Biosimilar Entry and the Pricing of Biologic Drugs*

Josh Feng, Thomas Hwang, Jacob Klimek, Luca Maini†

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Abstract

Unlike small-molecule drugs, biologics cannot be exactly replicated and instead face post-exclusivity competition from non-identical copies called biosimilars. Under a stylized model with a loyal segment of consumers, greater differences between incumbent and entrant can lead incumbents to "fight" rather than "acquiesce." Consistent with this prediction, we find that, on average, biologics respond to biosimilar entry by sharply reducing net-of-rebate prices to maintain volume—unlike small molecule incumbents. In addition, we provide suggestive evidence that proxies of biosimilar entrant quality and loyal segment size are associated with smaller price responses.

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†Josh Feng: University of Utah Eccles School of Business, josh.feng@eccles.utah.edu. Thomas Hwang: Harvard Medical School, tjhwang@bwh.harvard.edu. Jacob Klimek: UNC Chapel Hill, jklimek@live.unc.edu. Luca Maini: Harvard Medical School, maini@hcp.med.harvard.edu.

1 Introduction

Pharmaceutical market regulation grants temporary property rights to new drugs through patents and market exclusivity rights.[1] Once these protections expire, generic drugs that contain the same exact active ingredient can enter through an abbreviated approval process established in the United States by the Hatch-Waxman Act of 1984. Evidence shows that, after generic entry, incumbents typically do not reduce their prices and do lose almost all of their market share to generic entrants (Grabowski and Vernon, 1992; Berndt and Aitken, 2011; Grabowski et al., 2016).

The traditional brand-to-generic life-cycle of pharmaceutical products, however, breaks down for biologic drugs—large, complicated molecules that are grown from organic tissue—because potential "copycat" entrants cannot replicate the incumbent exactly.[2] As a result, entrants that replicate an incumbent biologic product—so-called *biosimilars*—may have a different effect on market outcomes.

In this article, we study the reaction of originator biologics to the entry of biosimilar products in the United States. We first present a model of competition between an incumbent and a "copycat" competitor that incorporates loyal consumers and vertical quality differences within a logit demand system. The model predicts that an incumbent is more likely to compete on price when: (i) The incumbent faces fewer copycat entrants; (ii) entrants have lower quality; and (iii) the loyal segment is small. We empirically evaluate the model's predictions by examining the effect of biosimilar entry on list and net price, volume, and insurance coverage; we use a generalized difference-in-differences framework. We then compare the reaction of biologic incumbents to that of small molecule brands that face generic entry.

Our model predicts that originator biologics are more likely to compete on price with copycat entrants than do small-molecule brands for two reasons: First, because generic entry costs are lower than biosimilar entry costs, we expect small-molecule brands to face a greater number of generic entrants, holding all else equal.[3] Second, because biosimilars cannot replicate biologic originators exactly, and because they are

[1] White (2020) notes that the presence of patents sometimes increases market power, but should not automatically be viewed as creating a monopoly.

[2] Biologic drugs are manufactured from organic tissue, unlike their small-molecule counterparts that are chemically synthesized. The former is a more complex process, and potential entrants cannot copy the incumbent exactly because they do not have access to the same input material and manufacturing conditions.

[3] See remarks made by FDA Commissioner Scott Gottlieb to the America's Health Insurance Plans' National Health Policy Conference on March 7, 2018 (https://www.fda.gov/news-events/speeches-fda-officials/capturing-benefits-competition-patients-03072018, retrieved November 3, 2020).

relatively new to the market, we expect patients and providers to perceive generics as closer in quality to their branded counterparts than are biosimilars to their branded counterparts.[4]

Our results are consistent with the predictions of our model: After each biosimilar entry, originator biologics experience: a significant decrease in net price of about 13%; a small, noisy decline in the volume of sales; and a small but statistically significant decline in coverage. Conversely, small-molecule brands that face generic entry keep net prices constant and experience dramatic losses in volume.

To support our model further, we provide two additional tests that leverage variation in entrant quality and loyal market size within the sample of biologic and biosimilar drugs: First, we compare incumbent responses to biosimilar originators that were approved through pathways that require a different degree of clinical evidence. Approximately half of the biosimilar products in our sample were approved through an abbreviated pathway that was introduced in 2010, whereas the rest were approved through more traditional pathways. Entrants that take advantage of the abbreviated pathway may be perceived as being supported by weaker clinical evidence, which could lead to differences in quality perception. Consistent with our model, we find that incumbents reduce prices more aggressively when competing against entrants that relied on the abbreviated pathway.

Second, we show that incumbents are more likely to compete more aggressively on price when the underlying market is growing. Growing markets include a greater share of new patients, who are less likely to be loyal to a given product.

Our findings shed light on the forces that shape equilibrium outcomes in markets with biosimilar competitors, and add to the evidence on why biosimilar takeup has been lagging relative to expectations (see, e.g., Atteberry et al., 2019; IQVIA Institute for Human Data Science, 2020). Our results suggest that, as more biosimilars enter the market and more evidence of their equivalence with originator biologics is generated, originator biologics may choose to "retreat" to the loyal market segment and concede volume.

