Incentive Programs for Neglected Diseases

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Honors Thesis submitted in partial fulfillment of the requirements for Graduation with Distinction in Economics in Trinity College of Duke University.

Duke University

Durham, North Carolina

2020

Acknowledgements

I would like to thank my faculty advisors, Professor David Ridley and Professor Pino Lopomo, for their unrelenting guidance and support throughout this project. Their patience, valuable feedback, and genuine willingness to help have greatly contributed to my learning at Duke University and beyond. This thesis would not be possible without their mentorship. I would also like to thank my honors seminar instructor, Professor Michelle Connolly, for nurturing my idea from its early stages, providing vital feedback, and lending herself as a wonderful resource. Next, I would like to thank my friends for tirelessly listening to my ideas and encouraging me. Last but not least, I owe an immense amount of gratitude to my parents for supporting my education every step of the way and helping me become the person I am today.

Abstract

We propose and evaluate an auction mechanism for the priority review voucher program. The 2007 voucher program rewards drug developers for regulatory approval of novel treatments for neglected tropical diseases. Previous papers have proposed auctioning vouchers for the priority review voucher program but have offered neither a mathematical model nor a framework. We present a mechanism design problem with one pharmaceutical company producing one drug for a neglected tropical disease. The mechanism that maximizes the regulator's expected surplus is a take-it-or-leave-it offer, with three different offers based on low, intermediate, and high neglected disease burdens. We demonstrate how mechanism design can be applied to settings in which the buyer pays for public access to a product with regulatory speed. Finally, this paper may be useful to policymakers seeking to improve access to voucher drugs through modifications of the program.

1   Introduction

Neglected tropical diseases are communicable diseases that prevail in tropical and subtropical conditions in 149 countries (World Health Organization, 2020).[1] They affect more than one billion people and cost developing economies billions of dollars every year. They primarily affect people living in poverty (World Health Organization, 2020). Examples of neglected diseases include malaria, cholera, Chagas disease, leprosy, and lymphatic filariasis.

Despite their pressing effects on global health, neglected diseases have been historically ignored by the pharmaceutical industry. Of the 850 new therapeutic products registered with the U.S. Food and Drug Administration (FDA) between 2000 and 2011, less than 1% were indicated for neglected diseases (Weng, Chan, and Wang, 2018). Similarly, only 66 novel products designed to treat or prevent neglected diseases entered Phase 1 clinical trials from 2010 to 2014. This represents less than 2% of the 4006 phase I trials in that period (Weng et al., 2018). This phenomenon can be explained by the inherently costly and risky nature of drug development, and low expected returns for neglected disease drugs (Barofsky & Schneider, 2017). The significant investments in capital and time for a pharmaceutical company to develop a neglected disease drug create barriers to innovation.

To address this lack of innovation, the FDA Priority Review Voucher System was established as part of the Food and Drug Administration Amendments Act (FDAA) of 2007 (Ridley, 2020). Initially proposed by Duke University professors David Ridley, Henry Grabowski, and Jeffrey Moe (2006), the program grants one transferrable priority review voucher (PRV) to a company developing a drug for a neglected disease. Two drugs receive priority review for each voucher: the drug for the neglected disease winning the voucher as well as any other new drug application. Under priority review, the FDA aims to complete drug review in six months, instead of the standard 10 months. Ridley and Régnier (2016) show that earlier approval by a few months can be worth hundreds of millions of dollars. The voucher can also be transferred or sold an unlimited number of times (Ridley et al., 2006). This transferability has created an active secondary market, commanding voucher sales up to $350 million. Vouchers were initially introduced to encourage development for neglected diseases but have been since amended to include rare pediatric diseases and medical countermeasures. The FDA has awarded a total of 34 vouchers, with 22 for rare pediatric disease, 11 for neglected disease, and two for medical countermeasures by the end of 2019 (Gaffney, Mezher, and Brennan, 2020). A medical

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[1]Henceforth, we will refer to neglected tropical diseases as "neglected diseases".

countermeasure is a product used in the event of a potential public health emergency stemming from bioterrorism or biological warfare (U.S. Food and Drug Administration, 2018).

Implementation of the priority review voucher program has created significant impact in the neglected disease space. Innovative products such as Dengvaxia, a vaccine for the protection of dengue fever developed by Sanofi, and Krintafel, the first treatment for relapse of P. vivax malaria developed by GlaxoSmithKline, are products of the priority review voucher (Sanofi, 2019; GlaxoSmithKline, 2018). The voucher has made investors more willing to fund entrepreneurs developing drugs for neglected diseases (Ridley, 2020). In a recent report by the U.S. Government and Accountability Office (2020), all seven drug sponsors that were interviewed said that the voucher was a factor in their drug development decisions. Despite these outcomes, many have also criticized the voucher program and raised questions surrounding its efficacy in providing access to the developed drugs and addressing the burden of neglected diseases. Many critics argue that the program does not mandate the company to ever sell the drug or set any standards regarding feasibility or cost-effectiveness for implementation in low resource settings (Gaffney et al., 2020).

Previous literature has explored the idea of tying the priority review voucher reward with the company's willingness to bring the neglected disease drug to market. Various stakeholders have called upon the FDA to mandate drug sponsors to submit an access plan to be eligible for the voucher program. This would ensure that the drugs reach the populations in need of treatment. Some have suggested alternative mechanisms, such as an auction designed by the FDA, as a potential improvement to the voucher program. Economics literature has largely ignored theoretical models of the voucher program.

We propose and evaluate an auction mechanism for the priority review voucher program, incorporating access mandates as part of the mechanism. We demonstrate how mechanism design can be applied to settings in which the buyer pays for public access to a product with regulatory speed.

2 Literature Review

2.1 Federal Auctions

Many U.S. federal agencies conduct auctions as a means of allocating resources. The U.S. Department of the Interior holds the mineral rights to offshore lands and began auctioning rights to these lands in 1954 (Milgrom & Weber, 1982). Robert H. Porter's paper, "The Role of Information in U.S. Offshore Oil and Gas Lease Auctions", analyzes bidding strategies for these leases and equilibrium models for these decisions (1995). The U.S. Treasury also sells billions of dollars of notes and bills through auctions (Milgrom & Weber, 1982). Robert Weber, co-author of "A Theory of Auctions and Competitive Bidding" with Paul Milgrom, argued that uniform-price and ascending-bid auctions would yield greater revenue for the Treasury than discriminatory price auctions (Weber, 1992). Roberts and Sweeting (2012) study federal auctions of timberland in California, where the U.S. Forest Service sells logging contracts to individual bidders such as mills and loggers. The authors make a variety of assumptions in their model that could be applied to an auction sponsored by the FDA. They assume independent private values for bidders, non-collusive bidder behavior, imperfect signals of value to bidders, and participation costs for entry to the auction (Roberts & Sweeting, 2012). Their analysis demonstrates that in an environment where it is costly for potential buyers to participate and where buyers receive imperfectly informative signals about their values prior to entry, a sequential auction mechanism generates higher revenues for the sellers and is more efficient (Roberts & Sweeting, 2012). Drug development also represents an environment where it is costly for buyers to participate and where there may be imperfect information in the market. Thus, Roberts' and Sweeting's work provides critical insight in constructing an auction for the voucher program. Economists have suggested auctions to federal agencies as mechanisms of greater social welfare and economic efficiency. Ronald Coase explored this idea with a seminal paper in 1959 on the Federal Communications Commission (FCC) and broadcasting licenses. At the time, broadcasting licenses were not issued automatically but rather granted or withheld at the discretion of the FCC (Coase, 1959). Coase argued that the system in place would naturally result in misallocation of resources. He advocated for competitive market forces by letting the rights to broadcast be disposed to the highest bidder. Though Coase was initially harshly criticized for his ideas, the FCC has auctioned licenses for the electromagnetic spectrum since 1994 (Hazlett, 2009). The FCC's transition to auctioning licenses provides a relevant

parallel to the FDA's proposed switch. The literature on auctions run by various federal agencies provides an important foundation for proposing an auction run by the FDA, imparting insight into optimal auction types, bidding strategies, and valuable theoretical models.

2.2 Auction-Based Mechanisms for Vouchers

Ridley, Grabowski, and Moe (2006) discuss the potential of auctioning a priority review voucher to a drug manufacturer. The authors suggest that the proceeds of the auction be paid to the developer of a treatment for a neglected disease. Kevin Outterson and Anthony McDonnell (2016) investigate the idea of an auction-based voucher mechanism specifically for antibiotic vouchers. Antibiotic vouchers are different than priority review vouchers in that they extend the market exclusivity period for any other drug or biologic product by a year rather than accelerate review. Therefore, an antibiotic voucher would delay generic entry of a competing drug (Outterson & McDonnell, 2016). Outterson and McDonnell (2016) suggest a mechanism where the government would directly auction several twelve-month vouchers each year and put the proceeds into an antibiotic innovation fund. The authors argue that if the fund was large enough, it could reward companies for certain milestones related to access, conservation, and innovation. This approach, if applied to priority review vouchers for neglected diseases, could resolve many of the concerns echoed by critics of the program.

