Regulation and welfare: evidence from paragraph IV generic entry in the pharmaceutical industry

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This article estimates welfare effects of accelerated generic entry via Paragraph IV challenges. Using data from 2000–2008 for hypertension drugs in the United States, we estimate demand using a random-coefficients logit model. We find consumers gain $42 billion whereas producers lose $32.5 billion from entry. This modest $9.5 billion gain in social welfare is consistent with our observation that overall consumption does not increase after entry—generic sales displace branded sales, shifting surplus downstream from producers to consumers, insurance companies,

and retailers. We demonstrate significant cross-molecular substitution and discuss challenges in determining what fraction of downstream surplus actually goes to consumers.

1. Introduction

■ The Drug Price Competition and Patent Term Restoration Act, informally known as the "Hatch-Waxman Act," was passed in 1984 and designed to balance access to pharmaceutical products while incentivizing pharmaceutical innovation in the United States. An important provision in this legislation allows generic manufacturers to attempt to enter the market *before* patents protecting original branded products have expired. Using this mechanism, known as a Paragraph IV (Para-IV) certification or challenge, generic manufacturers seek to enter patent-protected markets either by claiming noninfringement or invalidity of the branded product's patent. Even though the Para-IV challenge has been available to generic manufacturers since the passage of Hatch-Waxman, for reasons we will discuss, the number of challenges did not grow significantly until the late 1990s. Using unique and novel data we quantify, for the first time, the welfare effects of this accelerated generic entry as a result of Para-IV challenges.

We focus on the hypertension market in the United States, which is relatively large in terms of pharmaceutical revenues and disease prevalence. As a benchmark, we estimate the welfare effects of generic entry using the nested multinomial-logit demand model popularized by Berry (1994). However, given the restrictive assumptions and shortcomings associated with the nested-logit model, we focus our analysis on the results obtained from a full random-coefficients logit model (Nevo, 2000a, 2000b). Estimation of this model on quarterly data for the 2000–2008 period suggests consumer welfare gains from Para-IV entry of $42 billion. These are significant gains, but they are largely offset by declines in producer surplus. Our estimates suggest that Para-IV entry reduces producer surplus by $32.5 billion, leading to net social gains of approximately $9.5 billion. Importantly, the net social gains do *not* arise from an expansion in the total quantity of drug consumption as prices fall—for reasons we will discuss later, even large price declines do not appear to bring large numbers of inframarginal consumers into the US market for prescription drugs. Instead, the net social gains appear to be driven, in part, by an expansion in product variety associated with Para-IV entry. As we will see, branded producers often respond to Para-IV entry by launching reformulations of existing products that offer additional benefits to at least some patients; this does not appear to expand the total quantity of drug consumption but expands variety in a way that generates additional consumer surplus.

Our use of the term "consumer surplus" suggests that the benefits of entry and lower prices accrue directly to consumers, but we acknowledge in this article the reality that consumers interact with drug manufacturers through a complicated chain of intermediaries that include prescribing physicians, drug retailers, and insurance companies. It is really this nexus of parties that chooses drugs and collectively appropriates the gains from lower drug prices. It may therefore be more accurate to speak of "downstream" surplus rather than consumer surplus, though we use the latter term to avoid confusion and maintain continuity with the literature. Determining exactly what component of the aggregate downstream surplus actually goes to consumers is not possible, even with the rich data at our disposal. We return to these issues later in the article and describe future work that might help us disaggregate the downstream surplus into its various components.

In addition to welfare gains, we also document a high degree of cross-molecular substitution in this market. Cross-molecular substitution occurs when patients shift their hypertension drug consumption from a branded product to the generic version of a *different* branded product, based on a different molecule. We present anecdotal evidence suggesting that insurance companies encourage this shift among their customers and show that the scope for cross-molecular substitution

in hypertension appears to be substantial.[1] The implications of cross-molecular substitution are profound; a branded product's intellectual property protection, within a market, is only as strong as their weakest patent of its branded competitors. A high degree of cross-molecular substitution thus amplifies the *positive* impact of generic entry on consumer welfare and the *negative* impact of entry on producer profits.

Hatch-Waxman was originally designed to balance access to cheaper drugs on the one hand while preserving appropriate incentives for innovation on the other. We demonstrate in this article that Para-IV challenges have been an effective mechanism in terms of providing accelerated access to inexpensive generic drugs. Has this rising generic entry had an impact on the rate and direction of drug research and development activity? A full consideration of that question is beyond the scope of this article. However, ongoing research by the authors seeks to examine and quantify this effect (Branstetter, Chatterjee, and Higgins, 2014). Preliminary results suggest that the rising generic entry in US markets has significantly reshaped the nature of global drug development activity.

The article proceeds as follows. Section 2 offers a brief discussion of the regulatory environment in which pharmaceutical firms operate in the United States. Section 3 discusses the relevant prior literature. Our data and methodology are presented in Sections 4 and 5. Section 6 presents results, and we discuss the implications of our work and conclude in Section 7.

2. Regulatory environment and early generic entry

☐ **Hatch-Waxman and paragraph IV challenges.** The current regulatory environment faced by pharmaceutical companies in the United States can be traced to the passage of the Hatch-Waxman Act in 1984. This legislation expedites Food and Drug Administration (FDA) approval for generic entry while extending the life of pharmaceutical patents in order to compensate innovators who lost time on their "patent clocks" waiting for FDA approval (Grabowski, 2007). This balance was deemed necessary to equalize two conflicting policy objectives: giving pharmaceutical firms incentives to conduct drug research while improving consumer welfare by enabling generic firms to quickly bring copies to market (Federal Trade Commission (FTC), 2002).

When a pharmaceutical company submits a New Drug Application (NDA) to the FDA for approval they are required, by law, to identify all relevant patented technologies necessary to create the drug; these patents are subsequently listed in the *FDA Orange Book*.[2] Upon approval of a drug, the FDA will restore patent term to the pharmaceutical firm for time used by the FDA in the approval process (Grabowski, 2007).[3] In addition, the FDA will also grant each new approved product regulatory protection lasting for five years ("data exclusivity") that runs concurrently with patent protection.[4] During this data exclusivity period, regardless of the status of the underlying patent(s), no generic entry may occur. At the conclusion of data exclusivity, only patents protect branded products. The period running from the cessation of data exclusivity to the expiration of a drug's patents is commonly referred to as "market exclusivity" (see Figure 1).

Prior to the passage of Hatch-Waxman, generic manufacturers seeking to sell their products in the US market had to demonstrate the safety and efficacy of their products by putting them through clinical trials. Although the outcome of these trials lacked the uncertainty involved in the

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[1] See Aitken, Berndt, and Cutler (2009), who also draw attention to this phenomenon.

[2] During our sample period, there was no regulatory pathway through which generic producers could certify their products as "bioequivalent" to existing biologic drugs. The Affordable Care Act created the legal basis for entry, but the FDA did not approve such a product until March 2015. We thank an anonymous referee for urging us to clarify this point.

[3] There are limits to this. Pharmaceutical firms cannot receive a patent extension of more than five years, nor are they entitled to patent extensions that give them effective patent life (post approval) of greater than 14 years.

[4] There are exceptions, for example, orphan drugs receive seven years and reformulations receive three years of data exclusivity. A pediatric indication can receive an additional six months of data exclusivity. With the recent passage of the GAIN Act, certain antibiotics are eligible for five additional years of data exclusivity.

FIGURE 1

EXCLUSIVITIES AND INNOVATION IN PHARMACEUTICALS
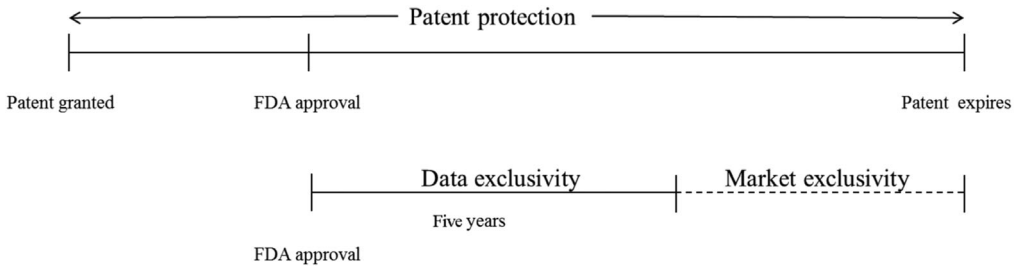
Notes: This figure demonstrates the two types of protection conferred on new drugs. When a new drug is approved by the FDA, the first five-year period (seven years for orphan drugs and five and a half years for pediatric drugs) carries with it a regulatory protection called "data exclusivity" that runs concurrent with underlying patent protection. Data exclusivity protects the underlying clinical data. At the conclusion of data exclusivity, a drug is protected only by its patents until they expire, a period termed "market exclusivity." Para-IV challenges occur only during the market exclusivity period.

trials of an innovative new drug, the time and expense involved were a significant disincentive for generics manufacturers to put products on the market, because they could not charge a premium price to offset the costs of clinical trials. During this time period, it is estimated that more than 150 products existed without any patent protection and without any generic entry (Mossinghoff, 1999). Although Hatch-Waxman did not lessen the burden of the clinical trials process for new branded drugs, it eliminated the requirement for separate clinical trials for generic manufacturers. Instead, generic manufacturers were merely required to demonstrate "bioequivalence" with branded products. This requirement can be satisfied through the simple demonstration that the active ingredient in the generic product diffuses into the human bloodstream in the same manner as the original branded product, using a tiny sample of a few dozen human subjects.

In theory, generics should be perfect substitutes for branded drugs as they are bioequivalent. Cleanthous (2002) shows that the data do not support this relationship but suggests this is the result of "spurious product differentiation," which he defines as arising "... when consumers perceive physically identical products to differ in quality." Recent evidence, however, suggests that consumer perceptions may have merit and although drugs may be bioequivalent, they may indeed differ in quality. For example, these differences can arise because of color allergies or allergic reactions to inert ingredients.[5] In addition, in some disease categories, practitioners have found that some patients react quite differently to generics versus branded drugs and to different generic versions of the same brand for reasons that are still not well understood. Several articles appeared in the April 17, 2007 edition of the prestigious journal, *Neurology*, discussing the high incidence of break-through seizures associated with the use of generic antiepileptic drugs. In recognition of this clinical reality, insurance companies such as Blue Cross Blue Shield of Georgia allow pediatric customers to stay on branded antiepileptic medications even though generics are available.

Hatch-Waxman provides four pathways (or "Paragraphs") that generic firms may follow in order to gain entry into a market. The process starts with the filing of an Abbreviated New Drug Application (ANDA) by a generic manufacturer with one of the four Paragraph certifications. A Paragraph I certification is one for which the originator firm has not filed patent information for its branded product. Paragraph II certification relates to cases when the branded product's patent has already expired (i.e., the end of market exclusivity), and Paragraph III certification relates

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[5] We thank an anonymous referee for making this important point.

FIGURE 2

ANDA PATENT CERTIFICATION OPTIONS FOR GENERIC MANUFACTURERS

Paragraph	Definition	Outcome
Paragraph I	Required patent information has not been filed	FDA may approve ANDA immediately; one or more generic applicant may enter
Paragraph II	Patent has expired	FDA may approve ANDA immediately; one or more generic applicant may enter
Paragraph III	Patent has not expired but will expire on a particular day	FDA may approve ANDA effective on the date the patent expires; one or more generic applicant may enter
Paragraph IV	Patent is invalid or is noninfringed by generic applicant	Generic applicant provides notice to the patent holder and NDA filer; entry of the first-filer may or may not occur

Notes: The regulatory pathway for generic entry in the united states can occur in one of four ways. Paragraph I, Paragraph II, and Paragraph III are used by generic manufacturers for drugs whose patents are either not listed in the *FDA Orange Book* or for those patents that have expired (or will expire). Paragraph IV is the only pathway that facilitates generic entry before expiry of patents or the conclusion of market exclusivity. Source: FTC (2002).

to cases when the generic manufacturer, notes that the patent on the branded product *will* expire on a certain date and that it seeks to enter only after patent expiry or end of market exclusivity. The fourth certification, Paragraph IV, establishes that the generic manufacturer does not infringe on a branded product's patents or that those patents are invalid.[6] This certification allows the generic manufacturer to enter the market and compete with the incumbent before the expiration of the patents protecting the innovator's drug. The FDA can act on a Para-IV certification after the conclusion of *data exclusivity* anytime during the market exclusivity window (see Figure 2).[7] If successful, these challenges can significantly decrease the effective patent life of branded products, bringing generics to the market earlier than otherwise would be the case (Grabowski and Kyle, 2007; Higgins and Graham, 2009).

When a generic manufacturer files an ANDA with a Para-IV certification, the generic manufacturer is obligated to notify the incumbent. Upon receipt, the incumbent pharmaceutical firm has two options: (i) do nothing, or (ii) sue the generic manufacturer (for patent infringement) within 45 days. If the incumbent firm chooses not to file suit and does nothing, then the FDA is entitled to approve the generic version of the branded product. If, however, the incumbent firm chooses to file suit, then that action automatically triggers a 30-month stay, on FDA action. During this stay, the FDA is unable to take any action on the ANDA unless there is a first court ruling. If the court rules in favor of the incumbent firm, the Para-IV challenge fails and the FDA is unable to authorize generic entry until the branded product's patents expire. On the other hand, upon a first court ruling in favor of the generic manufacturer, the FDA may approve the ANDA.

