BCG WHITE PAPER

Adverse Consequences of OECD Government Interventions in Pharmaceutical Markets on the U.S. Economy and Consumer

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THE BOSTON CONSULTING GROUP

Adverse Consequences of OECD Government Interventions in Pharmaceutical Markets on the U.S. Economy and Consumer

A White Paper prepared by

THE BOSTON CONSULTING GROUP, INC

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Preface

This white paper summarizes the findings of a Boston Consulting Group study commissioned by Pharmaceutical Research and Manufacturers of America (PhRMA) and conducted between April and May 2004. The objective of the study was to evaluate the impact of pharmaceutical cost controls in non-U.S. OECD markets on the U.S. consumer and economy, and inform the U.S. policy debate in the context of the Medicare Prescription Drug, Improvement and Modernization Act of 2003.

Our study drew on four main strands of research:

- a detailed review of the approaches taken by a cross-cutting sample of OECD countries to controlling drug costs: Canada, France, Germany, Japan, Poland, Spain, the United Kingdom, and the United States
- a survey of the extensive literature including academic studies and reports
- a detailed analysis of primary data from IMS for a selected set of disease areas and the commercial experience of drug therapies in the outpatient setting (including anti-diabetics, anti-psychotics, anti-depressants, statins, and selected anti-cancer agents)
- a series of interviews with pharmaceutical executives.

A detailed description of the methodology and sources used in this analysis – including the rationale for selection of countries and diseases studied – is laid out in the appendices. Where appropriate, we have also noted sources in footnotes.

Note: In this document, we use the term "OECD" to refer to OECD countries excluding the United States.

Executive Summary

Healthcare represents a significant share of OECD economies, 10 percent of GDP across the OECD, 14 percent in the United States itself. Demographic forces and therapeutic innovation are fuelling a steady growth in this sector of the economy and OECD governments are finding it even more difficult to balance this increasing demand for healthcare products and services with the ability of the healthcare system to finance it. Pharmaceutical spending represent one of the smaller shares of total healthcare cost (10.5 percent in the United States), but it is one that government policy makers can address more easily because of the limited number of manufacturers and distributors.

In addressing the need to ensure that the dollars spent on pharmaceuticals are optimally applied, the United States relies mostly on competition and market forces. By contrast, most other OECD countries have traditionally intervened to limit drug costs through government-mandated controls on price, volume and overall spend control. This difference in approach raises an important question for the United States: to what extent do these policies of other countries produce negative consequences for the US economy and consumer? Our analysis shows that OECD interventions do appear to keep drug expenditures lower in the OECD countries – but at a cost, both to themselves and to the United States.

Within OECD countries, patients experience reduced access to innovative medicines – launch delays of 1-2 years are typical, adoption rates are slower, and even peak penetration rates lag U.S. rates by 15-20 percent – and therefore are prevented from receiving the full therapeutic benefits of these drugs. Also, OECD countries spend significantly more on branded versions of drugs that are off-patent compared with the United States which focuses spend on the cheaper

pure generic copies. And there is evidence that the cost control policies in OECD countries have contributed to the migration of R&D activities out of those countries to the United States.

To measure the full impact of such distortions on the United States, we evaluated a counter-factual situation in which the OECD government interventions did not exist. Under different scenarios for correcting the pricing level and consumption level in the OECD, we find that drug revenues per treated OECD patient would increase by a factor of two to three, and that global drug revenues would increase by 35-45 percent, equating to an incremental $17-22 billion that would have been invested in biopharmaceutical R&D in 2003.

From this dynamic, several negative consequences for economies and patients globally emerge: specifically, fewer medicines, the missed opportunity for lower pricing from incremental competition and fewer jobs. Supposing that a level of incremental R&D investment had materialized over the past decade culminating in the incremental $17-22 billion R&D spend in 2003, we estimate there would be 10-13 extra drug launches a year – a 50 percent increase. In addition, there would potentially be 110-140 additional drugs overall in the global pharmacopoeia, of which 35-40 would likely be in new drug classes. In the United States, we estimate, there would be 20-30 thousand extra R&D jobs (with even greater increases overseas), 15-20 thousand extra pharmaceutical jobs, and a further – 55-65 thousand elsewhere in the economy.

1. Overview of Government Interventions in the OECD

Types of government intervention

Across the OECD,[1] governments have for some time intervened in markets to control the sales and distribution of pharmaceuticals. Whether intended to limit the consumption or the cost of drugs, or motivated by a desire to protect the local pharmaceutical industry, these interventions are intensifying. Because these controls tend to focus on the point at which drugs first enter the national health systems (at launch), they usually end up targeting the newest and most innovative medicines.

The control strategies deployed by OECD governments are many and varied. They can be directed either at the supply of medicines (the manufacturers) or at the demand (wholesalers, retailers, doctors, and patients). And they are deployed in environments where the state funds part or all of health care, acting effectively like a monopsony. They do have a common goal, however: to limit the total cost of drugs for the national health system. This goal can be achieved in three ways: price controls, volume controls, and spend/profit controls. (***Exhibit 1*** and ***Exhibit 2***)

[1] As noted in the preface, OECD references in the following pages exclude the United States.

EXHIBIT 1

OECD GOVERNMENTS EMPLOY A RANGE OF INTERVENTIONS TO CONTROL DRUG COST

	Price controls	x	Volume controls	=	Spending controls
Supply	• Cost plus pricing • Pharmacoeconomic criteria • Molecule/class reference pricing • Cross-country reference pricing • Mandatory rebates • Price cuts/price freezes		• Marketing spend limits • Product volume caps		• Profit controls • Revenue controls
Demand	• Co-payments/co-insurance • Generic substitution incentives		• Prescribing guidelines • Positive/negative lists • Formularies • Parallel import dispensing targets/incentives		• Physician Rx budgets • Physician healthcare budgets

Note: Molecule/class reference pricing: pricing/reimbursement the same for drugs with same active ingredient or therapeutic benefit; Mandatory rebates: one-off discounts or 'voluntary contributions to budget deficits; Positive lists similar to formularies; formularies can be used to steer prescribing among reimbursable drugs;

EXHIBIT 2

GOVERNMENT INTERVENTIONS CONTINUE TO PROLIFERATE

Tools currently used by governments to manage drug costs in their state health insurance systems

			U.K.	Germany	France	Spain	Poland	Japan	Canada
SUPPLY	Price	• Cost plus pricing							
		• Pharmacoeconomic criteria							
		• Molecule/class reference pricing							
		• Cross-country reference pricing							
		• Mandatory rebates							
		• Price cuts/price freezes							
	Volume	• Marketing spend limits							
		• Product volume caps							
	Spending	• Profit controls							
		• Revenue controls							
DEMAND	Price	• Co-payments/co-insurance							
		• Generic substitution incentives							
	Volume	• Prescribing guidelines							
		• Positive/negative lists							
		• Formularies							
		• Parallel import dispensing targets/incentives							
	Spending	• Physician Rx budgets							
		• Physician healthcare budgets							

Date of initial implementation: 1970s-1980s | 1990s | 2000s

Note: Analysis is summary of individual country studies

The Boston Consulting Group published a detailed survey of these interventions in 1999; here we offer a few summary highlights:[2]

Price controls

Price controls – in various forms – are used across almost all countries in the OECD. One of the most common approaches to controlling price is to set the reimbursement price of a drug to some selected benchmark. For example, Germany's molecule/class reference-pricing scheme is based on a drug-class benchmark, and caps the government-approved reimbursement price to the lowest third of prices of other drugs within the same drug class. And Canada's Patented Medicine Prices Review board uses cross-country reference pricing to set the government-approved price for a drug to its median price in a basket of other countries. Other countries resort to direct price-setting methods: in France, for example, where the reimbursed price of a drug is directly set by the Economic Committee on Medicines and subject to repricing every four years.[3]

Volume controls

Lower prices achieved through price controls can encourage increased utilization, and thereby could mitigate the broader objective of reducing cost. Hence the various forms of volume

[2] Analysis of cost control tools was developed from the following sources: United Kingdom: U.K. Department of Health (http://www.dh.gov.uk/PolicyAndGuidance/MedicinesPharmacyAndIndustryServices/fs/en); "United Kingdom – Pharmaceutical Pricing and Reimbursement Policies," LSE study on healthcare, http://pharmacos.eudra.org/F3/g10/p6.htm; ABPI; Germany: LSE study on healthcare in Germany, http://pharmacos.eudra.org/F3/g10/p6.htm; "International Review of Pharmacoeconomic, pricing and reimbursement news in the second half of 2003," Decision Resourses, March 12, 2004; France: "France – Pharmaceutical Pricing and Reimbursement," LSE study http://pharmacos.eudra.org/F3/g10/p6.htm; "International Review of Pharmacoeconomic, pricing and reimbursement news in the second half of 2003," Decision Resources, March 12, 2004; Spain: "World Pharmaceutical Market Spain," Epsicom Business Intelligence February 14, 2003; "Pharmaceutical regulation in Europe," Parlos Kanavos, Harvard Medical School; "Spain – Pricing and Reimbursement of Pharmaceuticals," LSE study, http://pharmacos.eudra.org/F3/g10/p6.htm; Japan: j"Japan – Pricing and Reimbursement of Pharrmaceuticals," LSE study, http://pharmacos.eudra.org/F3/g10/p6.htm; "Pricing of Prescription Drugs,"U.S. International Trade Commission, 2000; "World Pharmaceutical Markets – Japan," Epsicom Business Intelligence, March 2003 ; "Pharmaceutical Administration and Regulations in Japan," JPMA 2003; Canada: Annual Report 2002 of the Patented Medicine Prices Review Board, Canada; "Canada – Pharmaceutical Pricing and Reimbursement," LSE study, http://pharmacos.eudra.org/F3/g10/p6.htm

[3] Cross-national prices for drugs are checked by the Economic Committee on Medicines when setting prices. Also since 2003, France has reference pricing for certain products with generic substitution rates below 45% and extended it to products with generic substitution rates of less than 60% in 2004.

controls that have also been widely deployed across the OECD. These can be directed at reducing supply, as with France's product volume caps included in individual "framework agreements" between each pharmaceutical company and the Economic Committee of Medicines. Much more frequently, however, interventions aim at controlling demand through prescribing guidelines and various kinds of formularies or positive/negative lists which take the prescribing decision out of the hands of the physician treating a patient.

Spend controls

In general, spend controls aim to limit overall spending, and are usually deployed to supplement various measures for controlling price and volume. The United Kingdom attempts to control spend by capping returns to pharmaceutical manufacturers through the Pharmaceutical Price Regulation Scheme (PPRS), requiring any returns above a defined benchmark to be paid directly to the National Health Service. And in Spain, pharmaceutical companies have since 1994 been limited to an annual sales increase of 7 percent, and are required to transfer profits to the government if they exceed this limit.[4]

OECD countries – proliferating interventions

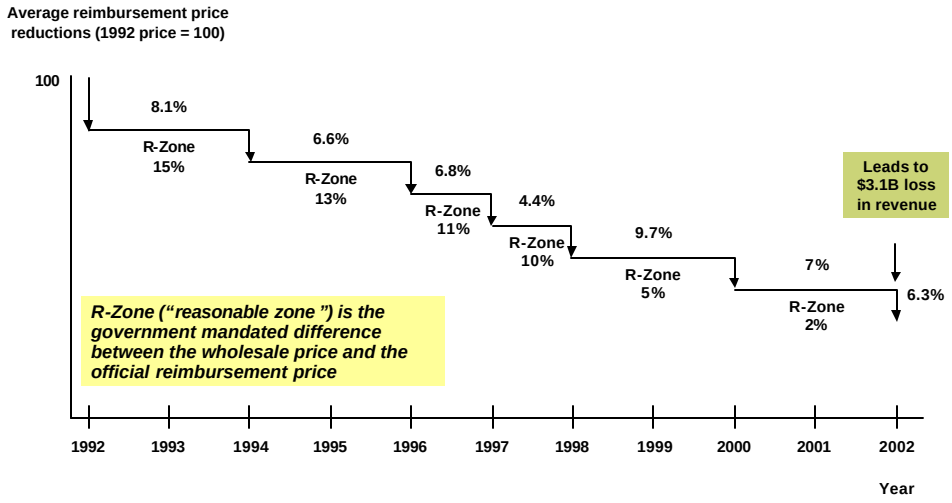
In keeping with their philosophy, many OECD governments have in recent years actually been expanding and intensifying their interventions in pharmaceutical markets. The French government, for example, having levied a "contribution" from the pharmaceutical industry in 1996, announced in 2004 the imposition of a further "one-time contribution" of $120 million. The German government, meanwhile, has imposed minimum quotas for pharmacists to import

[4] In 2002, the industry paid back $81M to the government as pharmaceutical expenditure had grown faster than the three percent excess over adjusted nominal GDP agreed with the government in 2001. See Farmaindustria Annual Report 2002, http://www.farmaindustria.es/Index_secundaria_ingles.htm

drugs from countries with lower drug prices,[5] despite evidence that the bulk of the potential savings on these imported drugs is captured by distributors and that little is passed on to the payor or consumer.[6] Further, Germany recently introduced mandatory rebates on on-patent drugs, and has since raised these mandatory rebates from 6 percent in 2003 to 16 percent in 2004. The Japanese government similarly has set about mandating price cuts every two years over the past decade, with each cut averaging 6-7 percent. (***Exhibit 3***).