2.3 Access Mandates for the Voucher Program

Kesselheim, Maggs, and Sarpatwari (2015) argue that regardless of the voucher's success in improving drug innovation, it does not ensure affordable access to the products in the U.S. or overseas. Pécoul and Balasegaram (2015) concur with this criticism of the program, citing access issues with miltefosine as evidence. Knight Therapeutics received a voucher in 2014 for miltefosine, a leishmaniasis drug. However, due to large minimum purchasing requirements and stringent distribution rights, organizations like Doctors without Borders and the Drugs for Neglected Diseases initiative have struggled to purchase affordable miltefosine and meet supply shortages. The authors recommend that Congress amend the voucher so that companies are required to ensure affordable access to any treatment that receives a voucher (Pécoul & Balasegaram, 2015). David Ridley, one of the co-authors of the program, has also supported mandatory access plans (2017).

2.4 Mechanisms for Encouraging Innovation

Various researchers have discussed mechanisms, incentives, and prizes for encouraging innovation. Though the priority review voucher program already represents an incentive for developing drugs in the neglected disease space, literature on alternate mechanisms can provide relevant background for structuring an auction for the program. Michael Kremer (1998) suggests that patent buyouts could potentially eliminate monopoly price distortions and incentives for duplicative research, while increasing incentives for original research. Kremer explores a mechanism for buying out patents and discusses key elements such as informational advantages, substitute and complementary patents, preventing collusions, and ceiling prices in the context of pharmaceuticals (1998). He concludes that governments could offer to purchase patents at their estimated private value, as determined in an auction, times a markup that covers the difference between the private and social values of the invention (Kremer, 1998). Petra Moser and Tom Nicholas, when analyzing data from the Crystal Palace Exhibition in 1851, found that ex post prizes that are awarded to high-quality innovations may encourage future innovation (2013). Furthermore, their paper suggests that publicity may be an effective mechanism by which prizes encourage innovation, in absence of a cash reward (Moser & Nicholas, 2013). Curtis Taylor presents a research tournament in which contestants compete to find the innovation of highest value to the research sponsor (1995). When the prize is large enough to support full participation, a symmetric research tournament has a unique subgame-perfect equilibrium in which each invited firm enters and employs a stopping strategy (Taylor, 1995). A stopping strategy is when a company stops doing research once it discovers an innovation worth more than some critical value. He also shows that free entry is not optimal, because high levels of entry give rise to low levels of research effort in equilibrium. Finally, the paper concludes that an optimally designed tournament balances the probability of overshooting the first-best quality level against the probability of falling short (Taylor, 1995). Taylor's work on research tournaments provides relevant information on tournament design, entry costs, and subgame-perfect equilibria for the model presented in this paper.

3   Theoretical Framework

3.1   One Company and One Disease

The design of an auction mechanism for the priority review voucher program can be simplified to a case with one pharmaceutical company developing one drug for a neglected disease. Time periods are defined in years by the variable t, with $t = 0$ marking the present day.

Company $\mathcal{C}$ can produce drug U, which can cure neglected disease α in an underserved population. Neglected disease α also poses some public health burden D on the world.[2] If brought to market, drug U generates a privately known current expected net profit π_{Ut} for Company $\mathcal{C}$. From the point of view of the FDA, π_{Ut} is drawn from a distribution f_U and support $[\underline{\pi}_U, \overline{\pi}_U]$, where $\overline{\pi}_U < 0$.

Company $\mathcal{C}$ can also produce another drug W to cure a profitable indication such as heart disease or cancer in a Western population. If brought to market, drug W generates a privately known current expected net profit π_{Wt}, and is perceived by the FDA as drawn from a distribution with a density f_W and support $[\underline{\pi}_W, \overline{\pi}_W]$, where $\underline{\pi}_W > 0$. π_U always takes negative values, but π_W is positive by definition. This is meant to capture an empirically relevant aspect of the pharmaceutical industry in the United States.

The FDA decides when Company $\mathcal{C}$ can start selling each drug. We assume that the FDA will approve both drugs, making both of their probabilities of approval equal to one. Standard approval of a drug by the FDA takes 10 months, while priority review aims for approval in six months. In this paper, we make the assumption that standard priority review occurs in six months. The FDA cannot feasibly review a drug in less than six months without compromising safety.

Additionally, it is assumed that no secondary voucher market is allowed. The total expected payoff of Company $\mathcal{C}$ is the sum of the payoff of producing drug U and the time value benefit of priority review on drug W. It is given by:

$$\mathbb{E}\left(\widetilde{\prod}\right) = q \cdot \sum_{t=.5}^{.5+T_U} \frac{\pi_{Ut}}{(1+r)^t} + \sum_{t=\epsilon}^{\epsilon+T_W} \frac{\pi_{Wt}}{(1+r)^t} - \sum_{t=\frac{10}{12}}^{\frac{10}{12}+T_W} \frac{\pi_{Wt}}{(1+r)^t}$$

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[2]D can be thought of as the number of disability-adjusted life years incurred by the disease. We expand upon this concept in Section 4.1.

where π_{Ut} and π_{Wt} represent the expected profits for drug U and drug W at time t. $q \in (0, D)$ is the scale at which drug U is brought to market or disease α is cured, and $\epsilon \in [.5, \frac{10}{12}]$ is the amount of time it takes for the FDA to approve drug W in years. We introduce ϵ to capture the idea that a voucher for drug W could hypothetically translate to a regulatory review slower than the standard priority review of six months. r is a discount rate, T_U is the duration of market exclusivity for drug U, and T_W is the duration of market exclusivity for drug W.

To simplify notation, define:

- $\Pi_U \equiv \displaystyle\sum_{t=.5}^{.5+T_U} \frac{\pi_{Ut}}{(1+r)^t}$ where Π_U is the net present value (NPV) of drug U at time t.

- $S \cdot \Pi_W \equiv \displaystyle\sum_{t=\epsilon}^{\epsilon+T_W} \frac{\pi_{Wt}}{(1+r)^t} - \sum_{t=\frac{10}{12}}^{\frac{10}{12}+T_W} \frac{\pi_{Wt}}{(1+r)^t}$ where Π_W is the NPV of drug W at time t. $S \in (0, B)$,

  or speed, quantifies the value of priority review.[3] B, or the FDA's budget, represents maximum speed in the drug approval process. Maximum speed corresponds to a voucher with FDA approval in six months, four months faster than the standard 10 month review.

Furthermore, we remove time variables to simplify notation. The simplified payoff is as follows:

$$\mathbb{E}\left(\widetilde{\prod}\right) = q \cdot \Pi_U + S \cdot \Pi_W$$

This payoff can be normalized by Π_W to make it more convenient to work with:

$$\mathbb{E}\left(\prod\right) = \mathbb{E}\left(\frac{\widetilde{\prod}}{\Pi_W}\right) = S - q \cdot c$$

where $c = -\dfrac{\Pi_U}{\Pi_W}$ represents a cost ratio. Since $\dfrac{\Pi_U}{\Pi_W}$ is always negative, we can think of c as a net relative cost. From the FDA's point of view, c appears to be drawn from a distribution with density f and support $[c_L, c_H]$. Furthermore, we assume that f is continuously differentiable on $[c_L, c_H]$. Figure 1 illustrates the support $[c_L, c_H]$.

This payoff proves to be more relevant to the priority review voucher market, as drug W is highly profitable and thus isolating the speed on W, or S, is of high interest. The FDA can reward the scale at which Company $\mathcal{C}$ brings drug U to market by accelerating the review of drug W.

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[3]Ridley and Régnier (2016) show that faster regulatory review creates value for the manufacturer through three effects: the competitive effect, the time value of money effect, and the patent effect. In this definition, we focus on the time value effect.

