Peltzman Revisited: Quantifying 21st-Century Opportunity Costs of Food and Drug Administration Regulation

Casey B. Mulligan *University of Chicago*

Abstract

Peltzman's work is revisited in light of two recent opportunities to quantitatively assess trade-offs in drug regulation. First, reduced regulatory barriers to drug manufacturing associated with the 2017 reauthorization of generic-drug user fee amendments were followed by more entry and lower prices for prescription drugs. A simple, versatile industry model and historical data on entry indicate that easing restrictions on generics discourages innovation, but this cost is more than offset by benefits from enhanced competition, especially after 2016. Second, accelerated vaccine approval in 2020 had unprecedented net benefits as it improved health and changed the trajectory of the wider economy. Evidence suggests that cost-benefit analysis of Food and Drug Administration (FDA) regulation is incomplete without accounting for substitution toward potentially unsafe and ineffective treatments that are outside FDA jurisdiction and heavily utilized before FDA approval. Moreover, the policy processes initiating the regulatory changes show an influence of Peltzman's findings.

> Consumer losses from purchases of ineffective drugs or hastily marketed unsafe drugs appear to have been trivial compared to gains from innovation. (Peltzman 1974, p. 82)

1. Introduction

An important fraction of improved living standards in the past, and likely the future, has originated from new medical products. Both markets and regulators have the potential to contribute to, or detract from, the innovative process. On the market side are concerns that competition may erode financial rewards to innovation or that large firms may be too bureaucratic to foster the consideration of new products and methods (early analyses appear in Schumpeter 1943; Arrow

I appreciate discussions with Dennis Carlton, Troy Durie, Kevin Murphy, Sam Peltzman, Tom Philipson, Andrei Shleifer, Alex Tabarrok, Bob Topel, and Cliff Winston and financial support from the University of Chicago's Initiative on Enabling Choice and Competition in Healthcare.

[*Journal of Law and Economics,* vol. 65 (November 2022)]

1962; Schmookler 1972). Meanwhile, government stands as a gatekeeper for new medical products for the stated purpose of protecting consumers.

A leading example of the regulation of new medical products is the 1962 Drug Efficacy Amendment (EA) to the Federal Food, Drug, and Cosmetic Act, which made proof of efficacy a requirement for the approval of new drugs by the Food and Drug Administration (FDA). Peltzman (1973) pioneered cost-benefit analysis of the EA by estimating the consumer benefit (if any) of curtailing the sale of ineffective drugs and comparing it with the opportunity cost of effective drugs that were not introduced into the US market owing to the additional approval costs created by the EA. Peltzman (1973, p. 1079) concludes that the EA imposed a net cost on consumers in magnitude similar to a "5–10 percent excise tax on all prescriptions sold."

Given the sudden and obvious reduction in the rate at which new drug formulas were introduced into the market after 1962, perhaps the greatest challenge Peltzman faced was quantifying the degree to which the forgone drugs would have been ultimately deemed ineffective by consumers and their physicians. Two drug market events between 2017 and 2021 offer fresh perspectives on the consumer costs and benefits of the entry barriers created by the FDA approval processes. One relates to the FDA regulation of the manufacturing of generic drugs, for which there is little scope for protecting consumers from ineffective products because, as a group, consumers accumulated years of experience while the drug was produced under patent. The other relates to approval delays of COVID-19 vaccines, which have particularly concrete opportunity costs and further illustrate some of Peltzman's influence on public policy.

Section 2 briefly reviews Peltzman's methodology. Section 3 describes the US generic-drug market in recent years. A simple and versatile conceptual model of prices and entry is provided in Section 4 for the purpose of quantifying the welfare benefits of the deregulation of the entry of generics (hereafter, generic entry) that has occurred since 2012, without restricting the values of the price elasticity of demand or the level of marginal cost. In this light, the generic-entry data suggest that easing restrictions on generics discourages innovation, but this cost is more than offset by consumer benefits from enhanced competition, especially since 2016. Section 5 describes the timing of COVID-19 vaccine development and approval. An excess-burden framework is applied to better measure the opportunity cost of regulatory delays, including substitution toward potentially harmful remedies that need not demonstrate safety or effectiveness because they are outside FDA jurisdiction. Section 6 concludes.

2. Peltzman's Methodology

Peltzman's most memorable finding is a sharp and persistent decline in new chemical entities (NCEs) beginning in 1963, at the same time that drug market trends suggested that the number of NCEs would have been similar to what it was in the 1950s. His point estimate of the effect of the 1962 EA is a reduction of

NCEs from 41 per year to 16 (about 60 percent, with a standard error of less than 2.5 NCEs). He also notes that US NCEs fell 54 percent relative to British NCEs (Peltzman 1973, pp. 1055, 1057).

Peltzman acknowledges that the EA was intended to reduce the number of NCEs by eliminating the ineffective ones that prior to the EA consumers were purportedly duped into purchasing until experience revealed their true value. Indeed, his examination of drug evaluations by the American Medical Association (AMA) shows that AMA-designated "ineffective drugs" were more common before 1963 and that such drugs lost market share after introduction. However, this category of drugs was a somewhat greater percentage of drug sales after the EA than before it. Moreover, NCEs as a whole did not maintain sales over time any better after the EA, when the FDA was certifying them as effective.

A significant part of his paper, and this one, is dedicated to quantitatively assessing the trade-offs of regulating drug market entry. Peltzman (1973, p. 1090) concludes that the net effect of the EA on consumers was "comparable to their being taxed something between 5 and 10 percent on their . . . drug purchases."

Peltzman's paper influenced both academics and policy makers. Klein and Tabarrok (2002) cite a wide range of academics sharing Peltzman's conclusions. For example, Temin (1980, p. 206) says that "whether or not people are capable of understanding the relevant information, I still would favor giving people more choice for their own well-being than the current [FDA] system allows." Philipson and Sun (2008) and others followed Peltzman in evaluating the effects of new FDA regulation on drug approvals. Philipson et al. (2008), for example, find that 1992 FDA reforms significantly increased consumer surplus and the returns to innovation with a minimal cost in terms of drug safety, which influenced further FDA deregulation efforts under George W. Bush and later in the Trump administration when Philipson was part of the senior White House staff.[1]

Pointing specifically to Peltzman's paper, the *1975 Economic Report of the President* (Council of Economic Advisers [CEA] 1975, p. 159) concludes that "existing laws and institutions are imposing significant costs on the economy." The 1987 *Economic Report of the President* also cites Peltzman's paper as part of its discussion of recent FDA changes, including rules around generic entry, intended to relax "[u]nnecessarily stringent regulatory requirements [that] can lead to more deaths and lower health levels" (CEA 1987, p. 194). The 1989 *Economic Report of the President* lists several possible changes to FDA regulation, citing Peltzman's results as to the agency's dramatic effect on the rate of innovation (CEA 1989, pp. 218–20). Several reports from the Trump administration focus on the fact that FDA regulation often discourages entry into prescription drug manufacturing (CEA 2018a, 2018b, 2019a, 2019b, 2020).

[1] These deregulation efforts, and an emphasis on medical innovation, are described further in Mulligan (2020b). The *2018 Economic Report of the President* (Council of Economic Advisors [CEA] 2018b) has a full chapter about the health sector, including the sections "Improving People's Health through More Access to Medical Innovations" and "Encouraging Innovation, and Making It Affordable." The *2019 Economic Report of the President* (CEA 2019a) looks at the possible negative innovation effects of a proposed federal ban on for-profit health care.

3. Generic-Drug Approvals and Prescription Drug Prices

As Peltzman recognized, the challenge to interpreting the welfare effect of FDA entry barriers is that the barriers are often tied to the agency's certification of effectiveness. Generic-drug approvals are interesting in this regard because they involve drugs familiar to the market that had been certified as effective when the FDA approved them as NCEs.[2] Although empirical relationships between drug prices and the number of generic manufacturers have been estimated in previous work, it is not easy to identify the reasons why some markets have more generics than others. Recent changes in generic-drug regulation thereby offer a unique new opportunity to assess welfare effects of FDA entry barriers.

About 90 percent of US prescriptions are filled with generics (Pew Charitable Trusts 2019). A manufacturer aspiring to sell an off-patent generic drug must submit an abbreviated new-drug application (ANDA) for FDA approval, as distinct from the new-drug application (NDA) required for introducing a new compound into the market. Although not requiring the safety and effectiveness studies that are part of NDAs, ANDAs are still costly. As of 2015, the FDA had thousands of ANDAs pending, which resulted in a median approval time of 42 months (Pew Charitable Trusts 2019, table 1).[3] About a quarter of markets, and likely more, had only one generic manufacturer approved (Berndt, Conti, and Murphy 2017).[4]

Reduced barriers to generic entry have the potential to significantly reduce drug prices by increasing competition. According to FDA (2017b), the generic was sold at only a 6 percent discount on the branded drug when the market had only one approved generic but at 48 and 56 percent discounts when the market had two and three approved, respectively.[5] With less than 3,000 extant markets at a point in time (FDA 2021), these findings suggest that a policy increasing a year's approvals by, say, 300 could reduce drug prices by 2 percent over a 1-year time frame in addition to any effect they had on the branded price or on prices in the markets for therapeutic substitutes (on the importance of such competition, see Lichtenberg 2021). Using data on quantities purchased and measuring prices before and after ANDA approval, Conrad et al. (2017) estimate that the ANDA

[2] For this reason, Tabarrok (2015) and others argue for international regulatory reciprocity for generic drugs. Namely, American consumers should be permitted to import generic drugs that have been approved abroad, are no longer protected by US patents, and have new-drug applications approved by the Food and Drug Administration (FDA).

[3] The Hatch-Waxman Act requires FDA approval within 180 days (21 U.S.C. 355[j][5][A]) but provides no enforcement mechanism.

[4] For application purposes, the FDA (2017b) defines a market as an active ingredient(s), dosage form, and route of administration, "ignoring differences in strength and package sizes." According to the FDA Orange Book, 1,447 markets in 2015 had at least one approved generic manufacturer, and 323 of those had exactly one. Moreover, 1,275 markets had no generic manufacturers. Later the FDA (2017c) found that hundreds of such markets had no exclusivities or blocking patents. See also Berndt, Conti, and Murphy (2017, figure 11).

[5] Caves, Whinston, and Hurwitz (1991) find only modest changes in brand prices when generic entry occurs. However, their data are from 1976 to 1987, when brand quantity shares (measuring conditional on generic competition or for the sector as a whole) were triple or quadruple what they would be in the 2010s (Grabowski et al. 2016).

approvals in 2017 alone would reduce annual consumer expenditures by $16 billion in a $324 billion prescription drug market (IQVIA Institute for Human Data Science 2018). This includes changes in the branded price in the same market with ANDA approval but not price changes for therapeutic substitutes.

The 1984 Hatch-Waxman Act requires the FDA to approve or disapprove ANDAs within 180 days. Rarely meeting this requirement, the FDA asserted that it needed more funds to hire review staff (US Senate 2016). With the 2012 Generic Drug User Fee Amendments (GDUFA I), Congress authorized user fees that add a cash barrier to entry but are "dedicated toward expediting . . . the review of human drug applications" (Pub. L. No. 112-144, sec. 101[b]). Between 2012 and 2015, the median time from ANDA receipt to approval increased from 32 months to 42 months (Pew Charitable Trusts 2019, table 1). The number of final and tentative approvals failed to increase.[6] The number of foreign and domestic facilities manufacturing generic drugs declined.

