

Preliminary- Comments Welcome

Price Controls and the Evolution of Pharmaceutical Markets

By

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Abstract

Many countries have essentially nationalized their health care systems. One byproduct of this is that pharmaceutical prices and volumes (utilization) are the subjects of explicit government directives and decisions, rather than the outcome of a market process. This paper synthesizes the substantial economic literature that has emerged that has studied the impact of these factors. Evidence suggests that drug prices and volumes are significantly lower outside the U.S. than they are inside the U.S. There is also evidence that these lower volumes are associated with trade factors. Domestic generic manufacturers often control a large share of the domestic generic market, often leading to an inefficient use of limited healthcare resources by governments with price controlled markets. The paper provides commentary on the literature that tracks the impact of lower revenue pharmaceutical research. That literature suggests that revenue reductions lead to reduced research and development activity and less drug discovery. The final section evaluates the impact of reduced drug discovery on health costs and outcomes, highlighting key evidence that the foreign price controls have significant human and economic costs associated with them.

I. Introduction

Economists have often found that attempts to centrally control markets lead to wildly suboptimal outcomes. Central planners have yet to discover an information revelation mechanism that can rival that of price in a free market. The world pharmaceutical industry is perhaps the most striking current test of this observation. Intrusive and aggressive price regulation by governments exists in almost every developed country other than the United States. The large difference in policies affords researchers the opportunity to investigate the impact of price controls on the evolution and organization of markets.

The pharmaceutical industry is an especially interesting test case for price controls because so much of the profit and improvements in social welfare associated with the industry depends on the success of risky research and development efforts. Recent examples of pharmaceutical innovation are impressive, with advances in medical oncology providing cancer patients with increased survival rates¹ and new cholesterol-lowering treatments providing encouraging outcomes for patients with heart disease.² While the science and research behind these innovations is complex, the mechanism by which they were developed is not random. In the context of pharmaceutical advancement, investment in research and development drives innovation.

Accordingly, one might expect that government intervention in pharmaceutical markets could have an unusually large impact on the pharmaceutical industry because of the extraordinary dynamism associated with rapid technological change. As will be documented

¹ For example, the U.S. Center for Disease Control recently reported a dramatic increase in cancer survivorship,(link: <http://www.cdc.gov/cancer/survivorship/#science>).

² Lewin Group (2000)

extensively below, the evidence suggests that the different regulatory climates have led to massive changes in the world pharmaceutical industry. Conceptually, one could think of the U.S. as an island ecosystem that has survived the ravages of some global ecological disaster, while Europe has lost the leadership it had just a few years ago.

Since research leads to new discoveries, the impact of price controls on the health of the world's citizens is likely significant. Though many innovative drugs, particularly those under patent, are more expensive than the older drugs they replace, the improved health outcomes they provide often create economic benefits that significantly outweigh the increased drug cost. A large and growing economics literature tracks the myriad impacts that these price controls have on the behavior of U.S. firms and patients, as well as the behavior of foreign governments, foreign doctors, and foreign patients.

The purpose of this short paper is to review the most important findings in this large literature. The next section of the paper begins by detailing price control policies employed by non- U.S. countries (I shall henceforth call them PCC's for "Price Control Countries") and provides specific examples of such mechanisms in practice. The section concludes by tracking the effect of these controls on actual prices, which are found to be significantly lower in PCC countries. Lower prices, of course, do not necessarily lead to lower revenues, since quantities used might be higher in response to these lower prices. The third section provides a discussion of the pharmaceutical usage in PCCs, and documents that it too, is generally below the level found in the U.S. In order to lay the background for understanding the theoretical effects of lower revenues, section four provides a discussion of the economics of drug discovery, with an emphasis on establishing the optimal behavior of a pharmaceutical firm in a world with many countries. The next section relates this optimal behavior to practice, with particular focus on the

relationship between revenue and research and development expenditure, which ultimately drives drug development. Lower revenues will, the evidence suggest, lead to less drug development. Understanding the impact of reduced drug development requires a sense of the efficacy and utility of new drugs. The fifth section of this paper reviews the substantial literature attributing health and cost benefits to drug development and innovation. The final section concludes.

II. How Do Price Controls Work?

Across the Organisation for Economic Co-operation and Development (OECD) there exists a broad and highly diverse range of mechanisms employed by countries to control the cost of pharmaceuticals.³ While the United States employs mostly market-oriented institutions to determine prices and value, other OECD governments tend to intervene more directly in the pharmaceutical industry to control costs. With state-run national health systems, these governments can effectively act like monopoly buyers (monopsonists) to reduce pharmaceutical prices to their national health budgets by implementing pharmaceutical price controls.

These interventions can be grouped broadly into three main categories: price controls, volume controls, and spending controls. PCC countries each use these measures with varying degree, with countries using individual combinations of these interventions. Taken together, pharmaceutical price control measures in PCCs can be described as comprehensive in so far as each category of intervention— price, volume, or spending — can be directed to affecting either the supply-side or the demand-side of the pharmaceutical market. It is also important to note

³ The primary source for this review is a 1999 Boston Consulting Group review.

from Silverstein, Brouwers and Wolff (2004) that the application of the controls described below is actually *increasing*. The following is an overview of these price control measures in PCCs grouped by method, including a review of their net price effect.

Supply- Side Interventions

Many PCCs employ price control mechanisms to regulate the supply-side of the pharmaceutical industry. While there are a number of mechanisms that PCCs use to accomplish this, there are a few important examples that highlight the level of government intervention in the market. One of the most pointed forms of such supply-side price control is the use of direct price control, wherein governments establish price ceilings at which manufacturers may sell pharmaceuticals.

Menon (2001) describes such a mechanism in Canada, wherein the Patented Medicine Prices Review Board (PMPRB) regulates prices of patented drugs by ensuring that prices are not “excessive,” which is determined by set guidelines. Some examples of the government’s price strictures are that a drug’s price may not increase more than the Consumer Price Index and the price of new, patented drugs must not exceed the price of the costliest drug already on the market in the same therapeutic class. Companies that are found to be pricing drugs at what the PMPRB deems “excessive” must either take action to voluntarily account for excess revenues, be ordered by the Board to make such amends, which could include mandated price reductions for the drug deemed excessive, forced settlements with the government reflecting revenues garnered by excessive prices, or the reduction in price of another patented drug by the same manufacturer.

Another form of cap on the supply side is accomplished by reducing the volume of drugs sold. Perhaps the most common mechanism of supply-side volume control is by negotiated price-volume agreements. These are contracts, or typically components of larger pricing agreements,

that stipulate allowable volume sales for drugs, based upon sales forecasts supplied by manufacturers. If suppliers exceed the prescribed volumes, prices are reduced to compensate for the volume overage. This mechanism is employed with increasing frequency, with countries that make use of price-volume agreements including Australia, Austria, and France.⁴

Spending controls are implemented to further limit overall pharmaceutical costs to national health services in conjunction with other price control mechanisms. The most striking example of this policy in practice is in the United Kingdom, wherein the government, through the Pharmaceutical Price Regulation Scheme, regulates the return to capital investment made by pharmaceutical companies. According to the Association of the British Pharmaceutical Industry⁵, which negotiates with the Department of Health on behalf of the industry to formulate the PPRS, British pharmaceutical companies are subject to profit caps. Any overage must then be reduced by price cuts, repaying the excess profit directly to the National Health Service, or by restricting or delaying any previously negotiated future price increases.

Demand-Side Interventions

Governments may also apply spending restrictions on the demand side of the market. These policies are typically in the form of budgetary restrictions on physicians, either in terms of total health care spending or more narrowly tailored prescription budgets, whereby doctors have a fixed budget for health care (if a broad based budget) or pharmaceutical expenditure (if budgetary considerations are restricted to prescription costs). It is important to note that if doctors exceed their respective budget, they will not cease filing prescriptions, but can be faced with penalties, or conversely if they under utilize their budget, they may be eligible for rewards,

⁴ Kanavos, Panos, “Overview Of Pharmaceutical Pricing And Reimbursement Regulation in Europe,” LSE Health and Social Care, 2001

⁵ http://www.abpi.org.uk/publications/publication_details/pprs/section5.asp

according to Kanavos (2001). Countries using physician budgets include the United Kingdom and Germany.