Figure 1
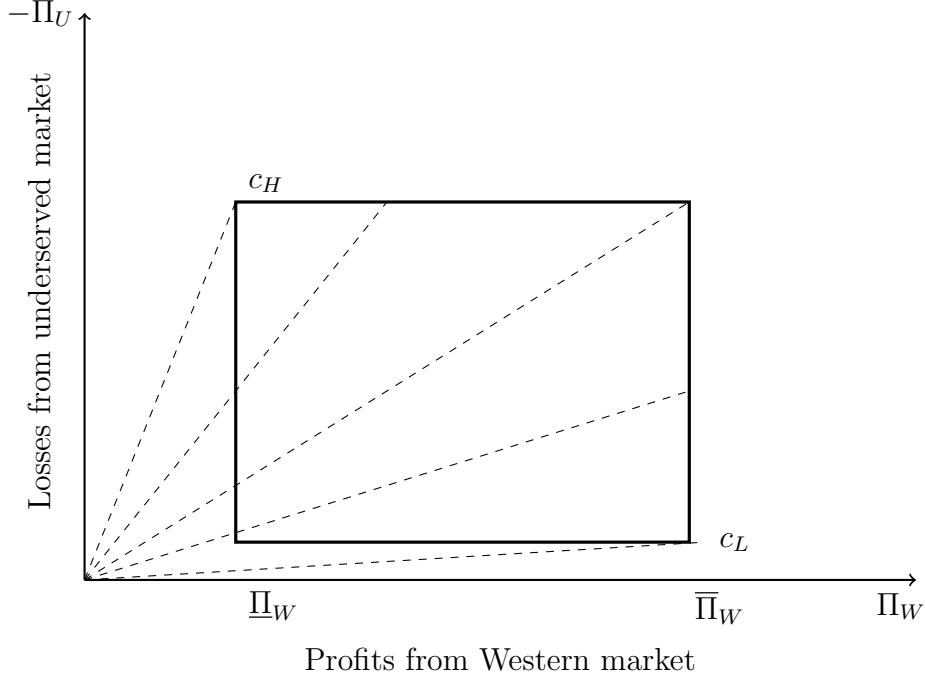
The values that the FDA puts on bringing drug U and drug W to market are v_U and v_W respectively. We assume that the FDA dislikes speeding the review of drug W. Furthermore, without loss of generality, we can normalize $v_W = 1$. The FDA's payoff is presented below:

$$\mathbb{E}\left(\prod\right) = q \cdot v_U - S \cdot v_W = q \cdot v_U - S$$

3.2 Symmetric Independent Private Values Model

In this part, we introduce a Symmetric Independent Private Values (SIPV) auction model where a buyer seeks to buy an indivisible good and faces a set $N \equiv \{1, ..., N\}$ of ex-ante identical suppliers.[4]

We present a model where the FDA is the buyer and Company $\mathcal{C}$ is the single supplier. Company $\mathcal{C}$ is privately informed about its cost ratio c. Given imperfect information, the best the FDA can do is offer a menu of choices to Company $\mathcal{C}$ based on its perceptions of c. The problem at hand is to design a menu.

The revelation principle states that given some mechanism and an equilibrium for that mechanism, there exists a direct mechanism in which 1) it is an equilibrium for each buyer to report his or her value truthfully and 2) the outcomes are the same as in the given equilibrium of the original

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[4] "Ex-ante" refers to before the game, while "ex-post" refers to after the game.

mechanism (Krishna, 2009). The revelation principle allows us to restrict attention to direct revelation mechanisms. Effectively, we use a menu and optimize over the classes of all conceivable menus.

Formally, a direct mechanism specifies:

- A function Q where $Q_i(x)$ is the probability that buyer i receives the object

- A function M where $M_i(x)$ is the payment made by buyer i

In our problem, we think of drug U's delivery to the underserved market as the object that the FDA, or buyer, receives from Company $\mathcal{C}$. This is parallel to an access mandate for the drug, or a requirement that Company $\mathcal{C}$ brings the neglected disease drug to market. The payment made by the FDA is through regulatory speed in the review of drug W, or a priority review voucher, to Company $\mathcal{C}$.

Thus, a direct mechanism specifies:

- The scale $q(c)$ in which drug U is brought to the underserved market

- The speed $S(c)$ in reviewing drug W

Formally, the interaction between the FDA and Company $\mathcal{C}$ is modeled as a three stage game:

Stage 0: Nature draws the profile of Company $\mathcal{C}$'s type from a distribution with density $f(c)$. Company $\mathcal{C}$ observes the realization of its type c privately and the FDA observes none of these realizations.

Stage 1: The FDA publicly commits to a feasible mechanism.

Stage 2: Company $\mathcal{C}$ decides whether to participate; if it declines to participate, the game ends and all parties earn zero payoff. If it decides to participate, Company $\mathcal{C}$ reports a cost value $\hat{c} \in [c_L, c_H]$ to the FDA.

Stage 3: Trade takes place and payoffs are realized according to the mechanism chosen in Stage 1 and cost profile reported in Stage 2.

3.3 The Buyer's Problem

The design problem for the FDA is

$$\max_{q,S} \int_{c_L}^{c_H} [q(c) \cdot v_U - S(c)] \, f(c) \, dc \tag{1}$$

subject to

$$q(c) \in [0, D], \quad \forall c \in [c_L, c_H]; \tag{2}$$

$$S(c) \in [0, B], \quad \forall c \in [c_L, c_H]; \tag{3}$$

$$S(c) - c \cdot q(c) \geq S(c') - c \cdot q(c'), \quad \forall c, c' \in [c_L, c_H]; \tag{4}$$

$$S(c) - c \cdot q(c) \geq 0, \quad \forall c \in [c_L, c_H]; \tag{5}$$

The constraints in 4 and in 5 impose Incentive Compatibility and Individual Rationality ex post. A mechanism is incentive compatible if the participants are best off reporting their true values (Krishna, 2009). Constraint 4 implies that Company $\mathcal{C}$ is better off reporting its true type c than lying and reporting some untruthful c'. A mechanism is individual-rational if an agent can always achieve as much expected utility from participation as without participation (Krishna, 2009). Constraint 5 implies that Company $\mathcal{C}$ is no worse off from participating in the mechanism. Thus, the strategy of reporting the true type and participating in the mechanism is weakly dominant, hence "belief-free" and "regret-free".

Before solving this problem, we present a method developed by economist Roger B. Myerson to simplify our design problem (Myerson, 1981).[5] We will show how the buyer's problem can be restated with only q variables.

Define

$$\widehat{\pi}(c', c) \equiv -c \cdot q(c') + S(c') \qquad \text{and} \qquad \pi(c) \equiv -c \cdot q(c) + S(c) \tag{6}$$

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[5]This technique is in a seminal paper that was a key component of Myerson winning the Nobel Prize in 2007.

Lemma 1. *A mechanism $\{q, S\}$ satisfies all inequalities in (4) and (5) if and only if it satisfies*

$$\pi(c) = \pi(c_H) + \int_c^{c_H} q(t)dt \tag{7}$$

and

$$q \quad nonincreasing \tag{8}$$

The proof of Lemma 1 is in the Appendix.

The equalities in (7) can be rewritten as

$$\forall c \in [c_L, c_H]: \quad S(c) = c \cdot q(c) + \int_c^{c_H} q(t)dt + \pi(c_H) \tag{9}$$

which implies

$$
\begin{aligned}
\int_{c_L}^{c_H} S(c) \cdot f(c) \cdot dc &= \int_{c_L}^{c_H} c \cdot q(c) \cdot f(c) \cdot dc + \int_{c_L}^{c_H} \int_c^{c_H} q(t) \, dt \cdot f(c) \cdot dc + \pi(c_H) \\
&= \int_{c_L}^{c_H} c \cdot q(c) \cdot f(c) \cdot dc + \int_{c_L}^{c_H} q(c) \cdot F(c) \cdot dc + \pi(c_H) \\
&= \int_{c_L}^{c_H} \left(c + \frac{F(c)}{f(c)} \right) \cdot q(c) \cdot f(c) \cdot dc + \pi(c_H)
\end{aligned} \tag{10}
$$

We substitute this result into the objective function in (1) and set $\pi(c_H) = 0$. The simplified design problem is presented below.

$$\max_q \int_{c_L}^{c_H} \left(v_U - c - \frac{F(c)}{f(c)} \right) \cdot q(c) \cdot f(c) \, dc \tag{11}$$

subject to

$$q(c) \in [0, D], \quad \forall c \in [c_L, c_H]; \tag{2}$$

$$c \cdot q(c) + \int_c^{c_H} q(t)dt + \pi(c_H) \in [0, B], \quad \forall c \in [c_L, c_H]; \tag{12}$$

$$q \quad nonincreasing \tag{8}$$

Thus, when we eliminate all payment variables $S(c)$ from the buyer's problem, the virtual valuation is:

$$\forall \in [c_L, c_H] \qquad w(c) \equiv v_U - c - \frac{F(c)}{f(c)} \tag{13}$$

w is the surplus that can be captured given incomplete information, where $\frac{F(c)}{f(c)}$ is information rent. Incomplete information is when parties in an economic situation may not possess full information about each other. Information rent is the expected profit that the supplier, Company $\mathcal{C}$, earns from private information. Alternatively, w is the FDA's net payoff expressed as gains from trade minus information rent.

