Reducing Drug Prices without Depressing Innovation *

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Abstract

Prices of biopharmaceuticals in the United States exceed the prices of the same drugs negotiated by foreign governments which, in turn, exceed their marginal costs of production. We construct a tractable theoretical model that accounts for these stylized facts while taking account of the structure of the industry. We consider two cases: personal arbitrage by patients at the retail level and commercial arbitrage by firms at the wholesale level. We use our model to predict the consequences of four policies proposed to reduce domestic drug prices: (1) facilitating drug imports from the European Union and Canada; (2) requiring that Medicare pay the same prices for drugs as foreign governments; (3) financing the services of downstream players (wholesalers, insurance companies, pharmacy benefit managers, and pharmacies) from developer profits instead of from markups over developer prices, and (4) lowering entry barriers in the downstream channel. All but the last of these price-reducing policies would eventually depress drug innovation. Finally, we identify the least expensive complementary policy the government can utilize to maintain the lower domestic price while restoring innovation to its previous level.

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1 Introduction

How to lower biopharmaceutical prices 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 two puzzling stylized facts: (1) Americans pay much more than Europeans and others for the same drugs, and (2) even the European price vastly exceeds the marginal cost of production.[2] For concreteness, consider drugs to treat the hepatitis C virus (HCV). Americans pay at least $65,000 (Sovaldi lists for $84,000) for the same HCV cure that Europeans buy for $40,000 even though the marginal cost of producing this cure is estimated to be less than $140.[3]

The standard explanation for the first stylized fact 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 second 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 US $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 (US dollars) for 12-week courses of HCV DAAs [direct-acting antivirals] 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 are so low but why they are so high. They are perhaps low relative to US prices (Sovaldi lists for $84,000 in the United States), but they are high relative to their marginal costs of production.

The prediction that foreign governments will bargain prices down to the marginal cost of production 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, convinces us that the markets *are* in some way connected. This is no mere academic quibble. For if the markets are

[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]Berndt (2007) and others regard the price in the two markets as a consequence of traditional third-degree price discrimination (Robinson, 1933). While this model does predict that the price in Western Europe should exceed the marginal cost of production, it also predicts that it should exceed the US price. The traditional model predicts that prices should be higher in Europe because, as Kyle et al. (2008) and Kanavos and Costa-Font (2005) emphasize, demand in Western Europe is more inelastic than US demand. The traditional model is inapplicable since it assumes that developers are free to set prices in foreign markets and that foreign governments play no role in price-setting.

[3]We accept here as a stylized fact the widespread view that the prices of drugs in the United States exceed the prices of those same drugs abroad. However, it must be recognized that the *magnitude* of this excess is impossible to quantify, since the rebates and discounts manufacturers routinely offer their customers in the United States and abroad are shrouded in secrecy. If American buyers receive large rebates, net prices received by manufacturers might not be so much higher in the United States than they are abroad.

[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.

[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.

connected, any attempt to make foreigners pay their "fair share" for future drug innovation by forcing up the price they currently pay for drugs will have the unwanted consequence of driving up US prices as well.

Logically, negotiated prices exceed marginal costs for one of two reasons: either (1) manufacturers would reject demands for prices closer to marginal cost or (2) manufacturers would accept such demands but negotiators have no desire to bargain so aggressively. Egan and Philipson (2013) make the latter 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, we are skeptical that foreign governments desire no lower prices on this account.

We think 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 $84,000 at domestic pharmacies but could acquire the same drug from Canadian or European online pharmacies reliably certified as safe for as little as $140 (marginal cost). To prevent the massive arbitrage that would ensue, developers limit how low they are willing to set the foreign price in negotiations with foreign governments.

While current price differentials are insufficient to induce massive imports from Canada, the more daring among us have long had their prescriptions filled in Canada. In response, drug company representatives gave some Canadian drugstores an ultimatum: pay a price closer to the US price or receive no new drugs. According to the New York Times (Simon 2003), one drug industry executive in the US threatened the Canadian pharmacies exporting their product: "From now on, if the Canadians don't give us a price close to our United States price, I'm not selling it there." In a letter to Canadian pharmacies, Pfizer forbade the export of its products: "This includes not selling, transferring or distributing products to any person that you know, or have reasonable grounds for believing, will or may export Pfizer products out of Canada. Any breach of the terms of this letter will result in Pfizer refusing all further sales to you." Foreign governments stop just short of triggering massive arbitrage when bargaining prices down, recognizing that manufacturers would resist any further concessions.[6]

In our view, the *threat* of arbitrage is what connects the low- 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 developers fund surreptitiously (Kopp and Bluth 2017) lobby Congress to preserve the import ban using the pretext that imports from Canada or Western Europe are "unsafe." However, a private firm, PharmacyChecker.com, has developed extensive methods to determine which online foreign pharmacies are safe (Honest Apothecary 2013). Sampling from pharmacies certified safe by PharmacyChecker.com has demonstrated convincingly (Bate et al. 2013) that drugs purchased from these certified online foreign pharmacies are as safe as drugs purchased in domestic, brick-and-mortar pharmacies.[7] 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.[8]

[6]As Danzon and Furukawa (2008) emphasize, manufacturers sometimes withhold the latest medications from foreign governments which reject as exorbitant the price that they propose. Like the rest of the theoretical literature, we abstract from lags in the introduction of new drugs.

[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 US 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."

[8]Pharmaceutical companies have employed a variety of strategies to prevent international arbitrage inside the European Union. These include strategic use of marketing authorizations, patents, trademarks, vertical restraints, launch timing, and refusals to supply.

In our model, we recognize that importing drugs sold initially in Canada or Western Europe is illegal but assume that if the price difference exceeds some threshold, massive arbitrage would occur anyway. We treat this threshold as exogenous. If the threshold is sufficiently high, the markets are unconnected and the negotiated foreign price equals the marginal cost of production while the expected price in the United States is 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 was sufficiently great.[9] Our formulation permits consideration not only of the extremes but also of the *intermediate* case where the threat of arbitrage induces 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 at just small enough to deter massive arbitrage. Hence, in the equilibrium of the "connected case" the only arbitrage that occurs is from a small set of inframarginal agents with unusually low thresholds. In our model, policies that benefit US 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 *avoid* arbitrage.[10]

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. Ganslandt and Maskus (2004) explicitly exclude personal arbitrage from their analysis and consider only commercial arbitrage. In this paper, we first consider personal arbitrage at the retail level by patients and then consider commercial arbitrage at the wholesale level by firms. 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. According to an April 2017 poll by the Kaiser Family Foundation, 72% of respondents favored allowing Americans to buy prescription drugs imported from Canada. 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: Sanders, Booker, Gillibrand, Harris, Klobuchar, and Warren. The bill instructs the Secretary of Health and Human Services within a half year to issue regulations allowing wholesalers, licensed US 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

[9] In reality, limited arbitrage occurs, since some inframarginal agents have lower thresholds.

[10] The CBO (2004) concludes that policies to reduce the exogenous threshold, such as legalizing arbitrage or reducing misleading safety warnings, will confer little benefit on US consumers. In reaching this conclusion, CBO disregards potential reductions in domestic drug prices and confines its estimate of benefits to increases in the quantity arbitraged from the European Union and Canada. CBO bases its estimates on the experience of the European Union after the introduction of parallel trade in pharmaceuticals. Under this approach, CBO would erroneously conclude that *none* of the policies we consider in our model would confer *any* benefit on domestic consumers.