OECD governments also use price controls to intervene on the demand side of the pharmaceutical market. One of the most common forms of this mechanism is the requirement of patient co-payment on prescription sales. With the objective of lowering national health care expenditures, PCCs use co-payments to pass some costs on to patients. It is important to note however, that PCC co-payment schemes are part of an overall price control apparatus employed by PCC governments. Thus an efficient co-payment system could obviate other more aggressive use of price control mechanisms in the same system to achieve lower national pharmaceutical expenditures. PCC co-payment systems however can be heavily laden with exceptions, caveats, and other regulations that ultimately diminish the utility of co-payments in diminishing national pharmaceutical expenditures. Indeed, while the U.S. health care system makes use of co-payments, the level of co-payment is subject to the laws of free markets, whereby providers must engage in price competition. This starkly contrasts with government mandated co-payment schedules employed in many PCCs. Kanavos (2001) provides a detailed description of European co-payment schedules.

Volume controls can also be employed on the demand-side; indeed many countries use such mechanisms as part of their overall price control apparatus. One of the most common forms of demand-side volume control is exacted through the use of positive or negative lists. This regime is either exclusive, wherein manufacturers must apply to have their drugs approved for reimbursement, which would place the drug on a positive list; or inclusive, wherein drugs that are not approved are placed on negative lists. According to Kanavos (2001), this method of volume control, in either exclusive or inclusive form, is widely employed in European countries.

Price Effects: PCCs versus the U.S.

The most obvious net effect of these interventions (both supply and demand) is to provide PCC patients with drugs at much lower prices than prevail in the U.S. (the impact on volume is explored in the next section). A recent PPRS study, for example, found that prices for 60 drugs launched between 1995 and 2000 were often about 40 percent lower than prices that prevail in the U.S.⁶ A recent Australian government report found that prices in the U.S. are about double those in France and Australia.⁷ Complementary findings were recently reported by a PPRS study that found that OECD countries typically see sales prices for new pharmaceuticals that are significantly below those in the U.S., often 40-50 percent lower.⁸ It is worth noting, however, that other factors beyond price controls have been cited in the literature as possibly contributing to differentials. Manning (1997), for example, finds that U.S. litigation costs contribute significantly to higher U.S. prices.

III. Pharmaceutical Usage in PCCs

Introducing a new drug has many regulatory costs. To the extent that cross-border trade leads to exports from low price countries, firms may also face a pecuniary cost to introducing a new drug in a PCC. Higher sales there may undercut revenues elsewhere.

From the trade perspective, it is important to note that a country may face protectionist pressures to avoid the significant adoption of a new drug as well. Many countries produce

⁶ Health, Department of and the Association of the British Pharmaceutical Industry, "PPRS: The Study into the Extent of Competition in the Supply of Branded Medicines to the NHS," December 2002

⁷ Commission, Productivity, "International Pharmaceutical Price Differences" (July 2001). Productivity Commission Paper No. 1670. <http://ssrn.com/abstract=277602>.

⁸ Department of Health and the Association of the British Pharmaceutical Industry, "PPRS: The Study into the Extent of Competition in the Supply of Branded Medicines to the NHS," December 2002

generic drugs domestically, and the emergence of a new patented drug could significantly undermine the profitability of a domestic generic manufacturer. Accordingly, one might expect that adoption patterns might vary significantly across countries, and be correlated with the pricing and trade policies of those countries. As discussed in Kessler (2004), there is a relatively large body of work documenting that this is this case. For example, Danzon, Wang, and Wang (2003) find that the expected profit in a specific country has a large and statistically significant effect on the diffusion of new drugs into a country. Kyle (2003) also found significant launch delays into price-controlled countries.

Silverstein, Brouwers and Wolff (2004) provide a detailed analysis of the impact of lower prices on introduction and delayed diffusion into PCCs. The authors analyzed data from a cross-section of seven OECD countries in four disease areas that include diabetes, antidepressants, statins (cholesterol lowering drugs) and antipsychotics. They also examined in detail the experience of two “breakthrough” drugs, Gleevec and Herceptin. Gleevec and Herceptin are especially interesting cases, as each is a highly successful cancer drug for which there is no substitute. Gleevec has been shown to significantly slow the progression of cancer for patients with chronic myeloid leukemia. Herceptin is a new immune therapy that has been shown to be effective in the treatment of metastatic breast cancer. Since both of these drugs have clear life-saving effects, any delay in launch resulting from government-controlled systems will have significant adverse consequences.

The results are reproduced in Figures 1 and 2. Figure 1 shows the launch delay in each of the price-controlled countries for new drugs in each of the four classes, and for Gleevec and Herceptin. The average launch delay across these countries for new diabetes compounds was found to be 18 months. For antidepressants, the delay was 24 months. For statins, the delay was

13 months, and for antipsychotics, the delay was 21 months. The average delay for Gleevec was 6 months, and for Herceptin 23 months.

After introduction, one might expect that PCCs would take up the use of the new and patented drug faster. Indeed, if trade concerns were irrelevant, then one might expect to see a slower introduction followed by a jump to a consumption level at or above the U.S. rate, since the data suggest that the PCCs pay lower prices for the patented medicines. However, if protectionism or budget pressure is a factor, then PCCs may discourage the use of the new pharmaceuticals, and the subsequent path of use of the drugs may stay below that of the U.S. for many years.

Silverstein, Brouwers and Wolff (2004) documents that the latter is the case. As can be seen in Figure 2, the PCCs maintain a strikingly low level of use of new pharmaceuticals for years after the introduction of newly patented drugs. Only in one case (Gleevec) did the PCC consumption rise to the level of the U.S. during the sample period. Even in that case, however, it took more than two years from the launch of the drug in the U.S. for PCCs to lift their use to the same level as that in the U.S. For Herceptin, the diffusion was found to be startlingly slow, with end-of-sample use of this important compound less than half the frequency of the U.S. Given the efficacy of Herceptin, this suggests that the large gap in survival rates for breast cancer between the U.S. and PCCs may well be increasing.⁹

Of course, one possible explanation for the higher reliance on patented medicines in the U.S. might be that the U.S. uses prescription drugs too often. As is discussed in greater detail later in this paper, published literature finds that, according to U.S. professional guidelines, there

⁹OECD, "A Disease-based Comparison of Health Systems: What is Best and at What Cost?" OECD Publication Service, 2003

is a large amount of underuse of medicines in the United States, which indicates that lower levels of medicine use in PCCs may not be medically appropriate.

Price Controls, Protectionism and the Drug Mix

The U.S. market-based system both rewards innovation through market prices for brand innovation and promotes widespread use of unbranded generics (leading the OECD in the use of such drugs). The flip side of the slow adoption of new drugs in the non-US OECD is that PCCs provide larger rewards for treatments that are older and often off-patent. Since off-patent drugs can be produced by domestic generic manufacturers, there is a key trade aspect to health practice. The German generic market for example, considered the largest such market in Europe, is dominated by German generic manufacturers: Ratiopharm, Hexal, and Stada. The market prevalence of domestic manufacturers, however, is not limited to Germany, with this regime also seen in France, and, presumably, other countries not yet studied.¹⁰ The data suggest that there is a very high correlation between drug use and trade factors. For example, Silverstein, Brouwers and Wolff (2004) found that the share of drug volume in PCCs that is attributed to branded generics, which compete partly by promoting brand image in contrast to competing strictly on the basis of price,¹¹ (and which often have an inefficiently high price) is often above 50 percent. In Germany, it is about 65 percent. Thus, the government intervention affects not only the total outlays on pharmaceuticals, but also the mix. Silverstein, Brouwers and Wolff (2004) found that PCCs could save about 20 percent of total annual pharmaceutical spending if they simply reduced their reliance on branded generics to levels equal to those in the U.S. These savings could then be reallocated to provide greater access to newer, innovative, patented products.

¹⁰ IMS, "IMS Generic Focus 2003-2007," IMSworld Publications, June 2003

¹¹ Danzon, Patricia M, and Michael F. Furukawa, "Prices and Availability of Pharmaceuticals: Evidence From Nine Countries," *Health Affairs Web Exclusive*. October 2003

Given a desire to minimize social expenditures on drugs, it is nonetheless the case that expenditure should have an optimal mix given the constraint. It is a serious indictment of the trade practices of the PCCs that they rely so little on the best and newest therapies while inefficiently managing crucial health care dollars by encouraging the use of branded generics. Unless, of course, the case can be made that their practices do not sacrifice the health of their constituents. The literature reviewed in subsequent sections suggests the practice does affect the health of citizens of PCCs.

