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The Effect Of Regulation On Pharmaceutical Revenues: Experience In Nineteen Countries

If the United States implemented price controls and negotiations similar to those in other developed countries, U.S. revenues would fall by as much as 20.3 percent.

by Neeraj Sood, Han de Vries, Italo Gutierrez, Darius N. Lakdawalla, and Dana P. Goldman

ABSTRACT: We describe pharmaceutical regulations in nineteen developed countries from 1992 to 2004 and analyze how different regulations affect pharmaceutical revenues. First, there has been a trend toward increased regulation. Second, most regulations reduce pharmaceutical revenues significantly. Third, since 1994, most countries adopting new regulations already had some regulation in place. We find that incremental regulation of this kind had a smaller impact on costs. However, introducing new regulations in a largely unregulated market, such as the United States, could greatly reduce pharmaceutical revenues. Finally, we show that the cost-reducing effects of price controls increase the longer they remain in place. [*Health Affairs* 28, no. 1 (2009): w125-w137 (published online 16 December 2008; 10.1377/hlthaff.28.1.w125)]

RAPID GROWTH IN PHARMACEUTICAL SPENDING is a worldwide phenomenon. According to a recent study, spending on pharmaceuticals in Organization for Economic Cooperation and Development (OECD) countries has increased by an average of 32 percent in real terms since 1998, reaching more than U.S.\$450 billion in 2003.¹ However, there is wide variation in the growth of pharmaceutical spending across countries. For example, during this period, the annual growth rate of pharmaceutical spending in the United States (9.6 percent) was nearly triple the growth rate of spending (3.5 percent) in Germany.

This growth in pharmaceutical spending has increased demands for regulating

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pharmaceutical markets by imposing limits on prices, profits, or total spending on pharmaceuticals. The likely effect of such regulations on social welfare is a contentious and much-debated public policy issue.² On the one hand, regulations curb expenditures and thus potentially improve the welfare of the current generation. On the other hand, such regulations limit incentives for research and development (R&D) and thus might hurt future generations by reducing the pace of innovation.³ In addition, some argue that pharmaceutical regulations might also have negative consequences for consumers today. For example, price regulation can lead to less competition in markets for generic drugs, delay launch and limit availability of new drugs, and could lead firms to follow costly strategies to “game” regulations.⁴

Pharmaceutical regulation thus involves a potential trade-off between curbing costs today and having fewer drugs to treat current and future generations. Thus, the first step in examining this trade-off is estimating the effect of regulations on pharmaceutical revenues. However, there is little consensus about whether or not real-world pharmaceutical regulations have any impact on revenues. Some believe that these regulations have little “bite,” especially over time, as pharmaceutical firms learn to work their way around them. Others believe that regulations have big impacts on revenues and consequently limit the pace of innovation.

The lack of consensus is driven in part by the lack of systematic information about current trends in pharmaceutical regulation and its effect on revenues. One strand of existing studies compares pharmaceutical prices or spending across regulated and unregulated markets.⁵ For example, a recent study by the U.S. Department of Commerce reviewed pricing in eleven OECD countries and found that for patented drugs that were best sellers in the United States, the prices in other OECD countries were 18–67 percent less than U.S. prices, depending on the country. The study concluded that price deregulation in these countries would increase pharmaceutical revenues by 25–38 percent.⁶ In general, these studies are limited by their reliance on cross-sectional variation in revenues or prices and by their resulting vulnerability to heterogeneity across countries in type of regulation and other determinants of prices.

There are some studies that address the heterogeneity problem by analyzing longitudinal data and comparing pharmaceutical spending before and after policies take effect.⁷ For example, Nina Pavcnik estimated a 10–26 percent decrease in drug prices as a result of a reference pricing policy introduced in Germany after 1989.⁸ However, most of these studies only examine the effects of a limited range of regulations in one country or a small group of countries.