EXHIBIT 3

JAPAN HAS MANDATED PRICE REDUCTIONS THROUGH 1990s



Source: "Pharmaceutical Administration and Regulations in Japan", JPMA 2003; "World Pharmaceutical Markets – Japan", Epsicom Business Intelligence, March 2003; OECD Health Data 2003

It is important to note that these interventions are imposed in the context of state-run health-insurance systems—essentially, centralized environments where consumers or employers are not free to make choices among health plans that offer varying levels of access to innovative pharmaceuticals.

[5] These are called parallel imports within the European Union. Typically countries with more aggressive systems of price control end up exporting drugs under this system.

[6] See LSE health and Social Care, January 2004, special research paper "The Economic Impact of Pharmaceutical Parallel Trade in European Union Member States." The study estimates that 86 percent of the price difference is gained by parallel importers, 13 percent is gained by payors, and 1 percent is gained by pharmacists, leaving none for consumers.

The contrasting U.S. approach – market-driven

The United States is not free of drug cost management tools in pharmaceutical markets either – whether in the private or public sector.[7] In the private sector, however, the cost controls are designed to leverage market forces across the spectrum of consumers, payors, intermediaries and manufacturers. Some of these private payors and pharmaceutical benefit managers (PBMs) represent formidable consolidated buying power. For example, the top PBMs have memberships between 35 and 60 million enrollees,[8] effectively larger than the patient populations of many OECD countries. These payors/PBMs are able to use their size, and their ability to shift market share, to negotiate with manufacturers – often invoking cost-control tools such as formularies and patient co-payments to drive substitution, all towards the goal of managing cost. (***Exhibit 4***)

EXHIBIT 4

U.S. PRIVATE PAYERS USE BROAD ARRAY OF TOOLS TO MANAGE DRUG COSTS

Target	Drug cost management levers	Description
Manu-facturers	• Concentration of buying power (e.g., PBMs)	• Pool drug purchasing volume to increase negotiating leverage
Physicians	• Formularies • Prior authorization • Physician incentives/capitation • Generic substitution • Counter-detailing • Disease management • Step therapy	• List of preferred drugs • Pre-approval for specific high cost branded drugs • Allowable monthly budget per patient • Physician notified of generic alternative • Plan-sponsored info on value/cost • Protocol and treatment guidelines • Initial therapy with least expensive option
Enrollee	• Co-insurance • Tiered co-pays • Mail-order substitution • Script limits • Covered lowest-cost drug	• Patient cost sharing • Co-pay increases with drug cost to payer • Encourage use of mail-order to lower cost • Monthly limit on total scripts per patient • Only lowest-cost drug covered; all other drugs available only at patient expense

[7] For example, state Medicaid programs and the Tricare system for the Department of Defence.
[8] As of December 31, 2002 as per Wachovia Securities, "Mining For Profits", September 24, 2003

The PBM industry itself confirms the importance of scale in influencing its relationships with pharmaceutical companies. As one PBM executive from Medco explained: "What we do at a macro level is leverage our size and our book of business to drive fundamental scale advantages and value for our customers… our broad client base makes us very attractive to the brand manufacturers who we negotiate with directly on rebates."[9]

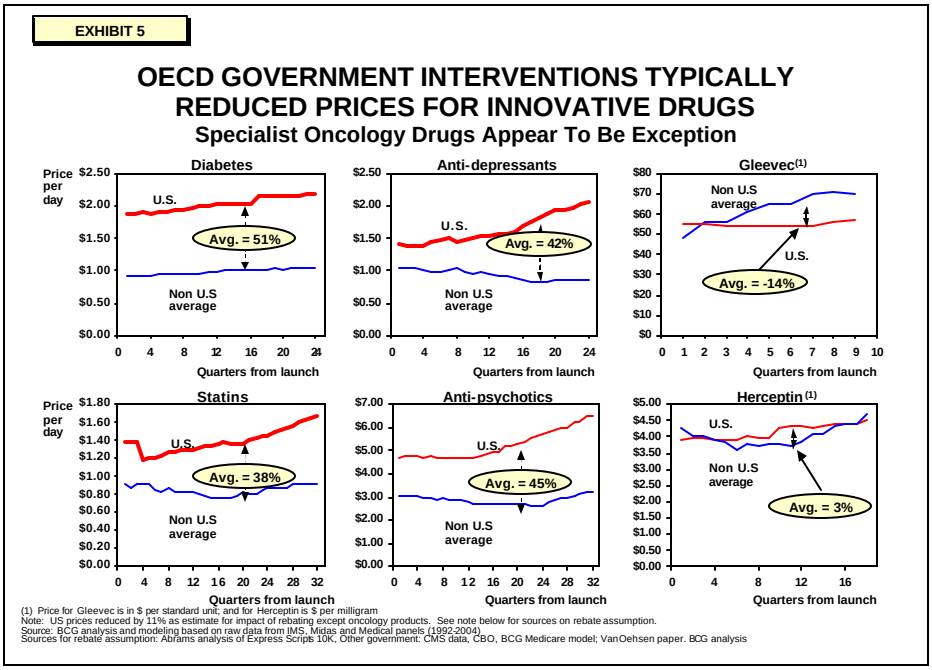
Given the competitive environment, how and when payors/PBMs deploy such controls is driven by market dynamics. Payors/PBMs have to compete for customers on the basis of the quality and cost of their coverage. In such a competitive market, they must respond to market preferences in managing the trade-offs between cost control and patient benefit – for instance, in determining which drugs to drop from a formulary, or which drugs to place in a non-preferred, higher co-pay tier. In this way, the U.S. system is able to achieve the very high usage of generics, for example, compared with the OECD countries we analyzed.

2. Adverse consequences for OECD consumers and countries

What has been the effect of the various market interventions imposed by OECD governments? It does appear that controls achieve some of the political and social objectives for which they were designed. Specifically, they seem to have been effective at holding down the aggregate growth of drug spending where applied, especially since the mid-1990s.[10] While U.S. prescription drug costs grew at an annual rate of 10 percent between 1992 and 2001, other countries saw slower rates of growth ranging from 0 percent (Japan) to 4-5 percent (France and the United Kingdom) to 7.5 percent (Canada). (It is worth noting that according to recent research by the Office of the Actuary at the Centers for Medicare and Medicaid Services (CMS), the overall drug cost growth in the United States in recent years has been driven mainly by higher volumes and by shifting the

[9] Timothy C. Wentworth, Group President, National Accounts, Medco, 14th Annual Wachovia Securities Nantucket Equity Conference, June 23, 2004.
[10] OECD Health Data 2003.

mix toward newer, more innovative medicines rather than by increased pricing across a fixed basket of medicines.[11] This reflects the impact of the many new drug categories introduced over the past decade as well as the introduction of more innovative products in existing categories). The evidence does suggest that government interventions succeed in extracting price concessions from manufacturers, and thus achieving lower prices for new medicines than in the United States. In OECD countries, manufacturers' sales prices for most new drugs appear typically to be about 40-50 percent below U.S. prices[12] even after U.S. rebates[13] are taken into account (although selected innovations in oncology and anti-virals have much more similar pricing in the U.S. and OECD markets). (***Exhibit 5***)



[11] C. Smith (from National Health Statistics Group, Office of the Actuary, at the Centers for Medicare & Medicaid Services), "Retail Prescription Drug Spending in the National Health Accounts," *Health Affairs*, 23 (Jan/Feb 2004): 1, 160-167. According to this analysis, the average annual growth in drug expense from 1994-2002 was 14.5 percent, of which 10.6 percent was driven by volume and mix shift and 4.0 percent was driven by price growth.

[12] This pricing differential is confirmed in PPRS "Study into the Extent of Competitiveness" in "The Supply of Branded Medicines to the NHS" December 2002.

[13] In the United States, rebates are a crucial aspect of pricing, but they tend to go unobserved, being part of confidential negotiations between payor and manufacturer. We allow for an average U.S. rebate of 11 percent, based on an evaluation of various public data sources including: (1) Abrams, Lawrence "Estimating the Rebate-Retention Rate of Pharmacy Benefits Managers", April 22, 2003; (2) CMS; (3) CBO; (4) Van Oehsen, William H. "Pharmaceutical discounts Under Federal Law: State Program Opportunities", Public Health Institute, May 2001

While our purpose is not to assess the overall societal impact of health care policy for OECD countries, it is worth noting that there is an emerging literature which suggests that market interventions do lead to adverse effects for the OECD. A recent study by Bain, for example, concludes that market interventions in Germany actually leads to a net economic loss for the society.[14] Let us review some of the particular adverse consequences of interventions that emerged from our analysis of selected disease areas and are relevant for policy making in the United States.

Trade-off's for OECD consumers

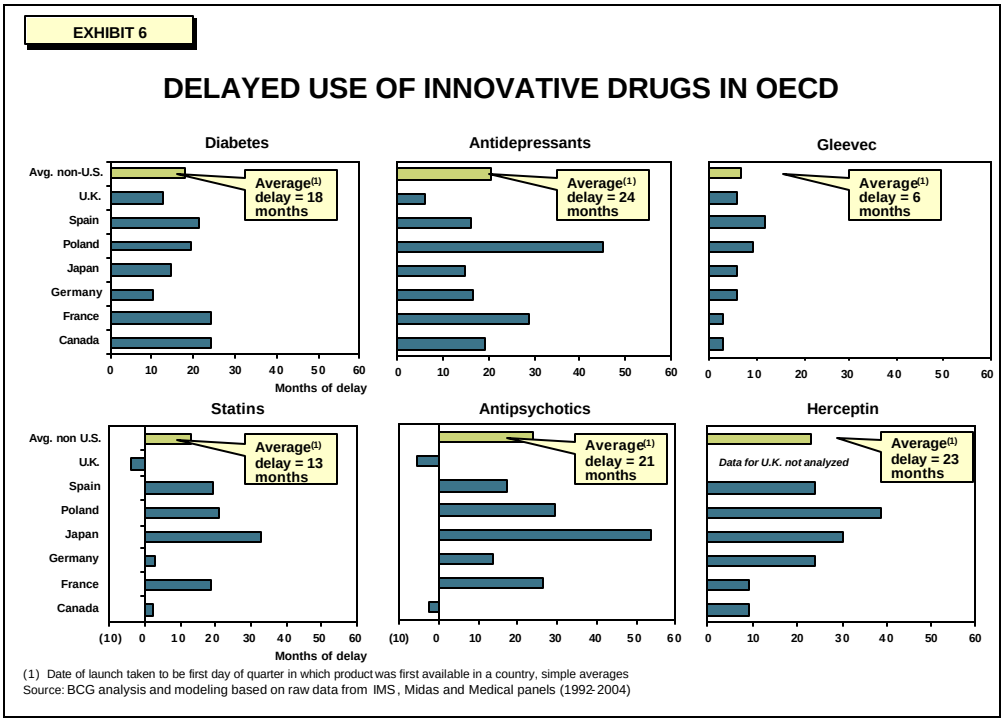
Whatever the short-term cost benefits, OECD patients are in other ways *dis*advantaged by the market interventions imposed by their governments: they have less chance of getting the latest drugs, and their chances of recovery or effective relief are to that extent compromised.

Reduced access to innovation

Patients in OECD countries typically gain access to innovative medicines – if at all – only after a substantial delay and at a level of availability usually well below that enjoyed by U.S. patients.

[14] Gilbert, Rosenberg, "Imbalanced innovation: The High Cost of Europe's Free Ride", In Vivo, 2004. Gilbert and Rosenberg are with Bain.

Regarding speed of access, we measured the lag between the U.S launch and the OECD launch for our sample therapeutic categories.[15] This lag is a function both of the administrative burden imposed by the market interventions and of the disincentives that biopharmaceutical companies face when launching medicines.[16] Among medicines used to treat chronic conditions, we found that the delay ranged from a low of 13 months for statins to a high of 24 months for anti-depressants. Even in the case of breakthrough first-in-class drugs such as Herceptin and Gleevec,[17] two drugs with significant therapeutic benefits for cancer patients and despite having pricing levels very similar to the U.S., average launch delays were substantial – 23 months and 6 months respectively. (***Exhibit 6***)



[15] Danzon, Wang and Wang (2003) studies the same topic and uses a broadly similar metric: the difference between a drug's "global" launch (measured as when the drug was launched in either the United States or the United Kingdom) and its local launch (measured by the launch date recorded in the IMS database, rather than the quarter in which sales are first recorded which is used in this study). The unweighted average delay estimated by Danzon, Wang and Wang (2003) for the same basket of countries analyzed in the current study is ~15 months.