The CBO's presumption that there would be no price declines in the high price market conflicts with the assumptions in Ganslandt and Maskus (2004) and in Kyle et al. (2008). In their pioneering study, Ganslandt and Maskus (2004) found that the high Swedish price declined between 12% and 19% after the legalization of pharmaceutical trade within the European Union. Although Kyle et al., using data from a broader set of countries, "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 US market in exercises like the one CBO conducted: "Important differences between the European Union and US 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. Unlike national health insurance programs in European countries, many patients in the United States purchase prescription drugs on a self-pay basis or within tiered copayment structures. Because these patients are more sensitive to drug prices than their European counterparts, parallel trade may have greater opportunity to impact prices 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).

regulatory standards that are comparable to US standards.[11]

We consider the effects of various interventions to lower the prices that US consumers pay: (1) reducing concerns about the safety of importing biopharmaceuticals from licensed pharmacies or wholesalers in the European Union and Canada; (2) allowing Medicare to pay the price negotiated by foreign governments (reference pricing); (3) financing the services of downstream players out of the domestic revenue of developers instead of from markups over the developer prices; and (4) reducing the markup over the developers' price by increasing competition in the channel. Our model is so tractable that we deduce the effects of most policies graphically.

Typically, a policy anticipated to lower prices in the US 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 biopharmaceutical research is conducted in universities and independent laboratories rather than inside big pharmaceutical companies. According to Shepherd (forthcoming), "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 from the academics, surmount the remaining FDA hurdles, and bring the drugs to market. Manufacturers anticipating lower profits 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.[12] 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.[13] The government has a choice: it 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. We refer to this counterintuitive property 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 developers seek to deter personal arbitrage at the retail level. In section 3, we analyze the effects of the same policies when developers seek to deter commercial arbitrage at the wholesale level. In Section 4, we turn to the effects of these policies would have on developer profit and innovation. We explain the paradox of sterilization and provide intuition for this counterintuitive property. Section 5 concludes the paper.

2 Personal Arbitrage

Personal arbitrage typically occurs when a patient with a valid US 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 US prescription and the patient history and write a new prescription ("co-signing") for the

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

[12]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.

[13]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. The RAND team's approach relies on hazard functions and exploits historical data. Our model abstracts from these transitory, intergenerational effects and focuses on the long-run, steady-state consequences that price-reducing policies would have. The RAND model is heavily empirical and focuses on the transition to the long-run, steady-state equilibrium if price-reducing policies are allowed to depress subsequent innovation. Our model abstracts from these transitory effects and shows how the government can ensure at least cost that future innovation does not fall when price-reducing policies are imposed. Hence, in our view, the two approaches nicely complement each other.

foreign version of the medication. Although importing prescription drugs into the US for own use is technically illegal, no one has ever been prosecuted for this "crime," which is victimless. Some have suggested traveling to a foreign country such as Canada or even France, filling the prescription, and returning home.[14] 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 certified by PharmacyChecker as safe instead of from an American pharmacy, there would be *massive* personal arbitrage. We assume the threshold difference in prices is exogenous and denote it Δ. We follow Ganslandt and Maskus (2004)[15] in assuming developers sell directly to consumers rather than to wholesalers but relax this assumption at the end of the section. Let p^U denote the price the developers set in the US and p^N denote the price for the same medication abroad. We assume that massive imports will occur if $p^U - p^N > \Delta$ and none (apart from inframarginal imports, assumed negligible) if $p^U - p^N < \Delta$. The US government can lower Δ exogenously by scaling down misleading 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 US consumers about the safety of prescriptions filled at such pharmacies, which patients abroad routinely use to treat the same diseases.

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.[16] The negotiator proposes this price sequentially to each of the n drug developers (hereafter referred to as "developers" in recognition of the many activities these firms do to develop a promising molecule into a marketed drug). If a developer is unwilling to pay the price demanded by the negotiator, the negotiator buys nothing from that developer. Each developer publicly announces whether he has accepted or rejected the negotiator's proposal. Those rejecting the proposal then produce and sell only in the unnegotiated (US) 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. The same equilibrium arises if the n developers accept or reject the negotiator's proposal simultaneously instead of sequentially.[17]

Given the extremely low marginal costs of production for HCV cures (Hill et al. 2014) reported in Section 1, we assume that producing additional units is costless. Developers benefit if they accept the negotiator's proposal since each developer sells more of a drug that is costless to produce. However, with Q^N more drugs in circulation, there is also a threat that supplies sold to Canada and Western Europe would flow into the United States if the price differential between the two regions exceeds the exogenous threshold Δ dollars per cure. The threat of arbitrage ensures that the price in the US market will not exceed the price in the rest of the world by more than Δ. The consequences of any developer accepting the negotiator's proposal is thus a price for every cure sold in the US market of at most Δ more than the price abroad.

We assume that the drugs in this therapeutic class are perfect substitutes and therefore sell at the same price. In fact, the new cures for HCV do appear to be very close substitutes.[18] Throughout, we make assumptions on the domestic demand function ($D(p)$) sufficient for (1) the total revenue function ($pD(p)$)

[14]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."

[15]See their equation 3.

[16]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. However,our comparative-static results would be largely unchanged if we had assumed instead that Q^N is an inelastic function of p^N.

[17]However, in the simultaneous-move version, there is also a spurious equilibrium where every firm accepts the negotiator's proposed price even if he offers only a penny. We discuss the non-spurious equilibrium further in footnote 17.

[18]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 developer that it would not put its drug on Express Scripts formulary unless the company lowered the price to that of the second drug."

to be concave and to pass through the origin, (2) the exogenous threshold price difference triggering arbitrage to be smaller than the revenue-maximizing monopoly price ($\Delta < argmax_{p \geq 0} pD(p)$), and (3) a unique Cournot equilibrium to exist.

2.2 Equilibrium

The negotiator approaches each developer 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 developers that accept. Each developer accepts or rejects the proposal, and the negotiator moves on to the next developer. To determine the subgame-perfect equilibrium, we first determine the payoffs in the various subgames that can arise.

If no developer accepts the negotiator's proposal, then each of the n developers simultaneously decides how much to produce and sell in the US market. In the equilibrium of this subgame, every developer acts like a symmetric Cournot oligopolist selling a perfect substitute. Developers receive an exogenous the Cournot profits generated.

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

If, however, one or more developers accept the negotiator's proposal and $p^N + \Delta < p^{Cournot}$, then every developer would realize that imported drugs would flood the US market if the domestic price strictly exceeded $p^N + \Delta$. In these subgames, *limit-pricing* occurs. Each developer sells more than its Cournot output ($D(p^N + \Delta)/n > D(p^{Cournot})/n$). No developer would unilaterally sell less than this, since doing so would lower its sales without raising the price per cure ($p^N + \Delta$). Nor would any developer 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 $p^N < p^{Cournot} - \Delta$, the price in the US market would be $p^N + \Delta$, but no importing would occur.

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

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

In situation (3), the developer always rejects the negotiator's proposal. For, the developer anticipates that if it is rational for the last developer to reject the proposal, then it must also be rational for every prior developer to reject that proposal since, unlike the last developer, prior developers 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 developer is pivotal: if the developer accepts the proposal, this induces everyone subsequent to this developer to accept it also.

Note that each developer 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 developer in the sequence will accept.[19] Denote this price as $\mathbf{p}^N$. This price is defined as the smallest solution to the following equation, assuming it is nonnegative.[20]

$$p^N Q^N + \frac{(p^N + \Delta) D(p^N + \Delta)}{n} = \frac{\pi^{Cournot}(n)}{n}. \tag{2.1}$$

[19] In the simultaneous-move version of this game, the lowest price the negotiator can demand without all n developers rejecting his proposal is defined implicitly by equation (2.1). If everyone rejects the proposed price, each developer 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.

[20] The smallest solution will be negative if $\Delta > p^{Cournot}$. In this "corner" case, $\mathbf{p}^N = 0$, and the US 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 developer in this case earns $R(n)/n = \pi^{Cournot}(n)/n$.