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[6] In practice, both findings of noninfringement and findings of invalidity of the original patent of the branded firm are important legal pathways to successful Para-IV entry. For a more detailed analysis of these legal strategies, see Palermo et al. (2015).

[7] Generic manufacturers may file a Para-IV challenge up to one year prior to the end of data exclusivity, but the FDA may not act on it until the conclusion of data exclusivity.

FIGURE 3

PARA-IV CHALLENGES ARE INCREASING IN THE UNITED STATES
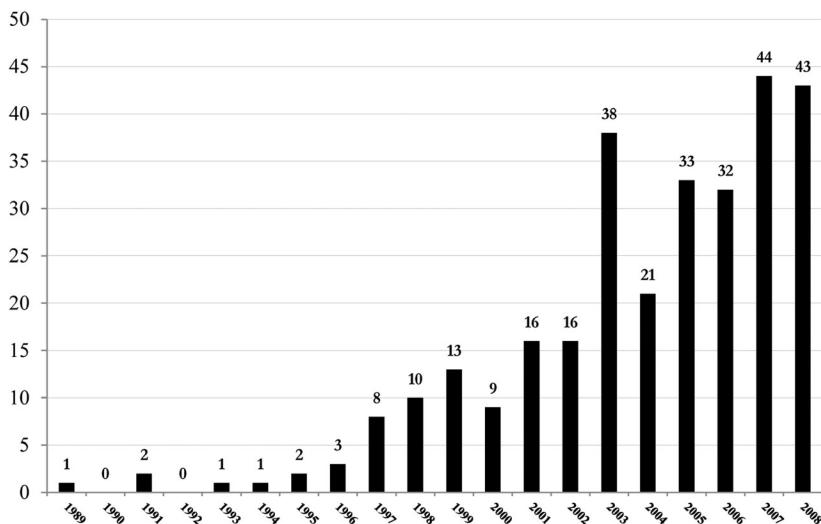
Notes: The number of Para-IV challenges has steadily increased since 1998. Source: Higgins and Graham (2009), Berndt et al. (2007), and FDA.

The first generic challenger is awarded 180 days of exclusivity.[8] During this 180-day exclusivity period, the first challenger is the sole generic provider and occupies a position of duopoly with the original branded provider.[9] Once this exclusivity period ends, any generic producer can enter the market, and, in our data, we see significant additional entry and rapid price declines. This, in turn, has a substantial impact on the revenues of the branded incumbent firms. During the first year after Para-IV entry, branded pharmaceutical product revenues declined by an average of 56%; in later years, branded revenues declined by an average of 89% relative to preentry levels.

Even though Para-IV challenges have been available to generic manufacturers since the passage of Hatch-Waxman in 1984, the number of challenges remained low until the late 1990s (see Figure 3). The acceleration of challenges since then can be tied to a series of court decisions, changes in FDA policy, and passage of the Medicare Act of 2003.[10] Over time, the ability of pharmaceutical firms to delay generic entry has been limited in important ways, dramatically intensifying competition and accelerating generic entry. In the early years, after passage of Hatch-Waxman, pharmaceutical firms were allowed to appeal initial judgments against the validity of their patents (or findings of noninfringement), and the FDA could not approve generic entry until all appeals had been exhausted. This was a time-consuming process that often held generic manufacturers at bay until patents expired or were about to expire. Starting in 2000, the FDA has approved entry as soon as courts issue a first ruling in favor of the generic challenger. Throughout the 1990s, incumbents often followed a practice of taking out additional patents after an initial Para-IV filing (or just before an anticipated Para-IV filing), thereby invoking nonconcurrent

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[8] The FDA may approve an ANDA upon a first court ruling in favor of the generic manufacturer. If that ruling is overturned on appeal, the generic manufacturer exposes itself to damages for lost revenue. This is a gamble many generics manufacturers are willing to take; the number of cases in which the first ruling has been reversed on appeal is limited.

[9] Note that the Para-IV provision operates at the level of an individual form-strength, and it is possible that different generic firms are successful for different form strengths. We thank an anonymous referee for stressing this detail.

[10] In 1998, *Mova v. Shalala* changed the interpretation of 180-day exclusivity. In 2000, the FDA started allowing generic entry following a first favorable court decision irrespective of a final court ruling. In 2003, the FDA started giving 180-day exclusivity to multiple applicants filing on the same first day.

30-month stays for each patent allegedly infringed (see Bulow, 2004).[11] In more recent years, due to changes in the Medicare Act of 2003, pharmaceutical firms have been limited to one 30-month stay per product. Generic manufacturers have also been given greater leeway in their use of the 180-day exclusivity period granted to first-filers under the law. Finally, legal experts claim that recent court rulings have made it easier to demonstrate patent invalidity and harder to demonstrate infringement (Knowles, 2010).[12] As a consequence of all these factors, the number of Para-IV challenges has surged from just one in 1994 to 44 in 2007 and to 230 in 2010. By the end of the 2000s, Para-IV challenges accounted for more than 40% of generic entry (Higgins and Graham, 2009; Berndt et al., 2007).

One strategy employed by branded firms in response to Para-IV entry is to launch a modified version of the original product, as a way of steering users away from the generic equivalent of the original product. The industry term for these modified drugs is "reformulations." Sometimes, the reformulation is an "extended release" or "once per day" version of the original drug, which helps ensure patient compliance with a regular drug treatment regime. In other cases, the reformulation combines the original active ingredient with other medications or alters the formula in other ways that limit side effects. In all cases, however, reformulations undergo limited clinical testing and are provided with three additional years of data exclusivity upon FDA approval. We find evidence in our data that at least some consumers value the features incorporated into these reformulations, and one can even think of the additional product variety induced by generic entry as a potential source of additional consumer welfare gains. However, these new product introductions do not generally prevent significant revenue losses following Para-IV entry, nor is there any evidence that, on average, reformulations expand the total quantity of drugs being consumed within a narrowly defined therapeutic area.

☐   **Cross-molecular substitution.** Most prescription health plans in the United States allow for the use of branded products until generics become available. Once that occurs, patients are given the generic by retail pharmacies unless the prescription is written "Dispense as written" or if the patient explicitly asks for a branded drug (in which case, there is usually a much higher copayment). Recently, insurance firms have started incentivizing patients to switch to different drugs, based on different molecules, for which a generic equivalent is available. As an illustrative example, let us assume there exists three branded products in a particular market, *Drug A*, *Drug B,* and *Drug C*, sold by three different pharmaceutical firms, and that *Drug B* just lost a Para-IV challenge in court. A generic version of *Drug B*, *Generic B*, has entered the market and is selling at a substantial discount to the prices of all three branded drugs. Insurance companies could attempt to profit from the entry of *Generic B* by encouraging patients taking *Drug A* or *Drug C* to switch to *Generic B*. Although insurance firms cannot force patients to move, they can entice them with lower (or no) copayments for *Generic B*. Table 1 provides a real-world example extracted from a letter Blue Cross Blue Shield of Georgia (BCBSGA) sent to patients suggesting generic alternatives to different branded products across several therapeutic categories. In the letter, BCBSGA offered to pay for the generic copay for a period of three months.

Because physicians, not patients or insurance companies, write prescriptions, these financial incentives will only shift drug consumption to the generic products if physicians also consent to the change. However, in many therapeutic markets, practicing physicians have long regarded different drugs, based on different molecules and/or different biochemical pathways to attack the disease, as equally effective therapies for the underlying illness. In such markets, physicians would generally consent to switching drugs if it saved their patients money. We refer to this

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[11] Industry insiders refer to this practice as patent "evergreening."

[12] Knowles (2010) provides a detailed review of the *KSR v. Teleflex* (2006) and *MedImmune v. Sun Pharma* (2007) cases, arguing that the former led to a new, higher standard for nonobviousness and the latter established a new, higher standard for noninfringement.

TABLE 1   Blue Cross Blue Shield of Georgia's Efforts to Profit from Cross-Molecular Substitution

Drug Class	Brand Name	Generic Suggested Through Generic Select Program
Angiotensin Receptor Blocker/Angiotensin Converting Enzyme Inhibitor	Cozaar, Diovan/HCT, Hyzaar, Altace (2.5, 5, or 10 mg), Atacand/HCT, Avapro, Avalide, Benicar/HCT, Micardis/HCT, Teveten	Benazepril, Enalapril, Enalapril HCTZ, Lisinopril, Lisinopril HCTZ
Antidepressant	Cymbalta, Effexor XR, Lexapro, Prozac (2 mg/ 5 ml solution), Effexor, Luvox/CR, Paxil/CR, Pexeva, Celexa, Zoloft, Prozac (nonsolution formulations)	Citalopram, Sertraline, Fluoxetine
Calcium Channel Blocker	Sular, Adalat CC, Cardene/SR, Norvasc, Plendil, Procardia XL	Amlodipine
Statin	Lipitor, Crestor, Pravachol, Zocor, Lescol, Lescol XL, Vytorin, Mevacor	Simvastatin, Lovastatin
Triptan	Maxalt, Maxalt–MLT, Zomig, Zomig–ZMT, Amerge, Axert, Frova, Imitrex, Relpax	Sumatriptan Tablets (Limit to 9 tabs/rolling 30 days)

This table presents data from a consumer communication sent by Blue Cross Blue Shield of Georgia to patients taking the brand name products listed in the second column. The letter provided a financial incentive in terms of a subsidized copayment if they would consider asking their physician to switch them to one of the respective generics identified in the third column. This communication provides an example of insurance companies seeking to profit from the opportunities for cross-molecular substitution in these therapeutic categories.

possibility of substitution across drugs and molecules within a therapeutic category in response to emerging price differentials as that category's degree of *cross-molecular substitution*.[13]

Where cross-molecular substitution is pervasive, the implications for pharmaceutical companies and consumers are quite significant. For pharmaceutical firms with branded products, cross-molecular substitution implies that their drug's market protection is only as strong as the weakest patent protecting a branded drug in a particular market. In the example given above, the transition from *Drug A* and *Drug C* to *Generic B* is occurring irrespective of the underlying Intellectual Property (IP) protection or exclusivity periods for those drugs. This activity has obvious welfare implications; the gains to consumers are potentially larger as patients using *Drug A* or *Drug C* can potentially benefit from the entry of *Generic B*. However, the producer loss will also be larger because the incumbents that market *Drug A* and *Drug C* will lose revenue. Of course, the extent of these impacts will vary across therapeutic categories, as some drugs are more easily substitutable. For example, we would expect higher substitutability in markets such as hypertension and allergy drugs, and lower substitutability in markets such as depression and epilepsy.

To give the reader a sense of the magnitude and scope of cross-molecular substitution in hypertension, we would direct the reader's attention to Figure 4. This figure illustrates the movement of sales, in quantity terms, across the major categories of hypertension drugs—Beta-Blockers, ACE-Inhibitors, and Calcium Antagonists. These drug categories use different biochemical pathways to treat the underlying illness; accordingly, they are assigned to different categories within the anatomical therapeutic chemical (ATC) classification system used by the pharmaceutical industry, which we will discuss in greater detail later in the article. Roughly midway through the sample period, there were important Para-IV challenges to successful brands in the ACE-Inhibitor category that opened the floodgates of generic competition and brought prices crashing down. These successful challenges followed on the heels of patent expiration for two successful brands, and added substantially to the overall momentum of growth in generic ACE-Inhibitor drugs. At that point, there was a major shift in demand, with the new ACE-Inhibitor generic drugs not only drawing substantial demand from other drugs in the same category, but also from Calcium Antagonists and Beta-Blockers.

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[13] Aitken, Berndt, and Cutler (2009) note a similar phenomenon.

FIGURE 4

EVIDENCE OF CROSS-MOLECULAR SUBSTITUTION IN HYPERTENSION DRUGS, 2000–2008
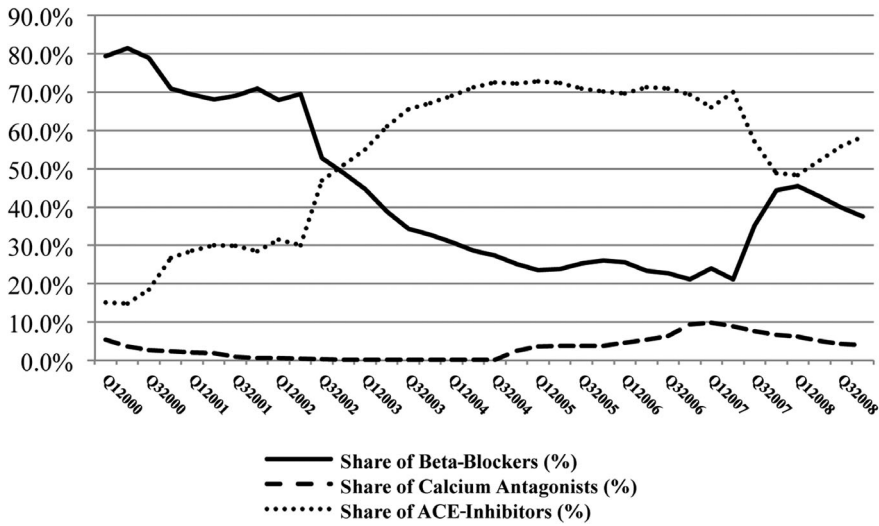
Notes: The figure plots the quarterly percentage shares of the three major classes of hypertension drugs (Beta-Blockers, Calcium Antagonists and ACE-Inhibitors) as measured by quantity sold (SU). Patients appear to be switching to ACE-Inhibitors from Beta-Blockers starting around the ninth quarter in our sample. However, by the 30th quarter, patients appear to be rotating back to Beta-Blockers. Over the entire time period, the share of calcium antagonist drugs remain low. The *x*-axis covers 36 quarters from Q1:2000 to Q4:2008. Source: IMS MIDAS™.