In this paper we attempt to fill this gap in the literature by characterizing the pharmaceutical regulatory environment in nineteen developed countries over a thirteen-year period. We take advantage of the substantial variation in pharmaceutical policies within a country to identify the causal effect of a wide variety of pharmaceutical regulations on revenues. We also examine the extent to which dif-

ferent regulations complement or substitute for each other. For example, to what extent are the effects of a particular policy on drug revenues determined by other regulations that were already in place before the new policy was introduced? Finally, we examine whether the effects of regulations change over time.

Study Data And Methods

■ **Pharmaceutical regulations.** There is no single source of information on pharmaceutical regulations in OECD countries. Some publications report current regulations for several countries, but historical data on regulations are less widely reported.⁹ We collected data on pharmaceutical regulations in nineteen OECD countries for the years 1992–2004 from a variety of sources. Data were abstracted from peer-reviewed journal articles obtained through a structured search in the PubMed and EconLit databases and publications from other sources.¹⁰ We verified the data through expert interviews with two researchers or policymakers in pharmaceutical regulation in each country, and country experts from a leading multinational pharmaceutical firm.

The nineteen countries included in our analysis are Australia, Canada, Denmark, Finland, France, Germany, Greece, Hungary, Italy, Japan, the Netherlands, New Zealand, Norway, Portugal, Spain, Sweden, Turkey, the United Kingdom, and the United States. There is tremendous heterogeneity in regulations across countries, and in some cases, historical data on the actual implementation and detailed design of the regulations were not available from either the literature or the country experts. To make these diverse regulations amenable to analysis, we grouped them into eleven major categories. Below we describe the regulations in each of these categories.

Global budgets. These are policies that impose a maximum annual limit on pharmaceutical spending. The nature of global budgets differs across countries. For example, in some countries, budgets cap the entire country's spending (Italy), while in others, budgets cap the spending of specific regions (Germany until 2001). There is also variation in these policies in whether they apply to the sum of all drug spending or to spending on individual products or groups of products.

Prescribing budgets. These imply that physicians face an annual budget for prescriptions, with financial sanctions in the event of overruns.

Profit controls. The regulator imposes a maximum annual limit on the profits or profit growth rates of pharmaceutical companies.

Direct price controls—external reference pricing (ERP) only. The regulator sets a maximum reimbursement level or market price for patented drugs based on prices of similar drugs in other countries. Variation exists across countries in the set of reference countries and pricing algorithms.

Direct price controls, price negotiations, and others. Here the regulator sets prices of patented drugs using price negotiations, imposed maximum prices, cost-plus formulas, price freezes, and so on, none of which depends exclusively on prices of

similar products in other countries (although it may be one criterion considered).

Generic reference pricing (GRP). In this case, the regulator sets a reference price—that is, a level above which consumers will not be reimbursed for the cost of a drug. The reference price depends on the prices of similar products (that is, products containing the same active substance) within the country. Only generic prescription drugs are subject to these reference prices.

Therapeutic reference pricing (TRP). The regulator sets a reference price, as above. However, both generic and patented drugs are subject to reference prices. The reference price for a patented drug can depend on the price of generics (sometimes referred to as therapeutic reference pricing, or “jumbo” groups).

Economic evaluations required or strongly encouraged. An economic evaluation must be considered when one is deciding on the inclusion of a drug in the benefit package offered by the national health insurance, government, or private insurers or when determining the level of reimbursement.

Generic substitution. Pharmacists are allowed to substitute generics with the same active ingredient without doctor’s consent, unless the doctor indicates otherwise on the prescription.

Incentives for generic prescribing. Doctors receive direct financial or nonfinancial incentives to prescribe generics, apart from those indirectly imposed by prescribing budgets.

Degressive pharmacy fee structure. Pharmacists receive a degressive fee or margin for dispensing drugs. In other words, the higher the cost of the drug, the lower the margin that the pharmacist receives. Therefore, this policy aims at promoting the substitution of cheaper (generic) drugs for expensive (branded) drugs.