Since at this price every developer will accept the proposal, each firm will receive $1/n^{th}$ of the additional Q^N sales. The n developers produce in aggregate $Q^N + D(\mathbf{p}^N + \Delta)$. They sell Q^N units in the negotiated market and $D(\mathbf{p}^N + \Delta)$ in the unnegotiated market. Denote the revenue received by each of the n developers as $R(n)$. Each developer earns revenue

$$R(n) = \frac{\mathbf{p}^N Q^N}{n} + \frac{(\mathbf{p}^N + \Delta)D(\mathbf{p}^N + \Delta)}{n}. \quad (2.2)$$

$$= \frac{\pi^{Cournot}(n) - (n-1)\mathbf{p}^N Q^N}{n}, \quad (2.3)$$

where the last line is obtained by substituting into (2.2) the solution to (2.1). Equation (2.3) 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 (2.1) as follows:

$$(p^N + \Delta)D(p^N + \Delta) = \pi^{Cournot}(n) - np^N Q^N. \quad (2.4)$$

The right-hand side is a decreasing linear function of p^N with vertical intercept $\pi^{\text{Cournot}}(n)$ and slope $-nQ^N < 0$. The left-hand side is a strictly concave function with vertical intercept $\Delta D(\Delta) \geq 0$. Given our assumptions that $pD(p) = 0$ when $p = 0$ and that $0 \leq \Delta < argmax_{p \geq 0} pD(p)$, the single-peaked function $\left(p^N + \Delta\right)\left(D(p^N + \Delta)\right) > 0$ is strictly increasing at its vertical intercept.

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 ($\Delta < p^{Cournot}$), the domestic and foreign markets are connected and $p^U = p^N + \Delta$, where the "hat" denotes the equilibrium value of the negotiated price; in the second case ($\Delta \geq p^{Cournot}$), the two markets are unconnected and $p^U = p^{Cournot}$. 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,

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

In the connected case, the horizontal component of the point of intersection is the negotiated price ($\mathbf{p}^N$), and the vertical component is the total revenue in the domestic market. In the unconnected case, the negotiated price equals the marginal production cost (assumed, for simplicity, to be zero), and the price in the US market is the Cournot price. We depict the solution in the connected case in Figure (2.1):

2.3 Comparative Statics

We now consider three 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) increasing competition among developers ($n \uparrow$); and (3) 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 developer. Under each of these policies, developer profit falls when the domestic 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 5.

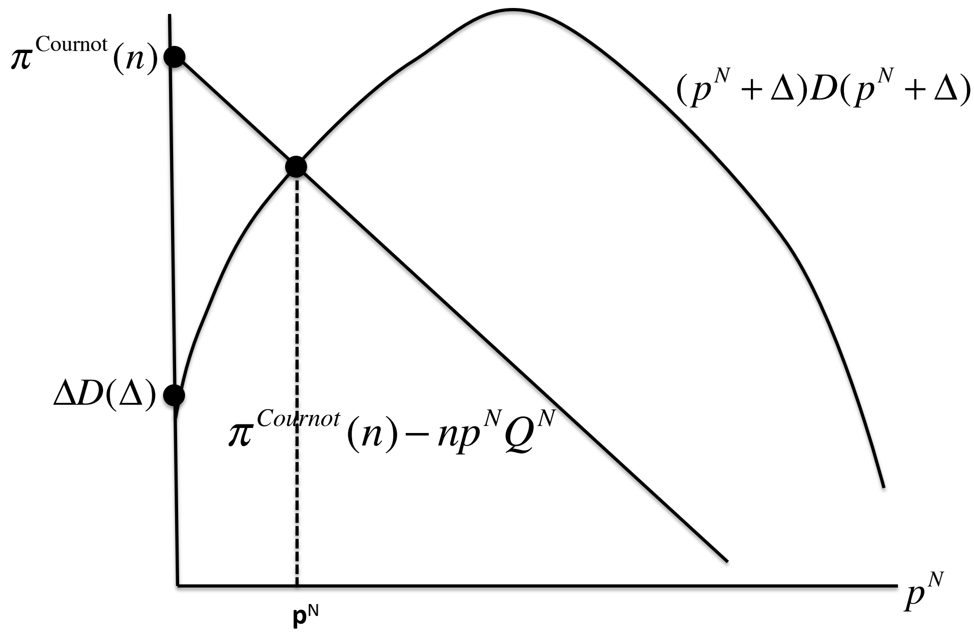
In analyzing the effects of a change in each exogenous parameter, we first consider the case where the two markets are connected and then the case where they are unconnected. The former case can easily be deduced from Figure 2.1. Results for both cases are summarized in Table 1.

2.3.1 Reducing Δ

If the US government reassured US 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

[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 2.1: Determination of the Negotiated Price



raise the foreign negotiated price. For if the negotiated price did not change, developers would earn strictly more by selling exclusively in the domestic market and would reject the negotiator's proposed price (see equation (2.1)). To acquire any drugs, therefore, the negotiator would have to propose a higher price. The domestic price ($\mathbf{p}^N+\Delta$), however, must strictly fall. Otherwise, the left-hand side of (2.1) would strictly exceed the right-hand side.

In terms of Figure (2.1), 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 Δ, $(p^N+\Delta)D(p^N+\Delta)$ 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 (2.3) implies that, since a reduction in Δ will cause $\mathbf{p}^N$ to rise, it must cause R to fall. Each developer loses more from the price decrease in the US market than it gains from the increase in the negotiated price.

If Δ is initially so large that the two markets are unconnected ($\Delta \geq p^{Cournot}$), then a reduction in Δ within this region will affect neither the two prices nor any developer's profit.

2.3.2 Increasing the Number of Developers

An exogenous increase in the number (n) of developers will cause the negotiated price to fall. For if the negotiated price did not change, the developers would strictly prefer to sell in both markets rather than to sell exclusively in the US market (see equation (2.1)), and the negotiator would seize the opportunity to propose a lower price. For the price differential to remain unchanged, the domestic price must fall by the same amount. Each developer's profit would also fall, since total revenue in each market falls (equation 2.2) and must be divided among a larger number of developers. Graphically, an increase in n does not

Table 1: Comparative Statics

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

affect the domestic industry revenue curve in Figure (2.1) 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 developers also causes the line to steepen. As a result, the intersection point has a smaller horizontal component (the negotiated price) and a smaller vertical component (domestic industry profit).

If Δ is so large that the two markets are unconnected ($\Delta \geq p^{Cournot}$), an exogenous increase in the number of developers 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 developers would result in lower profits per developer. We summarize these comparative-statics results in Table 1.

2.3.3 Switching HCV Sufferers from the Market-Determined Price to the Negotiated Price

If Medicare is allowed to pay the price that foreign governments negotiate with developers, some HCV sufferers in the US market would switch to paying the negotiated price. We assume that at any price, $D(p)$ shifts leftward, reflecting the loss of the demands of these domestic HCV sufferers on Medicare. Since the total number of infecteds globally (W) is unchanged, $Q^N + D(0) = W$. As a result, when Q^N increases, $D(p)$ shifts leftward by an equal amount.

If the markets are connected, the negotiated and market-determined prices either both rise or both fall, as does the profit of each developer. It turns out that both prices must fall provided relatively weak assumptions on demand specified in the Appendix are satisfied. If the two markets are unconnected,[22] an exogenous increase in the number paying the negotiated price and a simultaneous decrease in the number paying the market-determined price (which equals the Cournot price) will leave the negotiated price unchanged and will depress the market-determined price. The revenue of each developer will decline. These claims are established in the Appendix.

When campaigning, candidate Donald Trump advocated that Medicare Part D sufferers cease to pay the market-determined price and begin to pay a negotiated price. As president, he has proposed that Medicare pay developers the price negotiated by foreign governments. While this recent proposal was limited to drugs administered in doctors' offices or hospitals, we investigate here what would happen if this policy were extended to *all* HCV drugs (or whatever pharmaceutical is under consideration). Since Q^N would then increase, this policy would lower the US price. But it would also lower developer profit, depressing innovation.

[22]The markets are connected if $Q^N \in [0, W - m(n+1)\Delta)$ and unconnected if $Q^N \in [W - m(n+1)\Delta, W - 2m\Delta)$.

2.4 Discussion

It is instructive to compare our model of personal arbitrage to the model of commercial arbitrage proposed by Ganslandt and Maskus (2004). Like us, they envision developer sales in two markets, each with a different price. Like us, they assume that production costs are zero. However, they assume a single developer and we assume that there are several developers ($n > 1$).