As far as the economics of drug development is concerned, the key observation from the previous two sections is that foreign governments significantly reduce both the price and the volume of patented drug use. Accordingly, it follows that revenues from PCC's are significantly lower than would likely be achieved in a free market. Understanding the impact of those lower revenues on the economics of drug development requires a short economic diversion.

IV. The Economics of Patents and Innovation

Economists and policymakers have long recognized that research and development activity suffers from a severe free-rider problem. If there are no enforceable property rights for a discovery, then there will be little incentive for firms to invest in the up-front costs. The patent system emerged for this reason, allowing those who make discoveries to exercise "monopoly" rights (or exclusive rights to a product) for those discoveries (but not for non-infringing discoveries that compete in the same market) for a specific amount of time. While there are many theoretical concerns about patent design, and a great deal of disagreement about the appropriate length of patents, econometric work has identified a number of positive and significant effects of patents on research activity and economic growth. In an exhaustive work

exploring the 150 year history of patents, Lerner (2000) found that relatively wealthier countries are more likely to have patent systems, to give longer patents, and to enter into cooperative agreements with other countries to respect each other's patent rules. However, Lerner found significant variance across countries in the respect for each other's property rights. Notably, he found that many European countries have a long history of ignoring the rights of others. For example, "French family countries, while early to adopt patent protection, have consistently discriminated against foreign patentees."¹² Thus, the literature has found that the free-rider problem has been solved better within countries than across countries. Put differently, patent protections have been found to be a successful method to induce innovation, but those who own patents have often found their property rights threatened by the actions of foreign governments. Patents are an empirical success story, but that disguises a great deal of historical conflict below the surface.

Why do patents work? Assuming that a patent is enforceable, the economics of patents and their relationship to research and development is quite straightforward. Firms invest until the expected revenue from a new discovery is just equal to the cost of that discovery at the margin. During the period when the firm has patent protection, it charges a price that is higher than the marginal cost of production for the product. Accordingly, it is generally true as both a theoretical and an empirical matter that more research activity will be planned when firms expect to receive higher revenues in the future.¹³ Moreover, social welfare clearly benefits from the existence of patents, since a significant fraction of economic growth over time is attributable to technological progress, as has been recognized since the pioneering work of Samuelson and Solow (1953).

¹² Lerner (2000), p. 2.

¹³ I will return to the relevant literature in this area in section V.

The connection between patents and this economic wellbeing has been made in a number of recent studies. Eaton and Kortum (1995) document a tremendous positive impact of patents on growth. They estimated that doubling the number of researchers in the U.S. would increase average OECD growth from 2.5 to 4.3 percentage points per year. They also found, to continue the free-rider theme, that most growth generating discoveries emanated from the U.S. More recently, Moser (2003) found in a cross-country study that patents had a profound impact on the research efforts of individuals in different countries. Countries with weak patent systems tended to see more research into things such as foodstuffs that depend on “secret” recipes.

While patents grant a short-term monopoly right, they do not create a system that requires strict economic regulation. If drug companies made sufficient profits over many years, then additional firms would enter the market to compete away those profits. The relatively low threshold to entry in pharmaceutical research is highlighted by the enormous variety of new startups that currently exist, and by the fact that, as Scherer (2001) states, “rates of return on pharmaceutical industry R&D investments tend to exceed risk-adjusted capital costs by only modest amounts.”¹⁴ For example, as of December 31, 2003 there were 315 biotech companies listed on either the NASDAQ, NYSE, or AMEX.¹⁵

Economists studying R&D intensive industries have even gone so far as to argue that patents alone might not be enough to stimulate all of the research that would be optimal from the point of view of society. Firms engage in R&D with the hope of developing new products that will generate healthy profits. Patents allow firms to capture some of those profits, but R&D is a classic example of an activity that has external benefits: when a firm uncovers something new,

¹⁴ Scherer (2001), p 220.

¹⁵ Burrill & Company, *Biotech 2004 – Life Sciences: Back on Track* (San Francisco, CA: Burrill & Company, 2004).

the knowledge will help some other firm perform its own R&D. It is often hard to predict where these spillovers will occur, but it is generally accepted by those who study R&D that breakthroughs often create a kind of snowball effect, spreading innovation and productivity increases to the far reaches of the economy. Think, for example, of how many everyday appliances have been changed by computer technology. The benefits to society of R&D are likely to be higher than the benefits to individual firms doing research, since firms tend to look only at their own payoffs. This theoretical observation was confirmed by Hall (1996), and is so widely accepted that a recent review addressed why there is so little funding for R&D in the U.S.¹⁶ If the effectiveness of patents were undermined, then the problem of too little R&D would be exacerbated.

In a global economy, a firm that has a patented product will be able to obtain revenue from many different countries. If the economic characteristics of countries vary, and markets are effectively separate, then different prices for each country may be optimal to maximize revenues during the patent period (if the economic characteristics of countries vary, e.g. per capita GDP). Then the higher revenues will spur higher research activities at home, and higher welfare for citizens who benefit from new discoveries.

However, there will also often be a political tension associated with patent policies. This is because the optimal *ex ante* policy is to encourage active research by guaranteeing firms patent protection. However, *ex post*, politicians will always face the temptation to take the patent away and win popularity with consumers who will then receive the product at a lower price. Current estimates suggest that it costs approximately \$800 million to develop a new drug and 12.8 years

¹⁶ Hall (2002)

to deliver it to market.¹⁷ Such a dynamically inconsistent policy of removing patent incentives in a research- intensive industry would discourage future discoveries, but the damage may be difficult for voters to see in the short run. One reasonable speculation regarding the abysmal record of continental Europe with regard to discoveries that lead to economic growth (again, see Eaton and Kortum, 1995) may well be that dynamically inefficient policies that disregard prior promises have been a significant enough factor that entrepreneurs have chosen to take their best ideas elsewhere. Under this view, the U.S. may have been able to maintain the strong environment for research because its market is large enough to allow successful entrepreneurs to capture adequate profit even if the Europeans effectively disregard the patent (such as through price controls that degrade its value). As I will discuss in section V, this view is supported by recent trends in the location of pharmaceutical industry, but suggests that policy changes that move U.S. practice toward that of Europe may eliminate the key factor supporting innovation in the U.S.

When contemplating the possible effects of pharmaceutical price controls as a special case of the patent literature, it is essential at the outset to compare the existing international market order to the standard conceptual framework. Most countries other than the United States have health sectors that are predominately government run. Firms that make new discoveries expose these to market forces in the U.S., but must engage in a different and idiosyncratic price discovery process in most other countries.

Accordingly, the key question is whether non-U.S. prices deviate significantly from domestic prices, and from those that would occur if prices were established optimally in a competitive market. If prices do vary significantly from the ideal, then the theory of the damage

¹⁷ see DiMasi (2000) and Dickson and Gagnon (2004)

is straightforward. Lower revenues will mean less research. Lesser research will mean fewer discoveries. Armed with the value of a typical discovery, policy-makers can then assess the harm to patients in the U.S. and abroad, and to the economy as a whole.

Of course, understanding the predictions of theory will only provide part of the answer. More important is evidence on the importance and magnitude of the different effects from the existing empirical record. In the remainder of this paper, I will explore these links in detail, and, where possible, attempt to draw conclusions concerning the likely magnitude of the various effects from the existing empirical literature.

The empirical literature points to a significant free-rider problem in the pharmaceutical industry. This dynamic is one that is quite similar to past problems documented by Lerner (2000). Many PCCs impose significant price controls on U.S. firms. These government interventions discourage the diffusion of new drugs into PCCs, and discourage research and development activity as well. Thus, many countries are engaged in behavior that significantly undermines the return to discovery. As noted above, the literature suggests that this behavior of other countries is likely as much a trade issue as it is a pharmaceutical policy issue. Patients in PCCs receive fewer patented U.S. drugs, but receive relatively more “branded” generic drugs. Finally, the literature also allows one to estimate the impact of foreign price controls on overall drug development. I will turn to that in the following section.

