Redesigning the Orphan Drug Act:
Examining the Government’s Use of Subsidy and Exclusivity for Incentivizing Drug Development

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Abstract

The Orphan Drug Act incentivizes the development of drugs for rare diseases using R&D subsidies and years of market exclusivity. My thesis examines how the government can improve upon the social welfare generated by the orphan drug industry with a more refined distribution of these two incentive tools. I find that incentivizing drugs with subsidy instead of exclusivity optimizes the social benefit offered by the drugs, because subsidy incentivizes drug development without generating any of the deadweight loss that is created by monopoly pricing during exclusivity. However, subsidy is constrained by the government’s budget, so I propose a subsidy priority ranking system based on characteristics of consumer demand. Drugs that experience the greatest deadweight loss during exclusivity are incentivized entirely with subsidy, while the remaining drugs are incentivized entirely with exclusivity. Unlike the current Orphan Drug Act, which spreads subsidies across all approved drug projects, my proposed incentive system, in which only drugs facing the greatest deadweight loss qualify for subsidy, ensures that subsidy funds are being allocated most effectively.
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1 Introduction

In 1983 the United States Congress passed the Orphan Drug Act, creating an incentive program to stimulate the development of drugs for rare diseases (Asbury, 1985). Without government intervention, these drugs, known as orphans, would remain largely undeveloped, rendered unprofitable by their small patient populations and the high costs of pharmaceutical development. The law provides two means of incentive for pharmaceutical companies. The first incentive, R&D subsidies, typically covers 50% of orphan drug development costs. The second incentive, years of market exclusivity, grants orphan drugs seven years of monopoly control of the market. Drugs qualify for orphan status so long as their intended patient population is less than 200,000. All orphan drugs, regardless of any other characteristics, receive the same set amount of subsidy and the same set amount of exclusivity. This blunt application of the incentive tools prevents the government from discriminating between drug development projects. In turn, this fails to incentivize pharmaceutical firms to consider the social benefit of the orphan drugs they choose to develop. My thesis examines how the government can improve upon the social welfare generated by the orphan drug industry with a more refined distribution of subsidy and exclusivity.

More precisely, I model the government as a socially benevolent entity that seeks to maximize the discounted future social benefit of all drugs that get developed, and I model pharmaceutical companies as profit-maximizing firms that will undertake drug development projects if and only if they are profitable. Subsidies and years of market exclusivity affect the profitability of drugs, so the government can influence which drugs firms choose to develop by adjusting the levels of these two incentives. Subsidy makes a
drug more profitable by reducing development costs upfront, while exclusivity enables the firm to capture more profit from a drug by protecting it from competition. Both incentives increase the expected profit from a drug, so a pharmaceutical firm can be sufficiently incentivized to develop a drug with either incentive.

Unlike exclusivity, subsidy is limited by the government’s budget. In order to deal with this constraint, the government currently spreads the two incentives evenly across orphan drug projects, awarding all projects the same combination of subsidy and exclusivity. This evenhanded combination of both subsidy and exclusivity prevents the government from determining where its limited subsidy funds will be most effective. The government would be better served by identifying the drugs for which subsidy dollars will have the greatest impact on social welfare. These drugs should be sufficiently incentivized with subsidy, while the remaining drugs can be sufficiently incentivized with exclusivity. I propose a ranking system for subsidy priority based on characteristics of consumer demand for the drugs. Thus in contrast to current policy, my solution suggests that most drugs should receive either only subsidy or only exclusivity – not both.

In my model the government calculates the social benefit provided by an orphan drug by considering the consumer surplus it generates, both during and after exclusivity, as well as the cost of the subsidy grant. Consumer surplus serves as a proxy for the health benefit provided by a drug, assuming that a drug’s medical benefit drives consumers’ willingness to pay. Although exclusivity does not have a direct monetary cost for the government, it comes with opportunity cost for social welfare. Each year of exclusivity is a year that the drug is subject to monopoly pricing and the associated deadweight loss. Exclusivity increases firm profits by enabling a transfer of surplus away from consumers
to the firm, but the transfer is not one-to-one because monopolies generate deadweight loss. While firms are largely indifferent between subsidy and exclusivity, as both incentives increase the potential profit from a drug, consumers bear the opportunity cost from exclusivity. When the socially benevolent government is not constrained by a budget, it prefers to incentivize drugs with subsidy due to the opportunity cost of exclusivity. Subsidy incentivizes drug development without generating deadweight loss or delaying any consumer surplus. When a drug is incentivized exclusively with subsidy, meaning there are no exclusivity rights, the drug is immediately made subject to competitive pricing, enabling more patients to purchase the drug and reap its health benefits sooner. Unfortunately, every orphan drug cannot be incentivized entirely with subsidy, because the government’s budget is constrained. I show that, in order for the limited funds to be allocated across orphan drugs in the most socially beneficial manner, drugs that are likely to experience greater deadweight loss from monopoly pricing should receive higher subsidy priority.

The size of the deadweight loss and the amount of surplus that a firm extracts from consumers during exclusivity, depend on the shape of consumer demand curve for the drug. The government’s current policy of awarding the two incentives evenly across drugs disregards the wide range of orphan drugs being produced, and thus disregards the variations in consumer demand for the drugs. More precisely, it disregards the possibility that there are greater benefits from subsidizing some drugs than others. We can look to the FDA’s recent orphan drug approvals in order to illustrate this issue. In December 2015 the FDA approved a novel drug called Kanuma to treat a rare disorder known as Wolman disease that typically kills children in their first year of life (FDA, 2015a).
Kanuma, the first and only treatment available for Wolman disease, gives sick children an opportunity for survival that had not existed before. In the same month, the FDA approved another orphan drug, Uptravi, which treats a rare type of high blood pressure that typically affects older adults (FDA, 2015b). Uptravi offers only a marginal improvement over eight treatments previously approved by the FDA for the same disease. Thus Uptravi has many close substitutes, while Kanuma has none. Because Kanuma has fewer substitutes and treats a more serious disease, it is likely that demand for Kanuma is more price inelastic than demand for Uptravi. All else equal, greater price inelasticity means greater deadweight loss generated by monopoly pricing, making the opportunity cost of awarding exclusivity to Kanuma larger than the opportunity cost of awarding exclusivity to Uptravi. Therefore, if the government only has funds to subsidize one of the two drugs, Kanuma should be prioritized.