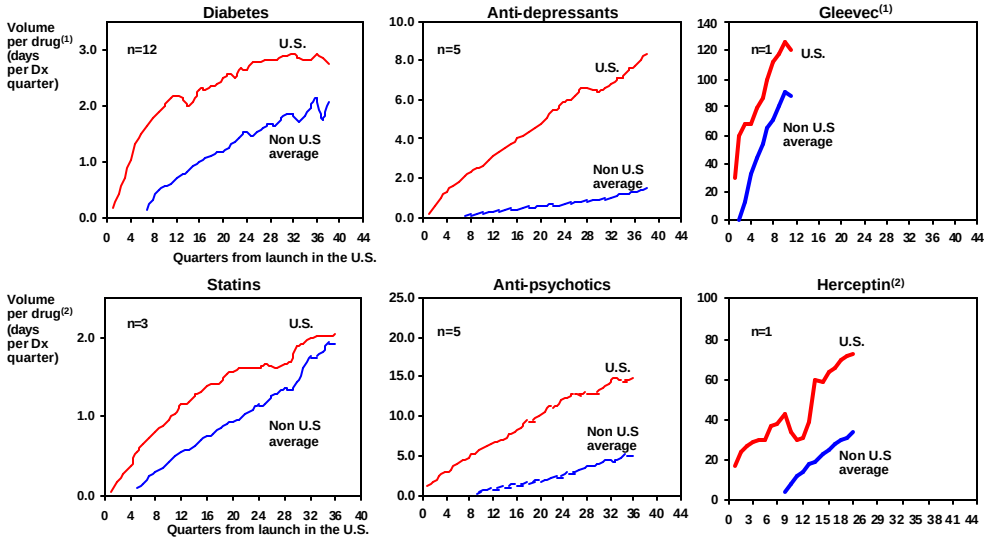
[16] Danzon, Wang and Wang (2003).

[17] Herceptin went from clinical trials to regulatory approval in less than 3 years, relative to the typical 6-9 years in development; Gleevec's FDA approval from filing came through in just 3 months, relative to the typical 12 months.

Even once a new drug is launched, the slower uptake still keeps utilization rates at about 50 percent of U.S. levels even up to three years after launch. Even 8 years after launch, volumes in the OECD can lag 15-20 percent behind U.S. rates. (***Exhibit 7***)

EXHIBIT 7

LOWER PENETRATION OF INNOVATIVE DRUGS IN OECD

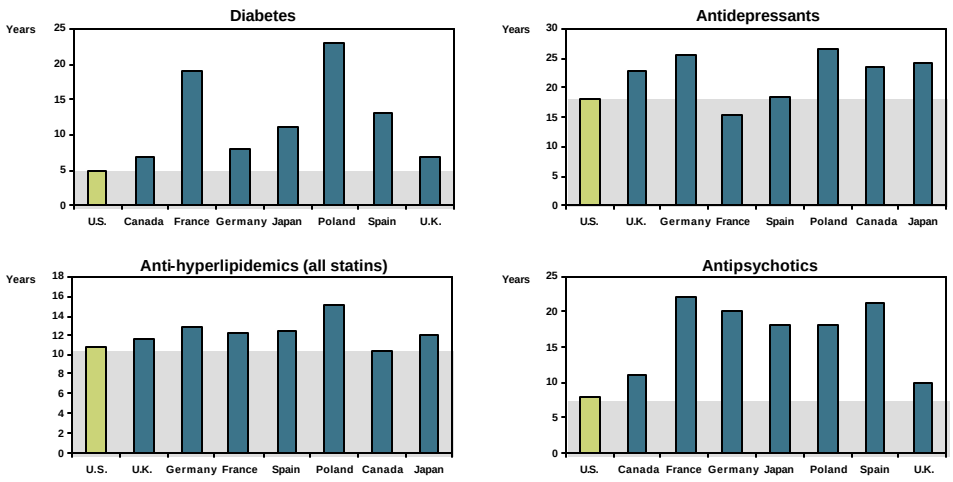


(1) Volume measure forGleevec is standard units per Dx
(2) Volume measure forHerceptin is grams of active ingredient per capita
Source: BCG analysis and modeling based on raw data from IMS, Midas and Medical panels (1992-2004)

The result is that OECD patients face a mix of therapies that is weighted toward older drugs, often drugs already superseded in most U.S. physicians' guidelines. For instance, the weighted average age of diabetes drugs in the United States is 5 years, as against 7-8 years in Canada, Germany and the United Kingdom, and as much as 19-23 years in France and Poland. As for anti-psychotics, U.S. patients are treated with drugs that are on average 8 years old, while patients in most of the other sample OECD countries receive drugs that are on average 18-21 years old.[18] (***Exhibit 8***).

EXHIBIT 8

OLDER DRUGS USED TO TREAT DISEASES IN OECD
Weighted Average Age of Drug Therapies Used



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

This delay is partly due to the fact that, in Europe, after new drugs have received regulatory approval, pharmaceutical companies must obtain approval from each national government for the prices they charge.

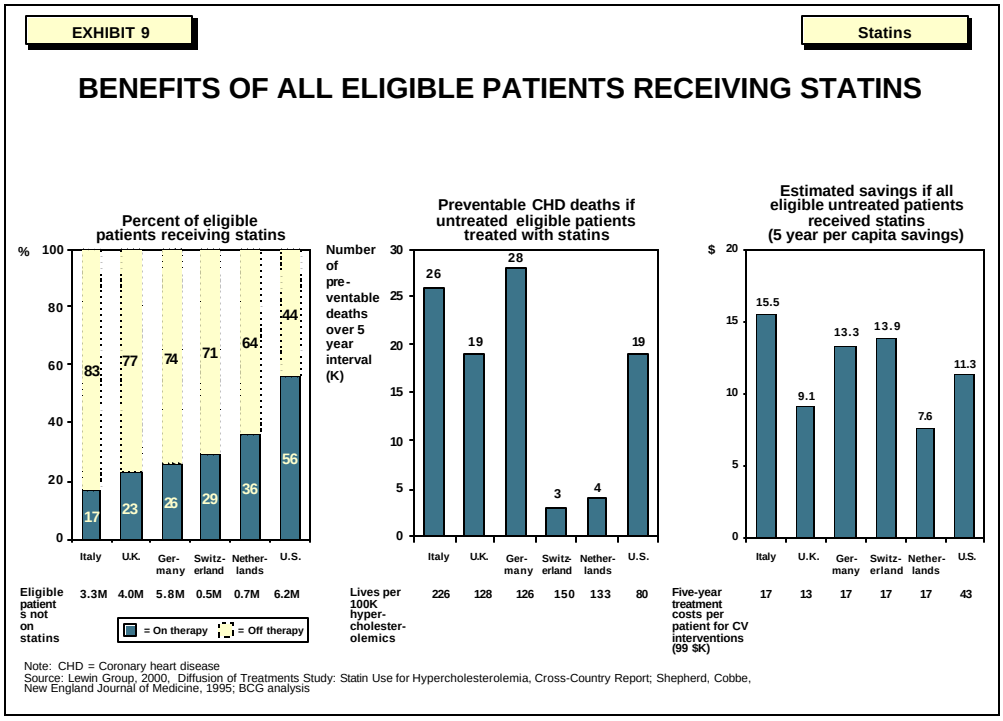
[18] Canada and the United Kingdom are exceptions, with drugs that are 11 and 10 years old on average.

Health consequences of reduced access

For many patients, older medicines prove efficacious. Furthermore, there is a rich academic literature that asserts that curtailed access to innovative drugs has a negative impact on health outcomes. For example, one study found that the availability of new drugs (measured by NCE launches) was responsible for 40 percent of the increase in life expectancy over a 14-year time period from 1986-2000.[19] Certainly for the disease areas we studied, reduced access can lead to compromises in health outcomes for afflicted patient populations.

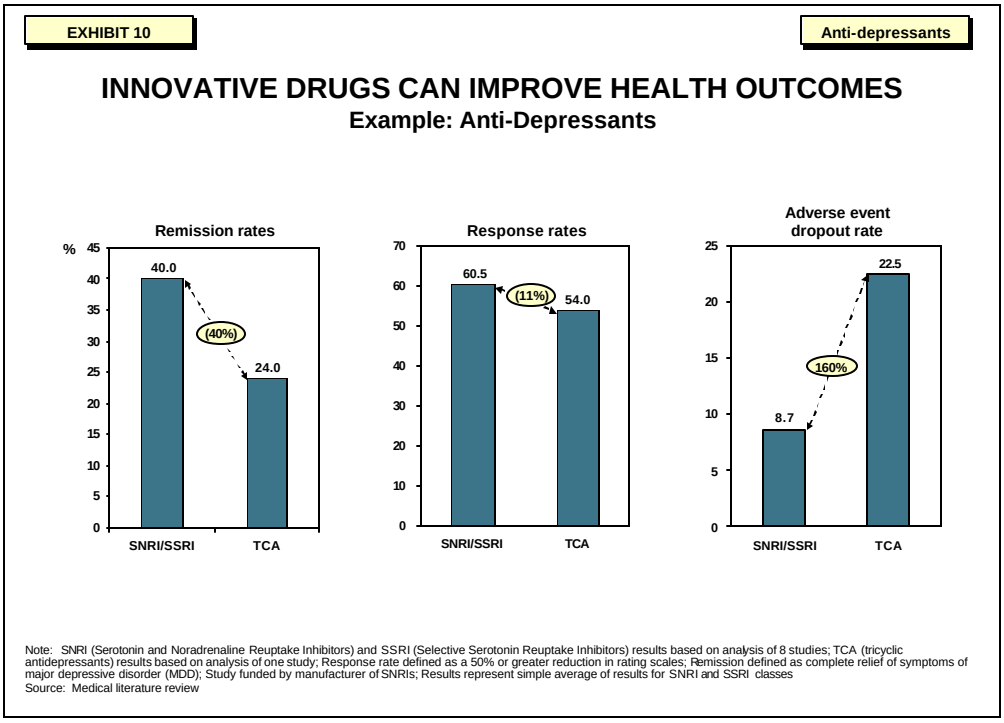
[19] "The Impact of Drug Launches on Longevity: Evidence from Longitudinal, Disease-Level Data from 52 Countries, 1982-2001," Frank R. Lichtenberg, NBER working paper # 9754, June 2003

In the case of hyperlipidemia, statins are widely recognized as effective in reducing cholesterol, and recommended as a preventative treatment for high-risk patients. In spite of their obvious clinical advantages, statins are still underutilized – far more so in OECD countries than in the United States. One study from 2000 reported that while 56 percent of eligible U.S. patients were taking statins – itself far from adequate – the figures for Italy and the United Kingdom were significantly lower, at 17 percent and 23 percent respectively. The study estimated that many lives could be saved if all eligible patients were on statin therapy, and, furthermore, that health care system would experience significant cost savings due to a reduction in emergency room care and hospital stays. (***Exhibit 9***)



Psychosis is a disease that has a highly disruptive effect on its affected patients' lives, on the economy and on society in general. Patients using newer "atypical" anti-psychotics, rather than the traditional typical anti-psychotics, show marked improvements in both so-called negative and positive side effects,[20] and have higher compliance rates.[21]

In treating depression, patients taking SSRIs and more recently the SNRIs experience superior health outcomes to patients on older therapy such as tricyclics. Study evidence suggests that the newer drugs yield higher remission and response rates, coupled with a lower incidence of adverse events – side effects that drive patients to end therapy prematurely. (***Exhibit 10***)



[20] See literature review in Wertheimer, Levy and O'Connor "Too many drugs? The clinical and economic value of incremental innovations" in *Investing in Health: The Social and Economic Benefits of Health Care Innovation*, volume 14, Elsevier Science, 2001.
[21] Medical literature review

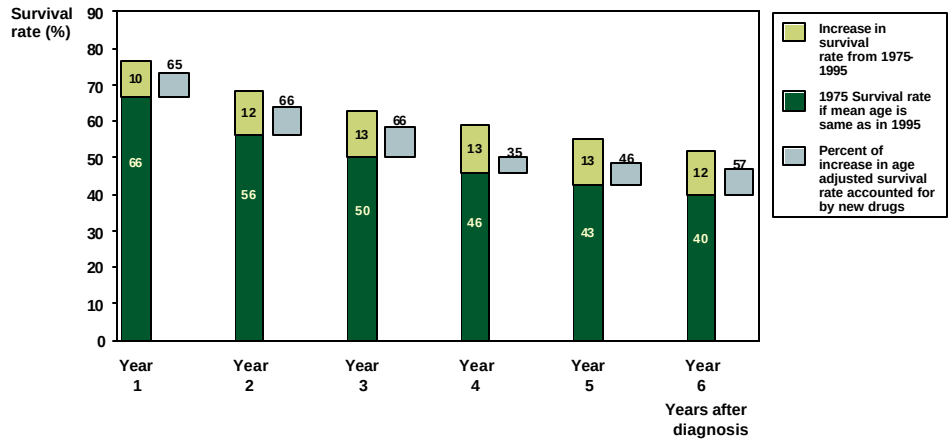
In addition to the immediate health benefits for patients, these newer therapies can also provide second-order benefits, by reducing the number of physician visits and hospitalizations.[22]

Finally, in the case of cancers, the differential benefits of newer drugs are even more pronounced. Recent innovations in oncology are widely recognized for the improved survivorship of cancer patients.[23] (***Exhibit 11***)

