Reducing Drug Prices without Depressing Innovation *

Stephen W. Salant

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Abstract

Prices of patented pharmaceuticals in the United States exceed the prices of the same drugs which foreign governments have negotiated which, in turn, exceed marginal costs of production. This paper provides a tractable theoretical model that explains these stylized facts while taking account of the structure of the industry. The explanation involves arbitrage-deterrence due to oligopolistic limit-pricing: manufacturers would reject proposed foreign prices any closer to the marginal cost of production because the resulting price differentials would trigger massive arbitrage into the higher price U.S. market. The model is used to predict the consequences of policies proposed to reduce domestic drug prices such as (1) international reference pricing to insure that Medicare pays the price negotiated by foreign governments, (2) legalization of commercial arbitrage and (3) creation of an FDA white list of foreign pharmacies where U.S. patients can safely fill prescriptions. It is shown that when each policy is set to achieve the same reduction in the domestic retail price that the loss in manufacturer profits is far greater under international reference pricing than under the other two policies. In calibrated simulations, the profit loss under international reference pricing is at least 5 times as large as under either of the other two policies. All price-reducing policies would depress manufacturer profit per drug and hence future drug innovation. So I conclude by identifying the least expensive complementary policy the government could utilize to maintain the lower domestic price while restoring innovation to its previous level.

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1 Introduction

How to lower the prices of brand-name pharmaceuticals in the United States without deterring innovation of new drugs (CEA 2018) constitutes a major policy dilemma.[1] Before sensible policy can be devised to resolve this dilemma, it is necessary to understand the determinants of drug innovation and of drug pricing in the U.S. and abroad.

Any model of the international pharmaceutical market must explain three stylized facts: (1) Americans pay much more than Europeans and others for the same brand-name drugs, (2) drug prices abroad result from bargaining between drug manufacturers and foreign governments, and (3) even the lower foreign price vastly exceeds the marginal cost of production.

For concreteness, consider the Direct Action Antivirals (DAA) used to treat the hepatitis C virus (HCV). There are four patented drugs, each of which can cure genotypes 1-4. Sovaldi is the oldest and most well-established.[2] Americans pay at least $65,000 to cure their HCV with Sovaldi while Europeans pay $40,000 even though the marginal cost of producing this cure is estimated to be less than $140.[3]

Berndt (2007) and others have sought to use the traditional model of third-degree price discrimination (Robinson, 1933) to explain these facts. While this model does predict that a manufacturer would charge different prices exceeding marginal cost in different markets, it assumes that every price is set by the manufacturer without any negotiation. Moreover, according to experts on parallel trade in pharmaceuticals within the EU, "...many patients in the United States purchase prescription drugs on a self-pay basis or within tiered copayment structures [and]...these patients are more sensitive to drug prices than their European counterparts..." (Kyle et al., 2008). Given the relative elasticities, the traditional model predicts that the European price should exceed the U.S. price.

The popular explanation for the lower foreign price is that in Europe, Canada, and elsewhere, governments use their considerable bargaining power to get lower prices from manufacturers, whereas no comparable bargaining occurs in the United States. As the Council of Economic Advisers noted: "Most OECD nations employ price controls in an attempt to constrain the cost of novel biopharmaceutical products, e.g. through cost-effectiveness or reference pricing policies."

But bargaining alone cannot explain the third stylized fact. For, as the Council of Economic Advisers goes on to say "...in price negotiations with manufacturers, foreign governments with centralized pricing exploit the fact that once a drug is already produced, the firm is always better off selling at a price above the marginal cost of production and making a profit, regardless of how small, than not selling at all. *Thus, the foreign government can insist on a price that covers the marginal production cost—but not the far greater sunk costs from years of research and development—and firms will continue to sell to that country.*" (CEA 2018, 15; emphasis added).[4]

The data strongly conflict with this prediction. The prices negotiated by Canada and the governments in Western Europe are sometimes many hundreds of times larger than the marginal costs of production. For example, no price in Western Europe for a 12-week course of the HCV drug Sovaldi is below $40,000. And yet "a recent study estimated the cost of production of sofosbuvir [Sovaldi] to be U.S. $68-$136 for a 12-week course of treatment based on the same manufacturing methods used in the large-scale generic production of HIV/AIDS medicines (Hill et al., 2014), and its findings have not been challenged" (Iyengar et al. 2016). Nor is Sovaldi unique in this regard. "Predicted manufacturing costs (U.S. dollars) for 12-week courses of HCV DAAs were $21-$63 for riba-virin, $10-$30 for daclatasvir, $68-$136 for sofosbuvir, $100-$210 for faldaprevir, and $130-$270 for simeprevir" (Hill et al. 2014).

The real question is not why prices in Western Europe and Canada are so low but why they are so high! They are low relative to U.S. prices, but they are high relative to the marginal costs of production.

The prediction that foreign governments will bargain prices down to the marginal cost of production

[1] If reducing domestic drug prices does not lower innovation below the socially optimal level, of course, there is no policy dilemma to resolve. For a discussion of why medical innovation may currently exceed the socially optimal level, see Garber et al. (2006).

[2] The other three are Mavyret, Vosevi, and Epclusa.

[3] It is widely acknowledged that the prices of drugs under patent in the United States exceed the prices of those same drugs abroad, although admittedly the *magnitude* of this excess is impossible to quantify given the secret rebates and discounts manufacturers routinely offer their customers.

[4] The academic literature (Grossman and Lai 2008, 386 and Figure 1) also predicts that when re-imports are illegal, governments imposing price controls will bargain down to the marginal cost of production under the plausible assumption that these countries are not too sizable compared with the region that innovates.

implicitly assumes that negotiated prices are "unconnected" to prices in the United States.[5] That prices in the European Union and Canada greatly exceed the marginal cost of production, however, strongly suggests that the markets *are* in some way connected. This is no mere academic quibble. For if the markets are connected, the Trump administration's goal of making foreigners pay their "fair share" for future drug innovation by forcing up the price they currently pay for drugs would, unless safety concerns about importing were simultaneously reduced, have the undesirable consequence of driving up U.S. prices as well.

Logically, negotiated prices exceed marginal costs for one of two reasons: either (1) government negotiators have no desire to bargain so aggressively although manufacturers would accept such demands or (2) government negotiators anticipate that manufacturers would reject demands for prices closer to marginal cost. Egan and Philipson (2013) make the former argument. They contend that foreign governments refrain from bargaining for even lower prices out of fear of depressing future innovation (innovation costs for current drugs being sunk). Given that the discovery of promising molecules and their development into drugs takes more than a decade and is fraught with uncertainty, it seems unlikely that foreign governments would refrain from pressing for lower prices on this account.

A more plausible explanation for why government negotiators do not demand prices closer to marginal cost is that they anticipate drug manufacturers would reject such demands out of fear of arbitrage. Imagine what would happen if Americans seeking medication to cure their hepatitis C continued to be charged tens of thousands of dollars at domestic pharmacies but were reassured that they could safely acquire the same drug from designated Canadian or European online pharmacies for as little as $140 (marginal cost). There would be massive arbitrage, but manufacturers would quickly act to block it. Manufacturers would invest heavily in misinforming buyers that it is unsafe to import from *any* foreign pharmacy, and they would narrow the difference in the prices between the two markets until massive imports ceased. Neither of these tactics could be employed when these manufacturers sought to block pharmaceutical trade within the EU since (1) importing from another EU country is legal and safe and (2) demand within Europe is relatively insensitive to price reductions in the importing country.[6]

In our view, the *threat* of arbitrage is what connects the low-price and high-price markets. As internet shopping expands, the threat that cheaper medicines will be purchased from abroad can only grow in importance. The evidence that manufacturers recognize that massive arbitrage would endanger their profits is the huge sums they spend to prevent it. In the United States, where importing drugs is illegal, manufacturers and the nonprofit "pro-consumer" organizations that manufacturers fund surreptitiously (Kopp and Bluth 2017) lobby Congress to preserve the import ban using the pretext that all pharmaceutical imports from Canada or Western Europe are, without exception, "unsafe." They have also enlisted FDA in this disinformation campaign (Levitt, 2019).