By spreading subsidies across all orphan drugs, instead of concentrating them more judiciously, the government currently dilutes the social benefits from public funding of drug development. The use of public funds is not the only consideration, though. Since the Orphan Drug Act was passed, the orphan drug segment of the pharmaceutical industry has experienced exponential growth, with global orphan drug sales expected to top $178 billion by 2020 (EvaluatePharma, 2015). Because of government incentives that make the drugs profitable, billions of dollars of private investment are being funneled into orphan drug development. The government is missing an opportunity to incentivize firms to use this private funding in a more socially beneficial manner.
The rest of the paper proceeds as follows: In section 2, I provide background on
the Orphan Drug Act, as well as motivation for the problem I identify with the current law’s incentive policies. In section 3, I develop a model for drug development that includes the government’s social welfare function and the firm’s profit function. In section 4, I solve for the government’s optimal incentives policy by first solving for the firm’s problem with the given set of incentives. Finally in section 5, I explore more practical interpretations of my results.

2 Background

The United States considers a disease rare when it affects less than 200,000 domestic patients. By 1983, only 38 approved drugs existed for rare diseases. These drugs were largely the products of university-run labs and only ten of them were ever marketed (EvaluatePharma, 2015). With the large costs associated with drug development, pharmaceutical companies knew they could not generate enough revenue to justify R&D investments in drugs for limited numbers of patients. Thus, drugs for rare diseases went largely undeveloped and patients with rare diseases went largely untreated. This lack of treatments inspired massive lobbying efforts by patient groups in the 1970’s, particularly by the National Organization for Rare Diseases, which brought the issue into the national spotlight (Asbury, 1985). In order to alleviate the apparent medical inequity, Congress passed the Orphan Drug Act in 1983, creating an incentive program to stimulate the development of drugs for rare diseases, known as orphan drugs. The law argues that these drugs would never be developed without the government intervening to “reduce the costs of developing such drugs and to provide financial incentives to develop such drugs,” and
insists that it is “in the public interest to provide such changes and incentives for the development of orphan drugs” (Orphan Drug Act of 1983).

Once a drug is ready for clinical testing, the pharmaceutical company can apply to the FDA for orphan designation. This means that the set of drugs that the government considers for orphan designation consists of treatments for rare diseases that have already progressed through initial development and pre-clinical stages. Although success in human trials is in no way guaranteed, the basic science of these potential orphan drugs is already established. The government is not considering chemically impossible drugs, for example. So long as the potential treatment seems viable and the intended disease has less than 200,000 patients, the drug is granted orphan status, making it eligible for the law’s two main incentive tools. The first incentive, a tax credit, refunds 50% of the drug’s clinical drug testing costs (Orphan Drug Act of 1983). This subsidy directly lowers the cost of conducting human clinical trials, which are required to test the efficacy and safety of drugs. Due to the length of time and number of participants they require, clinical trials are costly undertakings, typically accounting for 2/3 of total new drug development expenditures for drugs. Although orphan drug clinical trials are typically smaller and shorter, and thus less expensive than clinical trials for non-orphan drugs, human clinical trials still account for the largest percentage of orphan drug development costs (DiMasi, 2003). Thus, the subsidy significantly diminishes the cost of the most expensive part of the drug development process, which not surprisingly comes at great cost to the government. In 2007, after a little more than two decades of the orphan drug program, the development subsidies had cost the government a total of $2 billion in lost tax revenue. With the expansion of the orphan drug industry in recent years, the government has
begun spending more than that annually. In fact, the White House predicts that the government will spend $38.9 billion subsidizing orphan drugs between 2015 and 2020 (U.S. Office of Management and Budget, 2016).

The second incentive is seven years of market exclusivity (Orphan Drug Act of 1983). Unlike simple patent protection, which protects the chemical compound of a drug from being manufactured and sold by competitors, exclusivity prohibits competitors from marketing any new drug for the treatment of the same disease. This ensures that the pharmaceutical company has monopoly control of the entire market for that disease. Exclusivity only begins once a drug is approved, while patent protection on the chemical compound usually starts before clinical trials even begin. On average it takes between ten and fifteen years to develop a single drug, but exclusivity helps ensure monopoly control of the disease market, even typical twenty-year patent is close to expiring by the time the drug goes to market (DiMasi, 2003). Sometimes pharmaceutical companies take existing chemical compounds from the public domain and develop them as treatments with new indications for orphan diseases. In these cases no patents are available, but, with exclusivity, the pharmaceutical companies receive at least seven years of monopoly control of the revenue stream for treating those diseases. While subsidies reduce costs of drug development upfront, exclusivity expands potential revenue from the drug in the future. Both increase the expected profitability of orphan drugs.