EXHIBIT 11

RESULTS OF LICHTENBERG STATISTICAL ANALYSIS ON IMPACT OF NEW DRUGS ON CANCER SURVIVAL RATES

Effect of Increase in 1975 – 1995 Stock of Drugs on Increase in Survival Rates

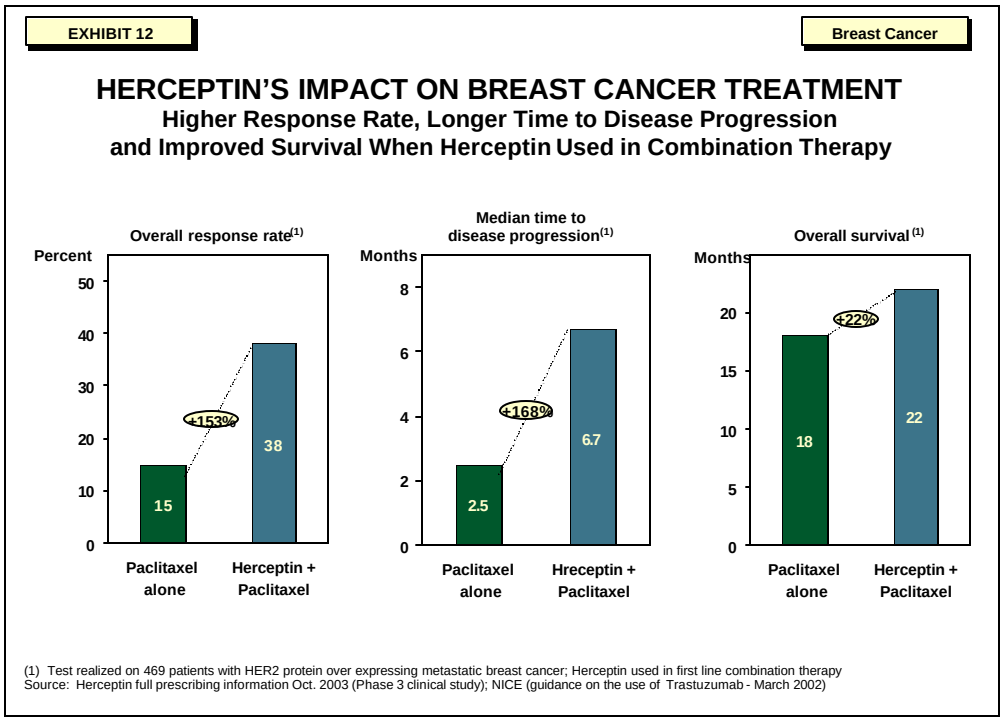


Source: "The expanding pharmaceutical arsenal in the war on cancer," F. R. Lichtenberg, Columbia University, 26 January 2004

[22] Medical literature review

[23] Lichtenberg "The expanding pharmaceutical arsenal in the war on cancer" (2004)

Studies have shown that Herceptin, for example, when used in combination with other drug therapies, produced marked improvements in response rate, disease progression and median survival from time of diagnosis. (***Exhibit 12***).



Negative consequences for OECD economies

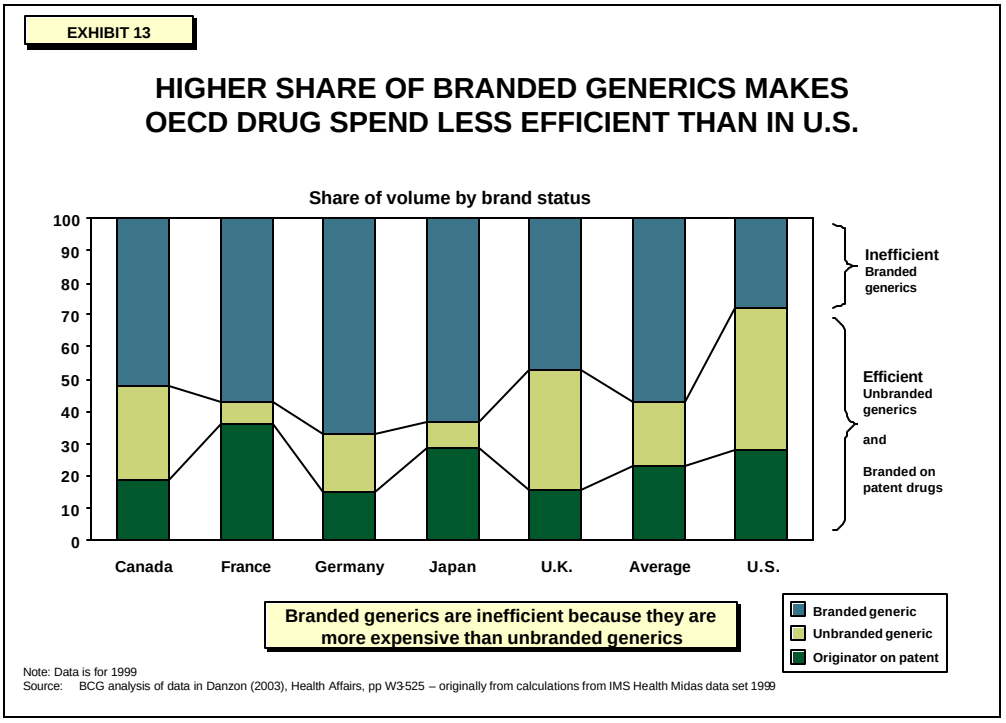
For the economies of the OECD countries, interventions produce two key adverse consequences: first, misallocation of resources to older drugs, and second, an erosion of the vitality in the research-based biopharmaceutical industry.

Inefficiency through misallocating resources to older drugs

If market interventions are designed to minimize spend on newer branded drugs, presumably they would strive to minimize spend on older branded drugs which have lost their patent

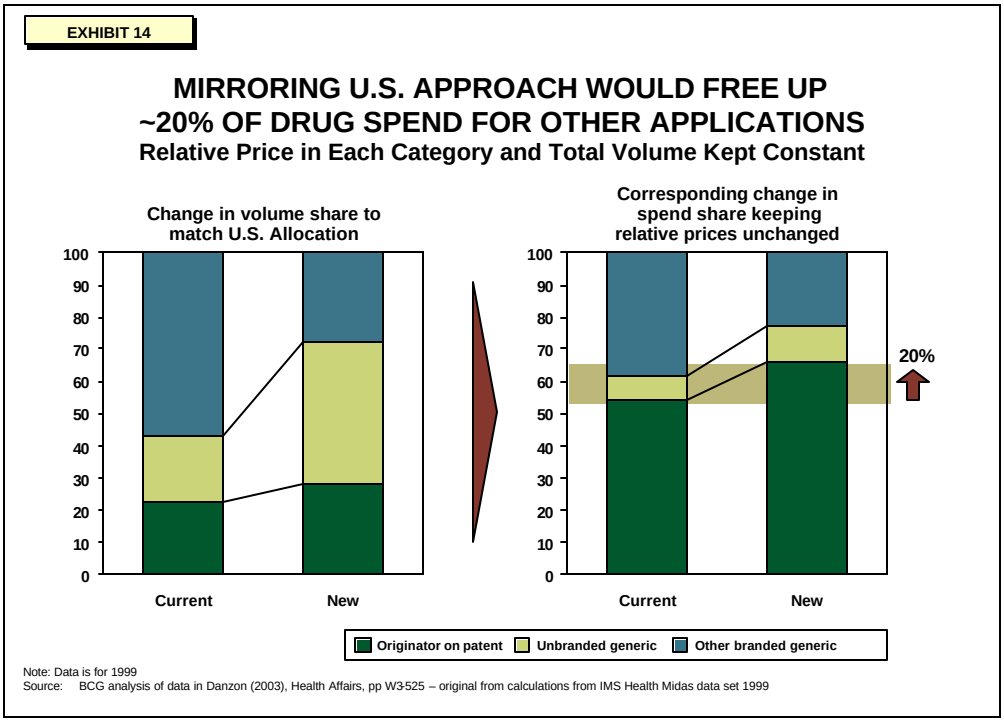
protection. It turns out that that is not the case in many OECD countries. Consider what happens with off-patent drugs. As soon as a drug loses patent protection, several companies typically start manufacturing it in direct competition with one another. In OECD markets, some of these manufacturers will attempt to brand and market their versions as the original manufacturer has. Others produce pure generics. Interestingly, based on historical data, the new "branded generics" usually obtain a higher price than the "pure generic" copies do. The spend that goes into branding the generic provides negligible incremental benefit for the patient or the health system over the pure generic copy.

Competitive markets understand this. The share of pure generics in the U.S. market is accordingly about twice that of the branded versions. Across European countries, by contrast, the share of pure generics is only about one-third that of the branded versions.[24] (***Exhibit 13***)



[24] BCG analysis of data in Danzon (2003), Health Affairs, p. W3-525.

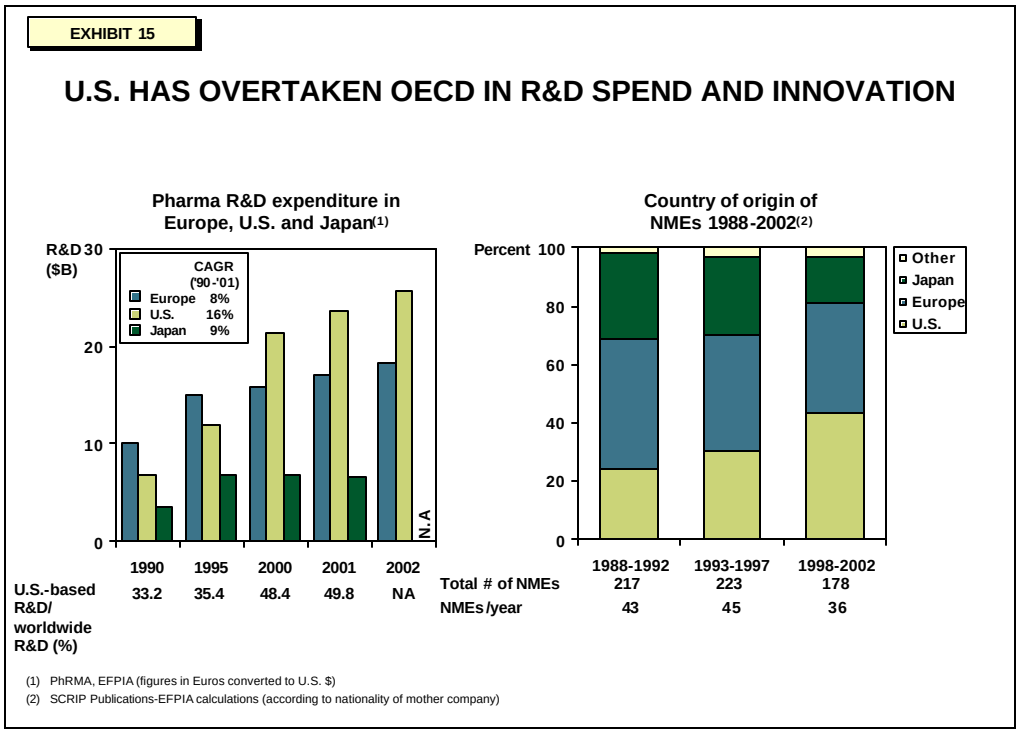
As a result, if the OECD countries were to shift their usage of pure generics to match U.S. proportions, we estimate that their health care systems could save as much as 20 percent of their annual overall drug spend. These resources could be reallocated to provide consumers greater access to more innovative drugs – and their accompanying health benefits — without any budget compromise. (***Exhibit 14***)



Struggling local pharmaceutical industry

By curbing the adoption of newer drugs, and skewing the rewards away from innovation, governments in Europe and Japan have likely contributed to the relative decline of their respective research-based pharmaceutical industries. The figures are compelling. In 1990, the United States accounted for just about a third of the global pharmaceutical R&D spend, while

Europe had almost half. Today, the United States and Europe have in effect reversed positions.[25] (***Exhibit 15***)



What happened? A number of factors have contributed to the greater success of the U. S. pharmaceutical industry, including the large public research funding in the United States[26] and the greater availability of capital to support research-based ventures[27]. A further decisive driver,

[25] PhRMA, EFPIA, SCRIP Publications, EFPIA calculations.
[26] In 2002, the U.S. government dedicated $18.4 billion to medical research, about five times the amount ($3.7 billion) spent by the entire European Union. See K. Murphy and R. Topel (editors), *Measuring the Gains from Medical Research: An Economic Approach* (Chicago, IL: The University of Chicago Press, 2003).
[27] Witness the much larger pool of venture capital financing available in the United States. In 2003, in the U.S. there were $2.8B in new venture financing for biotech companies and $11.1B in follow-on financings; this compares with a little over $1.0B in venture financing and $1.6B in follow-on financings. Ernst & Young "Resurgence: Americas Perspective Global Biotechnology Report" (2004)

however has been the greater ability of U.S. based companies to invest in their own growth through R&D.

Because the U.S. market rewards innovation better than other markets, and U.S.-headquartered companies have a disproportionate share of the U.S. market, they have a greater ability—and incentive—to invest in R&D. In this context, a number of international pharmaceutical companies have been increasing their presence and investment in the United States. Novartis has moved their Research headquarters to the United States, and many other companies are rebalancing their center of gravity towards the United States (for example, GSK and Aventis) at least partially reflecting the benefits of keeping research and development activities near the most important market.

3. Negative Consequences for the U.S. consumer and economy

Lower revenues to fund global pharmaceutical research

The adverse consequences of OECD market interventions are also borne by U.S. consumers. By imposing government controls on prices and restraining the market penetration of innovative therapies in their home markets, OECD governments are, in effect, sharply reducing the *global* returns to pharmaceutical innovation and the global pool of cash available for research on new medicines. Our analysis highlights the disparate contributions made across countries. Take the case of diabetes: on a per-patient basis (that is. for each person diagnosed with diabetes), revenues for innovative drugs in the OECD are just one-third those of the United States over the lifecycle of the drug.[28] This great disparity is driven both by lower usage of innovative drugs in

[28] As noted below, this estimate is based on an analysis of the experience of new drugs for diabetes and hyperlipidemia.

OECD countries (as a result of delays in launch, slower adoption rates and lower peak penetration), and by the lower pricing imposed through government interventions.