This simple figure speaks to the reality that substitution possibilities in hypertension extend not just within but also across the most basic categories of hypertension drugs. In the final years of our sample, there was another major inflection point. Successful generic entry in the key Beta-Blocker market brought prices sharply down. Demand shifted from the previously ascendant ACE-Inhibitor category to Beta-Blockers, with these two categories occupying far more equal shares of the total market by the end of our sample period. Again, we see evidence of large shifts across major therapeutic categories. Based on standard dosage frequency, we can infer roughly how many patients with chronic hypertension were shifted across therapeutic categories as brands lost patent protection and prices shifted. The magnitude of the rise in ACE-Inhibitor consumption in the middle of the figure implies a shift in the prescription patterns of approximately 24 million patients.[14] The reversion to Beta-Blockers at the end implies a shift of roughly 21 million patients.[15]

☐ **Generic entry leads to lower prices, but not increased drug utilization.** The previous sections demonstrate that Para-IV entry can lead to significant shifts in demand from branded drugs to generic versions of the same drug and, in some cases, to generic versions of *different* drugs. Surprisingly, though, we find no evidence that the shift to low-priced generics leads to an increase in the quantity of total drug consumption. The lower prices available to consumers after generic entry do not appear to induce inframarginal consumers to start using these drugs. What

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[14] In Q2:2002, ACE-Inhibitors accounted for 30% of overall quantity in the market or 1.3 billion Standard Units (SUs), equivalent to 14.4 million patients. By Q2:2007, the market share of ACE-Inhibitors increased to 70%, equivalent to 3.5 billion SUs, or some 38.5 million patients.

[15] In Q2:2002, Beta-Blockers accounted for 69.5% of overall quantity in the market or 3 billion SUs in our sample. This translated into approximately 33.3 million patients consuming these drugs, assuming chronic intake through the quarter. By Q2:2007, Beta-Blockers accounted for 21.2% of the total quantity or 1.06 billion SUs, equivalent to 11.7 million patients.

this implies is that the increase in consumption of generics we observe in the data appears to be offset (usually more than offset) by a decline in the consumption of branded drugs, so that prices decline, but the physical quantity of drug consumption does not increase.

In order to depict this reality, we estimated the following simple equation:

$$q_{it} = \sum_{t=1}^{10} Lead_t + \sum_{t=1}^{10} Lag_t + \alpha_i + \beta_i y_t + \varepsilon_{it}, \tag{1}$$

where q is the total sales of all drugs in ATC four-digit category i at time t, both branded and generic, measured in quantity (standard unit) terms, the αs are molecule-specific fixed effects, the βs are molecule-specific linear time trends, and we estimate a set of dummy variables for the 10 quarters leading up to generic entry (*Lead*) and the 10 quarters after generic entry (*Lag*). This is not put forward as a structural model of drug supply, nor do we interpret any of the coefficients in a causal way—we simply want to examine if, on average, total drug consumption goes up after generic entry occurs. We explicitly include reformulations launched in response to a Para-IV entry in our quantity calculations. In our baseline regressions, we pool data from Paragraph III and Paragraph IV entry episodes. However, we also present results based solely on markets that experienced Para-IV entry.

The regression coefficients associated with six alternative specifications of (1) are provided in Table 2. Model 1 includes all hypertension molecules over the 2000–2008 time period. Model 2 adds an overall time trend to Model 1. Model 3 adds molecule-specific time trends. Models 4 to 6 also include molecule-specific time trends but focus on various subsamples of the data, starting with the subsample of molecules that witnessed Para-IV entry (Model 4). The final two models focus specifically on ACE-Inhibitors, as this submarket witnessed especially intense Para-IV entry. Model 5 includes only ACE-Inhibitors whereas Model 6 includes only ACE-Inhibitors that witnessed Para-IV entry. The coefficients from the full sample that includes molecule-specific time trends (Model 3) are plotted in Figure 5, along with the 95% confidence bounds associated with *Lead* and *Lag*. The results of Model 3 do not qualitatively change with the inclusion of a full set of time fixed effects.

Clearly, there is no evidence that generic entry causes the physical quantity of drug consumption to go up. If anything, it goes down. We are not the first researchers to find this pattern in drug sales data. Lichtenberg and Duflos (2009) and Huckfeldt and Knittel (2011) find broadly similar results.[16] Despite the fact that others have documented similar results, they still appear to be counterintuitive. The simple models of monopoly pricing taught to undergraduates emphasize the deadweight loss of foregone consumption at high prices. It is the increase in the volume of consumption after prices decline that generates most of the net social gains from greater competition. Why is it that consumption of hypertension drugs does not increase after prices decline?

The reason is that these are prescription drugs. Consumers cannot legally purchase these drugs without a prescription from a practicing physician. The vast majority of patients who have interacted with a physician intensively enough to receive a diagnosis of hypertension and a prescription for one of the drugs in our sample are likely to have some kind of health insurance—and that insurance often has some degree of coverage for prescription drugs. In fact, for the nine drugs for which we have transactions-level copay data, we find that more than 93% of all drug purchases involved the use of some kind of prescription drug plan obtained through health insurance. The price declines brought about by generic entry allow insured patients to switch from branded drugs to generic drugs, but we see little evidence in the data that these price declines somehow induce large numbers of patients who did not have a diagnosis of hypertension and a prescription for one of the drugs in our sample to acquire one after entry. Field interviews with

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[16] Lakdawalla, Philipson, and Wang. (2006) also find evidence of a short-run decline in utilization when generic entry occurs.

TABLE 2 **Coefficients from the Quantity Regressions**

| Variables	(1) lnq	(2) lnq	(3) lnq	(4) lnq	(5) lnq	(6) lnq
	All Sample 00–08	All Sample 00–08 with Time Trends	All Sample 00–08 w/Mol-Time Trends	All Sample 00–08 - Only P4 Molecules	All Sample 00–08 - Only ACE-Inhibitors	All Sample 00–08 - Only ACE-Inhibitors & P4 Molecules
Lead10	0.640***	0.512***	0.309***	0.354***	0.356***	0.404***
	(0.127)	(0.104)	(0.0642)	(0.0706)	(0.0809)	(0.0905)
Lead9	0.633***	0.492***	0.321***	0.376***	0.356***	0.423***
	(0.121)	(0.117)	(0.0674)	(0.0764)	(0.0833)	(0.0942)
Lead8	0.635***	0.531***	0.347***	0.396***	0.395***	0.457***
	(0.124)	(0.121)	(0.0732)	(0.0867)	(0.0896)	(0.105)
Lead7	0.625***	0.559***	0.360***	0.419***	0.412***	0.468***
	(0.132)	(0.123)	(0.0807)	(0.0998)	(0.0974)	(0.126)
Lead6	0.665***	0.610***	0.394***	0.423***	0.445***	0.475***
	(0.136)	(0.118)	(0.0848)	(0.109)	(0.108)	(0.140)
Lead5	0.667***	0.649***	0.419***	0.429***	0.488***	0.494**
	(0.140)	(0.116)	(0.0927)	(0.124)	(0.115)	(0.159)
Lead4	0.644***	0.665***	0.422***	0.433***	0.490***	0.496**
	(0.140)	(0.120)	(0.0995)	(0.135)	(0.124)	(0.176)
Lead3	0.644***	0.702***	0.446***	0.447***	0.514***	0.505**
	(0.141)	(0.120)	(0.107)	(0.149)	(0.133)	(0.196)
Lead2	0.690***	0.725***	0.431***	0.457**	0.486***	0.502**
	(0.148)	(0.112)	(0.115)	(0.158)	(0.148)	(0.213)
Lead1	0.648***	0.721***	0.417***	0.445**	0.486***	0.508*
	(0.148)	(0.116)	(0.127)	(0.172)	(0.161)	(0.230)
Lag1	0.168	0.317**	−0.00687	0.0425	0.0856	0.215
	(0.182)	(0.146)	(0.127)	(0.203)	(0.154)	(0.247)
Lag2	0.00124	0.188	−0.146	−0.115	−0.0552	0.0627
	(0.195)	(0.162)	(0.132)	(0.220)	(0.153)	(0.272)
Lag3	−0.168	0.0565	−0.287*	−0.306	−0.207	−0.152
	(0.213)	(0.176)	(0.151)	(0.260)	(0.184)	(0.352)
Lag4	−0.221	0.0415	−0.312*	−0.384	−0.224	−0.230
	(0.224)	(0.184)	(0.161)	(0.281)	(0.192)	(0.378)
Lag5	−0.196	0.0856	−0.262*	−0.255	−0.168	−0.0584
	(0.215)	(0.188)	(0.136)	(0.244)	(0.143)	(0.288)
Lag6	−0.179	0.0562	−0.232*	−0.292	−0.171	−0.121
	(0.198)	(0.179)	(0.131)	(0.250)	(0.134)	(0.283)
Lag7	−0.262	−0.0116	−0.262*	−0.372	−0.178	−0.172
	(0.215)	(0.188)	(0.150)	(0.282)	(0.148)	(0.307)
Lag8	−0.159	0.0507	−0.204	−0.288	−0.163	−0.174
	(0.161)	(0.166)	(0.148)	(0.293)	(0.160)	(0.346)
Lag9	−0.130	0.0363	−0.154	−0.207	−0.180	−0.272
	(0.169)	(0.161)	(0.136)	(0.280)	(0.165)	(0.382)
Lag10	−0.250	−0.0463	−0.239	−0.251	−0.215	−0.343
	(0.188)	(0.154)	(0.157)	(0.309)	(0.168)	(0.416)
Constant	9.372***	10.46***	10.50***	10.85***	10.47***	10.60***
	(0.0427)	(0.284)	(0.0194)	(0.0794)	(0.0464)	(0.0932)
Time trend	N	Y	N	N	N	N
Molecule time trend	N	N	Y	Y	Y	Y
Observations	1,295	1,295	1,295	539	719	323
R^2	0.081	0.276	0.735	0.677	0.692	0.670
Number of mcode	36	36	36	15	20	9

Robust standard errors in parentheses.

***$p<0.01$, **$p<0.05$, *$p<0.1$.

This table presents results from estimating equation (1). Models 1–3 were estimated on the full sample with all molecules and other controls. Models 4–6 were estimated on various subsamples with molecule-specific time trends. We observe absence of expansion in quantities in hypertension markets with generic entry.

FIGURE 5

CHANGES IN DRUG QUANTITY BEFORE AND AFTER GENERIC ENTRY
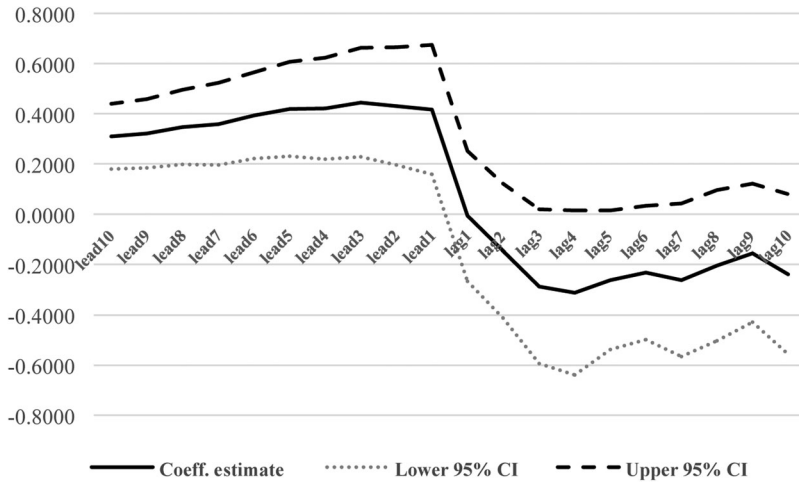
Notes: This figure plots the coefficients from model 3, Table 2, along with respective 95% confidence bounds estimated over the full sample of all molecules with molecule-specific time trends. On the horizontal axis, observations are for the 10 quarters *prior* to generic entry, lead10 to lead1, respectively. Observations 11–20 are for the 10 quarters after generic entry, lag1 to lag10, respectively. There does not appear to be evidence that total drug consumption goes up after generic entry.

numerous family physicians, those most likely to treat hypertension, confirmed this reality. None of the physicians could recall a patient coming to seek treatment on the basis of the entry of a generic medication in the market. To put it simply, drugs do not appear to be like minivans or breakfast cereals.

This reality constrains the level of net social gains we should expect following generic entry. To the extent that low-income patients with hypertension are failing to utilize potentially helpful drugs, the real barrier is probably not high drug prices but lack of regular access to competent primary care physicians who can diagnose the illness and prescribe the drug. Unfortunately, generic entry does not procure that access for the undiagnosed. This helps rationalize our modest estimates of net social gains. The first-order impact of generic entry is to shift surplus downstream from producers to consumers and the intermediaries (e.g., pharmacies and insurance companies) that link actual consumers to drugs.