V. What is the Effect of Price Controls on Revenues and R&D?

The foreign price controls appear to have had a dramatic effect on the structure of international industry and activity. First, lower revenues abroad have significantly eroded the resources available to U.S. firms for R & D investment. As Scherer (2000) has documented, and

as is illustrated by Figure 3, taken from Silverstein, Brouwers and Wolff (2004), pharmaceutical firms have historically poured a significant fraction of their free cash flow back into research and development activity. Numerous studies have found a significant link between profitability and research and development activity.¹⁸ There is also a significant link between R&D expenditures and new discoveries, with the seminal work in the area being Jenson (1987), who documented a positive link between R&D and the discovery of new compounds.

These studies collectively confirm ample research into the behavior of firms more generally. For example, Hassett and Hubbard (2002) review the literature on the determinants of business fixed investment and find that there is consistent evidence that firm investment responds, as economic theory suggests it should, to key marginal cost and profit variables. Cummins, Hassett, and Oliner (1999) found a significant link between profit forecasts of stock analysts and the current investment activity of firms.

Accordingly, the free riding of foreign nations likely carries significant external costs. Research is diminished, and the discovery of new treatments is slowed, harming the U.S. economy and consumers. Silverstein, Brouwers and Wolff (2004) attempt to assess the net impact of foreign price controls on the number of compounds available in the market place, utilizing the literature that links free cash flow to future investment, and investment to future discoveries. They concluded that revenues would increase by 35-45 percent if PCC's removed their price controls, and that R&D expenditure would rise by \$17-22 billion. This extra research would, they estimate, lead to between 10 and 13 new compounds a year. This analysis is conservative compared to that of Acemoglu and Linn (2003) who predicted enormous responsiveness of drug development to revenue changes. They found that a 1 percent increase in

¹⁸ These include Gambardella (1995), Giacotta, Santerre, and Vernon (2003), Grabowski and Vernon (2000) and Lichtenberg (2004c).

the potential market size for a drug category would lead to a 4 to 6 percent increase in the number of new drugs in that category. While their study was concerned more with the location of research across different sized patient pools, a simple application of their results suggests that a 35-45 percent increase in revenues might lead to more than a doubling of the number of new compounds available. In light of the value of new medicines as discussed above and in greater detail later in the paper, the negative consequences for the U.S. of OECD price controls that suppress R&D investment are evident.

There is also evidence that the pharmaceutical industry itself has suffered significantly in the PCCs. A recent Ernst and Young study reports that in the biotechnology sector alone, the U.S. employed 142,900 workers in its biotech industry. The total in Europe was only 33,304. The total in Canada was 7,785, and the total in all of Asia only 9,764.¹⁹ (Of course, total employment in the U.S. pharmaceutical sector industry is far larger than in the biotechnology sector alone.) Indeed, large foreign firms have begun locating their research activities in the U.S., with Novartis and GSK two recent examples.

There has yet to be an academic study that has attributed the out-migration of R&D specifically to price controls. However, the evidence presented in this study leads to a reasonable speculation. The price and revenue associated with a patented new product decline over time. Accordingly, it is important to introduce any new product as soon as possible in the markets that have the highest profitability.

¹⁹ Ernst and Young, "Beyond Borders: The Global Biotechnology Report 2003," July 2003

VI. What Are the Health and Cost Effects of U.S. Practice?

To close the loop on the economics of price controls, it is necessary to explore the impact of drug development on welfare. After all, if the research that is foregone because of the intrusions of foreign governments would only produce close substitutes of existing drugs, then the impact may not be dramatic.

In this section, the role of pharmaceutical innovation is examined, considering the health benefits and the economic benefits derived from those health gains.²⁰ This is followed by an assessment of the effect that new drug introductions have on market structure. I then evaluate the effects of pharmaceutical advances on selected health conditions, first assessing the outright health benefits, then the economic benefits of pharmaceutical innovation specific to those conditions.

Health Benefits of New Drugs

The positive health effects of new and innovative pharmaceuticals on the population at large have been well documented. A number of recent studies have found that increases in the overall stock of pharmaceuticals and the development of newer, more innovative medications have reduced morbidity, the number of hospital stays, and have increased longevity. Moreover, these improved health outcomes translate into significant economic benefits realized through decreased hospital stays, fewer workdays missed, and lives saved.

Lichtenberg (2004a) calculated the stock of drugs available in a given year and compared the pharmaceutical stock with mortality rates to assess the effect of drug stock and health outcomes over the period 1979 to 1998. The drug stock was calculated by combining FDA data,

²⁰ Portions of this section are drawn from Kessler (2004)

which indicates when a drug was introduced, with data from First DataBank's National Drug Data File, which provides a comprehensive list of all drugs medically indicated for treatment of each disease included in the study. For the specific diseases studied, an increase in drug stock over the period observed was found to both increase the average age at which individuals died as well as to reduce the overall likelihood of death before age 65. Thus, overall drug development can be credited with improving health outcomes for patients. This finding was also observed in Lichtenberg (2003a), which was a broader study that observed treatment information across 52 countries from 1982 through 2001.

Beyond increases in overall drug stock, drug innovativeness has been shown to have a significant and positive effect on pharmaceutical treatment outcomes. Lichtenberg (2003b) examined over three historical periods the effect of new drug share to overall stock on treatment outcomes across diseases. The study found a significant relationship between new drug use and mortality reduction in the periods observed, noting that, "over 45 percent of the variation across diseases in the 1970-91 reduction in mortality is explained by the new drug share."²¹ Drug innovativeness has also been credited with improved health outcomes for specific conditions, for example CASCADE (2003) notes survival rates of HIV patients increasing after the introduction of new antiretroviral treatments.²²

Health cannot be simply defined as the binary relationship of life or death, it is therefore important to look beyond survival and mortality rates in evaluating the impact of pharmaceutical innovation. Patient hospital stays is an important indication of the state of health beyond mortality rates. Indeed, hospital stays require patients to leave work and pay for hospital

²¹ Lichtenberg (2003b), pg. 103

²² CASCADE Collaboration, "Determinants of Survival Following HIV-1 seroconversion after introduction of HAART," *The Lancet*, 362 (2003):1267-1274

services, all while suffering the effects of an affliction of such severity as to merit hospitalization. The extant literature on pharmaceutical advancement, in addition to showing strong correlation between innovation and increased survival, also observes a significant decline in patient hospital stays with the utilization of newer drugs, which in turn can translate into significant overall health care cost savings.

Lichtenberg (1996) examined the correlation between drug utilization and hospital care. Comparing the 1980 and 1991 National Ambulatory Medical Care Survey Drug Mentions file, the study was able to measure the growth in the total number of prescriptions for the 93 diseases listed in the survey. The study was also able to assess the innovativeness of the prescribed drugs with an index that gauges the increasing dissimilarity of prescribed drugs between the 1980 and 1991 surveys. Lichtenberg (1996) observed the largest decrease in hospital stays was for those diagnoses with the greatest increase in total drugs prescribed and the greatest change in the distribution of drugs. Indeed, the study estimated that an increase of 100 prescriptions implies a corresponding reduction, by 16.3 days, in hospital care. Though savings would be partially offset by increased ambulatory care expenditures, the study found that an additional \$1 increase in pharmaceutical expenditure relates to a corresponding drop by \$3.65 in hospital care expenditures. This indicates that hospital stays, and attendant costs, decreased for patients with diseases for which there was the most pharmaceutical innovation, in terms of increases in pharmaceutical expenditures and increases in the use of more innovative drugs.

Lichtenberg (2001) was able to provide a more detailed analysis that also included the age of the drugs being prescribed. Using the 1996 Medical Expenditure Panel Survey (MEPS), the study confirmed the earlier findings indicating a high correlation between drug innovativeness and hospital stays, observing that patients consuming newer drugs had

significantly fewer stays than those patients that consumed comparatively older drugs.

Lichtenberg (2001) also observed decreases in mortality, as well as other indicators of morbidity such as lost workdays. This study was later updated in Lichtenberg (2002) to include a larger sample size, by incorporating the 1997 and 1998 MEPS data, as well as including some methodological changes to improve precision. The updated study maintained the observed decreases in hospital stays, mortality and other indicators of morbidity such as workdays lost with the consumption of newer drugs.