Because we consider personal arbitrage rather than purchase for subsequent re-sale, each of our arbitrageurs buys only enough medication for his own use (1 cure) and exerts no market power. In Ganslandt and Maskus (2004), arbitrage occurs in equilibrium whereas we attribute the arbitrage that occurs to a negligible set of patients willing to import even when the price differential is relatively small; developers find such inframarginal arbitrageurs unprofitable to deter.[23] In Ganslandt and Maskus, the price in the low-priced market is exogenous. In our model, however, that price is determined in a negotiation between the government in the low-priced region and the n developers.

In Ganslandt and Maskus, consumers are assumed to pay the price set by the developer; there are no markups by players downstream in the distribution chain. To simplify, we provisionally made the same assumption but now discuss relaxing it.

Assume instead that developers continue to sell at the price p^U in the US and p^N abroad but the cures are purchased by wholesalers instead of by consumers. Assume wholesalers and pharmacies mark up these developer prices so that consumers pay retail prices of $p^U(1+\tau)$ and $p^N(1+\tau)$. For example, Sood et al. found that for every \$100 paid by US consumers for medication, developers received only \$54, implying $(1+\tau) = 100/54 = 1 + .85$. In that case, massive arbitrage would occur if $p^U(1+\tau) - p^N(1+\tau) > \Delta$ or, equivalently, $p^U - p^N = \hat{\Delta}$, where we define $\hat{\Delta} = \frac{\Delta}{1+\tau}$. That is, if the developers charge wholesalers in the two regions developer prices that differ by more than $\hat{\Delta}$, there would be massive personal arbitrage at the retail level.

How does the inclusion of the downstream markup affect our conclusions? In the connected case, equation (2.1) would be revised as:

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

where $\hat{D}(x) = D\left(x(1+\tau)\right)$ and $\hat{\pi}^{Cournot}$ denotes industry profit in Cournot equilibrium with industry revenue curve $p^U \hat{D}(p^U)$.

Profit per developer would be:

$$\hat{R}(n) = \frac{\mathbf{p}^N Q^N}{n} + \frac{(\mathbf{p}^N + \hat{\Delta})\hat{D}(\mathbf{p}^N + \hat{\Delta})}{n}. \tag{2.6}$$

instead of equation (2.2). Since $\hat{\Delta} \neq \Delta$ and $\hat{D}(\cdot) \neq D(\cdot)$ inclusion of a markup over the developers' price does alter the *levels* of the endogenous variables. But since $\hat{\Delta}$ is still a constant and $\hat{D}(\cdot)$ is still decreasing, taking account of markups would not affect the qualitative comparative statics we derived for the total revenue of the developers and the pair of prices they charge. The changes in the two retail prices would be proportional to the changes in the two developers' prices to maintain the constant ratio of $(1+\tau)$.

3 Commercial Arbitrage

Under current US law, firms may not import medications purchased abroad in order to re-sell them within the US. Unlike the law against personal arbitrage, the law against *commercial* arbitrage is strictly enforced. Suppose, however, that the U.S. legalized commercial arbitrage.

Kyle et al. (2008, 1312) emphasize that within the European Union "parallel trade usually occurs at the wholesale level rather than the retail level." Assume, therefore, that if it were legalized, commercial arbitrage would occur at the wholesale rather than the retail level. For foreign wholesalers to sell to the

[23] It is straightforward (but tedious) to take account of such arbitrageurs. Since their numbers are small and their behavior obscures our point that the *threat* of arbitrage alone can induce developers to lower the price in the US even if no actual arbitrage occurs, we neglect these inframarginal arbitrageurs.

commercial arbitrageurs what they could otherwise have sold to local pharmacies, they would have to receive the same markup that these pharmacies are willing to pay. In addition, commercial arbitrageurs must incur transport costs. Finally, arbitrageurs would have to incur costs to overcome legal barriers which would otherwise prevent their profiting from the price differences. Denote the *sum* of these costs as Δ^c. Hence, if the developers sell to US wholesalers at p^U and foreign wholesalers at p^N, they would need to set $p^U - p^N \leq \Delta^c$ to deter commercial arbitrage. We assume that Δ^c is exogenous and $\Delta^c << \hat{\Delta}$. Hence, when developers set the prices they charge wholesalers in the two markets to deter commercial arbitrage, massive personal arbitrage would cease to be a threat. [24]

Currently four types of intermediaries operate in the US market:wholesalers, pharmacies, PBMs, and insurers. To simplify, we assume that there are M intermediaries, each performing all four functions. We refer to them as "multifunction channel players". We assume that each multifunction channel player exercises market power in the product market. This seems to us appropriate since, according to Sood et al. (2017), the top three PBMs have a market share of more than two-thirds, the top three wholesalers have a market share of more than four-fifths, and the top three pharmacies have a market share of roughly one-half.

To describe the strategic interaction between the upstream drug developers and the downstream domestic channel players, we modify the model of successive Cournot oligopoly first proposed by Greenhut and Ohta (1979) and further analyzed by Gaudet and Long (1995). We follow Ganslandt and Maskus (2004) and Gaudet and Long (1995) in assuming zero marginal costsand linear retail demand: $D(p) = a - mp$. The Cournot equilibrium in this case is well-known:

$$p^{Cournot} = \frac{a}{m(n+1)} \tag{3.1}$$

$$Q^{Cournot} = \frac{an}{n+1} \tag{3.2}$$

$$\pi^{Cournot} = \frac{na^2}{m(n+1)^2}. \tag{3.3}$$

One property of the Cournot model with linear demand and constant marginal cost deserves mention since it arises repeatedly below. The equilibrium Cournot price is always a weighted average of the marginal cost (c) and the choke price (a/m), with the marginal cost receiving the weight $\frac{n}{n+1}$.[25] Thus, in conformity with equation (3.1), $p^{Cournot} = \left(\frac{1}{n+1}\right)\frac{a}{m} + \left(\frac{n}{n+1}\right)0 = \frac{a}{m(n+1)}$.

We briefly review the standard model of successive Cournot oligopoly in subsection 3.1 and then modify it in subsection 3.2 for the case where there is a threat of commercial arbitrage at the wholesale level from abroad.

3.1 The Standard Model: No Threat of Arbitrage

Suppose the M multifunction channel players, in their capacity as wholesalers, buy cures from the n independent developers and then, in their capacity as pharmacies, sell them to customers at a markup over the developers' price. Assume the given inverse demand curve is linear:

$$p^R(Q) = (a - Q)/m, \tag{3.4}$$

where p^R denotes the retail price.

To compute the subgame-perfect equilibrium, we first determine how much the M downstream channel players would order for any given developers' price, and then, given their anticipated ordering behavior, how much the n upstream developers would sell to them.

[24] In a richer model, of course, each component of Δ^c might be endogenized.

[25] This is easily establised. The first-order condition for a Cournot oligopolist can be written as $p - \frac{1}{m}\frac{(a-mp)}{n} = c$, where the second term on the left is the inframarginal loss in revenue resulting from a unililateral marginal increase in output. Solving for p, we conclude: $p = (\frac{1}{n+1})(\frac{a}{m}) + (\frac{n}{n+1})c$.

The downstream stage is exactly like a traditional Cournot oligopoly model except that the acquisition cost p^U, which channel players take as given, replaces the constant marginal cost of production.[26] Channel player i chooses how much (q_i) to purchase from developers at the given price p^U and resell to consumers to maximize

$$\left(\frac{a - q_i - Q_{-i}}{m}\right) q_i - p^U q_i.$$

In the symmetric Nash equilibrium, each channel player (in its capacity as a pharmacy) sells to consumers the same amount that it has purchased (as a wholesaler) from the developer, an amount that equates perceived marginal revenue to the cost of acquiring additional units:

$$\frac{a - Q}{m} - \frac{Q}{Mm} = p^U. \tag{3.5}$$

Solving (3.5), we conclude that the upstream firms order:

$$Q = \frac{M}{M+1}(a - mp^U). \tag{3.6}$$

That is, whatever developers' price they pay, the downstream firms order only the fraction $\frac{M}{M+1}$ of what they would have ordered if they had charged consumers the developers' price, p^U, instead of the retail price, p^R.

