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The effect of regulation on pharmaceutical revenues: experience in nineteen countries

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Abstract

This paper describes the pharmaceutical regulatory environment in 19 developed countries from 1992 to 2004 and examines how changes in regulatory policies affect pharmaceutical revenues. Several important findings emerge from our analysis. First, we document a trend towards increasing pharmaceutical regulation over this 13-year period. Second, we find that a majority of regulations reduce pharmaceutical revenues significantly. Third, we find that most countries that adopted new regulations since 1994 already had some regulations in place for controlling costs. We find that such additional regulation had a smaller impact on further controlling costs. However, we find that introducing new regulations in a largely unregulated market, for example the US, could reduce pharmaceutical revenues significantly. Finally, we show that the effects of price controls increase over time.

Introduction

Rapid growth in pharmaceutical spending is a worldwide phenomenon. According to a recent study, OECD spending on pharmaceuticals has increased by an average of 32% in real terms since 1998, reaching more than US \$450 billion in 2003. 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 US (9.6%) was nearly triple the growth rate of spending (3.5%) in Germany.

This growth in pharmaceutical spending has increased demands for regulating 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 (Henry and Lexchin, 2002; Santerre and Vernon, 2006). On the one hand, regulations curb costs and thus potentially improve the welfare of the current generation. However, some argue that pharmaceutical regulations might also have negative consequences for consumers. For example, price regulation can lead to less competition in markets for generic drugs (Danzon and Chao, 2000), delay launch of new

drugs (Danzon, Wang and Wang, 2005), and limit the availability of new drugs (Danzon and Ketcham, 2003). In addition, such regulations might reduce the pace of innovation, by limiting pharmaceutical revenues and the profitability of investing in research and development (Acemoglu and Linn, 2003).

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. For example, a recent study by the U.S. Department of Commerce reviewed pricing in 11 OECD countries and found that, for patented drugs that were best sellers in the United States, the prices in other OECD countries were 18 to 67 percent less than U.S. prices, depending on the country. They conclude that price deregulation in these countries would increase pharmaceutical revenues by 25 to 38% (Department of Commerce, 2004). Similarly, Martikainen, Kivi and Linnosmaa (2005), found that wholesale prices for newly launched reimbursable pharmaceuticals were highest in countries where manufacturers are free to set their own prices. Another study, Ekelund and Persson (2003), find that in contrast to the unregulated market in the US, prices of new drugs in all classes fall faster in the regulated market of Sweden. Finally, Danzon and Chao (2000) found a negative relation between strict price regulation and the price of older molecules. However, they also found that generic competition is more effective in reducing prices in the US compared to more stringently regulated markets. In general, existing studies are limited by their reliance on cross-sectional variation in revenues or prices, and 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 expenditure before and after policies take effect. For example, Pavcnik (2002) estimated a 10–26% decrease in drug prices as a result of a reference pricing policy introduced in Germany after 1989. Pekurinen and Häkkinen (2005) suggested that voluntary generic substitution and prescribing policies had no affect on expenditures in Finland, but that compulsory generic substitution decreased prices and led to cost savings in the first year after introduction. 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 19 developed countries over a 13-year period. Next, we exploit 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 different pharmaceutical regulations are complements or substitutes of each other. For example, to what extent are the effects of a particular policy on pharmaceutical revenues determined by other regulations that were already in place before the new policy was introduced? Finally, we assess whether the effects of regulations change over time.

Several important patterns emerge from our analysis. First, we find that a majority of regulations reduce pharmaceutical revenues significantly. Second, we find that most

countries that adopted new regulations since 1994 already had some regulations in place for controlling costs. We find that such additional regulation had smaller impact on further controlling costs, though this is an average effect across all regulations introduced since 1994, including both enforced and poorly or un-enforced policies. However, we find that introducing new regulations in a largely unregulated market, for example the US, could reduce pharmaceutical revenues significantly. Finally, we show that the effects of price controls increase over time – price controls not only reduce the level of pharmaceutical revenues but also reduce the rate of growth of pharmaceutical revenues.

