to current Canadian guidelines, they may fail to account for important benefits to society.[98]

6.1.3 Deliberative processes

Deliberative processes have been adopted as a mechanism to bring appropriate actors together when there are important societal decisions that involve evidence and value. They are intended to improve the quality of decision making my allowing for mutual decision-making based on facts. Culyer suggests that deliberative processes must be considered differently from consultation or public

[89] Drummond MF, et al. *Methods for the Economic Evaluation of Health Care Programmes*, Third Edition (Oxford University Press, 2005)
[90] See Jacobs, Using Canadian Administrative Databases to Derive Economic Data for Health Technology Assessments, CADTH, 2009 www.cadth.ca/media/pdf/H0483_Canadian_Admin_Databases_mg_e.pdf
[91] See, for example, the Ontario Case Costing Initiative - www.occp.com/mainPage.htm
[92] CADTH, *Guidelines for the Economic Evaluation of Health Technologies* (Canadian Agency for Drugs and Technologies in Health, 2006)
[93] Ibid
[94] Claxton K, et al. *Appropriate Perspectives for Health Care Decisions*. CHE Research Papers 54 (York: Centre for Health Economics, 2010)
[95] Ibid
[96] Available: www.cirano.qc.ca/publications_detail.php?lang=en&id=2012RP-13 [Unpublished report]
[97] CADTH, *Guidelines for the Economic Evaluation of Health Technologies* (Canadian Agency for Drugs and Technologies in Health, 2006); Garrison LP Jr, et al. Good Research Practices for Measuring Drug Costs in Cost-Effectiveness Analyses: A Societal Perspective: The ISPOR Drug Cost Task Force Report—Part II. *Value in Health* 2010;13(1):8–13
[98] Garrison Jr, et al. *Good Research Practices for Measuring Drug Costs in Cost-Effectiveness Analyses*

commentary; "Neither consulting nor commenting involves mutual deliberation – there is limited interchange, there is restricted participation – and neither is an arrangement for the actual taking of decisions, whereas deliberative processes can be. These are what make deliberative processes different."[99]

Deliberative processes are currently used in processes to judge the value and price of new medicines and technologies. Examples of these in Canada include PMPRB's HDAP, CADTH's CDEC, and Ontario's CED. They typically incorporate membership based on subject expertise (health economics, epidemiology). Some have incorporated "patient" representatives. In Ontario, the committee to evaluate new non-drug medical technology (called the Ontario Health Technology Advisory Committee) also has producer representatives on the committee. Some international jurisdictions, such as Scotland, have adopted this approach for the value assessment of new medicines.

6.1.4 Assessment of opportunity costs

In Canada, the opportunity costs from adopting new medicines or other interventions within the health system have never been empirically measured. Similarly, absolute thresholds for decision-making have never been declared by decision-makers. A commonly cited framework published by researchers Laupacis and colleagues proposed decision rules based on economic evaluation and suggests technologies that fall below an ICER of $20,000/QALY provide strong evidence for adoption but technologies up to and over $100,000/QALY gained might be considered depending on the circumstances.[100]

More recent analyses of recommendations of new medicines based on economic evidence reveal this framework may still apply. In an examination of CDR decisions between 2003-08, Clement and colleagues reveal that in 32/114 (28%) unique drug/indication submissions where cost per QALY was thought to be relevant to the new drug recommendation, ICERs assessed by the manufacturer to be above ~CAD $80K never resulted in a decision to list (see Figure 8). A similar analysis of recommendations from 2003-2009 corroborated these findings.[101]

Consistent with empirical evidence, the ICER from the manufacturer-funded analysis was generally believed to be exaggerated after scrutiny by CDR analysts.[102] A "real" ICER estimate based on a best guess by the Canadian Drug Expert Committee (CDEC, formerly the Canadian Expert Drug Advisory Committee) suggested the revealed threshold was closer to $125K/QALY.[103] An examination of the first 15 submissions to Canada's new pan-Canadian oncology drug review process revealed similar concerns about exaggerated economic value in some submissions;

[99] Culyer. *Deliberative Processes in Decisions About Health Care Technologies: Combining Different Types of Evidence, Values, Algorithms and People*

[100] Laupacis A, et al. How Attractive Does a New Technology Have to Be to Warrant Adoption and Utilization? Tentative Guidelines for Using Clinical and Economic Evaluations. *Canadian Medical Association Journal* 1992;146(4):473–81

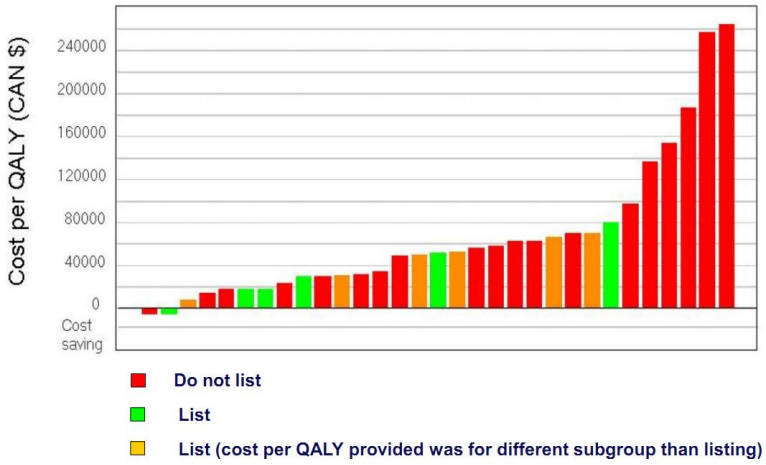
[101] Rocchi A, et al. Common Drug Review Recommendations: An Evidence Base for Expectations? *PharmacoEconomics* 2012;30(3):229–46

[102] Bell CM, et al. Bias in Published Cost Effectiveness Studies: Systematic Review. *BMJ (Clinical Research Ed.)* 2006;332(7543):699–703, doi:10.1136/bmj.38737.607558.80

[103] Harris A, Clement FM. Using Effectiveness and Cost-effectiveness to Make Drug Coverage Decisions: A Comparison of Britain, Australia, and Canada. *JAMA* 2009;302(13):1437–43, doi:10.1001/jama.2009.1409

nonetheless, a positive listing decision for one cancer therapy was obtained based on a manufacturer-derived ICER of $144K/QALY.[104]

Figure 8: Ranked ICERs for CDR submissions ICERs were relevant (2003-08)



(Sources, [105] and [106])

6.1.5 Other elements of value

Despite it being an excellent measure to compare health gains and losses across different parts of the health system, the QALY has well-known shortcomings including not accounting for health equity.[107] QALY measures do not differentiate between the very sick and those healthier at treatment and those with limited versus longer life expectancies. There are other shortcomings of this measure, and other measures have been proposed. Despite this, the QALY continues to enjoy widespread uptake in value assessments of new medicines with other approaches being used to supplement its potential shortcomings. These include soliciting the views of patients (as is seen in the CDR process), or weighting QALYs according to length of expected life (as is done in the UK).[108]

More recently, it has been suggested that all elements of value to society could be aggregated mathematically (using a technique called multi-criteria decision analysis, or MCDA) to produce a single metric of value that could include QALYs. Several proposals for MCDA-like approaches have been proffered, often naively violating principles of decision science by confusing what can technically constitute criteria for decision-making and how these criteria can be correctly applied.[109]

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[104] Chabot I, Rocchi A. How Do Cost-Effectiveness Analyses Inform Reimbursement Decisions for Oncology Medicines in Canada? The Example of Sunitinib for First-Line Treatment of Metastatic Renal Cell Carcinoma. *Value in Health* 2010;13(6):837–45, doi:10.1111/j.1524-4733.2010.00738.x

[105] Adapted from Manns B, Presentation at Institute of Health Economics Methodology Forum, Sept 2010

[106] Clement FM. *Using Effectiveness and Cost-effectiveness to Make Drug Coverage Decisions*