In the upstream stage, developers recognize that if they sell a larger quantity, channel players will buy that larger quantity only if the developers' price is reduced. That is, they regard (3.5) as an inverse demand curve with slope $\frac{dp^U}{dQ} = -\frac{M+1}{Mm} < 0$.

The n developers decide independently how much to sell to the channel players. In the symmetric Nash equilibrium, each developer sells an amount which maximizes his profit by equating his perceived marginal revenue from additional sales to the marginal cost of production (assumed by us to be zero).[27]

$$\left(\frac{a - Q}{m} - \frac{Q}{Mm}\right) - \frac{Q}{n}\left(\frac{M+1}{Mm}\right) = 0. \tag{3.7}$$

From equation (3.7), we conclude:

$$\bar{Q} = \frac{M}{(M+1)}\frac{an}{(n+1)} = \frac{M}{(M+1)}Q^{Cournot}, \tag{3.8}$$

where the "bar" denotes variables determined in the subgame-perfect equilibrium. Aggregate sales are smaller in this two-stage oligopoly than in one-stage oligopoly because of the markup above the developers' price. In the case of linear inverse demand, aggregate output is smaller by the factor $\frac{M}{M+1}$. Evaluating $p^U(Q)$ and $p^R(Q)$ at $\bar{Q}$, we conclude:

$$\bar{p}^U = \frac{a}{m(n+1)} = p^{Cournot} \tag{3.9}$$

$$\bar{p}^R = \frac{a(M+n+1)}{m(M+1)(n+1)}. \tag{3.10}$$

Note that, in the absence of a threat of arbitrage, the markup over the price developers' charge domestic wholesalers is not constant.[28] Note also that developers would charge channel players a developers' price equal to $p^{Cournot}$, the same price that they would have charged final consumers if they had dealt with

[26] PBMs often claim that they exercise oligopsony power. In the absence of unambiguous evidence to support such claims, we follow the literature on successive oligopoly and assume that downstream firms take the developer's developers' price as given.

[27] Although the cost of an additional course of a drug (a "cure") is negligible, the costs of developing that drug are substantial (DiMasi et al. 2003; DiMasi and Grabowski 2007). These costs do not figure into our calculations, however, because they are sunk before the strategic interactions modeled here begin.

[28] As can be verified from equations (3.9) and (3.10), in the traditional model of successive oligopoly, $\frac{p^R}{p^U} = 1 + \frac{n}{M+1}$.

them directly; the channel players then add their own markup, reducing the quantity sold to $\frac{M}{M+1}$ times its former level. Intuitively, the developers' price when there is a markup equals the Cournot price because the quantity ordered by the channel players is $\frac{M}{M+1}$ as large at every developer price. Since this is like a mere scaling of the units used to measure quantity, it does not affect the equilibrium price per cure.[29] It does, of course, reduce each developer's profit by the factor $\frac{M}{M+1}$:

$$\bar{R} = \left(\frac{M}{M+1}\right)\frac{a^2}{m(n+1)^2} = \left(\frac{M}{M+1}\right)\frac{\pi^{Cournot}}{n}. \tag{3.11}$$

3.2 Accounting for the Threat of Commerical Arbitrage

We now modify the standard model for the case where downstream developers have the opportunity to sell additional units at a price foreigners negotiate, but these domestic developers risk arbitrage if the domestic manufacturer price exceeds the negotiated price by more than Δ^c.

Arbitrage would be deterred if it is strictly cheaper for channel players (wholesalers) to order the cures directly from the developers ($p^{Cournot} < p^N + \Delta^c$). But suppose it is more than Δ^c cheaper to purchase cures from commercial aribtrageurs: $p^{Cournot} > p^N + \Delta^c$. Channel players would never pay more than $p^N + \Delta^c$ when they could simply buy from arbitrageurs whatever they wanted at that price. Allowing any arbitrage, however, would not be optimal for the developers since their marginal production cost is negligible. They would instead expand their sales at the developers' price of $p^N + \Delta^c$ to satisfy the *entire* aggregate demand of the multifunction channel players. Hence, provided $p^N + \Delta^c < p^{Cournot}$, the threat of arbitrage would drive down the developers' price:

$$p^U = p^N + \Delta^c < p^{Cournot}.$$

Substituting this reduced developer price into (3.6), we conclude that the channel players would order:

$$Q = \left(\frac{M}{M+1}\right)\left(a - m(p^N + \Delta^c)\right). \tag{3.12}$$

It remains to determine the lowest negotiated price that at least one developer would accept. As before, the negotiator approaches developers sequentially and offers to purchase a total of Q^N additional cures, equally divided among the developers accepting his offer, at the proposed price. By accepting the proposal, each developer sells more cures, but as in Section 2, the developer's profits in the domestic market are smaller than they would have been if commercial arbitrageurs had no supplies to resell to the channel players.[30] The arguments in Section 2 for determining the negotiated price still apply. The lowest negotiated price that would be acceptable to the n developers must make the last developer in the sequence indifferent between accepting and rejecting the proposed price if the other developers had rejected it. Hence, in the model with the markup over the developer price, the negotiated price (denoted $\tilde{p}^N$) must satisfy the following equation:

$$p^N Q^N + \frac{\left(\frac{M}{M+1}\right)(p^N + \Delta^c)(a - m[p^N + \Delta^c]}{n} = \left(\frac{M}{M+1}\right)\frac{\pi^{Cournot}}{n}. \tag{3.14}$$

[29]As a check on these calculations, note that the retail price is a weighted average of the choke price on the consumer demand curve and the marginal cost $\bar{p}^U$, where the latter receives a weight of $\frac{M}{M+1}$. Moreover, the developers' price is a weighted average of the choke price on the downstream firms' demand curve (which also equals a/m) and the marginal production cost of zero, where the latter receives a weight of $\frac{n}{n+1}$. The second of these calculations reproduces $\bar{p}^U$ in equation (3.9). Substituting that into the first of these calculations reproduces $\bar{p}^R$ in equation (3.10).

[30]To show this, we use equation (3.5) to express the aggregate profit of the developers as

$$R^{ag} = Q\left(\frac{a-Q}{m}\right) - \frac{Q^2}{Mm}. \tag{3.13}$$

Differentiating twice, it is straightforward to show: (1) R^{ag} is globally concave ($\frac{d^2R^{ag}}{dQ^2} < 0$) and (2) since $\frac{dR^{ag}}{dQ} = \frac{aM-2Q(M+1)}{Mm}$, this first derivative is negative when evaluated at $\hat{Q}$. Together, these two observations imply that when aggregate sales increase, the profit of every developer declines.

The left-hand side is what the last developer in the sequence would receive from sales in the two markets if he alone accepts the proposal and the right-hand side is what he would receive from sales in the domestic market if he rejects it. Multiplying every term by $\frac{n(M+1)}{M}$) and transposing the first term, we conclude:

$$(p^N + \Delta^c)(a - m[p^N + \Delta^c]) = \pi^{Cournot} - p^N nQ^N \left(\frac{M+1}{M}\right). \tag{3.15}$$

The left-hand side is a concave parabolic function of p^N like the one in Figure 2.1. The right-hand side is a linear function of p^N with vertical intercept $\pi^{Cournot}$. It is like the linear function in Figure 2.1 except that its slope flattens as M increases. If the solution to this quadratic equation is nonnegative, $\tilde{p}^N$ denotes its smaller root. If the solution is strictly negative, then the negotiator drives the developers' foreign price down to marginal cost (zero). In both cases, the price developers charge domestic wholesalers is $\tilde{p}^U = \min(\tilde{p}^N + \Delta^c, p^{Cournot})$.