If instead, we eliminate all q variables, the coefficient of each variable $S(c)$ in the objective function is given by $\psi(c) \cdot f(c)$. ψ is also the FDA's net payoff expressed as gains from trade minus information rent. However, the difference with respect to w is that ψ captures the marginal effect of changing S instead of q. We present ψ below.

$$\forall c \in [c_L, c_H] \qquad \psi(c) \equiv v_U \left(\frac{1}{c} - \frac{1}{c^2} \cdot \frac{F(c)}{f(c)} \right) - 1 \tag{14}$$

The following lemmas and assumptions will be used in our main theorem later on. Their proofs are presented in the Appendix.

Lemma 2. *The following lemma highlights a relation between w and ψ.*

$$\forall p \in [c_L, c_H] \qquad \int_{c_L}^{p} w(c) \cdot f(c)\, dc - p \cdot w(p) \cdot f(p) = -p^2 \cdot \psi(p) \cdot f(p) \tag{15}$$

Assumption 1. *The function ψ is strictly decreasing, and $\psi(c_L) > 0$.*[6]

Lemma 3. *Under Assumption 1, $w(c_L) > 0$ and w is strictly decreasing.*

Lemma 3 states that if ψ is monotonically decreasing, so is w.

Let

$$c_w \equiv \arg\min_c |w(c)| \quad \text{and} \quad c_\psi \equiv \arg\min_c |\psi(c)| \tag{16}$$

Here we define our threshold costs, c_w and c_ψ. c_w is the point at which w crosses the x-axis, if this point exists. Otherwise, $c_w = c_H$. Similarly, c_ψ is the point at which ψ crosses the x-axis, if this point

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[6]Assumption 1 is mild as it is satisfied by almost all distributions.

exists.

In light of Assumption 1 and Lemma 3, c_w and c_ψ are well defined in $(c_L, c_H]$.

Lemma 4. *We have $c_L < c_\psi \leq c_w \leq c_H$, with $c_\psi < c_w$ if and only if $\psi(c_H) < 0$.*

We are now ready to state the main theorem of this section. The proof can be found in the Appendix.

Theorem 1. *Under Assumption 1, the FDA's problem* (1) – (5) *is solved by the mechanism (q_1, S_1), given by*

$$\forall c \in [c_L, c_H] \qquad q_1(c) \equiv \min\left\{\frac{B}{c_\psi}, D\right\} \cdot \mathbf{1}_{[c<p]} \qquad and \qquad S_1(c) \equiv \min\left\{B, c_w \cdot D\right\} \cdot \mathbf{1}_{[c<p]} \qquad (17)$$

where

$$p = \begin{cases} c_w, & if \ c_w \cdot D \leq B \\[2mm] \dfrac{B}{D}, & if \ c_\psi \cdot D \ < \ B < c_w \cdot D \\[2mm] c_\psi, & if \ B \leq c_\psi \cdot D \end{cases} \qquad (18)$$

Theorem 1 establishes that, for any budget level $B > 0$, the mechanism that maximizes the FDA's expected surplus is a take-it-or-leave-it offer. A take-it-or-leave-it offer means that Company $\mathcal{C}$ can only accept or deny the offer, as the FDA will not come back with a better offer. There are three possible offers based on varying neglected disease burdens. We present them below:

- Company $\mathcal{C}$ will be granted a voucher with a priority review less than four months if it addresses the full disease burden D and its cost ratio is below the threshold c_w. This is if the disease burden is "low", i.e. $c_w \cdot D \leq B$;

- Company $\mathcal{C}$ will be granted a voucher with a standard priority review of four months if it addresses the full disease burden D and its cost ratio is below the threshold $\dfrac{B}{D}$. This is if the disease burden is "intermediate", i.e. $c_\psi \cdot D \ < \ B < c_w \cdot D$;

- Company $\mathcal{C}$ will be granted a voucher with a standard priority review of four months if it addresses the disease burden at scale $\dfrac{B}{c_\psi}$ and if its cost ratio is below the threshold c_ψ. This is the case if the disease burden is "high", i.e. $B \leq c_\psi \cdot D$.
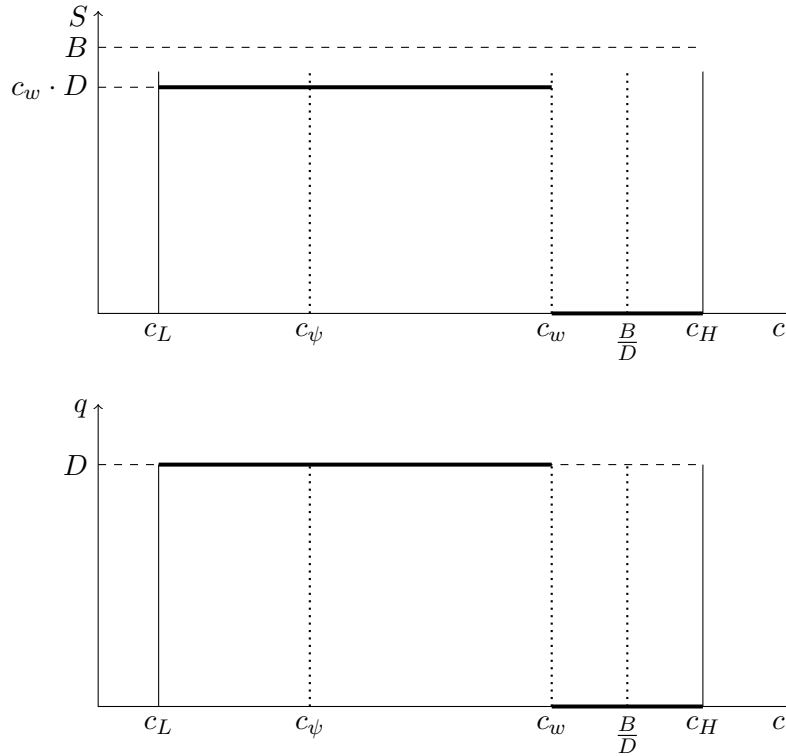
Table 1 illustrates the optimal mechanism defined in (17) and (18), for each disease burden.

Table 1: Optimal Mechanism with One Pharmaceutical Company

	$B \leq c_\psi \cdot D$	$c_\psi \cdot D < B < c_w \cdot D$	$c_w \cdot D \leq B$
q	$\dfrac{B}{c_\psi}$	D	D
S	B	B	$c_w \cdot D$
$p = \dfrac{S}{q}$	c_ψ	$\dfrac{B}{D}$	c_w

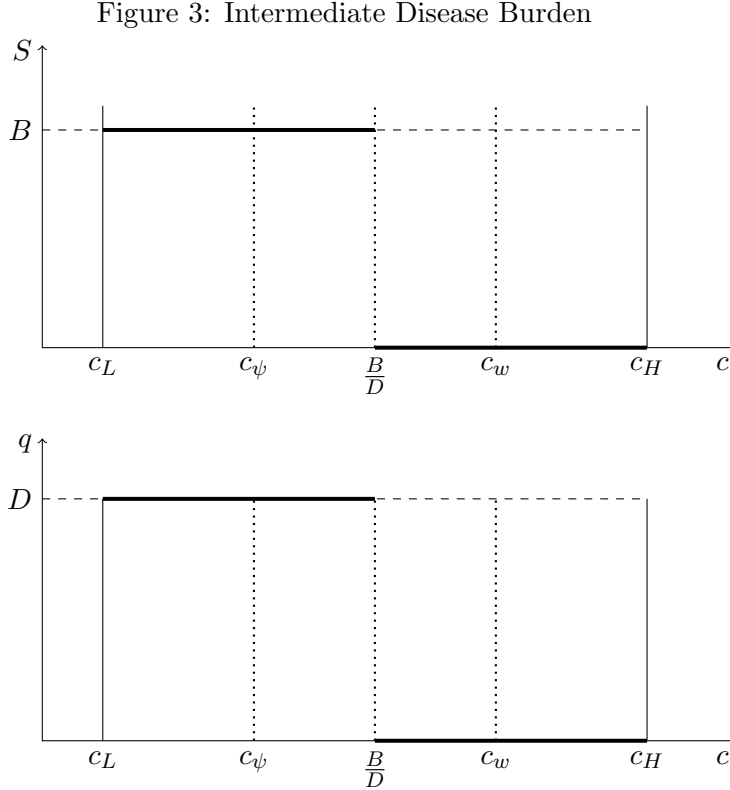## 3.4 Low Disease Burden Case

Figure 2: Low Disease Burden

The figure above illustrates the low disease burden case. In this case, neglected disease α poses a low disease burden D. The FDA, without knowledge of Company $\mathcal{C}$'s cost ratio c, tells the Company that it will receive speed $S = c_w \cdot D$ in review of drug W if it is willing to cure the disease at full scale D. In the context of the voucher program, this would be a priority review less than four months.