The application of subsidy and exclusivity has stimulated the development of orphan drugs. Once considered an unprofitable liability, adding an orphan designated drug to the development pipeline now increases a firm’s market value (Rzakhanov, 2008). According to the FDA’s orphan drug database, since the law was passed in 1983,
3693 drugs have received orphan designation, 526 of which have been approved for sale. The law was considered so successful that it has subsequently been adopted in other important markets, notably Japan in 1993 and the European Union in 2000 (Evaluate Pharma, 2015). Orphan drug sales are now growing at double the rate of the rest of the prescription market, and orphan drugs are making up larger percentages of pharmaceutical company’s drug portfolios than before. Not only are orphan drugs proving profitable, becoming big business for pharmaceutical companies, they are also benefitting patients. In a 2013 study, Lichtenberg determined that new orphan drug approvals had reduced premature mortality from rare diseases in the United States and France over the previous decade. In the United States, potential years of life lost to rare disease before age 65 had declined at an average annual rate of 3.3%.

In a separate paper, Lichtenberg demonstrates that by incentivizing the development of drugs for rare diseases, the Orphan Drug Act reduces the dependence of patients’ health on the market size of their disease. He asserts though that it remains unclear whether this effect is efficient for total welfare (Lichtenberg, 2003). Many people disagree with spending such large sums of public and private funds on diseases affecting only a small percentage of the population. As a 2014 survey suggests, most citizens, unaware of the existing Orphan Drug Act, do not actually support the idea of funding drugs for rare diseases at the cost of treatments that could help more people (Drummond, 2014). There is an opportunity cost for each dollar spent on orphan drug development, because those funds could be spent on diseases and medical treatments that affect more people. From a strictly utilitarian perspective, funding the development of orphan drugs that help so few people is difficult to justify (Paulden, 2015). The government is instead
valuing an ethical obligation to help the small minority suffering from untreatable rare diseases in order to ensure all citizens a basic minimum standard of health (Paul, 2002).

It still remains unclear whether the incentives in the law are being awarded in an efficient manner. Analyzing the law’s success by looking at drug approval numbers ignores the differences between the types of drugs that get developed, particularly the difference between drugs that represent true pharmaceutical innovation and those that represent only marginal improvements on pre-existing drugs (Yin, 2008). A novel drug is one that represents a significant medical advance, providing treatment where it did not exist before. Although orphan drugs typically constitute around 50% of all the novel drugs approved by the FDA each year, far less than half of approved orphan drugs are novel. According to the FDA drug database, in 2014, 46 orphan drugs were approved, but only 17 were considered novel. This means that a significant portion of orphan drugs, receiving all the incentives provided by the law, may offer only marginal improvements over previously existing treatments. Although these marginal improvements still provide health benefits to consumers, they do not provide as much health benefit as the novel drugs for which there are far fewer alternative treatments. Thus, orphan drug subsidy funds spent on these marginal improvements are not generating as much social benefit as subsidy funds spent on novel drugs would. Despite this opportunity cost of subsidizing the marginal improvement drugs, the FDA does not differentiate between orphan drugs when awarding subsidy and exclusivity.

As the number of orphan drugs continues to grow and the subsidies create a greater strain on government resources, it seems increasingly necessary to develop criteria for differentiating between orphan drugs when granting subsidies. Bioethicists
have long argued that cost-benefit analyses should be applied to the healthcare system and more cost-beneficial drugs should receive some preference for subsidy (Paul, 2002). This implies that the government should consider other characteristics that are indicative of a drug’s benefit to consumers, beyond just the patient population limit for orphan drugs, when awarding subsidy. For example, the health benefits offered by a drug and the number of existing substitutes for that drug both affect how much the drug will benefit consumers. The fact that the amount of subsidy currently awarded is not a function of these kinds of considerations, which drive consumer demand for the drug, fosters a disconnect between pharmaceutical firms and patients. Pharmaceutical companies embark on the most profitable drug development projects, such as the marginal improvements on existing drugs, which are less expensive projects, as opposed to the most socially beneficial drug projects, like novel drugs. This dilutes the power of the funds that taxpayers are putting towards orphan drug development.

Although exclusivity does not come at a direct monetary cost to the government, it shifts the cost burden of drug development to consumers. Henry Waxman, the very congressman who originally sponsored the Orphan Drug Act, has since acknowledged “the pharmaceutical industry has taken advantage of the incentives to charge excessive profits and to reap windfalls far in excess of their investments in the drug” (Seattle Times, 2013). As Garber explains, “Orphan drugs have commanded extraordinary profits because the Orphan Drug Act offered exclusive rights to sell a drug in a price-insensitive market” (Garber, 1994). Pharmaceutical companies can take advantage of patients desperate for new treatments by using the monopoly power granted by exclusivity to charge high prices. Without exclusivity rights, new drugs would enter the competitive
markets sooner, driving down their price and enabling more sick patients to access treatment. Exclusivity increases profits, ensuring that orphan drugs get developed and making patients better off overall, but the burden of exclusivity on consumers varies between drugs. For example, exclusivity on a drug that has many preexisting substitutes creates less of a burden on consumers than exclusivity on a drug for a disease without any other treatments, a more desperate case. This more desperate case is the same drug that would generate more social benefit from subsidies, suggesting that incentivizing the drug more with subsidy than exclusivity would be beneficial for consumers.

The Orphan Drug Act is widely criticized in the media for enabling pharmaceutical companies to generate large profits. Proposed reforms for the law have included implementing price regulation and requiring subsidies to be paid back once the drug becomes profitable. While both of these options would reign in the profits being commanded by orphan drugs, they would also hinder orphan drug development by weakening the incentives and scaring off potential developers (Wellman-Labadie, 2010). Rather than hindering drug development, the government could focus on making the law’s existing incentives more efficient, by adjusting the method of subsidy and exclusivity allocation. My model examines the burden of exclusivity on consumers based on characteristics of their demand, as discussed above, and explores how the government can optimally allocate subsidies and award exclusivity accordingly, ensuring an efficient use of limited funds.
3. **A Model of Drug Development**

My model of drug development is a one-shot game between the government and pharmaceutical companies. The government first considers the exogenously given set of available drug projects, the set of scientifically feasible drugs that have advanced through preclinical trials and are ready for human clinical trials. The government then determines the level of subsidy and exclusivity offered to each drug. The firms move second, reacting to the policy and determining which drug projects to continue developing based on the policy. The firm’s binary development decision, whether or not to continue development, is based on the profitability of the drug, which is affected by the government’s incentives.