In the connected case, the n developers produce in aggregate $Q^N + \left(\frac{M}{M+1}\right)(a - m(\tilde{p}^N + \Delta^c))$. They sell Q^N cures in the negotiated market and $\left(\frac{M}{M+1}\right) D(\tilde{p}^N + \Delta^c)$ in the unnegotiated market. Denote the revenue received by each of the n developers as $\tilde{R}(n)$. Each developer earns revenue

$$\tilde{R}(n) = \frac{\tilde{p}^N Q^N}{n} + \frac{\left(\frac{M}{M+1}\right)(\tilde{p}^N + \Delta^c)(a - m[\tilde{p}^N + \Delta^c])}{n}. \tag{3.16}$$

The comparative statics for the case where there is a threat of commercial arbitrage are recorded in Table 2. The last row and last column are new. Since we derived the comparative statics for the model of personal arbitrage from the same Figure 2.1, the remainder of the table merely repeats the entries in Table 1.

To derive the entries in the last row of Table 2, we utilize equations (3.15) and the associated Figure 2.1 as well as equation (3.16). Note that in the connected case, the downward-sloping line in Figure 2.1 has a slope of $-n\frac{M+1}{M}Q^N$. Since the downward-sloping line flattens when M increases, $\tilde{p}^N$ increases. $\tilde{p}^U$ must increase by the same amount since the developers' price in the two regions must differ by Δ^c. Since the developers earn more for the same volume of sales abroad, their revenue increases in the foreign market. They also increase in the domestic market. To see this, recall that developers charge domestic wholesalers a price less than $p^{Cournot}$ which in turn is smaller than the monopoly price. When M increases, developers marginally raise the price they charge domestic wholesalers and their revenue from these sales would increase even if the factor $\frac{M}{M+1}$ did not change. However, this factor itself increases, insuring that developer revenue increases when M increases. The factor increases because, with more channel players, the markup is smaller and so the loss in sales due to the markup is smaller.

In the unconnected case, each developer earns nothing from foreign sales and $\left(\frac{M}{M+1}\right) p^{Cournot}(a - mp^{Cournot})$ in the domestic market. An increase in M does not affect either developer price. However, with more downstream players, the markup above the developers' unchanged Cournot price is smaller and so wholesalers order more from the developers. Hence, developer revenue increases.

To derive the entries in the last column of Table 2, note that in both the connected and the unconnected cases, developers charge domestic wholesalers $\tilde{p}^U = \min(\tilde{p}^N + \Delta^c, p^{Cournot})$ and that the domestic retail price is a weighted average of the what developers charge domestic wholesalers ($\tilde{p}^U$) and the choke price (a/m):

$$\tilde{p}^R = \left(\frac{1}{M+1}\right) a/m + \left(\frac{M}{M+1}\right) p^U. \tag{3.17}$$

This implies, as in the standard model of successive oligopoly, that $\frac{\tilde{p}^R}{\tilde{p}^U}$ is endogenous.[31] If more people switch from paying the US price to the negotiated price ($Q^N \uparrow, a \downarrow$), then the retail price falls. An increase in Q^N with an offsetting reduction in a reduces both the choke price (a/m) and (from Table 2) the price developers charge domestic wholesalers in both the connected and the unconnected cases. Since the weights do not change, the retail price must fall in both cases.

[31] With a threat of commercial arbitrage at the wholesale level, $\frac{\tilde{p}^R}{\tilde{p}^U} = \frac{1}{M+1}\frac{a/m}{\tilde{p}^U} + \frac{M}{M+1}1$.

Table 2: Comparative Statics when Channel Players Are Financed by Markups

	$\tilde{p}^N$	$\tilde{p}^U$	$\tilde{R}$	$\tilde{p}^R$
Q^N	− (NC)	− (−)	− (−)	− (−)
n	− (NC)	− (−)	− (−)	− (−)
Δ^c	− (NC)	+ (NC)	+ (NC)	+ (NC)
M	+ (NC)	+ (NC)	+ (+)	? (−)

If the number of developers (n) increases, the retail price falls in both the connected and unconnected cases. This follows since the weights are unchanged, the choke price is unaffected, but the lower developers' price decreases in both cases (see Table 2).

If Δ^c is larger, then the retail price rises in the connected case but does not change in the unconnected case. In the connected case, the increase in Δ^c increases the developers' domestic price (see Table 2) without affecting the choke price or the weights. So the retail price increases. In the unconnected case, the developers' price remains $p^{Cournot}$ and, since the weights and the choke price do not change, the retail price is unaffected.

If the number of channel players (M) increases, less weight is put on the choke price and more on the developers' domestic price, which is smaller. Although the choke price is unchanged, the developers' domestic price increases when M increases (see Table 2) so the effect on the retail price cannot be established without further analysis. However, in simulations with a calibrated model, the retail price falls in response to an increase in the number of channel players.[32]In the unconnected case, an increase in M does not affect the choke price or the developers' price but increases the weight on the lower component. Hence, the retail price declines monotonically. Indeed, it approaches the developers' price ($p^{Cournot}$) in the limit. Promoting entry in the downstream market seems a noteworthy policy since, unlike the others we consider, it induces an increase in developer profits and innovation while at the same time lowering the domestic retail price in the unconnected case and probably in the connected case as well.

3.3 Transparency in Retail Pricing: An Alternate Way to Finance Downstream Players

In the US, the public blames developers for the high cost of prescription drugs and developers in turn blame "middle men" (wholesalers, pharmacies, pharmacy benefit managers) who markup the the developers' prices to finance their activities downstream. Various proposals have been made to increase "transparency."

One solution would be to compensate these downstream channel players directly out of the revenues developers earn from domestic sales instead of out of markups over developer prices in the US. If that were done, consumers would know that the price they pay is the price the developers set: $\tilde{p}^U$.

A federal law could mandate that developers publish their prices and that downstream players would not mark them up. Developers could negotiate with domestic players downstream contractual agreements to compensate them out of the revenue from developer sales in the domestic market. This policy can easily be monitored and enforced. Any wholesaler or pharmacy downstream that unilaterally broke the agreement and marked up the developer's price would be easily identified by consumers and swiftly reported to the relevant developer. That developer would report the legal violation and in doing so would be released from his obligation to provide the offending intermediary with the share of developer profits which the contract specifies. If the offender was a pharmacy (resp. a wholesaler), it would have no

[32]I am endeavoring to show this result analytically.

choice but to continue to markup the developer's price and consumers (resp. pharmacies) would seek out competitors selling the same product for less. Hence, markups would not occur in equilibrium.

Suppose developers paid downstream channel players a fraction of their domestic revenue and retained for themselves only the fraction $\Gamma \in (0, 1)$. In that case, the foreign price would be negotiated down to p^N satisfying:

$$p^N Q^N + \frac{\Gamma(p^N + \Delta^c)(a - m[p^N + \Delta^c]}{n} = \Gamma \frac{\pi^{Cournot}}{n}. \tag{3.18}$$

and developer revenue would be:

$$R(n) = \frac{\tilde{p}^N Q^N}{n} + \Gamma(\tilde{p}^N + \Delta^c)\frac{(a - m(\tilde{p}^N + \Delta^c)}{n}. \tag{3.19}$$

As a benchmark, suppose the "tax" on developers' domestic revenue is set so that $\Gamma = \frac{M}{M+1}$. Then developers will charge wholesalers in the two markets the same prices as before since, with this tax rate, equation (3.18) is identical to equation (3.14) . However, domestic consumers will pay what the developers charge the domestic wholesalers. The domestic retail price would therefore be much lower and some patients who could not previously afford to fill their prescriptions would be able to fill them. Developers would earn exactly the same revenue as when downstream channel players were compensated by markups. Revenue in the foreign market would be unchanged. Developers would continue to charge domestic wholesalers $\tilde{p}^U = \tilde{p}^N + \Delta^c$, but these wholesalers would expand their orders by the factor $\frac{M+1}{M}$ to accommodate the increased demand which removal of markups would stimulate. However, since the benchmark tax is $\Gamma = \frac{M}{M+1}$, developers would earn, after the tax, the same revenue as when the downstream domestic distributors financed their activities using markups.

