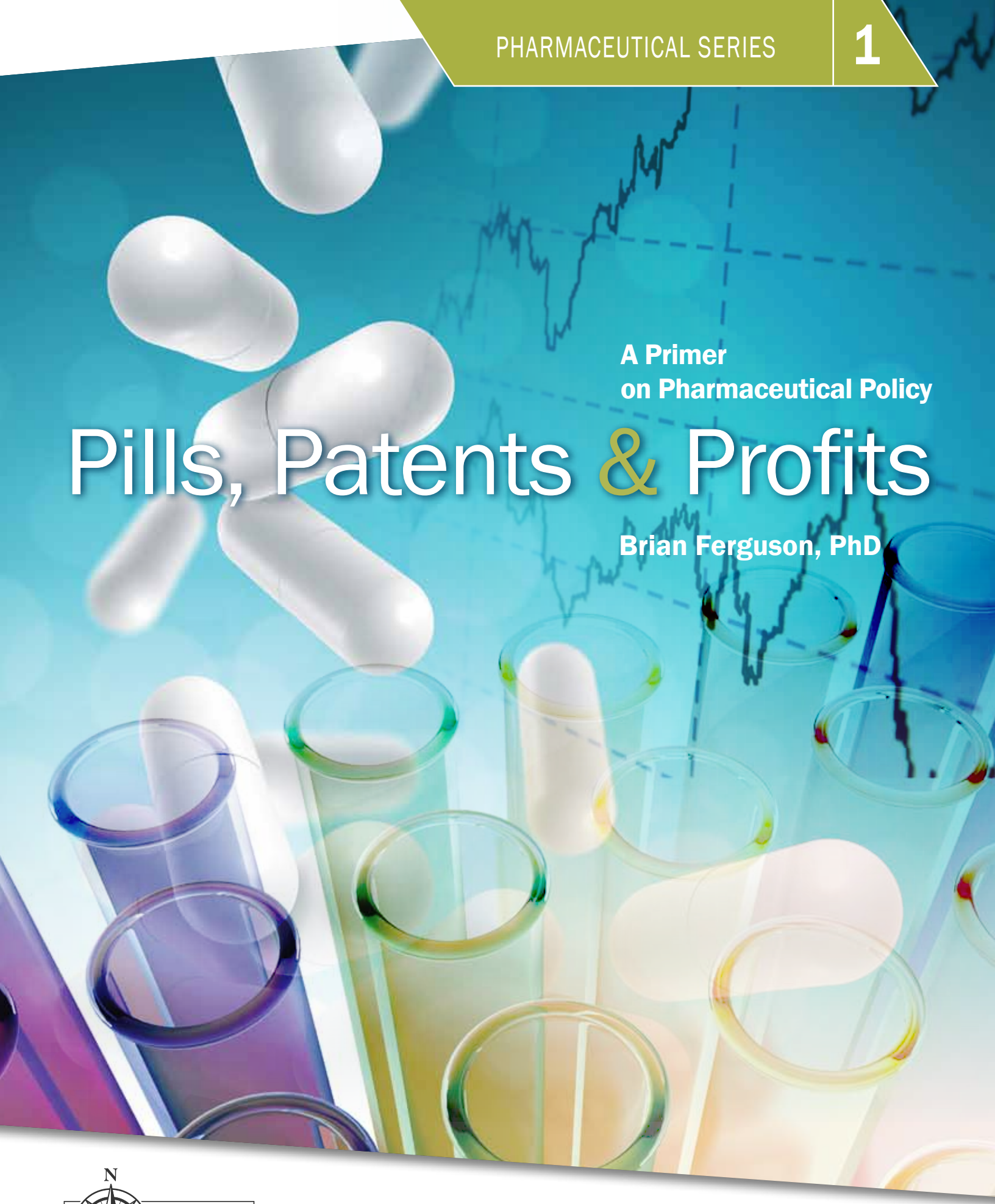
PHARMACEUTICAL SERIES 1



A Primer
on Pharmaceutical Policy

Pills, Patents & Profits

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MLI

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Executive Summary

Pharmaceutical policy is vitally important to health care in Canada because of the high cost of drugs and their increasingly central role in further advances in health care. Unfortunately, discussion of the relevant issues is too often marked by a disregard of elementary economics, documented practical experience and common sense. This paper, preparing the way for a series of more detailed papers, lays out the key areas of pharmaceutical policy and the most important questions that must be asked and answered if we are to have any hope of creating a sensible policy framework for pharmaceutical policy that actually serves the interests of Canadians. Those questions are five in number. This paper explains why they are the right questions to ask, and each subsequent paper in this series will answer one of these five questions.

Question # 1: What is the best way to recognise and protect the intellectual property that underlies new pharmaceutical products while keeping costs under control and ensuring a stream of new products? Patents have been criticized for creating temporary monopolies but also praised for ensuring a decent reward for the often enormous time and effort required to invent medicines that, once invented, are not expensive to manufacture.

Question # 2: Just how much does it really cost to invent new drugs? The pharmaceutical industry is a complex one and some important research takes place in universities at public expense, and measuring the real cost of drug companies' R&D is as complicated as it is essential.

Question #3: How do we strike a balance between rewarding the research work of "brand name" pharmaceutical firms and encouraging "generics" to manufacture more affordable versions of drugs? This question is obviously related both to the real cost of R&D and the appropriateness of patents.