The apparent lack of success of GDUFA I may seem surprising given its apparent similarities to the 1992 Prescription Drug User Act (PDUFA), which required the FDA to meet performance goals in processing of NDAs in exchange for collecting fees from manufacturers. Perhaps PDUFA was successful in reducing approval times (Cantor 1997; Vernon et al. 2009) because it simultaneously benefited manufacturers, consumers, and the FDA. In contrast, accelerated processing of ANDAs includes a significant amount of redistribution to consumers from expired patent holders (and perhaps also the generic manufacturers participating in markets with only one generic), which I quantify in Section 4.

Three related changes occurred in 2017. By May 9, Scott Gottlieb was nominated and confirmed to head the FDA. He had been an outspoken critic of the FDA's slow approval process, which he described as "evading the law" (Gottlieb 2010). He immediately told Congress that his FDA would prioritize competition (US House 2017). In June, the FDA (2017a) announced the Drug Competition Action Plan with procedural details published in November (FDA 2017d). The FDA (2017c) immediately promulgated, and subsequently maintained, a list of drugs with no blocking patents or exclusivities but still no approved generics. Section 801 of GDUFA II, which became law in August 2018, instructs the FDA to prioritize the review of drugs with no blocking patents or exclusivities that have three or fewer ANDAs or NDAs already approved. On paper at least, the FDA appeared to be looking toward competition rather than purely bureaucratic metrics such as numbers of applications and approval times.

Table 1, based on the FDA's Orange Book listing of approved NDAs and ANDAs, shows approvals at a higher rate during Gottlieb's tenure as compared with either the 2 years before it or the 2 years after it. Before Gottlieb's leader-

[6] The FDA Orange Book shows 433, 400, and 483 abbreviated new drug application (ANDA) final approvals in fiscal years 2013–15 as compared with 413, 454, and 510 for the prior 3 fiscal years (before the 2012 Generic Drug User Fee Amendments). The FDA reports similar results for the sum of final and tentative ANDA approvals (see Uhl 2016, slide 18; Berndt, Conti, and Murphy 2018, figure 2).

Table 1
Entry and Price Changes in Drug Markets

	May 2015–April 2017	May 2017–April 2019	May 2019–April 2021
Abbreviated new drug applications approved	1,286	1,754	1,475
New-drug applications approved	184	229	202
Biosimilars approved	4	16	15
New biologics approved	73	82	62
Prescription drug price change relative to all items (%)	3.7	−1.5	−5.1
Inflation-adjusted changes in unit cost between calendar years (%)	−.1	−3.6	N.A.
Medicaid/CHIP enrollment change per capita (%)	3.4	−5.3	12.8

Sources. Food and Drug Administration (FDA) Orange Book and Purple Book; Bureau of Labor Statistics consumer price index (CPI) series CUSR0000SEMF01 and CUSR0000SA0; Express Scripts/Evernorth Drug Trend Reports (Express Scripts 2019).
Note. The CPI and Medicaid changes are from April to April. Unit cost is per-prescription consumer expenditure, including insurance plan expenditures net of rebates and discounts. Scott Gottlieb was FDA commissioner May 2017–April 2019. Biosimilars and new biologic approvals include supplemental biological license applications. CHIP = Children's Health Insurance Program; N.A. = not applicable.

ship, and therefore also before GDUFA II, the FDA averaged 54 approvals per month (1,286 for the 24 months). The average was 73 per month during Gottlieb's tenure (through April 2019) and 61 in the subsequent 24 months.[7] Table 1 also shows that FDA approvals of new drugs were also high during his tenure. The corresponding approvals for biosimilars and biologics are from the FDA's Purple Book; they are a large share of expenditures on physician-administered drugs but a small share of retail prescription drugs.[8]

Drug market performance appears to reflect additional competition. Berndt, Conti, and Murphy (2018) find that, as of April 30, 2017, Teva Pharmaceutical owned 1,611 ANDAs of about 10,000 in existence. The second largest owner was Mylan Inc., with 668 ANDAs. Teva's stock crashed in the summer of 2017, with its chief executive officer reporting that the company would henceforth be less profitable owing to "greater competition as a result of an increase in generic-drug approvals by the U.S. FDA" (Sheetz 2017). Real retail prescription drug prices fell 1.5 percent during Gottlieb's tenure, as compared with a 3.7 percent increase in

[7] All but 3 of these 48 months were under the 2017 amendments. The number of drugs coming off patent seems to be fairly constant over time after peaking between 2012 and 2014 (CEA 2018a, figure 3). The *t*-statistic for the hypothesis that Gottlieb's rate was the same as the combination of the prior and subsequent 24 months is 4.7 ($p < .001$). See also CEA (2019b).

[8] Biologics, which include vaccines, gene therapy, and insulin, have applications akin to NDAs (biological license applications [BLAs] under 351[a] of the Public Health Service Act) and ANDAs (BLAs under 351[k]). Both types of BLAs are approved by the FDA's Center for Biologics Evaluation and Research and are tabulated in the FDA's Purple Book. Note that biologics are more than 70 percent of total drug spending under Medicare Part B (physician-administered drugs) and less than 10 percent of total drug spending under Medicare Part D (retail prescription drugs) (Nguyen and Sheingold 2020; Anderson-Cook and Maeda 2019).

the prior 2 years and a 5.1 percent decrease in the subsequent 2 years.[9] These findings are consistent with the hypothesis that GDUFA II, Gottlieb's management, or some combination thereof increased drug-market competition by reducing entry barriers.

Duggan and Scott Morton (2006) argue that Medicaid enrollment is also an important driver of prescription drug prices because Medicaid reimburses on the basis of the average price in the commercial market. Drug companies setting their commercial prices know that raising them will reduce utilization among their commercial customers but would automatically increase Medicaid revenue with hardly any effect on Medicaid utilization. The relative importance of these factors depends on the share of customers enrolled in Medicaid versus commercial plans. Between April 2015 and April 2017, per capita Medicaid enrollment increased 3.4 percent and then fell in the subsequent 24 months. Real drug prices show a similar qualitative pattern, except in the third period when real drug prices and Medicaid enrollment moved sharply in opposite directions. More research is needed to determine how much of the pattern Duggan and Scott Morton find across drug markets is expected to be observed in the national time series.

4. Welfare Consequences of Generic-Entry Barriers

4.1. Competition, Entry Expenditure, and Innovation Costs

Entry barriers associated with ANDAs have three kinds of welfare consequences: a competition effect, an entry expenditure effect, and an innovation effect. One effect is the static effect on ongoing competition for the supply of drugs after patent expiration. Social welfare increases with the quantity of drugs sold to consumers for which marginal value exceeds the marginal cost of production. A second effect is that entry barriers are real costs, in the form of delays and labor effort at the FDA and manufacturers, that are incurred to the extent that entry occurs. Costs are imposed by NDAs too, except that they are paid by the first manufacturer of the drug, whereas ANDA costs are paid by generic manufacturers. It is theoretically possible that barriers relax, but do not eliminate, new entry enough to increase aggregate expenditure on ANDAs and that this added cost exceeds the benefit of more competition. As I show below, much can be said about the sum of these two costs with minimal assumptions about industry demand and supply.

A third effect of ANDA barriers is that, by limiting entry, they indirectly encourage innovation by protecting incumbents, including the incumbent that brought the product to market in the first place. Quantifying this effect requires,

[9] The CEA (2019b) explains why the consumer price index (CPI) indicates the contribution of prescription drugs to the cost of living and how it relates to other drug price inflation measures. As a cost-of-living index, the CPI is based only on price changes within product and (unlike unit cost) does not reflect any increase from the introduction of a new expensive product because consumers can opt not to purchase it. Table 1 shows results for unit cost measured from the Express Scripts (now Evernorth) database of US consumer costs for prescription drugs, which is one of the largest in the world.

in addition to static information about entry and the distribution of surplus among producers, information or assumptions about the effect of postpatent profits on the number of new drugs brought to market. Entry costs that are high enough to prevent all generic entry, and thereby not paid in equilibrium, would be the economic equivalent of an infinite patent life. Lesser generic-entry barriers also resemble infinite patent life by indefinitely elevating incumbents' profits, except that such barriers elevate profits less than the infinite patent would and involve generic-entry costs, which are real costs that would not be incurred if patent lives were infinite. Nevertheless, if actual patent lives were enough shorter than the social-surplus-maximizing patent life, generic-entry barriers could have a net social benefit through their oblique transfer of surplus to patent holders after their patents expire.

To focus issues, this paper evaluates the third welfare effect of generic entry, assuming that the optimal patent duration has already been achieved, and leaves it to future research to assess whether patent lives are too short or too long (see Izhek, Saxell, and Takalo 2020).[10] The elasticity of new drugs with respect to innovators' profits is assumed to be constant with a value that exactly offsets the static benefits (evaluated at pre-GDUFA entry) of marginally shortening the patent's life. The optimal-duration assumption by itself implies a significant innovation benefit of a marginal increase in innovators' profits, while the constant-elasticity assumption dictates the rate at which the marginal benefit to innovation diminishes.

Reducing generic-entry costs enough to induce exactly one generic entrant necessarily increases aggregate expenditure on entry. Because generic entry can reduce innovation and, by some estimates (FDA 2017b), can have a limited competition effect, social welfare can be less with one generic entrant than with none. But further entry barrier reductions (enough to have more than one generic) would be associated with greater competition effects, smaller marginal effects on innovation, and potentially less entry expenditure. This theoretical result is interesting to consider in light of GDUFA II's emphasis on second and third generic entrants, in contrast to previous FDA metrics that weighted all ANDAs equally regardless of their market consequences.

4.2. Cournot Competition with Unit Pass-Through

Just a few market assumptions deliver a number of quantitative results about the relationship between entry barriers and market performance. First, I assume that market demand is the same before and after patent expiration with all manufacturers in the same market producing perfect substitutes. Second, I assume Cournot competition after the patent expires, which means that each entrant chooses its quantity taking as given the quantities produced by other manufac-

[10] See Morris (2012) on pharmaceutical patent life before and after the Hatch-Waxman Act. Hughes, Moore, and Snyder (2002), using a linear demand model, conclude that an effective patent life of 9 years yields significantly more social welfare than a patent life of 0 would. Boldrin and Levine (2008) disagree.

turers. The competition is symmetric, except that the innovator does not pay ANDA costs. Third, pass-through of common marginal costs is one-for-one regardless of the number of entrants. This pass-through implies that all (infinite) potential entrants face the same ANDA cost and marginal production cost, which I denote a and c, respectively. It also follows that market demand has a constant semielasticity with respect to price (Vives 1999, p. 104).[11] Conversely, any market demand curve with constant (negative) semielasticity has unit pass-through in the Cournot equilibrium conditional on the number of entrants.