Data

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 is less widely reported. We collected data on pharmaceutical regulations in 19 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, in addition to publications from the World Health Organization and OECD, along with grey literature (e.g. IMS), as listed in Appendix A. We verified the data through expert interviews with two researchers and/or policy makers in the field of pharmaceutical regulation in each country, and country experts from a leading multinational pharmaceutical firm. The list of country experts consulted is available from the authors upon request. The 19 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, United Kingdom, 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 was not available either from the literature or from the country experts. For example, we know which countries adopted or repealed a maximum annual limit on pharmaceutical expenditures. However, in several cases, we do not know the exact expenditure limit that was implemented or whether it was enforced in practice. To make these diverse regulations amenable to analysis, we grouped them into 10 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 expenditure. The nature of global budgets differs across countries. For example, in some countries, budgets cap the entire country's spending (e.g., 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 pharmaceutical expenditure (as in Italy and Germany), or to spending on individual products or groups of products (New Zealand had negotiated expenditure caps for products such as fluoxetine and acyclovir, and in aggregate across proton pump inhibitors and H2-receptor antagonists). Finally, in some countries such policies are imposed (e.g. Germany), while in others they are negotiated as price-volume agreements. For example, in Hungary the pharmaceutical industry faced mandatory paybacks on excess revenues, in addition to price-volume agreements since the middle of 2003. In Portugal, the government and pharmaceutical industry agreed to a voluntary budget cap for the year 1997. In some cases (e.g. Italy until 1998), a budget cap exists, but is routinely exceeded in practice. In such cases the policy is defined based on its appearance in the law, and not upon the extent to which it is enforced in practice. However, in general, the industry is required to repay any revenue in excess of the negotiated or predetermined amount to the government or national health insurance program.

Prescribing budgets—These imply that physicians face an annual budget for prescriptions, with financial sanctions in the event of overruns. For example, German doctors faced a cap on prescription volume in 1998 and from 2001 onwards. The cap is set through a process in which physicians' associations negotiated a prescription drug budget with Statutory Health Insurers. The budget is then split into medical specialty-specific budgets, and converted into an average budget per patient, based on historical volume. The annual prescription budget for each individual doctor is the number of patients treated in a year by that doctor times the average budget per patient.

Profit controls—The regulator imposes a maximum annual limit on profits or profit growth rates of pharmaceutical companies. For example, profits of pharmaceutical firms in the UK were not allowed to exceed 17–21% until 1998 and 29% afterwards. Spain had limits on profit growth rates of 7% for 3 years starting July 1995. This agreement was revised in 1996 and 1998. Until 2004, Turkish pharmaceutical firms faced a maximum limit on profits of 15% at the corporate level and 20% on individual products, even though these figures were rarely achieved in practice.

Direct price controls - Only external reference pricing (ERP)—The regulator sets a maximum reimbursement level or market price for patented drugs based on prices of similar drugs in other countries. For example, since 1996 prescription drug prices in the Netherlands are based on wholesaler prices in Belgium, France, Germany and the UK. Variation exists across countries in the set of reference countries. For example, the set of reference countries used in Italy was France, Germany, Spain and UK until 1998, and all European countries from 1998 to 2003. In addition, variation exists in the pricing algorithm and the initiating party. For example, from 2004, Turkey annually chose 5 EU countries and used prices from the two countries with the lowest ex-manufacturer prices as the reference, whereas in Denmark since 2001, the Association of the Pharmaceutical Industry unilaterally agreed that prices will not exceed the European Average Price (EAP).

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, etc., none of which depends exclusively on prices of similar products in other countries (although it may be one of the criteria considered). For example, in 1994, the government of Denmark negotiated an agreement with the industry that imposed price ceilings on prescription drugs.

Generic Reference pricing (GRP)—In this case, the regulator sets a reference price, i.e., 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 (i.e. products containing the same active substance) within the country. Only generic prescription drugs are subject to these reference prices. For example, in Denmark starting in 1996, the reference price (reimbursement level) for generics is equal to the level of the lowest priced generic equivalent available on the market. In case a generic has a price higher than the reference price, patients have to pay the difference between the actual price and the reference price out-of-pocket.