However, a private firm, PharmacyChecker.com, has developed extensive methods to determine which online foreign pharmacies are safe (Honest Apothecary 2013). Using Raman spectroscopy, the same technique that FDA uses to distinguish *bona fide* medicine from counterfeits and adulterated pharmaceutical products (Witkowski, 2005), Bate et al. (NBER, 2013) conclude that drugs purchased from foreign pharmacies certified safe by PharmacyChecker.com are just as safe as drugs purchased from domestic, brick-and-mortar pharmacies. Since the accurate information PharmacyChecker.com provides threatens manufacturer profits, it is now classified by Big Pharma as among those firms that "put your family at risk."[7]

[5]It also assumes that foreign governments have complete information and propose prices on a take-it-or-leave-it basis, and information is assumed to be complete.

[6]Since parallel trade within the European Union is legal, these same companies, at considerable cost, have had to devise other strategies to limit the damage massive parallel trade would do to their profits. These include strategic use of marketing authorizations, patents, trademarks, vertical restraints, launch timing, and refusals to supply.

[7]Firm profit, not consumer safety, motivates these lobbying expenditures. As Kesselheim and Choudhry (2008) emphasize, "Concerns about the integrity of imported brand-name and generic drugs from these markets [Canada and Europe] are often exaggerated, and U.S. regulators should be able to readily ensure the safety of imported products." According to Outterson (2005), "The most thorough recent analysis . . . concludes that Canadian drug supply is actually safer on balance than that of the United States. . . . The EU has many years of experience with parallel trade in pharmaceuticals, without significant safety issues." Outterson (2005) points out that the behavior of manufacturers itself reflects a disregard for consumer safety."By cutting off direct supplies to exporting pharmacies, the pharmaceutical companies force additional intermediaries into the supply chain, which increases safety and handling problems, increases inefficiencies and increases the opportunity for spoilage and introduction of counterfeits. If the concern is truly patient safety, supply restrictions are a crude and counterproductive tool."

Importing drugs sold initially in Canada or Western Europe is illegal but, if the price difference exceeds some threshold, I assume that massive arbitrage would occur anyway. This threshold is assumed to decrease as the accuracy of information about the safety of foreign pharmacies increases exogenously. If the threshold is sufficiently high, the markets are unconnected and the foreign retail price equals the marginal cost of production while the retail price in the United States equals the oligopoly price, $p^{Cournot}$. At the other extreme of a threshold of zero, arbitrage is legal and the markets are perfectly connected. These are the two extremes on which Grossman and Lai (2008) focus in their valuable article on parallel trade. In our view, however, there is a neglected intermediate case of importance where reselling drugs is illegal but nonetheless the markets are connected. Banning pharmaceutical imports does not eliminate importation; it merely makes engaging in it more costly. Massive arbitrage would still occur if the price difference were sufficiently great. Our formulation permits consideration not only of the extremes but also of the *intermediate* case where the threat of arbitrage leads manufacturers to reject prices in Canada and Western Europe any closer to the marginal cost of production.

In the equilibrium of the connected case, manufacturers set the price differential just small enough to deter massive arbitrage. Hence, in the equilibrium of the "connected case" the only arbitrage that occurs is from inframarginal agents with unusually low thresholds; such agents—typically poor, desperate, and uninsured—would continue to buy from foreign pharmacies even if their prices were closer to the U.S. price.

In our model, policies that benefit U.S. consumers do not do so by stimulating more arbitrage. The benefits arise instead because these policies motivate profit-maximizing manufacturers to lower domestic prices to *deter* arbitrage.[8]

It is important to distinguish two kinds of arbitrage that can be triggered if price differences between markets are sufficiently large: (1) personal arbitrage by patients seeking the least expensive cure for their illness and (2) commercial arbitrage by firms which buy and then re-sell whatever quantity of cures maximizes their profits. While both forms of arbitrage are illegal, personal arbitrage for own use has never been prosecuted. On the other hand, the law against commercial arbitrage is strictly enforced.

That may change. Bills have been proposed to legalize both kinds of arbitrage. In January 2019, the"Affordable and Safe Prescription Drug Importation Act" (H.R. 447 and S.97) was introduced in both the House and the Senate. Virtually every Senator running for president is a co-sponsor of the Senate bill. The bill instructs the Secretary of Health and Human Services within a half year to issue regulations allowing wholesalers, licensed U.S. pharmacies, and individuals to import qualifying prescription drug manufactured at FDA-inspected facilities from licensed Canadian sellers and, after two years, grants the Secretary authority to permit importation from OECD countries that meet specified or regulatory standards that are comparable to U.S. standards.[9]

Since the threat of personal arbitrage is what currently determines manufacturer pricing, we focus on that form of arbitrage. However, since there is a slim possibility that one of the pending bills will become law, we also discuss the consequences of relaxing the prohibition on commercial arbitrage.

The following interventions to lower the prices that U.S. consumers pay are examined: (1) reducing concerns about the safety of importing brand-name pharmaceuticals from licensed pharmacies in the

[8]The CBO (2004) concluded that policies to reduce the exogenous threshold, such as legalizing arbitrage or reducing misleading safety warnings, would confer little benefit on U.S. consumers. In reaching this conclusion, CBO disregarded potential reductions in domestic drug prices and confined its estimate of benefits to increases in imports from the European Union and Canada. Under this approach, CBO would have disregarded the policy-induced price changes in our model and, since these are accompanied by no changes in pharmaceutical imports, would have erroneously concluded that no policy change affects consumers.

CBO based its forecast of how changes pharmaceutical import policies affect consumers in the U.S. on the experience of consumers in the European Union after the introduction of parallel trade in pharmaceuticals. But authorities on parallel trade in the EU explicitly warn against such reasoning, regarding it as based on a false analogy. Although Kyle et al. "found little evidence that parallel trade affected price dispersion of prescription drugs over a 12-year period," they emphasize that in many countries in their sample, regulations leave pharmacies and patients with no incentive to purchase cheaper offerings of the same product. Hence, manufacturers would have no incentive to reduce the price in the higher-priced market. Kanavos and Costa-Font (2005) explained their statistical findings in the same way. Kyle et al., therefore, emphasize that their conclusions *should not be applied* to the U.S. market in exercises like the one CBO conducted: "Important differences between the European Union and U.S. markets regarding the regulation of parallel trade and other aspects of pharmaceutical markets make it difficult to predict how parallel trade would fare in the United States. Kyle et al. conclude: "parallel trade may have less effect in the European Union than it would in higher-price markets like the United States, where pharmacists, insurers, and patients have greater incentive to switch to less expensive prescription drugs" (Kyle et al., 2008).

[9]The threat of imports from OECD countries is vastly more important quantitatively because of its greater population size.

European Union and Canada; (2) legalizing commercial arbitrage; (3) promoting entry into drug manufacturing; and (4) allowing Medicare to negotiate or, equivalently, to pay the price negotiated by foreign governments (international reference pricing).

Typically, a policy anticipated to lower prices in the U.S. market will depress innovation and the expected number of future drugs that will be produced. If the policy reduces drug innovation, a second government policy can be used to restore it.

Most drug innovation results from research conducted in universities and independent laboratories rather than inside big pharmaceutical companies. According to Shepherd (2018), "Approximately three-fourths of new drugs are externally sourced. Internal R&D is no longer the primary source, or even an important source, of drug innovation in large pharmaceutical companies." The role of the large pharmaceutical companies is to acquire promising molecules that academics have discovered and taken over preliminary FDA hurdles, to surmount the remaining FDA hurdles, and to bring the drugs to market. Manufacturers anticipating lower profit per drug because of government intervention would pay academic researchers less for the promising molecules they discover and, expecting lower reward for their discoveries, those researchers with the lowest probabilities of finding a promising molecule would cease to search for one.[10] As a result, there would be less innovation.

To restore innovation to its previous level, thus "sterilizing" the effect of the price-reducing policy on innovation, a second policy instrument is required.[11] Two candidates are considered. The government can replace the money the drug companies cease paying academics who succeed in finding promising molecules, so that the academic who was just indifferent between searching for a molecule and abandoning the search continues to be indifferent. Or the government can pay *everyone* who commits to search for a molecule *prior* to the outcome of their research gambles just enough that the marginal academic remains indifferent. Both of these sterilization strategies would restore innovation, but one always turns out to be less expensive for the government. It is always cheaper for the government to pay everyone *before* discoveries are made, even though vastly more people must be compensated, than to reward only those researchers who succeed in their research gambles. This counterintuitive property is referred to as the "paradox of sterilization."