If Company $\mathcal{C}$ accepts, the FDA knows that its cost ratio was below threshold c_w. Otherwise, its cost

ratio was above c_w.

3.5 Intermediate Disease Burden Case

Figure 3: Intermediate Disease Burden

The figure above illustrates the intermediate disease burden case. In this case, neglected disease α poses an intermediate disease burden D. The FDA, without knowledge of Company $\mathcal{C}$'s cost ratio c, tells the Company that it will receive the maximum speed $S = B$ in review of drug W if it is willing to cure the disease at full scale D. It is worth pointing out that it is still optimal for the FDA to request full scale intervention i.e. $q = D$. The FDA covers as many cost types as it can to keep the scale at the highest level. In the context of the voucher program, maximum speed corresponds to a voucher with FDA approval in six months, four months faster than the standard 10 month review.

If Company $\mathcal{C}$ accepts, the FDA knows that its cost was below $\dfrac{B}{D}$, a ratio equal to the value of priority review over the value of curing disease D at full scale. $\dfrac{B}{D}$ is in between thresholds c_ψ and c_w. Otherwise, Company $\mathcal{C}$'s cost was above $\dfrac{B}{D}$.

3.6 High Disease Burden Case

Figure 4: High Disease Burden
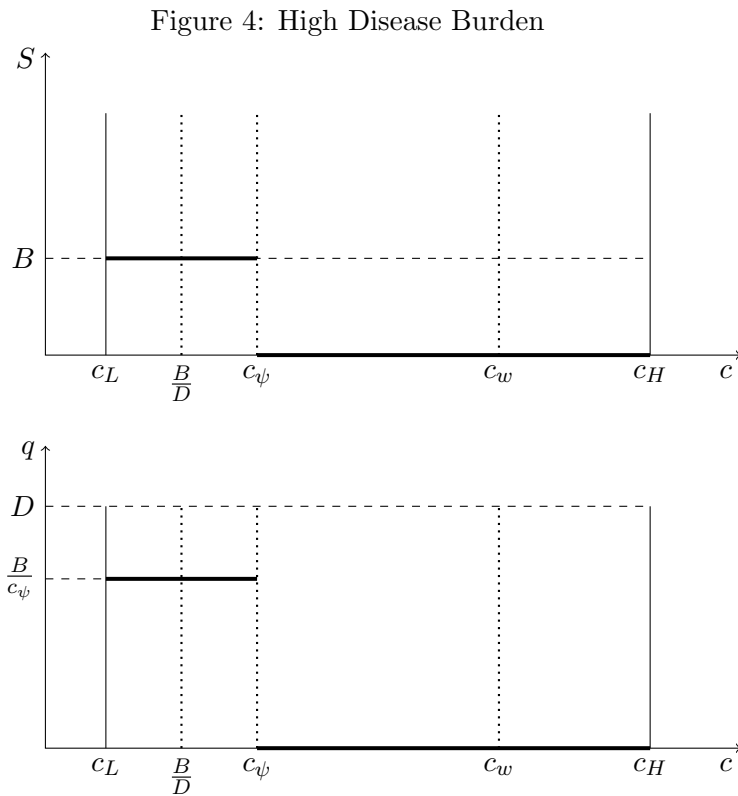
The figure above illustrates the high disease burden case. In this case, neglected disease α poses a high disease burden D. The FDA, without knowledge of Company $\mathcal{C}$'s cost ratio c, tells the Company that it will receive the maximum speed $S = B$ in review of drug W, if it is willing to cure the disease at scale $\dfrac{B}{c_\psi}$. $\dfrac{B}{c_\psi}$ is equal to the value of the priority review over threshold cost c_ψ. In the context of the voucher program, maximum speed corresponds to a voucher with FDA approval in six months, four months faster than the standard 10 month review.

If Company $\mathcal{C}$ accepts, the FDA knows that its cost was below c_ψ. Otherwise, Company $\mathcal{C}$'s cost was above c_ψ.

4   Empirical Application and Discussion

We have designed an auction where the FDA is the buyer and a pharmaceutical company developing a drug for a neglected disease is the single supplier. We have shown that the mechanism that maximizes the FDA's expected surplus is a take-it-or-leave-it offer, with three possible offers based on varying neglected disease burdens. In this section, we will calibrate data from a previously awarded voucher to quantify the optimal scale q, speed S, disease burden D, budget B, and cost thresholds c_ψ and c_w for these offers.

## 4.1   Classifying Disease Burdens

Before calibrating the model, we will classify the neglected diseases eligible for a voucher into one of the three disease burden cases presented in our framework: low, intermediate, or high.

Disease burden, or D, can be quantified using a global health metric called Disability-Adjusted Life Years (DALYs). One DALY can be thought of as one lost year of a "healthy" life. DALYs for a particular disease are calculated as the sum of the Years of Life Lost (YLL) due to premature mortality and the Years Lost to Disability (YLD) for people living with the disease and its consequences (World Health Organization, 2020). Using data from the Global Burden of Disease Study in 2017, we plotted total DALYs of each neglected disease against the percent burden of the disease in rich countries on a logarithmic scale.[7] All neglected diseases with a global disease burden less than one million in 2017 are classified as low burden. Those with a global disease burden between one and 10 million are intermediate burden. Finally, neglected diseases with a burden over 10 million are high burden (Figure 5).[8] Further details on the methodology for this classification can be found in the Appendix.

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[7]The World Bank classifies countries into one of four income groups: low income, lower middle income, upper middle income, and high income. We define "rich countries" as those in the high income or upper-middle income categories.

[8]Figure 5 was adapted from Exhibit 3 in Ridley, Grabowski, and Moe (2006).

Figure 5: Neglected Disease Burden Classification
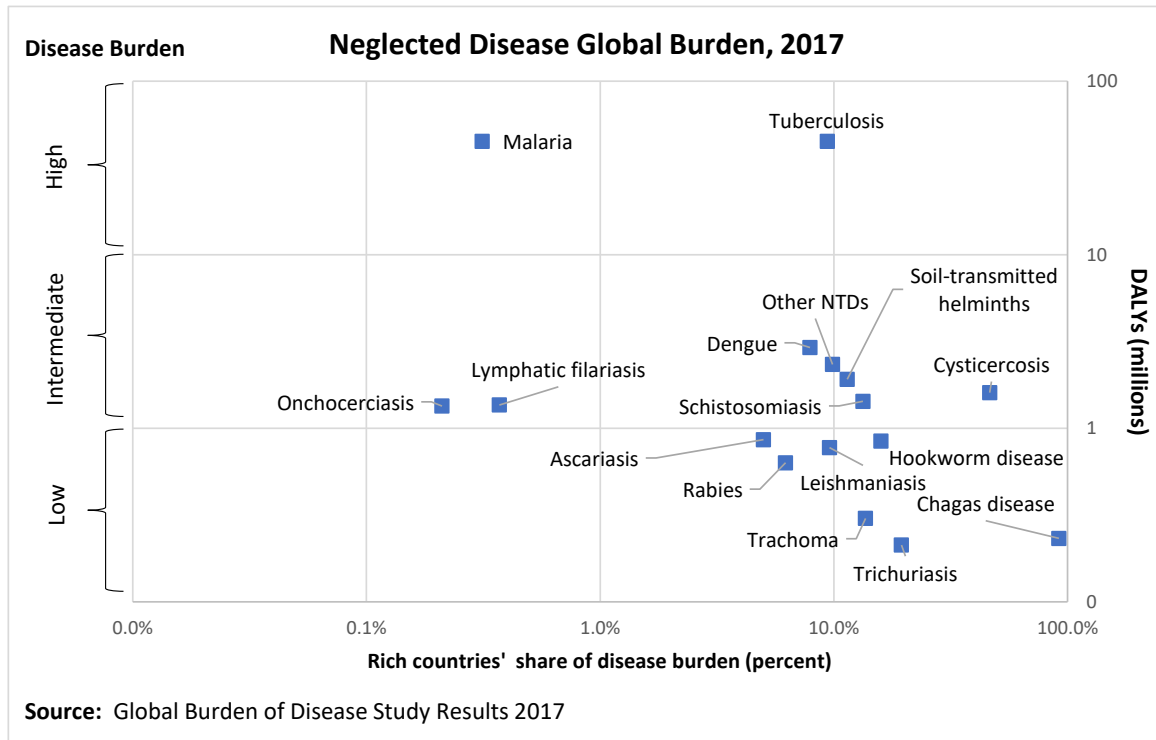
4.2   Case Study: Bedaquiline

To calibrate the model, we use an awarded voucher that mirrors many of the assumptions in the theoretical framework. Considering that our model did not account for secondary voucher sales, we selected a voucher that was awarded to and redeemed by the same company. The FDA granted a voucher to a subsidiary of Johnson & Johnson Company (J&J) in December 2012 for bedaquiline, a tuberculosis drug. J&J redeemed the voucher in November 2016 for guselkumab, a drug treating patients with moderate-to-severe plaque psoriasis (U.S. Government and Accountability Office, 2020).

