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Examining the link between price regulation and pharmaceutical R&D investment

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Summary

This paper examines the link between price regulation and pharmaceutical research and development (R&D) investment. I identify two mechanisms through which price regulation may exert an influence on R&D: an expected-profit effect and a cash-flow effect. Using established models of the determinants of pharmaceutical R&D, I exploit a unique fact to quantify firm exposure to pharmaceutical price regulation: relative to the rest of the world, the U.S. pharmaceutical market is largely unregulated with respect to price. Using this fact within the context of a system of quasi-structural equations, I simulate how a new policy regulating pharmaceutical prices in the U.S. will affect R&D investment. I find that such a policy will lead to a decline in industry R&D by between 23.4 and 32.7%. This prediction, however, is accompanied by several caveats. Moreover, it says nothing about the implications for social welfare; therefore, these issues are also discussed. Copyright © 2004 John Wiley & Sons, Ltd.

Keywords price regulation; R&D Investment; pharmaceuticals; pharmaceutical innovation; pharmaceutical profitability

Introduction

In this paper I examine a potential link between price regulation and investment in pharmaceutical research and development (R&D). Because it is through R&D that new drugs are discovered and brought to market, it is important to understand what effect, if any, price regulation has on a firm's decision to allocate resources to this activity. I describe two potential channels through which price regulation may exert an influence on R&D investment. First, price regulation may affect the expected returns to R&D, which may be thought of as a demand-side effect (for R&D). Second, if capital market imperfections exist in the market for R&D finance (and impart a lower cost of capital to internal funds relative to external debt and equity), then price regulation may also affect R&D through a cash-flow effect (i.e., a supply-of-funds effect).

To quantify pharmaceutical price regulation in this paper I will utilize a unique stylized fact: relative to the rest of the world, the U.S. pharmaceutical market is largely unregulated with respect to price. Methods of pharmaceutical price regulation outside the U.S. are quite heterogeneous, and include, for example, direct price regulation through price controls (e.g., France and Italy), indirect price regulation through limits on reimbursement under social insurance programs (e.g., Germany and Japan), and indirect price regulation through profit controls (e.g., the United Kingdom).[a] Therefore, firms with a high proportion of their pharmaceutical sales coming

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from non-U.S. markets will be more exposed to price regulation than firms whose sales come primarily from the U.S. market. This fact will play a key role to identifying the potential links between price regulation, pharmaceutical profitability, firm cash flows, and R&D investment.

This article will proceed as follows. First, the theory is presented and a system of quasi-structural equations that govern the firm R&D investment process is defined. This will be done within the context of two broadly classified markets: a price-regulated market (i.e., non-U.S. pharmaceutical markets) and a 'free' market (i.e., the largely unregulated – with respect to price – U.S. market). I will rely heavily on the prior research by Grabowski and Vernon [3–6], which has established a robust empirical framework for analyzing the determinants of pharmaceutical R&D investment intensity. Next, the various data sets used are described and my empirical results are discussed. Following this, a policy of introducing price regulation into the U.S. pharmaceutical market is simulated. I will model this by assuming price regulation (or re-importation) drives U.S. pharmaceutical profit margins down to the average level observed in non-U.S. pharmaceutical markets. This, I will argue, will reduce both future pharmaceutical profit expectations and firm cash flows. Potential welfare implications will also be considered in this section. The final section concludes.

Theory and empirical specifications

Basic economic theory predicts that firms invest in capital up to the point where the expected marginal efficiency of investment (MEI) is just equal to the firm's marginal cost of capital (MCC). This equilibrium may be thought of in the classic way: as the intersection of a demand (for investment) and supply curve (for investment funds).

A firm's MEI schedule is derived by arranging potential investment projects in a decreasing order with respect to each project's risk-adjusted expected rate of return. Firms will undertake the most profitable investment projects first – those offering the highest risk-adjusted expected rate of return – and continue to undertake additional investment projects so long as the expected rate of return from the next project exceeds the firm's marginal cost of capital. This classic supply and demand framework for capital investment may be applied directly to investment in pharmaceutical R&D.

The MCC reflects the supply price of funds on the margin. In a neoclassical world, with perfect information and well-functioning capital markets, the MCC schedule would be constant at the real market rate of interest, implying that firms consider the source of investment finance irrelevant [7]. Recent research, however, both theoretical and empirical, suggests the source of finance does matter, and cash flows, because they have a lower cost of capital relative to external debt and equity, exert a positive influence on firm investment spending [8–10].[b] Grabowski and Vernon [3–6] have demonstrated this to be particularly true for pharmaceutical R&D investment.

Therefore, mathematically, a pharmaceutical firm's equilibrium level of R&D investment may be described by the following optimality condition:

$$\text{MEI (RD, } \mathbf{X}) = \text{MCC (RD, } \mathbf{Y}) \tag{1}$$

In Equation (1), X is a vector of variables influencing the expected returns to R&D investment (i.e., the demand for R&D) and **Y** is a vector of variables influencing the opportunity cost of investment capital (i.e., the supply price of funds); RD is, of course, the firm's level of R&D investment. Solving Equation (1) for RD yields the following reduced-form solution for a firm's equilibrium level of R&D investment:

$$\text{RD}^* = f(\mathbf{X},\ \mathbf{Y}) \tag{2}$$

In their most recent study of the determinants of pharmaceutical R&D expenditures, Grabowski and Vernon [6] analyzed panel data for eleven firms from 1974 to 1994. They found pharmaceutical profit expectations and cash flows to be the principal explanatory variables of firm-level R&D investment. This finding was consistent with their earlier studies, which examined different time periods and firms. Grabowski and Vernon's general empirical specification, which was quite robust statistically, was the following:

$$\frac{R_{it}}{S_{it}} = \beta_0 + \beta_1 E\pi_t + \beta_2 \frac{C_{it-1}}{S_{it-1}} + \sum_{i=2}^{11} \beta_{i+1} F_i \tag{3}$$

The variables in Equation (3) are defined as follows: R_{it} is firm i's R&D expenditures in year t; S_{it} is firm i's total sales in year t; $E\pi_t$ is an index of the expected returns to pharmaceutical R&D in

year t; C_{it-1} is firm i's cash flow in year t-1; and F_i is a dummy variable for firm i (for $i = 2$ to 11).