We proceed as follows. In Section 2, we introduce our model and use it to analyze the effects of policies to lower domestic retail prices when manufacturers seek to deter personal arbitrage at the retail level. At the end of the section we simulate the model to illustrate that when each policy is set to achieve the same reduction in the U.S. retail price, FDA reassurance that importing from specific foreign pharmacies is safe reduces manufacturer profit less than international reference pricing. In Section 3, we turn to the effects of these policies on manufacturer profit and innovation. We explain the paradox of sterilization and provide intuition for this counterintuitive property. Section 4 concludes the paper.

2 Arbitrage

Personal arbitrage typically occurs when a patient with a valid U.S. prescription orders online from a foreign pharmacy. Many foreign pharmacies receiving a prescription from an American patient routinely fill the order with the version of that drug approved in their own country. In countries where pharmacists are required to receive a prescription from a *local* doctor, the current practice is for the local doctor to review the U.S. prescription and the patient history and write a new prescription ("co-signing") for the foreign version of the medication. Although importing prescription drugs into the U.S. for own use is technically illegal, no one has ever been prosecuted for this "crime," which is victimless. Some have travelled to a foreign country such as Canada or a member of the EU, filled their prescriptions, and

[10] It is important to note, however, that those least likely to succeed are the ones who abandon the search. The lower their success probabilities relative to the academics who continue to search, the less their departure will depress innovation.

[11] Price-reducing policies which would depress future innovation would harm future generations of consumers. A model developed by researchers at RAND (Lakdawalla et al. 2009) focuses on this intergenerational trade-off using historical data and a hazard function approach. Their model describes the transition to the long-run, steady-state equilibrium if price-reducing policies are allowed to depress subsequent innovation. In contrast, our model is conceptual. It abstracts from the transitory effects which are the focus of the Rand model and shows how the government can ensure that future innovation does *not* fall when price-reducing policies are imposed. Hence, the two approaches nicely complement each other.

returned home.[12] Enforcement then seems even more problematic since a patient can always disguise the drug purchased abroad by putting it in empty bottles (either from old prescriptions or over-the-counter medications). Even if the authorities were capable of stopping personal arbitrage, it seems unwise politically to separate a grandmother from the only medication she can afford to treat her cancer.

We hypothesize that if patients with valid prescriptions could save enough money by purchasing from a foreign pharmacy instead of from an American pharmacy, there would be *massive* personal arbitrage. We denote the threshold difference in retail prices as Δ.

Let p^U denote the price the manufacturers set in the U.S. and p^N denote the price they set for the same medication abroad. Let $\tau \geq 1$ denote the exogenous combined markup of wholesalers and retailers at home and abroad, so that the *retail* prices are, respectively, τp^U and τp^N. We assume that massive personal arbitrage will occur if $\tau(p^U - p^N) > \Delta$ and none (apart from inframarginal imports) if $\tau(p^U - p^N) \leq \Delta$. The U.S. government can lower Δ exogenously by scaling down misleading FDA warnings about the safety of medications routinely dispensed by licensed pharmacies in other developed countries; legalizing personal arbitrage would have similar effects since it would reassure U.S. consumers about the safety of prescriptions filled at such pharmacies.

Let $\tau_w \leq \tau$ denote the markup foreign wholesalers apply when selling to pharmacies the drug obtained from the manufacturers at price p^N. Commercial arbitrage occurs if the per-unit profit from this activity, $p^U - \tau_w p^N$, is sufficiently large. The second term is the cost foreign wholesalers would require to sell the drug to a commercial arbitrageur instead of a foreign pharmacy; the first term is the price the commercial arbitrageur can obtain if the U.S. wholesaler buys a unit from the arbitrageur instead of from a manufacturer. Denote by Δ^c the exogenous threshold beyond which massive commercial arbitrage occurs. Then no commercial arbitrage occurs if:

$$p^U - \tau_w p^N \leq \Delta^c. \tag{2.1}$$

where Δ^c denotes the exogenous threshold above which massive commercial arbitrage would occur. Since commercial arbitrage is illegal and the ban is strictly enforced, Δ^c is assumed to be very large; but that would change if the pending bills become law.

We consider $n \geq 1$ manufacturers producing patented perfect substitutes (such as the four Direct Action Antivirals to cure hepatitis C) at zero marginal cost and selling them at a market-determined price in the U.S. and at a negotiated price-ceiling in the European Union (E.U.) and Canada. These assumptions are very similar to those in the arbitrage-deterrence model sketched briefly by Ganslandt and Maskus (2004) as background for their main model. There are two key differences: (1) the price cap in their model is exogenous and (2) they limit attention to a monopolist manufacturer ($n = 1$).[13] G-M do not conduct comparative-statics in their preliminary model. But since our goal is to assess the effects of alternative policies on the equilibrium, endogenizing the negotiated price cap is crucial. We allow there to be more than one manufacturer so that our model can be applied to markets where several manufacturers offer patented drugs that are therapeutically equivalent (like the market for Direct Action Antivirals to cure hepatitis C). The cap is set in the following game between the n manufacturers and the negotiator. The equilibrium would be unchanged if the manufacturers instead responded simultaneously to the negotiator's proposed price cap instead of sequentially.[14]

2.1 Description of the Game

We envision the following game. A single negotiator specifies a discounted price p^N per cure at which to purchase medication for each of the (exogenous) Q^N HCV sufferers he represents.[15] The negotiator proposes this price sequentially to each of the n drug manufacturers. If a manufacturer is unwilling to

[12] In a signed letter to the *New York Times* (Hanauer, 2019), a rheumatologist observed that "A patient could fly first class to Paris, stay at the Ritz, dine at a top Michelin restaurant, buy a one-year supply of Humira [a rheumatoid arthritis drug] at local prices in France, fly back home and finish with enough profit to hire a registered nurse to administer the injection every two weeks."

[13] They also omit the "unconnected case" where, even if the domestic price were set at the monopoly level, no arbitrage would occur because the combined cost of acquiring and transporting drugs is too high to make arbitrage profitable.

[14] See footnote 16.

[15] Given the observations of Kyle et al. (2008) and others that regulations make patient demand in the European Union much less elastic than in the US, we assume that Q^N is completely insensitive to price.

pay the price demanded by the negotiator, the negotiator buys nothing from that manufacturer. Each manufacturer publicly announces whether he has accepted or rejected the negotiator's proposal. Those rejecting the proposal then produce and sell only in the unnegotiated (U.S.) market. Those accepting it not only sell in the domestic market but also share equally the Q^N additional sales at price p^N per cure in foreign markets.

Given the extremely low marginal costs of production for HCV cures (Hill et al. 2014) reported in Section 1, we assume (as do Ganslandt and Maskus) that producing additional units is costless. We assume that the drugs in this therapeutic class are perfect substitutes and therefore sell at the same price. For example, the new cures for HCV are very close substitutes.[16] Throughout, we make assumptions on the domestic retail demand function ($D(p)$): (1) $D(0)$ is finite, (2) $pD(p)$ is concave, (3) $\Delta < argmax_{p \geq 0} pD(p)$, and (4) there is a unique Cournot equilibrium in the game where the n manaufacturers sell simultaneously and the retail price is τ times the price they receive.

Manufacturers benefit if they accept the negotiator's proposal since each manufacturer sells more of a drug that is costless to produce. On the other hand, with Q^N more drugs in circulation, there is also a threat that supplies sold abroad would flow into the United States if the retail price differential between the two regions exceeds the exogenous threshold Δ dollars per cure. The threat of arbitrage ensures that the retail price in the U.S. market will not exceed the retail price in the rest of the world by more than Δ. The consequences of any manufacturer accepting the negotiator's proposal is thus a retail price for every cure sold in the U.S. market of at most Δ more than the retail price abroad.

The negotiator approaches each manufacturer in sequence and proposes to pay p^N per cure for $\frac{Q^N}{l}$ cures, where $l = 1, \ldots, n$ is the number of manufacturers that accept. Each manufacturer accepts or rejects the proposal, and the negotiator moves on to the next manufacturer. To determine the subgame-perfect equilibrium, we first determine the payoffs in the various subgames that can arise.

If no manufacturer accepts the negotiator's proposal, then each of the n manufacturers simultaneously decides how much to produce and sell in the U.S. market. In the equilibrium of this subgame, every manufacturer acts like a symmetric Cournot oligopolist selling a perfect substitute. Manufacturers receive the Cournot retail profits generated minus the distribution chain markups.

If instead one or more manufacturers *accept* the negotiator's proposal but it is so high that $\tau p^N + \Delta \geq p^{Cournot}$, then the retail price in the U.S. market remains $p^{Cournot}$. In these subgames, manufacturers rejecting the proposal would earn Cournot profits minus markups while the l firms accepting it would each earn an additional $p^N Q^N / l$.