■ **Pharmaceutical revenues.** We obtained data on pharmaceutical revenues from various editions of the *IMS World Review*. The dollar values of revenues represent local currency sales converted into U.S. dollars on a quarterly basis, using the prevailing average exchange rate for the quarter. Sales values are standardized at the manufacturer level. We extracted sales data for the period 1992–2004 for each of the nineteen countries, except, because of missing values, Hungary (1992–1993) and New Zealand (1992–1993).

■ **Empirical strategy.** We merged the data on pharmaceutical revenues and regulations for each country and year to create the analytic data set for this research. The unit of observation is a country-year, with detailed information on the regulations and revenues for each country-year observation. We used these panel data to estimate the effect of a variety of regulations on revenues. The dependent variable is the natural logarithm of pharmaceutical revenues (in millions of dollars). The key independent variables are a vector of indicators for the presence of different regulations. The empirical model includes country fixed effects to account for the substantial heterogeneity across countries. The model also includes time fixed effects to account for secular changes in the time trend of revenues. We also included exchange rates as a regressor to account for potential confounding because of local currency

appreciations or depreciations. Finally, we also included an indicator variable for whether pharmacy chains were allowed, because it may be argued that pharmacy chains have more bargaining power to obtain discounts from the manufacturers. The model was estimated using generalized least squares (GLS) and allowed for first-order serial correlation in revenues within a country where the coefficient on the auto-regressive process is specific for each country.¹¹ In particular, we used the `xtgls` command with `corr(psarl)` option implemented in Stata version 9.

In the first model, we considered the impact of six different types of regulation on revenues: budget controls, both global and physician; direct price controls, both ERP and price negotiations; reference pricing, for both generics and patented drugs, as well as generics only; number of incentives for generic use, which includes incentives for generic prescribing, pharmacy fee structure, and permission for generic substitution; economic evaluations; and profit controls.

Although comparisons across these six categories were quite useful, we explored several alternative specifications as well. First, we disaggregated regulations further to test whether more-stringent policies of a particular type have larger effects. Second, we estimated the interaction effects between policies, to assess the extent to which different regulations are complements or substitutes. For example, the extent to which the effects of a particular policy on pharmaceutical revenues are determined by which other regulations were in place when the particular policy was introduced. Finally, we examined the dynamic effects of regulations and, specifically, whether the effects of policies change over time.

Study Results

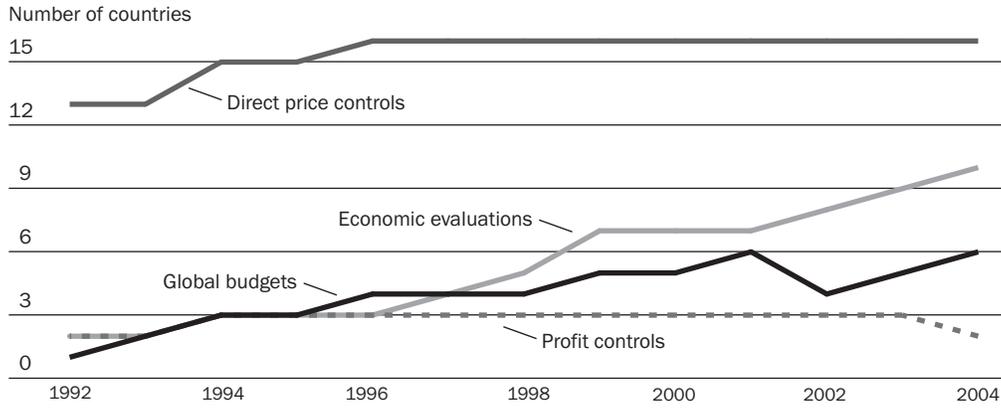
■ **Trends in pharmaceutical regulation.** Exhibits 1–3 show an overall trend toward increased regulation in OECD countries during 1992–2004. However, there is much variation in adoption rates of different regulations. Below we describe trends in specific regulations, and we provide examples of countries that changed their policies.