Huckfeldt and Knittel (2011) find that overall utilization of the compounds targeted by generics falls, but that this decline is significantly offset by the introduction of reformulations by the branded manufacturers.[17] These authors attribute both the declining utilization of the original compound and the rise in utilization of the reformulation to advertising. Although we do not dispute these results or the authors' interpretation of them, we note that in hypertension, clinical practice allows for a high degree of cross-molecular substitution, and this, in turn, limits the scope for branded manufacturers to offset loss in market share to generics with the introduction of reformulations. Even though reformulations do not lead to a larger market, in terms of quantity consumed, they can still enhance consumer welfare by expanding product variety and providing at least some consumers with additional product features that are valued and useful. In the

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[17] In unreported regressions, we ran an analysis where we examined how the quantities of reformulations evolved over time and with generic entry. The results suggest that sales of reformulations increase after generic entry, but not by enough to expand the overall quantity of drugs consumed. These results appear broadly supportive of Huckfeldt and Knittel (2011).

welfare calculations that follow, we will see substantial consumer welfare gains attributable to the introduction of reformulations.

3. Related literature

■   This article draws upon a large literature on welfare estimation and demand modelling with differentiated products that dates back to Trajtenberg's (1989) pioneering work on the Computed Tomography (CT) scanner industry and includes the seminal contributions of Berry (1994), Berry, Levinsohn, and Pakes (1995, 2004), and Nevo (2000a, 2000b, 2001). These approaches have been applied to the pharmaceutical industry in earlier studies, although researchers have had to confront some additional challenges unique to this sector. For example, agents of the consumer (i.e., doctors) often make the choice of a particular product. Consumer choice can also be influenced by the presence (or absence) of insurance coverage. Notwithstanding these difficulties, Ellickson, Stern, and Trajtenberg (2001) explore patient welfare from new drugs. Stern (1996) employs a discrete-choice framework to evaluate patterns of substitutability between branded and generic drugs. Ellison et al. (1997) model demand in order to compute substitution elasticities between branded and generic antibacterial drugs. More recently, Cleanthous (2002) and Dunn (2012) find large welfare gains from drug innovation in antidepressants and anticholesterol drugs, respectively. Bokhari and Fournier (2013) report welfare gains due to first-time generic entry, and Dutta (2011) and Chatterjee, Kubo, and Pingali (2015) analyze the welfare impact of stronger intellectual property (IP) protection and differential pricing for pharmaceuticals in India. Other complementary work has focused on the enhancements to social welfare through reductions in mortality, morbidity, and total medical expenditures, Lichtenberg (1996a, 1996b, 2001, 2003, 2005).

In addition to work that quantifies welfare effects from product innovation using discrete-choice models, this article also relates to other work focusing on various dimensions and implications of generic entry, starting with Caves, Whinston, and Hurwitz (1991). Saha et al. (2006) report the dramatic rise in generic introductions since the passage of Hatch-Waxman, whereas Reiffen and Ward (2005) show that the cost to obtain generic drug approval has decreased. Time to market for generics after branded product patent expiration has also declined substantially, from approximately three years prior to Hatch-Waxman to only one to three weeks (Congressional Budget Office, 1998).[18] Other research has focused on entry decisions by generic manufacturers (Hurwitz and Caves, 1988; Grabowski and Vernon, 1992, 1996; Frank and Salkever, 1997; Scott Morton, 1999, 2000; Hudson, 2000; Berndt et al., 2003, 2007; Appelt, 2015), prices (Danzon and Chao, 2000a, 2000b), price controls (Danzon, Wang, and Wang, 2005; Lanjouw, 2005; Kyle, 2007), and entry costs (Djankov et al., 2002).

Hemphill and Sampat (2011, 2012) analyze Para-IV challenges to incumbent firms across a wide range of therapeutic categories, and these authors find that most Para-IV challenges in their sample do not challenge the key or essential patent that identifies and protects the principal innovation within the drug. Instead, the authors argue that most Para-IV challenges are directed at ancillary or additional patents strategically taken out by branded incumbents after the original drug discovery—ometimes long after that discovery—as a way of extending the period of market exclusivity. This practice is referred to in the industry as "evergreening." Hemphill and Sampat contend that Para-IV challenges have (appropriately) constrained this evergreening, by successfully invalidating or working around the ancillary patents. When this effort to extend market exclusivity is thwarted, the consumer gains could be large. On the other hand, Hemphill and Sampat argue that because Para-IV challenges have not generally shortened the life of many "key" or "essential" patents, they are not weakening the incentives for fundamental or basic innovation.

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[18] Berndt and Aitken (2011) provide an excellent summary of the increase of generic competition in the United States over the last decade.

In this article, we do not take a stand on which of the patents associated with a product represents the key or essential innovation, and which are taken out as part of an effort to extend monopoly life, nor do we take a stand on the length of patent protection that might constitute "fair" compensation to the innovator for the introduction of a novel drug. Our study here is designed to measure the changes in consumer and producer surplus that results when Para-IV entry allows generic competition to occur before patents expire. In that sense, we are closely aligned with Hemphill and Sampat, who recognize that successful Para-IV challenges could lead to substantial consumer surplus gains. The patterns of Para-IV entry we find in hypertension over our sample period appear to be broadly consistent with those documented in Hemphill and Sampat (2011, 2012); Para-IV entrants in hypertension generally do not challenge the earliest patent associated with the product.

In Table 3, for each Para-IV challenge in our sample, we list the challenge date, the entry date, the expiration date of the earliest expiring patent associated with the branded firm's product, the expiration date of the latest expiring patent associated with this product, and the expiration date(s) of the earliest patent(s) litigated in the Para-IV challenge. Interestingly, the litigated patents are often not the latest expiring patents associated with the product, and entry often occurs when this litigation is successful, even though the *FDA Orange Book* lists later expiring patents for which there is no record of a legal challenge. This may indicate that some of the patents associated with branded drugs in the *FDA Orange Book* are either only tangentially associated with the products of record or are viewed by the courts, the incumbent branded firm, the generic challengers, and the FDA as constituting no effective barrier to generic entry.

Our welfare analysis presumes that the patents challenged by Para-IV entrants, and identified as such in Table 3, would have protected the branded incumbent's monopoly position in the absence of the challenge. Our counterfactual calculations presume that these monopoly positions would have continued until the expiration of the litigated patent(s) or the end of our data window, whichever comes first. This method of constructing the counterfactual suggests that the producer surplus losses associated with Para-IV entry are quite large, exceeding $32 billion over our sample period under our baseline treatment of producer costs. If Para-IV entry really reduced branded firm revenue by such a large amount, then it is at least theoretically possible that Para-IV entry led to some reductions in Research and Development (R&D) investment by branded firms.[19] This theoretical possibility has been recognized in prior work. For example, Hughes, Moore, and Snyder (2002) show in a theoretical model that providing greater access to a current stock of prescription drugs yields large benefits to existing consumers. However, this access comes at a cost in terms of lost consumer benefits from reductions in the *flow* of future new drugs. Other recent articles have discussed this possibility (e.g., Grabowski and Kyle, 2007; Higgins and Graham, 2009; Knowles, 2010; Panattoni, 2011), and this stream of research has provided (mostly indirect or anecdotal) evidence *suggesting* that acceleration of generic entry has undermined incentives for R&D.

However, to the best of our knowledge, no published study has yet provided direct econometric evidence demonstrating that generic entry has *caused* a change in the rate or direction of R&D investment in new drugs. The extent, to which this occurs in practice, if at all, remains an open question. An analysis of the relationship between generic entry and R&D is beyond the scope of the current article. Instead, this article focuses solely on documenting the (large) short-run gains to consumer welfare and the (more modest) gains to overall social welfare driven by Para-IV entry in hypertension. A related article (Branstetter, Chatterjee, and Higgins, 2014) explores the relationship between generic entry and drug development, and finds evidence of an impact that is statistically and economically significant. In yet another article, Gilchrist (2015) demonstrates

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[19] This could be true even if all Para-IV challenges target ancillary or derivative patents taken out to extend a monopoly rather than the patent that documents the new compound. All that is necessary for this theoretical possibility to hold is that some of the revenues derived from extension of a monopoly would have been invested in R&D.

TABLE 3 Sample Molecules that Experienced Early Para-IV Entry with Quarter of Entry

Molecule	Challenged Brand	NDA Approval Date	Data Exclusivity Expiration	Earliest Patent Expiration	Latest Patent Expiration	Entry Date	Earliest Challenge Date	Earliest Expiration of Litigated Patent
AMLODIP BES/BENAZ (3)	Lotrel	Mar-95	Jul-00	Feb-04	Dec-17	Q2:2007	Feb-04	Dec-17
AMLODIPINE (2)	Norvasc	Jul-92	Jul-97	Jul-06	Sep-07	Q1:2007	Feb-04	Mar-07
METOPROLOL SUCCIN (1)	Toprol XL	Jan-92	Jan-97	Apr-92	Sep-10	Q4:2006	Feb-06	Sep-07
CARVEDILOL (1)	Coreg	Sep-95	Sep-00	Sep-07	Aug-16	Q3: 2007	Jun-07	Jun-15
FELODIPINE (2)	Plendil	Jul-91	Jul-96	Dec-01	Oct-07	Q4: 2004	Jul-01	Apr-07
FOSINOPRIL (3)	Monopril	May-91	May-96	Dec-00	Jan-10	Q4: 2003	Apr-03	Jul-09
FOSINOPRIL/HCTZ (3)	Monopril HCT	Nov-94	Nov-99	Dec-00	Jan-10	Q4: 2004	Apr-03	Jul-09
METOPROLOL/HCTZ (1)	Lopressor HCT	Dec-84	Dec-89	Apr-92	Dec-93	Q3:2004	Jul-04	May-07
MOEXIPRIL (3)	Univasc	Apr-95	Apr-00	Oct-00	Aug-07	Q2: 2003	Nov-01	Feb-07
MOEXIPRIL HCL/HCTZ (3)	Uniretic	Jun-97	Jun-02	Oct-00	Aug-07	Q1: 2007	Apr-04	Feb-07
QUINAPRIL (3)	Accupril	Nov-91	Nov-96	Oct-00	May-15	Q4: 2004	Mar-99	Feb-07
QUINAPRIL HCL/HCTZ (3)	Accuretic	Dec-99	Dec-04	Oct-00	Aug-07	Q2: 2004	Mar-99	Feb-07
RAMIPRIL (3)	Altace	Jan-91	Jan-96	Jan-05	Aug-20	Q4: 2007	Mar-03	Oct-08
TRANDOLAPRIL (3)	Mavik	Apr-96	Apr-01	Jun-07	Apr-15	Q1: 2007	Dec-04	Jun-07
VERAPAMIL (2)	Verelan PM	Nov-98	Nov-03	Jun-07	Jun-07	Q3: 2007	Sep-06	Jun-07

This table identifies sample molecules that experienced Para-IV entry and when that entry occurred during our sample period. Also included are detailed approval and exclusivity information. Earliest litigated patent expiration is taken as the earliest date of expiration of a litigated patent, available from our various data sources in case of two different dates for the same focal litigated patent. The molecules are further subdivided across three categories: Beta-Blocking Agents and Combinations (1); Calcium Antagonists Plain (2); ACE-Inhibitors and Combinations (3). Patent expiration month and year identify the end of market exclusivity. Source: Perry Ashford Publications (www.paragraphfour.com), *FDA Orange Book*, USPTO Patent Term Extension Database, and IMS MIDAS™. We are also indebted to Bhaven Sampat for providing us additional patent data.

a causal impact between first-in-class exclusivity (i.e., the length of time before generics are able to enter the market) and subsequent innovation in that class.

4. Methodology

■   The richness of data at our disposal allows us to consider two alternative empirical methodologies. We start by modelling demand using a nested multinomial-logit framework. This approach allows us to "nest" drugs into submarkets with other especially close substitutes, but also allows for substitution across these submarkets. As Berry (1994) has shown, this approach can be easily implemented with standard instrumental variable (IV) regression techniques. However, there are several limitations to the nested-logit approach. First, the results will be affected by the presumed nesting structure, which may or may not fully reflect actual patterns of substitution in the market. Second, the nested-logit model abstracts from any interaction between patient characteristics and product demand. In order to get around these restrictions, we also implement a full random-coefficients logit model (Nevo, 2000a, 2000b). Recent research has strongly favored the latter approach, and we view that approach as providing the most credible estimates of welfare impact. In the interests of space, we have omitted any derivation of the nested-logit approach. The interested reader is directed to our earlier article (Branstetter, Chatterjee, and Higgins, 2011) for a full discussion.

Our potential market is all prospective US hypertension patients who might consume one of a number of drugs spread across three specific drug categories used broadly to treat hypertension.[20] Our product-level data are organized in a taxonomy known as the anatomical therapeutic chemical (ATC) classification system, and we will refer henceforth to ATC codes and categories. Chemically distinct products are assigned to different categories. A drug containing a single active ingredient is treated differently from a drug that combines multiple active ingredients; each chemically distinct category in our data will be classified as a "molecule" (even though some substances may combine multiple active ingredients) and will be assigned to a distinct four-digit ATC category.

□   **Nested-logit model.**

Computing consumer surplus using the nested-logit model. When presenting estimates of consumer surplus based on the nested-logit model, we estimate aggregate consumer surplus in each quarter of our sample period by following Small and Rosen (1981) and Train (2003):

$$CS_{actual} = \frac{1}{\alpha} * P * \ln \left[1 + \sum_{m \in M_n} \sum_{j \in J} exp^{\frac{\delta_{jm}}{(1-\sigma)}} \right]. \tag{2}$$

Here, the subscript on the consumer surplus (CS) variable denotes the fact that we are calculating CS using the actual configuration of products in the market at a given point in time. Time subscripts are suppressed here and elsewhere to simplify exposition. *P* provides our measure of disease prevalence at time *t*, which corresponds to sample-weighted estimates taken from the National Health Interview Survey (NHIS) data. We convert the estimated number of patients into a drug consumption estimate by assuming standard chronic dosage frequency and treatment length. Within the bracketed term, 1 represents the utility obtained by the average consumer from consuming the outside good; the remaining expression estimates the indirect utility obtained by the average consumer from consumption of hypertension drugs. This is calculated by multiplying the regression coefficients associated with each product characteristic by the characteristics of the products in the market at time *t* (Train, 2003).[21] The double summation term implies that the

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[20] The ATCs used to define the market are: (i) C7 Beta-Blockers; (ii) C8 Calcium Antagonists; and (iii) C9 ACE-Inhibitors. Angiotensins and their combinations with Calcium Antagonists or diuretics were excluded, as they did not face patent expiration or Para-IV challenges during our sample period.