[107] Nord E, Daniels N, Kamlet M. QALYs: Some Challenges. *Value in Health* 2009;12(Suppl 1):S10–15, doi:10.1111/j.1524-4733.2009.00516.x

[108] Sussex, Towse, Devlin. *Operationalizing Value-based Pricing of Medicines: a Taxonomy of Approaches*

[109] Goetghebeur M, et al. Evidence and Value: Impact on DEcisionMaking–the EVIDEM Framework and Potential Applications. *BMC Health Services Research* 2008;8(1):270

Examples of failure to understand this approach are seen in proposals containing costs or cost-effectiveness as criteria, and uncertainty or clinical uncertainty as criteria.[110]

Others have suggested that decisions based on cost-effectiveness thresholds will not always lead to optimal allocation of resources. This is mostly due to the fact that cost-effectiveness threshold-based decision rules are grounded in assumptions that do not typically hold true.[111] While arguments about the fallibility of decision rules based on thresholds are technically valid, there have been no other feasible solutions offered in response to these arguments, and there is general consensus that adhering to a threshold framework for assessing value is not misguided and is better than not using any framework.[112]

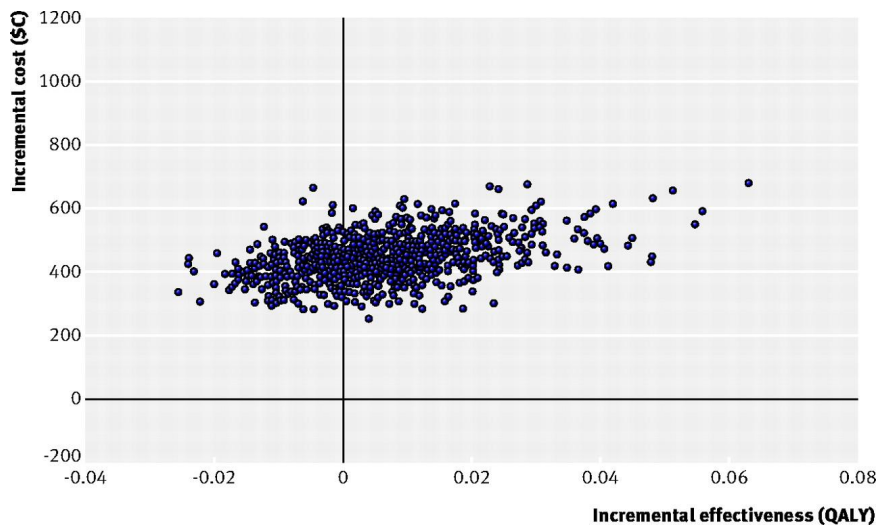
6.2 Current Approaches to Dealing With Uncertainty

Somewhat unique to new pharmaceutical markets is the amount of uncertainty surrounding the value of any new drug. This uncertainty arises as new medicines are not guaranteed to work in everyone. New drugs have only a *chance* of causing an individual benefit and a *chance* of causing individual harm for patients. Some of this chance can be accurately inferred from the studies conducted to obtain regulatory approval. However there are other factors beyond errors from measurement and sample size that can lead to additional levels of uncertainty. Some examples of these factors include the unexpected effects of new drugs in populations not previously studied (e.g., the very sick or very old), patients who are less compliant in the real world, or from other real-world factors. These systematic biases may lead to different (better or worse) average therapeutic benefits in the real world than were observed in regulatory studies.

Along with uncertain benefits are associated uncertain costs. As with clinical outcomes, some costs and their associated uncertainty can be inferred from clinical studies. Taken together, uncertain costs and uncertain health outcomes lead to decisional uncertainty. Figure 9 depicts this uncertainty. Each node in the graph represents a decision to use a new drug versus a valid comparator given current uncertainty. Rather than a single estimate of value (in this case QALYs compared to health system costs), there are a range of possible health and cost outcomes. In all cases, decisions lead to increased costs to the system and it appears in a majority of decisions, health gains are realized. Under this scenario, we can calculate a probability that a new drug would be cost-effective because we do not know this with certainty. The authors of this analysis reported that the intervention had a "99% probability that the cost per QALY gained is <$50,000" meaning only 1% of decisions had either sufficiently low QALY gains or sufficiently high incremental costs to lead to incur "opportunity costs".[113]

[110] Guindo LA, et al. From Efficacy to Equity: Literature Review of Decision Criteria for Resource Allocation and Healthcare Decisionmaking. *Cost Effectiveness and Resource Allocation* 2012;10(1):9, doi:10.1186/1478-7547-10-9
[111] Gafni A, Birch S. Inclusion of Drugs in Provincial Drug Benefit Programs: Should 'Reasonable Decisions' Lead to Uncontrolled Growth in Expenditures? *Canadian Medical Association Journal* 2003;168(7):849–51
[112] Gold M, Bryan S. A Response to Birch and Gafni – Some Reasons to Be Cheerful About NICE. *Health Economics, Policy and Law* 2007;2(02):209–16, doi:10.1017/S1744133107004021
[113] Manns B, et al. Population Based Screening for Chronic Kidney Disease: Cost Effectiveness Study. *BMJ* 2010;341(nov08 1):c5869–c5869, doi:10.1136/bmj.c5869

Figure 9: Depiction of decision uncertainty



Source [114]

Uncertainty about sales (and budget impact) is an additional uncertainty related to value (but unrelated to cost-effectiveness) that must be considered in the value-based price of a new drug. There have been several notable instances where sales were not accurately predicted by either payers or producers, resulting in unforeseen payer fiscal pressures (and producer profits). For example, the introduction of new non-steroidal anti-inflammatory drugs in 2000 led to unexpected increases in prescribing of NSAIDS. Relative increases in use of 29% and 64% over expected values were reported in the provinces of British Columbia and Ontario respectively.[115] As price must be based on sales, excessive sales will lead to consumer losses and producer gains. Conversely, underprescribing at a price based on assumed sales can unfairly harm producers (in the long term) at the benefit of consumers (in the short term).

6.2.1 The Value of information

To reduce our uncertainty about the incremental cost-effectiveness of a new drug would require more information. Acquiring this information requires resources and associated costs. These costs are ultimately borne by society, either through funding of research paid through tax revenues or through the profits earned by producers passed on to consumers. Because resources used for research can also be used to produce health, uncertainty has both a financial and human health cost. (i.e., they are interchangeable) An illustrative example of this trade-off is provided in Figure 9.

In this illustrative example based on Claxton[116], decisions to use a new drug result in either a net benefit or net loss due to uncertainty. The net effect of using the drug is calculated by subtracting

[114] Ibid
[115] Mamdani M, et al. Changes in Rates of Upper Gastrointestinal Hemorrhage After the Introduction of Cyclooxygenase-2 Inhibitors in British Columbia and Ontario. *Canadian Medical Association Journal* 2006;175(12):1535–38, doi:10.1503/cmaj.050192
[116] Claxton, Sculpher, Carroll. *Value Based Pricing for Pharmaceuticals: Its Role, Specification and Prospects in a Newly Devolved NHS*

the health benefits (in terms of QALYs) lost from using new resources to fund the drug from the health benefits gained from funding it. Based on existing information, we can predict that each time we use either drug we will incur either a net benefit or loss. In the first decision, new drug B produces an additional QALY. This means it was able to produce one QALY more health than using the same resources required to produce the next-most-expensive health gains elsewhere. However, the old drug could produce even more additional health (4 QALYs) with the same resources.

These decisions are based on uncertainty. With additional decisions, the effect of uncertainty becomes clear. Sometimes the new drug performs better, sometimes not as well. On average, the net health benefit of the new technology (NHB (New drug)=11) can be predicted to be greater than current treatment (NHB (Old Drug)=10). So at current prices, early access to the new technology is expected to offer one additional QALY per patient.