The equilibrium pricing function conditional on the number of manufacturers $n \geq 1$ is the sum of marginal cost c and a term inversely proportional to n. Policies that change a, which are the focus of this section, trace out this pricing function. In particular, the monopoly and duopoly prices can be many times greater than the perfectly competitive price c. For many purposes, these theoretical pricing results are a good approximation of empirical findings for drug markets (FDA 2017b; Dave et al. 2017; Conrad and Lutter 2019). In contrast, drug markets are poorly described by Bertrand competition (for a homogeneous product), which has trouble explaining costly entry, as it predicts that price would be c regardless of whether the market has one generic or 10.[12]

More surprising, the pass-through assumption delivers a number of quantitative static welfare conclusions—that is, conclusions about the sum of the competitive and entry expenditure effects—without restricting the values of the price elasticity or semielasticity of demand or the level of marginal cost. The relationship between the ANDA cost a and aggregate expenditure on it, $(n-1)a$, follows a single-peak Laffer curve shape. Aggregate ANDA expenditure is 0 both in the monopoly case and in the limit as a goes to 0. Ignoring integer constraints, the peak ANDA expenditure is at the ANDA cost supporting $(3+\sqrt{5})/2$ (about 2.6) manufacturers, as shown in Appendix A.

Ignoring integer constraints, the static marginal benefit of relaxing ANDA barriers is 0 in the neighborhood of the entry barrier supporting $n = 1$ as an equilibrium. The innovation (opportunity) costs are strictly greater than 0, which means that the first generic entrant can have a net social cost. However, static social surplus strictly declines with ANDA cost a at any value of a supporting $n > 1$. Reducing a in the amount that induces exactly one more entrant creates the most

[11] A demand curve with a constant semielasticity is consistent with any (negative) value for the equilibrium price elasticity of demand. Like many other demand curves, it is more price elastic at higher prices. Although the demand curve has no choke price, the area under the demand curve is finite.

[12] The tension between Bertrand competition and costly market entry is known as the Bertrand paradox (Mukherjee 2005). Indeed, for explaining drug-market pricing, even the Cournot model may not be far enough from Bertrand because the former predicts that the first generic entrant reduces the markup by a factor of 2, which appears to be more than occurs empirically. Also note that the crucial assumption of the Cournot model for my purposes is not that manufacturers set quantities rather than prices but that each manufacturer perceives that it must select an own quantity and price combination from a demand curve (inclusive of all competitors' strategic reactions) that has the same slope as the market demand curve.

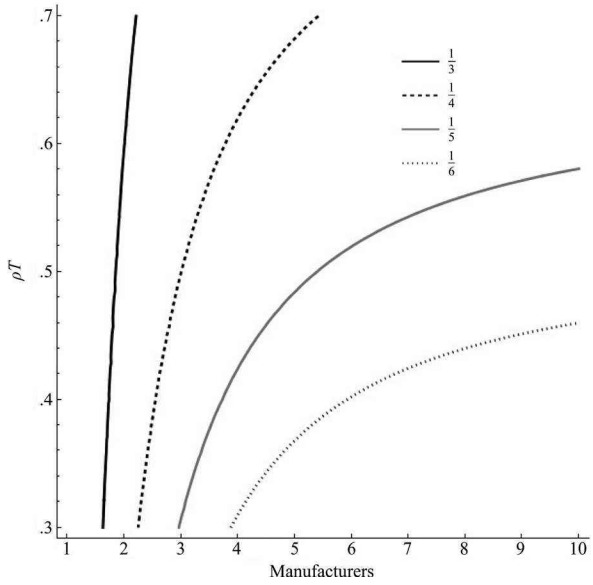

Figure 1. Level curves of the innovator's share of surplus

static welfare when it is adding a third manufacturer (that is, a second generic) and the second most when adding a fourth manufacturer.[13]

This model also says a lot about how the social benefits of innovation are allocated between the innovator and consumers. It predicts innovators' profits and social surplus for the T years that the patent is effective and the years after its expiration. The ratio of the present value of the innovator's profits to the present value of social surplus is shown in equation (1):

$$\text{Innovator Share} = \frac{1}{2} - \frac{n_1^2 - 1}{2} \frac{1}{1 + n_1^2 + (e^{\rho T} - 1)2n_1^2 e^{-(n_1 - 1)/n_1}} \in \left(0, \frac{1}{2}\right), \quad (1)$$

where ρ is the annual discount rate and $n_1 > 1$ is the number of manufacturers after patent expiration. The discount rate reflects not only the time value of money but also any exponential trends in market demand, such as decay that may occur as therapeutic substitutes come on the market (Lichtenberg and Philipson 2002). The fact that the share is significantly less than 1 means that the social benefit of innovation significantly exceeds what the innovator spends on it. Without any assumption about the relative costs and benefits of a T-year patent life, Figure 1 shows level curves of the innovator's share as a function of ρT and n_1 and sug-

[13] In decreasing order of static social welfare increments, the subsequent additions are fifth, second, sixth, and seventh manufacturers and so forth. Note that, even by the static criterion, the Cournot equilibrium has excessive entry at any given level of a (Mankiw and Whinston 1986).

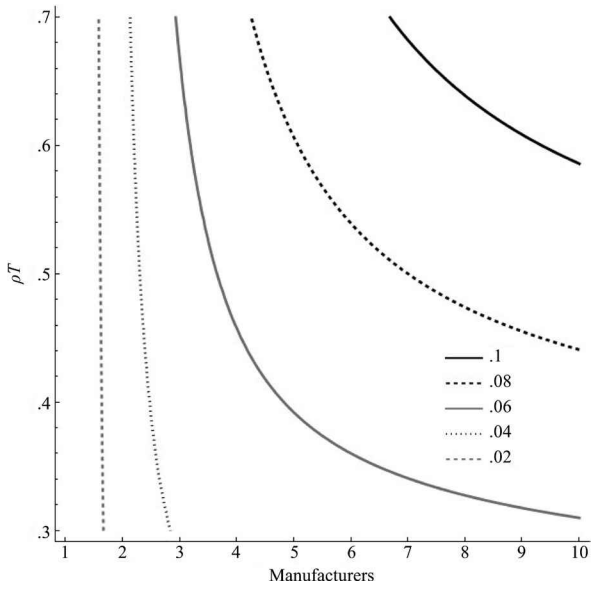

Figure 2. Level curves of the elasticity of innovation with respect to profit that justifies the actual patent length.

gests that innovators capture about a quarter of the social surplus.[14] Not surprisingly, this share increases with the patent's duration and the discount rate but decreases with the number of postpatent competitors.

Figure 2 shows level curves for the elasticity of the quantity of new drugs with respect to innovators' profits that justifies T years as the optimal patent life. This is the critical elasticity I use in what follows to weight the innovation benefits of protecting incumbents against the static social benefits of enhanced competition.

Table 2 shows the welfare consequences of increasing generic entry by one manufacturer, achieved through reduced ANDA barriers, beginning with the case in which one generic enters a postpatent market that had none. Each entry is simulated by reducing the ANDA cost a from the value supporting n_1 equilibrium generics to the value supporting $n_1 + 1$. For the impacts on postpatent flows of surpluses and costs, the units are normalized so that the profit flow under patent is 1. Row 1 is the competition effect, which unsurprisingly is greatest for the first generic entry because of the large gap between marginal cost and marginal social value under monopoly. Even though the innovator loses profit, combined producer and consumer surplus increase by an amount that is 47.3 percent of the profit a monopoly manufacturer would earn. The increments to surplus fall with

[14] The relationship between innovation share and n_1 in equation (1) and Figure 1 is a parametric relationship traced out by changing the ANDA cost a. Using a linear demand assumption, Philipson and Jena (2006) estimate a smaller share for human immunodeficiency virus drugs. Nordhaus (2004) estimates an even smaller share for the economy as a whole, which includes innovations without legal intellectual property rights. See also Jones and Summers (2020).

Table 2

Welfare Consequences of Reducing Generic-Entry Barriers

	Increase in Generic Manufacturers				
	Zero to One	One to Two	Two to Three	Three to Four	Four to Five
Impact on postpatent flows:					
1. Consumer and producer surplus, ignoring entry costs	.473	.124	.049	.024	.014
2. Aggregate generic-entry costs	.412	.021	−.036	−.041	−.037
3. Static surplus after expiration (rows 1 − 2)	.061	.103	.085	.065	.050
Impact on annuitized values, discount rate 6 percent:					
4. Static surplus after expiration	.031	.052	.043	.033	.025
5. Innovation benefit with elasticity .076	−.053	−.024	−.012	−.006	−.004
6. All three welfare components (rows 4 + 5)	−.023	.028	.031	.026	.021
7. Cumulative from zero generics	−.023	.005	.036	.063	.084
Impact on annuitized values, discount rate 4 percent:					
8. Static surplus after expiration	.038	.065	.054	.041	.032
9. Innovation benefit with elasticity .060	−.056	−.028	−.014	−.008	−.005
10. All three welfare components (rows 8 + 9)	−.018	.038	.039	.033	.027
11. Cumulative from zero generics	−.018	.020	.059	.092	.119

Note. Present values are from the perspective of the effective beginning of the patent and are then annuitized (over a perpetual horizon) to compare with the profit flow under patent. This comparison profit flow does not vary across columns or rows. Discount rates and patent lives matter only as a product. Patent life is 11.5 years. A negative innovation benefit is a cost. Row values may not add because of rounding.

each subsequent generic entrant. On the other hand, ANDA costs are incurred with the first generic that would not be incurred under monopoly. This expenditure amounts to 41.2 percent of the profit a monopoly manufacturer would earn. Reducing per-entrant costs enough to induce a second entrant also increases aggregate entry costs, although much less than the first entrant did. Further reductions in per-entrant costs reduce aggregate costs. Although not shown in Table 2, in the limit aggregate entry costs go to 0 even though the number of entrants is unbounded.

Row 3 in Table 2 shows the net of the previous two rows. This static surplus is positive for all increments although, as noted previously, it is greater for the second, third, and fourth generic than for the first. As with results shown in Figures 1 and 2, this part of Table 2 does not depend on the magnitude of the semielasticity of demand with respect to price. Moreover, because it refers only to postpatent flows, it does not depend on the discount rate or patent duration.

Although not shown in Table 2, the redistribution from innovator to consumers due to the first generic is almost 10 times the addition to static surplus shown in row 3 (see also Appendix A). The amount of redistribution not only speaks to the political economy of generic-entry policy but also raises concerns that generic entry may discourage innovation. Table 2 also accounts for the innovation effects under two alternative assumptions about the product ρT of the discount rate and patent length. Those products are 6 and 4 percent of 11.5 years.[15]

Generic-entry policy affects surplus flows, such as those shown in rows 1 and 3, after patent expiration. Using the two alternative discount factors, rows 4 and 8 discount the values in row 3 back to the date when the innovator's product entered the market and converts them into perpetual annuities. As a result, the annuitized values of static surplus in row 4 are about half of their corresponding entries in row 3. The discount factor used to calculate row 8 is farther from 0 owing to the lower discount rate.

Generic entry reduces innovators' profit, which reduces the supply of new drugs to the marketplace (Vernon et al. 2009). The patent life would have been optimal on average prior to GDUFA I if the elasticity of new drugs with respect to innovators' profit were .076 and .060, which are the values assumed for the second and third sections of Table 2, respectively.[16] The present value of the forgone social surplus associated with the forgone new drugs is shown in rows 5 and 9 as negative numbers because the forgone drugs are a cost. Rows 6 and 10 show the sum of the innovation benefit and the postpatent static surplus. For the first ge-

[15] The Congressional Research Service (Schacht and Thomas 2012) estimates the average effective patent life for drugs to be 11.5 years, including the extensions provided by the Hatch-Waxman Act. The effective life is less than the statutory life (20 years) owing to the patent time used during the FDA approval process. The results in Table 2 would be identical if instead, for example, the products were taken as 3 and 4 percent of 23 years.