If, however, one or more manufacturers accept the negotiator's proposal and $\tau p^N + \Delta < p^{Cournot}$, then every manufacturer would realize that imported drugs would flood the U.S. market if the domestic manufacturer price strictly exceeded $p^N + \Delta/\tau$. In these subgames, *limit-pricing* occurs. Each manufacturer sells more than its Cournot output ($D(\tau p^N + \Delta)/n > D(p^{Cournot})/n$). No manufacturer would unilaterally sell less than this, since doing so would lower its sales without raising the price per cure ($p^N + \Delta/\tau$). Nor would any manufacturer unilaterally sell more since, with every firm producing an output exceeding the Cournot level, the (right) marginal revenue is strictly negative. Hence, in the equilibrium of subgames that follow acceptance of any proposed p^N, the retail price in the U.S. market would be $\tau p^N + \Delta$, but no importing would occur.

2.2 Equilibrium

We now consider how each manufacturer in the sequence would respond to any proposed p^N if the sales behavior described above was anticipated. Each manufacturer in the sequence will find itself in one of three situations: (1) some previous manufacturer has accepted the negotiator's proposal; (2) no previous manufacturer has accepted the proposal, but it is nonetheless still in the interest of the last manufacturer to accept the negotiator's proposal; or (3) no previous manufacturer has accepted the proposal, and it is also in the interest of the last manufacturer to *reject* the proposal.

[16] According to Newsweek (Wapner 2017), "A curative drug [for hepatitis C] was approved a few years ago but was incredibly expensive. When a second curative treatment [for hepatitis C] emerged, Express Scripts told the first manufacturer that it would not put its drug on Express Scripts formulary unless the company lowered the price to that of the second drug." See also footnote X, where the three perfect substitutes of Sovaldi are listed.

Table 1: Payoffs to Manufacturer i

Manufacturer i accepts	$\frac{p^N Q^N}{l} + \frac{(\tau p^N + \Delta)}{\tau n} D(\tau p^N + \Delta)$
Manufacturer i rejects but other(s) accept	$0 + \frac{(\tau p^N + \Delta)}{\tau n} D(\tau p^N + \Delta)$
Every manufacturer rejects	$\frac{\Pi^{Cournot}}{\tau n}$

In situations (1) and (2), the manufacturer anticipates that no matter what it does, the retail price in the unnegotiated market will be $\tau p^N + \Delta$. Since in either situation accepting the proposal results in additional sales at no cost, the manufacturer will always accept the proposal.

In situation (3), the manufacturer always rejects the negotiator's proposal. For, the manufacturer anticipates that if it is rational for the last manufacturer to reject the proposal, then it must also be rational for every prior manufacturer to reject that proposal since, unlike the last manufacturer, prior manufacturers would have to divide up the Q^N additional sales among themselves and hence the negotiator's offer is less valuable to them. Thus, in situation (3), each manufacturer is pivotal: if the manufacturer accepts the proposal, this induces everyone subsequent to this manufacturer to accept it also.

Note that each manufacturer in the sequence is a copycat: it makes the same decision as the one it anticipates the last firm will make. Anticipating this response, the negotiator will choose the lowest price that the final manufacturer in the sequence will accept.[17]

We will denote the equilibrium value of a variable using bold face. Thus, the equilibrium foreign manufacturer's price is $\mathbf{p}^N$. This price is defined as the smallest solution to the following equation, assuming it is nonnegative.[18]

$$p^N Q^N + \frac{(\tau p^N + \Delta) D(\tau p^N + \Delta)}{\tau n} = \frac{\pi^{Cournot}(n)}{\tau n}.\ ^{19} \tag{2.2}$$

Figure (2.1) describes the determination of the negotiated price. The price the manufacturers charge U.S. wholesalers is on the vertical axis and the price they charge foreign wholesalers is on the horizontal axis. The U.S. retail price never exceeds what n manufacturers would charge as Cournot oligopolists but will be lower if that price would induce massive personal arbitrage. The pair of manufacturer prices that would just deter personal arbitrage is depicted as the line sloping up at a 45 degree angle with vertical intercept Δ/τ. There is no incentive for personal arbitrage if manufacturer prices are on or below this line.

[17] In the simultaneous-move version of this game, the lowest price the negotiator can demand without all n manufacturers rejecting his proposal is defined implicitly by equation (2.2). If everyone rejects the proposed price, each manufacturer receives the payoff on the right-hand side of this equation; if one player unilaterally accepts the proposal, he receives the profit on the left-hand side.

[18] The smallest solution will be negative if $\Delta > p^{Cournot}$. In this "corner" case, $\mathbf{p}^N = 0$, and the U.S. retail price will be $p^{Cournot}$. Since the price differential between the two regions is strictly smaller than Δ, no one will be tempted to import. Each manufacturer in this case earns $R(n)/n = \pi^{Cournot}(n)/\tau n$.

[19] As long as the arbitrage from abroad would be sufficiently massive, every manufacturer would have an incentive to deter it. In particular no manufacturer would unilaterally deviate from arbitrage-deterrence as long as $p\left(D(\tau p) - \frac{n-1}{n} D(\tau \mathbf{p}^N + \Delta) - Q^N\right) \leq \frac{(\tau \mathbf{p}^N + \Delta) D(\tau \mathbf{p}^N + \Delta)}{\tau n}$ for all $p > \mathbf{p}^N + \Delta/\tau$. The right-hand side is the payoff a manufacturer gets in the U.S. market if arbitrage is deterred and the left-hand side is the payoff from a unilateral deviation. This inequality is clearly satisfied if $Q^N \geq D(\tau \mathbf{p}^N + \Delta)$ since the left -hand side would then be negative. But Q^N does not need to be so massive to satisfy it. In the case of the HCV drugs, the inequality is clearly satisfied since the European and Canadian markets combined exceed 25% of the U.S. market.