While a detailed review of their model is not necessary for the purposes of this research, one important characteristic of the model does deserve attention because of its relevance to the current analyses. Grabowski and Vernon utilized an *industry-wide* proxy of the expected returns to pharmaceutical R&D.[c] This is in contrast to their earlier studies in which they employed *firm-level* proxies of expected returns.[d] While their industry-wide variable was statistically significant, the fact that it was measured at the industry level – and not the firm level – could be problematic. This would be the case if there existed heterogeneity in firm pharmaceutical profit expectations. Grabowski and Vernon argued that parallel paths of research and increasing R&D spillover opportunities, which began in the early 1980s [11,12], would tend to result in uniform pharmaceutical profit expectations within the industry. While this is not implausible, it seems more likely that firms *will* have different expectations about their future pharmaceutical profitability. Indeed, as Vernon [13,14] has discussed, some firms consistently profit more than others from their R&D activities, and they do this by being more successful at penetrating the highly profitable U.S. pharmaceutical marketplace: the only marketplace that remains largely unregulated with respect to price.[e] The obvious question then becomes: why are some firms better than others at infiltrating the U.S. market? One plausible explanation is that firms have divergent capabilities in discovering, developing, and marketing pharmaceutical products for the U.S. market.[f] Indeed, this is what Grabowski and Vernon assumed in their earlier studies when they utilized firm-level measures of pharmaceutical profitability and productivity to proxy for expected future returns to R&D. The theoretical arguments for the existence of sustainable heterogeneities in firm capabilities (e.g., R&D capabilities) are numerous, and have their origins in the resource-based theory of the firm [15,16]. In addition to firm capabilities, intra-industry barriers to entry, such as trademarks, goodwill, and advertising might also contribute to a sustained divergence across firms with respect to their abilities to develop commercially successful pharmaceuticals (which significantly penetrate the U.S. market).

Therefore, in forthcoming analyses of how price regulation affects R&D investment, I will employ a firm-level proxy of pharmaceutical profit expectations – one that is identical to Grabowski and Vernon's industry-level variable. I will use a firm's current period pre-tax pharmaceutical profit margin to proxy expected future profitability.[g] More will be said about this variable momentarily. The key question now becomes how, within this model of firm R&D investment, does pharmaceutical price regulation enter? This question is addressed next.

The link between pharmaceutical price regulation and firm R&D investment

It has been widely argued in the literature that pharmaceutical price regulation exerts a negative influence on a firm's expected returns to R&D investment (see, for example, Scherer [19]; Grabowski [20]; Helms [21]; Green [22]; and Vernon [13]).[h] Within the framework of the model just described, this regulatory influence will reduce the demand for R&D through the X vector in the MEI equation. Theoretically this seems appropriate because a firm's returns to R&D come in large part from sales of newly launched, patented, pharmaceuticals – those products for which price regulation is the most stringent in non-U.S. markets [2]. Therefore, the greater the proportion of a firm's pharmaceutical sales coming from outside the U.S., the greater a firm's exposure to price regulation, and, importantly, the lower a firm's expected returns to R&D, ceteris paribus.

The second principal way in which pharmaceutical price regulation may influence firm R&D investment is through a cash-flow effect. Unlike profit expectations, which operate through the X vector in Equation (2), and are based on forward-looking expectations, this influence will occur through the Y vector, and the firm's level of internally generated funds. The former influence may be thought of as a demand-side effect (for R&D investment) and the later a supply-side effect (for investment funds). Figure 1 illustrates these two effects within the context of the preceding discussion.

Regarding Figure 1, there is an important point to keep in mind: firms in the pharmaceutical industry are often highly diversified into other industries (e.g. consumer products, medical devices, and industrial chemicals). As such, a firm's

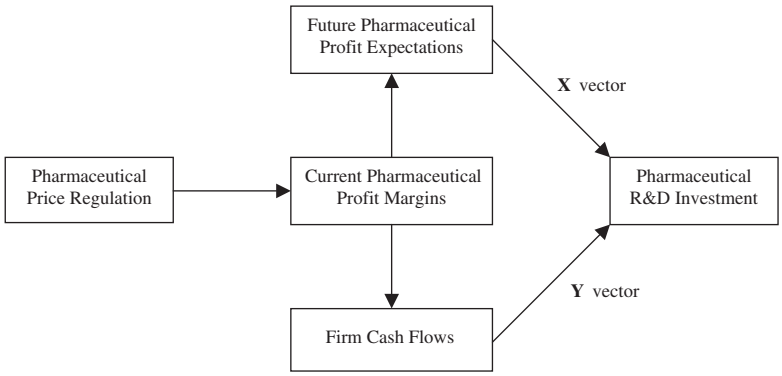

Figure 1. The paths through which pharmaceutical price regulation may affect R&D

cash flow will be determined by both its pharmaceutical and non-pharmaceutical business operations. This distinction is highlighted in the following system of quasi-structural equations that define the relationships between price regulation, pharmaceutical profitability, firm cash flows, and R&D investment intensity.

$$\frac{R_{it}}{S_{it}} = \beta_0 + \beta_1 \frac{\pi_{it}}{S^P_{it}} + \beta_2 \frac{C_{it-1}}{S_{it-1}} + \sum_{i=2}^{n} \beta_{i+1} F_i \tag{4}$$

$$\frac{\pi_{it}}{S^P_{it}} = \lambda_{it} M^R_{it} + (1 - \lambda_{it}) M^F_{it} \tag{5}$$

$$C_{it-1} = I_{it-1} + D_{it-1} + (1 - \tau) R_{it-1} \tag{6}$$

$$I_{it-1} = (1 - \tau)(\pi_{it-1} + \tilde{\pi}_{it-1}) \tag{7}$$

The new variables appearing in Equations (4)–(7) are the following: π_{it} is firm i's pre-tax pharmaceutical profits in year t; $\tilde{\pi}_{it-1}$ is firm i's pre-tax non-pharmaceutical profits in year t; S^P_{it} is firm i's total pharmaceutical sales in year t; λ_{it} is the percentage of firm i's pharmaceutical sales in year t from non-U.S. markets; M^F_{it} is firm i's average pre-tax profit margin on pharmaceuticals products sold in the U.S. market in year t; M^R_{it} is firm i's average pre-tax profit margin on pharmaceuticals products sold in non-U.S. markets in year t; I_{it-1} is firm i's net income in year $t-1$; D_{it-1} is firm i's depreciation expense in year $t-1$; and τ the corporate tax rate.

The first equation is the firm R&D investment equation. It is similar in specification to the formulation used by Grabowski and Vernon in their most recent study; however, as was previously mentioned, the industry-wide proxy for expected returns to R&D has been replaced. An equivalent firm-level version of this variable is used instead.[i]

Equation (5) is an identity, and reflects the fact that a firm's pre-tax pharmaceutical profit margin can be decomposed into a weighted average of its pre-tax pharmaceutical profit margin in the U.S. and its pre-tax pharmaceutical profit margin in non-U.S. markets.[j] This decomposition is derived and discussed in the appendix.

Equation (6) is also an identity, and defines how the cash flow variable was constructed for this study. Following Grabowski and Vernon [6] and Hall [9], this definition was designed to measure a firm's internally generated funds before the payment of dividends and investment in R&D and other capital assets. Because R&D, unlike other capital assets, is expensed for tax purposes, after-tax R&D was added to after-tax net income and depreciation to obtain an estimate of a firm's pre-investment cash flow. A flat tax rate of 33% was used for this purpose.[k] Lastly, Equation (7) reflects the fact that a firm's net income is the sum of its after-tax pharmaceutical and non-pharmaceutical profits.