[16] For the pre-2012 optimal-patent-life analysis, an average of three generic entrants is assumed after a patent's expiration. Each assumption with a different discount rate therefore corresponds to its own point in Figure 2 at a horizontal position of four manufacturers. See Appendix B for the algebra deriving the innovation elasticity and its derivative calculations in rows 5 and 9 of Table 2.

neric entrant, the forgone innovation dominates, but the static surplus dominates for subsequent entrants. After the second entrant, the static surplus is a good approximation of the total welfare consequences.

Rows 7 and 11 show the cumulative welfare consequences—that is, the net benefit of having additional generics compared with none. Contrary to what is suggested by the static surplus, social welfare is lower with one generic than with zero. But the zero-generic surplus is still less than the surplus from two or more generics. Comparing these values shows how the results are fairly insensitive to the discount term ρT. The priority given by GDUFA II to second and third entrants may have an economic justification in Table 2.

Table 3 applies the results from Table 2 to the empirical distribution of drug markets as measured in the FDA's Orange Book. Following FDA protocol for NDAs and ANDAs, I define a drug market to be the cross between active ingredient(s), dosage form, and route of administration, "ignoring differences in strength and package sizes" (FDA 2017b). For each market and month, I use the Orange Book to track the number of NDAs and ANDAs so far approved for that market.[17] The total number of approved manufacturers for each cell is then merged with the cumulative benefits and costs shown in Table 2, extended to include results for more than five generic manufacturers. Each cumulative benefit and cost is then averaged across markets at a point in time, with the results shown in the the first three columns of Table 3,[18] which also shows changes over time.

Rows 1 and 2 of Table 3 show how first (and perhaps second) generic approvals were comparatively important between 2012 and 2016 because, on average, competition benefits increased more during that period (.018) than during 2016–20 (.014), but so did entry costs. Combined static surplus increased more during the latter period: .019 compared with .013. Rows 5 and 8 suggest that innovation opportunity costs increased about the same amount during the two periods, so the combination of all three welfare components increased almost twice as much (about .008) between 2016 and 2020 than it did during 2012–16. Over the 8 years the combined benefits are, amortized over time, over 1 percent of the profit flow received by the patent holder prior to the patent's expiration. Assuming that a significant majority of drug revenue prior to expiration goes toward patent holders' profit, then the net social benefits are an amount equivalent to about 1 percent of revenue prior to expiration. This appears to be of the same order of magnitude as, although likely smaller than, Peltzman's estimate of the net costs of the

[17] Applicants with more than one approved NDA or ANDA are counted only once. A weakness of the Orange Book data is that "both FDA and industry personnel believe a substantial number of approved ANDAs are no longer marketed, but it is unknown how large is their number" (Berndt, Conti, and Murphy 2018, p. 139). To the extent that ANDA exit occurs in low-volume markets, it may not be important for the industry surplus results of this paper.

[18] If none of the markets at a point in time had a generic, then the values in the first two rows of the corresponding column in the left half of Table 3 would be 0. If every market had exactly one generic, then those entries would be the same (for example, .473 and .412) as the entries in Table 2.

Table 3

Welfare Consequences of Generic Entry

	Empirical Distributions Compared with No Generics			Changes over Time		
	2012	2016	2020	2012–16	2016–20	2012–20
Impact on postpatent flows:						
1. Consumer and producer surplus, ignoring entry costs	.320	.337	.351	.018	.014	.031
2. Aggregate generic-entry costs	.174	.178	.173	.004	−.005	−.001
3. Static surplus after expiration (rows 1 − 2)	.146	.160	.179	.013	.019	.032
Impact on annuitized values, discount rate 6 percent:						
4. Static surplus after expiration	.073	.080	.090	.007	.009	.016
5. Innovation benefit with elasticity .076	−.044	−.047	−.049	−.003	−.002	−.005
6. All three welfare components (rows 4 + 5)	.029	.033	.040	.004	.007	.011
Impact on annuitized values, discount rate 4 percent:						
8. Static surplus after expiration	.092	.101	.113	.008	.012	.020
9. Innovation benefit with elasticity .060	−.049	−.052	−.055	−.003	−.003	−.006
10. All three welfare components (rows 7 + 8)	.044	.049	.058	.005	.009	.014

Note. The various costs and benefits from the constant-semielasticity model are averaged across numbers of producers using the Food and Drug Administration's Orange Book cross-market empirical distribution as weights. For each market, the total number of extant manufacturers with approved abbreviated new drug applications is measured in December 2012, 2016, and 2020. A market is the cross between active ingredient(s), dosage form, and route of administration as reported in the Orange Book. Patent life is 11.5 years. The innovation benefit is a cost. All changes in the empirical distributions of numbers of generics are assumed to be derived from entry costs. Rows 7 and 11 are not relevant and are omitted. Row values may not add because of rounding.

1962 EA, which he found to be about 8 percent of industry revenue (Peltzman 1973, p. 1075).[19]

5. Barriers to the Marketing of Pandemic Vaccines

Pandemic vaccines provide a unique opportunity to measure the consequences of regulatory barriers to drug approval. The opportunity costs of pandemic vaccines and treatments are less speculative than those for most other drugs. For example, Peltzman (1973) finds that there were 25 fewer new drugs per year as a result of the 1962 EA. Because those drugs were not produced, it is difficult to know which diseases they would have treated and what benefits they would have conferred. In contrast, a pandemic vaccine prevents a specific disease. The opportunities forgone during a pandemic without an available vaccine are primarily familiar, and normal activities are curtailed as individuals and organizations seek to avoid infection.

In addition, the experience with pandemic vaccines, tests, and treatments suggests that the opportunity costs of approval barriers may have a fat right tail. Especially dangerous pandemics occur just once or twice per century and did not occur during Peltzman's sample period.

The COVID-19 pandemic also shows how FDA approval barriers can, in some instances, have the opposite of the effect intended for the 1962 EA, which is to reduce the number of unsafe and ineffective interventions used by consumers. The demand for interventions during a pandemic is high enough that many interventions are supplied outside FDA jurisdiction, especially while treatments or vaccines under FDA jurisdiction are delayed by its approval process.

5.1. Changes in Federal Pandemic Vaccine Approval Policy

In addition to the large economic literature critical of FDA approval barriers generally, a couple of strands of research influenced federal pandemic policy. One focuses on vaccine demand functions, incentivizing innovation, and whether effective vaccines can be expected to eradicate an infectious disease (Berndt et al. 2007; Geoffard and Philipson 1996, 1997; Glennerster, Kremer, and Williams 2006; Kremer 2000; Philipson 1996). Another includes Murphy and Topel (2003), Cutler and Kadiyala (2003), Lichtenberg (2003), Nordhaus (2003), Becker, Philipson, and Soares (2005), and work by others estimating the value of lifesaving medical innovations. Another is work on the application of Bayesian decision theory to new-drug approval (Berry 1985; Isakov, Lo, and Montazerhodjat 2019) noting that the trade-off between speed and safety or speed and efficacy is disease specific. Counterterrorism experts concerned with the use of viruses as bioweapons bring urgency to vaccine innovation (Borio et al. 2002; Clark and Pazdernik 2016).

[19] The revenue base in Peltzman (1973) includes revenues from drugs both on and off patent.

In 2018, Luciana Borio was working in the White House as national security director for medical and biodefense preparedness and asked Tomas Philipson of the CEA that the CEA undertake an economic analysis of pandemic vaccine innovation. The CEA (2019c, pp. 23, 1) concluded that "improving the speed of vaccine production is more important for decreasing the number of infections than improving vaccine efficacy" and emphasized the need for large-scale manufacturing and the possible advantages of "public-private partnerships." Borio and the CEA vaccine report prompted a 2019 executive order, also before the pandemic, noting that "viruses emerge from animals . . . that can spread efficiently and have sustained transmission among humans" and concluding that "[v]accination is the most effective defense" (Exec. Order No. 13,887, 84 Fed. Reg. 49,935 [September 19, 2019], p. 1).

Moderna finalized its messenger RNA sequence of the SARS-CoV-2 virus on January 13, 2020, and manufactured its first clinical vaccine batch by February 7, only 1 day after the first American died (in Wuhan, China) from COVID-19 (Moderna 2021; Zhong and Wong 2020). At that time, there were only 12 known cases in the United States (Centers for Disease Control and Prevention 2020). Nevertheless, experts were pessimistic as to the duration of vaccine development. The director of the National Institute of Allergy and Infectious Diseases told the US Senate in March 2020 that "a vaccine . . . will take at least a year or year and a half" largely because, he said, approval by the FDA necessarily requires a year or more (NBC News 2020). The *New York Times* put the potential vaccine-development timeline out to the year 2034 (Thompson 2020). Even the Pharmaceutical Research and Manufacturers of America (2020), the trade association for pharmaceutical manufacturers, said on March 13 that "12 to 18 months . . . is a best case estimate" of the amount of time it would take for a vaccine to be available to the public.[20]

Contrary to the above assertions, "when COVID-19 emerged, the White House was ready and expeditiously applied the [CEA] report's deregulatory and fiscal lessons to streamline FDA approval for vaccines and their parallel manufacturing on a large scale" (Grogan and Philipson 2020). The $20 billion federal program Operation Warp Speed launched in April 2020 to encourage and accelerate the development and mass manufacturing of COVID-19 vaccines, streamline federal approval for vaccines and their manufacture, and provide federal funds for private vaccine research and advance-purchase orders. Pfizer's vaccine was given emergency use authorization by the FDA on December 11, and Moderna received it on December 18 (FDA 2020; Moderna 2020). By the end of that month, at least 14 million vaccine doses had been manufactured and distributed in the United States (Hawkins and Kornfield 2020).

[20] The Pharmaceutical Research and Manufacturers of America deleted this wording on March 24.

5.2. *Excess Burden as an Analytical Framework for Measuring Opportunity Costs*

Let E denote exposure to the disease per unit of time and t denote the health cost of exposure. For example, t could be the value of a statistical life times the fatality rate per exposure. The arrival of a vaccine is a change in t: $dt < 0$. Let $U(E)$ denote the economic benefits of exposure, without regard for the health costs tE.[21] Therefore, reducing exposure by $-dE$ involves an opportunity cost $U'(E)dE$. The net benefit of the arrival of a vaccine is

$$d[U(E) - tE] = d[U(E)] - d[tE]. \tag{2}$$

In this formulation, one way to measure the opportunity cost of vaccine delay is as the effect of delay on the value of economic activity, which is the $d[U(E)]$ term, net of the effect on equilibrium health costs $d[tE]$. I refer to equation (2) as the excess-burden method.

Rearranging terms in equation (2) gives

$$d[U(E) - tE] = [U'(E) - t]dE - Edt. \tag{3}$$

If the amount of exposure equated benefits and costs at the margin, then the first term on the right-hand side of equation (3) would disappear, and there would be a second measurement method, which is the product of equilibrium exposure E and the effect dt of the vaccine on health costs conditional on exposure. In principle, dt would be revealed in double-blind clinical trials by comparing the vaccinated and the unvaccinated.[22] For example, if the health costs of exposure were entirely deaths valued at the value of a statistical life (VSL) and the vaccine reduces the disease's mortality by 90 percent, then Edt would be 90 percent of the mortality cost that would be incurred without the vaccine. I refer to Edt as the envelope method.