The benefits of reduced morbidity and mortality as observed in the study were also realized as cost savings. Lichtenberg (2002) noted that for every measured increase in drug expenditure there was a corresponding reduction in non-drug expenditures on the order of 7.2 times the original drug expenditure increase. For example, reducing the mean age of drugs used to treat a condition from 15 years to 5.5 years is estimated to increase prescription drug spending by \$18 but reduce other medical spending by \$129, yielding a \$111 net reduction in total health spending. These savings are mainly derived from reduced hospital and physician office-visit expenditures. Further studies have also observed the broad cost savings derived from increased pharmaceutical consumption. Indeed, a recent study conducted by the Tufts Center for the Study of Drug Development at Tufts University observed that disease management organizations believe that increased spending on prescription drugs reduces hospital inpatient costs. According to Kenneth I. Kaitin, Tufts Center Director, “Since prescription drugs account for less than 10% of total current U.S. health care spending, while inpatient care accounts for 32%, the increased

use of appropriate pharmaceutical therapies may help moderate or even reduce growth in the costliest component of the U.S. health care system.”²³

The Medicare population was also included in Lichtenberg (2002), for whom a decrease in the age of drugs consumed reduced non-drug expenditure by all payers (including those covered under Medicare, private supplemental insurance, Medicare for dually eligible individuals and for out of pocket payments) 8.3 times as much as it increases drug expenditure and reduced Medicare non-drug expenditure 6.0 times as much as it increased drug expenditure.

The Role of Competition

While innovative new drugs are clearly beneficial, one criticism of industry research of late has been that too much effort is expended developing “follow on” drugs in a therapeutic area. Follow on drugs may have different effects, side effects, indications, contra-indications, and may work differently for different patients. At the same time, to the extent that drugs are good substitutes for one another, then new entrants will likely reduce the price paid by consumers. Insurers acknowledge the powerful competitive forces at work in the U.S. market place as there are additional entrants in the same therapeutic class. For example, in a May 24, 2002 letter to the National Association of Insurance Commissioners, a number of managed care organizations (including American Association of Health Plans, Blue Cross and Blue Shield Association, Health Insurance Association of America, Academy of Managed Care Pharmacy, Pharmaceutical Care Management Association, AdvancePCD, Express Scripts, Inc., and the National Association of Health Underwriters) note that, “The constantly advancing market is producing therapeutically similar drugs to compete with other brand name products, creating the

²³ "Disease Managers Say Increased Spending on Prescription Drugs Cuts Hospital Inpatient Costs," press release from Tufts Center for the Study of Drug Development, March 12, 2002

potential for driving down the cost of the class of drug.”²⁴ The effect on competition on drug prices has been examined further in DiMasi (2000), who found that new drugs in a class are often priced lower than existing drugs in the class. DiMasi (2000) examined the pricing of new entrants to drug subclasses in eight therapeutic categories, which account for half of the total prescription drug expenditures in 1999. The study found that most new drug entrants examined were launched at discounts (sometimes substantial) relative to both the class price leader and to the average price in the class. The study further concluded that average prices for drug subclasses did not on the whole increase substantially over general price inflation, and in many cases were shown to be either flat or to have declined slightly. An additional article on this topic, Lee (2004) published in the *New England Journal of Medicine*, found that prices for follow-on medicines are often lower than the first medicine in a class. Lee finds that additional entrants in a market, “reflect and create competition among drug and device manufacturers, and that competition is also a powerful driver of better quality and lower costs.”²⁵

These findings echo economic modeling that demonstrates downward pressure on prices by new entries in markets, assuming those products are substitutable. For example, a standard theoretical model of oligopoly, the Cournot model, is often applied to circumstances where entry occurs in the presence of market power.²⁶ The model suggests that the price of product will be, under some circumstances, proportional to the inverse of the number of firms competing in the market. According to Silverstein, Brouwers and Wolff (2004), the model produces similar results when applied to the pharmaceuticals market.

²⁴ <http://www.amcp.org/data/legislative/analysis/530021.pdf>

²⁵ Lee (2004) p. 211- 212.

²⁶ For a recent application to telecommunications economics, see Clark, Ivanova, Hassett and Kotlikoff (2004).

Thus, new drug introduction has been found to provide significant health benefits, and also, through competition, to reduce pharmaceutical costs.

Impact of Pharmaceutical Utilization on Health and Economic Outcomes

According to the National Center for Health Statistics, as of 2001, heart disease and cancer were the first and the second leading causes of death in the United States, respectively, accounting for over forty percent of recorded deaths in the U.S. It is clearly of national interest to combat these diseases, and pharmaceutical innovation has made a demonstrable contribution to the reduction of deaths attributable to these diseases. For example, the use of statins, can significantly reduce the incidence of heart disease by reducing LDL, or “bad,” cholesterol. Indeed, the most recent guidelines, Adult Treatment Panel 3 (ATP 3) for treatment for high cholesterol issued by the National Heart Lung Blood Institute (NHLBI) are predicated on the effectiveness of statins in reducing coronary heart disease. According to NHLBI Director Dr. Claude Lenfant, if the ATP III recommendations were followed, heart disease “would no longer be the No. 1 killer.”²⁷ The case of statin therapy serves as an important exemplar for pharmaceutical innovation; both for the objective health benefits provided by such drugs, and the important economic effects derived from their utilization.

A recent study by MEDTAP²⁸ found that for Medicare patients who have suffered a heart attack, every additional dollar spent on the overall treatment of heart attack has produced health gains valued at \$1.10. Specifically, statin therapy in heart attack survivors was found to generate gains valued as high as \$9.40

²⁷ G. Kolata, “U.S. Panel Backs Broader Steps to Reduce Risk of Heart Attacks,” *The New York Times*, 16 May 2001, sec. A., p. 1.

²⁸ MEDTAP International, Inc. *The Value of Investment in Health Care*. Bethesda, MD: 2004. Available at: <http://www.medtap.com/Products/policy.cfm>. Accessed (June 24, 2004).

The introduction of new pharmaceuticals has also had a noted impact on cancer treatment. Lichtenberg (2004b), for example, noted the compelling link between pharmaceutical advances and survival rates. Observed over the period 1975-1995, the study used longitudinal, annual, cancer-site-level data with a sample size of 2.1 million people. The study found that increases in drug stock had a significant (50 to 60 percent in this case) contribution to the increase in the age-adjusted survival rate 6 years after diagnosis. It is important to note that the survival rates increased most for those cancers for which there was the most growth in drug stock. The same study determined that the surge in pharmaceutical introductions during this period increased the life expectancies of individuals diagnosed with cancer by about one year, which, assuming a 40% risk of being diagnosed with cancer, translates into pharmaceutical innovation in medical oncology accounting for 10.7 percent of the total increase in life expectancy for the population at large observed during the same period. The study concluded by noting that the average expenditure on pharmaceuticals by a patient from time of diagnosis until death in 1995 was below \$3000, significantly below the \$150,000 value of the one-life year added to the life expectancy of people diagnosed with cancer over the period observed in the study.

The Importance of Innovation

As detailed above, PCC policies have led to a reduction in new innovative medicines made available to OECD consumers. Additionally, due to the demonstrated positive impact on health from new and innovative medicines, these price control policies are harmful to American consumers.

In a study on the value of medical technology advances, Cutler and McClellan (2001) report on the costs and benefits of medical technology changes affecting care of heart attacks,

low birth weight babies, depression, cataracts, and breast cancer. Medicines, while not the sole type of technology advances, are central to the treatment of four of these conditions. The authors conclude that benefits from lower infant mortality and better treatment of heart attacks alone are about equal to the entire cost increase for medical care over time. Additionally, they explain that their findings imply that the quality-adjusted price of medical care is actually falling over time.

In the instance of comparing the costs and benefits of heart attack treatments (including prescription drug treatment), Cutler and McClellan report that for every dollar spent on technology, the gain has been \$7. Furthermore, they state, “the net benefit of technology changes is so large that it dwarfs all of the uncertainties in the analysis.”²⁹ In the case of depression, the authors cite to research showing that the introduction and uptake of a new class of medicines has meant that treatment efficacy has improved for roughly the same cost as older forms of treatment, and that the value of treatment expansions facilitated by improved medicines has been six times greater than the cost of treatment, even before considering gains from persons’ being able to work and produce more.

As noted above, OECD price control policies have a large effect in retarding technological progress. This study is suggestive of the extraordinary loss of welfare accruing to Americans as a result of those policies.

The gains made by pharmaceuticals against this nation’s top killing diseases are compelling, but the scale of these conditions is such that every marginal advance can have a dramatic effect. Murphy and Topel (2003) cite that a 10% permanent reduction in death rates for heart disease would yield \$5.1 trillion in prospective gains and the same reduction in death rates for cancers would yield \$4.4 trillion in prospective gains. Clearly, the cost of pharmaceutical

²⁹ Cutler and McClellan (2001) p. 18

development and innovation is vastly outweighed by benefits that are objectively health related, in terms of lives saved or improved, and by the economic gains realized by such advancements.