What we can observe is that despite the new drug being more cost-effective on average, of three decisions made, there is a 33% chance that the new treatment may not be cost-effective, as it was inferior the first time we decided to use it. Additional information could be acquired to reduce uncertainty to improve decision-making. "The maximum value of having more information is the difference between the best that can be done if we could resolve this uncertainty by collecting more information and the best that can be done if we base our decision on current information. As it turns out, we gain one QALY per patient by being more certain about the health gains through acquiring more information."[117]

Figure 9: The value of early access and the value of evidence. Two treatments are compared: Drug A (current treatment) and Drug B (new treatment)

	NHB, QALYs (Drug A)	NHB, QALYs (Drug B)	Maximum NHB, QALYs
1	4	1	4
2	10	10	10
3	16	22	22
Average	10	11	12

Value of Access

Value of Evidence

NHB=Net Health Benefit
QALYs=Quality-adjusted life-years

Adapted from Husereau[118] and Claxton[119]

This example attempts to illustrate that reducing uncertainty and providing access to a new drug both lead to the same consequences of consumer benefit. In some cases, the value of obtaining more information outweighs the value of paying for a new drug at its given price.

[117] Husereau and Cameron. *Value-Based Pricing of Pharmaceuticals in Canada: Opportunities to Expand the Role of Health Technology Asessment?*
[118] Ibid
[119] Claxton K, Sculpher M, Carroll S. *Value-based Pricing for Pharmaceuticals: Its Role, Specification and Prospects in a Newly Devolved NHS* (Centre for Health Economics, University of York, February 2011). Available: http://EconPapers.repec.org/RePEc:chy:respap:60cherp

Although the current approach to dealing with uncertainty in Canada reflects the principles of reducing price (due to reduced value) under uncertainty, it is a blunt instrument in its current form. Canadian decision makers have typically relied on a two-tiered approach to evidence evaluation; as described in a report of Ontario's Drug Quality and Therapeutics Committee (now the Committee to Evaluate Drugs), clinical evidence is first considered and if clinical outcomes from the use of a new drug are considered valuable, an economic evaluation follows.[120] Although the CADTH CDR process suggests evidence of clinical, economic and patient values are considered for each new drug, there is significant evidence that rather than a simultaneous consideration of costs and consequences, the current approach used employs a hierarchy where clinical evidence is considered first and then economics.[121] For example, Clement and colleagues noted that economic evidence was only considered to be relevant to decision making in 27% (31/114) of submissions to the CDR within a 4-year period. In a subsequent analysis of 138 final recommendations, Rocchi and colleagues noted:

> *Ultimately, clinical uncertainty was the strongest predictive factor, and clinical uncertainty was frequently cited as the reason for a DNL. This finding supported the empirical hypothesis that there was a hierarchical consideration of variables, with clinical factors considered first.*
> (Source, 122 , p. 241)

Creating a preliminary "Do Not List" recommendation is similar to valuing a new drug at $0 rather than its current price. A "Do not list at the submitted price" recommendation does not specify how much the price should be lowered, but implies anything below the current value should be considered. Through the CDR process, these embargoed recommendations could lead to a lower submitted price from the producer. If the producer chooses to keep the price, the final recommendation may trigger regional price negotiations or more recently, collective negotiations through the newly established pan-Canadian purchasing alliance.[123]

The current approach to dealing with uncertainty about benefit within the PMPRB is to categorize the new drug as having "Slight or No Improvements". This approach does not distinguish between a new drug where there is substantial evidence of no benefit and no evidence of a benefit.

6.2.2 Product listing agreements and negotiation

Another approach to managing considerable uncertainty, beyond asking for price reductions or not paying, is to pay conditionally based the collection of further information. Intended to provide patient access under uncertainty, these agreements between payers and producers have been called product listing, risk-sharing or managed entry agreements.[124] Typically, this involves an agreement to pay a drug at a certain price and up to a certain volume. Revenue earned beyond the price-volume cap is returned to the payer.

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[120] PausJenssen AM, Singer PA, Detsky AS. Ontario's Formulary Committee: How Recommendations Are Made. *PharmacoEconomics* 2003;21(4):285–94
[121] Rocchi, et al. *Common Drug Review Recommendations an Evidence Base for Expectations?*
[122] Rocchi, et al. *Common Drug Review Recommendations*
[123] Dempster B. Provincial Purchasing Alliances — Drivers, Challenges And Implications. *Prescription Reimbursement Advisor*, 2011
[124] Nason E, Sproule J. *Industry-Payor Agreements for Pharmaceuticals Backgrounder for Roundtable* (Edmonton, AB: Institute of Health Economics, 2011). Available: www.ihe.ca/documents/Industry-payor%20agreements%20for%20pharmaceuticals_v1%200%20(2)-1.pdf

There are other forms of access agreements that could be used and include outcome-based schemes (conditional coverage and performance-linked reimbursement) and non-outcome- based schemes (market share, utilization caps and manufacturer funded pilots). A taxonomy of the various approaches is depicted in Figure 10. However agreements beyond price-volume agreements have been more difficult to implement. For example, a study linked to reimbursement and intended to assess outcomes associated with the use of a new biologic in Alberta required 3 years to begin, due to legal and bureaucratic challenges, despite the willingness to participate by all parties.

In 2009, a meeting was held in Canada to develop a Consensus Statement on Principles of Good Practice in the Design of Access with Evidence Development Approach.[125] A report of these principles reflects some of the various challenges with creating these agreements including 1) Defining specifically what information is important 2) Designing systems to capturing information in a way that is unambiguous and 3) Ensuring the scheme is suited to the health system and has an independent governance structure.[126]

In Canada, as with the rest of the world, agreements to collect information beyond price and utilization to inform a product listing agreement are an exception rather than a rule due to their various challenges.[127] A 2010 OECD report noted that despite holding promise, "there is insufficient evidence to be confident in their utility."[128] Despite several attempts to conduct these agreements in Canada, a 2011 report similarly reflected that despite perceived benefits by all parties, these agreements appear to be risky, costly, and difficult to implement when there are barriers to trust.[129] Nonetheless, price-volume agreements informed by assessments of value are still an appropriate complement to any value-based pricing approach.

[125] Menon D, et al. Principles of Design of Access with Evidence Development Approaches: a Consensus Statement from the Banff Summit. *PharmacoEconomics* 2010;28(2):109–11, doi:10.2165/11530860-000000000-00000
[126] Ibid
[127] Neumann PJ, et al. Risk-sharing Arrangements That Link Payment for Drugs to Health Outcomes Are Proving Hard to Implement. *Health Affairs (Project Hope)* 2011;30(12):2329–37, doi:10.1377/hlthaff.2010.1147
[128] Organisation for Economic Co-operation and Development, *Value for Money in Health Spending.* (Paris: Organisation for Economic Co-operation and Development, 2010)
[129] Nason and Sproule. *Industry-Payor Agreements for Pharmaceuticals Backgrounder for Roundtable*

Figure 10: Access with evidence development approaches to resolve uncertainty between payers and producers