Tuberculosis is a high burden disease (Figure 5). The global burden of tuberculosis in 2017 was approximately 45 million DALYs (Institute for Health Metrics and Evaluation, 2018). To measure the financial value of this burden, we need to estimate the value of a statistical life year. If we conservatively assume that the value of a statistical life year is $1000, the financial burden of tuberculosis every year would be $45 billion per year.[9] Over a decade and assuming a 10% discount rate, the net present value of this burden would be $277 billion.[10]

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[9]According to the World Bank (2020), average income per capita in Sub-Saharan Africa was $1235 in 2017.

[10]The calculation of the financial burden of a disease was adapted from a working paper by Ridley, Kroetsch, and Kleinrock (2020).

We now assume that J&J participates in our proposed auction model for the voucher, where drug U is bedaquiline and drug W is guselkumab. We also assume that J&J faces no competitors in the tuberculosis or plaque psoriasis market for bedaquiline or guselkumab. Additionally, J&J cannot sell the voucher in the secondary market.

The FDA, not knowing J&J's cost type c, offers the company maximum speed, or $S = B$, in review of guselkumab if it is willing to address the burden of tuberculosis at scale $\dfrac{B}{c_\psi}$. Maximum speed corresponds to a voucher with FDA approval in six months, four months faster than the standard 10 month review. This is consistent with the offer outlined in the high disease burden case in section 3.6.

We will now quantify the value of a maximum priority review, $S = B$, for guselkumab. One approach to estimating the value of priority review on a drug is by using the drug's fifth year sales and the approval acceleration in months (Ridley & Régnier, 2016). Launched in 2017, guselkumab's projected sales in 2022 are \$1.56 billion (Helfand, 2017). Ridley and Régnier estimate that a voucher is worth \$384 million if used on a drug with fifth-year sales of \$1.5 billion and if accelerating approval by four months (2016). Thus, we estimate that $S = B = \$384$ million.

We now estimate J&J's cost type $c = -\dfrac{\Pi_U}{\Pi_W}$, a ratio of the NPV of bedaquiline over the NPV of guselkumab. Under the assumption that bedaquiline's net revenue is zero, we estimate that $-\Pi_U$ is \$1.872 billion or the average capitalized cost of a neglected disease drug (Barofsky & Schneider, 2017). Π_W, or the NPV of guselkumab at time of approval, was \$6.392 billion (Evaluate, 2018). Dividing $-\Pi_U$ by Π_W, we find that $c = .29$.

The values for our threshold cost c_ψ is determined by the virtual valuation function $\psi(c)$. $\psi(c)$ is dependent on v_U, the value the FDA places on the drug U, and the density f from which c is drawn. Given that f is uniform, we estimate that the support $[c_L, c_H]$ is [.094, 1].[11] Assuming that c_ψ and c_w are at the 25th and 75th percentiles of this interval respectively, we approximate $c_\psi = .32$ and $c_w = .77$.

Because $c \leq c_\psi$, we know that J&J will accept the FDA's offer. As part of the offer, the company would be required to address the global burden of tuberculosis with bedaquiline at scale $\dfrac{B}{c_\psi} = \dfrac{\$384,000,000}{.32} = \$1.2$ billion over the course of ten years. This amounts to 0.43% of the global burden of tuberculosis. In exchange, J&J receives a maximum priority review of guselkumab worth \$384 million.

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[11]The calculation for this interval can be found in the Appendix.

We do not claim precision with these estimates. Rather, we have shown how real-world data can be adapted to our framework.

Table 2: Bedaquiline Case Study Results

Variable	Definition	Value
U	Neglected disease drug	bedaquiline
W	Western drug	guselkumab
α	Neglected disease	Tuberculosis
D	Disease burden	45 million DALYs or \$277 billion
$S = B$	Maximum speed	\$384 million
c	Cost type	.29
c_ψ	Cost threshold	.32
$q = B/c_\psi$	Scale of access	\$1.2 billion

4.3   Limitations and Future Research

There are limitations to the mechanism presented in this paper. We present a mechanism with only one supplier; the mechanism could be expanded to two suppliers and eventually to N suppliers. Furthermore, we only consider cases where drug U generates a negative expected net profit and cases where the FDA dislikes drug W. Future iterations of this model should account for cases where drug U may generate a positive, albeit small profit and cases when the FDA likes accelerating the review of drug W. It would be worthwhile to consider how the model would change if the firm's profit π_i was observable. Further research is needed to numerically explore solutions to the model and conduct sensitivity analyses on its parameters.

Our model would be strengthened by simulations and further calibration from empirical data. In our case study, we calibrated data from a high disease burden case. Future research should use data across a variety of indications and disease burdens. Certain assumptions used in the J&J case study would have to be relaxed to accomplish this. For example, maximum speed, $S = B$, could be thought of in terms of the market value of the voucher, which is approximately \$100 million (Gaffney et al., 2020). Assumptions behind the estimation of the financial burden of D and disease burden classifications should be more rigorously tested. The model should also account for voucher resales to better reflect market behavior.

Finally, our model lends itself to some interesting and pertinent extensions. First, how would welfare change if the government removed any possible priority review for drug W? Second, what if the prices for drugs U and W were capped? If they were capped, what would be the optimal price cap be so that gains from reducing deadweight loss and reducing negative externalities would outweigh any losses from a neglected disease drug not being developed? Third, what if eligibility for the priority review voucher introduced a profit cap for the neglected disease drug? If drug U for neglected disease α generated enough profits on its own, it may not be necessary to award a voucher for drug W.

5   Conclusion

In this paper, we have designed an auction model for the priority review voucher program, tying access mandates to the issuance of a voucher. In our model, the FDA is the buyer and a pharmaceutical company is the single supplier. We have shown that the mechanism that maximizes the FDA's expected surplus is a take-it-or-leave-it offer, with three different offers based on varying neglected disease burdens.

This paper is the first to propose and evaluate an auction mechanism for the voucher program and incorporate access mandates in that mechanism. This provides a concrete response to critics of the program who would like to see the FDA require access mandates from companies that receive vouchers.

On a fundamental level, our model shows how to think about incentives for pharmaceutical development. We formally demonstrate how incentives for pharmaceutical companies should be tied to the effect of the drugs they create. In our framework, we have presented a tiered system that rewards companies for both the burden of the disease they address and the scale in which they address that burden.

The priority review voucher program is relevant to lawmakers and society. During the COVID-19 global pandemic of 2020, a member of Congress introduced H.R. 6019: "Cure the Coronavirus Act", a bill that would expand the neglected disease voucher program to reward the developer of a drug or vaccine for the novel coronavirus (Jeffries, 2020). Furthermore, the extensions of the voucher to rare pediatric diseases and medical countermeasures are set to expire in 2020 and 2022 respectively (U.S. Government Accountability Office, 2020). Our model can inform policymakers voting to modify the program's incentive structure and eligibility.

On a broader scale, we have applied principles of mechanism design to a novel setting. Our model provides a framework to think about faster regulatory review and the optimal use of FDA resources. The ideas in this paper may also be relevant to other settings in which government agencies conduct regulatory review.

6 Appendix

Proof of Lemma 1 Using the definition in (6), we can rewrite the IC constraint for any pair c, c' as

$$
\begin{aligned}
\pi(c) \ &\geq S(c') - c \cdot q(c') \\
&= S(c') - c \cdot q(c') + c' \cdot q(c') - c' \cdot q(c') \\
&= \pi(c') - q(c') \cdot (c - c')
\end{aligned}
$$

or equivalently as

$$
\pi(c) - \pi(c') \geq -q(c') \cdot (c - c') \tag{19}
$$

Switching the roles of c and c', we also have

$$
\pi(c') - \pi(c) \geq -q(c) \cdot (c' - c)
$$

or equivalently

$$
\pi(c) - \pi(c') \leq -q(c) \cdot (c - c') \tag{20}
$$

Combining (19) and (20) yields

$$
q(c) \cdot (c - c') \ \geq \ \pi(c) - \pi(c') \ \geq \ q(c') \cdot (c - c') \tag{21}
$$

For any $c > c'$, dividing through (21) by $(c - c')$ yields

$$
-q(c) \ \geq \ \frac{\pi(c) - \pi(c')}{c - c'} \ \geq \ -q(c') \tag{22}
$$

The inequalities in (22) immediately imply that q is *nonincreasing*, as claimed in (8).

Finally, since monotonicity implies continuity almost everywhere, taking the limit as $c \to c'$ in (22) yields

$$
\frac{d\pi(c)}{dc} = -q(c) \quad \text{a.e.} \tag{23}
$$

and integrating both sides yields (7).