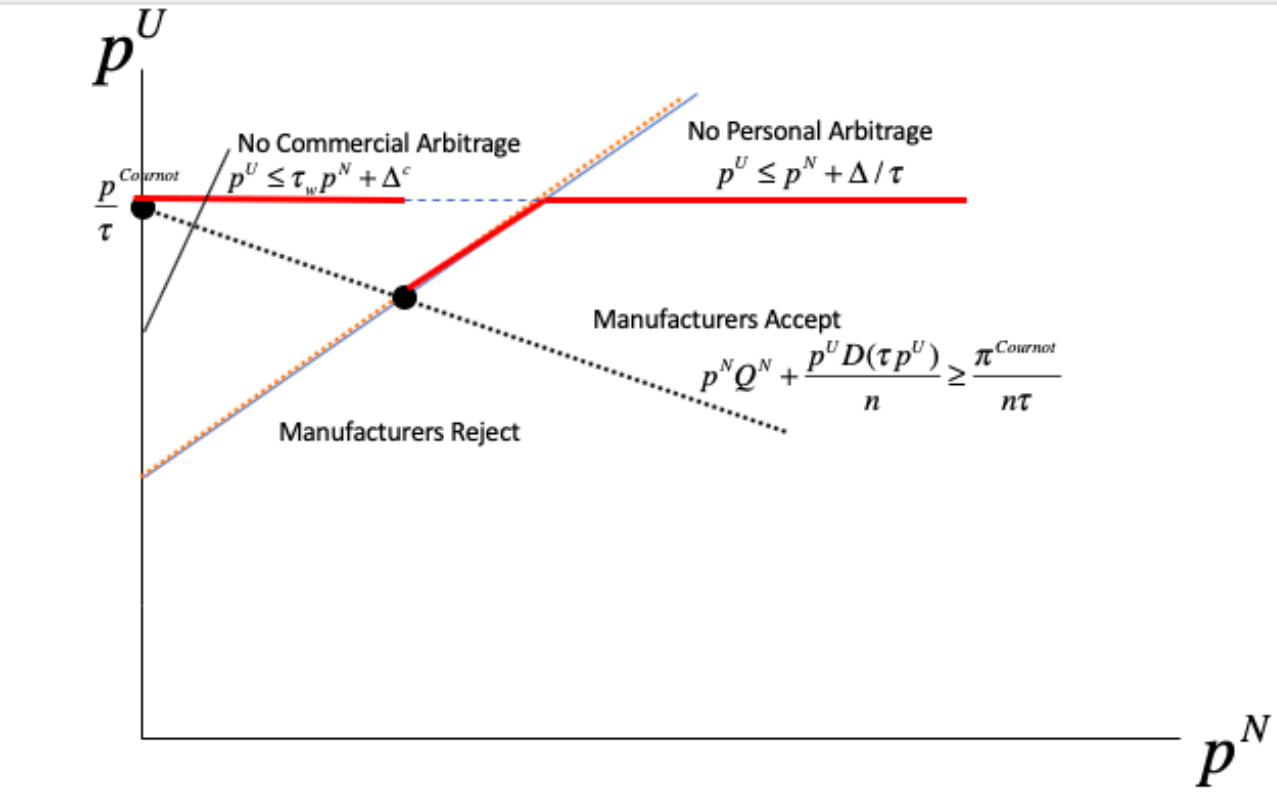


Figure 2.1: Determination of the Negotiated Price

The proposed foreign price p^N that would just be acceptable to manufacturers if they charged domestic wholesalers p^U lies on the downward-sloping locus. Any foreign price proposed by the negotiator to the left of this locus would be rejected. If the markets are connected, the equilibrium negotiated price is the *smallest* p^N that (1) deters massive arbitrage[20] but (2) is acceptable to the manufacturers. This occurs where the downward-sloping line intersects the upward-sloping line. For future use, we have also inserted a second upward-sloping line below which no *commercial* arbitrage would occur.

As we will see when we turn to comparative statics, policies that shift the downward-sloping locus against an unchanged upward-sloping locus will result in the U.S. price and negotiated foreign price changing in the same direction. Policies that shift the upward-sloping locus against an unchanged downward-sloping locus will result in the two prices changing in opposite directions.

If the markets are connected, every manufacturer will accept proposal $\mathbf{p}^N$, each firm will receive $1/n^{th}$ of the additional Q^N sales. The n manufacturers sell Q^N units in the negotiated market and $D(\tau\mathbf{p}^N + \Delta)$ in the unnegotiated market.

Denote the revenue received by each of the n manufacturers as $R(n)$. Each manufacturer earns revenue

$$R(n) = \frac{\mathbf{p}^N Q^N}{n} + \frac{(\tau\mathbf{p}^N + \Delta)D(\tau\mathbf{p}^N + \Delta)}{\tau n}. \tag{2.3}$$

$$= \frac{\pi^{Cournot}(n)}{\tau n} - \frac{n-1}{n}\mathbf{p}^N Q^N, \tag{2.4}$$

where the last line is obtained by substituting into (2.3) the solution to (2.2). Equation (2.4) implies that in equilibrium each firm earns smaller profits when the n firms sell in both markets than it would if the n firms sold only in the domestic market. This counterintuitive property is common in games.[21]

It is helpful to rearrange equation (2.2) as follows:

$$(\tau p^N + \Delta)D(\tau p^N + \Delta) = \pi^{Cournot}(n) - \tau n p^N Q^N. \tag{2.5}$$

The right-hand side is a decreasing linear function of p^N with vertical intercept $\pi^{\text{Cournot}}(n)$ and slope $-\tau n Q^N < 0$. The left-hand side is a strictly concave function with vertical intercept $\Delta D(\Delta) \geq 0$. Given our assumptions about the function $D(\cdot)$, domestic total retail revenue $(\tau p^N + \Delta)D(\tau p^N + \Delta)$ is strictly increasing at $p^N = 0$.

Since Cournot profit is strictly smaller than monopoly profit (for $n = 2, \ldots$), the vertical intercept of the line is strictly smaller than the peak of the concave profit function. There are two possible cases. In the first case ($\Delta \leq p^{Cournot}$), the domestic and foreign markets are connected and $\mathbf{p}^U = \mathbf{p}^N + \Delta/\tau$; in the second case ($\Delta > p^{Cournot}$), the two markets are unconnected and $\mathbf{p}^U = p^{Cournot}/\tau$. The first case (respectively, the second case) arises if the vertical intercept of the single-peaked function lies below (resp. above) the vertical intercept of the downward-sloping line. In the two cases,

$$\mathbf{p}^U = \min\left(\mathbf{p}^N + \Delta/\tau, p^{Cournot}\Big/\tau\right).$$

In the connected case, the horizontal component of the point of intersection is the manufacturer's foreign price ($\mathbf{p}^N$), and the vertical component is the total retail revenue in the domestic market. In the unconnected case, the negotiated manufacturer's price abroad equals the marginal production cost (assumed, for simplicity, to be zero), and the retail price in the U.S. market is the Cournot price. We depict the determination of $\mathbf{p}^N$ in Figure (2.2):

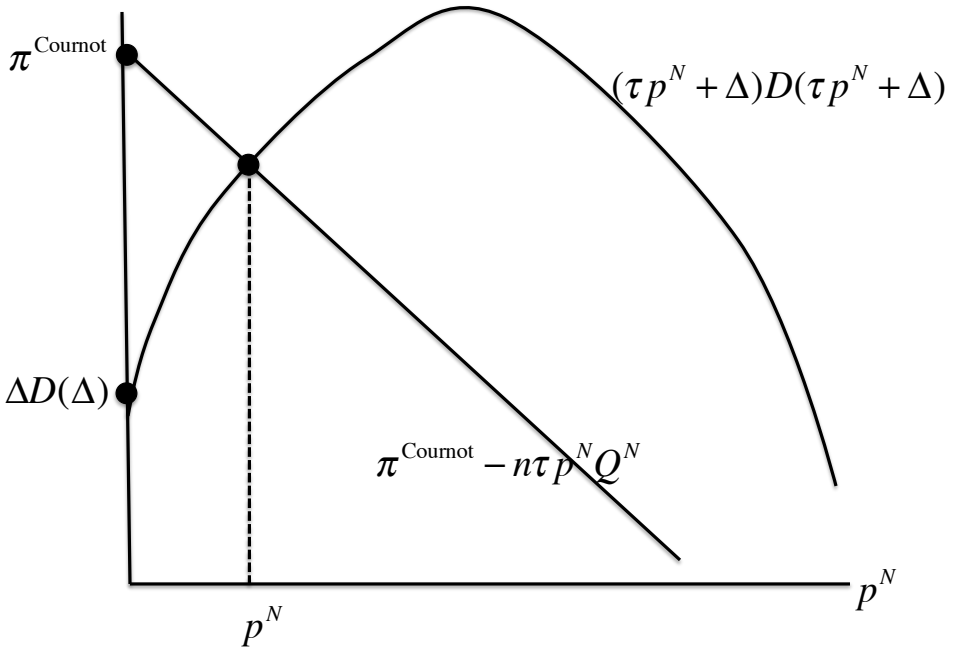
2.3 Comparative Statics

We now consider four government policies that would reduce the domestic price of prescription drugs: (1) ceasing to discourage imports from online pharmacies certified safe by PharmacyChecker.com ($\Delta \downarrow$); (2) legalizing commercial arbitrage ($\Delta^c \downarrow$); (3) increasing competition among manufacturers ($n \uparrow$); and

[20] We are focusing here on personal arbitrage because Δ^c is assumed to be large. In general the relevant upward-sloping line is $p^U = \min(p^N + \Delta, \tau_w p^N + \Delta^c, p^{Cournot}/\tau)$.

[21] For example, in the prisoner's dilemma full cooperation is preferred by each player to the equilibrium outcome and in a Cournot game, an equal share of the monopoly profit is preferred by each firm to the oligopoly equilibrium.

Figure 2.2: Determination of the Negotiated Price



(4) allowing Medicare to pay the price negotiated by foreign governments ($Q^N \uparrow, D(p) \downarrow$). We also show how these policies would affect the price negotiated by foreign governments and the profit of each manufacturer. Under each of these policies, manufacturer profit falls when the domestic retail price falls. As a result, innovation would fall unless a second policy instrument is used to offset the effect. We defer discussion of this second instrument until Section 4.

In analyzing the effects of a change in each exogenous parameter, we first consider the case where the two markets are connected and then the case where they are unconnected. Results for both cases are summarized in Table 2.

2.3.1 Reducing Δ

If the FDA reassured U.S. patients that they could safely import drugs online from foreign pharmacies certified by PharmacyChecker.com, Δ would be reduced. An exogenous reduction in Δ will raise the foreign negotiated price. For if that negotiated price did not increase, manufacturers would earn strictly more by selling exclusively in the domestic market and would reject the negotiator's proposed price (see equation (2.2)). To acquire any drugs, therefore, the negotiator would have to propose a higher price ($\mathbf{p}^N$). Since an exogenous reduction in Δ leads to an increase in $\mathbf{p}^N$, what can be said about $\tau\mathbf{p}^N + \Delta$, the domestic retail price. This sum must fall. Otherwise, the left-hand side of (2.2) would strictly exceed the right-hand side, and the negotiator could secure a lower price.