How can the impact of such distortions on the economics of the biopharmaceutical industry be measured? One way is to consider the counter-factual situation – one in which the OECD government interventions did not exist. By comparing the estimated figures of what the world would be without OECD interventions with those of the real world today, we can get a good idea of the cost that these interventions impose on the United States. In the hypothetical world without cost controls, revenues for the pharmaceutical industry would not be distorted; our assumption is that all OECD markets for pharmaceuticals would function more like the U.S. market, both in the receptiveness to new drugs (volume uptake) and in the rewards they offered manufacturers (price). Below we describe our approach and assumptions defining a reasonable upper and lower bound to both volume and price as they might have been under this hypothesis, and hence defining a range of estimates of the revenues lost to the industry:

Volume scenarios

Consider first of all the volume of drugs consumed per patient: To ascertain the difference between OECD and U.S. volumes for a specific disease, you need to distinguish two components:

(a) The total *amount* of drug treatment for the disease – measured, for example, by "days-of-treatment" prescribed per diagnosed patient. (For some diseases, such as diabetes, an OECD patient tends to receive more drug therapy than a U.S. patient does, while for other diseases, such as depression, the reverse holds true.)

(b) The *share* which innovative drugs have of the total treatment prescribed.

Using these two measures, we can devise two scenarios in which to calculate the volume of innovative medicines that would be prescribed in the OECD in the absence of government controls. In the first scenario, component (a) remains the same, but component (b) changes to match the U. S. experience. In other words, the current amount of drug treatment for a given disease remains unchanged (the same number of days-of-treatment per patient), but the *share* of innovative drugs shifts to match that of the United States. Implicit in this assumption is the view that local physicians retain their basic treatment strategies, using drug therapies, non-drug therapies, and no therapy in their actual current proportions. We call this scenario the "innovative share of total prescriptions" assumption. Note that it consistently leads to higher volumes of innovative drugs in OECD countries, since in the real world their adoption of innovative drugs in the diseases we studied always lags the U.S. adoption rates.

In the second scenario, component (a) changes as well as component (b) to reflect U.S. experience. The total amount of drug treatment per OECD patient – specifically, the number of days-of-treatment per patient – changes to match that of a U.S. patient. In other words, if U.S. physicians typically prescribe a specified number of days-of-treatment with innovative drugs per patient, then the OECD physician is assumed to do the same. Implicit in this assumption is the view that innovative drugs – through their greater perceived potency or other features – reshape the overall prescribing habits of physicians universally. For example, a drug offering a superior side-effect profile might be prescribed more frequently, resulting on average in more days-of-treatment for the patient population. We call this scenario the "volume of prescriptions" assumption.

Price scenarios

In the absence of government interventions, we assume that prices will rise for innovative drugs across the OECD. The question is: how much? Here again are two possible scenarios.

In the more conservative one, drug prices across the OECD are assumed to match the higher U.S. levels, though adjusted to reflect differences in the GDP per capita (which principally means adjusting prices in OECD countries to reflect their lower per capita GDP relative to the United States). Implicit in this assumption is the view that what consumers are willing to pay for drugs is somehow linked to their incomes. Some might view this as being reflective of local "ability to pay." If so, it is misconceived given the readiness of OECD consumers to pay equal or higher prices vis-à-vis U.S. consumers for products such as computers, music CDs, or movie tickets. We call this assumption "U.S. pricing adjusted for GDP per capita."

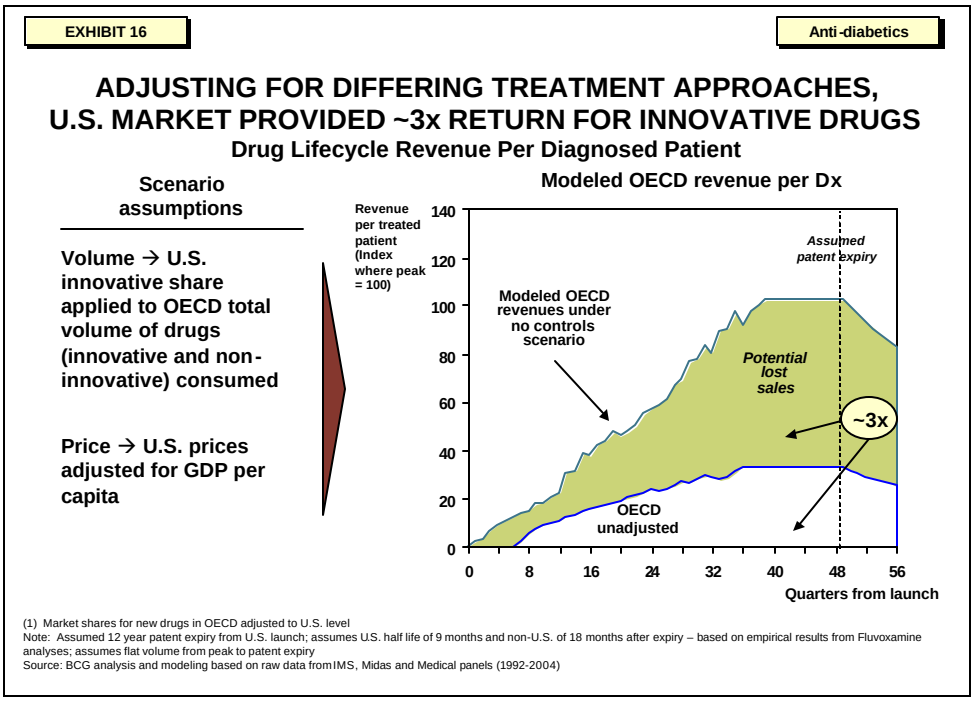
In the second scenario, drug prices in the OECD countries are assumed to match U.S. levels without any adjustment -- simply in accord with the currency exchange rate. Implicit in this assumption is the view that the underlying microeconomics which drives pricing decisions – including marginal revenue and marginal cost – works in the same basic way across OECD countries as it does in the United States. We call this assumption "unadjusted U.S. pricing."

The likely range

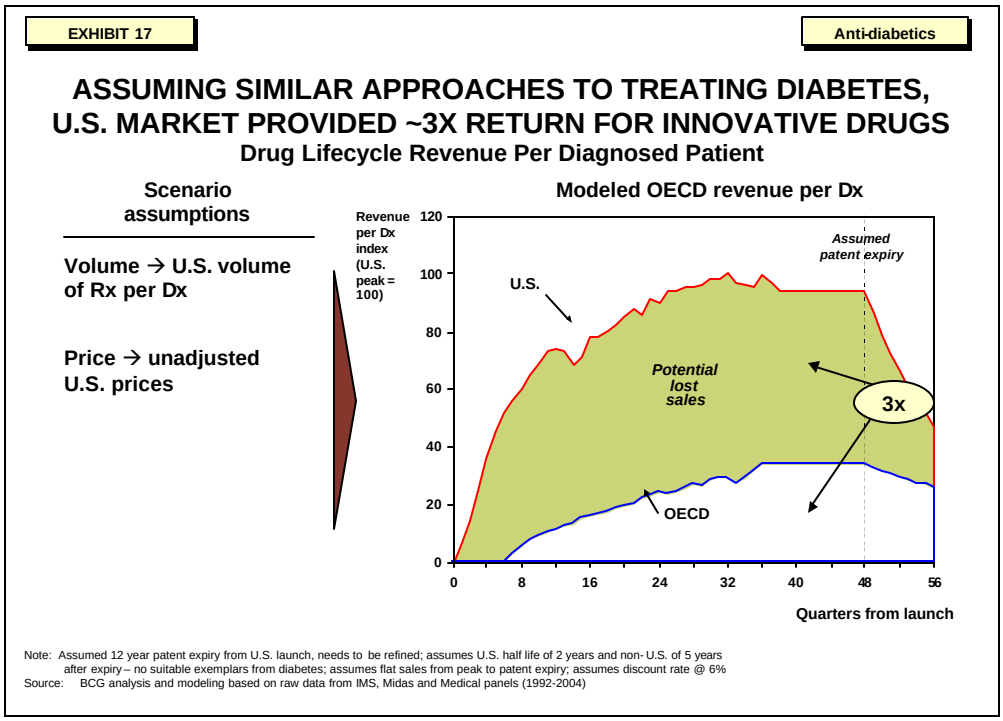
In our hypothetical intervention-free world, the total volume and the average pricing in OECD markets would likely lie somewhere between the two sets of assumptions in each case. So we can use the alternative scenarios to frame a reasonable range of how these markets would have behaved for each class of drugs in our sample.

In the case of **diabetes**, the typical OECD patient currently receives more "days of treatment" than the U.S. patient – but, as noted above, with drugs significantly older on average. Now, take scenario 1 for both volume and price – in other words, assume that, without government interventions, volume in OECD countries match the U.S. innovative share of total prescriptions and pricing in OECD countries would match U.S. prices adjusted for GDP per capita. In that

case, the latest diabetes drugs would provide the industry with about three times the revenues per OECD patient that they do today. (***Exhibit 16***)



And if you take scenario 2 for both volume and price, such that the OECD countries match the U.S. volume of prescriptions and match unadjusted U.S. pricing, the increase in revenues would again be about threefold.[29] (***Exhibit 17***).



For **statins,** a comparable analysis provides a range of two to two-and-one-half times the revenues per patient in the absence of government interventions.

Applying the same analysis to next generation **anti-depressants** and **anti-psychotics** shows an even greater increase in revenues for manufacturers. For anti-depressants, revenues per OECD patient would increase by as much as a factor of 12; for anti-psychotics, by a factor of 6

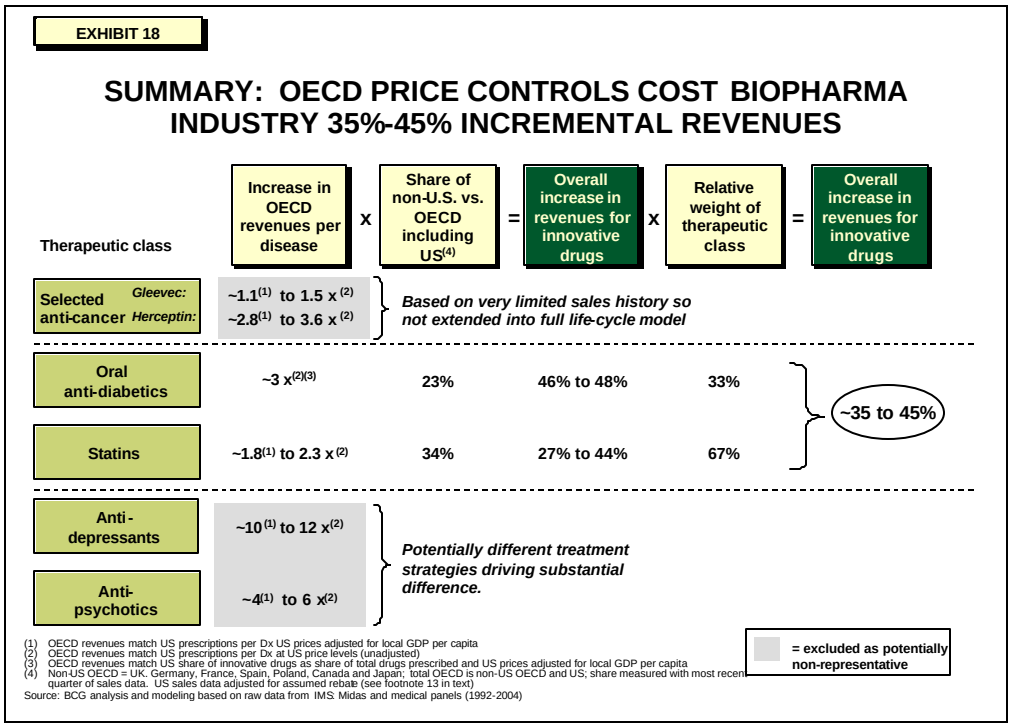
[29] Because OECD physicians typically prescribe more daily drug doses per diabetic than their U.S. counterparts, the first scenario for volume (assuming U.S. innovative share of prescriptions) actually results in a higher volume of innovative drugs per diabetic than is achieved in the United States. In the second scenario, the lower volume of prescriptions (relative to scenario 1) counterbalances the higher prices (relative to scenario 1).

(estimates under scenario 2 in each case in which OECD countries match the U.S. volume of prescriptions and the U.S. unadjusted price). One of the underlying reasons for the larger impact in these diseases compared with diabetes and statins is likely the greater difference in the OECD and U.S. approaches to treating the diseases, making these results potentially less reflective of the experience of other drug categories.

To sum up the analysis[30], the experience of innovative drugs across our diseases indicates a substantial potential to increase revenues in the absence of government cost controls. It also indicates a wide range depending on which disease areas are considered. Some of the difference is certainly reflective of differing patterns of treatment and some is probably due to the way that market interventions vary by disease area.