The reverse implication is well known (Krishna, 2009). □

Proof of Lemma 2.

Rewrite (15) as

$$\int_{c_L}^p w(c) \cdot f(c) \, dc = p \cdot w(p) \cdot f(p) - p^2 \cdot \psi(p) \cdot f(p) \tag{24}$$

The left-hand side of (24) is equal to $(v - p) \cdot F(p)$, because $\frac{d}{dp} ((v - p) \cdot F(p)) = w(p) \cdot f(p)$.

The right-hand side of (24), after substituting the definitions of w and ψ and simplifying, becomes

$$p \left(v - p - \frac{F(p)}{f(p)}\right) f(p) - p^2 \left(v \left(\frac{1}{p} - \frac{1}{p^2} \cdot \frac{F(p)}{f(p)}\right) - 1\right) f(p) = \left(p\,v - p^2 - p \cdot \frac{F(p)}{f(p)} - v\,p + v \cdot \frac{F(p)}{f(p)} + p^2\right) f(p)$$

$$= (v - p) \cdot F(p) \tag{25}$$

□

Remark 2. *The expression $(v - p) \cdot F(p)$ in (25) is the FDA's expected surplus if it makes a take-it-or-leave-it offer to buy a single unit at price p. The function $w(p) \cdot f(p)$ can be interpreted as the FDA's marginal surplus with respect to the price p*

$$\frac{d}{dp} ((v - p) \cdot F(p)) = -F(p) + (v - p) \cdot f(p) = \overbrace{w(p) \cdot f(p)}^{marginal\ surplus} = \overbrace{v \cdot f(p)}^{marginal\ wtp} - \left[\overbrace{p \cdot f(p) + F(p)}^{marginal\ cost}\right]$$

Proof of Lemma 3. By Assumption 1, we have $\psi(c_L) = v \cdot \dfrac{1}{c_L} - 1 > 0$ which implies $v - c_L = w(c_L) > 0$.

Define $\rho(c) \equiv \frac{F(c)}{f(c)}$, which is information rent. We have

$$w(c) = v - c - \rho(c)$$

hence

$$w'(c) = -1 - \rho'(c) = -[1 + \rho'(c)]$$

and

$$\psi(c) = v \left(\frac{1}{c} - \frac{\rho(c)}{c^2}\right) - 1$$

hence

$$\psi'(c) = v \left(-\frac{1}{c^2} - \frac{\rho'(c) \cdot c^2 - 2\rho(c) \cdot c}{c^4}\right) = v \cdot \frac{-c^2 - \rho'(c) \cdot c^2 + 2\rho(c) \cdot c}{c^4} = v \cdot \frac{c \cdot w'(c) + 2\rho(c)}{c^3}$$

By Assumption 1, we have $\psi'(c) < 0$, hence

$$c \cdot w'(c) + 2\rho(c) < 0 \quad \Rightarrow \quad w'(c) < -\frac{2\rho(c)}{c} < 0$$

$\square$

Proof of Lemma 4. If $c_w < c_H$, then $w(c_w) = 0$, hence $v = c_w + \frac{F(c_w)}{f(c_w)}$. Therefore

$$\psi(c_w) \;=\; \left(c_w + \frac{F(c_w)}{f(c_w)}\right) \cdot \left(\frac{1}{c_w} - \frac{F(c_w)}{c_w^2 \cdot f(c_w)}\right) - 1 \;=\; -\frac{F^2(c_w)}{f^2(c_w) \cdot c_w^2} \;<\; 0$$

Proof of Theorem 1

The proof consists in showing that, for each of the three neglected disease burdens (low, intermediate and high), the mechanism (q_1, S_1) defined in (17) and (18) solves a convenient relaxation of the FDA's problem. We begin with the low disease burden case. We report it here for completeness.

Lemma 5 (low disease burden). *If $c_w \cdot D \leq B$, the mechanism (q_L, S_L) defined by*

$$q_L(c) \equiv D \cdot \mathbf{1}_{[c < c_w]} \qquad \text{and} \quad S_L(c) \equiv c_w \cdot D \cdot \mathbf{1}_{[c < c_w]} \tag{26}$$

solves the FDA's problem (1) – (5).

Proof of Lemma 5.

Following the approach, we start by eliminating all payment S variables from the problem.

Claim 3. *The inequalities in* (4) *and* (5) *imply:*

$$\pi(c_H) \geq 0 \tag{27}$$

$$\forall\, c \in [c_L, c_H]: \quad \pi(c) = \pi(c_H) + \int_c^{c_H} q(t)\, dt \tag{28}$$

and

$$q \quad \text{is nonincreasing} \tag{29}$$

where

$$\pi(c) \equiv S(c) - c \cdot q(c) \tag{30}$$

Proof of Claim 3 The key step in the proof is to show that the IC constraints in (4) imply the "sandwich" inequalities in (34) below. Both (28) and (29) then follow from (34). For any c, $c' \in [c_L, c_H]$, the inequalities in (4) can be rewritten as

$$\begin{aligned}
\pi(c) \;&\geq\; S(c') - c \cdot q(c') \\
&= S(c') - c \cdot q(c') + c' \cdot q(c') - c' \cdot q(c') \\
&= \pi(c') - q(c') \cdot (c - c')
\end{aligned}$$

or equivalently as

$$\pi(c) - \pi(c') \geq -q(c') \cdot (c - c') \tag{31}$$

Switching the roles of c and c', we also have

$$\pi(c') - \pi(c) \geq -q(c) \cdot (c' - c)$$

or equivalently

$$\pi(c) - \pi(c') \leq -q(c) \cdot (c - c') \tag{32}$$

Combining (31) and (32) yields

$$-q(c) \cdot (c - c') \ \geq \ \pi(c) - \pi(c') \ \geq \ -q(c') \cdot (c - c') \tag{33}$$

The inequalities in (33) immediately imply that q is *nonincreasing*, as claimed in (29); and also imply

$$-q(c) \ \geq \ \frac{\pi(c) - \pi(c')}{c - c'} \ \geq \ -q(c'), \qquad \forall\, c, c': \ \ c_L \leq c' < c \leq c_H \tag{34}$$

Since q is monotone, it must be continuous almost everywhere. This implies that π is Lipschitz continuous, hence absolutely continuous. Therefore, taking the limit as $c \to c'$ in (34) yields

$$\frac{d\pi(c)}{dc} = -q(c) \quad \text{a.e.} \tag{35}$$

and integrating both sides yields (28). $\qquad\square$

It is now easy to see that any optimal mechanism must satisfy the participation constraint (5) for the highest type with equality. If not, lowering the payment for every type by a small amount will improve the objective without upsetting any constraint. From now on we will restrict attention to this class of mechanisms in which (27) holds with equality.

The equalities in (28) can be rewritten as

$$\forall\, c \in [c_L, c_H] \quad S(c) = c \cdot q(c) + \int_c^{c_H} q(t)\, dt \tag{36}$$

which implies

$$\int_{c_L}^{c_H} S(c) \cdot f(c) \cdot dc = \int_{c_L}^{c_H} c \cdot q(c) \cdot f(c) \cdot dc + \int_{c_L}^{c_H} \int_{c}^{c_H} q(t)\, dt \cdot f(c) \cdot dc + \pi(c_H)$$

$$= \int_{c_L}^{c_H} c \cdot q(c) \cdot f(c) \cdot dc + \int_{c_L}^{c_H} q(c) \cdot F(c) \cdot dc + \pi(c_H) \qquad (37)$$

$$= \int_{c_L}^{c_H} \left(c + \frac{F(c)}{f(c)} \right) \cdot q(c) \cdot f(c) dc$$

Using (37), the objective function (1) can be rewritten as

$$\int_{c_L}^{c_H} [v\, q(c) - S(c)]\, dF(c) = \int_{c_L}^{c_H} w(c)\, f(c)\, q(c)\, dc$$

It is now straightforward to verify that q_L solves (pointwise) the following problem

$$\begin{cases} \max_{q} \quad \int_{c_L}^{c_H} w(c)\, f(c)\, q(c)\, dc \\[2mm] \text{s. to} \\[2mm] \forall c \in [c_L, c_H] \quad 0 \leq q(c) \leq D \end{cases}$$

Since (q_L, S_L) satisfies all constraints of the FDA's problem (1) – (5), we conclude that (q_L, S_L) solves the FDA's problem in the low disease burden case. $\square$

Lemma 6 (high disease burden). *If $B \leq c_\psi \cdot D$, the mechanism (q_H, S_H) defined by*

$$q_H(c) \equiv \frac{B}{c_\psi} \cdot \mathbf{1}_{[c < c_\psi]} \qquad and \quad S_H(c) \equiv B \cdot \mathbf{1}_{[c < c_\psi]} \qquad (38)$$

solves the FDA's problem (1) – (5).