Therapeutic Reference pricing (TRP)—The regulator sets a reference price, as in the previous policy. 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). In Germany, for example, the reference price (i.e. reimbursement level) of specific therapeutic classes — statins, sartans, triptans, and proton-pump inhibitors — has been determined by the federal

associations of sickness funds (i.e., health insurance collectives) since 2004, and in general cannot exceed the highest price in the lowest third of the market for a particular therapeutic class.

Economic evaluations are required and/or strongly encouraged—An economic evaluation must be considered when 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. For example, New Zealand uses cost-utility analysis (based on measuring cost per quality adjusted life-year, QALY) as a key analytical tool in its management of drug subsidies.

Generic substitution is allowed—Pharmacists are allowed to substitute generics with the same active ingredient without doctor's consent, unless the doctor indicates otherwise on prescription. For example, since 2002, regulators have allowed German pharmacists to substitute generics for certain high-priced brands, without physician approval. Physicians can indicate on the prescription that substitution is not allowed.

Incentives for generic prescribing—Doctors receive direct financial or non-financial incentives to prescribe generics, apart from those indirectly imposed by prescribing budgets. For example, Japan increased the generic-prescribing fee received by providers in 2002.

Degressive pharmacy fee structure—Pharmacists receive a degressive fee or margin for dispensing drugs. Put it 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.

In addition to the above policies we also investigated the impact that *pharmacy chains* had on total revenues since it may be argued that pharmacy chains have more bargaining power to obtain discounts either from the wholesalers or directly from the manufacturers.

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 US dollars on a quarterly basis, using the prevailing average exchange rate for the quarter. Sales values are standardized at the ex-manufacturer level. We extracted sales data for the period 1992–2004 for each of the 19 countries with the following exceptions (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 dataset 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 this 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. In addition to the regulation variables, we included exchange rates as a regressor to account for movements in the dependant variable related to local currency appreciations or depreciations (e.g. the sharp depreciation of the Turkish Lira in year 2000). The model is estimated using generalized

least squares (GLS) and allows for first order serial correlation in revenues within a country.¹

In the first model, we consider the impact of 6 different types of regulation on revenues: budget controls, both global and physician; direct price controls, both external reference pricing and price negotiations; reference pricing, both for 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.

While 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 what 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.

Results

Trends in Pharmaceutical Regulation

Exhibits 1 to 4 show an overall trend towards increasing regulation in OECD countries over the years 1992 to 2004. However, there is substantial variation in adoption rates of different regulations. Below we describe trends in specific regulations, and provide examples of countries that changed their policies.

Global budgets—In 1992 only New Zealand had global budgets as a policy for controlling pharmaceutical costs. By 2004, five additional countries in our sample imposed global budget caps for pharmaceutical expenditures (France, Hungary, Italy, Spain and UK), bringing the total to six. Exhibit 1 shows that adoption was continuous and gradual until 2001, at which point Germany and Spain dropped the policy. Germany adopted (1993) and then repealed (2002) this regulation over the same period. Portugal introduced global budgets in one year (1997) and Spain displayed the most turbulence, introducing budgets in four years (1996, 1998, 2001 and 2004).

Prescribing budgets—The number of countries with prescribing budgets was very small. Until 1997, only the UK had prescribing budgets. In 1998, Germany joined the UK, but in the following year, both countries dropped the policy. Germany reintroduced it in 2001, and as of 2004 it remained as the sole country with such a policy in place.

Profit controls—Exhibit 1 shows that the number of countries with profit controls is small and fairly constant. Over this period, Spain and Turkey changed their policies, with Spain adopting profit controls in 1995, and Turkey repealing them in 2004. The UK had this policy in place over the entire sample period.

Direct price controls—Direct price controls were the most popular regulation over our entire sample period. In 1992, 13 out of 19 of the countries in the sample already had some

¹The 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 6. These sensitivity analyses are available from the authors upon request.

form of price regulations in place. In 2004, the number of countries with direct price controls (either just ERP or a combination of price negotiations and other mechanisms) was 16. 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 Netherlands (ERP since 1996).