[30] It was not possible to develop a fully comparable analysis for recent anti-cancer drugs (Gleevec, Herceptin) because of the limited data available

We base the rest of this analysis on the more conservative revenue multipliers emerging from the disease specific analyses and assume that, in the absence of government interventions in the OECD, revenues per patient in the OECD would be higher by a factor of two to three. This approach is reasonable given its conservatism, the broad importance of the disease categories analyzed,[31] the consistent direction in which our analyses of these diseases point. Given that the OECD markets today represent about 25-35 percent of the global revenues for patented drugs for the diseases we used in this analysis, we arrive at an average overall revenue for the industry increase of 35-45 percent. Plainly put, if the OECD cost controls did not exist, revenues for innovative drugs would increase by 35-45 percent. In light of our exclusion of the more extreme experience of the anti-depressants and the anti-psychotics, this finding can be regarded as fairly conservative. (***Exhibit 18***)



[31] See appendix on sample disease categories

Lower global R&D investment

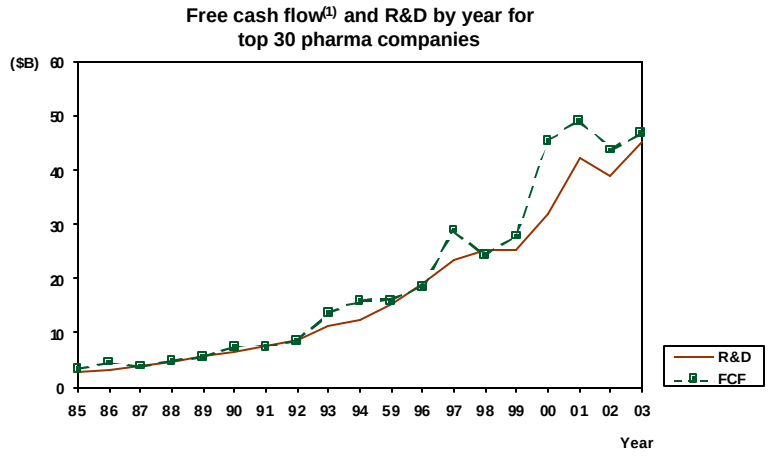
Such increased returns to innovation would have significant consequences for the level of R&D. The business of researching and developing drugs is a notoriously risky one. The Boston Consulting Group has estimated that almost three-quarters of investment in new drugs is spent on projects that fail somewhere along the research and development process.[32] But the high potential rewards attract investment and encourage the pursuit of riskier projects, whereas lower returns merely discourage overall investment and drive researchers toward more conservative projects.[33]

[32] Analysis based on the model, reported in The Boston Consulting Group "A Revolution In R&D" (2001).
[33] Basic portfolio management theory demonstrates that to achieve a certain targeted risk-adjusted return for a portfolio of projects, a company must consider four variables: the projected overall profits to the projects, the overall investment cost, the time horizon for investment and profit and the riskiness of projects. If the overall profits are lower, and a company cannot substantially change the investment cost or time horizon (for the pharmaceutical industry, these variables are determined more by science and regulation than by management policy), the company will tend to exclude riskier projects

Historically, the biopharmaceutical industry has maintained a close correlation between its R&D investment and its free cash flow.[34] (***Exhibit 19***)

EXHIBIT 19

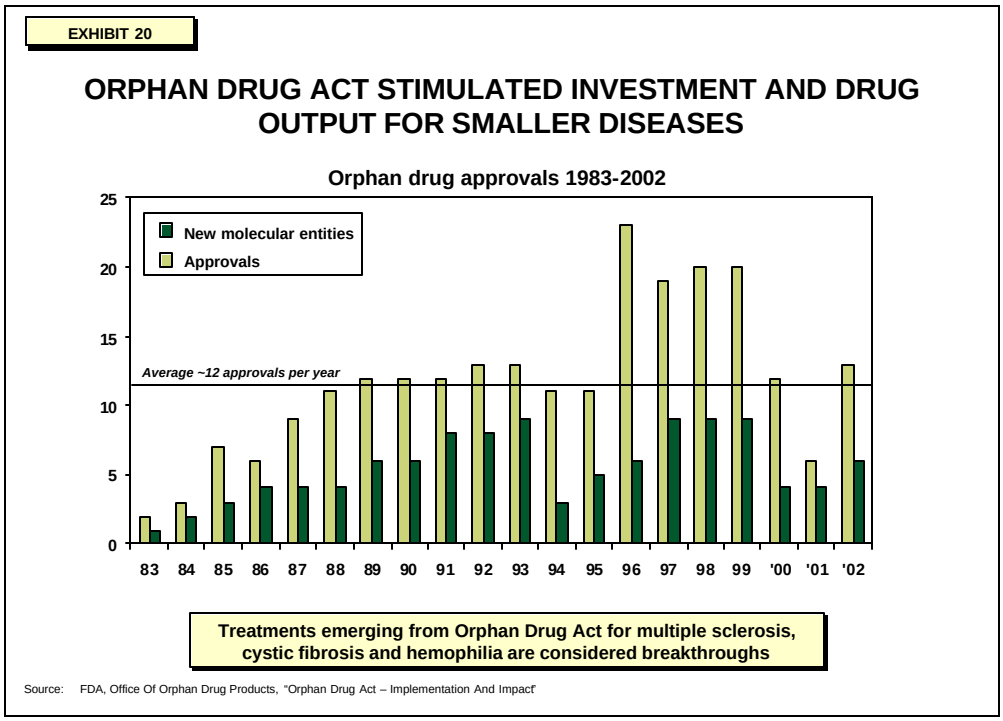
HISTORICALLY, INDUSTRY HAS MAINTAINED CLOSE RELATIONSHIP BETWEEN FREE CASH FLOW AND R&D SPEND



(1) EBITDA – Taxes – CapEx – Change in Working Capital
Source: Compustat; BCG Value Science center analysis of top 30 pharma companies

[34] Defined in our analysis as Earnings Before Interest, Depreciation and Taxes less Taxes less Capita Expenditures less Net Change In Working Capital. Note, Scherer (2001) Health Affairs developed a similar view regarding the relationship between gross profitability of the industry and R&D investment

The industry also has a record of responding to incentives stemming from changes in regulations or the environment. Witness the surge of investment that followed the Orphan Drug Act of 1983, where new rewards were created for a particular kind of R&D investment (diseases with fewer than 200,000 patients). The increased investment in R&D led to many new treatments for orphan diseases.[35] (***Exhibit 20***)



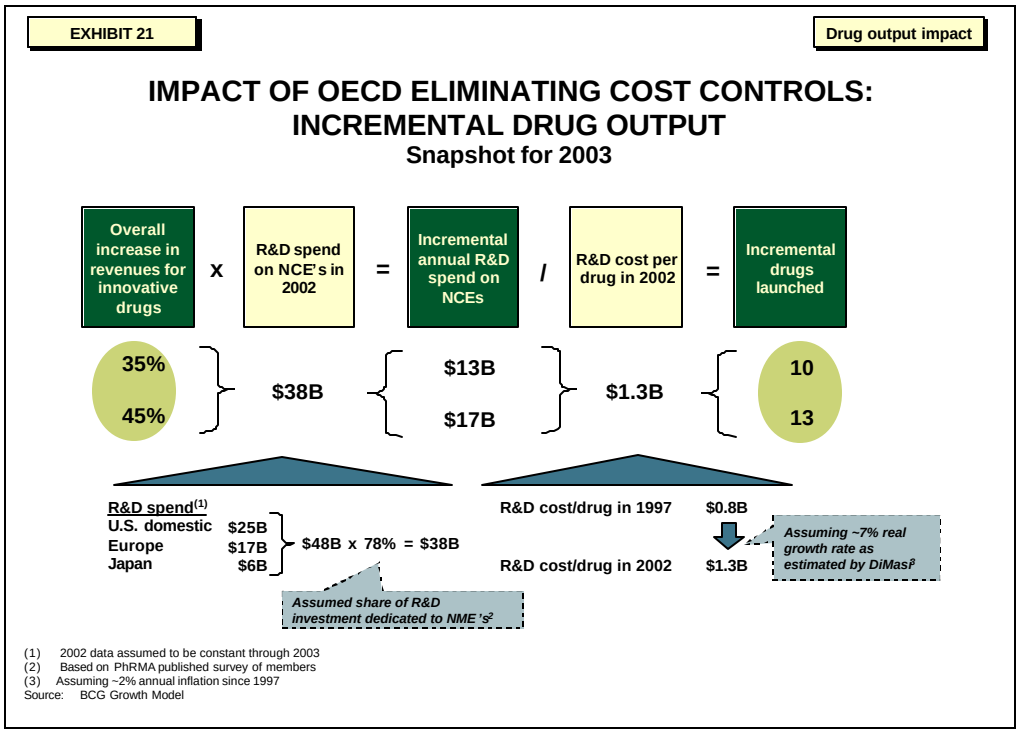
We assume that, if the industry experienced a 35-45 percent increase in revenues on its branded products, it would grow its R&D investment by the same 35-45 percent[36]. Applying these assumptions to the world in 2003, we can accordingly say that OECD government interventions are effectively discouraging the incremental investment of $17-22 billion in annual global biopharmaceutical R&D.[37] The U.S. consumer and economy bear their share of the consequences, in the form of fewer innovative medicines, fewer drugs competing in any given

[35] FDA, Office of Orphan Drug Products, "Orphan Drug Act – Implementation and Impact."
[36] Implicit in this assumption is the prediction that the industry cost structure remains fixed – in other words, the ratio of R&D spend to revenues would remain the same.
[37] Estimate for 2003; values for other years will vary but remain at about the same magnitude. Estimate is for a 35-45 percent increase in the $48 billion spent globally on research in innovative pharmaceuticals today.

category to drive prices lower, fewer jobs and a slower growth trajectory for one of the preeminent U.S. industries.

Fewer innovative therapies for U.S. consumers

Supposing that this level of incremental R&D had materialized over the past decade, culminating in the incremental $17-$22 billion R&D spend in 2003, we estimate that the result would have been 10-13 additional drug launches[38] in 2003 alone (which amounts to 50 percent of the new drugs approved in that year, approximately a third of the historical output). (***Exhibit 21***)



[38] Our analysis assumes that ~22 percent of the R&D spend is on approved molecules (for instance, new indications related to them or incremental innovations) and on other research not directly connected with producing new molecules, so the amount available for investing in new drugs would be $13-17 billion.

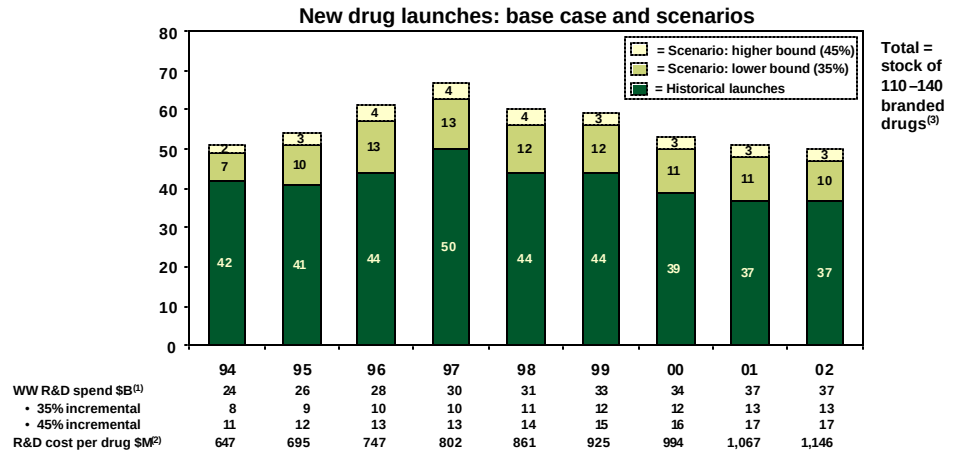
Furthermore, if the OECD controls had been absent in the past, the incentives for R&D investment would have been greater in the past as well as the present, and the industry would have produced more drugs in past years too. According to our analysis, there would have been as many as 110 to 140 more innovative drugs available to the U.S. health care system today. (***Exhibit 22***)

EXHIBIT 22

Drug output impact

IMPACT OF OECD ELIMINATING COST CONTROLS: INCREMENTAL STOCK OF AVAILABLE DRUGS

Potential Stock of Branded Drugs Available in 2003



	94	95	96	97	98	99	00	01	02
WW R&D spend $B(1)	24	26	28	30	31	33	34	37	37
• 35% incremental	8	9	10	10	11	12	12	13	13
• 45% incremental	11	12	13	13	14	15	16	17	17
R&D cost per drug $M(2)	647	695	747	802	861	925	994	1,067	1,146

(1) Estimated worldwide spend adjusted for an estimate 22% spent on product line extensions; (2) Derived from DiMasi 2003 assuming $902MM is for 1997 median launch date, 7.4% annual real cost growth rate and a verage 2% inflation; (3) Including estimate for 2003

Note: New drug launches for 2002 are estimated using 2001 data

Source: BCG analysis based on data from IMS, PhRMA, EFPIA,, JPMA, Di Masi et. al. (2003) assuming $802MM estimate is 1997 and 7.4% average annual real growth rate; BCG Growth Model

Bear in mind that the industry has historically introduced one entirely new class of drugs for every three drugs approved.[39] Applying these averages to the incremental stock of innovative drugs, our analysis suggests further that, without OECD controls, there would be about 35-40 entirely new drug classes today.