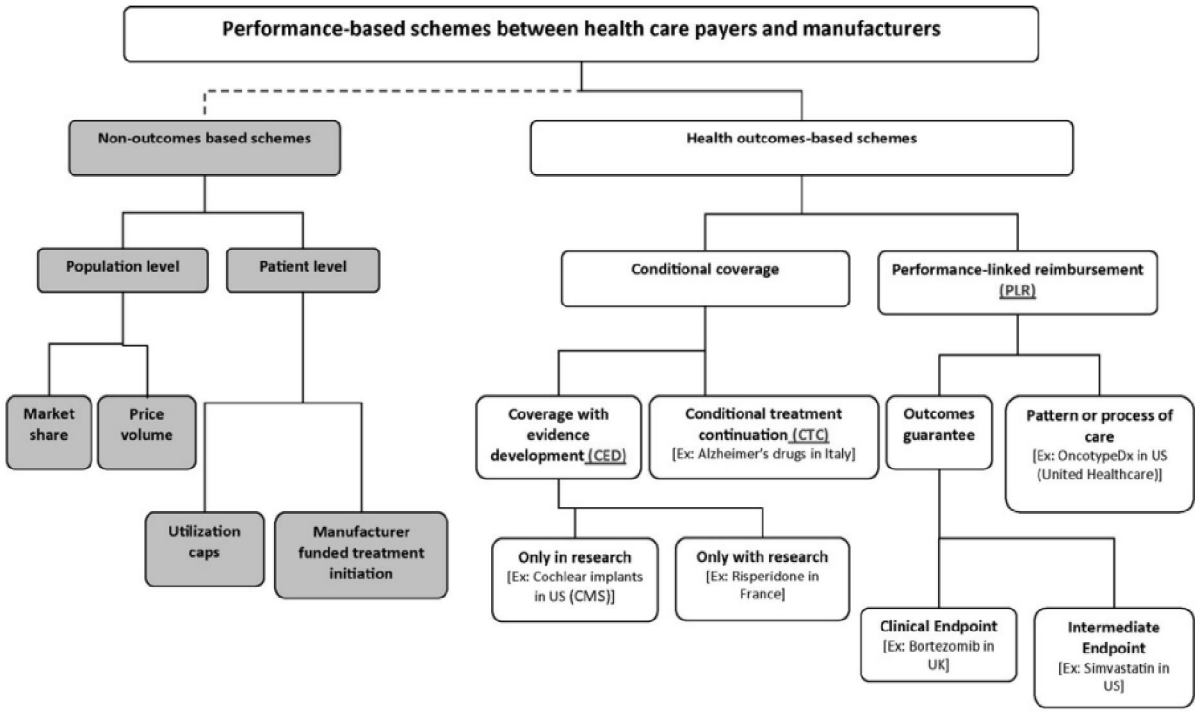


Fig. 1. Taxonomy of performance-based health outcomes reimbursement schemes. Performance-based schemes are broken into health outcomes-based and non health outcomes-based schemes. Our review focused on health outcomes-based schemes. We defined the subcategories as follows: (1) conditional coverage: schemes where coverage is granted conditional on the initiation of a program of data collection; (2) performance-linked reimbursement (PLR): schemes where the reimbursement level for covered products is tied to the measure of clinical outcomes in the "real world"; (3) coverage with evidence development (CED): binary coverage decision is conditioned upon the collection of additional population level evidence, from a pre specified scientific study, to support continued, expanded, or withdrawal of coverage; (4) only in research: coverage conditional on individual participation in research (i.e. only patients participating in the scientific study are covered); (5) only with research: coverage conditional on a scheme to conduct a study that informs the use of the medical product in the payer patient population; (6) conditional treatment continuation (CTC): continuation of coverage for individual patients is conditioned upon meeting short-term treatment goals (e.g. tumor response or lower cholesterol); (7) outcomes guarantees: schemes where the manufacturer provides rebates, refunds, or price adjustments if their product fails to meet the agreed upon outcome targets; (8) pattern or process of care: schemes where the reimbursement level is tied to the impact on clinical decision making or practice patterns (e.g. whether or not patients adhere to the treatment course suggested by a risk predicting genomic test). Of note, there were hybrid examples that had two or more of the above components.

Source, [130]

6.2.3 Timing of assessments

The primary approach to assessing the value of new medicines is to conduct an *ex ante* (prior to access) using a review of current literature. This process is employed by PMPRB, pCODR, CDR and regional processes. Predicting the performance of a drug is tricky business, and new medicines

[130] Carlson JJ, et al. Linking Payment to Health Outcomes: A Taxonomy and Examination of Performance-based Reimbursement Schemes Between Healthcare Payers and Manufacturers. *Health Policy* 2010;96(3):179–90

may end up performing much better or worse than is predicted by a review of evidence, typically randomized trials conducted for regulatory purposes. Ex ante assessment provides an opportunity for assessing the effect of uncertainty and heterogeneity, which can further create priorities for re-assessment and the design of product listing agreements.

Ex post (after launch) assessment not directly linked to reimbursement still continues as an academic exercise in Canada through calls for changes to market access policies (enhanced pharmacovigilance) and as various provincial ministries explore enhancing their capacity to conduct "real-world" studies of cost-effectiveness. Ex post assessment does not require local "real-world" data - many provincial ministries routinely re-assess publicly insured drugs by examining currently available literature. Provinces are also able to ask the CDR for new recommendations for listing based on new information.

In the realm of "real-world" studies, the Drug Safety and Effectiveness Network has been established by CIHR and Health Canada as a means of monitoring the safety and effectiveness of marketed drugs across Canada.[131] Also, provincial ministries, notably Ontario, BC, Saskatchewan and Manitoba have used population-based data to monitor the cost-effectiveness of new drugs. Various *ad hoc* registries have also been established by drug companies, clinical communities, private companies, the Canadian Institute of Health Information as well.[132] None, however, have an explicit remit to monitor cost-effectiveness.

6.3 Conclusions

Value-based pricing schemes require consistent approaches to value assessment, including measuring and valuing health system performance, drug utilization, associated costs and manufacturer sales (profits). They also require some notion of opportunity costs from investment. Canada currently has methods and data for conducting these assessments as well as national standard for economic evaluation, which is currently applied to assessments for the purpose of new drug reimbursement. The opportunity costs from adoption of new drugs has *not* been measured, but analysis of adoption decisions reveals preferences to fund drugs that fall below $125K/QALY and possibly larger for cancer-specific decisions.

Value-based pricing schemes also require mechanisms to manage uncertainty. This might involve asking for lower prices, not paying and/or re-assessing after launch either based on existing studies or drug performance in the real-world. Real-world assessment of new drugs can also be tied to purchasing arrangements, called product listing, risk-sharing, or managed entry agreements. Deliberative processes for translating evidence of benefit and costs to some notion of value are widely adopted.

[131] Canadian Institutes of Health Research Government of Canada. Webinars Announcing the Establishment of New Drug Safety and Effectiveness Network (DSEN) Collaborating Centres - CIHR. Available: *www.cihr-irsc.gc.ca/e/43190.html* (accessed 13 June 2011)

[132] Health Canada Government of Canada. Post-Marketing Pharmacosurveillance in Canada: A Background Paper Prepared for the Working Conference on Strengthening the Evaluation of Real World Drug Safety and Effectiveness [Health Canada, 2005]. Backgrounder, November 7, 2005. Available: *www.hc-sc.gc.ca/hcs-sss/pubs/pharma/2005-pharma-surveill-can/index-eng.php#a3_2_2*

7 CHANGING TO VALUE-BASED PRICING: KEY CONSIDERATIONS AND LESSONS FOR CANADA

Section 4 provided an overview of concepts related to pricing patented medicines. Through an examination of current theory and empirical evidence it suggested:

- External price referencing is not a means of optimizing consumer welfare and profits to producers.
- Value-based pricing *is* a means of fostering global innovation by signaling from consumers to producers what innovations are required.
- Value-based pricing *is not* a means of stimulating Canadian R&D or non-R&D investment by the pharmaceutical sector.
- Value-based pricing is not a mechanism to lower prices that are unaffordable; neither is it a mechanism to contain costs;

In Section 5, a review of current jurisdictions that have adopted or are considering adopting a value-based pricing approach was undertaken. This led to several lessons for Canada.

- There are no one-size-fits-all solutions.
- Value-based pricing requires knowledge of impact on benefits, costs and drug utilization.
- Value-based pricing requires an explicit declaration of opportunity costs from investment.
- Value-based pricing that is not directly linked to reimbursement creates a unique set of challenges that will require understanding and rule-setting.
- The importance of re-assessment is a consistent theme.