Proof of Lemma 6. The proof for this case mimics the proof of the low disease burden case. However, instead of eliminating all S variables we eliminate all q variables.

The equalities in (35) imply

$$\forall c', c'' \in [c_L, c_H] \qquad \int_{c'}^{c''} dS(c) = \int_{c'}^{c''} c\, dq(c) \qquad \forall c', c'' \in [c_L, c_H] \qquad (39)$$

which in turn implies

$$q(c') - q(c'') = -\int_{c'}^{c''} dq(t) = -\int_{c'}^{c''} \frac{1}{t} \, dS(t) = \frac{S(c')}{c'} - \frac{S(c'')}{c''} - \int_{c'}^{c''} \frac{S(t)}{t^2} dt \tag{40}$$

Setting $c' = c_H$ yields

$$\forall c \in [c_L, c_H] \qquad q(c) = \frac{S(c)}{c} - \int_{c}^{c_H} \frac{S(t)}{t^2} \, dt \tag{41}$$

Now using (41), the objective function (1) can be rewritten as

$$\int_{c_L}^{c_H} [v \, q(c) - S(c)] \, dF(c) = \int_{c_L}^{c_H} \psi(c) \, f(c) \, S(c) \, dc$$

It is straightforward to verify that S_H solves (pointwise) the following problem

$$\max_{S} \int_{c_L}^{c_H} \psi(c) \, f(c) \, S(c) \, dc \tag{42}$$

subject to:

$$\forall c \in [c_L, c_H] \quad 0 \leq S(c) \leq B \tag{43}$$

We conclude that (q_H, S_H) solves the FDA's problem in the high disease burden case. $\qquad\square$

Lemma 7 (intermediate disease burden). *If $c_\psi \cdot D < B < c_w \cdot D$, the mechanism (q_I, S_I) defined by*

$$q_I(c) \equiv D \cdot \mathbf{1}_{\left[c < \frac{B}{D}\right]} \qquad and \quad S_I(c) \equiv B \cdot \mathbf{1}_{\left[c < \frac{B}{D}\right]} \tag{44}$$

solves the FDA's problem (1) – (5).

Proof of Lemma 7. Note that (q_I, S_I) satisfies (2) – (5). It remains to show that q_I solves the following problem

$$\max_{q} \int_{c_L}^{c_H} w(c) \, f(c) \, q(c) \, dc \tag{45}$$

subject to

$$q(c_L) \leq D \tag{46}$$

$$c_L \cdot q(c_L) + \int_{c_L}^{c_H} q(t)dt \quad \leq B \tag{47}$$

$$\forall c, c' \in [c_L, c_H] \quad (c - c') \cdot [q(c) - q(c')] \leq 0 \tag{48}$$

$$-q(c_H) \leq 0 \tag{49}$$

Define $W(c) \equiv w(c) \cdot f(c)$ and $b \equiv \dfrac{B}{D}$. Next we provide a nonnegative "multiplier" for each relevant constraint. We will use the symbols: δ for the multiplier of the demand constraint in (46) for the lowest type, β for the multiplier of the budget constraint in (47) for the lowest type, $\mu(c)$ for the multiplier of the monotonicity constraints in (48), and $\mu(c_H)$ for the multiplier of the nonnegativity constraint in (49) for the highest type:

$$\begin{cases} \delta \equiv \displaystyle\int_{c_L}^{b} W(c)\,dc - b \cdot W(b) \\[2mm] \beta \equiv W(b) \\[2mm] \forall c \in [c_L, b] \quad \mu(c) \equiv \displaystyle\int_{c}^{b} W(x)\,dx - (b - c) \cdot W(b) \\[2mm] \forall c \in (b, c_H) \quad \mu(c) \equiv (c - b) \cdot W(b) - \displaystyle\int_{b}^{c} W(x)\,dx \\[2mm] \mu(c_H) \equiv (c_H - b) \cdot W(b) - \displaystyle\int_{b}^{c_H} W(x)\,dx \end{cases} \tag{50}$$

Claim 4. *All expressions in* (50) *are nonnegative.*

Proof of Claim 4. In light of (15), we have

$$\delta = \int_{c_L}^{b} W(c)\,dc - b \cdot W(b) = -b^2 \cdot \psi(b) \cdot f(b)$$

Since $c_\psi < b$, we have $\psi(b) < 0$ and thus $\delta > 0$. Since $b < c_w$, we have $\beta > 0$. Finally, we have $\mu'(c) = -W(c) + W(b) = -w(c)f(c) + w(b)f(b)$. Since w is decreasing and f is always positive, we have that $\mu'(c)$ is negative for $c < b$ and positive for $c > b$. Therefore μ is quasiconvex, and minimized at $c = b$, with $\mu(b) = 0$. $\qquad\square$

The next two equalities, which will be used shortly, follow directly from the definitions in (50).

$$\begin{aligned} \delta + \beta\, c_L - \mu(c_L) \;&=\; \int_{c_L}^{b} W(c)\, dc - b \cdot W(b) + W(b) \cdot c_L - \left(\int_{c_L}^{b} W(x)\, dx - (b - c_L) \cdot W(b) \right) \\[2mm] &= \int_{c_L}^{b} W(c)\, dc - b \cdot W(b) + W(b) \cdot c_L - \int_{c_L}^{b} W(x)\, dx + b \cdot W(b) - c_L \cdot W(b) \quad (51) \\[2mm] &= 0 \end{aligned}$$

and

$$\forall c \in (c_L, c_H) \qquad \beta - \mu'(c) = W(c) \tag{52}$$

In light of Claim 4, the inequalities in (46), (47), (48), and (49) imply

$$\delta\, q(c_L) + \beta\, c_L\, q(c_L) + \beta \int_{c_L}^{c_H} q(t)\, dt + \int_{c_L}^{c_H} \mu(c)\, dq(c) - \mu(c_H)\, q(c_H) \;\leq\; \delta D + \beta B \tag{53}$$

The second integral in (53) can be rewritten as

$$\int_{c_L}^{c_H} \mu(c)\, dq(c) \;=\; \mu(c_H)\, q(c_H) - \mu(c_L)\, q(c_L) - \int_{c_L}^{c_H} \mu'(c)\, q(c)\, dc \tag{54}$$

Substituting (54) back into (53), collecting terms and simplifying yields

$$\left[\delta + \beta\, c_L - \mu(c_L)\right] q(c_L) + \int_{c_L}^{c_H} \left[\beta - \mu'(c)\right] q(c)\, dc \;\leq\; \delta D + \beta B \tag{55}$$

Finally using (51) and (52), and the definitions of δ and β, we can rewrite (55) as

$$\int_{c_L}^{c_H} w(c)\, q(c)\, dF(c) \;\leq\; D \int_{c_L}^{b} w(c) f(c)\, dc \tag{56}$$

Since q_I satisfies (56) with equality, it maximizes the objective function in (45), subject to (56). Since any q that satisfies (46) – (49), also satisfies (56), q_I also solves the problem (45) – (49). Thus (q_I, S_I) solves the FDA's problem in the intermediate disease burden case.

This concludes the proof of Lemma 7 and Theorem 1 . $\qquad\square$

Note on Section 4.1

The dataset used for this section was sourced from the Global Burden of Disease Study 2017. Data was downloaded and filtered by World Bank Income group (low income, lower middle income, upper middle income, and high income).

Rich countries' share of DALY burden was calculated by aggregating DALY count from high income and upper middle income countries and dividing over total DALY burden. Diseases with no DALY count in rich countries were assigned a value of .01% since the logarithm of zero is invalid.

Ebola, leprosy, Zika virus, guinea worm disease, and African trypanosomiasis are excluded from Figure 5 but are considered low burden diseases. Asciarisis, trichuriasis, and hookworm diseases are considered soil-transmitted helminths but also shown separately in Figure 5.

Note on Section 4.2

We estimated the support $[c_L, c_H] \equiv [.094, 1]$ using the following methodology. Throughout the interval, we assumed that $-\Pi_U = 1.872$ billion, or the average capitalized cost of an NTD drug (Barofsky & Schneider, 2017). For type c_H, we set $\Pi_W = 1.872$ billion, no less nor greater than the cost of the average NTD drug. Thus, $c_H = -\dfrac{\Pi_U}{\Pi_W} = 1$. For type c_L, we assume that $\Pi_W = \$20$ billion. This reference for an upper bound on the NPV of drug W is based on an estimate of the most valuable R&D pharmaceutical project in 2019 (Evaluate, 2019). Thus, $c_L = -\dfrac{\Pi_U}{\Pi_W} = \dfrac{1.872}{20} = .094$.

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