Regardless of whether exposure equates marginal costs and benefits, it is likely that people reduce their exposure in response to additional severity. Formally, $dE/dt < 0$, so the arrival of a vaccine has a larger effect Edt on conditional health costs than its effect $d[tE]$ on equilibrium health costs. Indeed, nothing in this model rules out the possibility that exposure is elastic to severity in the relevant range, so the arrival of a vaccine that is effective at preventing death from the disease, but less than 100 percent effective, increases equilibrium deaths.[23] This possibility highlights the more general result that proper measurement of vaccine benefits either holds exposure constant (the final term in equation [3]) or accounts for the economic benefits or reduced excess burden $u'(E)dE$ of the additional equilibrium exposure (equation [2]).

[21] This is a simplified version of the notion in Philipson (1995) of a disease as a tax on at-risk activities E, levied at rate t.

[22] In practice, those treated in clinical trials may suspect that they were treated because they experienced different symptoms than members of the placebo arm. If the treated respond by increasing their exposure, then the health gap between the two arms involves a tdE term and not just the Edt term.

[23] That is, diseases can illustrate the Peltzman (1975) effect too. See also Iyengar et al. (2022).

Equation (2) is a static model, but in reality the distribution of a vaccine requires a prolonged period of time. Mass manufacturing is required, and a distribution network must be built and staffed. More individuals become convinced to take a valuable vaccine as they observe others experiencing it. Even though vaccine approval does not in reality create an immediate transition to the static equilibrium associated with the vaccine, the static model's comparative statics are useful because an x-month approval delay postpones each stage of the prolonged processes of manufacturing, distribution, and so on by approximately x months.

5.3. Examples of Substitution outside Food and Drug Administration Jurisdiction

The simple excess-burden framework reveals that medical innovation such as a vaccine reducing t has therapeutic substitutes, broadly construed. Namely, any action $dE < 0$ that individuals and organizations take to reduce exposure is a prevention substitute for vaccination. Many of these substitute interventions, such as remote work, closing schools, and canceling normal medical appointments, are beyond the jurisdiction of the FDA and can be utilized without any attempt to demonstrate their safety or efficacy. Indeed, rational individuals may use such substitutes merely because they suspect them to be sufficiently safe and effective, especially during periods of time when more proven treatments are still awaiting FDA approval and therefore are prohibited.

Closing schools to in-person learning is an important example of a prevention activity that was available, was applied to tens of millions of children in the United States, and was outside the FDA's jurisdiction, while vaccines were within its jurisdiction.[24] Closing schools significantly harmed student learning and created extraordinary household stress. Halloran et al. (2021, p. 2) find, for example, "that offering full in-person instruction rather than fully hybrid or virtual instruction reduces test score losses in math by 10.1 percentage points (on the base of 14.2 percentage points)" (see also Mulligan 2021c). In many public school districts, the resumption of in-person learning was conditioned on teachers' vaccination (Shapiro and Hubler 2020; Blume and Esquivel 2021).[25]

If closing schools prevented infection, the effect has proven difficult to detect because students, teachers, and other school employees engage in activities if they are not in school, and those activities may pose greater infection risk than closely supervised activities in schools. The COVID-19 risks of teaching and learning in person during the pandemic, without a vaccine and including secondary trans-

[24] The potential timings of school closings and vaccine distribution are not as different as they might appear. The first day of closed schools in most states was Monday, March 16, 2020, which is the same day that Moderna first administered its vaccine to humans. Of course, the two prevention measures are different in terms of the speed at which they can be scaled and command public acceptance. Tests for COVID-19 were created by commercial and academic labs in February, but they too were delayed in reaching the market by FDA approval processes (Baird 2020).

[25] The tie between vaccine availability and school openings might be blamed on school districts rather than the FDA, but the point here is that a proper cost-benefit analysis of FDA decisions must acknowledge the real world in which the FDA is embedded. That real world includes actors seeking potentially ineffective substitute interventions in the absence of FDA approval.

mission to teachers' and students' families, was comparable to the risk of driving a car a few miles (Mulligan 2021c). Indeed, closing schools may have contributed to spreading the disease. On either an absolute or hourly basis, students and teachers appear to have been more likely to be infected outside of school than in school, where prevention protocols were more likely implemented and followed (Mulligan 2021a). Obviously the FDA's effectiveness standard for vaccines differs from the effectiveness standard (if any) that school districts applied in deciding to close schools.

During the pandemic, 20 percent of adults skipped or delayed medical appointments for serious health problems (Findling, Blendon, and Benson 2020). Because those choices had other health consequences and already by April 2020 medical facilities proved to be more effective at slowing the spread than the wider community (Mulligan 2021a), this seems to be another instance in which vaccine delay encouraged unsafe and ineffective substitutes. The FDA's delays in approving tests had a similar effect. As Cochrane (2021) put it, "[S]omeone could sell you a thermometer to detect a COVID-19 fever, but if someone tried to sell you anything more effective, the FDA would stop them. . . . Unlike a drug, a test result cannot harm you. Sure, the test might not be perfect, but it would be a lot better than relying on thermometers."

The pandemic was not the first important instance that FDA barriers steered consumers toward unsafe treatments outside FDA jurisdiction.[26] In 2010, the FDA pursued a reformulation policy in which OxyContin, a leading prescription opioid, would be removed from the market and replaced with a new abuse-deterrent formulation that could not be crushed or dissolved as easily (a common recreational practice contrary to the prescribed method of delivery). Several studies conclude that this change pushed many consumers from opioid prescriptions to heroin and then illicit fentanyl, both of which are manufactured and sold illegally without FDA oversight (see Alpert, Powell, and Pacula 2018; Schnell 2018; Mallatt 2018; Evans, Lieber, and Power 2019; Ruhm 2019). Any reduction in OxyContin overdose deaths was dwarfed by the increase in deaths from fentanyl overdoses, which were enough to reduce nationwide life expectancy 2 years consecutively for the first time in at least 50 years (Mulligan 2020a).[27]

5.4. The Opportunity Costs of COVID-19-Vaccine Delays

For both estimation methods, the opportunity cost of delay depends on the duration of delay and the VSL. I use a 6-month delay in what follows; readers may rescale results to approximately consider longer or shorter delays. I use a VSL of

[26] Other licensing requirements have at least occasionally led consumers to pursue dangerous alternatives outside the licensing jurisdiction. Carroll and Gaston (1981, p. 963) find that licensing "restrictions that reduce the density of electricians are significantly associated with a rise in the rate of death from accidental electrocution," apparently as consumers do their own electrical work.

[27] Law enforcement and technological changes also contributed to an expansion of heroin and illicit fentanyl markets.

$2.1 million as the cost of each death from COVID-19, which is an estimate accounting for the age and morbidity of those who died from the disease.[28]

The simplest envelope method, based on equation (3)'s final term at taking the primary health costs of the disease to be mortality rather than morbidity, is simply the product of the duration of delay, the number of COVID-19 deaths per unit of time, the VSL, and the factor reflecting the percentage effectiveness of the vaccine in terms of preventing death. Sensitivity analysis is therefore straightforward rescaling. I take the number of US COVID-19 deaths as 500,000 annually and vaccine effectiveness as 90 percent.[29] Therefore, according to the envelope method, the cost of a 6-month delay is $.5 \times 500{,}000 \times \$2{,}100{,}000 \times .9 = \$.47$ trillion in the United States.

In Mulligan (2021b) I estimate the opportunity costs from a specific change in exposure E, namely, from normal levels to a complete shutdown of nonessential activities.[30] The costs include forgone market and nonmarket production, including human capital opportunity costs, and deadweight costs of relief policies. During much of the pandemic, and in parts of the country, exposure was not reduced this much, which I associate with a 25.4 percent reduction in the rate of goods and service production in the private sector and an annualized opportunity cost of $8.6 trillion for the United States (Mulligan 2021b). Because this paper's term $d[U(E)]$ reflects the opportunity costs of exposure from vaccine delays, it rescales the $8.6 trillion for various plausible effects of vaccine delay on the flow of economic activity. These results are shown in the third column of Table 4 and can be rescaled proportionally to accommodate alternative estimates of the costs of reducing exposure while a vaccine is delayed.

The fourth column of Table 4 shows estimates of the $d[tE]$ term. This term is smaller in magnitude than the Edt term used for the envelope method ($.47 trillion) as long as exposure E falls with severity t. Nevertheless, the sum of the two columns, which is the opportunity cost according to the excess-burden method, exceeds $.47 trillion. This discrepancy has two explanations. One is that my implementation of at least one of the methods has incorrectly calibrated one of the

[28] To arrive at my estimate of the value of statistical life (VSL), I begin with the Kniesner and Viscusi (2019) $10 million estimate for 2017. Following the convention in this field, I then adjust to 2019 according to the increase in nominal gross domestic product per capita. Because I am comparing the mortality costs with costs incurred during the pandemic, I then adjust for the ratio of pandemic consumption to 2019 consumption among the affected population, which I take to be .9. The result of these two adjustments is $9.8 million. The more important adjustment is for differences between the ages and comorbidities of the general population and the population dying from COVID-19. The middle estimate from Briggs (2020) is that those who died from COVID-19 had a discounted average of 4.1 remaining quality-adjusted life years (QALYs), as compared with 19.1 for the general population. My $2.1 million VSL is $9.8 \times 4.1/19.1$. A somewhat lower VSL would be obtained by using Briggs's undiscounted QALY or undiscounted life expectancy. Failure to adjust for the characteristics of those who died from COVID-19 would lead to overestimates of VSL.

[29] This estimate from the Institute for Health Metrics and Evaluation (2021) assumes that the clinical trials are double-blind, but vaccination has obvious side effects. These effects may induce behavioral changes offsetting some of the vaccine's effect with behavior constant, which is what is needed for the envelope method.

[30] See also the discussion in Castillo et al. (2021) of the health and opportunity costs of limits on vaccine capacity.

Table 4
Vaccine-Delay Opportunity Costs according to the Excess-Burden Method

	Assumed Impact of Vaccine Arrival (%)		Delay Costs ($Trillions)		
Scenario	Private Production	Mortality Cost	Reducing Exposure	Equilibrium Mortality	Sum
1	3	−33	.51	.17	.68
2	3	−50	.51	.26	.77
3	3	−67	.51	.35	.86
4	5	−33	.85	.17	1.02
5	5	−50	.85	.26	1.11
6	5	−67	.85	.35	1.20
7	10	−33	1.70	.17	1.87
8	10	−50	1.70	.26	1.96
9	10	−67	1.70	.35	2.05

Note. A full shutdown of nonessential activities is assumed to cost $4.3 trillion per 6 months, including nonmarket opportunity costs and the deadweight costs of relief packages, while reducing gross domestic product by 25.4 percent. The $4.3 trillion value is rescaled for reduced exposure. The 100 percent mortality cost is 250,000 deaths per 6 months valued at $2.1 million each. A 6-month delay in vaccine production is assumed.

parameters. Another explanation is that exposure during the pandemic was reduced excessively relative to a $2.1 million VSL, so the $[U'(E) - t]$ term in equation (3) is positive. Indeed, in hindsight this was the case with at least some prevention measures such as closing schools.