[21] Our specification detailed in Branstetter, Chatterjee, and Higgins (2011) includes the following product characteristics: number of contraindications, advertising, and price; we also estimate product-specific fixed effects.

indirect utility in each quarter is first summed across all products (brands, generics, and Para-IV generics) within a molecule and then across all molecules. The entire expression is then logged, and multiplied by P and by $\frac{1}{\alpha}$ (where α is the coefficient on price and is defined as the marginal utility of income) in order to express consumer surplus in dollar terms.

Estimating counterfactual consumer surplus using a nested-logit approach. In order to understand the impact of Para-IV generic entry, we need to establish the counterfactual that will allow us to determine the consumer surplus generated had there *not* been entry before patent(s) expiry by the generic entrants. In constructing the counterfactual consumer surplus series, we assume that generic entry would have been delayed until the expiration of the first litigated patent(s) identified in Table 3. When those patents expire, we assume the same pattern and level of generic entry that actually occurred at the end of the 180-day market exclusivity period.

We need to make several assumptions relating to pharmaceutical firm action in this counterfactual world. First, we assume that branded pharmaceutical firms would not launch the product reformulations or me-too drugs they launched in response to Para-IV entry, as they would end up cannibalizing sales of their existing products. Second, we assume that the pharmaceutical firm follows preentry trends in terms of price and advertising until the litigated patents identified in Para-IV litigation expire, after which they follow average postentry trends in the face of normal (non-Para-IV) generic entry. Following these assumptions, we are able to impute counterfactual estimates of product price and product-specific advertising expenditures from the quarter of Para-IV generic entry until patent expiry of the incumbent's product. We have tested the accuracy of our counterfactual predictions by using early sample data to estimate late sample prices, quantities, and advertising in markets where generic entry never occurred. We find that our predictions track actual values fairly closely.[22] We repeat the calculation outlined in equation (2) to create a $CS_{counterfactual}$ series by quarter with the difference between the two consumer surplus series giving us an estimate of the welfare gains from Para-IV entry.

□ **Random-coefficients logit model.**

Estimating demand using a random-coefficients logit model. The relative simplicity and ease of implementation of the nested-logit approach make it an obvious benchmark specification to employ in the context of our study. Nevertheless, the broader literature has moved to more sophisticated approaches that allow for richer substitution patterns and for interactions between consumer and product characteristics. We therefore follow Berry, Levinsohn, and Pakes (2004) and Nevo (2000a, 2000b, 2001) and implement a random-coefficients logit model. Much prior research suggests that the nested-logit approach tends to yield welfare impacts from new product entry that are much higher than those obtained from the more flexible and defensible random-coefficients logit approach—the results we present in this article are consistent with that pattern. Given the increasingly well-established nature of the random-coefficients logit approach and the closeness with which we follow prior work, we do not present a full derivation here. Instead, we reproduce a few key equations to establish the similarity of our approach to prior work, and refer the reader to the standard treatments cited above for a more complete exposition.

We start by modelling the utility of consumer i, buying a pharmaceutical product j at time t as:

$$u_{ijt} = x_{jt}\beta_i^* + \alpha_i^* p_{jt} + \xi_{jt} + \epsilon_{ijt} = V_{ijt} + \epsilon_{ijt}, \qquad (3)$$

where the taste of consumer i for product characteristics x_{jt} and prices p_{jt} vary given demographic characteristics. V_{ijt} is the indirect utility function and ϵ_{ijt} is a random shock to utility, distributed

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[22] We thank Brian Kovak for this suggestion. Results of this test are available from the authors upon request.

as i.i.d. extreme value. The coefficients (α_i^*, β_i^*) are individual-specific. Consumer preferences can be expressed as a function of observed and unobserved characteristics as follows:

$$\begin{pmatrix} \alpha_i^* \\ \beta_i^* \end{pmatrix} = \begin{pmatrix} \alpha \\ \beta \end{pmatrix} + \Pi D_i + \Sigma \nu_i, \quad \nu_i \sim N(0, I_{K+1}), \tag{4}$$

where K is the dimension of the observed characteristics vector, D_i is a $d \times 1$ vector of demographic variables, Π is a $(K+1) \times d$ matrix of coefficients that measure how the taste for drugs vary with demographics, and Σ is a scaling matrix. This specification allows for more flexible substitution patterns by accommodating "observed" and "unobserved" additional characteristics (D_i and ν_i, respectively). We also assume that there are unobserved product-specific characteristics that add to a consumer's utility for a molecule-brand. The demand system is completed with the outside good. Consumers may decide not to purchase any of the products, and in that case, the indirect utility from the outside option is:

$$u_{iot} = \xi_0 + \pi_o D_1 + \sigma_o \nu_{io} + \varepsilon_{iot}. \tag{5}$$

Product choice is the result of individual-specific characteristics as well as brand-specific characteristics and following Nevo (2000a, 2000b), one can show that the market share of the *jth* product as a function of the mean utility levels of all the *J+1* goods, given the parameters, is:

$$s_{jt}(x_{.t}, p_{.t}, \text{ and } \xi_{.t}; \theta) = \int_{A_{jt}} dP^*(D, \nu, \varepsilon) = \int_{A_{jt}} dP_\varepsilon^*(\varepsilon) dP_\nu^*(\nu) dP_D^*(D), \tag{6}$$

where P*(.) denotes the population distribution function. The second equality is a result of making an assumption of independence of *D*, ν, and ε (i.e., demographic and product-specific shocks). With aggregate share data, the model can be estimated by choosing the parameters that minimize the distance between the shares predicted by the equation above and the ones observed in the data (Nevo, 2000a, 2000b). We follow the prior literature in using the GMM estimator suggested by Berry (1995) and the inversion technique developed by Nevo (2000a, 2000b) to simplify this minimization problem. We deal with the potential endogeneity problem by using an instrument set similar to that employed in prior studies, which includes product fixed effects. For price, we use the average prices of other products a firm sells in the same market. That is, for product *i* of firm *j* in market *k*, we take an average of the prices of other products (excluding product *i*) marketed by the same firm, *j*, in the same market, *k*. Similar instruments are constructed for advertising. If there are no other products sold by firm *j* in market *k,* then we instrument for the potentially endogenous product characteristics by using the average characteristics of other firms' products in markets proximate to *k*.

Estimating real (and counterfactual) consumer surplus using the random-coefficients logit model.
Given the coefficient estimates on price and product characteristics, we compute quarterly consumer surplus (CS) in the full random-coefficients logit model following Nevo (2000a, 2000b, 2001), McFadden (1973), and Small and Rosen (1981), where aggregate consumer surplus at time *t* is given by:

$$CS_t = M * \int CV_{i,t} dP_D^*(D) dP_\vartheta^*(\vartheta), \tag{7}$$

where *M* is the total US population of hypertensive patients and P*(.) are distribution functions.[23] Individual *i's* consumer surplus is calculated using her compensating variation and is equal to:

$$CV_{it} = \frac{\ln \sum_{j=1}^{J} exp^{V_{i,j}}}{\alpha_i^*}. \tag{8}$$

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[23] Given the need to measure consumer characteristics with the highest possible degree of accuracy, we employ data from the Medical Expenditure Panel Survey, where each representative patient includes a weighting measure that is used to scale our sample to the hypertensive population, *M*.

Equation (8) computes indirect utility by applying the estimated α_i^* and β_i^* parameters to the realized observations of product characteristics and prices on the choice sets available in the real and counterfactual world. M provides our measure of disease prevalence at time t, which corresponds to sample-weighted estimates taken from NHIS data. We convert the estimated number of patients into a drug consumption estimate by assuming standard chronic dosage frequency and treatment length, as before. We estimate the indirect utility obtained from consumption of hypertension drugs by multiplying the regression coefficients associated with each product characteristic by the characteristics of the products in the market at time t.[24]

☐ **Potential endogeneity concerns.** Evidence suggests that Para-IV challenges are not only becoming more likely; they also appear to occur earlier in a branded product's life cycle (Scherer, 2001; Grabowski, 2004; Saha et al., 2006; Panattoni, 2011) and now affect a broader range of drugs, including smaller market drugs with yearly sales under \$100 million. "Blockbusters" are not the only target (Grabowski and Kyle, 2007).[25] However, even as the frequency of Para-IV entry has grown and the set of targets has broadened, entry remains a decision by a generic challenger, not a random assignment by an experimenter. Should we worry that the accuracy of our welfare calculations is somehow undermined by this reality? Our response to this important question relies on two important features of the particular market in which our study is set.

First, we hold the initial enactment of Hatch-Waxman and the various significant court rulings and administrative changes that have followed it to be plausibly exogenous to the actions of the individual branded and generic producers in our data set. Some readers might contend that we would have seen generic entry even in the absence of this Act, which created the Para-IV entry pathway. We cannot observe that counterfactual world, but we can note that, in the absence of Hatch-Waxman, would-be generic entrants would have had to bear the cost of clinical trials to establish the safety and efficacy of their drugs. These trials are extremely time-consuming and expensive. A back-of-the-envelope calculation suggests that most of the Para-IV generic entry we have seen in hypertension, over our sample period, would not have occurred without the passage of the Hatch-Waxman Act. We can reach this conclusion by looking at the revenues earned by the first generic entrant during the period in which broader generic entry was not yet allowed. We then create an annualized estimate of that revenue, make a modest and conservative adjustment for marketing costs, and compare the net revenue stream to what would have been required to offset the costs of clinical trials, plus the benchmark cost of capital. Even under aggressive assumptions, there are only 5 out of 17 product markets in which generic entry would have been remotely plausible.[26] This suggests to us that the vast majority of entry episodes observed are, in fact, a result of the policy change.

Second, as already indicated, to be successful, a Para-IV challenger has to find a "weak" patent that can either be rendered invalid in court or effectively invented around. The patents protecting the key innovations of the branded drugs were often written early in the research process, long before the true clinical value of the innovation was known. The need to secure patent protection before rival firms with similar research programs means that patents that later turned out to be critical to the financial well-being of the firm often received no more care or attention in the patent-writing process than patents that wound up "protecting" useless failures. Of course, once the value of the compound was known, it was not possible to go back and rewrite the patent application with greater care. This alone could plausibly introduce a large measure of randomness into the relative strength of a firm's patents. This element of randomness remains

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[24] Our specification includes the following product characteristics: number of contraindications, advertising, and price; we also estimate product-specific fixed effects.

[25] For incumbents, these challenges remain significant financial events. In a recent event study, Panattoni (2011), reports cumulative abnormal market losses of slightly over \$1 billion when an incumbent-branded pharmaceutical firm loses a Para-IV case in court.

[26] Table R1, a supplementary table shared with anonymous referees, shows the results of our calculations and is available upon request.

and is probably even strengthened if we consider the possibility that pharmaceutical firms have engaged in "evergreening" since the passage of Hatch-Waxman—that is, long after patents were granted on the key invention(s) embodied in the new drug, the branded firms took out subsequent patents on minor improvements of the active ingredient or elements of the production process with the purpose of delaying generic entry. Prior research, discussed above, has shown that, under the laws, administrative procedures, and legal interpretations that held sway from the 1980s through the late 1990s, branded firms were often able to forestall Para-IV challenges entirely or delay them for years, by using patents that would be considered quite narrow or weak today.

However, legal and administrative changes and shifts in the courts' interpretation of patents discussed above have made these strategies much less tenable in more recent years. These policy shifts have thus driven the surge in Para-IV challenges depicted in Figure 3. From the standpoint of the branded incumbents, these changes have limited the usefulness of some patents in blocking generic entry in ways that the patent counsel for branded pharmaceutical firms could not have anticipated *ex ante*.[27] Owners of patents for both blockbuster drugs and less lucrative drugs have discovered that some of the patents protecting their revenue streams are weak as the courts and regulators now define "weak." The fact that both kinds of drugs experience Para-IV challenges strengthens the view that generic firms are increasingly attacking weak patents wherever they find them.

The work of Hemphill and Sampat (2011, 2012), probably represents the most systematic research to date on the question of which pharmaceutical patents attract challenges from generic firms. These researchers conclude that most Para-IV challenges have focused on the sorts of patents associated with evergreening rather than those that protected the active ingredient of the original branded product. Nevertheless, the researchers also conclude that the (plausibly exogenous) policy changes that enabled the striking surge of Para-IV challenges over our sample period raised consumer welfare (and reduced producer surplus), probably substantially, by enabling the invalidation or narrow interpretation of patents that would have delayed or blocked entry under the policy settings that held through the late 1990s. Our approach to welfare estimation follows this logic almost exactly. It is not necessary for us to presume that generic entry was the outcome of random assignment by an experimenter—in fact, we readily concede that entrants strategically concentrated their attacks on "weak" patents. Instead, our estimates of the impact of Para-IV entry on welfare hinge on the presumption that the patents that were successfully challenged in the recent period of accelerated generic entry would have remained in force until their expiration— which was the usual outcome prior to the late 1990s/early 2000s. This strikes us as reasonable, given the institutional context of our study.