In terms of Figure (2.2), an exogenous decrease in Δ will shift the single-peaked function down in the neighborhood of the equilibrium. To see this, note that at a fixed $\Delta, (p^N + \Delta)D(p^N + \Delta)$ is strictly increasing in p^N where it intersects the downward-sloping line, and hence at a fixed p^N, this function must be strictly increasing in Δ. But if Δ decreases, it will shift the curve downward to the left of its peak (and upward to the right of its peak), and consequently the intersection with the unchanged downward-

sloping line will occur at a higher $\mathbf{p}^N$. Equation (2.4) implies that, since a reduction in Δ will cause $\mathbf{p}^N$ to rise, it must cause $\mathbf{R}$ to fall. Each manufacturer loses more revenue in the domestic market than it gains in the foreign market. For a reduction in revenue in the domestic market to occur, $\mathbf{p}^U$ must fall and so must the domestic retail price ($\tau\mathbf{p}^U$).

If Δ is initially so large that the two markets are unconnected ($\Delta > p^{Cournot}$) and there is no incentive for commercial arbitrage, then a reduction in Δ within this region will affect neither the two prices nor any manufacturer's profit.

2.3.2 Reducing Δ^c

Arbitrage (whether personal or commercial) occurs if $p^U > \min(p^N + \Delta/\tau, \tau_w p^N + \Delta^c)$. We have been assuming that the intersection of the personal arbitrage line and the downward-sloping manufacturer acceptance line occurs at a point below the commercial arbitrage constraint in Figure 2.1. If commercial arbitrage becomes legal, however, the commercial arbitrage constraint may shift downward and intersect the downward-sloping line at a point *below* the personal arbitrage constraint. In that case, personal arbitrage would be strictly unprofitable and the manufacturers would price so that massive commercial arbitrage would just be deterred. In that case, the negotiated foreign manufacturer price would rise and the U.S. manufacturer price would fall. Equation (2.4) still holds in the case of commercial arbitrage and it implies that, since a reduction in Δ^c will cause $\mathbf{p}^N$ to rise, it must cause $\mathbf{R}$ to fall.[22]

If Δ^c is initially so large that the two markets are unconnected ($\Delta^c > p^{Cournot}/\tau$) and there is no incentive for personal arbitrage, then a reduction in Δ^c within this region will affect neither the two prices nor any manufacturer's profit.

For the markets to be unconnected, there must be no incentive for either commercial or personal arbitrage. This occurs if and only if $\min(\Delta^c, \Delta/\tau) \geq p^{Cournot}/\tau$.

2.3.3 Increasing the Number of Manufacturers

An exogenous increase in the number (n) of manufacturers will cause the negotiated price ($\mathbf{p}^N$) to fall. For if the negotiated price did not decrease, the manufacturers would strictly prefer to sell in both markets rather than to sell exclusively in the U.S. market (see equation (2.2)), and the negotiator would secure a lower price. For the difference in manufacturers' prices to remain unchanged (Δ/τ), the domestic price ($\mathbf{p}^U$) must fall by the same amount as the negotiated price. Each manufacturer's profit would also fall, since total revenue in each market falls (equation 2.3) and must be divided among a larger number of manufacturers.

Graphically, an increase in n does not affect the domestic industry revenue curve in Figure (2.2) but shifts the intercept of the line down since, in a symmetric Cournot equilibrium, industry profits decline as the number of competitors increases. The increase in the number of manufacturers also causes the line to steepen. As a result, the intersection point has a smaller horizontal and a smaller vertical component. The horizontal component is the negotiated price. Since it falls, manufacturers collectively earn less in the foreign market. The vertical component is the aggregate revenue collected from domestic consumers. Since it falls, manufacturers collectively earn less in the domestic market. Since these reduced aggregate revenues are divided among more firms, the revenue per firm $\mathbf{R}$ also falls.

If Δ is so large that the two markets are unconnected ($\Delta > p^{Cournot}$), an exogenous increase in the number of manufacturers will leave the negotiated price at the marginal cost of production and will reduce the domestic price because there would be more Cournot competitors. In the foreign market, profits would continue to be zero while in the domestic market, the reduced industry revenue divided among a larger number of manufacturers would result in lower revenue per manufacturer ($\mathbf{R}$).

[22] To verify that equation (2.4) still holds, note that the manufacturer's revenue per firm in the U.S. market is now $\frac{\tau(\tau_w p^N + \Delta^c) D(\tau(\tau_w p^N + \Delta^c))}{\tau n}$. This term replaces the second term on the left of equation (2.2) and the second term on the right of equation (2.3). Substituting into the revised (2.3) the revised (2.2) one obtains equation (2.4) as before.

Table 2: Comparative Statics

	p^N	p^U	R
Q^N	− (NC)	− (−)	− (−)
n	− (NC)	− (−)	− (−)
Δ	− (NC)	+ (NC)	+ (NC)
Δ^c	− (NC)	+ (NC)	+ (NC)

2.3.4 International Reference Pricing

If Medicare either negotiates with drug manufacturers or pays an international reference price for medications instead of the unnegotiated domestic price, $D(p)$ decreases at every price and Q^N increases.

To capture this, assume that each of these functions depends on the shift parameter α with partial derivative $D_2(p;\alpha) > 0$ and derivative $Q^{'N}(\alpha) < 0$. An exogenous *reduction* in α reflects Medicare shifting marginally from paying the U.S. price to paying the negotiated price. Assume that (1) $D_{12}(p;\alpha) \geq 0$ and (2) $D_{11} \leq 0$. These assumptions are sufficient to show that the Cournot price and profit are increasing in α. [23]

Define $l(p^N;\alpha)$ as the distance in Figure 2.2 between the height of the downward-sloping line at a given p^N and the height of the upward-sloping curve at that p^N :

$$l(p^N;\alpha) = p^{Cournot}(\alpha)D\left(p^{Cournot}(\alpha);\alpha\right) - n\tau p^N Q^N(\alpha) - (\tau p^N + \Delta)D\left(\tau p^N + \Delta;\alpha\right) = 0. \tag{2.6}$$

Then, $\frac{dp^N}{d\alpha} = -\frac{l_2(p^N;\alpha)}{l_1(p^N;\alpha)}$. As Figure 2.2 reflects, $l_1(p^N;\alpha) < 0$. Partially differentiating Equation (2.6) with respect to α, we conclude:

$$\begin{aligned} l_2(p^N;\alpha) &= p^{'Cournot}(\alpha)\left(D(p^{Cournot}(\alpha);\alpha) + p^{Cournot}(\alpha)D_1(p^{Cournot}(\alpha);\alpha)\right) && (2.7)\\ &+ D_2\left(p^{Cournot}(\alpha);\alpha\right)\left(p^{Cournot}(\alpha) - (\tau p^N + \Delta)\frac{D_2(\tau p^N + \Delta;\alpha)}{D_2\left(p^{Cournot}(\alpha);\alpha\right)}\right) && (2.8)\\ &- n\tau p^N Q^{'N}(\alpha) > 0. && (2.9) \end{aligned}$$

The partial derivative is strictly positive because each of its three terms are positive. The first term (2.7) is the product of two factors. The Cournot price is increasing in α as established in the footnote below. The second factor is positive since the Cournot price is smaller than the revenue maximizing monopoly price. The second term (2.8) is again the product of two factors. The first is strictly positive because we defined α as a parameter which shifts the demand curve rightward. The second factor is strictly positive since it

[23] Define the Cournot first-order condition as $f(p^{Cournot};\alpha) = p^{Cournot} + \frac{D(p^{Cournot};\alpha)}{nD_1(p^{Cournot};\alpha)} = 0$. Then, $\frac{dp^{Cournot}}{d\alpha} = -\frac{f_2(p^{Cournot};\alpha)}{f_1(p^{Cournot};\alpha)}$. Differentiating partially and using our assumptions on $D(p;\alpha)$, it is straightforward to show that $f_1(p^{Cournot};\alpha) > 0$ and $f_2(p^{Cournot};\alpha) < 0$. Hence $p^{'Cournot}(\alpha) > 0$. Moreover, Cournot profit is also strictly increasing in α. Differentiating $\pi(\alpha) = p^{Cournot}(\alpha)D\left(p^{Cournot}(\alpha);\alpha\right)$ we conclude that $\frac{d\pi(p;\alpha)}{d\alpha} > 0$. Intuitively an increase in α with the price fixed, raises profit because the quantity demanded increases. An increase in price with α fixed will then increase profit since the Cournot price is below the revenue maximizing monopoly price.

is the difference between the Cournot price and the smaller U.S. retail price multiplied by a fraction no larger than 1 (since $D_{12} \geq 0$).