Reference Pricing—Exhibit 3 shows a strong upward trend in the number of countries with reference pricing for generics, ranging from two in 1994 to seven in 2004. Denmark, 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. Norway and Sweden abandoned this policy eventually: Sweden did so in 2003 and Norway in 2005.

The number of countries with therapeutic reference pricing is smaller and stayed between two and three for the period 1992–2002. After this it increased, to five in 2003 and six in 2004. Australia adopted therapeutic reference pricing in 1998; Hungary and Italy moved from generic reference pricing to therapeutic reference pricing in 2003. Germany abandoned therapeutic reference pricing in 1996 (for new drugs), but then reintroduced it in 2004².

Economic evaluations—From Exhibit 1 it becomes clear that many countries started to adopt the use of economic evaluations in their pricing policies over the years, from two countries in 1992 to ten countries in 2004. None of the countries ever abandoned this policy, thus whenever we observed a change in this policy it was an introduction, i.e. Canada in 1994, Italy in 1997, Portugal in 1998, Finland and the UK in 1999, Norway in 2002, Sweden in 2003, and Hungary in 2004.

Policies for increasing generic use—Exhibit 4 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 countries in 1992 to fourteen in 2004. Generic substitution was introduced in Australia (1994), Hungary (1995), Denmark (1997), France (1999), Italy (2001), Norway (2001), Spain (2001), Germany (2002), Portugal (2002), and Sweden (2003). Finland adopted such a policy in 1993, repealed it in 1996, and re-adopted in 2003.

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 and ten countries had them in 2004. The countries that imposed a degressive margin were Hungary (1993), Finland (1997), Italy (1997), Spain (2000), Sweden (2003) and Turkey (2004).

Effect of regulations on revenues

Exhibit 5 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 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. We also included a control variable for whether a country allows pharmacy chains. 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

²Although the German “jumbo” reference pricing policy was officially reintroduced early 2004, it took several months before the first reference baskets were established. Due to the limitations of our sample (ending in 2004) our subsequent results do not fully capture the effects of this particular policy.

economic evaluations and budgets. In particular, direct price controls reduce revenues by 18.3%, economic evaluations and budgets have a much smaller impact of around 6%. Note that the small impact of economic evaluations might in part be due to our definition of economic evaluations that includes both mandatory economic evaluations (which would probably have a larger impact) and regulations that strongly encourage pharmaceutical firms to conduct economic evaluations (which would probably have a smaller impact). It is important to note that since all the policy variables are dichotomous the size of the coefficient should be interpreted as an average of the short and long term impacts of the policy.

Model 2 disaggregates budgets, direct price controls and reference pricing into the subcategories that were discussed earlier. The results suggest that both global budgets and physician budgets reduce total revenues, with the latter having a stronger impact. This result seems logical since physician budget should create stronger incentives to reduce spending than global budget. Physician budgets are borne directly by prescribing doctors who are individually accountable.

The results in model 2 also show that price negotiations and other form of price controls reduce revenues by 18.7%, and less stringent price controls that rely on external reference pricing only reduce revenues by 13.5%. Finally, we found a positive effect (9.3%) of reference pricing for both generics and patented drugs, which is peculiar given the fact that these policies were introduced to contain cost. Model 3 provides a possible explanation for this unexpected result

In Model 3, we include aggregated policies, as in model 1, and an interaction effect between direct price controls and reference pricing. The results from this model show that reference pricing alone (i.e., in the absence of direct price controls) reduces pharmaceutical revenues by 10.9% and direct price controls alone (i.e. in the absence of reference pricing) reduce revenues by 26%. Furthermore, even when both regulations are implemented together they reduce revenues by roughly the same magnitude as price controls alone (24%). This suggests that the implementation of reference pricing alone reduced revenues considerably, but the implementation of reference pricing when price controls are already in place has very little or negligible additional effect on revenues. In contrast, implementing price controls on top of reference pricing can have a significant additional impact on industry revenues.