Question #4: How should government agencies approve or reject drugs for sale, determine what constitutes a fair sale price, and decide whether they should be covered by various provincial and territorial public health systems? This question is therefore about the appropriate regulatory machinery to govern the prescription drug industry.

Question #5: How should Canadians be insured against "catastrophic" drug costs? This is the increasingly important question of how to design an insurance program to cover patients whose quality of life depends either on a short course of very expensive medicine or, more often, a very long period of consuming drugs that, even if each dose is moderately priced, amounts to an enormous expenditure over months or years.

In all these areas, we cannot allow compassion to overwhelm judgement. If we want to do good things, we must do things well. And in pharmaceutical as in all other policy, we have no hope of the latter unless we understand what lessons can be drawn from both economics and practical experience and we then apply those lessons intelligently.

Sommaire

La politique pharmaceutique influence de façon cruciale le système de santé au Canada à cause des coûts élevés des médicaments et du rôle de plus en plus incontournable qu'ils jouent dans les améliorations à apporter aux soins. Malheureusement, les débats entourant les enjeux pertinents sont souvent caractérisés par une absence de prise en compte des lois fondamentales de l'économie, de l'expérience pratique documentée et du gros bon sens. Cet article, qui ouvre la voie à une série d'études plus détaillées, présente les principaux domaines de la politique pharmaceutique et les plus importantes questions si l'on souhaite mettre en place un cadre juridique et réglementaire pour le secteur pharmaceutique qui servira vraiment les intérêts des Canadiens.

Question # 1: Quelle est la meilleure façon de reconnaître et de protéger la propriété intellectuelle qui sous-tend la production de nouveaux médicaments, tout en maîtrisant les coûts et en s'assurant de maintenir un flot continu de nouveaux produits ? Les brevets ont été critiqués parce qu'ils créent une situation temporaire de monopole, mais ont aussi été louangés parce qu'ils garantissent une récompense décente pour le temps et les efforts souvent énormes que nécessite la conception de remèdes qui, lorsqu'ils ont été conçus, peuvent être fabriqués à des coûts très modestes.

Question # 2: Combien en coûte-t-il réellement pour concevoir de nouveaux médicaments? L'industrie pharmaceutique est complexe et certaines recherches importantes ont lieu dans les universités grâce à un financement public. Mesurer le coût réel de la R&D des compagnies pharmaceutiques est une démarche compliquée mais essentielle.

Question # 3: Comment trouver un équilibre entre récompenser le travail de recherche des fabricants de médicaments de marque et encourager les fabricants de médicaments génériques à produire des versions moins dispendieuses?

Question # 4: Comment les agences gouvernementales devraient-elles approuver ou rejeter des médicaments pour la vente, déterminer ce qui constitue un juste prix de vente et décider si ces médicaments devraient ou non faire l'objet d'une couverture par les divers systèmes de santé publics provinciaux et territoriaux ? Cette question touche l'organisation réglementaire qui devrait régir le secteur des médicaments obtenus sur ordonnance.

Question # 5: Comment les Canadiens devraient-ils être assurés contre les coûts « catastrophiques » des médicaments ? Il s'agit ici de la question de plus en plus importante qui concerne la mise en place d'un programme d'assurance visant à couvrir des patients dont la qualité de vie dépend soit d'un traitement relativement court nécessitant des médicaments très coûteux ; soit, comme c'est plus souvent le cas, d'un traitement prolongé où, bien que chaque dose soit peu coûteuse, finissent par coûter énormément cher.

Dans tous ces domaines, nous ne pouvons nous permettre de mettre notre jugement de côté sous prétexte qu'il faut faire preuve de compassion. Autant sur le plan de la politique pharmaceutique qu'en ce qui concerne les autres politiques publiques, on ne peut bien faire les choses qu'en acceptant les leçons à tirer à la fois de la science économique et de l'expérience pratique, et en appliquant ces leçons intelligemment.

Introduction

The role of pharmaceuticals in Canadian health care is once again a hot topic. A growing awareness of how much we spend on drugs is fuelling concerns, as are reports of high prices for new drugs for a whole range of hard-to-treat conditions, and limits on access to them. In this debate, governments have heard a wide range of policy options, the vast majority of which are not just wrong but would, if implemented, be positively harmful. Unfortunately the policy options which appeal most to those in government generally turn out to be the ones with the greatest potential to do harm.

In part, this is a consequence of a prevailing mindset among Canadian health policy analysts divorced from sound economic thought. Their world still contains many who appear to be direct intellectual descendants of the advisers who claimed King Canute could command the tides; in their minds, the government has but to command a perfect world and it will appear. And if things don't happen to turn out the way they'd hoped, it's not because their advice was flawed, rather it's because of someone else's evil intentions. In fact, when pharmaceutical (and other) policy fails, it's usually because the designers of the policy have not taken the economics of the sector they're trying to regulate properly into account. Simply put, bad economics leads to bad policy.

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There is good reason to believe that future advances in medical care will depend crucially on advances in pharmacology, and it is becoming more and more difficult to find those advances. Yet the "good old days," in which the objective was first to identify what bug was making people sick, and then to find a compound which would kill the bug without killing the patient, are gone. The process of making policy for the pharmaceutical sector will likely become more difficult and more important at the same time.

What are the key elements of the economics of the pharmaceutical sector? What are their implications for policy design?