Direct price controls. Direct price controls were the most common regulation over our entire sample period. In 1992, all but six of the nineteen countries in the sample already had some form of price regulations in place. By 2004, the number had risen to sixteen (Exhibit 1). The countries that introduced these regulations during this time were Italy (ERP in 1994 and negotiations since 1997), Denmark (a series of price cuts/freezes from 1994 to 2000 and international price comparisons since 2001), and the Netherlands (ERP since 1996).

Budget controls. In 1992 only New Zealand had global budgets as a policy for controlling pharmaceutical costs. By 2004, five more countries in our sample imposed global budget caps for pharmaceutical expenditures (France, Hungary, Italy, Spain, and the United Kingdom), bringing the total to six (Exhibit 1). In contrast, only two countries adopted prescribing budgets during our sample period.

Profit controls. The number of countries with profit controls is small and has

EXHIBIT 1
Trends In Various Regulatory Mechanisms In Nineteen Organization For Economic Cooperation And Development (OECD) Countries, 1992–2004



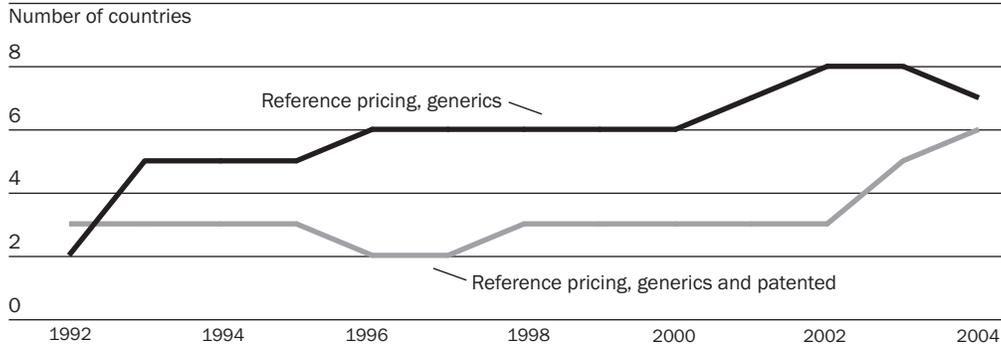
SOURCE: Based on data on pharmaceutical regulations for nineteen OECD countries, from literature review and expert interviews.

stayed fairly constant (Exhibit 1). Over this period, Spain and Turkey changed their policies, with Spain adopting profit controls in 1995 and Turkey repealing them in 2004. The United Kingdom had such a policy in place over the entire sample period.

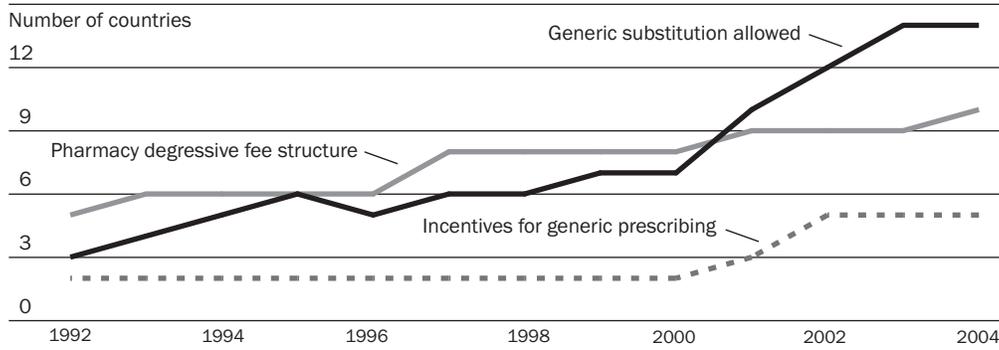
Economic evaluations. Economic evaluations were the fastest-growing policy; the number of countries with this policy increased from two in 1992 to ten in 2004 (Exhibit 1). None of the countries ever abandoned this policy; thus, whenever we observed a change in this policy, it was an introduction.