5. Data

■ Previous research in this area has struggled with data limitations. We are fortunate to have access to a range of comprehensive data sets that provide us with powerful leverage over some of the econometric challenges we confront. First, data from Parry Ashford Publications (www.paragraphfour.com) allows us to identify each Para-IV certification dating back to 2003.[28] These data provide full drug-level information about the challenge and outcome that we can link to our other data resources. For data prior to 2003, we filed a Freedom of Information Act (FOIA) request with the FDA. Next, we gathered demand-side information for the drugs (and markets) where challenges occurred. For this, we turned to the IMS MIDAS™ database that provides sales (quantity) and revenue information for every product sold by every firm,

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[27] Many of the patents successfully litigated in Para-IV entry cases were written before the increase of Para-IV entry. Under the prevailing law when they were granted, these patents would likely have forestalled or delayed generic entry. However, under the prevailing law in the early 2000s, many were invalidated or invented around.

[28] Para-IV certification data only became publicly available in 2003, In order to supplement the data prior to 2003, we filed a FOIA request with the FDA. Other researchers (Berndt et al., 2007) have used survey data to gather pre-2003 activity. In a recent study, Panattoni (2011) collected data from district court decisions.

across all therapeutic disease categories, branded and generic, in the United States This database also provides information on dosages and expected market exclusivity expiry dates. All branded products are also listed in the *FDA Orange Book*, and this database provides an alternative source for approval, data exclusivity, and patent expiry dates.[29] Our final data set covers the time period 2000 to 2008 and is chosen due to limitations on consumer characteristics data, discussed below, which is needed for our empirical specification.

Unlike most articles in the prior literature (e.g., Cleanthous, 2002; Dutta, 2011) that use annual data, we instead utilize quarterly data. This choice is necessary so that we can more accurately track initial entry (and subsequent entry after 180-day exclusivity periods granted to first-filers) by generics. A key aspect of our methodological framework is the definition of our market and how it relates to the measurement of the outside good. We choose to focus on the US hypertension market as our research setting. The market is economically large; for example, in 2007, the American Heart Association estimated the burden of hypertension on the healthcare budget to be close to $60 billion. This category of disease is medically significant too, with prevalence around 26% to 29% of the population in 2008.[30] We consulted experts at the Center for Disease Control (CDC) to help retrieve disease prevalence statistics for hypertension from the National Health Interview Survey (NHIS), which we discuss more fully below. Para-IV certifications have also been active in this market. Finally, discussions with physicians suggest a relatively high degree of substitution across different drugs, allowing for a high level of cross-molecular substitution.

☐ **Quantities and prices.** As we indicated above, our unit of observation is molecule-firm-brand-quarter, which means that if two branded firms and a generic firm are each selling chemically identical products, we still treat each of the three products as distinct, and we track sales on a quarterly basis. IMS MIDAS™ provides sales data in standard units (SU). The SU measurement is designed to equate different dosage forms (e.g., tablets, capsules, liquid) into comparable patient dosages. Products that have multiple dosage forms of a molecule sold by a single firm are aggregated together. Revenues are reported over the same period as SU and are converted into real dollars using a base year 2000 Gross Domestic Product (GDP) deflator. For each quarter observation, wholesale price is estimated by dividing revenues by the number of SU sold. The revenues are sales from the manufacturer to wholesalers. Our price measures are effectively unit values at the SU level, so that each measured price is an aggregate of multiple dosage forms.[31]

We view these unit values as a close approximation to the actual wholesale prices received by producers. They are thus, conceptually, the right prices to use when estimating producer surplus changes. On the other hand, as we acknowledge later in the article, these wholesale prices are not the prices faced by actual patients. Patients without health insurance pay a retail price that is much higher than the wholesale price, but only a small fraction of hypertension drug purchases take place at the full retail price over the course of our sample period.[32] Patients with health insurance are effectively participating in a complex web of transactions involving insurance companies and drug retailers as well as drug manufacturers. This nexus of downstream parties collectively shares the surplus generated by generic entry, and if we redefine "consumer surplus" to mean the surplus accruing to the entire nexus, then wholesale prices are conceptually the correct price to use here.

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[29] Only chemical-based drug data is included in the *FDA Orange Book*, but as already noted, because there was no pathway for generic biologic drugs to enter the market during our sample period, this limitation does not impact our analysis. We thank an anonymous referee for suggesting that we clarify this issue.

[30] See www.cdc.gov/nchs/data/databriefs/db03.pdf for a more complete discussion of hypertension awareness, treatment, and control in the United States.

[31] A significant body of prior research on the pharmaceutical industry uses earlier versions of the IMS Health data that we employ here. Like us, these prior researchers do not directly observe retail sales or prices. Although this is a shortcoming, the data are widely seen within the industry as the "gold standard" of pharmaceutical data.

[32] Examination of our raw data found that the "cash" or retail price was higher than the wholesale price. Only 6.6% of hypertension drug prescriptions were purchased at the retail cash price. This means that retail prices cannot be the "right" prices at which to value true consumer surplus. As a practical matter, retail drug prices are extremely hard to get.

We revisit the issue of drug prices and the related issue of just how to think about "consumer surplus" in this market context later in the article.[33]

We need to acknowledge another issue with these price data: unmeasured discounting (rebates) by drug manufacturers.[34] The largest drug purchasers appear to be extracting rebates from drug companies up to 61%.[35] However, the sales data recorded by IMS and the wholesale "price" data one can extract from IMS do not reflect this discounting. Firms allegedly record sales to their large customers at the "market" price and then engage in rebates that are concealed from other purchasers or rival sellers. There is simply no practical way to measure these discounts by drug or over time in an accurate way. After generic entry, the volumes of branded drug sales drop substantially, price-sensitive customers tend to adopt generic drugs, and the rationale for discounting on the part of the branded firms weakens considerably. How might this price mismeasurement affect our results?

To the extent that discounts during data/market exclusivity are pervasive, we are overestimating producer surplus before generic entry and therefore overestimating the decline in producer surplus that takes place when generic entry occurs. On the other hand, this same logic implies that we are underestimating consumer surplus before generic entry and therefore overestimating the increase in consumer surplus that occurs with generic entry. If the overestimated decline in producer surplus and the overestimated increase in consumer surplus roughly offset each other—not unreasonable, given the lack of an increase in physical consumption after generic entry—then the implications of mismeasurement for our estimates of social surplus may be limited. Given the data limitations, there is little more we can do other than acknowledge this problem.

☐ **Hypertension market and unconditional shares.** We consulted experts at the CDC to help retrieve and construct disease prevalence statistics for hypertension from the National Health Information Survey (NHIS). Specifically, for children and adults, we retrieve counts of the number of US residents taking the NHIS who answered that they ever had hypertension or the related conditions of high blood pressure, a heart condition, or coronary heart disease. CDC-recommended weights were then applied in order to back out national estimates of hypertension prevalence.[36]

To create a correspondence between sales data (pill-level) and prescription-level data or the number of patients consuming hypertension drugs, we impose an assumption on the length of treatment. For this, we assume chronic intake of hypertension drugs (i.e., patients stay on the drug throughout a year) and combine this with prescription-level data on average treatment days from the IMS National Prescription Audit™ (NPA) and the IMS National Disease and Therapeutic Index™ (NDTI), supplemented with information from medical references. We take our estimates of the number of patients with hypertension and multiply this by 90 (days in a quarter) and then by 4 (four quarters in a year). This multiplication yields the potential market size for hypertension drugs. We therefore define the unconditional share for a particular quarter, s_{jm}, as brand-level sales divided by our estimate of the potential market size, in SU.

☐ **Outside good share.** We create the outside good measure, s_0, or the number of potential patients with hypertension that are *not* actively receiving drug treatment. In any given quarter, we can sum hypertension drug sales across all relevant ATC categories and compare that with the overall *potential* market derived from the CDC NHIS data above; the difference is our measure

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[33] An examination of the copay data reveals problems with using these as price data. Simply put, there is limited variation in drug copays across consumers, drugs, and time. Efforts to estimate an indirect utility function using copay data demonstrated this; it was difficult to achieve convergence.

[34] We thank Iain Cockburn for pointing this out to us.

[35] www.forbes.com/sites/matthewherper/2012/05/10/why-astrazeneca-gives-insurers-60-discounts-on-nexiums-list-price/.

[36] For more information on the CDC weighting recommendation and methodology, please see: ftp.cdc.gov/pub/Health_Statistics/NCHS/Dataset_Documentation/NHIS/2009/srvydesc.pdf.

of the outside good. We experimented with the outside good measure in various ways, as its reasonable computation might have a bearing on the results. This involved imposing different assumptions on the length of treatment and reconciling all the measures of outside good shares with epidemiological estimates of US patients who are aware of their being hypertensive but are not getting treated (for a variety of reasons).[37]

☐ **Product characteristics.** Formal modelling of demand in this setting occurs in a manner such that the utility of a consumer from consuming a drug product, in a certain time period, is a function of product characteristics, observed and unobserved. Following the extant literature (e.g., Stern, 1996; Cleanthous, 2002; Dutta, 2011), we include information on drug side effects. More specifically, we use drug-label information, cross-checked with medical references, and define a variable, *Number of Contraindications*, as the number of contraindications (i.e., circumstances under which the drug cannot be safely taken) for each drug. Advertising expenditures on a product are also a significant determinant of sales, and the literature points to biases in demand estimates without advertising (Moul, 2006). As a result, we incorporate product-specific information from IMS MIDAS™ on advertising. Advertising data comprises three components: (i) direct journal advertising, (ii) direct mail advertising, and (iii) direct interactions ("detailing") between drug representatives and physicians. We define a variable, *Advertising*, which is the summation of these three forms of activity at the product level, converting all financial variables to real dollars. We do not possess quarterly data on direct-to-consumer advertising (DTC) but as physicians are acting as agents on behalf of patients (consumers), it can be argued that detailing is a critical component of a pharmaceutical firm's advertising strategy. Rosenthal et al. (2003) supports this notion and demonstrates that total promotion expenditures were approximately 14% of sales. Of this 14%, DTC comprised 2.2% whereas total physician promotion accounted for 11.8%. Finally, because there are important product attributes that are difficult to measure consistently across products, we include product-specific fixed effects. These fixed effects will vary across products but not over time.

☐ **Consumer characteristics.** Following Dunn (2012), data relating to consumer characteristics are drawn from the Medical Expenditure Panel Survey (MEPS) 2008 file. We utilize MEPS rather than NHIS as our source for these consumer data due to the former source's relative precision and quality of insurance and income data, and the availability of these data at the patient level (MEPS) instead of only the family level (NHIS). To identify our population of hypertensive patients in MEPS, we start by using the variable BPMLDX, which indicates that a patient has been identified as having hypertension on more than two physician visits. This variable is only available starting in 2000 and is used by MEPS for epidemiological studies to identify prevalence of hypertension (see MEPS Statistical Brief #315). Because we need high quality data on hypertensive consumer characteristics for our random-coefficients logit specification, the availability of this variable determines the beginning of the period over which we can estimate that specification. For each quarter, a sample of 500 patients is drawn from this hypertension population. Patients are dropped if they are under the age of 18 or have a recorded annual income below $5000. We are able to exploit epidemiological data in order to further ensure that our sample is reflective of the actual patient population. We continue our draws until we have a race distribution consistent with epidemiologic data: 27% white, 32% black, 18% Hispanic, and 22% other.[38] Once we obtain our final sample, we gather age and health insurance information for those patients. *Age* is defined as the age of the patient and *Insurance* is defined as an ordered variable 1, 2, or 3 for private insurance, public insurance, and no insurance, respectively.

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[37] Our findings remain robust to these various measures. Results of these robustness checks are available from the authors upon request.

[38] We use the epidemiologic data for the hypertension population summarized in MEPS Statistical Brief #315: meps.ahrq.gov/data_files/publications/st315/stat315.pdf. Accessed 1 May 2013.

TABLE 4   **Panel A. Descriptives Related to Demand Regression**

	Average	Standard Deviation	Minimum	Maximum
ATC market size ('000 USD)	2074335	520699.2	606641.2	2598465
Price ($ per SU)	1.96	8.58	0.02	116.4
SU (quantity) sold per quarter ('000)	27292.6	65527.9	1	474276
Number of contraindications	3.4	2.8	0	10
Product-level advertising per quarter ('000 USD)	665.7	2131.7	0.0	16061.7
Share of outside good (s_0)	0.4	0.03	0.38	0.48
Unconditional share (s_{jjm})	0.009	0.02	0	0.13
Number of firms per quarter	59.8	5.6	54.0	73.0
Consumer Characteristics for 500 draws used in Random-Coefficients Logit Estimation				
Age	58.7	14.7	18.0	90.0
Health insurance	1.46	0.62	1.0	3.0

Panel A presents the variables directly related to our demand estimation: market size, price, quantity sold, number of contraindications, product-level detailing (advertising), share of the outside good, and unconditional share. Price is dollar per standardized unit (SU). SU is a unit of measurement that equates different forms, for example, pills, capsules, and tablets. Advertising (detailing) are at the firm-product-quarter level over the sample period 2000–2008. Summary statistics for consumer characteristics used in draws for random coefficient logit model are also provided.