The main equation estimated in this paper will be the R&D equation. However, in order to demonstrate how price regulation (or possibly re-importation) influences R&D investment, Equations (5)–(7) must also considered. Therefore, repeated substitution and lagging are used to obtain an expanded version of the R&D equation, which contains λ, a measure of exposure to pharmaceutical price regulation.[l]

Equation (7) is first substituted into Equation (6) to yield the following form of the lagged cash

flow variable:

$$C_{it-1} = (1-\tau)(\pi_{it-1} + \tilde{\pi}_{it-1} + R_{it-1}) + D_{it-1} \quad (8)$$

Next, Equation (5) is lagged one period, multiplied through by S^P_{it-1}, and substituted into (8) to produce the following expanded version of lagged cash flow:

$$C_{it-1} = \{1-\tau\}\{S^P_{it-1}[\lambda_{it-1}M^R_{it-1} + (1-\lambda_{it-1})M^F_{it-1}] + \tilde{\pi}_{it-1} + R_{it-1}\} + D_{it-1} \quad (9)$$

Finally, Equations (5) and (9) are substituted into Equation (4). This results in a fully decomposed version of the R&D equation, one that is a function of λ (firm constant terms have been suppressed for algebraic convenience):

$$\frac{R_{it}}{S_{it}} = \underbrace{\beta_1[\lambda_{it}M^R_{it} + (1-\lambda_{it})M^F_{it}]}_{\text{Expected-profitability effect}} + \underbrace{\beta_2 \frac{\{1-\tau\}\{S^P_{it-1}[\lambda_{it-1}M^R_{it-1} + (1-\lambda_{it-1})M^F_{it-1}] + \tilde{\pi}_{it-1} + R_{it-1} + D_{it-1}}{S_{it-1}}}_{\text{Cash-flow effect}} \quad (10)$$

Equation (10) reveals the precise nature of the linkages between pharmaceutical price regulation and investment in R&D (at least within the context of the model described by Equations (4) through (7)). The first term is the expected-profitability effect, which enters the model contemporaneously.[m] The second term is the cash-flow effect, which influences R&D intensity with a one-period lag. Before proceeding to the empirical section of this paper, an interesting policy scenario is considered within the context of Equation (10).

Regulating pharmaceutical prices in the United States?

There has been much debate over whether or not the U.S., like the rest of the world, should begin regulating pharmaceutical prices. In fact, there have been several attempts to pass into law bills that would result in regulated pharmaceutical prices in the U.S. For example, the 1993 Health Security Act proposed by the Clinton Administration called for universal health insurance with price-regulated pharmaceuticals as part of the basic benefit package. In more recent times, however, individual states have begun filing bills that would enable state legislatures to set maximum prices for prescription drugs.[n] Similarly, the re-importation of pharmaceuticals from Canada and Europe has emerged as another potential means of curtailing the prices in the U.S.[o]

Within the context of Equation (10), a scenario of regulated pharmaceutical prices in the U.S. can in fact be modeled. This is possible because of the way price regulation is measured in the model: as the percentage of a firm's pharmaceutical sales coming from price-regulated (i.e., non-U.S.) markets. Consequently, if pharmaceutical prices in the U.S. were regulated in a manner equivalent to the average degree of price regulation found in non-U.S. markets, within Equation (10) this would be equivalent to setting $\lambda = 1$: all of a firm's pharmaceutical sales are subjected to price regulation of one form or another.

Mathematically, this scenario can be modeled as the limit of the R&D investment equation as both λ_{it} and λ_{it-1} approach unity. This limit is evaluated one year after the hypothetical policy is enacted because the cash flow effect operates with a one-year lag (again, firm constant terms are suppressed for convenience).[p]

$$\lim_{\lambda \to 1} \frac{R_{it}}{S_{it}} = \beta_1 M^R_{it} + \beta_2 \frac{[1-\tau][S^P_{it-1}M^R_{it-1} + \tilde{\pi}_{it-1} + R_{it-1}] + D_{it-1}}{S_{it-1}} \quad (11)$$

Subtracting Equation (11) from Equation (10), and then simplifying, quantifies the change in R&D that would accompany a policy of pharmaceutical price regulation in the U.S.:[q]

$$\Delta\left[\frac{R_{it}}{S_{it}}\right] = \beta_1 \underbrace{[(1-\lambda_{it})(M^F_{it} - M^R_{it})]}_{\Delta \text{ Pharmaceutical profit margin}} + \underbrace{\beta_2 \frac{\{1-\tau\}\{S^P_{it-1}[(M^F_{it-1} - M^R_{it-1})(1-\lambda_{it-1})]\}}{S_{it}}}_{\Delta \text{ Cash flows}} \quad (12)$$

In order to evaluate Equation (12), it is necessary to have parameter estimates of β_1, β_2, and average pre-tax pharmaceutical profit margins in both markets. Data on the other model variables may be obtained directly from firm financial statements and/or other sources. These parameters will be estimated in the following two sections. To be certain, this type of policy simulation is highly speculative, and any predictions that are generated need to be tempered with considerable caution for a number of reasons. Nevertheless, this is what is done in Section 4, along with a discussion of the caveats involved. First, however, empirical models of the determinants of R&D intensity will be estimated. This is done next using firm financial data on fourteen major pharmaceutical firms from 1994 to 1997.

Data and empirical estimates of the determinants of R&D investment

Financial data on the world's 30 largest pharmaceutical firms from 1994 to 1997 were collected from three primary sources: Standard & Poor Compustat files, Scrip Company League Tables (PJB Publications Ltd) and IMS America. The sample was restricted to top-30 firms to ensure that the selected firms had a specialization in innovative R&D. Several firms that ranked below 30, but above 50, were generic manufacturing drug firms (e.g., Watson and Mylan), which perform little, if any, innovative R&D. The sample time period was selected because of data availability for several of the model's key variables and merger activity.[r] These issues are discussed next.

Of the top-30 firms for which data were collected, complete observations (on all of the key model variables) were available for only 14 firms. There were two principle reasons for why some top-30 firms had to be excluded from the sample. First, if a firm experienced a merger during or after the sample time period, historical financial data prior to the merger could not always be reconstructed. This was because of the different reporting methodologies used by the three data sources. For example, IMS pools the financial histories of merged firms. Standard and Poor, on the other hand, assigns to the new firm the financial history of the larger of the two firms pre-merger. Only Scrip maintains records on the separate firms pre-merger. The second reason some firms were excluded from the sample was lack of data on firm *pharmaceutical* profitability. Most firms in the pharmaceutical industry are diversified into other, non-pharmaceutical industries; thus, a firm's total profit is comprised of both pharmaceutical and non-pharmaceutical business operations. Unlike a firm's total profits, pharmaceutical profits (or the profits generated by other business lines) are seldom reported in firm financial statements. Scrip, on the other hand, does report these data. However, because these data are based on survey responses (i.e., firms are not required to report these data), pharmaceutical profitability for several firms could not be obtained.[s]

Empirical analyses: the determinants of pharmaceutical R&D investment

To estimate the R&D investment equation from the last section, current-period pharmaceutical profit margins were used to proxy a firm's expected future pharmaceutical profitability. As previously argued, this variable should serve as a reasonable proxy for a firm's expectations per its ability to discover, develop, and market commercially successful pharmaceutical products (which typically penetrate the U.S. market in a significant manner).