We further investigated the idea that additional 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 independent variables, rather than the individual policies. Exhibit 6 presents the results from this specification, where all the combinations observed in our sample are incorporated in the model. There are two striking patterns in the results. First, the results show that all possible combinations of policies significantly reduce revenues. Second, the results do suggest that additional regulation has a smaller impact on revenues. In fact, the evidence suggests that having more than two or three regulations in place provides no significant additional impact on revenues. For example, we found that introducing price controls in an unregulated market reduced revenues by 22.5% and introducing price controls combined with budgets (in comparison to no regulation) reduced revenues by 31.3%. However, the impact of price controls, budgets and other policies was not higher than the previous numbers.

In general, the results suggest that price controls have the strongest impact on revenues, followed by budget controls. It is important to keep in mind that these effects are the average

effects for those countries that implemented the specific policy or combinations of policies, regardless of whether those policies or regulations were enforced. We come back to this issue in the next section, when we discuss the limitations of our study.

The regression specifications in Exhibit 7 consider the dynamic impacts of regulations. In particular we evaluate 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 (Danzon et al., 2005). Conversely, firms may learn about and exploit additional loopholes over time.

We analyzed the presence of these dynamic effects by estimating a model for direct price controls and economic evaluations with an added linear time trend relative to the introduction of the policy. We also kept the other broad policies in our models as additional controls³. Exhibit 7 (model 5) presents the results from this analysis. The results show that direct price controls reduce revenues by 13.7% in the year of introduction and by 14.8% one year after their introduction. In the case of economic evaluation, the point estimate indicates that the effects of economic evaluation grow overtime, however the point estimate is statistically insignificant. In model 6, we relax the assumption that the trend is linear, and analyze the impact of direct price controls and economic evaluations for 4 different time periods: year of introduction, 1–3 years after introduction, 4–6 years after introduction, and more than 6 years after introduction. The results from this specification are similar to our earlier results and 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 10.4% in revenues. However, the effects increase significantly in the years after introduction with an average reduction of 20.2% in revenues in years one to three years after introduction and a reduction of 23.9% six years after introduction. In the case of economic evaluations, our results suggest that economic evaluations reduce revenues by 2.8% in the year of introduction, although this effect is statistically insignificant. However, we do observe a significant reduction in revenues in the years after introduction. For example, economic evaluation reduce revenues by 9.4% in years one to three after introduction and by 10.4% in years four to six after introduction.

Limitations

It is important in evaluating these findings to understand the limitations and context of this study. In principle, the regulations we study could affect pharmaceutical costs or 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 type of drugs consumed (branded vs. generic or cost effectiveness of drugs sold). Unfortunately, due to limited data we are unable to distinguish between these effects on prices vs. quantity and type of drugs sold.

There are two empirical challenges in estimating the effect of regulations on 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.

³These coefficients are not reported in Exhibit 7. They are very similar to those obtained in Model 1 and are available from the authors upon request.

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 years⁴. 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 or capsule whereas for syrup forms the standard unit factor is one teaspoon (5 ml) and injectable forms it is one ampoule or vial. We used these limited data from IMS 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 are not able to identify the effects of some regulations due to the limited availability of the IMS data. In addition, the above analysis cannot shed light on whether regulations changed the type of drugs consumed. So even if standard units sold were unchanged by regulation, it is possible that a greater fraction of prescriptions were for generic drugs, which would reduce revenues even further for branded drugs. Our data do not allow us to estimate whether regulations affect prices or revenues of branded drugs more than that of generics. However, prior research shows that regulations typically limit prices and availability of branded drugs more than generics (Danzon and Ketcham, 2003), which is consistent with many of the regulations we described, as some were specifically designed to encourage greater reliance on generic drugs. As a result, it is likely our model underestimates the true impact on revenues for innovative, branded pharmaceutical firms.