3.1 **The Government**

The socially benevolent government’s objective is to maximize the social surplus generated by a drug, meaning the consumer surplus generated by the drug less the cost of the subsidy to the drug. Thus the socially benevolent government sets the amount of
subsidy and the number of years of exclusivity awarded to a drug in order to maximize this value. Consumer surplus acts as a proxy for the health benefits of the drug, because willingness to pay reflects consumer benefit from a social perspective. However, using willingness to pay to value health benefits is problematic because it disregards the fact that consumer surplus also reflects consumers’ ability to pay.¹ For example, consider two patients for the same drug. The first patient only receives moderate health improvement from the drug, but is comfortably able to purchase the drug because he is rich. The second patient sees major health improvements from drug, but struggles to purchase the drug because he is poor. Although the second patient receives greater health benefit from the drug, the first patient has a higher marginal value for the drug because he can afford to pay higher prices. In this example, the patient who experiences more health benefits generates less consumer surplus. For the sake of this model, I assume that the effect of income on willingness to pay is minimal and that consumer surplus adequately represents health benefit.

Consumer surplus during exclusivity ($J_i$), as labeled in figure 3.1, represents the benefit to consumers while the firm maintains monopoly pricing. I assume that the drug enters a perfectly competitive market after exclusivity expires. The consumer surplus after exclusivity ends ($G_i$) represents the benefit that consumers realize once the drug becomes subject to competitive pricing indefinitely. I assume that the marginal cost of producing the drug, simply manufacturing a pill, is constant, so I normalize the marginal cost to zero. Because competitive pricing makes the drug cheaper, consumer surplus is

¹ Some scholars have argued that there are actually reasonable adaptations of willingness to pay that can account for income distribution. As Bala explains, “statistical techniques can be used to adjust for income to estimate an income-adjusted willingness to pay.” (Bala, 1999)
greater after exclusivity ends, encompassing the entire triangle underneath the demand curve in figure 3.1. Adding years of exclusivity does not have a direct monetary cost. However, there is an implicit cost because each year a drug spends in exclusivity is a year consumers face monopoly pricing.

Figure 3.1: Aggregate Consumer Demand Curve

In order to develop a government objective function, we consider the consumer surplus generated during and after exclusivity, as well as the total number of years of exclusivity ($Y_i$) and amount of subsidy ($S_i$) awarded to the drug. For the sake of tractability, I will work with a continuous time framework instead of a discrete one. This assumes that years of exclusivity can be awarded in infinitely small increments. Future consumer surplus is discounted back by an exponential discount rate $\delta$ such that $\delta > 0$ in
order to generate the present value of future returns. Thus the social benefit of drug $i$ is represented by

$$\phi_i = -S_i + \int_0^{Y_i} e^{-\delta t}(J_i) \, dt + \int_{Y_i}^\infty e^{-\delta s}(G_i) \, ds$$

The first component of the social benefit function is the government’s outlay of subsidy funds during the development period. The second component is the consumer surplus that society captures once the drug is available for sale, at time 0, until the end of exclusivity in year $Y_i$. The third component is the full consumer surplus that society captures indefinitely after exclusivity ends.

The government wants to maximize social welfare by maximizing the sum of the social benefits of all $n$ unique drugs that get produced: $\sum_{i=1}^n \phi_i$. A summation of social benefits assumes that the marginal benefit of orphan drugs is not diminishing and that the social benefit values of orphan drugs are all independent of each other, meaning there is no overlap in R&D. The summation also assumes that the government is risk neutral. The government is subject to two constraints. The first constraint is the firm’s participation constraint. Firms will only continue develop drugs when expected economic profit is at least zero. This means that if the government wants a given drug to be developed, it must ensure that the firm receives enough incentive so that expected profit from the given drug is nonnegative. The second constraint is the government’s subsidy budget constraint, $\bar{S}$. If the government does not have unlimited money to spend on drug subsidies, then it must determine how to divide its budget amongst the $n$ drugs. This subsidy budget constraint is
determined by the amount of funds the government is willing to allocate to the orphan drug program. Thus, the government’s objective function is

$$W_n = \sum_{i=1}^{n} \phi_i(S_i, Y_i) \ s.t. \ \sum_{i=1}^{n} S_i \leq S \ and \ \pi_i \geq 0 \ \forall i = 1 \ldots n.$$ 

### 3.2 The Firm

When considering the expected profit a particular drug project offers, the firm considers the necessary fixed cost of development, as well as the per-period monopoly profits from selling the drug. Fixed cost of development ($C_i$) reflects research and development costs for the drug, while the aggregate demand curve for the drug reveals producer surplus under monopoly pricing ($A_i$), as depicted by the shaded region in figure 3.1. Again, I assume that the marginal cost of producing the drug is zero. Thus, the producer surplus value represents the returns from the drug during a year of exclusivity. When exclusivity ends, the drug becomes subject to competition, driving down the price (and economic profits) to zero. Thus under my assumptions, the firm only generates meaningful returns on a drug during exclusivity.