Reference pricing. Exhibit 2 shows a strong upward trend in the number of countries with reference pricing for generics, from two in 1994 to seven in 2004. Den-

EXHIBIT 2
Trends In Reference Pricing Policies For Nineteen Organization For Economic Cooperation And Development (OECD) Countries, 1992–2004



SOURCE: Based on data on pharmaceutical regulations for nineteen OECD countries, from literature review and expert interviews.

EXHIBIT 3**Trends In Policies Aimed At Increasing Use Of Generic Drugs In Nineteen Organization For Economic Cooperation And Development (OECD) Countries, 1992–2004**

SOURCE: Based on data on pharmaceutical regulations for nineteen OECD countries, from literature review and expert interviews.

mark, Norway, and Sweden introduced reference pricing for generics in 1993, Hungary in 1998, Italy and Spain in 2001, Turkey in 2002, and France and Portugal in 2003. However, Norway and Sweden eventually abandoned this policy.

The number of countries with TRP is smaller (between two and three for the period 1992–2002). It increased to six in 2004. Australia adopted TRP in 1998; Hungary and Italy moved from GRP to TRP in 2003. Germany abandoned TRP in 1996 (for new drugs) but then reintroduced it in 2004.

Policies for increasing generic use. Exhibit 3 shows a strong upward trend in the number of countries that had policies aimed at increasing use of generic drugs. The number of countries with generic substitution policies increased from three in 1992 to fourteen in 2004. Just two countries offered generic prescribing incentives until 2000, but three more adopted policies after that point: Spain (2001), Japan (2002), and Portugal (2002). Finally, there is a strong upward trend in countries that used a degressive pharmacy fee—only five countries had such policies in 1992, but ten had them in 2004.

■ **Effect of regulations on revenues.** Exhibit 4 presents the results of our regression analysis. Model 1 is the most general one and presents the impact of six broad categories of policies: profit controls, budgets (either global budgets or budgets at the physician level), direct price controls (of any kind), reference pricing (of any kind), economic evaluations, and number of policies for promoting generic use. The results from this specification show that three out of the six aggregate regulation groups reduce revenues significantly. Direct price controls have the largest impact on revenues, followed by economic evaluations and budgets. In particular, direct price controls reduce revenues by 16.8 percent; economic evaluations and budgets have a much smaller impact of around 6 percent. Finally, reference pricing, profit controls, and policies for encouraging generic use did not have a statistically significant impact on revenues.

EXHIBIT 4
Percentage Change In Revenues Following Introduction Of Pharmaceutical
Regulations In Nineteen Organization For Economic Cooperation And Development
(OECD) Countries, 1992–2004

	Percent change in revenues	
	Model 1	Model 2
Profit controls	-6.3	-4.3
Budgets	-5.9**	
Global budget		-4.4*
Physician budget		-16.5***
Direct price controls	-16.8**	
Only international comparisons		-12.7***
Price negotiations and others		-17.1***
Reference pricing	1.6	
Reference pricing for generics		3.4
Reference pricing for generics and on-patent drugs		9.7**
Economic evaluation	-5.9**	-4.3
Incentives for generic use		
1 out of 3 policies for prescribing/dispensing generics	-2.8	-0.8
2 or more out of 3 policies for prescribing/dispensing generics	-4.0	-3.0

SOURCE: Based on results from multivariate regressions using data on pharmaceutical revenues and regulations from nineteen OECD countries for 1992–2004.

NOTES: For the regressions, the dependant variable was log(Revenue). The key independent variables were dummy variables for each of the regulations outlined in model 1 and model 2. Other covariates included year fixed effects, country fixed effects, exchange rates, and indicator variable for whether pharmacy chains are allowed. Regression coefficients for regulation dummy variables were converted into percentage changes using methods outlined in P.E. Kennedy, "Estimation with Correctly Interpreted Dummy Variables in Semilogarithmic Equations," *American Economic Review* 71, no. 4 (1981): 801.