The costs of distributing or administering the vaccine are real, as evidenced by the fact that vaccine take-up was much less than 100 percent and was prolonged. Such costs are not included in Table 4 because it quantifies the costs of delay rather than the cost of forgoing a vaccine indefinitely. Even at a 10 percent annual interest rate at 250 million Americans vaccinated, distribution and administration costs less than $800 per vaccinated would be overwhelmed by the rounding error.

6. Conclusions

Decades ago, Peltzman concluded that the FDA was not stopping enough ineffective drugs to justify the costs to consumers of its barriers to valuable medical innovation. Recent drug market events reinforce his conclusion. Drug prices are higher, and quantities less, because FDA approval barriers limit competition. Generic-entry policy changes initiated in 2012 began to alleviate some of those costs but had little effect on entry and social surplus until after 2016, when FDA approvals accelerated and prioritized second and third generics (Table 3). I estimate that these changes reduced the value created by innovation at about the same rate before and after 2016, but owing to the time lag between innovation

and generic entry, this opportunity cost is dwarfed by the static benefits of generic competition. The pandemic vaccine approval process, although surprisingly accelerated during the COVID-19 pandemic, still has large and obvious opportunity costs on the order of a trillion dollars in the United States for just a half-year delay (Table 4) and has even more costs worldwide.

One of Peltzman's approaches to assessing the benefits of FDA screening is whether it stops drugs from making it to market that would be deemed ineffective by experts such as the AMA. However, the alternatives against which the AMA judges effectiveness or costs may differ substantially from the practical alternatives employed by patients. Approval delays for pandemic tests and vaccines pushed tens of millions of individuals and businesses into preventions and treatments that were both outside the FDA's jurisdiction and hardly safe or effective. The pandemic experience raises the question of whether, on the whole, consumers engage in more unsafe and ineffective practices than they would if FDA approval were not a prerequisite for pharmaceutical sales. It also highlights another pitfall in the use of government licensing and approval requirements as consumer protection against imperfect information.[31]

My welfare analysis of generic-entry barriers relies on a simple model of competition and entry. Future research needs to extend the model to allow for nonprice competition such as advertising or negotiated discounts, which are quantitatively important differences in the conduct of brand names and generics.[32] Such an extension may further reduce the static social benefit of the first generic entrant relative to the benefit of the second and third, thereby strengthening the conclusion from Table 3 that generic-barrier reductions after 2016 were more beneficial than those before 2016. As long as the optimal-patent-length hypothesis is maintained, it is unclear how this extension would affect the relative magnitude of the innovation cost of reduced generic-entry barriers.

The value of an institution's reputation is another interesting area for future research. Accelerating approvals may reduce the expected costs of a present disease but risk complicating future information in the contingency that the FDA suffers a reputational loss from an accelerated approval. However, such an analysis should also consider the reputational costs of other institutions such as school districts that serve the demand for less effective substitute interventions that were created by the FDA's delay.

[31] Winston (2021) reviews prepandemic studies of consumer-protection regulation. Tabarrok (2017, p. 403; 2020) notes the irony that FDA test-approval policy increasingly has the effect of "limiting the information that patients may discover about their own bodies." See also Bourne (2021). A related question is whether a drug should be made available over the counter or by prescription (Temin 1992).

[32] See Lakdawalla and Philipson (2012) on pharmaceutical advertising before and after patent expiration. Murphy et al. (2014) discuss the economics of negotiated discounts, which are a significant share of gross prescription drug expenditure (Roehrig 2018).

Appendix A

Cournot Competition Algebra with Unit Pass-Through

Here I show the algebra of the unit pass-through Cournot model, with emphasis on the quantitative results that are independent of the level of demand, the elasticity of demand, and the level of marginal cost. I consider a market with $Q < A$ aggregate units sold by n sellers at price $p > 0$ and constant marginal cost c. The market demand curve is exponential:

$$Q = Ae^{-p/\alpha}. \tag{A1}$$

I impose no restrictions on the demand constants a and α except that they are positive. The area under this demand curve is

$$u(Q) = \left(1 + \ln\frac{A}{Q}\right)\alpha Q. \tag{A2}$$

For a given number of producers, the Cournot equilibrium price p, aggregate quantity Q, and per-seller quantity q are

$$p = \frac{\alpha}{n} + c \tag{A3}$$

and

$$nq = Q = Ae^{(-1/n)-(c/\alpha)}. \tag{A4}$$

It is straightforward to verify that these equations are consistent with symmetry, the market demand curve (equation [A1]), and unit pass-through of c conditional on n. The profit-maximization problem for a Cournot competitor is

$$\max_q \left(\alpha \ln\frac{A}{q + (\text{Others})} - c\right)q, \tag{A5}$$

where the first term in parentheses is the market price as a function of own sales q and the sales of others. The first-order condition of expression (A5) is satisfied with symmetry if and only if q satisfies equation (A4).

While the patent is in force, $n = 1$. Ignoring integer constraints on the number n of competitors, the equilibrium number after patent expiration is implicitly defined by

$$a = \frac{\alpha A}{n^2}e^{(-1/n)-(c/\alpha)}, \tag{A6}$$

where a is the ANDA cost paid by every seller except the one with the original patent. The number of competitors implied by equation (A6) puts equilibrium profits at 0 for all sellers except the one whose profits are a. It follows that profits prior to patent expiration are the right-hand side of equation (A6) with n set to 1, which is $\alpha A e^{-1-c/\alpha}$. After expiration, the owner of the expired patent earns a.

The two static flows represented in rows 1 and 2 of Tables 2 and 3 are $u(Q) - cQ$ and $(n-1)a$, respectively, expressed as ratios to $\alpha A e^{-1-c/\alpha}$:

$$\frac{u(Q) - cQ}{\alpha A e^{-1-c/\alpha}} = \frac{n+1}{n} e^{1-1/n} \tag{A7}$$

and

$$\frac{(n-1)a}{\alpha A e^{-1-c/\alpha}} = \frac{n-1}{n^2} e^{1-1/n}. \tag{A8}$$

Note that these normalized flows depend only on $n \geq 1$ (generic manufacturers ≥ 0) and are thereby reported in Tables 2 and 3 without any quantitative assumptions about the demand parameters (A and α) or the level of marginal cost c. Equation (A8) is the single-peak Laffer-curve shape referenced in Section 4.2 with peak at $n = (3 + \sqrt{5})/2$.

The present value of profits of the owner of a T-year patent are, from the perspective of the effective beginning of the patent,

$$\frac{1 - e^{-\rho T}}{\rho} \alpha A e^{-1-c/\alpha} + \frac{e^{-\rho T}}{\rho} a. \tag{A9}$$

For reporting in Tables 2 and 3, these present values are annuitized (multiplied by ρ) and then divided by the flow of profits under patent, $\alpha A e^{-1-c/\alpha}$. After this normalization, expression (A9) depends only on n and the product ρT.

The static social surplus (the difference between equations [A7] and [A8]) is greater with one generic ($n = 2$) than none ($n = 1$), but the increment is dwarfed by the redistribution from the innovator to consumers. The share of the innovator's monopoly profit flow lost from the first generic is

$$1 - \frac{a}{\alpha A e^{-1-c/\alpha}} = 1 - \frac{\sqrt{e}}{4}. \tag{A10}$$

By comparison, as a ratio to the monopoly profit, the addition to social surplus is

$$5\frac{\sqrt{e}}{4} - 2. \tag{A11}$$

The redistribution in equation (A10) is almost 10 times the value of expression (A11).

Appendix B

Estimation of the Value of Forgone Innovation

Let P denote the probability of creating a new product, v denote the present social value of a new product, and m denote the present value accruing to the innovator conditional on discovering the new product. Under an alternative entry policy, their values would be P', v', and m', respectively. Consider the increment to expected present social value, normalized by P:

$$\frac{P'v' - Pv}{P} = \left(\frac{P'}{P} - 1\right)v' + v' - v. \tag{B1}$$

The second term is the effect of policy on the present value of static welfare. Converted to an annuity value, it is shown in rows 4 and 8 of Table 2. The first term in equation (B1) can therefore be interpreted as the innovation-value term, which is shown as annuity values in rows 5 and 9 of Table 2. Each of the values m, m', v, and v' depends on the discounting term ρT and the number of producers n after patent expiration. The ratio term in the parentheses in equation (B1) is $(m'/m)^{\eta}$, where a single elasticity η (regardless of ρT and n) is calibrated as follows.

There is only one patent policy even while generic barriers vary over time and drugs vary in terms of generic entry. If the patent life (about 11.5 years) maximized Pv for products that will have four producers after patents expire, then a marginal reduction in the patent life from 11.5 years would increase v by the same percentage that it reduces the probability of innovation P.[33] The first-order condition with respect to patent life is

$$\eta \frac{d\ln m}{dT} + \frac{d\ln v}{dT} = 0, \tag{B2}$$

$$\eta = \frac{m}{v}\frac{v_3 - v_0}{m_0 - m_3}, \tag{B3}$$

where equation (B3) is derived from equation (B2) using the fact that v is the weighted sum of v_0 (surplus flow under patent) and v_3 (surplus flow with four producers, three of which are generics), and similarly for m. The second ratio in equation (B3) features differences because the patent length changes the weights in the sums without affecting the flows conditional on patent status. The first ratio is the innovator's share of the present value of social surplus, shown in Figure 1 conditional on ρT and n; a value of $n = 4$ is used for the purpose of applying equation (B3). Application of equation (B3) yields the values $\eta = .076$ and $\eta = .060$ for $\rho = .06$ and $\rho = .04$, respectively.

Recall that η is the elasticity of new drugs with respect to innovators' reward, which has been the subject of previous studies such as Cerda (2003) and Acemoglu and Lin (2004). The latter, for example, estimates an elasticity of new drugs with respect to market size of about 4 to 6 by comparing drugs serving larger patient populations with those serving smaller ones. The discrepancy between their estimates and the values used in Table 2 suggests that the patent length is far short of maximizing expected social surplus, the (positive) elasticity of the innovator's return with respect to market size is close to 0, cross-sectional comparisons exaggerate the elasticity that is relevant for determining the optimal patent length, or some combination of these factors. As noted in the main text, to the extent that patent length is short of maximal, generic-entry barriers can enhance social surplus by serving as a backdoor method of extending patent life.

[33] In 2012, the average number of producers according to the Orange Book was 3.6. It was 3.9 in 2016.

References

Acemoglu, Daron, and Joshua Linn. 2004. Market Size in Innovation: Theory and Evidence from the Pharmaceutical Industry. *Quarterly Journal of Economics* 119:1049–90.

Alpert, Abby, David Powell, and Rosalie Liccardo Pacula. 2018. Supply-Side Drug Policy in the Presence of Substitutes: Evidence from the Introduction of Abuse-Deterrent Opioids. *American Economic Journal: Economic Policy* 10:1–35.

Anderson-Cook, Anna, and Jared Maeda. 2019. Prices for and Spending on Specialty Drugs in Medicare Part D and Medicaid. Report. Washington, DC: Congressional Budget Office. https://www.cbo.gov/system/files/2019-03/54964-Specialty_Drugs.pdf.