It follows that in the connected region p^N is increasing in α. Hence, when the policy is implemented and α decreases exogenously, p^N decreases. Since p^U and p^N differ by a constant, p^U must decrease at the same rate.

In the connected region, the decrease in α lowers revenue from sales in the U.S. Although the foreign manufacturers price (p^N) falls, volume (Q^N) rises due to increased Medicare demand so revenue from sales at the negotiated price may rise or fall. If $p^N Q^N$ falls, then manufacturer revenue falls in each market and hence overall revenue falls. If revenue in the foreign market rises, then the first term in Equation (2.4) falls and the second one rises, establishing that overall manufacturer revenue falls. In this latter case, the decrease in revenue in the U.S. market more than offsets the increase in revenue in the foreign market so that overall revenue falls.

If the two markets are unconnected, an exogenous increase in the number paying the negotiated price and an equal decrease in the number paying the market-determined price will leave the negotiated price unchanged (at the marginal cost, assumed to be zero) and will depress the market-determined price (since the Cournot price falls when the demand curve shifts inward). The revenue of each manufacturer will decline: foreigners who previously paid the negotiated price continue to pay zero; those who pay the domestic retail price, which has declined, pay less; and the people who switch from paying a positive amount to paying zero also pay less. Hence, revenue per firm (**R**) declines.

We summarize these comparative-statics results in Table 2.

2.4 How Policies Lowering U.S. Drug Prices by the Same Amount Would Affect Manufacturer Profits: A Simulated Comparison

While every policy which lowers retail drug prices in the U.S. reduces overall manufacturer profits and hence the development of new drugs in the future, some policies reduce profits less than others. We now consider three policies adjusted to lower the U.S price (p^U) by the same amount and determine which of them reduces manufacturer profits (R) and hence innovation the least.

The three policies are (1) mandating that Medicare either negotiate like foreign governments or pay an international reference price, (2) legalizing commercial arbitrage, and (3) requiring that FDA create a "white list" of foreign pharmacies safe for personal arbitrage. As Figure 2.1 illustrates, if policies (2) and (3) are set to achieve the same U.S. price ($\mathbf{p}^U$), they will induce the same negotiated price ($\mathbf{p}^N$). This follows since the equilibrium occurs where the lower envelope of the two upward-sloping arbitrage lines, one of which shifts down depending on the policy, intersects the unshifted downward-sloping manufacturer-acceptance line at the given U.S. price ($\mathbf{p}^U$). Since both policies result in the same U.S. price, both result in the same foreign price ($\mathbf{p}^N$). Moreover, since revenue per manufacturer is the same function of the foreign price under the two policies (as established in footnote 21), both reduce manufacturer revenue (**R**) by the same amount.

By design, all three policies are set to reduce the U.S. price by the same amount. Under policies (2) and (3), massive arbitrage would occur if manufacturers did not *raise* the foreign negotiated price ($\mathbf{p}^N$) to deter arbitrage. In contrast, the policy that increases the bargaining power of the negotiator (policy (1)) forces manufacturers to *lower* the foreign price ($\mathbf{p}^N$). One might anticipate that the policy which *lowers* the foreign price will reduce manufacturer revenue more than the two policies which raise that price.

To test this intuition we run a simulation calibrated to the market in HCV cures. We assume that retail demand in the U.S. is a linear function of the retail price ($D(p) = a - mp$) and that the exogenous parameters take on the following values:[24]

- $W = 7$ million
- $Q^N = 5$ million
- $a = 2$ million

[24]The first three numbers are based on the WHO Global Hepatitis Report, 2017, Table 2 (p. 14) Web Annex C. The number of manufacturers selling perfect substitutes reflects the 4 drugs that target genotypes 1-4 of HCV. The assumed markup is based on Sood et al (2017). The slope parameter has been set to generate retail prices roughly consistent with observation.

- $n = 4$
- $\tau = 1.85$
- $m = .5$
- $\Delta = \$10$ thousand

Because U.S. demand is assumed linear, Equation (2.2) simplifies to a quadratic in the variable p^N :

$$\tau n p^N Q^N + (\tau p^N + \Delta)(a - m[\tau p^N + \Delta]) = \frac{na^2}{m(n+1)^2} \tag{2.10}$$

$\mathbf{p}^N$ is the smaller of the quadratic's two roots, provided that root is nonnegative; in that case, the markets are connected. If the smaller root is negative, the markets are unconnected and $\mathbf{p}^N = 0$.

In the simulated equilibrium, the U.S. retail price is \$67.38 thousand. To reduce it by 10% by mandating that Medicare negotiate like foreign governments or pay the international reference price lowers profit per manufacturer by 12.83%. To reduce the retail price by 10% by identifying foreign pharmacies safe for engaging in personal arbitrage (reducing Δ) lowers profit per manufacturer by only 2.3%. The same 2.3% decrease could be achieved by legalizing commercial arbitrage or penalizing it less (lowering Δ^c to achieve the 10% cut in the retail price). If m is changed, these numbers change slightly but it remains true that the percentage reduction in profit per manufacturer is more than 5 times as large under international reference pricing as under either of the other two policies.

This is a general result. When Δ is reduced enough that the retail price decreases by a given amount (e.g. 10%), the domestic manufacturer price falls but the foreign manufacturer price rises. So while manufacturers lose revenue from sales in the U.S. market, these losses are partially offset by increased revenue in the foreign market.

On the other hand, when Medicare stops paying the U.S. price and starts paying the foreign price on enough transactions to lower the U.S. retail price by the same amount (e.g. 10%), *both* the U.S. and the foreign manufacturer's price fall. So revenue from foreign sales decreases. And while the revenue from U.S. sales would decrease by as much as under the other policy if no one switched (since the U.S. price is reduced by the same amount), revenue from U.S. sales in fact decreases *more* because some Medicare transactions occur at the foreign price, not the U.S. price.

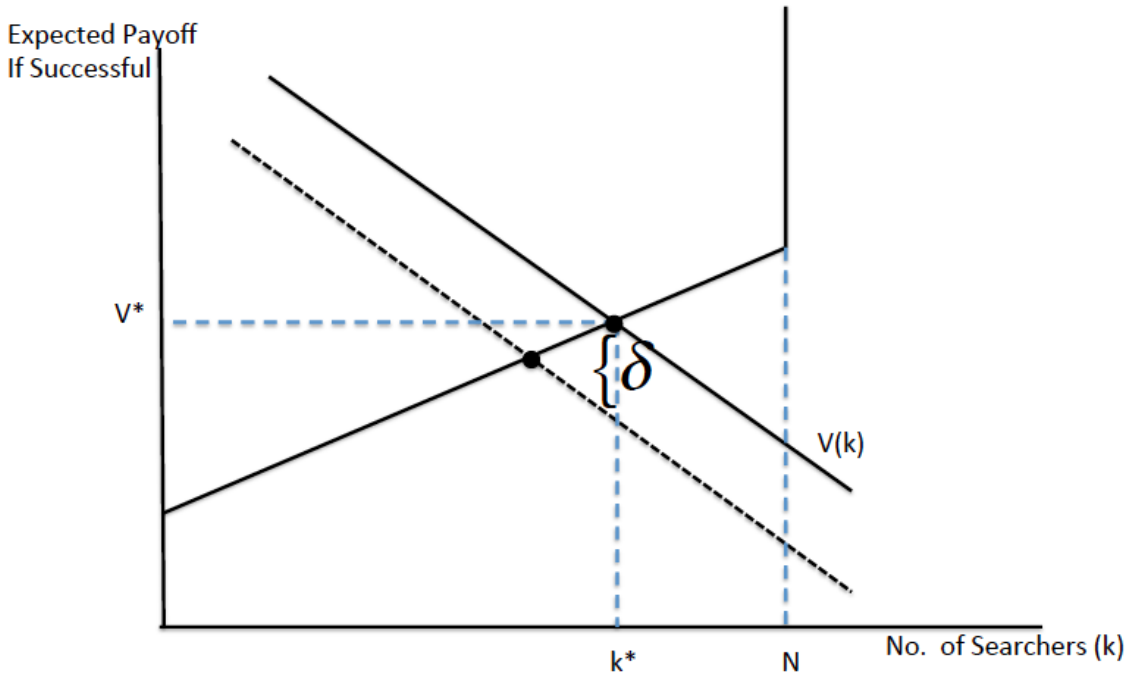
3 The Adverse Impact on Innovation of Price-Reducing Policies

As Table 2 reflects, policies which lower U.S. drug prices reduce manufacturer profits. No manufacturer would respond by withdrawing his drug from the market, however, since producing it has negligible cost. But in the long run, such reductions in profit will lead to less research and fewer new drugs on the market. We clarify why this would happen below and then compare the cost of two ways of preventing this reduction in research and new drugs.