History demonstrates that as new therapeutic categories are opened, significant clinical and economic benefits have emerged. One widely cited analysis by Lichtenberg estimates that NCE launches between 1986 and 2000 were responsible for about 40 percent of the overall increase in

[39] BCG analysis based on data from Evaluate plc

longevity achieved over the same time period.[40] Other analyses have underscored the high returns to drug treatments in individual diseases. Some examples: in heart disease, the return to adding statin therapy to heart attack survivors is estimated to range from four-to-nine times the incremental cost.[41] In Alzheimer's Disease, one recent study estimated that treatment of diagnosed patients with donepezil can substantially reduce overall annual patient costs, the savings being derived mostly from reduced in-patient hospitalizations and nursing facility expenditure.[42]

Quantifying the potential impact of these new medicines is beyond the scope of this study. However, many have tried to do this: For example, Murphy and Topol have estimated that a 10 percent reduction in mortality due to heart disease could yield a present value of as much as $5.5 trillion to current and future generations. A similar reduction in mortality due to cancer is estimated to have a present value of $4.4 trillion.[43]

Higher prices for drugs for U. S. consumers

Between 75 and 100 drugs of the incremental stock (which we estimate would be available in the absence of OECD cost controls) would likely have been added to existing categories. The addition of drugs to a class in this way can yield two benefits. First, the additional drugs can provide significant health benefits, by offering a differentiated therapeutic profile – efficacy, side effects, dosing requirements, delivery system and other features.[44] Second, the addition of new

[40] Lichtenberg, "Impact of New Drug Launches On Longevity: Evidence From Longitudinal, Disease Level Data From 52 Countries 1982-2001", NBER Working Paper 9754, 2003
[41] MEDTAP International, "The Value of Investment In Health Care" 2004
[42] Hill, et al, "The Effect of Donepezil Therapy on Health Costs In A Medicare Managed Care Plan", Managed Care Interface, March 2002. Total annual average costs per diagnosed patient were estimated at $12,000 without the therapy and around $8,000 with the therapy (including the cost of the drug).
[43] Murphy, Topol, *Measuring the Gains from Medical Research: An Economic Approach*, University of Chicago, 2003
[44] For a broad review of the literature, see Wertheimer, Levy and O'Connor "Too many drugs? The clinical and economic value of incremental innovations" *in Investing in Health: The Social and Economic Benefits of Health Care* Innovation, volume 14, Elsevier Science, 2001.

drugs into existing categories would likely have led to greater price competition and therefore lower prices for U.S. consumers.

Academic studies have highlighted the potential for price competition among potential therapeutic substitutes. One study, analyzing 130 drugs launched between 1978 and 1987, concluded that the number of existing drug substitutes had a significant downward effect on the manufacturer's launch price (not including rebates) of a new drug.[45] Another study,[46] analyzing retail drug prices (before rebates) between 1995 and 1999, found that, of 20 drugs launched within existing drug sub-classes, 13 were launched with at least a 5 percent discount relative to the average price of the sub-class and several drugs saw discounts ranging as high as 30-40 percent.[47] Another study found evidence that the later a new drug enters an existing class, the lower the list price of that drug.[48]

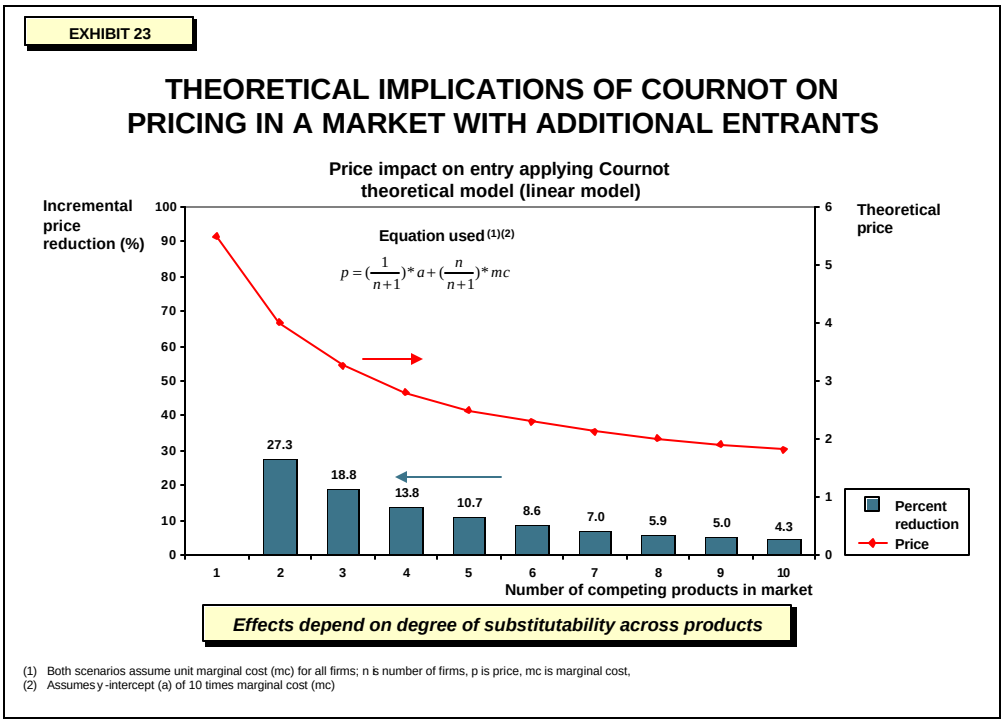
But list prices are not really the best lens for viewing prices, since in the United States much of the price competition takes place in the form of confidential rebates negotiated between manufacturers and payors.[49]. In these price negotiations, more competition among drugs certainly does provide the payors with leverage, as one industry executive testified: "In general, the level of the rebates increases if the PBM achieves a greater market share for a drug within a defined class of prescriptions with similar therapeutic effects…Rebates are usually not provided

[45] Lu and Comanor, "Strategic Pricing of New Pharmaceuticals", Review of Economics and Statistics, 1998.
[46] DiMasi, "Price Trends for Prescription: Pharmaceuticals" Report for HHS Conference on Pharmaceutical Pricing Practices, Utilization and Costs, 2000. Note impact of rebates were not included in this analysis
[47] Five of the drug launches were at the same approximately the same price as the existing drugs in the sub-class, although it is worth noting that four of these drugs were in the same sub-class in which new entrants were basically launched at parity (before rebates).
[48] Danzon, Chao "Cross national price differences for pharmaceuticals: how large and why?" Journal of Health Economics 19 (2000) 159-195. This study also found that a higher number of drugs in a class had no statistically significant effect on manufacturer list prices.
[49] In our model, we allow for an average U.S. rebate of 11 percent, based on an evaluation of various public data sources including: (1) Abrams, Lawrence "Estimating the Rebate-Retention Rate of Pharmacy Benefits Managers", April 22, 2003; (2) CMS; (3) CBO; (4) Van Oehsen, William H. "Pharmaceutical discounts Under Federal Law: State Program Opportunities", Public Health Institute, May 2001.

or they may be minimal for landmark or breakthrough drugs, since… no other comparable drug is available.[50]

Because rebates are confidential, they are of course unobservable for analysis. Accepted economic theory, however, offers a perspective on how additional entrants in a market can lead to lower pricing. The Cournot model, in particular, provides an approach to estimating the impact on the average price of a product as more competing products enter the market.

(***Exhibit 23***)



While there are some limitations on its applicability to drug markets[51], the model, along with the academic literature points in the same general direction, and does provide some evidence that

[50] Testimony of Carol J. McCall, EVP, Managed Care, Allscripts and formerly VP for Pharmacy Management with Humana, provided to United States Senate Committee on Finance, "Providing Prescription Drug Coverage Through Medicare – the Role of Pharmacy Benefit Managers", March 29, 2000.

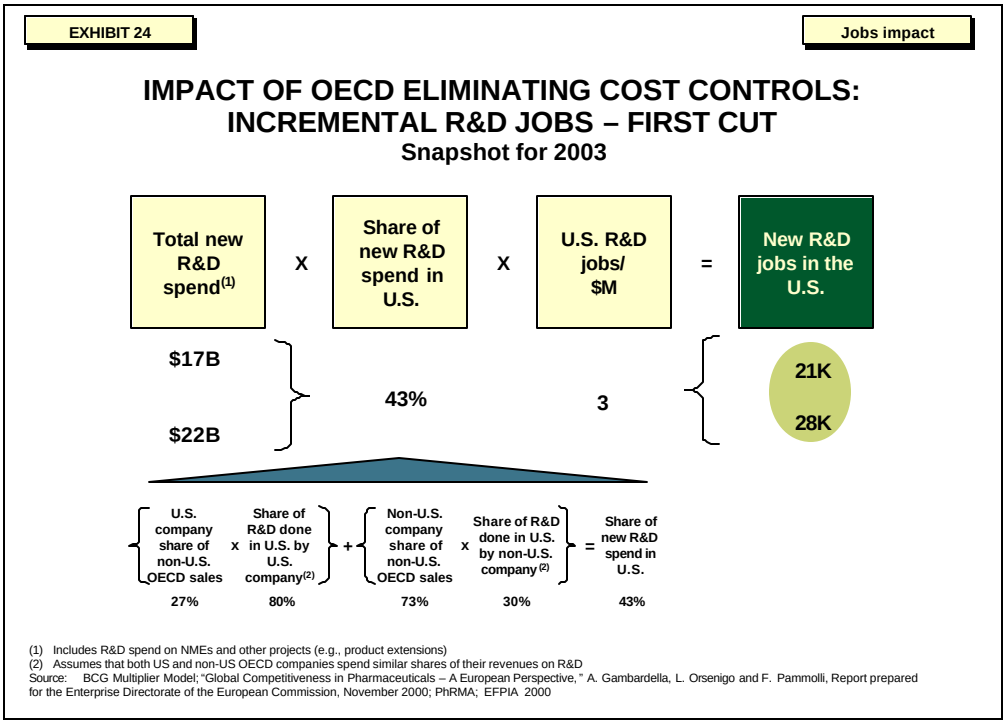
[51] It is worth noting that there are some limits to its applicability for branded drugs. Specifically, the model assumes that all products in the market are perfect substitutes, while very frequently drugs in the same class can offer quite different efficacy and side-effect profiles. Providing patients access to different trade-offs of efficacy and side-

more drugs could lead to lower net prices within the United States and, by implication, that OECD cost controls are imposing higher costs on U.S. patients.

Fewer jobs for the U.S. economy

Curtailed R&D investment also has a negative impact on the number of U.S. jobs through multiple levels.

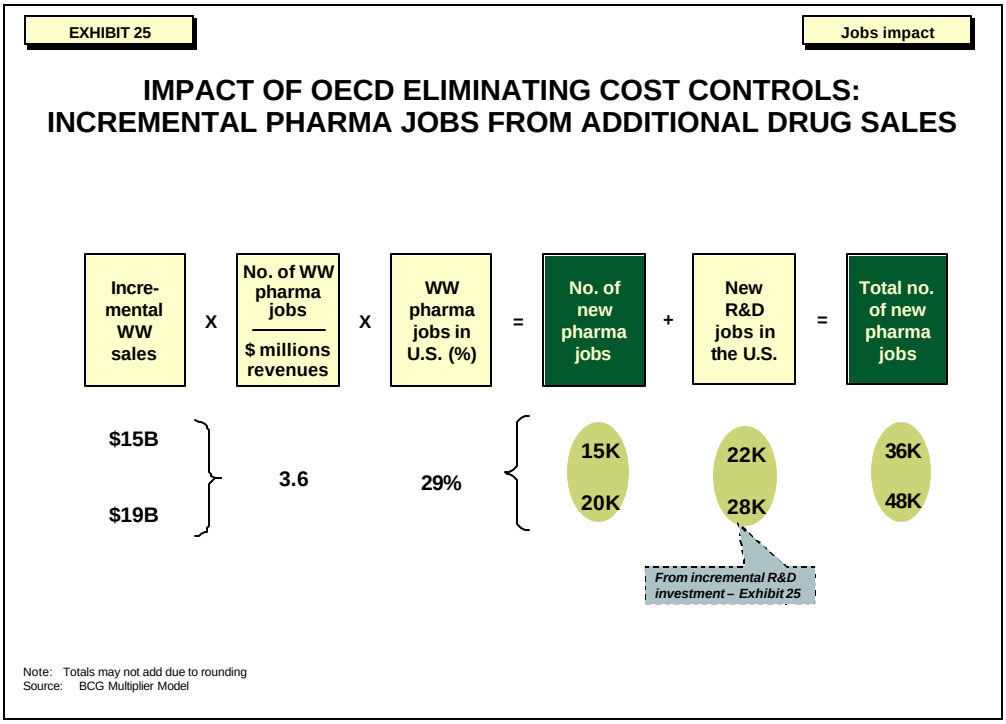
First, because so much of the industry's R&D spend occurs in the United States, the U.S. economy is obviously a major casualty when global R&D investment falls short. Supposing that the annual shortfall of $17-22 billion were added to the global R&D spend, we estimate that an additional 20-30 thousand R&D jobs would be created in the United States. (***Exhibit 24***)



effects and different results for patients with different conditions is of great value itself, even greater than the potential for price reductions. See Wertheimer (2001).