In Section 6, an analysis of important components of value-based pricing was undertaken. There are several important observations from this analysis:

- Value-based pricing requires a principled approach to economic evaluation – there are current National guidelines for economic evaluation of new drugs that may require adaptation to value-based pricing.
- Value-based pricing requires an approach to evaluating benefits – life-years and quality-adjusted life-years have been adopted as primary metrics of benefits in Canada as elsewhere
- Value-based pricing requires an approach to evaluating costs - information about costs is widely available and there are National guidelines for conducting analyses. These may not account for costs associated with R&D.
- Deliberative processes are commonplace in Canada for assessments of new medicines
- The opportunity cost threshold of adopting new medicines in Canada is unknown; there is evidence that new drugs with an unbiased estimate of $125K/QALY are attractive for adoption.
- The threshold for adopting new drugs in patients with cancer may be higher.

- For payers, the current approach to dealing with significant uncertainty is to ask for an undefined lower price or to not pay. For price determinations of patented medicines, the current approach is to assume no incremental benefit.
- The focus of assessment is before launch with some limited ex post assessment.

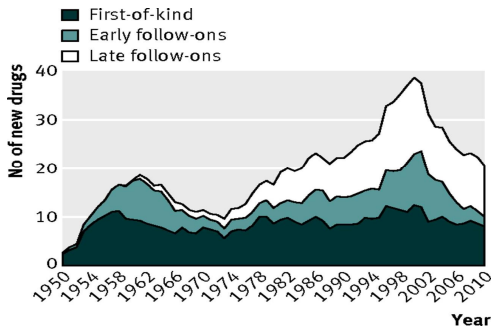
In the next section, we will use what we have learned to examine options for implementing a value-based pricing scheme in Canada. First, we will describe the effects of value-based pricing on relevant policy goals (providing health benefits, controlling costs, and fostering innovation.) We will then recommend some options for change based on the current system and provide a brief analysis of potential impacts on the current policy environment.

7.1 Effects of value-based pricing on health, costs, and innovation

Due to a predicted larger availability of generics (the patent 'cliff'), it would be expected that value-based pricing, that considers the price of generic comparators in its assessment, might realize short-term reductions in expenditures. However, in the long-term, producer responses to value-based pricing will be to re-direct R&D resources into therapeutic areas without medicines, or where there is substantial need. If these efforts are successful, value-based pricing could lead to longer-run cost increases but with corresponding benefits to society. In short, health and cost effects from value-based pricing policies will depend on the extent of innovation realized.

Value-based pricing will provide strong signals for innovation but it cannot be known whether more or less innovation will be realized. A recent analysis by Morgan and colleague suggests real innovation (first of a kind) in drugs has remained relatively stable over the previous decades with previous declines in productivity explained by fewer me-too (early and late follow-on) drugs. (Figure 11).

Figure 11: Five year averages of all therapeutic new molecular entities (NMEs) approved by the US Food and Drug Administration by degree of novelty, 1946-50 to 2006-10 from Morgan[133]



[133] Morgan SJ, Cunningham CM, Law MR. Drug Development: Innovation or Imitation Deficit? *BMJ (Clinical Research Ed.)* 2012;345:e5880

7.2 Lessons for Change

Although PMPRB's system of pricing involves an assessment of incremental benefit and therapeutic reference pricing, it cannot be called "value-based" for several reasons:

- Although some premiums are given for more therapeutically beneficial drugs, these premiums are based on external reference pricing, not the degree of benefit.
- It is not based on any consideration of tradeoffs of benefits to consumers or wider society given costs or overall budgets in either the short or long term.
- Similarly, benefits to producers in the short and long term are not directly factored into price determination.

In the current system, producers are given incentives to develop me-too therapies, therapies with high degrees of uncertain benefit, characterize their therapies in a lower therapeutic category or not obtain a patent. They may also be given incentives to use rent-seeking tactics outside of price regulation, such as trade agreements, introduction delays and sequencing, supplemental indications, or other available and legitimate opportunities to maximize revenue.

7.2.1 Consistent approaches to economic evaluation

LESSON 1: *A National standard for conducting economic evaluation is the basis for informing value-based prices*

Consistent with other jurisdictions, price evaluation will require (at minimum) an assessment of the costs and consequences of therapy along with the volume of new drug that will be sold. A cost/QALY framework will reflect the entirety of clinical benefits currently considered by the PMPRB. These include factors beyond direct benefits and harm including convenience, compliance and other measures of patient satisfaction.

Determination of the value of a new therapy that provides no additional benefit will need to be addressed. The current approach to pricing new drugs with similar or slight benefits is to give them a monopoly price, signaling to the innovator that me-too drugs are highly valued. However, a value-based pricing system should lead to a price of $0 for a drug of no incremental benefit with some additional price for providing additional alternatives for patients, a value to society from a supply-chain standpoint.[134]

A model that mimics prices in other markets would see first-in-class drugs with premium prices; second-in-class drugs with no incremental benefit would then be priced lower than first-in-class drugs but higher than a third-in-class drug which is priced higher than subsequent drugs with no added benefits. The price-demand curve for imitative drugs would require arbitrary definition based on societal preferences for additionally available drugs. This is separate from arguments that new drugs may benefit individuals where other drugs have failed.

This rule would apply to drugs with similar benefits in similar populations and not a drug that is beneficial in a population where no other agent has been shown to be beneficial. The case that someone unresponsive to alternatives might benefit is an empirical question, and will be addressed by evidence assessment.

[134] Kennedy I. *Appraising The Value Of Innovation And Other Benefits*, 2009. Available: www.nice.org.uk/media/98F/5C/KennedyStudyFinalReport.pdf

7.2.2 Determination of benefits

LESSON 2: *Single estimates of incremental benefits to consumers are important for supporting decisions about efficiency and compatible with the current reimbursement environment*

The current approach to assessing benefit conducted by the PMPRB is inadequate to inform price determinations that are comparable across the health system as a single metric of benefit has not been adopted. Adapting the current approach to one that uses an acceptable single metric of benefit (such as QALYs) will require additional analysis conducted by either the PMPRB or the applicants. Given these calculations are already being performed by producers for CDR and pCODR processes, requiring an applicant to provide this additional analysis is entirely feasible. It may be more difficult for exceptional products that are not subject to these processes. Sufficient resources will be required to allow considerable scrutiny of these estimates, which are prone to error and influenced by underlying assumptions which are not always apparent.

Aggregate measures of benefit, such as QALYs, provide a precise estimate of incremental benefit (and harm) but do not account for all factors that may be important to society or patients. Choosing QALYs would be consistent with current approaches in the UK, Australia, France and Germany[135]. However, if additional factors such as equity or the value of treating some conditions over others are required, a condition-specific approach (as in Germany) a modified QALY approach (as in UK) or MCDA approach to valuation of benefits will require adoption.

7.2.3 Determination of costs

LESSON 3: *Considering societal costs will require modification to existing guidance for economic evaluation. The value of information is also important to consider in pricing.*

Current guidance for economic evaluation lacks explicit direction about when to consider societal costs, and may lack some important societal cost categories that relate to R&D or benefits from non-R&D investment. Evaluation of costs for value-based pricing may require some modification to existing guidance or more-specific guidance.

The current approach to valuing uncertainty is also too blunt to consider the effects on costs associated with additional uncertainty. A more nuanced approach that considers the value of missing information will be necessary to inform price determination.

7.2.4 Opportunity cost threshold

LESSON 4: *Measuring the opportunity cost threshold for new medicines is an important avenue of future research, as an empirical measurement of impacts on life-years or quality-adjusted life-years is helpful for value-based pricing*

If feasible, it will be important to directly measure opportunity costs from adopting new medicines with Canada's health system. Otherwise, a revealed threshold, which may not accurately reflect a fair balance of consumer and producer benefits has been calculated and could be used. Some Canadian researchers have already developed proposals to measure this threshold but have not yet obtained funding to do so. Valuing new medicines using elements of value beyond life-years gained or QALYs will require estimates of opportunity costs using these elements, and will be infeasible at present.