If the tax rate $\Gamma = \frac{M}{M+1}$, then downstream distributors are shortchanged if and only if the following inequality holds:

$$(\tilde{p}^R - \tilde{p}^U)\tilde{Q} \overset{?}{>} (1 - \Gamma)\tilde{p}^U \left[\frac{M+1}{M}\right] \tilde{Q}, \tag{3.20}$$

where $\tilde{Q}$ denotes domestic sales in the equilibrium with markups. The left-hand side is compensation of the domestic downstream players when they are financed entirely from markups over the developers' domestic price. The right-hand side is their compensation when they are financed entirely out of developers' domestic revenues. That revenue equals the price developers charge domestic wholesalers multiplied by the quantity domestic wholesalers order from them. Note that orders are magnified by the factor $\frac{M+1}{M}$ since consumers order more in the absence of a markup. Since, as a benchmark, we are setting the tax rate $\Gamma = \frac{M}{M+1}$, the inequality simplifies to:

$$\frac{\tilde{p}^R}{\tilde{p}^U} \overset{?}{>} \frac{M+1}{M}. \tag{3.21}$$

With four downstream players, the right-hand side of (3.21) is 1.25. If inequality (3.21) fails to hold after commercial arbitrage is legalized, then the proposed tax benefits domestic consumers and downstream players while leaving developers and foreign consumers unaffected. It seems at least as likely, however, that the inequality will hold. In that case a larger tax on developer profits (a reduction in Γ) is necessary to fully compensate downstream players for relying on direct payments from developers instead of markups. Since reducing Γ has the same qualitative effect as reducing M in Table 2, restoring downstream revenue to its previous level would then reduce developer profits ($\tilde{R}$) across the two markets while raising the price developers charge foreign wholesalers. The domestic retail price would also increase if Γ decreased but we conjecture, based so far on simulations, that this increase would not offset the reductions in the retail price from eliminating domestic markups.

Therefore of the four policies we have considered to lower domestic drug prices, three cause developer profits to fall. Promoting entry of downstream players is the only policy that simultaneously reduces domestic prices and increases developer profits.

3.4 Comparing the Policies

In this section, we ask which of the policies we have considered lowers developer profits the least given that each of the policies is set to reduce domestic retail prices by the same amount.

[APOLOGIES. THIS SECTION IS INCOMPLETE. AWAITING MATLAB RESULTS]

4 The Adverse Impact on Innovation of Price-Reducing Policies

Since three of the policies to reduce developer prices reduce developer profits, we turn now to the long-run effects of these policies on innovation of new drugs. Most biopharmaceutical innovation is done by academics (Shepherd, forthcoming), some more capable of searching for a promising molecule than others. Assume there are N academics with distinct, strictly positive probabilities of finding a promising molecule if they commit to looking 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. In that case, the number of academics willing to search for a molecule is a strictly increasing step function of the payoff they expect to receive if they find a promising molecule. For any given expected payoff (denoted V), academics with sufficiently high success probabilities will gear up to search for a promising molecule, while those with insufficiently high probabilities will pass up the opportunity. We assume each academic takes V as given.[33]

We assume that a developer who expects to receive more revenue from sales of a drug it develops from a promising molecule is willing to pay academics more for their promising molecules. Hence, we assume that V is a strictly increasing function of R. The results in Table 1 and Table 2, therefore, can be reinterpreted as implying that an increase in downstream competition (an increase in M) raises V while promotion of imports from Canada or Western Europe or the requirement that Medicare pay the price that foreign governments negotiate lowers V. That is, $V_M > 0, V_{\Delta^c} > 0, V_{Q_N} < 0$. Recall that increasing the number of developers (n) competing in the product market lowers R and hence V. We assume that when more academics search for promising molecules, more are discovered and eventually more firms sell whatever drugs can be developed. Consequently V is a decreasing function of k.

We summarize this discussion in Figure 4.1. On the horizontal axis, we plot the number of academics who search for a promising molecule ($k \leq N$). The vertical axis is in dollars. The upward-sloping line depicts the number of academic searchers (k) as a function of the payoff they expect to receive if they are successful; this is a continuous approximation of the step function. The downward-sloping line is $V(k)$.[34]

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

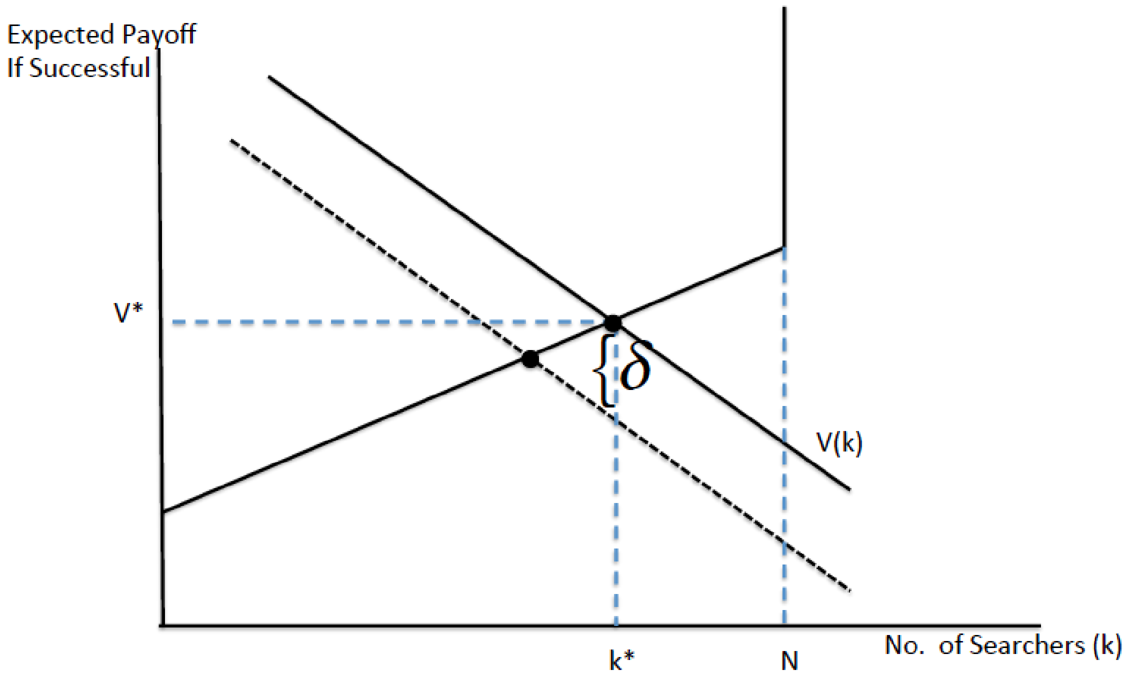
$V(k)$ will shift if the government intervenes in the product market in order to lower the domestic price of pharmaceuticals. Increasing competition downstream would lower the domestic price and would increase the profits of each developer selling a drug. Hence, $V(k)$ would shift up and, in the long run, innovation would increase. Since there is no adverse effect on innovation, there is no "policy tradeoff"; hence, there is nothing further to discuss.

On the other hand, reducing the domestic price by promoting the importation of biopharmaceuticals from Canada or Western Europe or by requiring Medicare to pay the same price that foreign governments have negotiated shifts down $V(k)$. In the long run, innovation falls. Note that the academics who cease to search for a promising molecule will be those with the *lowest* probabilities of finding one.

[33]How sensitive the supply of searchers is to the payoff they expect if they are successful depends on the vector of success probabilities. For simplicity, we assume that each success probability is distinct. As a result, the supply curve will have N steps and will steepen as the difference between the success probabilities grows. If instead we had assumed that all N academics had the same success probability, then all N of them would have the same asking price.

[34]Our results would not change if $V(k)$ were horizontal or even upward-sloping, provided it crosses the supply curve from above.