* $p < 0.10$ ** $p < 0.05$ *** $p < 0.01$

Model 2 disaggregates budgets, direct price controls, and reference pricing into the subcategories, to test whether more-stringent policies of a particular type have larger effects. The results suggest that physician budgets reduce total revenues by more than global budgets do. This result seems logical, because physician budgets are borne directly by prescribing doctors, who are individually accountable. The results also suggest that price negotiations and other forms of price controls reduce revenues by more than ERP only. Finally, we found a positive effect of reference pricing for both generics and patented drugs, which is peculiar, given the fact that these policies were introduced to contain costs.¹²

To explore this unexpected result, we estimated a model that allowed for an interaction effect between direct price controls and reference pricing. The results from this model show that the impact of reference pricing in the absence of direct price controls was indeed in the expected direction (10.5 percent reduction in revenues). However, this effect was disguised by the fact that price controls are typically already in place when reference pricing has been adopted; incremental to

“There are good reasons to expect the impact of direct price controls or other regulations to change over time.”

price controls, reference pricing has a limited impact on pharmaceutical revenue.

We further investigated the idea that incremental regulation may have a smaller impact on pharmaceutical revenues, by using mutually exclusive and exhaustive combinations of four major pharmaceutical regulations—profit controls, price controls, reference pricing, and budgets—as our explanatory variables, rather than the individual policies. Thus, these models measure the cumulative effects of regulations on pharmaceutical revenues. In contrast, the models in Exhibit 4 measured the incremental effects of regulations over and above existing regulations. Online Appendix B presents the results from this specification, where all the combinations observed in our sample are incorporated in the model.¹³ There are two striking patterns in the results. First, the results show that all possible combinations of these policies greatly reduce revenues. Second, the results do suggest that additional regulation has a smaller impact on revenues. For example, we found that introducing price controls in an unregulated market reduces revenues by 20.3 percent and that introducing price controls combined with budgets (in comparison to no regulation) reduces revenues by 27 percent.

Next, we evaluated whether direct price controls and economic evaluations have a different impact on revenues in the year they are introduced compared to their impact on revenues in later years. There are good reasons to expect the impact of direct price controls or other regulations to change over time. For example, policymakers might close loopholes over time. It is also possible that price ceilings imposed by regulations become more binding, especially when unregulated prices are rising rapidly. Finally, there is also evidence that regulations delay the launch of new drugs and thus suppress pharmaceutical revenues over time.¹⁴ Conversely, firms may learn about and exploit additional loopholes over time.

We analyzed the presence of these dynamic effects by estimating the impact of direct price controls and economic evaluations for four different time periods: year of introduction, one to three years after introduction, four to six years after introduction, and more than six years after introduction (Exhibit 5). The results show that the impact of direct price controls and economic evaluations on revenues increases over time. For example, in the case of price controls, the results suggest that the immediate impact of imposing such controls is a decline of 10 percent in revenues. However, the effects increase significantly in the years after introduction, with an average reduction of 18.4 percent in revenues one to three years after introduction and a reduction of 21.3 percent six years after introduction. In the case of economic evaluations, our results suggest that economic evaluations reduce revenues by 2.8 percent in the year of introduction, although this effect is statistically insignificant. However, we did observe a significant reduction in reve-

EXHIBIT 5
Dynamic Effects Of Direct Price Controls And Economic Evaluations On Revenues In
Nineteen Organization For Economic Cooperation And Development (OECD)
Countries, 1992–2004

Policy	Percent change in revenue
Effect of economic evaluations	
In year of introduction	-2.8
In years 1–3 after introduction	-9.0**
In years 4–6 after introduction	-9.9**
6 years after introduction	-7.0
Effect of direct price controls	
In year of introduction	-10.0**
In years 1–3 after introduction	-18.4***
In years 4–6 after introduction	-16.5***
6 years after introduction	-21.3***

SOURCE: Based on results from multivariate regressions using data on pharmaceutical revenues and regulations from nineteen OECD countries for 1992–2004.