[135] Note that Germany allows QALYs but does not restrict measures of therapeutic benefit to them

7.2.5 Timing of assessments

LESSON 5: *Systems for measuring real-world effectiveness will be required for re-assessing prices.*

There are some shortcomings in the current processes for ex ante assessment that are worth mentioning. First, value is determined by therapies that are immediately available at the time of decision-making and not future therapies that are known to be close to emerging. It is also based on what is known about a drug currently, and cannot account for ongoing trials whose results are yet to emerge. Similarly, costs reflect costs in the current environment.

The emergence of a generic drug over the lifetime of a patented medicine, which is uncertain due to a variety of legal and cost factors, is not entirely unknown. Although the emergence of generic drugs and new brand alternatives cannot be predicted with absolute certainty, these factors will have an influence on future consumption, value and price. *Ex ante* assessments could attempt to more reasonably capture uncertainty about these important events. By demonstrating the effect of these events, it could set an important precedence for when to conduct ex post assessment. One option is to create a "dynamic" perspective that assumes the emergence of technologies and associated costs.

Ex post assessment will be required to create an iterative system where value and price are fully aligned with undistorted signals to innovators. The PMPRB has no existing remit to conduct *ex post* assessment beyond monitoring whether prices are excessive compared to prices determined at onset and adjusted by inflation. A system of ex post assessment oriented to PMPRB decision-making would require leveraging current systems (such as DSEN or provincial payer-based systems) or conducting literature-based re-assessments to for these analyses. It will also need to consider how re-assessment can be linked to product listing agreements.

7.2.6 Determination of prices

LESSON 6: *Systems to support delivering and monitoring the use of medicine by indication are needed to develop menus of price-volume options based on cost-effectiveness*

As proposed by Claxton, a menu of price-volume options could be specified.[136] This would benefit both consumers and producers by creating a fair and level playing field for deliberation and negotiation of price. Without this, consumers or producers may "cherry-pick"; consumers and their agent insurers may demand a value-based price based on population averages be paid to a limited number of consumers (where a higher price is needed); producers may similarly demand a value-based price based on population average be paid for an expanded population (where a lower price is needed). The concept of a price-volume menu by Husereau and Cameron[137] is illustrated in Figure 12 below.

[136] Claxton K, et al. Value Based Pricing for NHS Drugs: An Opportunity Not to Be Missed? *BMJ* 2008;336(7638):251–54, doi:10.1136/bmj.39434.500185.25

[137] Husereau and Cameron. *Value-Based Pricing of Pharmaceuticals in Canada: Opportunities to Expand the Role of Health Technology Asessment?*

Figure 12: Value-based pricing (VBP Case Study): self-monitoring of blood glucose (SMBG) adapted from Husereau[138]

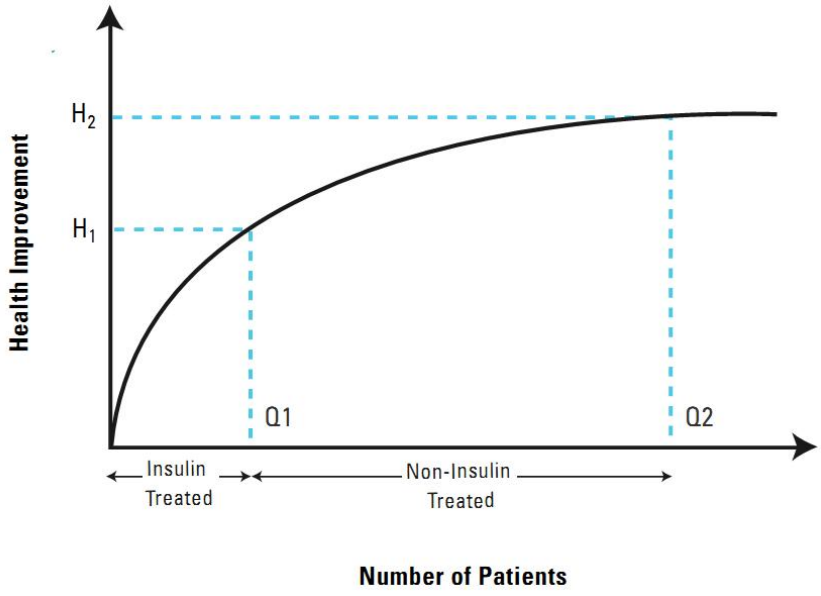
Consider a drug indicated for people with diabetes. Benefits of using the drug in people with diabetes have been shown, but there is more uncertainty surrounding these benefits in patients not using insulin. There are considerably more people with diabetes not using insulin (80%) than using insulin.

The figure below (12a) depicts this uncertainty. Treating all of the patients with insulin-treated diabetes will produce health gains (H1) with an associated average improvement of H1/Q1 for insulin-treated patients.

If all patients were treated, (i.e., including patients who are not using insulin), an incremental gain in health equal to H2 - H1 would be realized but with an average marginal improvement per patient that is smaller than the corresponding value for patients using insulin.

In this situation, the cost-effectiveness of the new medicine in patients not using insulin is likely to be less than in patients using insulin.