Pharmaceutical innovation has also seen impressive efficacy in the treatment of other important conditions, such as depression. Frank, McGuire, Normand, and Goldman (1999) describe the importance of developing newer drugs in the class of Selective Serotonin Reuptake Inhibitors (SSRIs). The study explains that the new drugs are not more powerful treatments than earlier pharmaceuticals, but are safer and pose lower risks of overdose, are easier to administer, and do not cause as many undesired side effects. Berndt, Bir, Busch, Frank, and Normand (2000) found that during the time period of 1991 to 1996, a period during which drugs such as SSRI's have largely replaced older drugs for the same condition, treatment costs for an episode of major depression have fallen by about 1.66 to 2.13 percent per year. Similarly, Frank, Berndt, Busch and Lehman (2003) reported that quality adjusted costs of treatment for schizophrenia dropped 5.5 percent per year between 1994-1995 and 1999-2000, with much of the gain attributable to the introduction of innovative new treatments.

Cost savings have been realized through the increased use of innovative pharmaceuticals in other treatment areas as well. In a recent study published in the *New England Journal of Medicine*, it was reported that in the 16 months since the introduction of antiretroviral therapy for the treatment of HIV, there was a 43 percent decrease in hospital inpatient care. According to Samuel A. Bozzette, a physician with the Veterans Affairs San Diego Healthcare System, who headed the study, "The drugs are almost a perfect substitute for hospital care. We can afford them because, in fact, we are already spending the money on HIV care" in the form of

hospitalization.³⁰ Further studies correlate the effectiveness of increased innovative pharmaceutical consumption³¹.

The impact of innovative treatment also has important cost benefits in terms economic productivity. Research supports the fact that new medicines and other medical technologies are also improving patients' health and functioning in the workplace and at home. In the case of depression, a study published in the *Journal of the American Medical Association* found that lost productivity resulting from employee depression could be reduced with the proper use of depression treatments. The study noted that the "combined lost productive time burden among those with depression and the low level of treatment suggests that there may be cost-effective opportunities for improving depression-related outcomes in the U.S. workforce."³² These findings are echoed by a National Committee for Quality Assurance report, which states that major depressive disorder is "the leading cause of disability in the United States" and "if every American with depression received care from a health plan or provider that was performing at the 90th percentile level, employers would recoup as many as 8.8 million absentee days per year."³³ In the case of allergies, evidence shows that workers who took newer nonsedating

³⁰ Bozzette, Samuel A., et al., "Expenditures for the Care of HIV-Infected Patients in the Era of Highly Active Antiretroviral Therapy," *New England Journal of Medicine* (Mar 15, 2001); 344(11):817-823

³¹ see Lichtenberg, Frank R., "Benefits and Costs of Newer Drugs: An Update," NBER Working Paper 8996 (2002)

CASCADE Collaboration, "Determinants of Survival Following HIV-1 seroconversion after introduction of HAART," *The Lancet*, 362 (2003):1267-1274

D. B. Matchar, G. P. Samsa, Secondary and Tertiary Prevention of Stroke, Patient Outcomes Research Team (PORT) Final Report - Phase 1, AHRQ Pub. No. 00-N001, Rockville, MD: Agency for Healthcare Research and Quality, June 2000

³² Stewart, Walter F. et al., "Cost of Lost Productive Work Time Among US Workers with Depression," *JAMA: the Journal of the American Medical Association* 289 (18 June 2003): 23, 3135-3144.

³³ National Committee for Quality Assurance, *State of Health Care Quality: 2002* (Washington, DC: NCQA, 2003).

antihistamines to treat their allergies were more productive than those taking sedating antihistamines.³⁴ The study found that workers taking nonsedating antihistamines experienced an average 5.2 percent increase in daily work output in the three days after receiving the medication, compared with a 7.8 percent reduction in work output for workers receiving sedating antihistamines.

In sum, PCC policies that suppress development of new medicines do extensive harm to U.S. consumers by reducing competition among drugs and by reducing the number of new molecules — which has a clear impact on improving health and economic outcomes.

Does the U.S. Use Too Many Patented Drugs, or Do PCCs Use Too Few?

Given these results, then, it is evident that the differences in drug use between the U.S. and PCCs cannot be explained by assuming that the U.S. uses too many patented drugs. The positive impact of the new drugs used has been extensively documented. Indeed, in the instance of statins, Lewin Group (2000) estimates that significant gains could be achieved in the U.S. if all relevant patients received recommended treatments.

Likewise, U.S. under-use of medicines has been documented across many other conditions. While only limited research indicates overuse of prescription drugs³⁵, there is much evidence that large numbers of patients underuse needed medical care, including prescription medicines, for many serious health conditions. According to study by McGlynn (2003), “The Quality of Health Care Delivered to Adults in the United States,” nearly half of all adults in the

³⁴ Cockburn, Iain M., et al., 1999, “Loss of Work Productivity Due to Illness and Medical Treatment,” *Journal of Occupational and Environmental Medicine* 41(11): 948–953.

³⁵ Kleinke, J.D., “Access Versus Excess: Value-Based Cost Sharing For Prescription Drugs,” *Health Affairs* Vol 23, Issue 1, 34-47, January/February 2004

United States fail to receive recommended health care.³⁶ In assessing underuse and overuse of health care services, the study included an examination of nine health conditions that require treatment with prescription medicines. The study determined that there was underuse of prescription medications in 7 of the 9 conditions. Conditions where underuse was found include asthma, cerebrovascular disease, congestive heart failure (CHF), diabetes, hip fracture, hyperlipidemia and hypertension. Asthma, diabetes, hyperlipidemia, and hypertension are considered “high priority” conditions by the Agency for Healthcare Research and Quality (AHRQ) and Institute of Medicine (IOM).³⁷ These findings are supported by a May/June 2003 study published in *the Journal of Managed Care Pharmacy*, which examined claims data from 3 of the 10 largest health plans in California to determine the appropriateness of prescription medication use based upon widely accepted treatment guidelines. This study found that of the four therapeutic areas for study – asthma, CHF, depression, and common cold or upper respiratory tract infections – asthma, CHF, and depression were undertreated. The researchers concluded that “the results are particularly surprising and disturbing when we take into account the fact that three of the conditions studied (asthma, CHF, and depression) are known to produce high costs to the healthcare system.”³⁸ Addressing these widespread patterns of underuse of needed, effective medicines can lead to better health outcomes and lower health care costs.

³⁶ McGlynn, Elizabeth. A. et al., “The Quality of Health Care Delivered to Adults in the United States,” *New England Journal of Medicine* 348 (23 June 2003): 26, 2635-2645

³⁷ AHRQ “high priority” conditions include cancer, diabetes, emphysema, high cholesterol, HIV/AIDS, hypertension, ischemic heart disease, stroke, arthritis, asthma, gall bladder disease, stomach ulcers, back problems, Alzheimer's disease, depression, and anxiety disorders.

³⁸ Gilberg, Karen, et al., “Analysis of Medication Use Patterns: Apparent Overuse of Antibiotics and Underuse of Prescription Drugs for Asthma, Depression, and CHF,” *Journal of Managed Care Pharmacy* Vol 9, No. 3 (May/June 2003): 232-237

Similarly, other studies³⁹ demonstrate that lower use of needed medicines can increase consumption of other health care services and increase other health care cost. Figure 4 for example, documents that while the U.S. use of statins is more than double that in the average PCC, the U.S. only successfully provides statins to 56 percent of the eligible patient population.⁴⁰ Italy, in contrast, provides statins to only 17 percent of the relevant patient population. Given the link between statins and heart disease, this practice difference is likely to produce striking differences in outcomes. As can be seen in the second panel of Figure 4, the total number of preventable deaths that will occur because of too little statin use is quite high. For example, the United States would experience 19,000 fewer deaths if everyone were optimally treated, compared with 26,000 preventable deaths in Italy, over 5 years.

VII. Conclusions

This paper reviewed a large literature on the effects of price controls in the pharmaceutical industry on the organization and practices of firms. The literature suggests a number of conclusions:

- 1) Price controls significantly reduce revenue for patented products.
- 2) Lower revenue generally results in lower R&D investment, delaying the introduction of new drugs.
- 3) Patents provide essential protections to costly research and development initiatives.
- 4) Lack of access to new drugs likely has significant negative health effects in PCC countries.
- 5) Lower R&D reduces the rate at which new compounds are discovered.