Figure 4.1: Effect of Reduction in Expected Payoff if Successful Reduces the Number of Academics Searching for a Molecule



4.1 When to Sterilize to Offset the Adverse Impacts

Suppose that in response to reduced revenue in the drug market, developers reduce payments for promising molecules. Innovation falls in the long run unless a second policy instrument is used. In particular, suppose that if k^* academics continued to search, they would receive $\delta > 0$ less than before the government's product-market intervention—only $V(k^*) - \delta$. The government can restore innovation by paying each academic who has discovered such a molecule δ to replace what the developers cease to pay. Alternatively, the government can restore innovation by paying each academic *before* he knows whether he has succeeded or failed an amount s just sufficient to restore innovation to its previous level. Which strategy is less expensive for the government?

If each of the k^* academics committed to searching is paid $s = p_{k^*}\delta$, the marginal researcher will continue to search and so will the $k^* - 1$ other researchers since they have an even better chance of finding a promising molecule. Multiplying by k^*, we conclude:

$$k^* s = k^* p_{k^*}\delta < (p_1 + p_2 + \ldots + p_{k^*})\delta. \tag{4.1}$$

The inequality follows because there are k^* terms in the parentheses on the right-hand side, strictly larger than p_{k^*}.[35] The left-hand side is the cost to the government of paying each of the k^* researchers s *before* they learn whether their research has succeeded or failed. The right-hand side, which is strictly larger, is the expected cost to the government of paying δ to each of the k^* researchers lucky enough to find a promising molecule.

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

[35]The inequality would also hold if at least one of the $k^* - 1$ probabilities strictly exceeds p_{k^*}.

paying the most. Nonetheless, as long as the marginal researcher continues to search for a promising molecule, so will the researchers with higher success probabilities.

5 Conclusion

The purpose of this paper is to explain the basic stylized facts in the international biopharmaceutical industry and, assuming that explanation is correct, to deduce from it the effects on future innovation of imposing product-market policies designed to lower domestic drug prices. Central to our explanation is the threat of arbitrage. While domestic sufferers paying $84,000 for an HCV cure do not en masse currently purchase medications from Canada or Western Europe, they would certainly do so if the same cures were available to them online from foreign pharmacies reliably certified to be safe at prices anywhere close to their $140 marginal cost of production. The price negotiated by foreign governments is no closer to the marginal cost of production because developers fear triggering massive arbitrage.

We considered four price-reducing policies, three of these would depress future innovation. To prevent this, a second instrument is required. One possibility is for the government to reward research success by exactly as much as developers 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 outcome of his molecule search is known. The latter policy is cheaper because the percentage reduction in the subsidy paid is always larger than the percentage increase in the number of recipients of the subsidy. 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*.

Although the model described here is conceptual and its results qualitative, it is the centerpiece of a calibrated simulation model (code to be made available in the summer of 2019) that can be used to *quantify* the effects of the alternative policies. We will describe the simulation model in a companion paper.

Appendix: Switching HCV Sufferers from the Market-Determined Price to the Negotiated Price

If some sufferers cease to pay the US price and instead pay the negotiated price, both prices must fall provided relatively weak assumptions on demand are satisfied. Let $D(p;a)$ denote domestic demand as a function of the endogenous domestic price p and the exogenous shift parameter a. Increases in a raise demand ($D_2(p;a) > 0$) and reduce the number of infecteds whom the negotiator represents ($Q'^N(a) < 0$). Assume that the Cournot price, $p^{Cournot}(a)$, is differentiable and weakly increasing in a in the neighborhood of the equilibrium. Together, these assumptions imply that Cournot profit is strictly increasing in a.[36] In addition, assume that $D_2(\check{p}, a) \geq D_2(p, a)$ for any $\check{p} \geq p > 0$. It is easy to verify that the linear demand function $D(p;a) = a - mp$ satisfies all of these restrictions. They are sufficient but not necessary for both the domestic and foreign prices to fall when HCV sufferers in the United States switch to the negotiated price.

Rewrite (2.4) as the following implicit function of the endogenous variable p^N and the exogenous variable a.

$$\left[p^{Cournot}(a)D\left(p^{Cournot}(a);a\right) - \frac{np^N Q^N(a)}{\left(\frac{M}{M+1}\right)}\right] - (p^N + \Delta)D(p^N + \Delta; a) = 0. \tag{5.1}$$

The left-hand side of equation (5.1) is the difference between the downward-sloping linear function of p^N (in square brackets) and the upward-sloping segment of the single-peaked function of p^N. Denote it $l(p^N;a)$. This function is strictly decreasing in p^N in the neighborhood of the equilibrium solution. We now show that $l(p^N;a)$ shifts up if a increases exogenously (for a given p^N). Hence, $\frac{dp^N}{da} > 0$. Since by assumption $Q'^N(a) < 0$, $\frac{dp^N}{dQ^N} = \frac{dp^N}{da}\frac{1}{Q'^N(a)} < 0$.

Holding p^N at its equilibrium value, partially differentiate $l(p^N;a)$ with respect to a and simplify this partial derivative to obtain:

$$\begin{aligned} &p'^{Cournot}(a)\left[D\left(p^{Cournot}(a);a\right) + p^{Cournot}(a)D_1\left(p^{Cournot}(a);a\right)\right] \quad + \\ &D_2(p^N+\Delta;a)\left[p^{Cournot}(a)\frac{D_2(p^{Cournot}(a);a)}{D_2(p^N+\Delta;a)} - (p^N+\Delta)\right] \quad + \quad \frac{-Q'^N(a)np^N}{\left(\frac{M}{M+1}\right)}. \end{aligned}$$

This partial derivative is, therefore, the sum of three terms. The first term is the product of two positive factors; the second factor is positive since the Cournot price is smaller than the monopoly price and the revenue function is increasing below the monopoly price. The second term is positive because it is the product of two factors each of which is positive; the second of these factors is positive because the domestic price is smaller than the Cournot price and the Cournot price is multiplied by a fraction weakly exceeding one. The third term is positive since $Q'^N(a) < 0$. An increase in a (or equivalently, a decrease in Q^N) increases p^N and, since the difference in the two prices must remain unchanged (Δ), the domestic price also strictly increases.

An increase in Q^N (or, equivalently, a decrease in a) would drive both prices down. Since the negotiated price falls but more sales occur at that price, the revenue generated from such sales ($p^N Q^N$) may increase or decrease. We consider each case in turn and show that in either case the profit of each developer falls.

If $p^N Q^N$ decreases, then (from equation 2.2) each developer earns less revenue in each market, and hence developer profits fall. If, on the other hand, the revenue from sales at the negotiated price ($p^N Q^N$) rises, the increase can never outweigh the revenue decrease in the domestic market. This follows from (2.3). The numerator in the right-hand side of (2.3) consists of the difference of two terms. Since $\pi^{Cournot}(a)$

[36] Developer revenue is strictly increasing in a. Differentiate the revenue function $p^{Cournot}(a)D\left(p^{Cournot}(a);a\right)$ to obtain:

$$p'^{Cournot}(a)\left[D\left(p^{Cournot}(a);a\right) + p^{Cournot}(a)D_1\left(p^{Cournot}(a);a\right)\right] + p^{Cournot}(a)D_2\left(p^{Cournot}(a);a\right).$$

The derivative is the sum of two terms. Each term is the product of two positive factors. The second factor of the first term is strictly positive because the Cournot price is strictly below the monopoly price.

strictly increases in a, the first term falls when Q^N rises. Since the second term rises when $p^N Q^N$ rises, the numerator falls. Therefore, when HCV sufferers formerly paying the market-determined price begin to pay the negotiated price, both prices fall and so does the profit of each developer.

If the two markets are unconnected,[37] an exogenous increase in the number paying the negotiated price and a simultaneous decrease in the number paying the market-determined price will leave the negotiated price (which equals the marginal cost of zero) unchanged and will depress the market-determined price (which equals the Cournot price) and the revenue of each developer.

[37] The markets are connected if $Q^N \in [0, W - m(n+1)\Delta)$ and unconnected if $Q^N \in [W - m(n+1)\Delta, W - 2m\Delta)$ for $n = 2, 3, \ldots$

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