Figure 12a

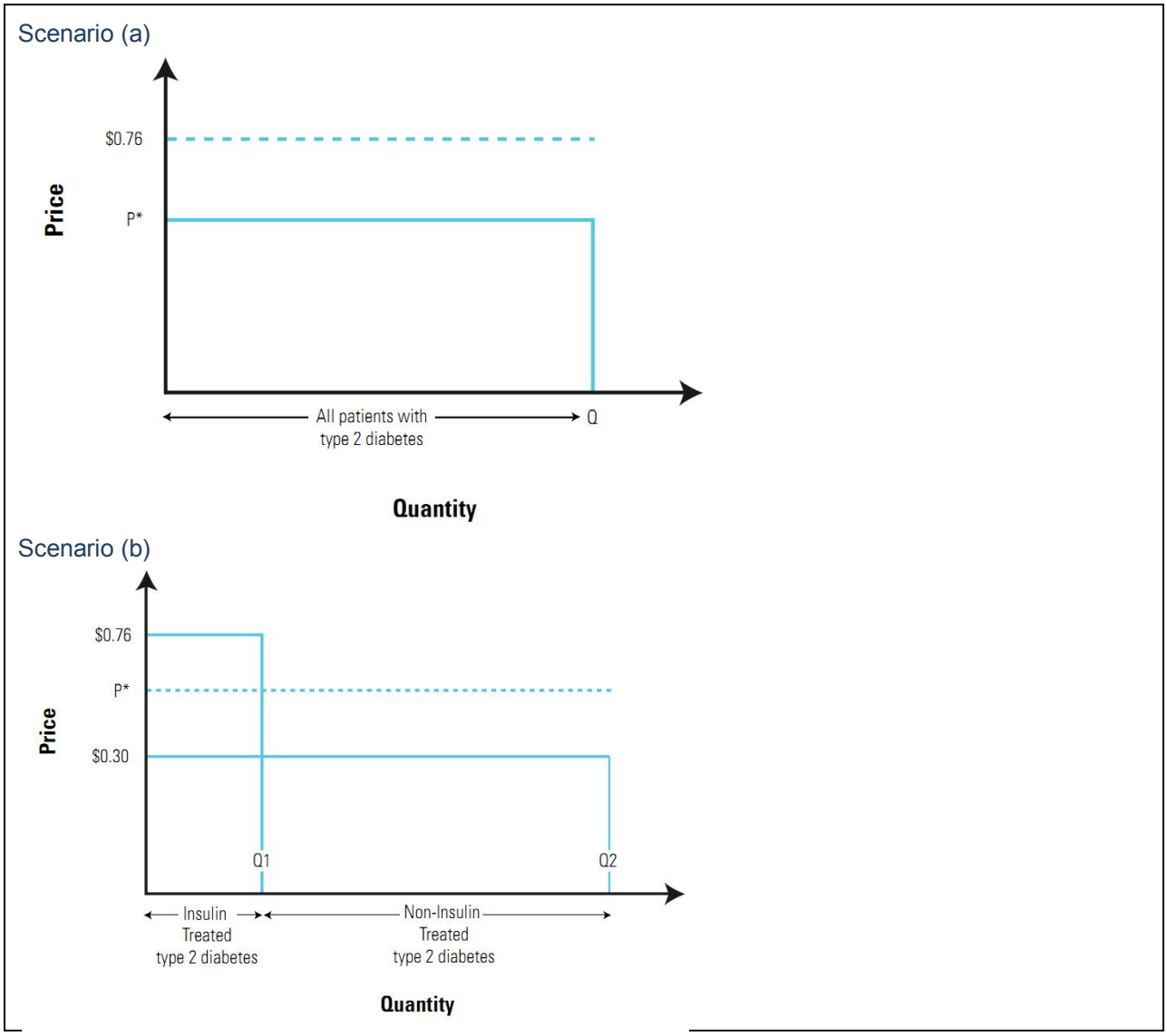


In Scenario (a) depicted below, a manufacturer hopes to charge $0.76 per daily course of therapy of the new drug. If the health system is paying value-based prices for drugs, the price of the new drug should be determined to be a maximum of P*. This is the price that leads to no short-term net benefits. The proposed price could be determined to be excessive, however, as it will result in health benefits gained that are much less than the health benefits foregone if the resources were invested elsewhere. At this price, the new drug would have a negative effect on the net health benefits of Canadians.

If we identify various groups who might benefit differently, we can create a menu of prices based on benefits and volume. For example, the two subgroups previously identified may have prices determined by their varying cost-effectiveness.

Scenario (b) depicts our choices. The drug can be sold only to those taking insulin for $0.76 OR (at volume, Q) or it can be sold at $0.30to all patients with diabetes.—insulin and non-insulin treated patients.

[138] Ibid



7.2.7 Negotiation

LESSON 7: *Value-based pricing requires a negotiation mechanism that is fair and transparent. This is best informed by deliberative processes that include all relevant experts and policy actors (patients, insurers, economists, and industry representatives).*

The long-term benefits provided to consumers and producers from pharmaceuticals are everybody's business. All Canadians will be affected by pharmaceutical pricing policies whether or not they are patients. Given the substantial opportunity costs from pricing decisions, transparent and structured processes for negotiating price informed by deliberative processes are paramount. Deliberative processes promote understanding and buy-in and will help to promote consistency over time.

7.2.8 Effect on Policy Environment

LESSON 8: *Value-based pricing must involve purchasers. Current initiatives oriented to support value-based purchasing (e.g., Reformulary Group, CDR and the pan-Canadian purchasing alliance) may eliminate the need for price regulation outside of purchasing arrangements.*

Although the real benefit of value-based pricing is to provide strong signals to innovators, there may be some untoward effects. Value-based pricing cannot be viewed as separate from value-based purchasing. Although uninsured consumers and those with private insurance coverage may benefit now and in the future from having prices that fairly reflect value, there is a potential for payers to exploit producers of medicines (i.e., to gain more than their share of the social surplus) if certain principles of negotiation are not adhered to (e.g., arbitrary price cuts are demanded beyond a value-based price).

The magnitude of discounts obtained in Canada through confidential producer rebates is not known but is estimated to be between 10%-30% based on anecdotal evidence and international evidence.[139] Although cost-reducing, these "discounts" are not based on any explicit notion of value; arbitrary discounting at a level that does not align itself with value (for example, 30% off in all cases) may send distorted signals to innovators and reduce consumer benefits if the discount does not accurately reflect potential welfare loss from uncertainty. It could also have the opposite effect by potentially harming producers if the discount demanded is too severe. Presumably, producers who have negotiated these prices as a fair reflection of value will simply refuse to cut prices further for public negotiation.

Any system of price regulation that is not accountable to a specific budget or does not sufficiently control prices across markets can lead to undesirable consequences from market forces that seek to maximize consumer welfare and producer profit through unforeseen tactics that undermine price regulation. This can paradoxically have adverse consequences for consumers and producers. In short, value-based pricing can only occur with the full participation and understanding of all provincial and national actors who can affect prices through their actions. If a high level of coordination with those who control the market (i.e., primarily payers and producers) cannot occur (as is seen in Germany, Sweden), then value-based pricing might not be a feasible option for the PMPRB in Canada. A more feasible option is to facilitate value-based pricing would be to support other organizations who wish to employ value-based purchasing, particularly at the level of pan-Canadian purchasing and price negotiation.

"Excessive" Pricing

Adoption of a value-based price casts a new definition on the existing PMPRB definition of excessive pricing. Although it is tempting to believe that prices can be viewed as excessive in comparison to other jurisdictions, excessive prices will require re-definition according to benefits to producers and consumers. Although comparisons of prices paid for goods across countries are commonplace, acknowledgment of the necessity of price discrimination will be required in an era of value-based pricing.

[139] Nason and Sproule. *Industry-Payor Agreements for Pharmaceuticals Backgrounder for Roundtable*

7.3 Conclusions

In order to be a feasible option for Canada, a value-based pricing approach will require a departure from the current approach to excessive price determination within the PMPRB. Notably, value-based pricing would require a much closer relationship with pharmaceutical public and private payers, and the institutions that support them, as prices can be further regulated in the marketplace. Any attempt to introduce value-based pricing for *ex-factory* prices will duplicate already existing systems that attempt to affect purchase prices based on cost-effectiveness, as seen across individual provinces and in the newly-formed pan-Canadian purchasing alliance.

We have developed eight lessons that would require consideration if value-based pricing were to be used for patented drug prices in Canada. These lessons highlight the need for consistent approaches that arrive at single estimates of benefits. Value-based approaches must also consider all costs relevant to consumers and producers.

Value-based pricing will require mechanisms to price based on quantity sold; detailed information will allow for re-assessment and flexible pricing options. Value-based pricing cannot be reduced to a mathematical algorithm; it requires the full participation and consent of representative societal actors who can deliberate and negotiate with information regarding how prices will affect the health and welfare of consumers now and in the future.

APPENDICES

Appendix A – List of Informants

The following individuals were consulted and made helpful comments and suggestions on various sections or conceptual aspects of this document. None reviewed the entire document or are responsible for its content.

1. Bill Dempster, 3Sicty Public Affairs Inc, Ottawa, Canada
2. Michael Drummond, Centre for Health Economics, The University of York, UK
3. Karl Claxton, Centre for Health Economics, The University of York, UK
4. Uwe Siebert, Department of Public Health, Medical Decision Making and Health Technology Assessment at the University of Health Sciences, Medical Informatics and Technology (UMIT) in Hall in Tirol, Austria
5. Paul Grootendorst, University of Toronto, Canada
6. Aidan Hollis, University of Calgary, Canada
7. Marc-Andre Gagnon, Carleton University, Canada
8. Marc Richard, Gowling Lafleur Henderson LLP, Ottawa, Canada

Appendix B: Description of Search Strategy

Value Based Pricing Search Strategy

Medline (Ovid Interface > 1998-Jan 30, 2013)

1. pharmaceutical preparations/ or drugs, generic/ or prescription drugs/
2. Drug industry/
3. drug costs/
4. Economics, Pharmaceutical/
5. pharmaceutical*.tw.
6. (medicines or medication*).tw.
7. prescription drugs.tw.
8. prescriptions.tw.
9. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8
10. (Health technology assessment or hta).tw.
11. technology assessment, biomedical/
12. Comparative Effectiveness Research/
13. comparative effectiveness.tw.
14. (cost-effectiveness adj10 threshold).tw.
15. value for money.tw.
16. or/10-15
17. (Incremental cost-effectiveness ratio or ICER).tw.
18. "costs and cost analysis"/ or "cost allocation"/ or cost-benefit analysis/ or "cost control"/ or "cost sharing"/
19. economic evaluation*.tw.
20. cost-per-QALY.tw.
21. or/17-20
22. reimbursement, incentive/
23. (pricing or purchasing or reimbursement).tw.
24. Insurance, Health, Reimbursement/ or Reimbursement Mechanisms/ or Insurance, Pharmaceutical Services/ec
25. 22 or 23 or 24
26. (Value-based adj5 (pricing or purchasing or reimbursement)).tw.
27. pay for performance.tw.
28. Risk Sharing, Financial/
29. risk-sharing.tw.
30. or/26-29
31. (value or pricing or price or prices or expenditure* or spending or reimbursement).ti.
32. 9 and 16 and 25
33. 9 and 21 and 25 and 31
34. 9 and 30
35. 32 or 33 or 34
36. limit 35 to yr="1998 -Current" (521 results)