Arrow, Kenneth J. 1962. Economic Welfare and the Allocation of Resources for Invention. Pp. 609–26 in *The Rate and Direction of Inventive Activity: Economic and Social Factors* by Universities—National Bureau Committee for Economic Research. Princeton, NJ: Princeton University Press.

Baird, Robert P. 2020. What Went Wrong with Coronavirus Testing in the U.S. *New Yorker,* March 16.

Becker, Gary S., Tomas J. Philipson, and Rodrigo R. Soares. 2005. The Quantity and Quality of Life and the Evolution of World Inequality. *American Economic Review* 95:277–91.

Berndt, Ernst R., Rena M. Conti, and Stephen J. Murphy. 2017. The Landscape of US Generic Prescription Drug Markets, 2004–2016. Working Paper No. 23640. National Bureau of Economic Research, Cambridge, MA.

———. 2018. The Generic Drug User Fee Amendments: An Economic Perspective. *Journal of Law and the Biosciences* 5:103–41.

Berndt, Ernst R., Rachel Glennerster, Michael R. Kremer, Jean Lee, Ruth Levine, Georg Weizsäcker, and Heidi Williams. 2007. Advance Market Commitments for Vaccines against Neglected Diseases: Estimating Costs and Effectiveness. *Health Economics* 16:491–511.

Berry, Donald A. 1985. Interim Analyses in Clinical Trials: Classical vs. Bayesian Approaches. *Statistics in Medicine* 4:521–26.

Blume, Howard, and Paloma Esquivel. 2021. Will California Campuses Reopen This School Year? It Depends on Vaccinating Teachers, Infection Rates. *Los Angeles Times,* January 26.

Boldrin, Michele, and David K. Levine. 2008. *Against Intellectual Monopoly*. Cambridge: Cambridge University Press, 2008.

Borio, Luciana, Thomas Inglesby, C. J. Peters, Alan L. Schmaljohn, James M. Hughes, Peter B. Jahrling, Thomas Ksiazek, et al. 2002. Hemorrhagic Fever Viruses as Biological Weapons: Medical and Public Health Management. *JAMA* 287:2391–2405.

Bourne, Ryan A. 2021. *Economics in One Virus: An Introduction to Economic Reasoning through COVID-19*. Washington, DC: Cato Institute.

Briggs, Andrew. 2020. Estimating QALY Losses Associated with Deaths in Hospital (COVID-19). Working paper. Avelon Health Economics, Morristown, NJ. https://avalonecon.com/wp-content/uploads/2020/04/COVID-19-QALYs-v3.pdf.

Cantor, David J. 1997. *Prescription Drug User Fee Act of 1992: Effects on Bringing New Drugs to Market*. CRS Report for Congress No. 97-838 E. Washington, DC: Congressional Research Service.

Carroll, Sidney L., and Robert J. Gaston. 1981. Occupational Restrictions and the Quality of Service Received: Some Evidence. *Southern Economic Journal* 47:959–76.

Castillo, Juan Camilo, Amrita Ahuja, Susan Athey, Arthur Baker, Eric Budish, Tasneem Chipty, Rachel Glennerster, et al. 2021. Market Design to Accelerate COVID-19 Vaccine Supply. *Science,* March 12, pp. 1107–9.

Caves, Richard E., Michael D. Whinston, and Mark A. Hurwitz. 1991. Patent Expiration, Entry, and Competition in the US Pharmaceutical Industry. *Brookings Papers on Economic Activity: Microeconomics,* pp. 1–66.

CEA (Council of Economic Advisers). 1975. *Economic Report of the President*. Washington, DC: Government Printing Office.

———. 1987. *Economic Report of the President.* Washington, DC: Government Printing Office.

———. 1989. *Economic Report of the President.* Washington, DC: Government Printing Office.

———. 2018a. *The Administration's FDA Reforms and Reduced Biopharmaceutical Drug Prices.* Washington, DC: CEA.

———. 2018b. *Economic Report of the President.* Washington, DC: Government Printing Office.

———. 2019a. *Economic Report of the President.* Washington, DC: Government Printing Office.

———. 2019b. *Measuring Prescription Drug Prices: A Primer on the CPI Prescription Drug Index.* Washington, DC: CEA.

———. 2019c. *Mitigating the Impact of Pandemic Influenza through Vaccine Innovation.* Washington, DC: CEA.

———. 2020. *Economic Report of the President.* Washington, DC: Government Printing Office.

Centers for Disease Control and Prevention. 2020. 2019 Novel Coronavirus (2019-nCoV) in the U.S. CDC.gov, February 7. https://web.archive.org/web/20200209003242/https://www.cdc.gov/coronavirus/2019-ncov/cases-in-us.html.

Cerda, Rodrigo. 2003. Drugs, Market Size, and Population. PhD diss. University of Chicago, Department of Economics.

Clark, David P., and Nanette J. Pazdernik. 2016. Biological Warfare: Infectious Disease and Bioterrorism. *Biotechnology* 2016:687–719.

Cochrane, John H. 2021. Free Markets Beat Central Planning, Even for COVID-19 Tests and Vaccines. *National Review,* January 12. https://www.nationalreview.com/2021/01/free-markets-beat-central-planning-even-for-covid-19-tests-and-vaccines/.

Conrad, Ryan, William Liu, Zachary Tillman, Alvin So, Andreas Schick, Clark Nardinelli, and Randall Lutter. 2017. *Estimating Cost Savings from Generic Drug Approvals in 2017.* Silver Spring, MD: FDA.

Conrad, Ryan, and Randall Lutter. 2019. *Generic Competition and Drug Prices: New Evidence Linking Greater Generic Competition and Lower Generic Drug Prices.* Silver Spring, MD: FDA.

Cutler, David M., and Srikanth Kadiyala. 2003. The Return to Biomedical Research: Treatment and Behavioral Effects. Pp. 110–62 in *Measuring the Gains from Medical Research: An Economic Approach,* edited by Kevin M. Murphy and Robert H. Topel. Chicago: University of Chicago Press.

Dave, Chintan V., Aaron S. Kesselheim, Erin R. Fox, Peihua Qiu, and Abraham Hartzema. 2017. High Generic Drug Prices and Market Competition: A Retrospective Cohort Study. *Annals of Internal Medicine* 167:145–51.

Duggan, Mark, and Fiona M. Scott Morton. 2006. The Distortionary Effects of Government Procurement: Evidence from Medicaid Prescription Drug Purchasing. *Quarterly Journal of Economics* 121:1–30.

Evans, William N., Ethan M. J. Lieber, and Patrick Power. 2019. How the Reformulation of OxyContin Ignited the Heroin Epidemic. *Review of Economics and Statistics* 101:1–15.

Express Scripts. 2019. *2018 Drug Trend Report*. February 6. St. Louis: Express Scripts. https://web.archive.org/web/20191216173635/https://www.express-scripts.com/corporate/drug-trend-report.

FDA (Food and Drug Administration). 2017a. FDA Tackles Drug Competition to Improve Patient Access. Press release. Washington, DC, June 27. https://www.fda.gov/news-events/press-announcements/fda-tackles-drug-competition-improve-patient-access.

———. 2017b. Generic Competition and Drug Prices. FDA.gov, November 28. https://wayback.archive-it.org/7993/20190423134204/https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm129385.htm.

———. 2017c. 2017 List of Off-Patent, Off-Exclusivity Drugs without an Approved Generic. FDA.gov, June. https://www.fda.gov/media/127816/download.

———. 2017d. Office of Generic Drugs. *Manual of Policies and Procedures No. 5240.3 Rev. 4*. November 9. Washington, DC: FDA Office of Generic Drugs. https://www.fdanews.com/ext/resources/files/2017/11/11-09-17-ANDAMAPP.pdf?1518765327.

———. 2020. FDA Takes Key Action in Fight against COVID-19 by Issuing Emergency Use Authorization for First COVID-19 Vaccine. Press release. Washington, DC, December 11. https://www.fda.gov/news-events/press-announcements/fda-takes-key-action-fight-against-covid-19-issuing-emergency-use-authorization-first-covid-19.

———. 2021. Orange Book Data Files. FDA.gov, August. https://www.fda.gov/media/76860/download.

Findling, Mary G., Robert J. Blendon, and John M. Benson. 2020. Delayed Care with Harmful Health Consequences: Reported Experiences from National Surveys during Coronavirus Disease 2019. *JAMA Health Forum* 1, art. e201463, 3 pp.

Geoffard, Pierre-Yves, and Tomas Philipson. 1996. Rational Epidemics and Their Public Control. *International Economic Review* 37:603–24.

———. 1997. Disease Eradication: Private versus Public Vaccination. *American Economic Review* 87:222–30.

Glennerster, Rachel, Michael Kremer, and Heidi Williams. 2006. Creating Markets for Vaccines. *Innovations: Technology, Governance, Globalization* 1:67–79.

Gottlieb, Scott. 2010. The FDA Is Evading the Law. *Wall Street Journal,* December 23, p. A17.

Grabowski, Henry, Genia Long, Richard Mortimer, and Ani Boyo. 2016. Updated Trends in US Brand-Name and Generic Drug Competition. *Journal of Medical Economics* 19:836–44.

Grogan, Joseph, and Tomas J. Philipson. 2020. How the White House Followed the Science to Enable a Quick Vaccine. *Newsweek,* December 11. https://www.newsweek.com/how-white-house-followed-science-enable-quick-vaccine-opinion-1553617.

Halloran, Clare, Rebecca Jack, James C. Okun, and Emily Oster. 2021. Pandemic Schooling Mode and Student Test Scores: Evidence from US States. Working Paper No. 29497. National Bureau of Economic Research, Cambridge, MA.

Hawkins, Derek, and Meryl Kornfield. 2020. Trump Administration Falls Far Short of Vaccination Goals as New Virus Variant Looms. *Washington Post,* December 31.

Hughes, James W., Michael J. Moore, and Edward A. Snyder. 2002. "Napsterizing" Pharmaceuticals: Access, Innovation, and Consumer Welfare. Working Paper No. 9229. National Bureau of Economic Research, Cambridge, MA.

Institute for Health Metrics and Evaluation. 2021. COVID-19 Vaccine Efficacy Summary. Institute for Health Metrics and Evaluation, June 4. http://www.healthdata.org/covid/covid-19-vaccine-efficacy-summary.

IQVIA Institute for Human Data Science. 2018. *Medicine Use and Spending in the U.S.* Plymouth Meeting, PA: IQVIA Institute for Human Data Science. https://www.iqvia.com/insights/the-iqvia-institute/reports/the-use-of-medicines-in-the-us.

Isakov, Leah, Andrew W. Lo, and Vahid Montazerhodjat. 2019. Is the FDA Too Conservative or Too Aggressive? A Bayesian Decision Analysis of Clinical Trial Design. *Journal of Econometrics* 211:117–36.

Iyengar, Karthikeyan P., Pranav Ish, Rajesh Botchu, Vijay Kumar Jain, and Raju Vaishya. 2022. Influence of the Peltzman Effect on the Recurrent COVID-19 Waves in Europe. *Postgraduate Medical Journal* 98:e110–e111.

Izhek, Olena, Tanja Saxell, and Tuomas Takalo. 2020. Optimal Patent Policy for Pharmaceuticals: Balancing Innovation and Access to New Drugs. Center for Economic Policy Research, August 25. https://voxeu.org/article/optimal-patent-policy-pharmaceuticals?qt-quicktabs_cepr_policy_research=0.