A few overarching themes should inform that discussion. The first is that the aim of pharmaceutical policy must be to maximize social benefit. A second is that drug companies, whether research-based or generic, are in business to make profit. Some commentators argue that this represents a fundamental flaw in the system, that having drugs made by for-profit firms drives up their cost. They believe that government could and should take over (or at least tightly regulate) the entire business, and thereby reduce the cost of drugs. They are just plain wrong in that; their solution would be highly damaging to the objective of maximizing social welfare.

No matter what sector we are talking about, we cannot escape the first, most fundamental law of economics – that people respond to incentives. In the case of the pharmaceutical sector, the people in question include not just the owners and managers of pharmaceutical firms but also consumers of pharmaceuticals. Much bad policy derives from ignoring the vital interplay between the incentives that motivate these players.

The primary objective of players on the supply side of the pharmaceutical sector is to maximize profits. This is key to understanding which policies will work and which will not. When we say that profit-maximizing entrepreneurs respond to the incentives they face, we mean that they will evaluate all the options open to them and adopt those yielding the largest profit.

This attribute is not, of course, unique to pharmaceuticals. Companies and individuals who seek to maximize profits by responding intelligently to incentives are the foundation of the dynamic market economy that, since the industrial revolution, has made the West unprecedentedly wealthy. Despite centuries of criticism of this approach, the historical record is clear. This supposedly selfish system creates social benefits no alternative economic and political regime has ever come close to providing. The burden of proof ought therefore to fall on those who criticize the use of this model in medical matters, not those who advocate it.

Unfortunately, the general concept of competition for profits driving benefits to consumers is so poorly understood generally that it is worth reviewing before examining its specific application to pharmaceuticals.

Economist William J. Baumol[1] has argued that there are two broad categories of entrepreneurial activity, productive and unproductive. Productive entrepreneurship involves maximizing profit by producing a product that consumers want to buy, selling it to them at a price they are willing to pay, and innovating as necessary to achieve this goal. Baumol's productive entrepreneurship is in part what Joseph Schumpeter[2] had in mind when he famously referred to "creative destruction" as the essential driving force behind economic growth. In this process, firms that do not respond nimbly to what the public wants are driven out of business by more effective rivals.

But Baumol's analysis continues with an important qualification. Successful profit-seeking by entrepreneurs would be productive, he argued, and would drive economic growth and add to social welfare only when the incentives built into the system within which they were working rewarded service to customers rather than manipulation of the system. Against productive entrepreneurship, Baumol placed unproductive entrepreneurship, activity which economists generally label rent-seeking behaviour.[3] Unproductive entrepreneurship basically involves an individual maximizing his profit not by improving the welfare of society as a whole but by arranging for some of the welfare of others to be transferred to himself, without offering them anything in exchange.

While this approach can involve criminal activity, it overwhelmingly involves persuading government to create laws and regulations that favour one group at the expense of another. In the context of the pharmaceutical sector, the key question is the best source of greater returns. Does it lie in producing new drugs and selling them at prices which consumers (patients) are willing and able to pay? Or is there a greater return from directing resources to lawyers and lobbyists, with the aim of persuading governments to twist the rules of the market until they favour one particular group.

In the context of the pharmaceutical sector, the key question is the best source of greater returns. Does it lie in producing new drugs and selling them at prices which consumers (patients) are willing and able to pay?

Baumol's key argument is that profit-maximizing firms will engage in either productive or unproductive entrepreneurship as their calculations show one or the other to be the more profitable, and that unproductive entrepreneurship will be the preferred activity if governments make it the more profitable. In the latter case, profit-seeking is not in the public interest, but that is the result of too much government involvement in markets, not too little. This point applies to markets generally, and to markets for medical drugs in particular.

Therefore the ultimate goal of any regulation of the pharmaceutical market must be to ensure that productive entrepreneurship is more profitable than is unproductive entrepreneurship.

Therefore the ultimate goal of any regulation of the pharmaceutical market must be to ensure that productive entrepreneurship is more profitable than is unproductive entrepreneurship. To say so does not dispose of a host of complex practical difficulties. But it does indicate the essential path to follow in an effort to solve them.

In this and future papers in this series, we will follow that path through the main areas of policy concern in the pharmaceutical sector and set out the economics of different aspects of it. This paper presents an overview of a range of these issues. Each of these particular topics merits papers of its own, but throughout these forthcoming discussions certain key ideas will pop up repeatedly. While each paper will have a different focus, the themes are not neatly separable. Each paper will make suggestions about policy design that follow from the analysis.

The aim is clarity about the effects of current policy design for drug-making and drug-regulating processes. What are the ultimate price consequences for consumers? What suggestions for redesign might improve that bottom line?

Pharmaceutical Policy Themes

Patents

In the effort to reward productive entrepreneurship in pharmaceuticals and not the unproductive kind, the first question is how best to reward innovation. Because an enormous share of the cost of "making" a drug is consumed in inventing and testing it, in this regard the pharmaceutical industry, though not unique, is unusual.

On the whole our system of property rights, which includes limited-term patents for inventors, has proven itself a superb instrument for creating wealth across virtually the whole range of economic activities. But it often strikes observers as unreasonable that drug companies charge dollars for pills whose physical manufacture costs pennies. Of course it is also expensive to create improvements in, say, automobiles. But it remains clear that when consumers pay thousands of dollars for a car, most of that price rewards the labour, physical plant and raw materials necessary to assemble the actual vehicle. With pharmaceuticals (and also things like computer software and, nowadays, music and video), the situation is very different.

As a result, patents are controversial in these areas, especially in medicine. It is widely believed that patents give drug companies monopolies over drugs, that those monopolies allow the companies to charge unconscionable prices, and that in the process they deny large segments of the population access to those drugs. This viewpoint contains a kernel of truth, but only a kernel.