There is also the possibility that countries may implement regulations in response to unobserved trends in spending. Countries with rapidly-rising pharmaceutical revenues (in ways not captured by our model) could lead to more regulation. As a consequence, we tend to underestimate their impact on pharmaceutical revenues. However, the effect need not work in this direction. For example, it may be that regulations reducing access to physicians are implemented simultaneously with pharmaceutical regulation. We estimated additional models that included total physician related expenses, the physician consultations per capita, and proportion of physician expenses paid by public sources as additional control variables. The results from this analysis were qualitatively similar to those presented in Exhibit 6. 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 analyze 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, physician opposition to physician prescribing budgets in Germany in the late 1990s led to a repeal of the regulation (which was not enforced due to the strong physician response). Inclusion of unenforced, or poorly enforced regulations will bias our estimates downward, of the impact of regulations on pharmaceutical revenues. Thus, our results are generalizable to future regulations to the extent that (1) new regulations mimic the modal regulation as it existed in the 1990’s and (2) pharmaceutical firms do not change their response to regulatory pressure. For example, although we find that additional regulations have smaller impacts on revenues, recent anecdotal evidence from the

⁴We do not have data on standard units for the years 1992 and 1993 for all countries. In addition, data from New Zealand is missing for all years, data from Norway is missing from 1992 to 1995, and data from Netherlands is missing from 1992 to 2000.

introduction of jumbo reference pricing in Germany suggests that new regulations might have reduced revenues significantly (Azar, 2006).

Conclusion

In this paper, we analyzed trends in pharmaceutical regulation and their impact on revenues. Over a 13-year period we find tremendous changes in the regulations within countries. Overall, we find a trend towards increasing regulation of pharmaceutical markets. However, there is significant variation in the adoption rate of various regulations with the biggest increase in economic evaluations and little change in profit controls.

Several important patterns emerge from our analysis. First, we find that a majority of regulations significantly reduce pharmaceutical revenues, with direct price controls, having the biggest impact on revenues.

Second, we find that most countries that adopted new regulations already had some regulations in place for controlling costs. We find that such additional regulation has a smaller impact on further controlling costs, though this represents the average impact of both enforced and poorly or un-enforced policies. However, the results also suggest that introducing new regulations such as price controls in a largely unregulated market, for example the US, could reduce pharmaceutical revenues significantly. For example, if the US implemented the price controls and negotiations similar to those found in other developed countries then revenues in the US would fall by as much as 22.5%.

The results also show that the impact of price controls increases over time. There are several possible explanations for this finding. For example, policy makers might become more familiar with implementation of the policy and close loopholes. It is also possible that price ceilings imposed by regulations become more binding overtime due to inflation in pharmaceutical prices. Finally, there is evidence that regulations suppress growth in pharmaceutical revenues by delaying the launch of new and high-priced drugs.

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 significantly reducing costs today. However, it is important to note that revenue reductions will affect future innovation. For example, price regulation can delay the launch of new drugs (Danzon, Wang and Wang, 2005), and limit the availability of new drugs (Danzon and Ketcham, 2003). Acemoglu and Linn (2003) estimate that each 1% reduction in pharmaceutical revenues in the United States would reduce the annual number of marketed chemical entities by 3.5%. 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. While there is much rhetoric on this point, little hard evidence exists on how global pharmaceutical policy affects the welfare of current and future generations. Although, such estimates are beyond the scope of this paper, it is an important avenue for future research.

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Global Budgets, Profit Controls and Economic Evaluations

Exhibit 1.

Trends in Global Budgets, Profit Controls and Economic Evaluations for 19 OECD countries 1992–2004

Direct Price Control Policies

Exhibit 2.

Trends in Direct Price Control Policies for 19 OECD countries 1992–2004

Reference Pricing Policies

Exhibit 3.

Trends in Reference Pricing Policies for 19 OECD countries 1992–2004

Policies Aimed at Generic Substitution and Prescribing

Exhibit 4.