NOTES: For the regressions, the dependant variable was log(Revenue). The key independent variables were dummy variables for each of the regulations interacted with dummy variables for years of introduction outlined above. Other covariates included year fixed effects, country fixed effects, exchange rates, and indicator variable for whether pharmacy chains are allowed. Regression coefficients for regulation dummy variables were converted into percentage changes using methods outlined in Kennedy (1981).

* $p < 0.10$ ** $p < 0.5$ *** $p < 0.01$

nues in the years after introduction. For example, economic evaluations reduce revenues by 9 percent one to three years after introduction and by 9.9 percent four to six years after introduction.

■ **Limitations.** In evaluating these findings, it is important to understand the limitations and context of this study. In principle, the regulations we studied could affect pharmaceutical revenues through several mechanisms, including (1) changes in prices, (2) changes in the use of drugs or quantity of drugs sold, and (3) changes in the types of drugs consumed (branded versus generic) or the cost-effectiveness of drugs sold. Unfortunately, because of limited data, we were unable to distinguish between these effects on prices versus quantity and types of drugs sold.

There are two empirical challenges in estimating the effect of regulations on the quantity of drugs sold. First, it is difficult to define a meaningful metric for quantity of drugs sold across several types of drugs. Second, data on quantity of drugs sold or consumed is very limited. Ideally, we would like data on how many people are taking drugs in each country and the standardized quantity of drugs taken per person, after adjusting for different dosing regimens across drugs. However, such data are not available. We do have limited data from IMS Health on “standard units” sold in some countries and years.¹⁵ The number of standard units sold is determined by taking the number of counting units sold divided by the standard unit factor, which is the smallest common dose of a product form as defined by IMS Health. For example, for oral solid forms the standard unit factor is one tablet

“Introducing new regulations such as price controls in a largely unregulated market could greatly reduce pharmaceutical revenues.”

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or capsule, whereas for syrup forms the standard unit factor is one teaspoon (5 ml) and for injectable forms it is one ampoule or vial. We used these limited data from IMS Health to estimate the effects of regulations on quantity or standard units. The estimates show that the regulations have an insignificant effect on standard units sold. However, our estimates of quantity effects are imprecise (large standard errors), and we were not able to identify the effects of some regulations because of the limited availability of the IMS data. In addition, the above analysis cannot shed light on whether regulations changed the types of drugs consumed.

Our data do not allow us to estimate whether regulations affect prices or revenues of branded drugs more than those of generics. However, prior research shows that regulations typically limit prices and availability of branded drugs more than generics, which is consistent with many of the regulations we described, as some were specifically designed to encourage greater reliance on generic drugs.¹⁶ As a result, it is likely that our model underestimates the true impact on revenues for pharmaceutical firms making innovative, brand-name products.¹⁷

There is also the possibility that countries may implement regulations in response to unobserved trends in spending. For example, countries might respond to rapidly rising pharmaceutical revenues (in ways not captured by our model) with more regulation. In this case, we would tend to underestimate the impact of regulations on pharmaceutical revenues. Or it may be that regulations reducing access to physicians are implemented simultaneously with pharmaceutical regulation. In this case, we would tend to overestimate the impact of regulations on revenues. Ideally, we would like to implement instrumental variable regressions to address these concerns, but it is difficult to find exogenous predictors of the regulations we studied. Another approach would be to control for other important predictors of pharmaceutical revenues that might confound our results. Thus, we estimated additional models that included total physician-related expenses, physician consultations per capita, and proportion of spending on physicians paid by public sources as additional control variables. The results from this analysis were qualitatively similar to those presented in Exhibit 4. A fuller exposition of the reasons why some countries implement or repeal regulations is beyond the scope of this paper but worthy of further scrutiny.