A number of misunderstandings surround the issue of patents, and in fact their role is controversial in economics. While most economists support the notion that property rights should apply to intellectual property (IP) in some form or another, a minority ar-

gues that these rights should be eliminated altogether. The most cogent arguments for this position are probably made by David K. Levine of Washington University in St. Louis.[4]

Virtually everyone agrees that patents do create a temporary monopoly and virtually everyone agrees that monopolies are, generally speaking, bad for society. Monopolies normally reduce the general welfare because they uncouple private gain from public welfare and allow the monopolist to profit at the expense of consumers in a way firms in competitive markets cannot.

If a monopolist reduces his own production, he or she reduces total production and pushes up the price and therefore the monopolist's profits, while firms with rivals simply lose sales if they reduce production. On the other hand, if a competitive firm finds a way to increase production, it can draw customers away from its rivals; a monopolist who increases production only pushes down the total price and therefore his profit per sale.[5]

This analysis, however, assumes that the product being monopolized already exists. It risks begging the question of how to encourage the creative activity which leads to the existence of the commodity in the first place.

Virtually everyone also agrees that some way must be found to reward successful inventors for their time and effort, especially given the fact that many inventors do not succeed. Patents are a proven way of doing so. But other ways besides patents exist for rewarding innovation and their merits and drawbacks deserve attention, especially in the context of pharmaceuticals.

The most important question regarding patents is whether the monopoly position that they create for the patent holder encourages or discourages invention. The pro-patent side is that the expectation of earning a return on inventive activity stimulates that activity; by protecting the inventor's IP rights, patents ensure that he has at least a chance of earning enough revenue to cover his costs and perhaps make a profit (depending on how the market receives his invention).

Without patent protection, according to this argument, inventions brought to market could be copied by anyone who could lay their hands on them. The copies could be sold at a price that does not have to cover the costs of research and development (R&D). Only fools and the independently wealthy would devote time and effort to devising improvements for the benefit of mankind.

Without patent protection... inventions brought to market could be copied by anyone who could lay their hands on them. The copies could be sold at a price that does not have to cover the costs of research and development (R&D).

In the case of pharmaceuticals in particular, to take drugs apart and determine what's in them – to "reverse engineer" them – is relatively easy. Without patent protection for the firm that did the original research, generic manufacturers would be able to flood the market with copies very soon after the original drug was released. That would drive prices down to a point where no one could afford to do significant research. The result would be a host of copycats, nothing to copy, and no advances in medicine for patients.

The anti-patent side makes two key arguments. One is that the incentive effects of patents on research are exaggerated. The other is that patent holders game their protection as a form of unproductive entrepreneurship, apply patents as widely as possible, and extend them as long as possible, in an effort to keep competitors out of the market. That allows the first firm producing a drug to milk their monopoly position for all it's worth. This gaming is all the more effective when a number of patents cover the component

aspects of a final product, so that violation of any one of those patents can block a competitor's access to the market. As a consequence, invention and drug development are retarded rather than encouraged by patents.

Again, this argument is not unique to the pharmaceutical sector. It goes right back to the early days of the modern patent system, during the industrial revolution that unleashed a never-ending stream of improved products and production techniques.

It applies most notably to the case of James Watt's patent on his improvements to the steam engine, which made it much more efficient than and, more importantly, fundamentally different from Thomas Newcomen's steam engine, already in use pumping water out of mines.[6] Watt's work on the steam engine was hampered, and on occasion put aside for several years, by his need to make a living. It only proceeded with any regularity when he obtained a patent in 1768, the strength of which persuaded John Roebuck to finance Watt's work.

As the initial patent was nearing expiry, Roebuck went bankrupt in a financial crash. Matthew Boulton was persuaded to buy out Roebuck's share of Watt's patent[7] but, because the patent was nearing expiry, he didn't formally come on board. He waited until 1775, when Parliament extended Watt's patent for another 25 years.[8]

At the time of expiry of the original patent, Watt still didn't have a commercially feasible steam engine. Had the patent not been extended, Boulton would not have financed him and he would probably have had to stop work on the engine. As it was, even granted the patent extension Boulton was gambling that Watt would be able to translate his models into a working, profitable piece of industrial machinery.

In the debate dealing with the extension of Watt's patent, Edmund Burke argued against it, on the grounds that patents created monopoly and stifled competing invention. But Parliament was convinced by the argument that, if he were to continue his work, Watt needed a reasonable expectation of being able to recover his costs of development. This would only be possible if he had a patent on the final product.

One of the hottest debates in the literature on pharmaceutical policy involves just what the costs of pharmaceutical innovation are and who actually bears them.

Critics of Watt[9] argue that, once he had the patent extension and a commercially feasible steam engine, he devoted most of his time to blocking entry by other engineers who were making improvements to his design. In particular, he blocked the development of high-pressure steam engines, an action which delayed the progress of the industrial revolution. Industrial steam power – steamboats, steam power in factories, ultimately steam locomotives – depended on high-pressure engines, not the low-pressure engine which Watt had designed to pump water out of mines more efficiently.

At least to date, defenders of the patent system seem to have made the stronger historical case. But the argument is by no means over. All of the issues raised on both sides in the 18th-century debate about Watt's patent are back today in the context of pharmaceutical patents. And a variety of alternative approaches – substitutes for patents – have been proposed to encourage research activity.