TABLE 4   **Panel B. Descriptives Related to Hypertension Products Experiencing Para-IV Entry**

	Average	Standard Deviation	Minimum	Maximum
Percent change in price after entry (brand and generic)	−12.0%	35.6%	−69.3%	53.0%
Percent change in branded drug price after entry	31.7%	20.7%	−9.2%	86.8%
Discount factor	32.4%	18.7%	7.5%	77.5%
No of entrants	8	6	1	21
Branded product revenue during year before first entry ($,000 USD)	599291	775387	12066	2559760
Branded product revenue during year after first entry ($,000 USD)	248531	330987	9639	966477
Revenue erosion during first year of generic entry (%)	55.2%	20.8%	−6.3%	80.1%
Revenue erosion after first year of generic entry (%)	82.3%	15.6%	37.2%	95.7%

Panel B presents descriptives for those hypertension products experiencing Para-IV entry over our sample period. Prices of drugs decrease, on average, whereas incumbents increase price, on average, after entry. Branded revenue erosion accelerates due to additional entry after the expiry of the first generic entrant's 180-day exclusivity period.

Toward the end of our sample period, in 2006, the implementation of Medicare Part D increased prescription drug coverage for some seniors. Zhang et al. (2010) and Li et al. (2012) explore the impact of this policy change on various factors, including the drug compliance of hypertensive senior patients who benefitted from this policy shift. Unfortunately, we do not possess individual-level drug consumption data; unlike the researchers cited in the previous sentence, we have no direct way of comparing the drug consumption or drug adherence of Medicare Part D participants to other categories of patients. We observe a broad increase in the total quantity of standard units of hypertension drugs consumed over our sample period, but there does not appear to be a sharp increase at the end that can be clearly ascribed to Medicare Part D.

6. Empirical results

☐ **Descriptive statistics.** Table 4 summarizes descriptive statistics for the hypertension market and the products we focus on in this study over the sample period (2000–2008). Panel A presents the variables directly related to our demand estimation: market size, price, quantity sold, number of contraindications, product-level advertising, share of the outside good, and

FIGURE 6

DISCOUNT FACTOR BY PARA-IV GENERICS IN QUARTER OF ENTRY ACROSS THERAPEUTIC
CATEGORIES
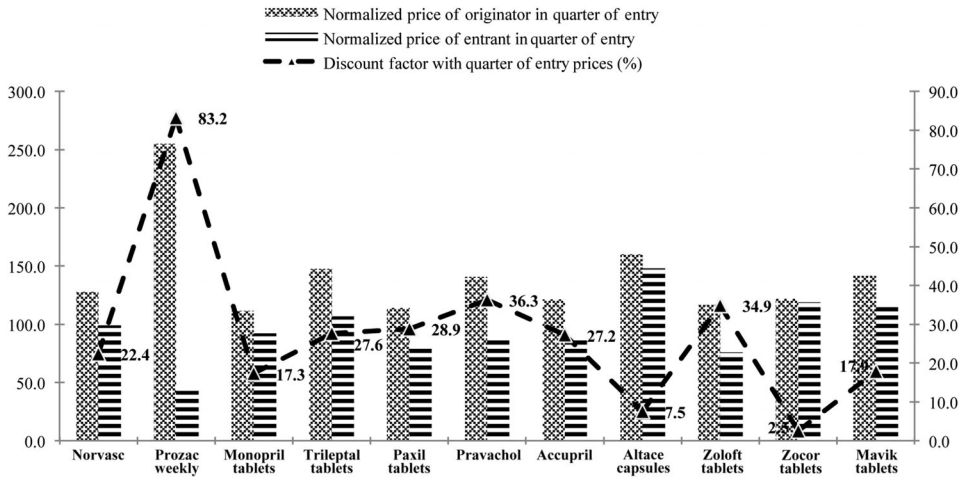
Notes: Preentry average originator price is normalized to 100. Originator price in quarter of entry on this scale is computed
and the exercise is repeated with generic price from Para-IV entrants. These prices are reported on the left-side y-axis. The
resulting discount factor is reported in the figure and along the right-side *y*-axis. The dashed line connects the discount
factors over several representative branded products across therapeutic markets. Source: IMS MIDAS™.

unconditional share. It also includes descriptive statistics for our patient characteristics utilized in
the random-coefficient specifications. Quarterly sales average $2.1 billion over our sample period,
and range between $0.6 billion and $2.6 billion. The average patient is 58 years of age. Average
real price per SU was approximately $1.96, and average sales were approximately 27 million SUs
each quarter. We note that the maximum price is in excess of $100 and is due to the presence of
injectable brands in our sample; we have four such branded products.[39] Although product-level
variation exists, there are, on average, three contraindications per product. Aggregate quarterly
advertising, on average, was $0.7 million for branded products and zero for generic products.
The share of the outside good averaged 41% whereas the unconditional share averaged 0.90%
per quarter. Finally, we observe that the number of firms per quarter, including both branded and
generic producers, ranged from 54 to 73 during our sample period.[40]

Panel B summarizes the impact of Para-IV entry on our branded hypertension products.
Prices, on average, decreased by 20% for all products after entry in challenged markets. For each
molecule where there was entry, the incumbent pharmaceutical firm increased branded price by
23%. This is not unexpected as the remaining brand consumers will have more inelastic demand
(Bhattacharya and Vogt, 2003). In the quarter of entry, we find that the average discount factor
offered by the generic entrant is approximately 38% of the branded product price. This discount,
however, varies widely (Figure 6). For illustrative purposes, we include drugs from other markets
in addition to hypertension to show the variability in these discount rates.

Another key feature in the data is the intensity of entry that follows a Para-IV challenge (i.e.,
other follow-on generic firms that enter once the generic entrant's 180-day exclusivity period

[39] Injectable versions are used in elderly or ill patients who are unable to ingest pills. These patient populations are
quite dependent on injectables; substitution possibilities are very limited. Results remain robust when these high-priced
injectables are excluded from the sample.

[40] These numbers are for disaggregate data. For our regression analysis, in order to avoid issues associated with
trivial market shares, we aggregate all generics, generating average prices for them weighted by sales. Incumbent brands
are retained with no modifications.

TABLE 5   Demand Estimation: Nested Multinomial-Logit and Full Random-Coefficient Logit Models

	Model 1: Nested Multinomial-Logit IV	Model 2: Random-Coefficient Logit
Price	−0.270***	−5.109***
	(0.052)	(0.931)
SD Price		1.123
		(0.920)
ln(s_{j|m}) (conditional share)	0.568***	
	(0.097)	
ln(Advertising)	0.770***	4.376***
	(0.146)	(0.138)
SD ln(Advertising)		0.972
		(3.717)
Number of contraindications	0.234	−4.903***
	(.202)	(0.061)
SD Contra		14.144***
		(4.215)
Age*Price		−0.627
		(1.388)
Insurance*Price		−1.360***
		(0.547)
Constant	−9.124***	
	(2.233)	
Product fixed effects	Y	Y
Observations	2935	3010
R^2	0.831	0.974
χ^2		73.37

Model 1 presents results from the nested multinomial-logit (with instrumental variables) specification. Model 2 presents results from the full random-coefficients logit specification. Instruments used in Model 1 include form number, number of firms in quarter, time since generic entry, and lags. Following Berry, Levinsohn, and Pakes (2004), instruments used in Model 2 include averages of prices and advertising for all other products sold by firm i, in focal product market j, in time t. For robustness tests with alternative specifications, see Branstetter, Chatterjee, and Higgins (2011).

ends). Across therapeutic markets there are, on average, 17 subsequent generic entrants. This subsequent follow-on entry drives down prices and compresses pharmaceutical firm revenue. For example, during the first year after Para-IV entry, average branded pharmaceutical product revenues eroded by an average of 56%; in later years, branded revenues fall by 89% relative to preentry levels.

□   **Demand estimation.**

Nested multinomial-logit coefficient estimates. The nested-logit demand regression results are reported in Table 5. Model 1 presents results obtained when we run the nested-logit specification (with instruments). Consistent with other studies (e.g., Stern, 1995, and Dutta, 2011) we use two competition-related instrumental variables and one related to product design. Using data from the FDA, our first instrument is the count of dosage levels in which a product is available. The second instrument we employ is the time since generic entry and is coded as 0 for all observations before entry into a molecule market, and this increases by one unit for each quarter that elapses after entry. Our final instrument is the number of firms (branded and generics) selling products across the market. For all instruments, we also used lagged values. (See Branstetter, Chatterjee, and Higgins, 2011, for more details.) The coefficients appear reasonable—the price coefficient is negative and statistically significant, and the value of the ρ parameter lies between 0 and 1, suggesting that our nests are not rejected by the data. The coefficient on contraindications is positive, but not statistically significant.

Random-coefficients logit estimates. Coefficient estimates from the random-coefficient logit model are reported in Model 2 of Table 5. The mean coefficient on *Price* is -5.109, significantly

higher than that estimated with the nested-logit approach, and it is strongly significant. It is within the range reported by prior work (Stern, 1996; Cleanthous, 2002; Dutta, 2011; Dunn, 2012). Advertising (*ln(Advertising)*) has a strongly significant and positive coefficient estimate of 4.376, suggesting a higher impact than that estimated with the nested-logit model. Contraindications (*Number of Contraindications*) negatively impact the utility of the consumer. The interaction between insurance and price (*Insurance*Price*) is strongly significant and negative (-1.360), suggesting a greater sensitivity to price as one moves from private insurance to public insurance to no insurance.[41] Although the interaction of age and price (*Age*Price*) is not significant, it is negative. We interpret this interaction as suggesting that price sensitivity rises with age.

We think it likely that the more flexible substitution possibilities captured by the random-coefficients approach are related to the stronger coefficient estimates it generates. In a world where cross-molecular substitution is high, and consumers not only cross nests but also two-digit ATC categories to take advantage of the opportunities generated by Para-IV entry, we would expect a higher estimated response to the low prices of generic entrants. Because advertising ceases when generic entry occurs, an approach that allows a greater response to the entry of low-priced generics could also produce a stronger estimated response to advertising. Many previous researchers have found that the estimated consumer welfare gains from new entry decline as one shifts from a nested-logit approach to a random-coefficients approach (e.g., Petrin, 2002); we find similar patterns in our analyses, which we discuss further below. As the exposition in this article makes clear, we regard the random-coefficients estimates as the most accurate and credible. We also believe that the rough equivalence between consumer surplus gains and producer surplus losses implied by the estimates based on the random-coefficients model reflects an important reality in this industry.

□ **Consumer surplus gains.** The social welfare gains associated with Para-IV entry are calculated as the difference between real consumer surplus (i.e. consumer surplus with Para-IV entry) and counterfactual consumer surplus (what would have been observed in the absence of Para-IV entry), minus the producer surplus losses associated with Para-IV entry. Estimates of social welfare gains, and the components of these gains, are provided in Figure 7 and summarized in Table 6. For the baseline nested multinomial-logit model, the cumulative consumer surplus was $217.7 billion. When we remove the Para-IV-facilitated generic entry from the sample and generate consumer surplus for the counterfactual world in which Para-IV entry did not take place, estimated cumulative consumer surplus drops to approximately $66.7 billion. The differences between real and counterfactual consumer surplus imply that early Para-IV generic challenges created substantial benefits for consumers—$151 billion in consumer surplus gains. These are large numbers. However, all the caveats and problems that attend the nested-logit approach lead us to discount them.

When we estimate the random-coefficients logit model, the coefficients imply that the cumulative consumer surplus was approximately $71.6 billion. When we remove the Para-IV-related generic entry from the sample and generate our counterfactual consumer surplus numbers, our results imply a cumulated consumer surplus gain due to Para-IV entry of approximately $42 billion. This is much smaller than the numbers implied by the nested-logit approach, but we believe it to be far more credible. As we have already noted, Para-IV entry induces some branded firms to create reformulations of their original products, and these reformulations sometimes capture a nontrivial share of the market. We sought to estimate the impact of reformulations on total consumer surplus gains by using the indirect utility function but then omitting the reformulations from our consumer surplus calculations. Alternatively, we reestimated the indirect utility function without the reformulations present, and recalculated consumer surplus with no consideration of these products. These alternative estimates suggest that reformulations could make a significant

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[41] Insurance coverage is measured with a categorical variable equal to 1 if the patient has private insurance, 2 if the patient has public insurance, and 3 if the patient has no insurance.

FIGURE 7

CONSUMER GAINS AND PRODUCER LOSES IN THE US HYPERTENSION MARKET
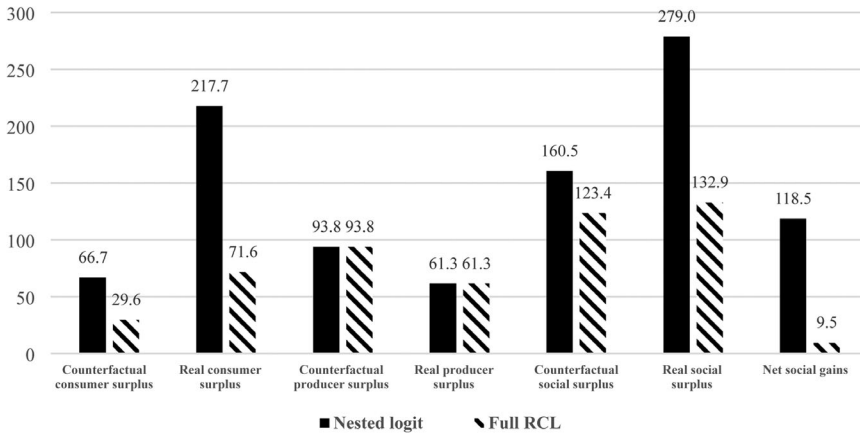
Notes: This figure plots (in billions) consumer surplus, producer surplus, and total welfare numbers derived from the coefficient estimates of the full-random coefficients logit model (Model 2, Table 5) and compares this to the welfare estimates with the nested multinomial-logit IV model (Model 1, Table 5). Total social gains estimated from the full-RCL model are $9.5 billion, whereas total social gains estimated from the nested multinomial-logit model are $118.5 billion.