The firm’s profit function depends on the amount of incentive the given drug will receive from the government. The total number of years of exclusivity ($Y_i$) and amount of subsidy ($S_i$) the drug receives are endogenous to the model, as they are chosen by the government. In the development stage, the firm loses money to development costs, but the loss is reduced by subsidies. Once the drug is available for sale, at time 0, the firm captures producer surplus until the end of exclusivity. After exclusivity ends, I assume
that the firm captures no producer surplus due to competition from generic entrants with the same constant marginal cost.\textsuperscript{2} Future producer surplus is discounted back with the same discount rate used in the government’s social benefit function in order to generate a present value for the producer surplus provided by the drug. Thus the expected profit of a drug i is represented by

\[
\pi_i = -(C_i - S_i) + \int_0^{y_i} e^{-\delta t} (A_i) \, dt + \int_{\hat{y}_i}^{\infty} e^{-\delta s} (0) \, ds
\]

The function demonstrates how both subsidies and years of exclusivity increase the drug’s profit. Although they operate differently, both incentives increase the expected profit from a drug. For some amount of subsidy, there is some number of years of exclusivity that could enable the drug to reach the same profit level. For example, if the government wants to boost a firm’s profits to zero using only subsidies, they have to award the difference between drug’s fixed costs and the drug’s future profits. If they want to boost profits to zero using only exclusivity, they have to extend years of exclusivity so that future profits equaled fixed costs. This suggests that the government is able to fully incentivize the firm using either subsidies or exclusivity, a notion that I demonstrate in the Results section. Ultimately the firm will enter in to a drug development project when the economic profit is made to be at least zero with either incentive, because firms are

\textsuperscript{2} Pharmaceutical companies typically expect to lose out on profits once their drug goes generic. As a 2011 New York Times Article explained, “Pfizer stands to lose a $10-billion-a-year revenue stream when the patent on its blockbuster cholesterol drug Lipitor expires and cheaper generics begin to cut into the company’s huge sales.” In fact, the article continues, “Consumers should see a financial benefit as lower-cost generics replace the expensive elite drugs.” (New York Times, 2011)
motivated to enter a market whenever there is expected profit. More precisely, the firm’s entrance constraint is nonnegative profit.

4 Results
Based on the set of available drug projects, the government chooses its incentive policy, determining the amount of the two incentives each drug project will receive, in order to maximize social welfare. The firm then chooses whether to go forward with each drug project based on the given incentives. We will now solve for the government’s optimal incentives policy using backwards induction, first solving for the firm’s problem for a given set of incentives.

As we saw in the model, the government seeks to maximize total social welfare subject to the firms’ entrance constraint on profit and the subsidy budget constraint.

$$\max_{S_i, Y_i} W_n = \sum_{i=1}^{n} \phi_i \quad s. t. \sum_{i=1}^{n} S_i \leq \tilde{S} \text{ and } \pi_i \geq 0$$

Without government assistance, orphan drugs would have negative profits. Firms will develop the drugs whenever the incentives make expected profits nonnegative, but the government does not want to over-incentivize orphan drug development. In order to avoid wasting subsidy funds or awarding excessive years of exclusivity, the government wants orphan drug profits to equal zero. Providing the firms with just enough incentives to have profits of zero ensures that orphan drugs are getting developed with the minimum amount of government assistance. The consumer is indifferent to the amount of profits generated by the firm, so long as the drug gets developed. Thus, there is no need for the
government to spend more than necessary for the drug to be incentivized. In order for the
government to maximize total social welfare, the firm’s entrance constraint binds at 0.

4.1 Unconstrained Government

To develop intuition we first consider the case where the government, unconstrained with
subsidies, wants to incentivize one drug. Although there are costs to the subsidies, the
constraint is unbinding. The government must decide how to incentivize this one drug,
meaning what combination of subsidy and exclusivity it should use, in order to maximize
the social benefit provided by the drug.

$$\max_{S_i} \phi_i(S) \text{ s.t. } \pi_i = 0$$

As discussed earlier, both subsidy and exclusivity increase the profitability of a drug. In
order to demonstrate that the government can use either tool to incentivize a firm, we first
confirm that both incentives unambiguously increase the profitability of a drug.

$$\pi_i = -(C_i - S_i) + \int_0^{Y_i} e^{-\delta t}(A_i) + \int_{Y_i}^{\infty} e^{-\delta s}(0)$$

$$\left. \frac{\partial \pi_i}{\partial S_i} \right|_{Y_i} = 1$$

$$\left. \frac{\partial \pi_i}{\partial Y_i} \right|_{S_i} = e^{-\delta Y_i}(A_i)$$
The partial derivatives of profit with respect to subsidy and with respect to exclusivity are both unambiguously positive when the other incentive is held fixed. If we start at some initial level of the two incentives such that drug profit equals zero, an increase in one incentive requires a decrease in the other in order to maintain profit at zero. Thus under optimal policy when subsidies increase, years of exclusivity must decrease, or visa versa, in order to keep profit constant. Due to this inverse relationship between subsidy and exclusivity when profit is constrained to zero, the social benefit of a single drug can be rewritten in terms of exclusively subsidies.