We analyzed the effects of broad regulation categories on pharmaceutical revenues as they existed from 1992–2004. As noted earlier, these regulation categories mask considerable heterogeneity within a category. For example, the estimated effect of “global budgets” represents an average global budget policy. This average policy in fact represents a range of policies, where the size of the budgets and the specific implementation of the policy might have varied. Furthermore, some of the

European regulations introduced during this period were not well enforced. For example, physicians' opposition to physician prescribing budgets in Germany in the late 1990s led to a repeal of the regulation (which was never enforced because of the strong physician response). Inclusion of unenforced or poorly enforced regulations will bias our estimates downward. Thus, our results are generalizable to future regulations to the extent that (1) new regulations mimic the modal regulation as it existed in the 1990s and (2) pharmaceutical firms do not change their response to regulatory pressure. For example, although we found that additional regulations have smaller impacts on revenues, recent anecdotal evidence from the introduction of jumbo reference pricing in Germany suggests that new regulations might have reduced revenues significantly.¹⁸

Concluding Comments

In this paper we analyzed trends in pharmaceutical regulation and their impact on revenues. Several important patterns emerge from our analysis.

First, we found that a majority of regulations greatly reduce pharmaceutical revenues, with direct price controls having the biggest impact on revenues. Second, we found that most countries that adopted new regulations already had some regulations in place for controlling costs. We found that such incremental regulation has a smaller impact on further controlling revenues. However, the results also suggest that introducing new regulations such as price controls in a largely unregulated market, such as the United States, could greatly reduce pharmaceutical revenues. For example, if the United States implemented price controls and negotiations similar to those found in other developed countries, then U.S. revenues would fall by as much as 20.3 percent. Finally, the results also show that the impact of regulations on revenues increases over time.

Whether governments should regulate pharmaceutical markets is a contentious and much-debated policy question. Our results show that introducing price controls and other regulations in largely unregulated markets will greatly reduce costs today. However, it is important to note that revenue reductions will affect future innovation.¹⁹ These innovation effects ultimately could hurt consumers. So the real question is: what is the net impact of regulations on the welfare of current and future generations? Such estimates, beyond the scope of this paper, are discussed in a companion paper.²⁰

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10. Appendix A is available online at <http://content.healthaffairs.org/cgi/content/full/hlthaff.28.1.w125/DC2>. Regulatory data are available from Neeraj Sood, sood@rand.org.
11. The first-order autocorrelation structure seems most consistent with the data. We found no evidence of unit roots, using the augmented Dickey-Fuller test. Moreover, models of second-order autocorrelation (with standard errors calculated according to the Newey-West covariance matrix) produced results qualitatively similar to those presented in Exhibit 4. These sensitivity analyses are available from the authors upon request; send e-mail to sood@rand.org.
12. One possibility advanced by the pharmaceutical industry is that cost savings from reference pricing of generics could be used to purchase more costly brand-name drugs.
13. See online Appendix B, as in Note 10.
14. Danzon et al., "The Impact of Price Regulation."
15. We do not have data on standard units for 1992 and 1993 for all countries. In addition, data from New Zealand are missing for all years, data from Norway are missing from 1992 to 1995, and data from the Netherlands are missing from 1992 to 2000. For a discussion of issues involved in measuring quantities of drugs sold across countries see E.R. Berndt, P.M. Danzon, and G.B. Kruse, "Dynamic Competition in Pharmaceuticals: Cross-National Evidence from New Drug Diffusion," *Managerial and Decision Economics* 28, no. 4–5 (2007): 231–250.
16. For example, financial incentives to physicians for prescribing generics and higher pharmacy margins for generics.
17. Danzon and Ketcham, "Reference Pricing of Pharmaceuticals for Medicare."
18. Azar, "What Is Your Health Worth to Your Bureaucrat?"
19. Acemoglu and Linn, "Market Size in Innovation"; and F.M. Scherer, "The Link between Gross Profitability and Pharmaceutical R&D Spending," *Health Affairs* 20, no. 5 (2001): 216–220.
20. D. Lakdawalla et al., "U.S. Pharmaceutical Policy in a Global Marketplace," *Health Affairs* 28, no. 1 (2009): w138–w150 (published online 16 December 2008; 10.1377/hlthaff.28.1.w138).