Costs of Drug Development

The high cost of developing drugs is obviously key to the question of how much patent protection pharmaceutical companies need in order to cover research overheads. It is surprising, though, that one of the hottest debates in the literature on pharmaceutical policy involves just what those costs are and who actually bears them.

The most commonly heard figure is the claim that bringing a new drug to market costs on the order of US$800 million. Some policy writers, however, reject this estimate, on the grounds that the pharmaceutical sector funds the university research centre which generated the figure and that it therefore cannot be trusted. Since other researchers have come up with numbers in the same ballpark, this *ad hominem* attack is not a particularly strong intellectual position.

Some analysts argue the substance of the question, and claim that the calculation is in fact wrong. They dispute the assumptions used to generate the $800-million figure, particularly the treatment of the cost of using retained earnings in the pharmaceutical sector; this leads into the question of the treatment of one type of what economists term opportunity costs (as distinct from those types which are easily observed on account books). Even so, these arguments tend to point to an estimate closer to the order of US$100–200 million, still a fairly hefty figure.

Another important issue is whether the current, patent-based system of rewarding innovation directs the lines of drug research into socially undesirable byways.

Who actually bears the costs of research? (This is not exactly the same question as who pays for it; significant non-monetary costs, including forgone opportunities for treatment, are also real.) Some analysts argue that government funding pays for the most important research, and that drug companies simply run clinical trials, claim that they've done research, and charge outrageous prices for drugs which someone else developed. This argument is false, but nonetheless one which a lot of people are predisposed to believe.

Closely related to this last argument is one which focuses on drug company claims about the riskiness of drug development, and the claim that drug companies need high returns to compensate for that risk. Beyond the assertion that the pharmaceutical industry doesn't really do any research, critics say that a look at rates of return for drug companies over time indicates very little risk in their income streams, and therefore nothing to compensate them for. As this issue is raised by some very thoughtful critics of the current structure of the industry, it deserves to be examined in some detail.

In large part, this set of issues comes down to the question of how to measure R&D costs in the pharmaceutical sector. It turns out to be more complicated than simply looking at each year's reported expenditure on this function. We also need to look carefully at the sources of R&D costs, at how they have changed over time, and at the degree of risk associated with the various stages in the drug-development process.

We need also to look at the evidence on the relationship between the drug industry and R&D activity. Related to this latter point is the often-heard claim that research-based pharmaceutical companies spend more on advertising than they do on drug development. Again, in this area we have to start by sorting out what is actually in the numbers (the figure most commonly cited as advertising expenditure, for example, is actually for administration and marketing combined), then ask what we can say about optimal R&D spending and how the drug industry compares with other industries in that regard. This necessarily links back to the question of patents, and also to the question of why generic drug companies do not, as a rule, become research-based companies.

Another important issue is whether the current, patent-based system of rewarding innovation directs the lines of drug research into socially undesirable byways. Pharmaceutical firms are often criticized for focusing on treatments for lifestyle-

based diseases found primarily in developed countries and ignoring life-threatening diseases which are endemic in poorer countries.[10]

The argument is also made that drug companies neglect (or, in more extreme versions of the argument, suppress) developments which might lead to cures for chronic diseases, including cancer. This position holds that companies can make more profit from patients who pay on a continuous basis than from a one-shot expenditure associated with preventing or curing cancer. Related to this argument is the claim that drug companies hide evidence of harmful side-effects from drugs in order to obtain regulatory approval to bring them to market: that they don't mind killing people so long as they can make a profit. These arguments also turn out to be weak but, as they resonate with a lot of people, they require serious attention.[11]

Finally, under this general heading comes the question of so-called "me-too" drugs. The argument is often made that drug companies should not be permitted to develop their own versions of drugs which their competitors have brought to market, but rather should be forced to concentrate on developing totally new drugs. This argument is usually framed along the lines of "How many versions of drug X do we really need?" Wouldn't social welfare be greater if we had fewer drugs for each condition, but drugs for more conditions?

It will not do to assume that generic companies are more virtuous than "big pharma" because they sell medicine more cheaply. The question is whether their entrepreneurship is productive or whether they are free-riding on the honest toil of others.

Economists generally argue that competition is good for consumers, in that it drives down prices. Drug-industry critics generally respond that this logic does not apply in the drug sector and that, even if it did, the monopoly power created by limiting the number of entrants in each field should be countered by price-setting regulation.

In addition to looking at the evidence whether price competition works in the pharmaceutical sector, we need to consider what me-too drugs really are, how exactly they mimic existing drugs, and how they fit into the pharmaceutical armamentarium beyond their role as devices to introduce competition. We also must look at how the concept of personalized medicine affects our understanding of me-too drugs.

Brand Name vs. Generic Drug Companies

One of the most interesting areas of pharmaceutical economics involves the relationship between research-based and generic drug manufacturers, the quintessential producers of me-too drugs.

The starting point for any assessment must be that both types of drug companies are in business to make a profit. But, by the nature of the rules under which they operate, their profit-maximizing strategies differ. Just as research-based firms have a self-interest in strong IP protection, generic manufacturers have a self-interest in weak IP protection. Each seeks to maximize its profits, but the question for policy-makers is what balance between the two serves the interests of consumers.

As with so much in the pharmaceutical policy field, part of the analysis of this question has to come back to patents. What, for example, is the optimal length of life of a drug patent, and do "big pharma" companies get appropriate recognition for their contribution to the success of the generics sector? It will not do, as too often happens in Canada, to assume implicitly that generic companies are more virtuous than "big pharma" companies because they sell medicine more cheaply. The question is whether their entrepreneurship is productive or whether they are free-riding on the honest toil of others.