Because the data sample was constructed from a panel of fourteen firms over only four years, it was a concern that the firm fixed-effects specification might obfuscate some of the key behavior relationships this paper seeks to identify.[t] Indeed, most of the sample variation in the dependent and independent variables occurred across firms, and not within firms over time. As a result, two other general model specifications were estimated: an ordinary least squares (OLS) specification and a random-effects specification. Table 1 summarizes the empirical results from these three regression equations.[u]

Consistent with earlier research, the results in Table 1 suggest that both pharmaceutical profit expectations and lagged cash flows are an important determinant of firm R&D intensity. The cash flow coefficient, which was significant at the 0.05-level or better in every equation, was found to be remarkably similar in magnitude to the coefficients obtained in earlier studies (studies that examined different time periods and different

Table 1. The determinants of R&D-to-sales for fourteen firms, 1994–1997 (white standard errors in parentheses)

Model specification	$\frac{C_{it-1}}{S_{it-1}}$	$\frac{\pi_{it}}{S_{it}^{P}}$	Adjusted R^2	Model F-Statistic
E.1: Ordinary least squares	0.285***	0.073*	0.822	43.2
	(0.071)	(0.039)		
E.2: Firm random effects	0.152**	0.073***	0.959	—
	(0.051)	(0.022)		
E.3: Firm fixed effects	0.106*	0.059*	0.958	257.5
	(0.046)	(0.025)		

Note: Intercepts and controls also included in equations.
*Significant at the 0.05-level.
**Significant at the 0.01-level.
***Significant at the 0.001-level or better.

firms). Specifically, in the current study this coefficient ranged from 0.11 to 0.29 (compared to a range of 0.12 to 0.31 obtained in previous studies). The variable designed to capture expected future pharmaceutical profitability (i.e., contemporaneous pharmaceutical profit margins) also performed well from a statistical perspective, and was similarly significant at the 0.05-level or better in every equation. However, the coefficient range for this variable, unlike that for the lagged cash flow variable, was quite narrow, and ranged from only 0.06 to 0.07.[v]

As discussed previously, given the short time series in the current panel, and the fact that most of the sample variation in the dependent and independent variables occurred across firms and not over time, a firm fixed-effects specification comes at a very high cost: it uses up fourteen degrees of freedom (25% of the data sample). Thus, it may obscure the influence cash flows and profit expectations have on R&D investment by not fully exploiting the variations in these variables across firms.[w] Indeed, the coefficients on the cash-flow variable and profit-expectations variable are smaller in the fixed-effects models relative to the OLS and random-effects models. This suggests that the firm fixed effects are picking up some of the time-invariant variation across firms in these explanatory variables. Before proceeding, however, it is necessary to mention that the random-effects specification is appropriate only if the firm effects are uncorrelated with the other model regressors. If they are correlated, then the random-effects model may suffer from inconsistency due to omitted variables. Therefore, a Hausman [25] test was performed. The null hypothesis of orthogonality between the random effects and other model regressors could not be rejected ($W = 4.88$). For this reason, the fixed-effects model results will not be used in the forthcoming policy simulation exercise.[x]

Pharmaceutical price regulation in the United States: potential consequences for Industry R&D investment

As described in detail in Section *Theory and Empirial Specifications*, it is possible to simulate, within the context of the R&D models estimated above, how a new policy regulating pharmaceutical prices in the U.S. might impact R&D investment. This was demonstrated mathematically by Equation (12). Before evaluating Equation (12), however, it is first necessary to estimate Equation (5), which is used to obtain measures of the average pre-tax pharmaceutical profit margins in U.S. and non-U.S. markets (i.e., in price-regulated and non-price-regulated markets). Vernon [14] has done this using a similar data sample, and determined that pre-tax pharmaceutical profit margins in the U.S. are approximately four times as large as those, on average, in non-U.S. markets (0.43 versus 0.12 in the most directly comparable sample). While there are certainly other factors that may be contributing to this observed difference (e.g., third degree price discrimination and medical practices), it seems likely that price regulation is indeed a prominent factor.[y] As will be seen momentarily, it is through the link between

price regulation and pre-tax pharmaceutical profit margins that this policy experiment will be modeled. Therefore, following Vernon, Equation (5) was rearranged algebraically and simplified as follows:

$$\frac{\pi_{it}}{S_{it}^P} = M_{it}^F - (M_{it}^F - M_{it}^R)\lambda_{it} \tag{13}$$

Defining $\delta_{it} = M_{it}^F - M_{it}^R$ and substituting this in (13) yields:

$$\frac{\pi_{it}}{S_{it}^P} = M_{it}^F - \delta_{it}\lambda_{it} \tag{14}$$

Using data on the variables π_{it}, S_{it}^P, and λ_{it} from the current sample, Equation (14) was used to estimate *average* U.S. and non-U.S. pre-tax pharmaceutical profit margins, $\bar{M}^F$ and $\bar{M}^R$, respectively. Specifically, the following equation was estimated:

$$\frac{\pi_{it}}{S_{it}^P} = \alpha_0 - \alpha_1\lambda_{it} \tag{15}$$

The constant term (α_0) may be interpreted as the average pre-tax pharmaceutical profit margin in the U.S. and this constant term less the slope coefficient ($\alpha_0 - \alpha_1$) may be interpreted as the average pre-tax pharmaceutical profit margin in non-U.S. markets. The appendix provides a detailed derivation of the theoretical model underlying this empirical specification. Table 2 summarizes the regression results from three separate statistical models: OLS, firm fixed effects, and firm random effects. The corresponding estimates of average pre-tax pharmaceutical margins are also reported.

The results from the three models are highly consistent with one another, and suggest that average pre-tax pharmaceutical profit margins are roughly four to five times higher in the U.S than they are in markets outside the U.S. Not surprisingly, in the fixed-effects model, the coefficient on λ_{it} was only marginally statistically significant ($p = 0.064$) relative to the significance levels obtained from the random effects and OLS models ($p < 0.001$). However, as Table 2 shows, the coefficient estimates from the fixed-effects model were very similar to those found in the OLS and random-effects models.

To further investigate the linkage between price regulation and pharmaceutical profit margins, Equation (14) was also estimated by OLS for each year in the sample. The results from these regressions were very similar to the pooled results, and both the intercept ($\hat{\alpha}_0$) and slope coefficient ($\hat{\alpha}_1$) were significant at the 0.001-level or better in each regression. The results from these single-year regressions are reported in the appendix.

The findings just presented may now be used in conjunction with the empirical work from Section 3 to model the *potential* consequences of regulating prescription drug prices in the U.S.