Jones, Benjamin F., and Lawrence H. Summers. 2020. A Calculation of the Social Returns to Innovation. Working Paper No. 27863. National Bureau of Economic Research, Cambridge, MA.

Klein, Daniel B., and Alexander Tabarrok. 2002. Is the FDA Safe and Effective? *FDAreview.org*.

Kniesner, Thomas J., and W. Kip Viscusi. 2019. The Value of a Statistical Life. In *Oxford Research Encyclopedia of Economics and Finance,* edited by Jonathan H. Hamilton. New York: Oxford University Press.

Kremer, Michael. 2000. Creating Markets for New Vaccines. Part I: Rationale. *Innovation Policy and the Economy* 1:35–72.

Lakdawalla, Darius, and Tomas Philipson. 2012. Does Intellectual Property Restrict Output? An Analysis of Pharmaceutical Markets. *Journal of Law and Economics* 55:151–87.

Lichtenberg, Frank R. 2003. Pharmaceutical Innovation, Mortality Reduction, and Economic Growth. Pp. 74–109 in *Measuring the Gains from Medical Research: An Economic Approach,* edited by Kevin M. Murphy and Robert H. Topel. Chicago: University of Chicago Press.

———. 2021. Are Drug Prices Subject to Creative Destruction? Evidence from the US, 1997–2017. *Health Economics* 30:1910–32.

Lichtenberg, Frank R., and Tomas J. Philipson. 2002. The Dual Effects of Intellectual Property Regulations: Within- and Between-Patent Competition in the U.S. Pharmaceuticals Industry. *Journal of Law and Economics* 45:643–72.

Mallatt, Justine. 2018. The Effect of Prescription Drug Monitoring Programs on Opioid Prescriptions and Heroin Crime Rates. Working paper. Bureau of Economic Analysis, Washington, DC.

Mankiw, N. Gregory, and Michael D. Whinston. 1986. Free Entry and Social Inefficiency. *RAND Journal of Economics* 17:48–58.

Moderna. 2020. Moderna Announces FDA Authorization of Moderna COVID-19 Vaccine in U.S. Press release. Cambridge, MA, December 18. https://investors.modernatx.com/news/news-details/2020/Moderna-Announces-FDA-Authorization-of-Moderna-COVID-19-Vaccine-in-U.S/default.aspx.

———. 2021. Moderna's Work on Our COVID-19 Vaccine. Modernatx.com, March 5. https://web.archive.org/web/20210330153008/https://www.modernatx.com/modernas-work-potential-vaccine-against-covid-19.

Morris, Emily Michiko. 2012. The Myth of Generic Pharmaceutical Competition under the Hatch-Waxman Act. *Fordham Intellectual Property, Media, and Entertainment Law Journal* 22:245–86.

Mukherjee, Arijit. 2005. Price and Quantity Competition under Free Entry. *Research in Economics* 59:335–44.

Mulligan, Casey B. 2020a. Prices and Federal Policies in Opioid Markets. Working Paper No. 26812. National Bureau of Economic Research, Cambridge, MA.

———. 2020b. *You're Hired! Untold Successes and Failures of a Populist President.* Alexandria, VA: Republic.

———. 2021a. The Backward Art of Slowing the Spread? Congregation Efficiencies during COVID-19. Working Paper No. 28737. National Bureau of Economic Research, Cambridge, MA.

———. 2021b. Economic Activity and the Value of Medical Innovation during a Pandemic. *Journal of Benefit-Cost Analysis* 12:420–40.

———. 2021c. The Incidence and Magnitude of the Health Costs of In-Person Schooling during the COVID-19 Pandemic. *Public Choice* 188:303–32.

Murphy, Kevin M., and Robert H. Topel. 2003. The Economic Value of Medical Research. Pp. 41–73 in *Measuring the Gains from Medical Research: An Economic Approach,* edited by Kevin M. Murphy and Robert H. Topel. Chicago: University of Chicago Press.

Murphy, Kevin, Robert Topel, and Edward Snyder. 2014. Competitive Discounts and Antitrust Policy. Pp. 2:89–119 in *The Oxford Handbook of International Antitrust Economics,* edited by Roger D. Blair and D. Daniel Sokol. Oxford: Oxford University Press.

NBC News. 2020. Dr. Fauci Explains Possible Timeline for Coronavirus Vaccine. NBCNews.com, March 3. https://www.nbcnews.com/video/dr-anthony-fauci-explains-possible-timeline-for-coronavirus-vaccine-talks-remdesivir-medication-79901253901.

Nguyen, Nguyen X., and Steve Sheingold. 2020. *Medicare Part B Drugs: Trends in Spending and Utilization, 2006–2017*. Assistant Secretary for Planning and Evaluation Issue Brief. Washington, DC: US Department of Health and Human Services. https://aspe.hhs.gov/sites/default/files/private/pdf/264416/Part-B-Drugs-Trends-Issue-Brief.pdf.

Nordhaus, William D. 2003. The Health of Nations: The Contribution of Improved Health to Living Standards. Pp. 9–40 in *Measuring the Gains from Medical Research: An Economic Approach,* edited by Kevin M. Murphy and Robert H. Topel. Chicago: University of Chicago Press.

———. 2004. Schumpeterian Profits in the American Economy: Theory and Measurement. Working Paper No. 10433. National Bureau of Economic Research, Cambridge, MA.

Peltzman, Sam. 1973. An Evaluation of Consumer Protection Legislation: The 1962 Drug Amendments. *Journal of Political Economy* 81:1049–91.

———. 1974. *Regulation of Pharmaceutical Innovation: The 1962 Amendments.* Washington, DC: American Enterprise Institute.

———. 1975. The Effects of Automobile Safety Regulation. *Journal of Political Economy* 83:677–725.

Pew Charitable Trusts. 2019. *FDA Approves More Generic Drugs, but Competition Still Lags.* Philadelphia: Pew Charitable Trusts. https://www.pewtrusts.org/-/media/assets/2019/02/fda_approves_more_generic_drugs_but_competition_still_lags.pdf.

Pharmaceutical Research and Manufacturers of America. 2020. *The Biopharmaceutical Industry Is Leading the Way in Developing New Vaccines and Treatments for COVID-19*. Washington, DC: Pharmaceutical Research and Manufacturers of America. https://web.archive.org/web/20200320202603/https:/phrma.org/-/media/Project/PhRMA/PhRMA-Org/PhRMA-Org/PDF/G-I/IndustryResponseCOVID19.pdf.

Philipson, Tomas. 1995. The Welfare Loss of Disease and the Theory of Taxation. *Journal of Health Economics* 14:387–95.

———. 1996. Private Vaccination and Public Health: An Empirical Examination for U.S. Measles. *Journal of Human Resources* 31:611–30.

Philipson, Tomas, Ernst R. Berndt, Adrian H. B. Gottschalk, and Eric Sun. 2008. Cost-Benefit Analysis of the FDA: The Case of the Prescription Drug User Fee Acts. *Journal of Public Economics* 92:1306–25.

Philipson, Tomas J., and Anupam B. Jena. 2006. Who Benefits from New Medical Technologies? Estimates of Consumer and Producer Surpluses for HIV/AIDS Drugs. *Forum for Health Economics and Policy* 9, art. 3, 31 pp.

Philipson, Tomas J., and Eric Sun. 2008. Is the Food and Drug Administration Safe and Effective? *Journal of Economic Perspectives* 22(1):85–102.

Roehrig, Charles. 2018. The Impact of Prescription Drug Rebates on Health Plans and Consumers. Altarum. https://altarum.org/sites/default/files/Altarum-Prescription-Drug-Rebate-Report_April-2018.pdf.

Ruhm, Christopher J. 2019. Drivers of the Fatal Drug Epidemic. *Journal of Health Economics* 64:25–42.

Schacht, Wendy H., and John R. Thomas. 2012. *The Hatch-Waxman Act: A Quarter Century Later*. Washington, DC: Congressional Research Service.

Schmookler, Jacob. 1972. *Patents, Invention, and Economic Change: Data and Selected Essays,* edited by Zvi Griliches and Leonid Hurwicz. Cambridge, MA: Harvard University Press.

Schnell, Molly. 2018. The Economics of Physician Behavior. PhD diss., Princeton University.

Schumpeter, Joseph A. 1943. *Capitalism, Socialism, and Democracy*. London: Allen & Unwin.

Shapiro, Eliza, and Shawn Hubler. 2020. If Teachers Get the Vaccine Quickly, Can Students Get Back to School? *New York Times,* December 15.

Sheetz, Michael. 2017. Teva Stock Plummets 18% after Rough Quarter in US Generic Drug Market. Yahoo Finance, August 3. https://finance.yahoo.com/news/teva-stock-plummets-18-rough-135334052.html.

Tabarrok, Alex. 2015. Generic Drug Regulation and Pharmaceutical Price-Jacking. Marginal Revolution, September 24. https://marginalrevolution.com/marginalrevolution/2015/09/generic-drug-regulation.html.

———. 2017. Discussion: The FDA Is Unprepared for Personalized Medicine. *Biostatistics* 18:403–4.

———. 2020. Frequent, Fast, and Cheap Is Better than Sensitive. Marginal Revolution, July 24. https://marginalrevolution.com/marginalrevolution/2020/07/frequent-fast-and-cheap-is-better-than-sensitive.html.

Temin, Peter. 1980. *Taking Your Medicine: Drug Regulation in the United States*. Cambridge, MA: Harvard University Press.

———. 1992. Realized Benefits from Switching Drugs. *Journal of Law and Economics* 35:351–69.

Thompson, Stuart A. 2020. How Long Will a Vaccine Really Take? *New York Times,* April 30.
Uhl, Kathleen. 2016. Office of Generic Drugs (OGD) Directors' Update. Paper presented at the Generic Pharmaceutical Association Fall Technical Conference, Bethesda, MA, October 24. https://web.archive.org/web/20170112025645/http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/UCM527918.pdf.
US House. 2017. Committee on Appropriations. Hearing before the Agriculture Subcommittee (testimony of Scott Gottlieb). 115th Cong., 1st Sess., May 25. https://www.youtube.com/watch?v=56crqzD_xDg.
US Senate. 2016. *Implementation of the Generic Drug User Fee Amendments of 2012 (GDUFA).* Hearing before the Senate Committee on Health, Education, Labor, and Pensions (testimony of Janet Woodcock). 114th Cong., 2d Sess., January 28. https://www.fda.gov/news-events/congressional-testimony/implementation-generic-drug-user-fee-amendments-2012-gdufa.
Vernon, John A., Joseph H. Golec, Randall Lutter, and Clark Nardinelli. 2009. An Exploratory Study of FDA New Drug Review Times, Prescription Drug User Fee Acts, and R&D Spending. *Quarterly Review of Economics and Finance* 49:1260–74.
Vives, Xavier. 1999. *Oligopoly Pricing: Old Ideas and New Tools.* Cambridge, MA: MIT Press.
Winston, Clifford. 2021. *Gaining Ground: Markets Helping Government.* Washington, DC: Brookings Institution Press.
Zhong, Raymond, and Edward Wong. 2020. First American Dies of Coronavirus, Raising Questions about U.S. Response. *New York Times,* February 9, p. A13.