Trends in Policies Aimed at Increasing Generic Use for 19 OECD countries 1992–2004

Exhibit 5

Static Effects of Pharmaceutical Policies on Revenues

Policy	Model 1 – Effect of Aggregate Measures of Policies on ln(Revenues)	Model 2 – Effect of Disaggregated Measures of Policies on ln(Revenues)	Model 3 – Effect of Aggregate Measures of Policies with Interactions [†] on ln(Revenues)
Profit controls	–0.064 (0.049)	–0.042 (0.054)	–0.068 (0.049)
Budgets	–0.061 (0.025) **		–0.049 (0.025) *
Global budget		–0.045 (0.024) *	
Physician budget		–0.180 (0.042) ***	
Direct Price Controls	–0.183 (0.037) ***		–0.260 (0.049) ***
Only international comparisons		–0.135 (0.040) ***	
Price negotiations and others		–0.187 (0.044) ***	
Reference pricing	0.016 (0.025)		–0.109 (0.064) *
Reference pricing for generics		0.034 (0.026)	
Reference pricing for generics and on-patent drugs		0.093 (0.039) **	
Interaction: RP and direct controls			0.131 (0.063) **
Economic evaluation	–0.061 (0.025) **	–0.044 (0.028)	–0.051 (0.025) **
Incentives for generic use			
1 out of 3 policies for prescribing / dispensing generics	–0.028 (0.027)	–0.008 (0.029)	–0.023 (0.027)
2 or more out of 3 policies for prescribing / dispensing generics	–0.040 (0.033)	–0.030 (0.035)	–0.037 (0.032)
Constant	7.834 (0.077) ***	7.819 (0.082) ***	7.896 (0.080) ***
Observations	243	243	243

Standard errors in parentheses.

* significant at 10%;

** significant at 5%;

*** significant at 1%.

[†] Between Direct Price Controls and Reference Pricing.

Exhibit 6**Static Effects of Combined Pharmaceutical Policies on Revenues**

Policy Combination	Model 4 – Effect of Combinations of Policies on ln(Revenues)
Only price controls	–0.225 (0.053) ***
Reference pricing only	–0.086 (0.067)
Price control + profit control	–0.341 (0.073) ***
Price control + reference pricing	–0.218 (0.056) ***
Budget + price controls	–0.313 (0.048) ***
Budget + reference prices	–0.249 (0.100) ***
Budget + price controls + profit controls	–0.340 (0.085) ***
Budget + price control + reference pricing	–0.326 (0.055) ***
Price control + profit control + reference pricing	–0.244 (0.078) ***
Budget + price control + profit control + reference pricing	–0.238 (0.087) ***
Economic evaluations	–0.036 (0.025)
1 out of 3 policies for prescribing / dispensing generics	–0.039 (0.028)
2 or more out of 3 policies for prescribing /dispensing generics	–0.045 (0.033)
Pharmacy chains allowed	0.003 (0.050)
Exchange rates	–0.003 (0.001) ***
Constant	7.867 (0.084) ***
Observations	243

Standard errors in parentheses.

significant at 1%

Exhibit 7**Dynamic Effects of Direct Price Controls and Economic Evaluations on Revenues**

Policy	Model 5 – Effect of regulation on ln(Revenues), t years after introduction (linear time trend)	Model 6 – Effect of regulation on ln(Revenues), t years after introduction (non-linear time trend)
Effect of economic evaluations in year of introduction	–0.064 (0.028) **	–0.028 (0.030)
Additional effect of economic evaluations t years after introduction	–0.006 (0.007)	
Effect of economic evaluations in years 1–3 after introduction		–0.094 (0.029) **
Effect of economic evaluations in years 4–6 after introduction		–0.104 (0.036) **
Effect of economic evaluations beyond 6 years after introduction		–0.071 (0.056)
Effect of direct price controls in the year of introduction	–0.137 (0.041) ***	–0.104 (0.051) **
Effect of direct price control t years after introduction	–0.011 (0.005) **	
Effect of price controls in years 1–3 after introduction		–0.203 (0.041) ***
Effect of price controls in years 4–6 after introduction		–0.179 (0.042) ***
Effect of price controls beyond 6 years after introduction		–0.239 (0.043) ***
Constant	7.560 (0.071) ***	7.573 (0.072) ***
Observations	243	243

Standard errors in parentheses.

* significant at 10%;

** significant at 5%;

*** significant at 1%.