Simulating the effects of a new U.S. policy on pharmaceuticals

Within the framework of the theoretical model described by Equations (4) through (7), the effect of regulating pharmaceutical prices in the U.S. can be illustrated by first evaluating the limit of Equation (5) as $\lambda_{it} \to 1$:

$$\lim_{\lambda \to 1} \frac{\pi_{it}}{S_{it}^P} = \lambda_{it}M_{it}^R + (1 - \lambda_{it})M_{it}^F = M_{it}^R \tag{16}$$

Table 2. Estimated pharmaceutical profit margins in the U.S. and abroad (white standard errors in parentheses)

Model specification	α_0	λ_{it}	$\bar{M}^F$	$\bar{M}^R$	Adj. R^2
E.4: Ordinary least squares	0.497*** (0.037)	0.392*** (0.067)	0.497	0.105	0.533
E.5: Firm random effects	0.497*** (0.030)	0.392*** (0.056)	0.497	0.105	0.573
E.6: Firm fixed effects	—	0.327* (0.211)	0.465	0.138	0.565

Note: $\bar{M}^F$ for the fixed-effects model is simply the average of the fixed effects.
*Significant at the 0.10-level.
***Significant at the 0.001-level or better.

Equation (16) captures firm i's pre-tax pharmaceutical profit margin under the new U.S. policy in year t, and highlights the central mechanism through which this policy simulation models the effect of price regulation on R&D investment: by driving a firm's average pharmaceutical profit margin down to the average level found in non-U.S. markets.[z] In other words, the assumption is that the new policy will cause U.S. pharmaceutical prices to be regulated in such a manner as to make U.S pharmaceutical profit margins equal, on average, to non-U.S. pharmaceutical profit margins. A new law legalizing the re-importation of pharmaceuticals into the U.S. would plausibly satisfy this requirement.[aa] It is critical to note, however, that to the extent other factors contribute to the observed divergence in pre-tax pharmaceutical profit margins across U.S. and non-U.S. markets, the forthcoming policy simulation might overstate the effect of price regulation in the U.S. Therefore, this policy simulation is really an analysis of how lowering pharmaceutical profit margins in the U.S., to the average level found in non-U.S. markets, will impact investment in R&D. This being said, however, as Vernon [3] has argued, it is quite likely that pharmaceutical price regulation is the prominent factor responsible for the observed divergence in profit margins across U.S. and non-U.S. markets.

Using the parameter estimates obtained from the random-effects and OLS model specifications in Sections 3 and 4 (i.e., models E.1, E.2, E.4, and E.5), Equation (12) from Section 2 was evaluated at the industry level. This was accomplished by using sample means of the relevant model variable.[ab] These forecasts are summarized in Table 3.

The results in Table 3 suggest that regulating pharmaceutical prices in the U.S. could lead to a decline in R&D intensity of between 23.4 and 32.7% (from 0.107 to between 0.082 and 0.072). Of this total decline in R&D, the cash flow effect accounts for between 44 and 60% of this drop, and the expected profit effect accounts for between 56 and 40%, depending on the model specification employed. This prediction is necessarily speculative for a couple of reasons. First, it implicitly assumes that the new policy will result in U.S. profit margins falling to the level of profit margins in markets outside the U.S. As has already been stated, it is likely that other factors – besides price regulation – may influence pharmaceutical profitability. Therefore, the estimates reported in Table 3 could simply represent a lower bound on the change in R&D that would accompany pharmaceutical price regulation in the U.S. However, given that price regulation is likely to be the prominent factor responsible for the divergence in pharmaceutical profit margins across U.S. and non-U.S. markets, this approximation may be quite reasonable. This would be particularly true if the policy under consideration is the re-importation of pharmaceuticals from non-U.S. markets *at* the prices for which those products are being sold at abroad.

A second reason these estimates are tenuous is because they are based on a significant deviation away from the sample (industry) average. The mean of λ_{it} in the sample was 0.494; the policy simulation assumed this value was driven to unity.

Table 3. Effect of pharmaceutical price regulation in the U.S. on R&D investment (Based Models E.1, E.2, E.4, E.5, and sample means)

	$\overline{\left(\frac{R_{it}}{S_{it}}\right)}$	$\overline{\left(\frac{\pi_{it}}{S_{it}^{P}}\right)}$	$\overline{\left(\frac{C_{it-1}}{S_{it-1}}\right)}$
Before New U.S. policy regulating Prices	0.107	0.303	0.248
1 Year After New U.S. policy regulating prices	00.082 to 0.072	0.105	0.176
Δ (R&D Intensity) From U.S. price controls	−0.025 to −0.035 (−23.4% to−32.7%)	−0.198 (−65.3%)	−0.072 (−29.0%)
Decomposition of decline in R&D intensity by effect:			
Δ (R&D Intensity) From cash flow effect	−0.011 to−0.021 (−10.3% to –19.6%)	—	—
Δ (R&D Intensity) From expected profit effect	−0.014 to −0.014 (−13.1% to –13.1%)	—	—

As a result, average firm profit margins were reduced from 0.303 to 0.105 in the simulations. Perturbations of this magnitude, for predictive purposes, may be inappropriate. There is no way to know if these models will continue to characterize industry conduct and performance under such circumstances.

These findings, while necessarily speculative, do appear to be highly plausible, and in accordance with economic theory. However, identifying the links between price regulation and R&D is of only limited value from a social welfare perspective. For example, to address how the regulation of pharmaceutical prices in the U.S. will impact social welfare, several additional considerations need to be examined. While this is beyond the scope of the current analyses, these considerations will be briefly mentioned.

What would the regulation of U.S. pharmaceutical prices mean for social welfare?

There are two interrelated issues that determine how pharmaceutical price regulation in the U.S. would affect social welfare. The first deals with the production function for pharmaceutical innovation, and the second, which is related to the first, deals with the tradeoff between static and dynamic efficiency. To illustrate the importance of the first issue, Figure 2 considers two simple

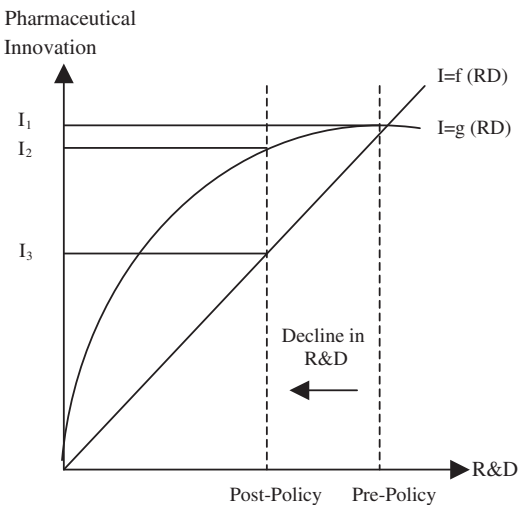

Figure 2. Two hypothetical production functions for pharmaceutical innovation

industry production functions for pharmaceutical innovation.[ac]

The shape of the innovation production function (over the range of R&D investment levels pre- and post-policy change) is critical in determining the consequences for pharmaceutical innovation that would be associated with regulating drug prices in the U.S. If there is a 'low' marginal productivity associated with R&D (at the current, pre-policy level of investment), as illustrated by production function *g*, then the fall in R&D associated with price regulation will have only a 'moderate' effect on innovation.[ad] The vertical distance I_1–I_2 depicts this level of forgone innovation.

If, on the other hand, the marginal productivity of R&D at the current pre-policy level is 'high', then price regulation could impose a very high cost in terms of forgone innovation. This would be the case if production function *f*, which assumes constant returns to R&D, characterized pharmaceutical productivity at the margin. The vertical distance I_1–I_3 depicts this cost.