TABLE 6   Welfare Analysis

	Cumulated CS Gains	Cumulated PS Gains	Cumulated Social Gains
NMNL IV	151	−32.5	118.5
RCL	42	−32.5	9.5
RCL / Alternative PS1	42	−31.7	10.3
RCL / Alternative PS2	42	−27.2	14.8

The increase in consumer surplus (CS) associated with Para-IV entry, the decline in producer surplus (PS) associated with Para-IV entry, and net social gains are reported across our various specifications. Values are in billions of real US dollars. NMNL IV denotes the nested multinomial-logit specification described in the text. RCL denotes the random-coefficients logit model. Alternative PS1 refers to an alternative approach to measurement of producer costs described in the text, which yields lower marginal costs and higher fixed costs. Alternative PS2 refers to a second alternative approach to measurement of producer costs, also described in detail in the same section, which also yields lower marginal costs but higher fixed costs. As can be seen in the table below, estimates of cumulated social gains are not very sensitive to these alternative assumptions.

contribution to total welfare gains—between $17 billion to $34 billion (depending on the approach taken) of the $71.6 billion in cumulative consumer surplus gains with the random coefficients-logit specification.

□   **Producer surplus losses.** A number of issues arise when considering these estimates of consumer surplus. First, how do these gains compare with producer surplus losses, and are there net social gains? Such a comparison requires an estimate of what producer prices and quantities would have been in a counterfactual world without Para-IV generic challenges. We find that we are able to predict incumbent sales and price outcomes with surprising accuracy, simply by extrapolating the trends found in early sample data for particular products to their later periods.[42] In many cases, the expiration of the litigated patent(s) lies beyond our sample period, so we can simply predict counterfactual producer behavior as a continuation of pre-Para-IV entry trends

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[42] We applied this procedure to markets that either never saw generic entry or saw it very late in the sample, and found that our "out of sample" predictions were accurate for price and quantity.

that extends to the end of our sample. In other cases, patent expiry occurs before the end of the sample. In those cases, we take the price and quantity declines observed after the initial 180-day exclusivity period, but redate these to the expiration of the patent rather than the successful Para-IV challenge.

Of course, calculating producer surplus requires that we subtract costs from revenue. Rather than use a formal model to derive an estimate of marginal cost, we take the late sample generic price as a measure of marginal cost.[43] Reiffen and Ward (2005) demonstrate that after 10 generic manufacturers enter, the market prices begin to approach long-run marginal cost. Moreover, conversations with industry insiders confirmed that significant generic entry tends to drive prices close to marginal cost, limiting the profits even for generic producers. We also subtract product-specific "detailing" expenditures from producer surplus. During our sample period, these detailing expenditures, aimed at marketing drugs to practicing physicians, represented the most important component of advertising expenditures. In calculating the counterfactual, we presume that advertising expenditures follow early sample trends. In the real world, producers tend to cut off advertising almost entirely after generic entry, and we use real-world expenditure levels in computing producer surplus for the actual market history we observe. Although we have total R&D spending for publicly listed pharmaceutical firms, we do not possess data on R&D spending for creation or improvement of particular products. As such, we assume that branded pharmaceutical firms spend as much on R&D as on advertising, and we deduct this from revenues to create a final measure of "producer surplus."

Generics producers earn profits in the real world that they would not have earned in the counterfactual world, but the intensity of generic competition compresses these profit flows very rapidly after the 180-day exclusivity period ends. Cumulatively, by the end of the sample period over which our random-coefficients welfare estimates are computed, the total loss in producer surplus in our baseline estimates comes to $32.5 billion. These producer losses offset most of the gains to consumers we compute when we use the more credible random-coefficients approach. Using those numbers, the net social gains are only $9.5 billion. Net social gains are much larger when we employ the welfare calculations based on the nested-logit model, but an impressive body of evidence suggests that these larger numbers need to be viewed with considerable skepticism, and we give them little weight in our welfare analysis.

We sought to test the robustness of these estimates to the use of different assumptions regarding marginal cost, advertising outlays, and R&D expenditures.[44] In the "baseline" approach detailed above, we calculate a separate "marginal cost" for each molecule, based on the lowest available generic price for that molecule at the end of our sample period. However, because generic competition was limited in some of our product markets, even at the end of our sample period, and even the lowest generic price could reflect some markup above marginal cost, we considered an alternative approach where we took the lowest price generics in each of the major categories of hypertension drugs considered in this article, and imputed that marginal cost for all products within the category. This led to lower estimates of marginal cost for many products.

Recognizing that, although detailing was the most important category of advertising expenditure for branded drugs during our sample period, it was not the only category; we considered alternatives in which firms were presumed to spend 7.5% of revenue on total advertising for each product in the quarters prior to generic entry. We also set R&D expenditure for all of our branded products equal to 15% of product revenues, reflecting the average R&D to sales ratio that held for the branded firms in our data set over our sample period. This proportional expenditure on R&D for our firms is consistent with numbers reported elsewhere in the literature (e.g., CBO, 2009).

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[43] For each molecule, we looked for the lowest late sample generic price and took that as our estimate of marginal cost for all producers in the molecule, In two cases of combination molecules, there was no generic entry, so we took the average of the lowest generic price for the element molecules in that combination.

[44] We thank the Editor for suggesting that we undertake these robustness tests as a way of confirming that our social surplus numbers were not simply an artifact of questionable assumptions about imperfectly measured fixed or marginal costs.

Moreover, the decision to set advertising at 50% of the R&D expenditure is also supported in the literature (e.g., Donohue, Cevasco, and Rosenthal, 2007; Staton, 2013). This first alternative, however, excludes the value of samples in the advertising expense. It will be included in our second alternative approach. We denote this first alternative approach "Alternative PS1."

As a final robustness check, we set advertising expenses equal to 15% of revenue for all products in all quarters prior to generic entry and label this approach "Alternative PS2." This increase in the advertising expenditure now reflects the retail value of samples (Donohue, Cevasco, and Rosenthal, 2007). Table 6 shows the difference these alternative assumptions make for our net welfare calculation. As it turns out, the impact is limited. The compression in producer surplus associated with Para-IV entry changes, depending on the assumptions we make, but not by much, and net social surplus varies from $10.3 billion to $14.8 billion. However we slice the data, we get fairly modest numbers for net social gains.

□   **The net gains in social welfare.** Figure 7 graphically depicts the various components of our social welfare calculations, identifying consumer, producer, and net social surplus in the real world and in the counterfactual world. This figure represents the first attempt that we are aware of to quantify the net social gains resulting from Para-IV entry under Hatch-Waxman. Table 6 summarizes the changes in consumer surplus and producer surplus associated with Para-IV entry. It also demonstrates how our estimates of net social gains change as we impose different measures of marginal cost and different assumptions about the evolution of fixed costs. The very significant price reductions and demand shifts generated by Para-IV entry lead to a massive shift of surplus from producers to consumers that measures in the tens of billions of dollars, but the net social gains are modest. As we have noted earlier in the article, within the molecular markets hit by Para-IV entry, there is no evidence of an increase in drug utilization after these price declines. If anything, utilization appears to decline rather than increase. If few consumers are brought into the marketplace, then our results actually make economic sense. Consumers benefit from significant price declines but nearly all of this comes at the expense of producers. The exact magnitudes of the producer surplus losses depend on the way we measure producer costs, but in all cases, these losses are large enough to offset most of the consumer surplus gains. If we omit the increase in consumer surplus that can be attributed to the reformulations introduced by branded firms in response to Para-IV entry, net social gains essentially disappear.

□   **Do consumer surplus gains really go to consumers?** The extent to which *final consumers*—that is, patients—actually realize the gains we have labelled as "consumer surplus" gains remains an open question. As we have already noted in this article, individuals do not purchase prescription drugs directly. Drug wholesalers, pharmacies, and insurance companies stand as intermediaries between patients and drug companies, and insured consumers pay a fraction of the retail price (the copay) at the point of purchase, with the rest being covered by prescription drug insurance. In effect, we have estimated in this article the decline in producer surplus and the increase in the surplus accruing to the entire downstream nexus of pharmacies and wholesalers, insurance companies, and patients that is generated by Para-IV entry. In a world in which pharmacies, doctors, and insurance firms acted in the best interests of their customers, patients, and policy holders, none of this would matter. Drug price declines would be passed through to consumers, either in the form of lower prices, lower copays, lower premiums, more generous coverage for nondrug medical procedures, or some combination of all three. The real world is considerably more complicated. Recent official reports by the FTC (2009, 2011) and the work of Alpert, Duggan, and Hellerstein (2013) suggest that pharmacies earn significant profit margins on generic drugs, at least in the short run. A long literature documents the reality that insurance companies extract surplus from their policy holders; recent industry consolidation may be exacerbating this (Dafny, Duggan, and Ramanarayan, 2012), and the limited data we have on copays suggests that insurance companies are probably appropriating some of the gains from lower generic drug prices for themselves.

Inspection of actual copay data from IMS NPA™ reveals the existence of a number of products in which insurance companies realize very significant declines in real drug cost but do not adjust patient copays by the same amount, in percentage change terms. Furthermore, although originator products' prices typically rise modestly after generic entry, the copays required of consumers who choose these products often go up by much more than the price, in percentage change terms. As an illustrative example, we observe the case of a branded drug, Altace®, which encountered very strong generic competition toward the end of the sample. Using copay data, we constructed a "pass-through" coefficient that measured the percent change in the branded drug's price after generic entry divided by the percent change in copay for patients who elected to continue to purchase the branded drug. This coefficient was about 0.55, well below one, demonstrating that the percent change in price was much smaller than the percent change in patient copay. On the other hand, the price of generic versions of the drug plummeted. However, patient copays fell only modestly. The ratio of the percent change in price over the pre and postentry periods to the percent change in copays was well above one, implying that copays fell by far less than the wholesale price for patients switching to generic versions.

Unfortunately, even with the rich data at our disposal, it is simply not possible to decompose the total gains in surplus accruing to this downstream nexus into the parts that go to pharmacies/wholesalers, insurance companies, and patients/consumers. This is because all of these parties participate in a complex web of transactions that are mostly missing in the IMS data sets. We do not come close to observing all the flows of rebates and reimbursements between large insurers and pharmacy chains, nor do we see how insurance companies might (or might not) pass on the benefits of lower generic drug prices to their insureds by lowering their premia. This is a significant limitation of our data and approach, but it is a limitation shared with virtually the entire economics of pharmaceutical consumption literature. In future work, a more complete and thorough consideration of the degree to which intermediaries such as pharmacies and insurance companies appropriate the gains generated by pharmaceutical price declines is certainly warranted.

7. Conclusion

■   This article estimates the impact of early generic entry facilitated via Para-IV challenges in the US hypertension market. Although Para-IV challenges have been legally possible since the passage of the Hatch-Waxman Act in 1984, a series of legal and institutional barriers kept their number quite low until the late 1990s. Since then, a series of court cases and procedural changes have significantly lowered the costs and raised the success probabilities of these challenges. We view these changes as constituting a slowly unfolding natural experiment. Using unusually rich data, we estimate structural discrete-choice demand models, and use these models to back out the first-known estimates of the net impact of these challenges on social welfare, inclusive of net gains to consumer surplus and declines in producer surplus.

In this article, we take two different econometric approaches to demand estimation: a nested-logit approach and a random-coefficients approach. The results based on a random-coefficients logit model, which we regard as most credible, suggest substantial consumer gains from Para-IV entry—gains on the order of $42 billion over the 2000–2008 period. However, these consumer gains are significantly offset by producer losses on the order of approximately $32.5 billion. To a first-order approximation, Para-IV entry has shifted surplus from branded incumbent producers to downstream drug purchasers. There has been effectively no increase in inframarginal drug consumption as prices have fallen, but that is not surprising given the institutional arrangements surrounding prescription drugs and the parallel recent findings of other researchers.

That being said, our estimates come with important caveats. Although we presume that a large fraction of the "consumer surplus" generated by increased generic availability and price declines actually goes to final consumers (i.e., patients), it is certain that insurance firms and/or pharmacies appropriate some of this downstream surplus. We intend to explore this issue more

thoroughly in future work. If it is the case that these actors are appropriating most of the consumer surplus generated from recent regulatory actions, then our estimates of "consumer gains" will need to be interpreted in a different light. Rising competition from generics could also diminish the incentives to conduct pharmaceutical R&D, at least in some product markets, and this could have a negative impact on future welfare from drug consumption. The impact of rising generic competition on pharmaceutical R&D is beyond the scope of the present article, but we are investigating it in ongoing work; preliminary results suggest a substantial impact of generic competition on pharmaceutical R&D (Branstetter, Chatterjee, and Higgins, 2014).

Finally, the hypertension market is just one of many important therapeutic categories in the US pharmaceutical industry. Future research should supplement the results described herein with results from other markets, many of which are plausibly characterized by significantly different levels of cross-molecular substitution (e.g., depression, epilepsy, and gastro esophageal reflux disease). Such analyses would enable a more complete judgment on the efficacy of Hatch-Waxman. As is usually the case in economic research, much more remains to be done.

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