Setting the drug profit function equal to zero yields:

\[ \pi_i = -(C_i - S_i) + \int_0^{Y_i} e^{-\delta t}(A_i) = 0 \]

\[ \int_0^{Y_i} e^{-\delta t}(A_i) = (C_i - S_i) \]

Solving for years of exclusivity yields:

\[ e^{-\delta Y_i} = 1 - \frac{\delta}{A_i} (C_i - S_i) \]

\[ Y_i = -\ln \left[ 1 - \frac{\delta}{A_i} (C_i - S_i) \right] / \delta \]

Plugging the years of exclusivity value calculated from the profit function above into the function for social benefit of the drug yields:

\[ \phi_i(S)_{\pi_i=0} = -S_i + \left( \frac{J_i}{\delta} \right) + \frac{1}{\delta} (G_i - J_i) \left[ 1 - \frac{\delta}{A_i} (C_i - S_i) \right] \]
In order to solve the maximization problem, the government must examine when awarding subsidy to the drug has a positive impact on the social benefit provided by the drug, which leads to the following derivative:

\[
\frac{d\phi_i(S)}{dS_i}\bigg|_{\pi_i=0} = \frac{G_i - A_i - J_i}{A_i}
\]

This total derivative of the drug’s social benefit with respect to the subsidy granted to the drug reflects the marginal social benefit of using subsidies over years of exclusivity to incentivize the drug. The numerator, \(G_i - A_i - J_i\), is the deadweight loss generated by monopoly pricing, as depicted in figure 1. The denominator, \(A_i\), is producer surplus. The derivative captures the amount of deadweight loss generated for every unit of surplus that is transferred from consumers to producers. Exclusivity makes drugs more profitable because it enables firms to earn back their R&D investment by extracting surplus from the consumer with monopoly pricing, but this transfer of surplus from consumers to producers does not occur at one-to-one rate. Rather, the deadweight loss acts as an implicit tax on the transfer of surplus. In order to increase producer surplus by one unit, consumers must lose one unit of surplus plus some deadweight loss.

The derivative is positive when consumer surplus from the drug under competitive pricing is greater than the sum of producer and consumer surplus from drug under monopoly pricing. More precisely, this derivative value is positive when some consumer surplus is lost during exclusivity. Unless the demand curve for a drug is perfectly elastic, which will never happen, there will always be some deadweight loss created by monopoly pricing, and so the derivative value will always be positive. The
derivative implies that the main benefit of using subsidy is that it allows a decrease in the number of years of monopoly control. Subsidy incentivizes the firm to develop the drug without any of accompanying deadweight loss, the implicit tax. Thus subsidy is always the preferred incentive because it incentivizes drug development without diminishing consumer surplus and creating deadweight loss. Although development costs do not appear in the derivative, but they do affect how much incentive the drug needs to become profitable. The greater the cost of the development, the more subsidy the drug will need to meet the zero profit constraint.

The previous argument can be expanded to the case where the unconstrained government wants to incentivize many drugs. Just as one drug’s social benefit can be written in terms of subsidies, the summation of the social benefits of many drugs can be written in terms of the subsidies to each drug. The government wants to maximize this summation of the social benefits and is constrained by zero profit entrance constraints for all the firms.

\[
\max_{s_i} W_n(S) = \sum_{i=1}^{n} \phi_i (S) \text{ s.t. } \pi_i = 0.
\]

Since social welfare is modeled as a summation of drugs’ social benefits, the derivative of social welfare with respect to the subsidies awarded to one single drug is the same as the derivative of that drug’s social benefit with respect to the subsidy.

\[
\frac{dW_n(S)}{dS_i} = \frac{G_i - A_i - J_i}{A_i}
\]
This derivative implies that subsidy is the preferred incentive for a drug. Because incentivizing a drug with subsidy positively affects the drug’s social benefit, incentivizing a drug with subsidy positively affects the sum of all n drugs’ social benefits. Since the marginal benefit of subsidy is positive for any drug in this model and the government has an unlimited budget, subsidy is the preferred incentive for all n drugs. Incentivizing all the drugs with subsidy ensures that no deadweight loss is generated by the monopoly pricing of any drug.

**Proposition 1:** Suppose the government is unconstrained with subsidies, then the optimal policy is to incentivize all drugs with zero years of exclusivity and sufficient subsidies to ensure that \( \pi_i = 0 \) for all firms receiving assistance.

The algebra that enables us to write the social benefit of the drug in terms of subsidy intuitively captures a scenario where the government buys out the firm with the subsidy payment. The government wants to “buy” the drug project because removing the drug from a state of exclusivity will positively increase the social benefit provided by the drug. In taking ownership of the drug, the government can combine the firm’s considerations for producer surplus and its own considerations for consumer surplus. The derivative of the drug’s social benefit with respect to subsidy, \( \frac{G_i - A_i - J_i}{A_i} \), is positive when the following inequality holds:

\[
G_i - J_i > A_i
\]
This means that the government wants to subsidize, or “buy” the drug project when the consumer surplus lost during exclusivity is greater than the surplus extracted by producers during exclusivity.

4.2 Constrained Government

In reality, the government does not have unlimited funds, so it must choose how to distribute its limited subsidies amongst the n drug projects. The government still prefers to incentivize drugs with subsidy because doing so prevents the deadweight loss generated by exclusivity, but the government cannot afford to incentivize every drug entirely with subsidy. The government still wants to maximize the social welfare generated by n orphan drugs, but is now subject to two constraints. The zero profit entrance constraint still holds for all drugs, and the amount of subsidy the government can award is now limited by the budget constraint.

\[
\max_{S} \mathcal{W}_n(S) = \sum_{i=1}^{n} \phi_i(S) \text{ s.t. } \sum_{i=1}^{n} S_i \leq \bar{S} \text{ and } \pi_i = 0
\]