³⁹ For further studies see Dor and Encinosa (2003 and Heisler et al. (2004)

⁴⁰ Lewin Group (2000)

- 6) Price controls often appear to be part of a protectionist strategy by PCC countries
- 7) Price controls appear have contributed to an economic environment in PCC countries that has undermined pharmaceutical research to a startling degree.

Moreover, disregard for the patent rights of U.S. firms appears to be part of a more general historical pattern. European countries have often been highly parochial in their devotion to intellectual property, to the detriment of consumer welfare.

In the past, the U.S. market has been large enough relative to the rest of the world that it has been able to support research despite these intrusions. The evidence reviewed here suggests that there could be devastating effects should our policy environment change.

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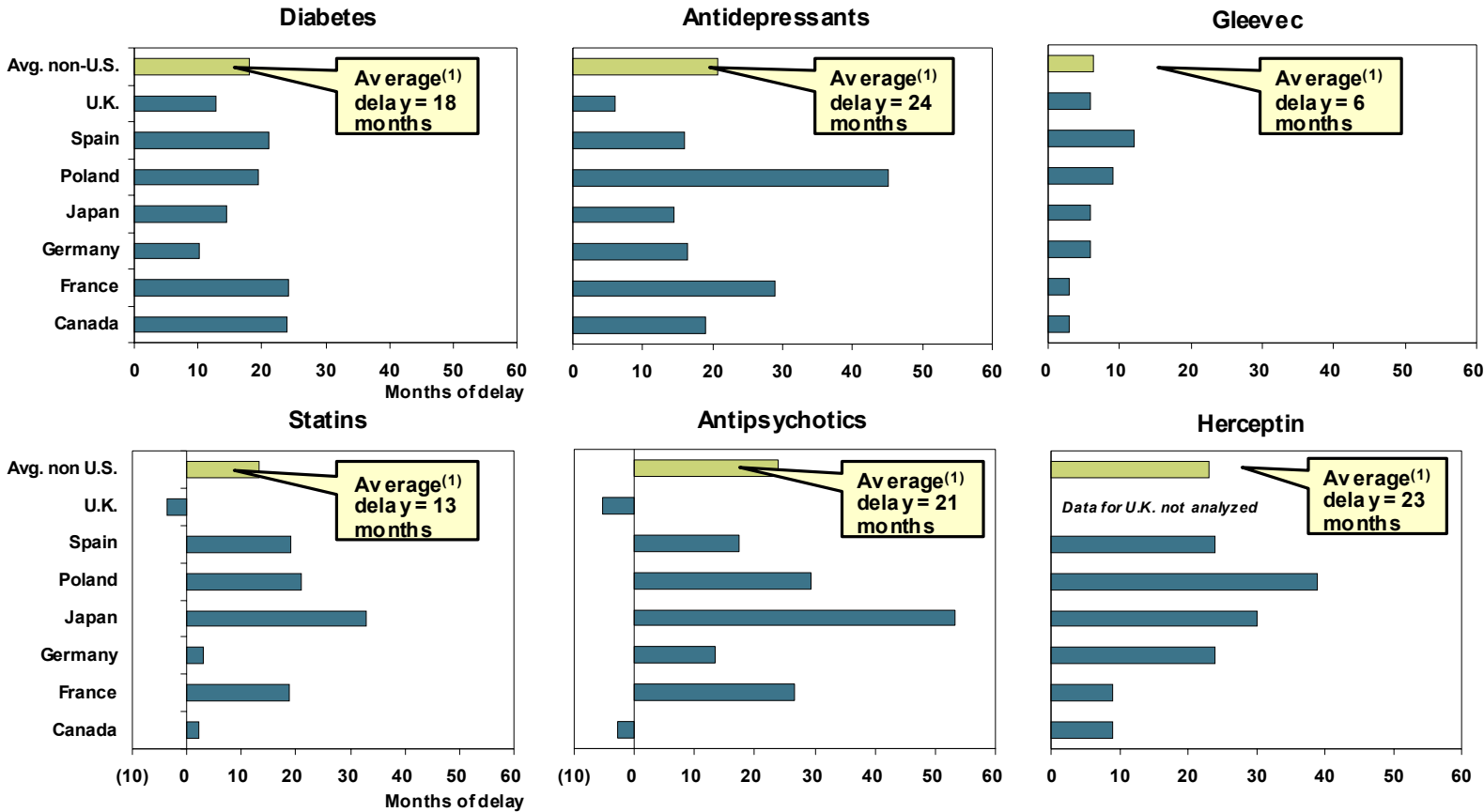
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Figure 1.

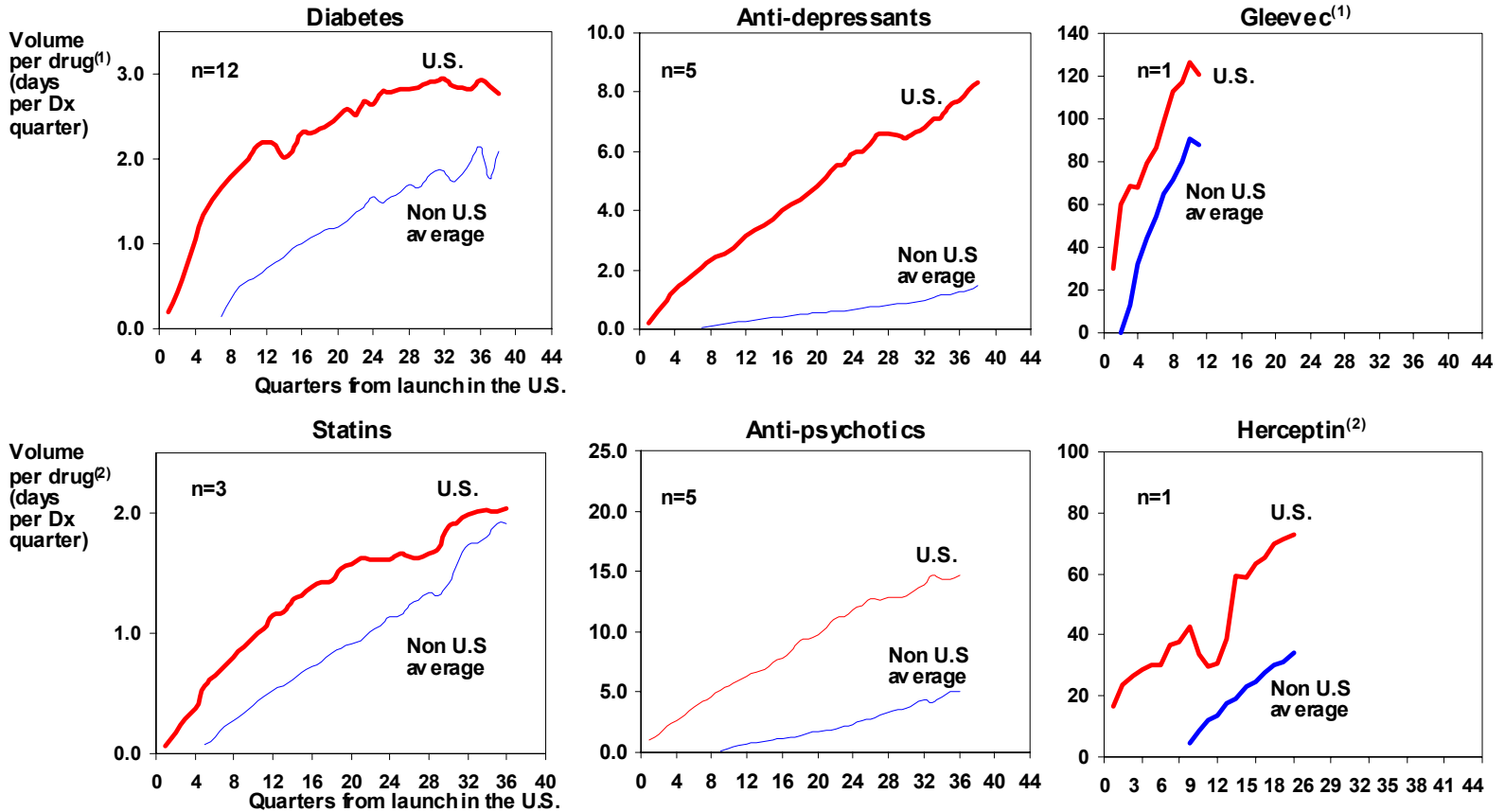
DELAYED USE OF INNOVATIVE DRUGS IN OECD



(1) Date of launch taken to be first day of quarter in which product was first available in a country, simple averages
 Source: BCG analysis and modeling based on raw data from IMS, Midas and Medical panels (1992-2004)

Figure 2.