In this area, the question of productive versus unproductive entrepreneurship looms large. We must consider the extraordinary efforts that patent-holding drug companies make to extend the life of their patents and to delay generic entry. Even firm supporters of the research-based sector are given pause by the number of resources devoted to the lawyers and lobbyists paid to fight these battles. We should consider alternative systems which would make it more difficult for patent holders to "evergreen" (i.e. to extend through rent-seeking activity) their patents. Finally, we will also consider the place of generic manufacturers in the world drug market, by looking at their activities in less developed as well as developed countries.

National Policy Bodies

It is not enough that a drug be invented. Regulators must also be persuaded to approve it as effective, safe, and suitable for sale. In Canada, they must also determine a sale price and suggest whether a drug should be covered by various provincial health plans. It is possible for government agencies to make mistakes; they may approve a drug that should not be for sale or they may reject one that should.

Regulators have difficult decisions to make and it is foolish to assume that agents of the state automatically and transparently make wise decisions in the public interest.

In both cases, patients and the public pay a heavy price, though not a monetary one. Regulators have difficult decisions to make and it is foolish to assume that agents of the state automatically and transparently make wise decisions in the public interest. It is therefore an important task of pharmaceutical policy to consider the incentives facing regulators as well as drug firms, and ask whether the rules under which they operate tend to reward excessive caution, excessive risk, political judgements rather than scientific ones, or something else other than sound medical practice.

A good starting point is to examine the process by which drugs receive approval for sale in Canada, and what factors are involved in the decision about whether a drug should be covered under one or more of a range of government drug programs. This requires that we consider the roles of three agencies: Health Canada, which makes the determination about whether a drug should receive marketing approval in Canada at all, the Patent Medicine Price Review Board, which regulates the prices of patented drugs, and the Common Drug Review, which provides guidance to the provinces on whether a drug should be covered under public plans.

Most developed countries have agencies which perform similar functions, to varying degrees, although the mechanisms adopted may differ. In a Canadian context, it makes sense to consider these three under a single heading because they represent three nationwide regulatory functions.

With respect to the first point, approval for use, Health Canada's role, through the Therapeutic Products Directorate (TPD), is similar to that of the Food and Drug Administration (FDA) in the United States. It involves a review of evidence from clinical trials on the safety and efficacy of proposed new drugs. A number of is-

sues have been raised in recent years about the whole process by which drugs are reviewed and about the Canadian process in particular.

With regard to the TPD process in particular, the main question has been the time it takes for a drug to receive approval for sale in Canada, and whether the process has become so slow as to delay unnecessarily the release of valuable drugs. The broader issue, though, is the logic of the approval process itself. Here questions have been raised about matters such as the standard against which a new drug is compared: should the trial comparator be a placebo or an existing drug for treating the same condition, when one is available?

Another issue is the question of who should make the judgment about whether the pluses of a new drug outweigh the minuses. All drugs have side effects, at least for some patients, and some of those side effects can be severe. In many cases, a drug which is beneficial in treating one disease can increase the risk of the patient's dying from another.

The basic question here is whether the patient or the regulator should be the one to decide whether the risk is worth taking. In some recent cases, the only drug found to be effective in treating extremely painful conditions in some patients carries the price of an increased risk of death from its side effects. Drug regulators have tended to pull those drugs from the market, while patients have demanded that they remain available.

Regulators tend to argue that patients do not have the information necessary to make judgments about whether a drug improves a patient's well-being. Patients argue that regulators are being paternalistic and are using a different measure of the patient's well-being than the patients themselves use. Interestingly, one of the most commonly used methods of judging the value of a treatment involves conducting surveys that ask how much of an increased risk of death patients would be willing to accept as the price of a cure for their condition. But those same patients who are trusted to provide answers to the survey questions on risk trade-offs are not allowed to make the final judgment in real life.

One of the most commonly used methods of judging the value of a treatment involves surveys that ask how much of an increased risk of death patients would be willing to accept as the price of a cure for their condition.

Related to this is the question of whether clinical trials should be required for drugs intended to treat fatal conditions for which no treatment currently exists. Regulators argue that clinical trials are necessary if we are to establish whether a new drug actually works at all. Their critics argue that it is unethical to deny patients the possibility of a benefit from a new drug when no treatment presently exists.

In part, this issue comes down to the way medical schools teach statistics. An argument can be made that many researchers overestimate the value of running what are known as double-blind, randomized clinical trials for no better reason than that they have not been given a proper exposure to the statistical principles which underlie alternative ways of evaluating the effectiveness of new drugs. We will consider this argument without getting too bogged down in the mathematics of the statistical argument.

On the second regulatory point, maximum price, the Patent Medicine Price Review Board (PMPRB) is the federal agency responsible for judging whether the price which a manufacturer proposes to set on a drug meets certain criteria of reasonableness, and should be approved. It is widely believed that the operations of the PMPRB are the reason why prescription drugs are cheaper in Canada than in the United States (although you can find analysts who make strong arguments the other way). Certainly a lot of American politicians believe that the PMPRB process is effective; that's why many

of them were pressing the FDA a few years ago to allow large-scale cross-border shopping for prescription drugs.