There are numerous complexities surrounding the productivity of R&D, and how it relates to the demand for innovative pharmaceuticals and investment in R&D itself. However, the objective of the current discussion is only to highlight an important fact: a decline in R&D investment of between 23.4 and 32.7%, as estimated in this paper, is of only limited value in the absence of a fuller understanding of what this would mean for pharmaceutical innovation. While it is probable that that innovation would decline, by how much it would decline is not at all clear.

Given the points just raised, it is now appropriate to consider the welfare implications that would be associated with this policy. To do this it is necessary to consider two types of economic efficiency: static and dynamic.

The primary product of pharmaceutical R&D is new knowledge, and the transfer of new knowledge often occurs at very low costs.[ae] From a static efficiency perspective – ignoring technological change and innovation, and focusing only on the optimal allocation of resources available in the present period – the socially optimal course of action would be to eliminate pharmaceutical patent protection all together. This would allow competitive forces to drive pharmaceutical prices down to (or close to) marginal manufacturing costs.

This eradication of intellectual property rights is not done for obvious reasons: it would eliminate all incentives to innovate. Indeed, the average new pharmaceutical spends 12–14 years in development and costs hundreds of millions of dollars to develop and bring to market [27]. Without the ability to price monopolistically through patent protection, firms would be unable to appropriate the rents from their innovations. Dynamic efficiency, therefore, must also be taken into account when considering the welfare implications of this policy.

While the regulation of pharmaceutical prices in the U.S. would certainly involve some gain in static efficiency, and some loss in dynamic efficiency, it is not clear what the net effect would be. On the one hand, price regulation (or allowing drugs to be re-imported into the U.S. from abroad) would result in prices that are closer to marginal costs. This would improve static efficiency. On the other hand, as has been the focus of this paper, the regulation of pharmaceutical prices in the U.S. will reduce the incentives to innovate (and will restrict the funds used to finance R&D). Therefore, the implications for dynamic efficiency must also be considered. This will depend largely on the innovative productivity of R&D, or, as illustrated in Figure 2, the shape of the industry's R&D production function.

If at the current levels R&D marginal innovative productivity is 'small', then forgone innovation will also be 'small'. If instead the marginal innovative productivity of R&D is 'large', then forgone pharmaceutical innovation will also be 'large'. Clearly then, from a social welfare perspective, the potential loss in dynamic efficiency from such a policy must be weighted against the potential gains in static efficiency. This tradeoff is illustrated in Figure 3.

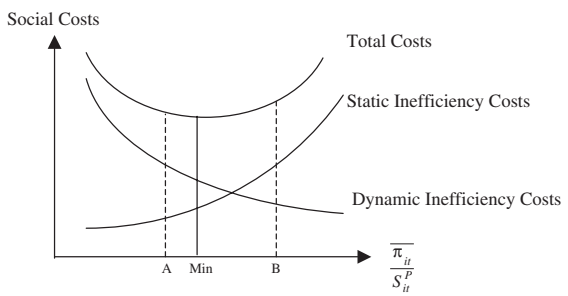

Figure 3. The tradeoff between static and dynamic efficiency under a U.S. policy regulating prescription drug prices

To determine whether a policy regulating pharmaceutical prices U.S. is, on net, good or bad for social welfare, it is necessary to know where along the horizontal axis (which is measured in terms of the industry's average pharmaceutical profit margin) we reside. If the current position is point B, then it is possible price regulation will be welfare enhancing, so long as the effect is not so great as to move industry profit margins below the level associated with minimum total social cost.[af] If instead society is currently at this minimum point, or to the left of it (i.e., point A), then the policy will unambiguously have a negative effect on social welfare.

In sum, it is critical to put the results presented in this paper into proper perspective, both because of the caveats associated with the results themselves and because of the uncertainty surrounding their implications for social welfare. The prediction that pharmaceutical price regulation in the U.S will lead to a decline in industry R&D investment from between 23.4 to 32.7% is insufficient for determining what the net effect of this policy will be on social welfare.

Conclusions

Using established R&D investment models from the literature, this paper has explored the possible links between pharmaceutical price regulation and firm R&D investment intensity. A unique fact has been employed to help identify these links: relative to the rest of the world, in the U.S., pharmaceutical prices are largely unregulated.

Data from fourteen major pharmaceutical firms have been collected for the years 1994 to 1997, and several models of the determinants of R&D investment were estimated. The estimated models have shown, like earlier research on this subject, that expected profits and lagged cash flows are the principal determinants of firm R&D-to-sales ratios.

It has then been argued that pharmaceutical price regulation influences R&D investment through both of these channels, resulting in an expected-profit effect and a cash-flow effect. The former effect influences R&D contemporaneously while the latter effect operates with a 1-year lag.

The empirical results from these models have then been used to simulate the effect of a

hypothetical U.S. policy that regulates pharmaceutical prices. This has been accomplished by assuming that the effect of such a policy would be to lower pre-tax pharmaceutical profit margins in the U.S. to the average level of profit margins observed in non-U.S. markets. My simulation exercises have predicted that the effect of such a policy would be to reduce industry R&D investment intensity by between 23.4 and 32.7%.

These predictions, it has been emphasized, are speculative for a number of reasons. However, they do appear to seem reasonable and in accordance with economic theory. Most importantly, I have underscored that from a social welfare perspective, the model's predictions themselves are of only limited value. An understanding of what this decline in R&D would mean for social welfare would require knowledge about the innovative productivity of the forgone R&D, as well as the precise nature of the static and dynamic efficiency tradeoffs involved.

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Notes

a. For a detailed summary of the different methods of pharmaceutical price regulation around the world, the reader is referred to Danzon's recent work [1,2].
b. Arguments for expecting a divergence in the cost of internal and external finance have been based on transactions costs, tax advantages, asymmetric information, agency costs, and the costs of financial distress. Hubbard [10] provides a review of these arguments.
c. In fact, they formulated and tested two proxies for expected returns: pre-tax pharmaceutical profit margins and an index of R&D productivity (defined as a moving average of new pharmaceutical product sales divided by lagged R&D expenditures).
d. In their earlier studies Grabowski and Vernon [4,5] employed a moving average of a firm's newly launched pharmaceutical sales divided by lagged R&D expenditures, which they found to be significant at normal confidence levels.
e. Vernon [14] has estimated that pre-tax pharmaceutical profit margins in the U.S. are on the magnitude of four to five times higher than those observed, on average, outside the U.S. and there was relatively little variability in the share of a firm's pharmaceutical sales coming from the U.S. market during the 1990s (the decade for which these data were available).
f. A related interpretation would be that truly exceptional drugs become blockbusters (which significantly penetrate the U.S. market), and current margins reflect past success in developing blockbusters; thus, current margins may serve as a reasonable proxy for a firm's expectations about its ability to develop blockbusters in the future, and it R&D productivity more generally. This interpretation is also consistent with Grabowski and Vernon's logic [4,5].
g. Lichtenberg [17] has criticized this approach and, specifically, Scherer's [18] suggestion that current margins are likely to be an important determinant of pharmaceutical R&D investment. Lichtenberg argues that firm market capitalizations, which should reflect the present value of the firm's expected future profits, are a more forward-looking measure of the expected returns to pharmaceutical R&D. This is likely to be true if markets are perfectly functioning and if the firm operates exclusively within the pharmaceutical industry. However, many of the firms in my sample, and indeed many of the firms in the pharmaceutical industry, are diversified across multiple industries and business operations; therefore, their market capitalizations should reflect the present value of expected future profits from all business operations, and not just pharmaceuticals (and pharmaceutical R&D more specifically). However, I did find a positive correlation between current pharmaceutical profit margins and various measures of firm market capitalization, and for firms that operated almost exclusively within the pharmaceutical business, this correlation was quite high ($\rho = 0.76$).
h. Indeed, this is the primary argument put forth by most opponents to the regulation of prescription drug prices in the U.S. The standard argument maintains that the unregulated U.S. pharmaceutical market (with respect to prices) supports industry-wide R&D incentives.
i. Industry-wide controls for changing profit expectations (i.e., year fixed effects) were also included, but these variables are repressed in Equation (4) for simplicity. Indeed, as will be discussed in the next section, several specifications of Equation (4) were estimated and modeled within the system of equations shown in (4)–(7).