Most discoveries of promising molecules are made by academic researchers, not by drug companies (Shepherd, 2018). When a drug company anticipates that acquiring a promising molecule and developing it into a new drug will generate smaller revenue, the company will pay an academic less to acquire it. Anticipating a smaller reward, some academics who would otherwise have committed to search for a promising molecule will choose not to hunt for one.

Assume there are N risk-neutral academics with distinct, strictly positive probabilities of finding a promising molecule if they search for one. Let $p_i > 0$ denote the success probability of academic i, where $p_1 > p_2 \ldots > p_N$. We assume that these academics do not differ in other respects. That is, they have the same expected cost of searching for a molecule (denoted C) and the same expected gain if successful (denoted V). Since C includes the cost of setting up a lab and re-directing one's professional activities, we assume that C is sunk when the academic initiates his molecule search. An academic will search if and only if $p_i V - C \geq 0$. No one would search if the expected prize was so small ($V < C/p_1$) that it is unattractive even to the academic with the highest success probability; similarly all N academics would

Figure 3.1: Effect of Reduction in Expected Payoff if Successful Reduces the Number of Academics Searching for a Molecule



search if the expected prize was so large ($V \geq C/p_N$) that it is attractive to even the academic with the lowest success probability.

Let k denote the number of academics who commit to searching for a promising molecule. Since k depends on V, we write $k(V)$. Note that $k(V)$ is a step-function.

For $V \in (C/p_1, C/p_N)$ some academics (those with success probabilities weakly higher than C/V) will search for a promising molecule while those with lower success probabilities will not. If V is reduced enough to alter the number of academics who commit to molecule hunting, those with the lowest probability of success choose another line of work. Hence, $k(V)$ is increasing.

We continue to assume that every FDA-approved drug in this therapeutic class is produced by a different manufacturer. For a fixed number of academic searchers (k), the number of promising molecules they discover is random and so is the fraction of them that become marketable drugs. Hence, for a fixed k, the reward that manufacturers offer successful academic searchers is random. The expected value (V) of this reward distribution, however, is deterministic. Since academics are assumed to be risk-neutral, only the expected value of the reward distribution affects their behavior. Given our comparative-statics result, V is a decreasing function of k and Q^N and an increasing function of Δ and Δ^c : $V = V(\overset{-}{k}; \overset{-}{Q^N}, \overset{+}{\Delta}, \overset{+}{\Delta^c})$. If the policy triple (Q^N, Δ, Δ^c) is fixed, an increase in the number of searchers (k) will result in more manufacturers competing on the market, lower profits per manufacturer and a lower expected payment for a promising molecule.

On the horizontal axis of Figure 3.1, we plot the number of academics who search for a promising molecule. On the vertical axis, we plot the expected reward (V) for the discovery of a promising molecule. The upward-sloping curve depicts the number of academic searchers (k) as a function of the payoff (V) they expect to receive if they are successful. Although $k(V)$ is a step-function, we represent it as smooth. The downward-sloping curve is $V(k; Q^N, \Delta, \Delta^c)$.[25]

Denote the intersection of the two curves as (k^*, V^*). This intersection point corresponds to the unique equilibrium: exactly k^* academics voluntarily search for molecules because they expect to receive V^*

[25]Our results would not change if the were horizontal or even upward-sloping, provided it crosses the supply curve from above.

dollars if successful, and manufacturers voluntarily pay each successful academic V^* dollars because of the revenue they anticipate receiving in the product market when k^* academics search for molecules.

Reducing the domestic price by having the FDA identify pharmacies safe for personal arbitrage, by legalizing commercial importation, or by instituting international reference pricing shifts down $V(k; Q^N, \Delta, \Delta^c)$. If the function shifts down, the expected prize (V) would fall. In the short run, the number of researchers committed to hunting for molecules would not change. But in the long run, anticipating that manufacturers would pay less for a promising molecule, searchers with the lowest success probabilities would choose pursuits expected to be more remunerative.

3.1 When to Sterilize to Offset the Adverse Impacts

Suppose that in response to reduced revenue in the drug market, each manufacturer reduces its payment for promising molecules by δ. In the short run, the number of manufacturers selling existing drugs and the number of academics searching for new ones will not change since their costs are sunk. But in the long run the number of academics searching for molecules would drop to k^{**} in Figure 3.1; and fewer promising molecules would be discovered and developed into marketable drugs.

To prevent this, the government could restore the payment to V^* by paying δ to everyone who finds a promising molecule. In that case, k^* academics would again search for promising molecules.

Alternatively, the government could pay each individual committed to searching for a promising molecule $p_{k^*}\delta$ before the outcome of his research gamble is realized. Each committed researcher would then earn $p_i(V - \delta) + p_{k^*}\delta$. Since this equals C for $p_i = p_{k^*}$ and exceeds C for $i < k^*$, the same set of researchers would commit to searching. Which of these policies to restore innovation is cheaper?

The aggregate cost of rewarding only those researchers who discover a promising molecule is a random variable with expected value $(p_1 + p_2 + \ldots + p_{k^*})\delta$. The aggregate cost of rewarding every committed researcher before knowing the outcome of his research gamble costs is certain: $k^* p_{k^*}\delta$

$$k^* p_{k^*}\delta < (p_1 + p_2 + \ldots + p_{k^*})\delta. \tag{3.1}$$

The inequality follows because there are k^* terms in the parentheses on the right-hand side, none smaller and at least one strictly larger than p_{k^*}.

The marginal researcher is indifferent whether the government pays him $p_{k^*}\delta$ before the realization of his research gamble or δ if he is successful. But *every* other researcher strictly prefers to receive δ if successful. In fact, since $p_{k^*}\delta - p_i\delta < 0$ for $i = 1, \ldots k^* - 1$, the higher the success probability of inframarginal researcher i, the more he loses if the government sterilizes before, rather than after, the realization of the research gambles. Sterilizing before the realizations of the research gambles redistributes inframarginal rents from researchers to the government, with those with the highest success probabilities paying the most.

4 Conclusion

In this paper, we identified three stylized facts about the international market in patented pharmaceuticals that seem undeniable. We then showed that no model in the literature explains these facts and constructed a new model consistent with them. Central to our explanation is the effect on manufacturer pricing of the threat of massive personal arbitrage; we can think of no other reason why foreign governments would have refrained from demanding that manufacturers set their price ceilings much closer to the marginal cost of production.

We use our model to predict the effects of several policies: (1) implementing international reference pricing for Medicare patients, (2) legalizing commercial arbitrage (or reducing the penalties imposed if it remains illegal), and (3) requiring the FDA to identify foreign pharmacies from which U.S. patients can order safely. We show using calibrated simulations that the loss in manufacturer profits under international reference pricing is more than 5 times as large as under either of the other two policies. The larger the loss in manufacturer profits, the fewer academics will search for promising molecules and the fewer new drugs will reach the market in the future.

If future pharmaceutical innovation is to be maintained while a policy is implemented to reduce domestic drug prices, a second policy instrument is required. One possibility is for the government to reward research success by exactly as much as manufacturers reduce their rewards when the product market becomes less profitable. We show, however, that a cheaper way to restore innovation is to reward each researcher looking for a molecule *before* the realization of his research gamble. The latter policy is cheaper even though the payment must be made to a larger group of people. It is cheaper because the percentage reduction in the subsidy paid is always larger than the percentage increase in the number of people receiving it. Subsidizing *ex ante* has notable redistributive effects. The marginal researcher is indifferent whether he is subsidized the smaller amount before the outcome of his research is known or the larger amount if and only if he is successful. But the higher the success probability of a researcher, the more he loses if the government subsidizes *ex ante*.

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