EMBASE (Ovid Interface >1998 - Jan 30, 2013)

1. drug/ or generic drug/ or new drug/ or prescription drug/
2. drug industry/
3. pharmacoeconomics/ or drug approval/ or "drug cost"/ or drug formulary/

4. (pharmaceutical* or medicines or medication* or prescription drugs).ti.
5. 1 or 2 or 3 or 4
6. biomedical technology assessment/
7. (Health technology assessment or hta).tw.
8. comparative effectiveness/
9. comparative effectiveness.tw.
10. (cost-effectiveness adj10 threshold).tw.
11. value for money.tw.
12. or/6-11
13. (Incremental cost-effectiveness ratio or ICER).tw.
14. cost per QALY.tw.
15. exp economic evaluation/
16. or/13-15
17. reimbursement/
18. reimbursement cost analysis/
19. price negotiation/
20. (pricing or purchasing or reimbursement).tw.
21. or/17-20
22. (Value-based adj5 (pricing or purchasing or reimbursement)).tw.
23. pay for performance.tw.
24. risk sharing.tw.
25. or/22-24
26. (value or pricing or price or prices or expenditure* or spending or reimbursement).ti.
27. 5 and 12 and 21
28. 5 and 16 and 21 and 26
29. 5 and 25
30. 27 or 28 or 29
31. limit 30 to yr="1998 -Current" (807 results)

International Pharmaceutical abstracts (Ovid Interface >1998-Jan 30, 2013)

1. (Health technology assessment or hta or comparative effectiveness or value for money or (cost effectiveness adj10 threshold)).tw.
2. (Incremental cost-effectiveness ratio or ICER or cost per qaly or economic evaluation*).tw.
3. (value or pricing or price or prices or expenditure* or spending or reimbursement).ti.
4. (Value-based adj5 (pricing or purchasing or reimbursement)).tw.
5. (pay for performance or risk-sharing).tw.
6. ((1 or 2) and 3) or 4 or 5
7. limit 6 to yr="1998 - 2013" (131 results)

EBM Reviews - HTA, NHS EED, and DARE only (Ovid Interface >1998-Jan 30, 2013)

1. (pharmaceutical* or medicines or medication* or drug*).ti.
2. (Health technology assessment or hta or comparative effectiveness or value for money or (cost effectiveness adj10 threshold)).tw.
3. (Incremental cost-effectiveness ratio or ICER or cost per qaly or economic evaluation*).tw.
4. ((value not "value of information") or pricing or price or prices or expenditure* or spending or reimbursement).ti.
5. (Value-based adj5 (pricing or purchasing or reimbursement)).tw.

6. (pay for performance or risk-sharing).tw.
7. 1 and (((2 or 3) and 4) or 5 or 6)
8. limit 7 to yr="1998 - 2013" (12 results)

Econlit (Ebsco Interface >1998-Jan 30, 2013)
S1: pharmaceutical* or medicines or medication* or drug*
S2: "value-based" OR "pay for performance" OR "risk sharing"
S3: ("Incremental cost-effectiveness ratio" or ICER or "cost per qaly" or "economic evaluation*" or "Health technology assessment" or hta or "comparative effectiveness" or "value for money" or ("cost effectiveness" and threshold)) AND (value or pricing or price or prices or expenditure* or spending or reimbursement)
S4: S1 AND (S2 OR S3) **Limiters** - Published Date from: 19980101-20121231 (119 results)

Academic Search Complete (Ebsco Interface >1998-Jan 30, 2013)
S1: TI (pharma* or medicines or medication* or drug*) OR SU (pharmaceutical* OR medications)
S2: "value-based" OR "pay for performance" OR "risk sharing"
S3: ("Incremental cost-effectiveness ratio" or ICER or "cost per qaly" or "economic evaluation*" or "Health technology assessment" or hta or "comparative effectiveness" or "value for money" or ("cost effectiveness" and threshold)) AND TI(value or pricing or price or prices or expenditure* or spending or reimbursement)
S4: S1 AND (S2 OR S3) **Limiters** - Published Date from: 19980101-20121231 (223 results)

Business Source Complete (Ebsco Interface >1998-Jan 30, 2013)
Same search as Academic Search Complete (123 results)

Health Business Elite & Health Policy Reference Center (Ebsco Interface >1998-Jan 30, 2013)
S1: TI (pharma* or medicines or medication* or drug*) OR SU (pharmaceutical* OR medications OR drug OR drugs)
S2: "value-based" OR "pay for performance" OR "risk sharing"
S3: ("Incremental cost-effectiveness ratio" or ICER or "cost per qaly" or "economic evaluation*" or "Health technology assessment" or hta or "comparative effectiveness" or "value for money" or ("cost effectiveness" and threshold)) AND TI (value or pricing or price or prices or expenditure* or spending or reimbursement)
S4: S1 AND (S2 OR S3) **Limiters** - Published Date from: 19980101-20121231 (282 results)

Web of Science (Web of Knowlege Interface> 1998-Jan 30, 2013)
((TS=((pharma* or medicines or medication* or drug*) AND ("value-based" OR "pay for performance" OR "risk sharing" OR (("Incremental cost-effectiveness ratio" or ICER or "cost per qaly" or "economic evaluation*" or "Health technology assessment" or hta or "comparative effectiveness" or "value for money" or ("cost effectiveness" SAME threshold)) AND (pricing or purchasing OR reimbursement))))) AND TI=(pharma* or "medicines" or medication* or drug* or value-based or "value for money" or pricing or price or prices or expenditure* or spending or reimbursement or "pay for performance" or "risk-sharing"))
Databases=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH
Timespan=1998-01-01 - 2013-02-01 (457 results)

RePEc (EconPapers)
S1: (pharma* or medicines or medication* or drug*) AND ("value-based" OR "pay for performance" OR "risk sharing") among working papers and articles and books & chapters

S2: (pharma* or medicines or medication* or drug*) AND ("Incremental cost-effectiveness ratio" or ICER or "cost per qaly" or "economic evaluation*" or "Health technology assessment" or hta or "comparative effectiveness" or "value for money" or ("cost effectiveness" NEAR threshold)) AND (pricing or expenditure* or reimbursement or purchasing) among working papers and articles and books & chapters
S3: S1 OR S2 (168 results) - Compared to refman file

SSRN (online_
"Value-based pricing" (11 results) No non-duplicate relevant
"value-based purchasing" (6 results) No non-duplicate relevant
"risk-sharing" pharmaceutical (2 results) No non-duplicate relevant
"risk-sharing" drug (4 results) No non-duplicate relevant
"pay for performance" drug (2 results) No non-duplicate relevant
"pay for performance" pharmaceutical (2 results)

Reference id numbers for VCP ref man database
Total #of articles before duplicate removal: 2880
Total after duplicate removal: 1705

	Ref ID numbers
Medline	1-520
Embase	521-1086
IPA	1087 - 1173
EBM	1174-1185
Econlit	1186-1275
Academic Search Complete	1276-1436
Business Source Complete	1437-1507
Health Business Elite & Health Policy Reference Center	1508-1580
Web of Science	1581-1825
REPEC	1826-1838

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