The fact that the American media more recently contains much less coverage about drug re-importation does raise another issue. Did the price differences really just reflect the fact that back then the Canadian dollar was worth about US$0.60, whereas today it is worth close to US$1.00? The debate at the time begged the question of why the US, if it really believed that the PMPRB process was valuable and effective, didn't simply introduce price controls of its own.

Whatever the answer to those questions, we will look at the evidence on the effectiveness of the PMPRB process and also on the mechanisms used by other countries to regulate the prices of prescription drugs. We will consider not just whether any of these mechanisms actually restrain drug-price inflation, but also whether they have unintended economic side-effects, particularly in their impact on drug companies' decisions about when or even whether to enter a particular country's pharmaceutical market.

Finally, given the structure of the Canadian public health care system, we will consider Canada's Common Drug Review process. The idea behind the CDR is simply that all of the provinces should have the same information available to them when they are deciding whether to cover a drug under one of their programs, and that that information should be collected as carefully and reliably as possible. The CDR process has rough parallels in other countries, most notably the operations of the National Institute for Clinical Evaluation[12] (NICE) in the UK, although with a key difference.

Regulators tend to argue that patients do not have the information necessary to make judgments about whether a drug improves a patient's well-being. Patients argue that regulators are being paternalistic and are using a different measure of the patient's well-being than the patients themselves use.

NICE has had the power to say "yea" or "nay" as to whether the National Health Service will cover a drug, whereas the CDR is strictly an information agency. The fact that its role is to provide information and recommendations but not to make final decisions about coverage has not shielded the CDR from criticisms from all sides – some from people who think that a positive CDR recommendation should impel a province to pay for a drug and others from people, drug companies and patients both, who object to a negative CDR recommendation.

In addition to considering the logic of the CDR process, we will also look at an issue that has become important in the UK, although not yet in Canada. That is what happens when courts intervene in the drug-review process. British courts have shown themselves willing to overturn and even pre-empt NICE decisions. While Canadian courts have, to this point, been less inclined to impose their judgment in this area of public administration, what has been happening in other countries raises interesting questions about the differences between different agencies' interpretation of social welfare.

A key issue relates to the broad question of regulatory approval in Canada. Do the CDR, the PMPRB, and the process by which provincial governments decide which drugs to cover under their various public programs foster unproductive entrepreneurship on the part of drug companies? Basically, do they encourage drug companies to try and determine the highest possible price which they can get past the regulators?

Interventionists assume that government regulation keeps prices down, but it is widely agreed that, in Canada, the various provincial regulations about the pricing of generic drugs are a key reason that generic drugs are more expensive in Canada than in the U.S. We need to consider whether the national bodies have a similar effect.

Catastrophic Drug Insurance

A final area of national policy concern is the matter of "catastrophic" drug insurance. The term generally suggests the dire situation of someone faced with a life-or-death choice whether to take a very expensive drug to treat an acute illness. From the perspective of the individual, though, the need to take moderately priced drugs in large quantities over a long time to treat a chronic illness may well seem a catastrophic expense, and is certainly one which most of us would like the option of insuring against.

At a technical level, the issue is more one of insurance design than of pharmaceutical economics. But the fact that so many drugs are being developed to treat chronic illnesses, and the possibility that drug treatment will turn acute illnesses into chronic ones (as has happened in the case of treatment for AIDS, for example), merits its inclusion in a series on the economics of pharmaceuticals.

We will look at the nature of insurance plans, both for-profit and mutual insurance systems, and discuss why chronic illness presents such a challenge. We will also look at efforts made in other countries, Australia and Germany for example, to tackle the problem of chronic illness, and the related question of guaranteed lifetime renewability of health insurance (which simply means ways of getting around the problem of pre-existing conditions).

The Canadian health care system is under unprecedented financial and demographic strain.

Conclusion

Even if we set aside the cloud of emotion and invective which has come to surround the Canadian debate on pharmaceutical policy, another major obstacle to meaningful debate emerges from the fray. The economics of the pharmaceutical sector differ in many ways from the models set out in textbooks. The problem is not, as some critics have suggested, that standard economics principles do not apply, but that the standard models have to be adapted to fit the particular circumstances of the pharmaceutical industry. When we do that, it becomes clear that economic analysis does apply; regrettably, it also becomes clear that this fact by itself does not make policy design easy.

The Canadian health care system is under unprecedented financial and demographic strain, and advances in medical care are increasingly dependent upon advances in pharmacology. That makes improvement in the design of national drug policy especially important. The task will require policy-makers, regulators and citizens to think about the matter in sound economic terms. That is the goal of this overview, and the papers in this series that will follow.

Endnotes

1 Baumol, William J. (1990): "Entrepreneurship: Productive, Unproductive and Destructive" *Journal of Political Economy* 98(5), October, 893-921

2 Joseph Schumpeter (1942): *Capitalism, Socialism and Democracy* Harper and Row.

3 It is an unfortunate term from the point of view of public debate because it has nothing to do with "rent" in the popular sense of what people pay to use a property they do not own.

4 See, for example Michele Boldrin and David K. Levine (2008) *Against Intellectual Monopoly* Cambridge University Press.

5 The technical economic term is that firms in competitive markets are "price takers" while monopolists are "price makers"; and as a result of the incentives they face (rather than any supposed character defects) the monopolist behaves in ways harmful to the welfare of fellow citizens. "Price takers" would of course prefer to be "Price Makers".

6 Thomas Newcomen himself had to go into partnership with Thomas Savery, who had a wide-ranging patent on a device to pump water by means of fire. Savery's device may well have been a copy of an idea published (but not patented) by Edward Somerset, Marquess of Worcester.