j. Following Vernon [14], the superscripts F and R are used. Thus drawing the distinction between the largely price-unregulated U.S. market (i.e., 'free' market) and the price-regulated pharmaceutical markets around the world.
k. This follows Grabowski and Vernon's approach in their most recent study.
l. As will be discussed more fully in a forthcoming section, and as Vernon [14] and Berndt [23] have discussed, there are likely to be several factors that contribute to the divergence in pharmaceutical prices (and profit margins) across U.S. and non-U.S. markets; however, it seems likely that price regulation is a prominent factor. Moreover, in the forthcoming simulation, all that is assumed is that price regulation (or allowing for the re-importation of pharmaceuticals from outside the U.S.) results in U.S. pharmaceutical profit margins being driven down to the average level observed in non-U.S. markets. This seems to be a reasonable assumption.
m. As already discussed, the implicit assumption here is that contemporaneous pharmaceutical profit margins serve as a reasonably good proxy for expected *future* pharmaceutical profit margins, and profitability more generally (refer to footnote g).
n. For example, in May of 2000, the state of Maine passed Bills S1026 and LD2599 into law, thus establishing discounted prices for all Maine residents without prescription drug coverage.
o. The issue of re-importation is not new. In fact, prior bills allowing re-importation were passed into law as early as 2000. However, these laws contain a provision requiring the Secretary of Health and Human Services certify that imported drugs will pose 'no additional risk' to consumers (NY *Times*, 21 July 2003). So far neither the Clinton nor Bush Administrations have been willing endorse such a claim, thus re-importation has remained illegal in the United States. However, the currently debated re-importation bill, HR 335, which was approved by the U.S. House of Representatives on 24 July 2003, contains no such 'poison pill' provision.
p. Clearly, only the profit effect would occur contemporaneously with the policy change. This highlights a significant limitation in the policy simulation exercise presented here: it implicitly assumes that the new policy is enacted without warning, and that firms did not foresee the new policy coming. This is indeed a dubious assumption: a major policy change of the magnitude described here would certainly be seen coming in advance (possibly a year or more in advance). Thus, for example, if current pharmaceutical margins are 'high', this period, but it is anticipated that U.S. pharmaceutical prices will be regulated next year, contemporaneous profit margins will 'overstate' future profit expectations.
q. The constant terms are *not* suppressed in Equation (12). Rather, like the other terms not interacting with λ, they simply drop out through differencing. Also note that, unlike the brackets underneath Equation (10), the brackets beneath Equation (12) are exclusive of the slope coefficients β_1 and β_2.
r. There were a number of mergers taking place in the pharmaceutical industry in the late 1990s. The window from 1994 to 1997 provided the best opportunity for collecting a balanced panel dataset. Furthermore, Scrip altered the type of pharmaceutical profit data it collected in 1994: it switched from collecting after-tax pharmaceutical profits to pre-tax pharmaceutical operating profits.
s. It is important to note that there did not appear to be any systematic reason why some firms reported these data in some years but not in others (or not at all). Some firms reported firm-wide profit margins exclusively. Moreover, when possible, data validity checks were performed on the Scrip data (i.e., by comparing the Scrip data to the same data reported by other sources – this could be done for firms that were not diversified outside of pharmaceuticals because total firm data is then identical to firm pharmaceutical data. These validity checks suggested that the Scrip data were reliable. The Scrip data (those reported at the firm level) were also found to be consistent with other data sources (e.g. total firm sales).
t. As Hsiao [24] states: 'When only a few observations are available for different [firms] over time, it is exceptionally important to make the most efficient use of the data across [firms] to estimate that part of the behavioral relationship containing variables that differ from one [firm] to another.
u. In additional to year fixed effects, an additional control was also employed: the ratio of a firm's pharmaceutical sales to its total sales. This control was used in several of Grabowski and Vernon's earlier studies [4,5] to control for the fact that firms have other, not insignificant research and development activities outside of pharmaceuticals, and firms that are more concentrated in pharmaceuticals will, all else held constant, have higher R&D intensities due to pharmaceuticals being among the most research intensive industries in the world. The use of firm fixed effects overcomes the need for this control variable (this variable was statistically insignificant in the fixed-effects model).
v. Models were also estimated using λ_{it} explicitly as a determinant of R&D intensity. This was done because pharmaceutical price regulation, which often results in significant marketing delays [26], could alter the cash-flow profiles of new products in a manner not captured by a firm's current period pharmaceutical profit margin [13]. These regression

results found λ_{it} and current-period pharmaceutical profit margins to be fairly substitutable.

w. Refer to the point made in footnote t.

x. A fixed-effects specification was more reasonable in the Grabowski and Vernon [6] study because the authors were working with a 21-year time series. Grabowski [3] similarly did not employ firm fixed effects; his sample also contained only 4 years of data (for 10 pharmaceutical firms).

y. An excellent discussion of these issues may be found in Berndt [23].

z. Equation (16) depicts the specific case for firm i in year t. In the forthcoming simulation exercises, however, sample means will be employed to estimate the average industry response to price regulation in the U.S.; in this context, $\bar{M}^R$ is the appropriate limiting value.

aa. In fact, this is precisely what is currently being debated in Washington, D.C. The re-importation bill, H.R. 2427, which was approved by the House of Representatives on July 24, 2003, would allow for the importation of pharmaceuticals from 26 countries. The US Senate has yet to vote on this bill.

ab. Full descriptive statistics are reported in the appendix.

ac. The horizontal axis could be labeled new pharmaceuticals, but because of the considerable heterogeneity in new pharmaceuticals, some of which may not be new at all (i.e., 'me-too' drugs), the more general variable, pharmaceutical innovation, was selected. How to measure pharmaceutical innovation is of course a challenging question, but it is not relevant for the current discussion.

ad. More precisely, the fall in innovation will depend on the average productivity between the pre- and post-levels of R&D. For small changes in R&D it may be sufficient to refer to the marginal productivity at the pre-policy level, but for large changes in R&D the average productivity between pre- and post-policy levels could significantly deviate from the marginal productivity at the pre-policy level.

ae. Regarding this point, Arrow [28] has noted: 'Information is a commodity with peculiar attributes, particularly embarrassing for the achievement of optimal allocation. In the first place, any information obtained, say a new method of production, should, from the welfare point of view, be available free of charge (apart from the cost of transmitting information). This insures optimal utilization of the information but of course provides no incentive for research...In a free enterprise economy, inventive activity is supported by using the invention to create property rights; precisely to the extent that it is successful, there is an underutilization of the information.'

af. Technically speaking, the policy could move industry margins below the minimum point and still be welfare enhancing: so long as margins were not displaced too far below the minimum point, and the sum of static and dynamic efficiency costs still declined relative to their pre-policy level.