An optimizing government awards subsidy where it will have the greatest positive effect on total social welfare. Marginal returns on subsidies are constant within an individual drug, but differ across drugs, meaning some drugs will consistently provide higher social benefit returns on subsidy than other drugs. Thus the government needs to prioritize subsidies based on these returns. The derivative of a drug’s social benefit with respect to subsidy, \( \frac{G_i - A_i - J_i}{A_i} \), as described in the previous subsection, captures the magnitude of the
positive effect that awarding subsidies to a given will have on total social welfare. This is because, for a given drug, every one dollar transfer from consumer to producer surplus through exclusivity experiences a constant deadweight loss “tax” that could be avoided by incentivizing with subsidy instead of exclusivity. Thus the government can rank all n drugs based on their marginal benefit of subsidy value. In order to maximize total social welfare, the government should award subsidies to drug projects in descending order of their marginal benefit of subsidy values, incentivizing higher priority drugs exclusively with subsidies until funds run out. These higher priority drugs will receive no years of exclusivity, but rather be incentivized to the point of development with just subsidies. Thus the derivative of a drug’s social benefit with respect to subsidy, \( \frac{G_I - A_I - J_I}{A_I} \), effectively operates as a “subsidy priority score” for the drug. All remaining drugs are incentivized with the necessary number of years of exclusivity to ensure that their expected profits equal zero and they get developed. Although this exclusivity will still create deadweight loss, these drugs with smaller subsidy priority scores will experience less deadweight loss from monopoly pricing than drugs with higher subsidy priority scores.

**Proposition 2:** Suppose that the government is constrained with subsidies, then the optimal policy is to award 0 years of exclusivity and sufficient subsidies to ensure that \( \pi_i = 0 \) to drugs in descending order of their \( \frac{d\Phi_I(S)}{dS_i} = \frac{G_I - A_I - J_I}{A_I} \) values. When no subsidies remain, all remaining drugs should be incentivized with sufficient years of exclusivity to ensure that \( \pi_i = 0 \).
When subsidies are constrained, the government can no longer “buy out” all drug projects, as discussed previously. The new intuition, in this constrained scenario, is that the government must pick which drug projects to buy with its limited subsidy budget. As Proposition 2 reveals, the government wants to subsidize, or “buy” the drug projects that experience the greatest marginal benefits of subsidy, as these drugs will provide the greatest social benefit gains when removed from exclusivity. Exclusivity enables firms to capture surplus from consumers, so the government wants to intervene and buy drug projects when the potential loss to consumers from exclusivity is at its greatest.

5 Discussion

The current Orphan Drug Act provides every orphan drug with a combination of subsidy and exclusivity, but my optimal incentives scheme establishes a more binary system of orphan drug incentives. In order to maximize the social welfare generated by the orphan drug industry, the government should incentivize every drug with entirely subsidy or entirely exclusivity, not a combination of the two. (At the point where subsidies run out, there could be a drug on the margin that receives both incentives.) This effectively establishes two types of orphan drugs, those that should receive subsidy and those that should receive just exclusivity. In practice it would be impossible for the government to perfectly discern the consumer demand for a drug and to employ a fluid subsidy priority ranking system, but by examining more evident characteristics of consumer demand, the government could strive to more broadly categorize orphan drugs as subsidy or exclusivity drugs as a matter of practicality.
5.1 Characteristics of Consumer Demand

As demonstrated in the Results section, the ratio of deadweight loss to producer surplus generated by a drug during exclusivity captures the marginal benefit of incentivizing a drug with subsidies as opposed to exclusivity. This ratio operates as the drug’s subsidy priority score and determines how the drug gets incentivized. In order to gain intuition about how particular characteristics of demand for a drug will affect the ratio, I examine an environment where drugs have polynomial demand curves of the general form

\[ Q(P) = a - bP - cP^2, \]

where \( a, b, \) and \( c \) are constant parameters. Given this quadratic equation of demand for a drug and my assumption that the marginal cost of producing a drug is zero, we can solve for the quantity \((Q_m)\) and price \((P_m)\) of the drug that will be produced by the profit-maximizing monopolistic firms. We solve for these monopoly levels by determining the point on the demand curve at which profit is maximized.

\[
\max(\pi = Q \times P):
\]

\[
\frac{d\pi}{dP} = a - bP - cP^2 + P(-2cP) = 0
\]

\[
P_m = \frac{-b + \sqrt{b^2 + 3ac}}{3c}
\]

\[
Q_m = Q(P_m) = a - \frac{b(-b + \sqrt{b^2 + 3ac})}{3c} - \frac{(-b + \sqrt{b^2 + 3ac})^2}{9c}
\]

These values allow us to solve for the producer surplus and deadweight loss generated by the quadratic demand curve. The producer surplus is the area of the square created by monopoly price and monopoly quantity, as seen in figure 5.1. The deadweight loss is
defined as the region between the monopoly quantity and the demand curve, integrated from the competitive price (0) to the monopoly price.

Producer Surplus = \( P_m \times Q(P_m) \)

Deadweight Loss = \( \int_{0}^{P_m} Q(P) - Q(P_m) \, dP \)

Figure 5.1: Polynomial Aggregate Demand Curve

Dividing deadweight loss by producer surplus yields the subsidy priority score.

Subsidy Priority Score = \( \frac{DWL}{PS} = \frac{\int_{0}^{P_m} Q(P) - Q(P_m) \, dP}{P_m \times Q(P_m)} = \frac{3c\left(\frac{b^3}{81c^2} - \frac{ab}{18c} \right) \frac{b^2}{81c^2} + \frac{2a\sqrt{b^2 + 3ac}}{27c}}{(-b + \sqrt{b^2 + 3ac})(a - \frac{b(-b + \sqrt{b^2 + 3ac})}{3c} \left(\frac{-b + \sqrt{b^2 + 3ac}}{9c}\right)^2} \)
We now have the subsidy priority score written in terms of the three parameters of the polynomial demand equation \((a, b, \text{ and } c)\), which means we can examine how the individual parameters affect the subsidy priority score. The contour map in Figure 5.2 reveals the effects of \(b\) and \(c\) on the subsidy priority score when \(a\) is held constant. As the map gets lighter, subsidy priority score increases.