7 Both Roebuck and, later, Boulton owned more of Watt's patent than Watt did.

8 In Watt's day, each patent required an individual Act of Parliament.

9 On this debate see Michele Boldrin and David K. Levine (2009): "Does Intellectual Monopoly Help Innovation", *Review of Law and Economics* 5(3) article 2, and George Selgin and John L. Turner (2009): "Watt Again? Boldrin and Levine Still Exaggerate the Adverse Effect of Patents on the Progress of Steam Power", *Review of Law and Economics* 5(3) article 7.

10 Again, this issue links to the issue of patent protection, since it is often argued that developed-country drug companies use patents to deny poorer countries access to critical medication.

11 As a starting point on the second of the two, consider the following question: which is going to yield a better revenue stream, Vioxx with harmful side-effects or Celebrex without?

12 This was NICE's original name, and is still the best name if you think that its name should tell you what an agency actually does.

About the Author

Brian Ferguson is Professor of Economics at the University of Guelph, where he has taught microeconomic theory, health economics, statistics and econometrics, advanced mathematical economics, the history of economic thought and business history and researches a range of issues in health economics and policy. He is also a member of the University of Guelph appeals committee, past chair of the University of Guelph College of Management and Economics Library Committee, a member of the editorial board of *Substance Use and Misuse* and a Fellow in Health Policy at the Atlantic Institute for Market Studies. He has also worked at Health Canada and been an academic visitor at the Kansas Health Institute and a visiting fellow in the Department of Economics at Australian National University, and served as chair of the University of Guelph Research Ethics Board from 2007-2010.

He has published in the major academic journals in health economics, testified before the Senate Committee on Social Affairs, Science and Technology on health issues and is co-author with G.C. Lim of *Introduction to Dynamic Economic Models* (Manchester University Press, 1998) and *Dynamic Economic Models in Discrete Time* (Routledge, London and New York, 2003).

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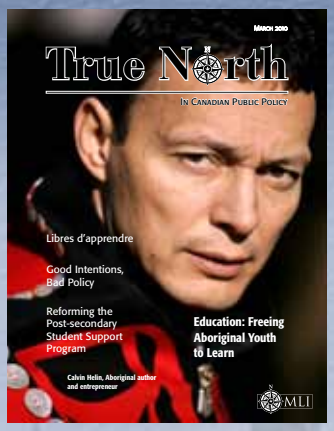

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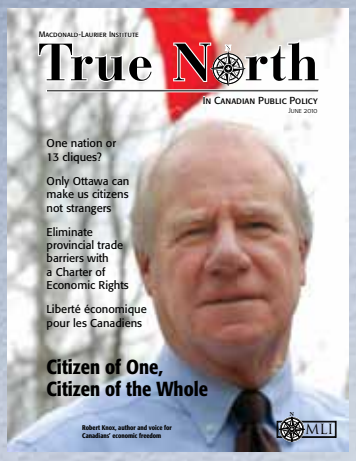

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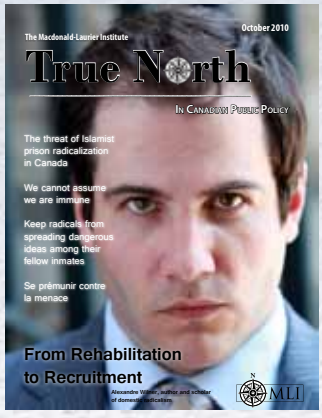

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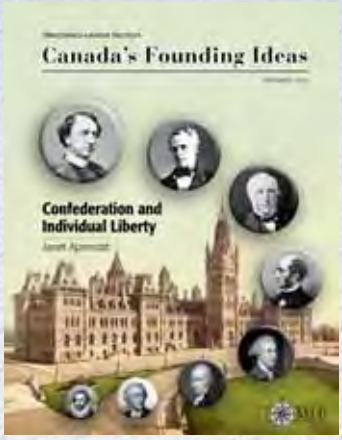

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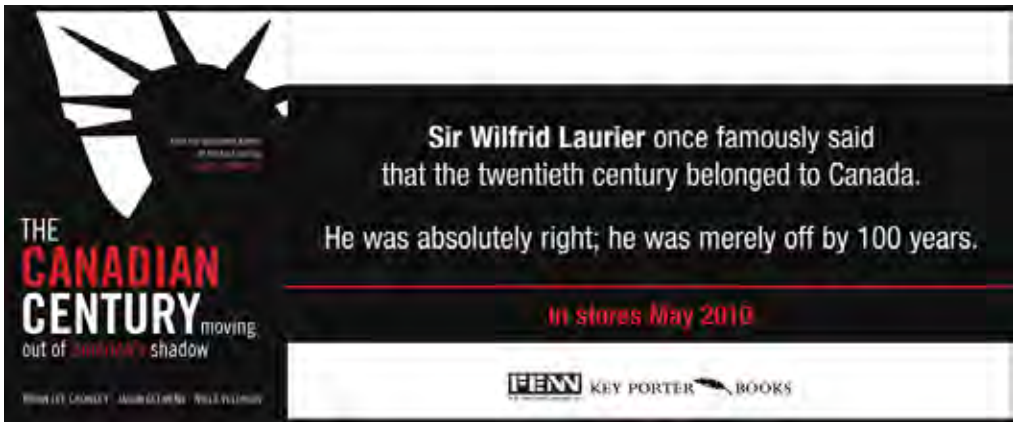

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