Appendix

Decomposing firm pre-tax pharmaceutical profit margins

To illustrate how a firm's pre-tax pharmaceutical profit margin can be decomposed into two components: a U.S. pre-tax profit margin and a non-U.S. pre-tax profit margin (i.e., a 'free' market and a price-regulated market profit margin), I develop a simple model in which a firm produces and sells a portfolio of n pharmaceutical products in two separate markets: market R, which is a price-regulated market, and market F, which is a free market. The firm's marginal cost of production for product i is assumed to be constant and equal to c_i.

Assume that the price of the firm's ith product is p_i^R and p_i^F in markets R and F, respectively. Further assume that $p_i^R < p_i^F$ for all $i = 1$ to n. The quantities sold in each market are q_i^R and q_i^F. Therefore, a firm selling it's product in both markets will have the following profit margin, π/S^P:

$$\frac{\pi}{S^P} = \frac{\sum_{i=1}^{n} p_i^R q_i^R + \sum_{i=1}^{n} p_i^F q_i^F - \sum_{i=1}^{n} c_i (q_i^R + q_i^F)}{\sum_{i=1}^{n} p_i^R q_i^R + \sum_{i=1}^{n} p_i^F q_i^F} \tag{A1}$$

Equation (A1) may be equivalently expressed in the following way:

$$\frac{\pi}{S^P} = \frac{\sum_{i=1}^{n} (p_i^R - c_i) q_i^R + \sum_{i=1}^{n} (p_i^F - c_i) q_i^F}{\sum_{i=1}^{n} p_i^R q_i^R + \sum_{i=1}^{n} p_i^F q_i^F} \tag{A2}$$

The numerator in Equation (A2) can then multiplied through by 1 as follows:

$$\frac{\pi}{S^P} = \frac{\left[\sum_{i=1}^{n} (p_i^R - c_i) q_i^R\right] \left[\frac{\sum_{i=1}^{n} p_i^R q_i^R}{\sum_{i=1}^{n} p_i^R q}\right] + \left[\sum_{i=1}^{n} (p_i^F - c_i) q_i^F\right] \left[\frac{\sum_{i=1}^{n} p_i^F q_i^F}{\sum_{i=1}^{n} p_i^F q_i^F}\right]}{\sum_{i=1}^{n} p_i^R q_i^R + \sum_{i=1}^{n} p_i^F q_i^F} \tag{A3}$$

Re-arranging terms in Equation (A3) yields:

$$\frac{\pi}{S^P} = \left[\frac{\sum_{i=1}^{n}(p_i^R - c_i)q_i^R}{\sum_{i=1}^{n} p_i^R q_i^R}\right]\left[\frac{\sum_{i=1}^{n} p_i^R q_i^R}{\sum_{i=1}^{n} p_i^R q_i^R + \sum_{i=1}^{n} p_i^F q_i^F}\right] + \left[\frac{\sum_{i=1}^{n}(p_i^F - c_i)q_i^F}{\sum_{i=1}^{n} p_i^F q_i^F}\right]\left[\frac{\sum_{i=1}^{n} p_i^F q_i^F}{\sum_{i=1}^{n} p_i^R q_i^R + \sum_{i=1}^{n} p_i^F q_i^F}\right] \quad \text{(A4)}$$

Inspection of the factors and terms in Equation (A4) reveals the presence of the previously defined variables from Equation (5) in the main text of the paper:

$$\lambda = \frac{\sum_{i=1}^{n} p_i^R q_i^R}{\sum_{i=1}^{n} p_i^R q_i^R + \sum_{i=1}^{n} p_i^F q_i^F} \quad \text{(A5)}$$

$$M^R = \frac{\sum_{i=1}^{n}(p_i^R - c_i)q_i^R}{\sum_{i=1}^{n} p_i^R q_i^R} \quad \text{(A6)}$$

$$M^F = \frac{\sum_{i=1}^{n}(p_i^F - c_i)q_i^F}{\sum_{i=1}^{n} p_i^F q_i^F} \quad \text{(A7)}$$

Finally, (A4) may be expressed in more compact terms as follows:

$$\frac{\pi}{S^P} = \lambda M^R + (1-\lambda)M^F \quad \text{(A8)}$$

Equation (A8) is thus identical to Equation (5) from the main text. It is important to emphasize that the derived results are contingent upon the separability of costs. This seems to be reasonable assumption; most pharmaceuticals are sold in both U.S. and non-U.S. markets and are produced in centralized manufacturing locations. They are then shipped to their final market destinations. Costs such as marketing expenses, however, may be greater in the U.S. than elsewhere in the world; this would be the case, for example, if direct-to-consumer advertising spending was proportionately greater in the U.S. relative to the rest of the world. Importantly, however, this would tend to buffer any differences in pre-tax profit margins across U.S. and non-U.S. markets. Finally, the assumption about constant marginal costs does not represent a threat to the model, it just provides for greater algebraic convenience. Thus, the constant marginal, c_i, could be replaced with a measure of the average cost of production. The variables M^R and M^F are, after all, averages

Table A1. Descriptive statistic for model variables

	$\frac{R_{it}}{S_{it}}$	$\frac{CF_{it-1}}{S_{it-1}}$	$\frac{\pi_{it}}{S_{it}^P}$	λ_{it}	$\frac{S_{it}^P}{S_{it}}$
Mean	0.107	0.248	0.303	0.494	0.544
Median	0.093	0.238	0.319	0.466	0.565
Range	0.050–0.263	0.115–0.506	0.050–0.724	0.070–0.894	0.105–1.000
Standard Deviation	0.046	0.090	0.106	0.199	0.282

Table A2. Estimated pharmaceutical profit margins in the U.S. and abroad (white standard errors in parentheses)

Year	α_0	λ_{it}	$\bar{M}^F$	$\bar{M}^R$	Adj. R^2
1994	0.433***	0.305***	0.433	0.128	0.718
	(0.028)	(0.048)			
1995	0.435***	0.321***	0.435	0.114	0.433
	(0.033)	(0.081)			
1996	0.502***	0.374***	0.502	0.128	0.612
	(0.039)	(0.066)			
1997	0.608***	0.558***	0.608	0.05	0.556
	(0.098)	(0.194)			

***Significant at the 0.001-level or better.

themselves. Vernon [14] discusses these assumptions in greater detail.

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