LOWER PENETRATION OF INNOVATIVE DRUGS IN OECD



(1) Volume measure for Gleevec is standard units per Dx

(2) Volume measure for Herceptin is grams of active ingredient per capita

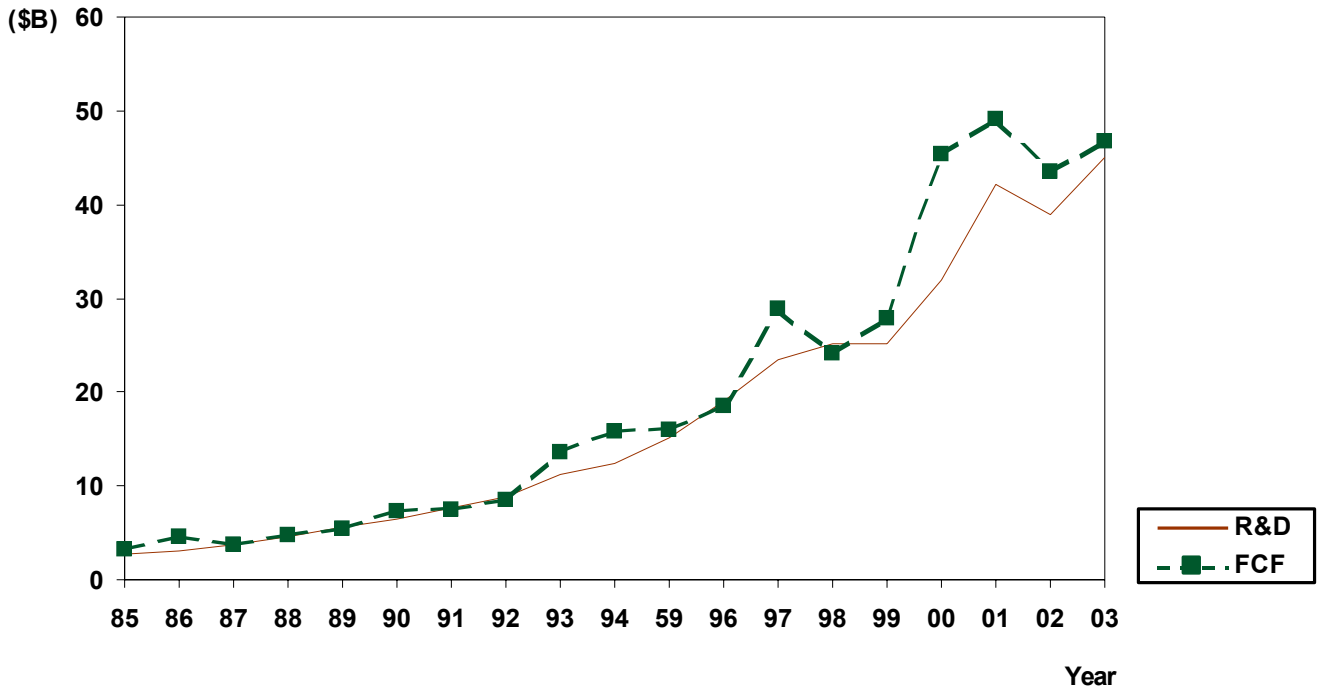
Source: BCG analysis and modeling based on raw data from IMS, Midas and Medical panels (1992-2004)

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Figure 3

HISTORICALLY, INDUSTRY HAS MAINTAINED CLOSE RELATIONSHIP BETWEEN FREE CASH FLOW AND R&D SPEND

Free cash flow ⁽¹⁾ and R&D by year for top 30 pharma companies



(1) EBITDA – Taxes – CapEx – Change in Working Capital

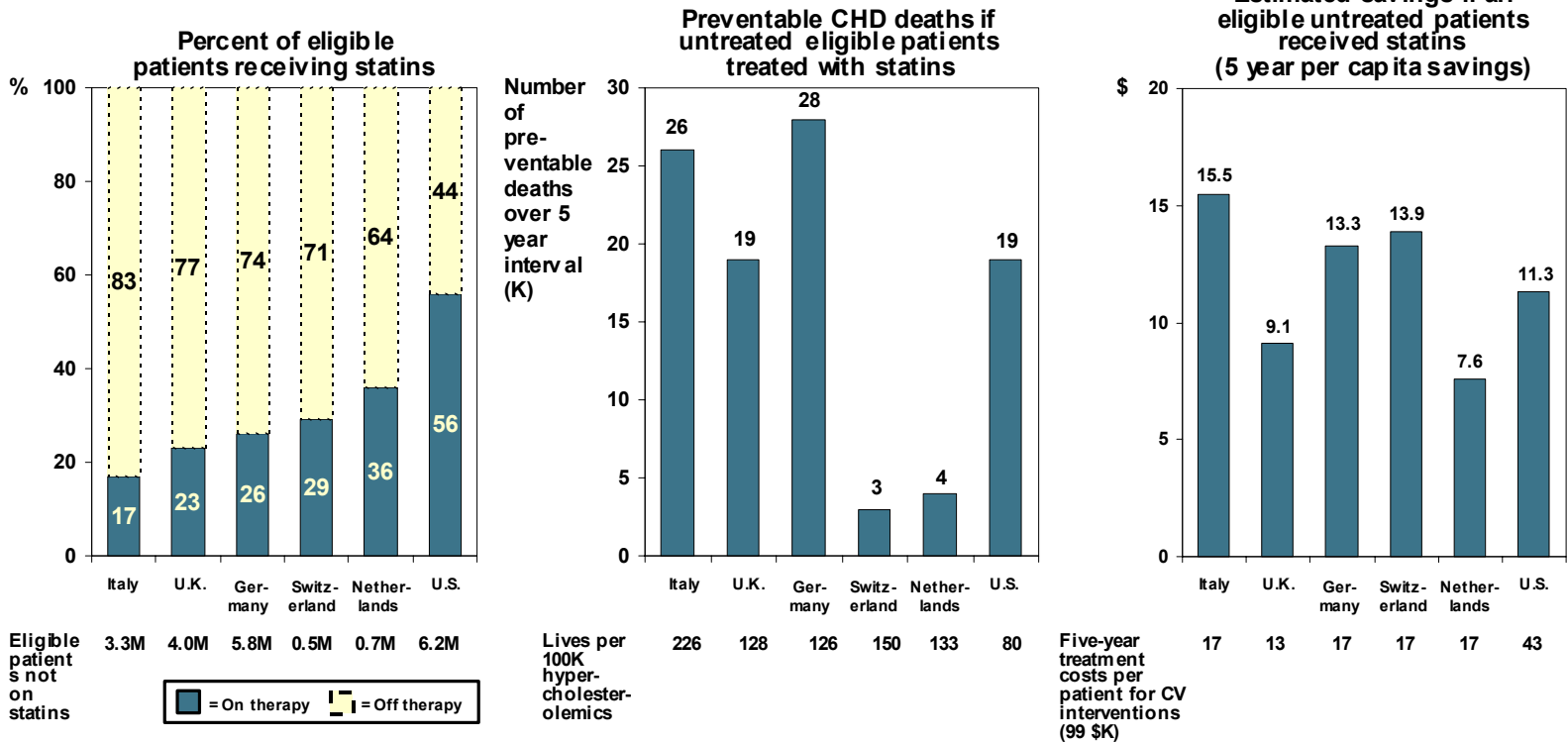
Source: Compustat; BCG Value Science center analysis of top 30 pharma companies

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Figure 4

Statins

BENEFITS IF ALL ELIGIBLE PATIENTS RECEIVED STATINS



Note: CHD = Coronary heart disease
 Source: Lewin Group, 2000, Diffusion of Treatments Study: Statin Use for Hypercholesterolemia, Cross-Country Report; Shepherd, Cobbe, New England Journal of Medicine, 1995; BCG analysis

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