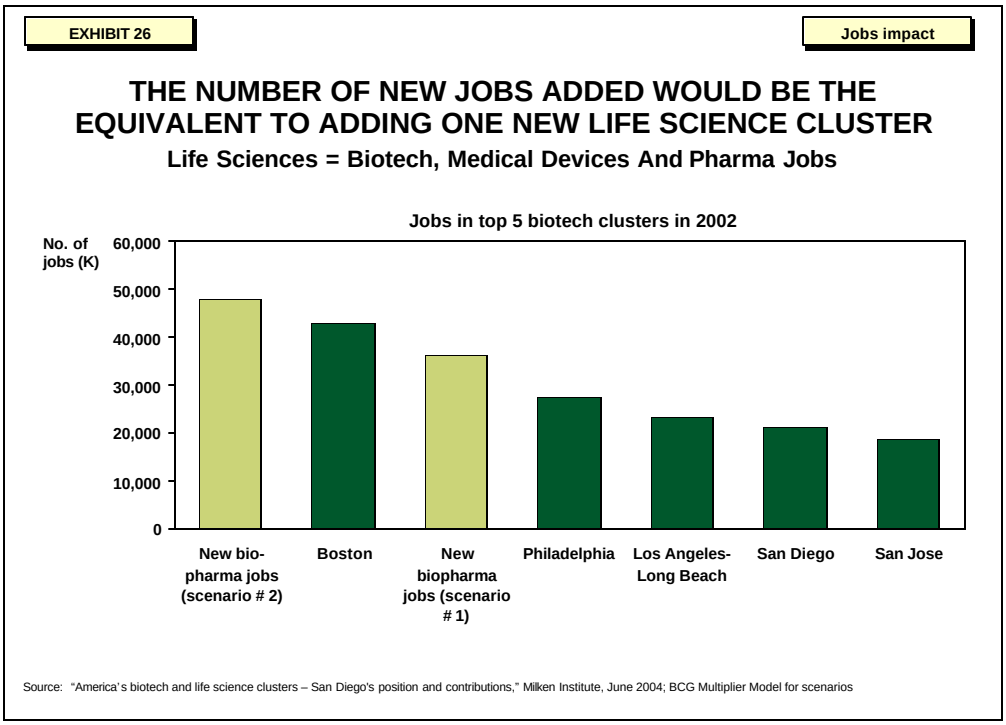
It is worth noting that, since the increase in revenues would be centered outside the United States and local pharmaceutical companies would benefit disproportionately, an even greater number of R&D jobs would be created outside the United States.

Second, the incremental R&D would lead to additional drugs being launched, which would in turn create additional revenues in the United States and additional job opportunities supporting those drugs in the U.S. market. We estimate that the incremental stock of drugs would create an additional 15-20 thousand pharmaceutical jobs, many of then supporting additional R&D investments.[52] (***Exhibit 25***)



[52] Assuming each incremental drug achieves peak incremental sales of $250 million and that progression from launch to peak is linear over a ten-year ramp-up. Any cannibalization of existing revenues would be in addition to the $250 million peak. But, of course, under this scenario, innovative drugs would, in general, achieve 35-45 percent more revenues still because the OECD cost controls would be absent. Historically, the industry has created ~3.6 jobs for every $1million in revenues, though only 29% have been in the United States. Based on BCG analysis using data from PhRMA Annual Membership Surveys, 2002, 2003 and 2004, EFPIA and JPMA.

Overall, there would be 35-50 thousand biopharmaceutical jobs, the equivalent of the large healthcare cluster in the Boston region. (***Exhibit 26***)



Finally, pharmaceutical jobs also create jobs elsewhere in the economy – a further 55-65 thousand, by our estimate. The total number of incremental jobs which the OECD cost controls are preventing ranges from 90 to 105 thousand jobs.

A few final considerations: Pharmaceutical jobs are much-valued jobs – technically sophisticated and well-paying given the level of expertise required. Because of the highly technical nature of the work and the high skills required, jobs in the pharmaceutical industry pay an average salary of $86,000,[53] implying a total of $3-4 billion in additional salaries. And job creation would not just occur in the United States. A substantial – in fact, disproportionate – share of the increased revenues stemming from the absence of OECD cost controls would flow to local research-based

[53] Bureau of Labor Statistics, Bureau of Economic Analysis

pharmaceutical companies in the OECD, encouraging them to invest further in R&D and create new jobs locally – not just R&D jobs, but also jobs supporting the commercialization of the resulting increment in patented drugs.

Appendix 1 – Methodology

Introduction

Our assessment of the impact of OECD government interventions derives from the analysis and modeling that we conducted on a set of volume and price data for a sample of drug classes and for a sample of eight countries – complemented by existing literature and macro-economic data. More specifically, this report draws on four main streams of research:

1) Analysis and modeling based on primary data from IMS, focusing on four disease areas[54] and selective anti-cancer agents[55]

2) A variety of secondary sources, such as academic publications and government reports.

3) A detailed review of the approaches taken by a sample of OECD countries to controlling drug costs: Canada, France, Germany, Japan, Poland, Spain, and the United Kingdom, as well as the United States.

4) A series of interviews with pharmaceutical executives

The purpose of this Appendix is to give a technical explanation of the first of these streams – the items of data, the selection of samples, and the analytical methods.

[54] Diabetes, hyperlipidimia, schizophrenia and depression
[55] Gleevec and Herceptin

Data

Sources

The volume and price data used in this study are for the period 1992-2003 from IMS Health, a global pharmaceutical market research company (it was in 1992 that fully reliable and comprehensive data first became available from IMS). The data are drawn from the IMS Midas and Medical panel databases, supplemented by the IMS institutional sales panel.

- The Midas data report sales through pharmacies, which for most products account for over 80 percent of sales in each country.

- The Medical panel data were used to correct for differences in prescribing patterns across different drugs – differences that could otherwise skew results.

- The institutional sales panel was used to analyze those drugs that are administered mainly in institutional settings – some cancer drugs, for instance.

We also used the Evaluate drug sales database[56] where noted below, as well as disease-prevalence data from various sources.[57]

Volume units

For volume of sales or consumption of any particular drug, we used the measure "days of treatment per diagnosed." It is calculated in the following way: We take standard units (single recommended dosage) as a starting point. The various other measures available, such as pack size or grams of active ingredient, all suffer from systematic aberrations.[58] We then refine this

[56] The Evaluate database contains net sales as reported in the financial statements of pharmaceutical manufacturers. It also contains useful details on each molecule, such as pharmacological class and technology (biotech, for example). The database is maintained by the British pharmaceutical data company Evaluate plc.
[57] For instance, the Diabetes World Atlas for diabetes prevalence, and several official sources for OECD economic and health care data. For a full list of sources, see the bibliography.
[58] See Danzon, Wang and Wang (2003) "Data and methodology" section for a review of the issues with these alternative measures

measure by correcting for different average daily doses across drugs. Otherwise, a "twice-a-day" drug might appear to provide greater volume of treatment than a "once-a-day" drug, for example. Finally, we correct for differing levels of prevalence across countries, by using a "per diagnosed" basis as opposed to a "per capita" basis for our metrics.

Currency units

Throughout our analysis, we use U.S. dollars as our unit. To convert local currencies into dollars, we used a dynamic exchange rate – the prevalent exchange rate for each time period – rather than a fixed exchange rate, and thereby smoothed out the changes over time that result from currency fluctuations. By contrast, using a constant exchange rate over a long period of time builds in systematic differences, and complicates the task of comparing prices across countries. Note, however, that it would not affect our analysis substantially.

Sample

Sample countries

Our analysis focused on seven (out of a possible 29) non-U.S. countries as a representative sample of the OECD: the United Kingdom, Germany, France, Spain, Poland, Canada, and Japan. This sample was carefully selected to ensure the following features: a large overall share of the OECD population and economy, a mix of higher- and lower-income countries, and a mix of drug-cost control strategies. The marginal refinement that any additional country might have provided was far outweighed by the data acquisition costs involved. Our sample is an ample one, representing: 61 percent of the total non-U.S. OECD GDP, 65 percent of the total non-U.S. OECD health care spend, and 51 percent of the total non-U.S. OECD population. (If you include the United States in the calculation, the figures are then 75 percent of the total OECD GDP, 80 percent of the total OECD health care spend, and 65 percent of the total OECD population.)

Sample disease categories

Our sample disease categories (which can encompass several drug classes) are anti-diabetics, anti-psychotics, anti-depressants, and anti-hyperlipidemics, as well as a pair of innovative oncology drugs. We arrived at this selection of samples by applying a set of objective criteria to the Evaluate database. We first ranked all drug classes according to two measures: the level of innovation, as measured by the lifetime-projected sales of drugs launched since 1992; and the presence of large patent expiries. A shortlist of six classes emerged, from which we discarded two: hypertension, because it was already a very mature market in 1992 (the earliest year for which IMS data are available), and because the large number of drugs made it an extremely expensive category to study; and drugs for treating Acid Reflux disease, because recent developments there – for instance, the launch of Nexium and the shift of Prevacid to over-the-counter – have not yet had a chance to play out across the OECD. Hence, our remnant of four main classes, all of them chronic categories. To this selection we then added a pair of oncology drugs, to represent breakthrough therapies and an acute category. The two oncology drugs were selected on the basis of conversations with physicians, who highlighted them as particularly innovative. The selected therapeutic categories jointly represent about 14 percent of the total global pharmaceutical market.[59]

Analysis

Using the IMS data, we developed a composite view of "per-patient product life-cycle revenue curves" for the OECD countries, singly and jointly, and for the United States. Each view is represented as a curve, and what it maps out is, essentially, the revenues for a "typical" innovative drug in each year. The sum of the area under the curve represents the total

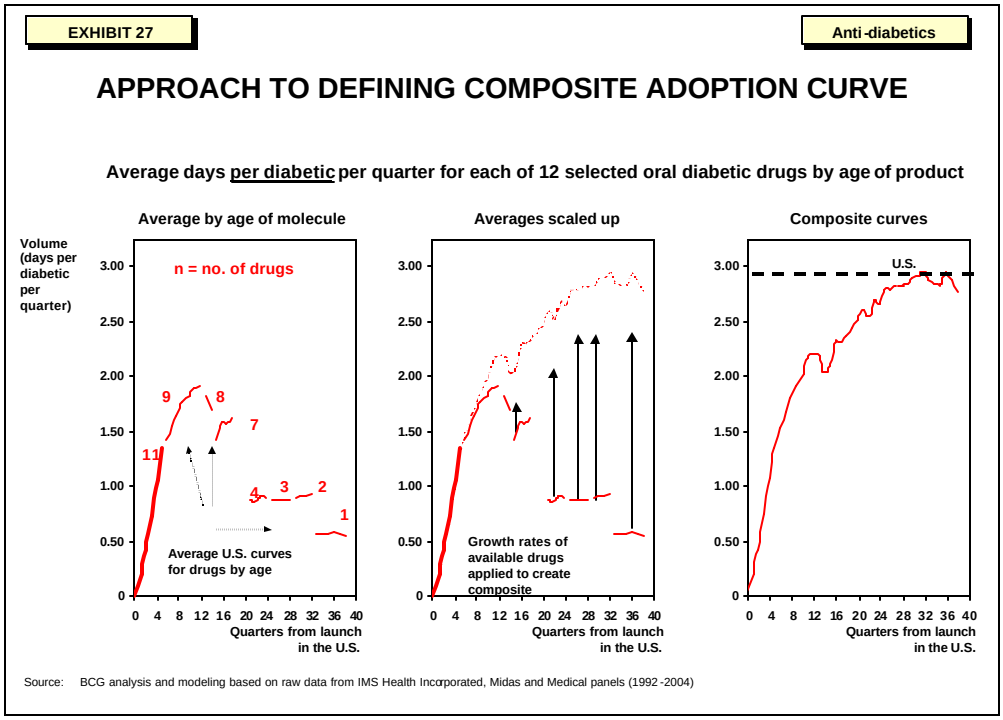
[59] Based on 2002 revenues as estimated by IMS audited worldwide revenue data. Total worldwide revenues are $400 billion, while the sum of anti-cholesterol (ranked #2, $21.7 billion), anti-depressants (ranked #3, $17.1 billion), anti-psychotics (ranked #6, $9.5 billion) and oral anti-diabetes drugs (ranked #8, $8.0 billion) is $56 billion. Analysis does not include the two oncology drugs we analyzed which would have marginal impact.

(undiscounted) revenue. This approach is similar though not identical to the "synthetic" life-cycles developed by Danzon and Kim (2002).

To develop the composite curve, we mainly used four sets of metrics: launch delay, adoption curve, price differential, and generic substitution post-patent expiry.

Launch delay: for drugs launched in more than three countries, we measured average launch delay in each country relative to the U.S. launch. The date of launch in each country is taken as the first day of the period for which IMS reports sales for the drug in that country.

Adoption curve: for the selected drugs in each country, we used average sales per diagnosed in the first quarter of sales to plot the curve for the first period. To define the growth rate for subsequent quarters in each country, we took the average growth in diffusion in each subsequent quarter, using "same-drug growth" as the measure for quarter-to-quarter growth. (***Exhibit 27***)



To develop the curve for the OECD countries jointly, we used a disease-prevalence-weighted average.

Price differential: across a number of drugs and classes, the average price difference between the OECD countries and the United States remained reasonably stable. Our measure was a simple average price of dosage strengths available in multiple countries indexed to the U.S. price. By using that simple average price, we could correct for differences resulting from a mix of dosage strengths.

Generic substitution: for all relevant examples, we calculated a "half-life" following patent expiry, to model the lifecycle curve post patent. This measure was, unavoidably, based on limited data, but that does not affect the overall picture significantly as it is also the least sensitive part of the model, being further out in time and corresponding to a period of declining sales.

Having created these composite curves, we were duly equipped to make the requisite comparison for a typical innovative drug – its lifetime revenue stream per diagnosed patient in the U.S. and OECD markets.

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