Figure 5.2: Subsidy Priority Score as Affected by Demand Parameters \(b\) and \(c\)

The contour map shows that as \(b\) increases and \(c\) decreases, moving towards the southeast corner of the graph, subsidy priority score increases. Increasing \(b\) while holding the other two parameters constant increases subsidy priority. Looking back to the equation for demand, the demand curve becomes less price responsive as \(b\) increase. This
mean as $b$ increases, the price elasticity of demand for the drug decreases. Thus all else equal, drugs with more inelastic demand curves receive higher subsidy priority. The number of substitutes available for a drug is one tangible factor that drives elasticity. Drugs with fewer substitutes have more inelastic demand curves, so their subsidy priority scores are higher. This confirms the intuition in the Introduction that, all else equal, a novel drug like Kanuma should receive more subsidy than a drug with many substitutes, like Uptravi.

The contour map shows that increasing $c$ while holding the other two parameters constant decreases the subsidy priority score. Looking back to the equation for demand, as $c$ approaches 0, the demand curve approaches a linear shape because $c$ is the parameter in front of the quadratic term. If $c$ becomes negative, the demand curve becomes concave. This creates a certain distortion across the demand curve. As $c$ decreases, price responsiveness decreases more quickly in the higher price region of the curve than the lower price region of the curve. When the demand for the drug is less elastic at higher prices, and more elastic at lower prices, the monopolist will price the drug at a higher price point in order to take advantage of the price inelasticity of consumers who are willing or able to pay more. This higher monopoly price will cut off all the consumers with lower price points from receiving the drug. As $c$ decreases, the size of this cut off population increases relative to the number of consumers that will purchase the drug. Thus, as the number of consumers cut off from purchasing the drug because of monopoly pricing increases, the drug’s subsidy priority score increases. This suggests that a drug for a disease that has a few wealthy patients and many poorer patients should receive
government subsidy because the pharmaceutical company will price the drug to capture profits from the wealthy patients, depriving poorer patients of crucial health benefits.

This simplification of demand curves and characteristics enables us to get a sense of how current orphan drugs would be incentivized under a more practical application of our optimal incentives scheme. The presence of substitutes and the distribution of the disease across the population can help inform whether a drug should receive subsidy or exclusivity.

6 Conclusion

When the government enacted the Orphan Drug Act in 1983, pharmaceutical firms responded vigorously, entering into thousands of orphan drug development projects. The orphan drug industry continues to grow at an accelerating pace, rendering the current incentives program inefficient and unsustainable. The government must eventually cap its budget for orphan drug subsidies and strive for a more optimal allocation scheme of the law’s two incentive tools, subsidies and years of market exclusivity. My thesis solves for an optimal incentive program and identifies the amount of deadweight loss experienced by an orphan drug under monopoly pricing as the key determinant of the drug’s subsidy priority. The deadweight loss represents the opportunity cost of market exclusivity, the amount of total surplus that is lost in order to increase the firm’s profits. This cost of exclusivity, dependent on characteristics of consumer demand, varies between drugs. In order to maximize the social welfare generated by the orphan drug industry, the government must identify the drugs that would experience the greatest deadweight loss from monopoly pricing and incentivize them fully with subsidies. Spending subsidies on
these drugs represents a more effective use of limited funds than spending them on drugs that would experience less deadweight loss during exclusivity.

Although the government cannot practically determine the deadweight loss that would be generated by a given drug, the government can identify certain characteristics of consumer demand, like number of available substitutes, and strive to more generally categorize orphan drugs as those that receive subsidy and those that receive exclusivity. For example, a novel life-saving drug like Kanuma should be incentivized with subsidy, in order to assure that patients without any alternative treatments are not subject to preventative monopoly pricing.

In my model I assume that the government’s subsidy budget is exogenously determined, meaning the government has some set amount of money that they want to spend on orphan drug development. In reality, the government has many ways they can spend public funds. They could spend the money incentivizing non-orphan drugs, or they could spend it on projects completely unrelated to healthcare. These other options create an external opportunity cost to orphan drug subsidies. In my model I assume that the only opportunity cost to subsidies is that they could be spent on different orphan drug projects. In the future, I would like to expand my model to account for the external opportunity cost to these subsidies. Accounting for the opportunity cost would more accurately capture the government’s operations in their entirety and would likely prevent subsidies from being as strongly favored as they are in my model.

In my model, I also assume that all orphan drug projects are completely independent from each other, meaning there is no overlap in their research and development efforts. In reality, the research a firm carries out for one drug development
project can likely be put to use in future drug development projects. Anushree Subramaniam, a current Ph.D candidate at University of Chicago, has examined the effects of this research “spillover.” She finds that there is a high degree of spillover between orphan and non-orphan drugs, which means orphan drugs can wind up being more profitable investments for pharmaceutical companies than initially expected (Subramaniam, 2015). In the future, I would also like to expand my model to include the degree of research spillover than an orphan drug offers. Presumably, if the research done for an orphan drug will serve as a valuable asset for more profitable projects down the line, the firm likely requires less government incentive to develop the drug.

As it currently stands, the Orphan Drug Act has expanded medical horizons and saved lives, but a more careful analysis of the benefits provided by orphan drugs to both consumers and the pharmaceutical firms would enable the government to more efficiently allocate subsidies and exclusivity. A more refined distribution of these incentives would enable the government to optimize the social welfare generated by a booming industry.

References


Drummond, M., & Towse, A. (2014). Orphan drugs policies: A suitable case for


U.S. Office of Management and Budget. (2016). *Analytical Perspectives, Budget of the*