Moreover, policies that aim at increasing patient and physician confidence in the effectiveness of biosimilars (e.g., the Advancing Education on Biosimilars Act, S.164 of

[4] A survey that focused on prescribing physicians found that about 40% were unaware that biosimilars were as safe or had the same efficacy as their reference counterparts (Cohen et al., 2016). In addition, according to a recent HarrisX poll, 65% of Americans admit to not being familiar with the term "biosimilars" (harrisx.com/wp-content/uploads/2020/03/Biosimilars-topline-poll-public-memo-VF.pdf, retrieved November 13, 2020).

the 117th Congress, 2021) or that provide monetary incentives for prescribing biosimilars over originator biologics (e.g., the Inflation Reduction Act, H.R. 5376, 2022) could help accelerate this process.[5]

1.1 Contributions to the Literature

This article contributes to the growing literature on the impact of biosimilars (see, e.g., Scott Morton et al., 2018; Karaca-Mandic et al., 2019; Chen et al., 2020; Dean et al., 2021; Frank et al., 2021) by studying the competitive interactions between biologic originators and biosimilars. We propose an explanation that can potentially reconcile the contrasting views on biosimilar entry in the U.S. market. Several papers in this literature (see e.g., Atteberry et al., 2019; Trusheim et al., 2019; Zhai et al., 2019) have described the current regulation of biologics markets as an overall failure due to the inability of biosimilars to gain meaningful market share and the absence of a list price response by originator biologics. Other studies, however, have identified some positive contributions in the form of lower net prices (see e.g., Brill and Ippolito, 2019; San-Juan-Rodriguez et al., 2019; Frank et al., 2021).

We find heterogeneous responses: Whereas some originator biologics seem to have "accommodated" biosimilar entry, others have actively fought their biosimilar competitor and have managed to maintain their pre-entry volume and insurance coverage. Our theoretical model points to perceived quality differences as a potential driver of these different outcomes.

More broadly, we contribute to the literature on competition in pharmaceutical markets: We join a series of recent papers that show that strategic behavior of pharmaceutical companies is rarely reflected in widely available list prices, but instead becomes apparent only through movements in net price, which are much harder—but not impossible—to track (see, e.g., Kakani et al., 2020; Feng et al., 2023). In addition, our work is one of a small but growing number of studies that examines access in the pharmaceutical market by using insurance coverage data (see, e.g., Lavetti and Simon, 2018; Geruso et al., 2019; Dean et al., 2024).

Prior work in the literature has analyzed the data separately to study: pricing trends in the industry; how reference pricing affects negotiations between manufacturers and

[5]The Advancing Education on Biosimilars Act requires the FDA to create and disseminate materials on biosimilars to providers and patients, including the comparability of biosimilars to originator biologics. The Inflation Reduction Act of 2022 slightly increased the amount hospitals receive when administering a biosimilar while keeping the reimbursement for the originator unchanged.

payers; and coverage choice incentives for payers across types of plans. Our analysis combines the two data sources to measure competition between drug manufacturers. We also add to work that studies the implications of consumer loyalty in affecting market outcomes (Frank and Salkever, 1992, 1997; Feng, 2024; Feng and Maini, 2024).

2 Biologics, Biosimilars, and Marketing Approval

Biopharmaceutical products—which are more commonly known as biologic drugs or biologics—are large, complex molecules that are grown from organic material. Examples of biologic drugs include: insulin; interferons (which are used to treat multiple sclerosis, some types of cancers, and hepatitis); and monoclonal antibodies (which are used to treat rheumatoid arthritis, psoriasis, and ulcerative colitis).

Because they are grown inside living organisms, biologics cannot be reproduced exactly. Only the company that manufactures the original biologic drug has access to the specific cell line that is used in the production process. Therefore, no other company can create an exact copy. Thus, biologics are fundamentally different from "small-molecule" drugs, which are synthesized using perfectly replicable chemical processes. Nonetheless, it is still possible to create a "biosimilar" version of an existing biologic drug: one that contains the same components but may present small differences that are due to the complexity of the production process.[6]

The impossibility of reproducing exact copies of biologic drugs means that most existing regulations that manage drug competition over the product life-cycle do not apply to biologics. For example, generic drugs have enjoyed access to the "abbreviated new drug application" (ANDA) since the passage of the Hatch-Waxman Act in 1984. The ANDA waives the requirement to provide clinical trial data for generic products. Instead, biosimilar drugs, until recently, had to undergo clinical testing as completely new drugs.

The Biologics Price Competition and Innovation Act (BPCI Act) of 2009 attempted to address the gaps in the regulation of biosimilars by creating an abbreviated approval pathway for these drugs. The BPCI Act sets two main criteria for the approval of a biosimilar product: (i) presentation of chemical data showing that the product is highly similar to the originator biologic in structure; and (ii) evidence of "equivalence" with

[6] As defined by the FDA, a "biosimilar" is a biologic that is highly similar to, with no clinically meaningful differences from, an existing biologic that is already in production. The phrase "meaningful differences" refers to the efficacy and safety of the biosimilars in comparison to the originator biologic.

the originator biologic from a clinical trial. The BPCI Act significantly reduced entry costs, because clinical trials that are aimed at proving statistical equivalence typically have much smaller enrollments than do trials for gaining approval as a new drug. However, a smaller enrollment likely leads to perceptions of lower quality, as can be found in the evidence on physician behavior and trial representation in Alsan et al. (2024).

Although the BPCI Act makes it easier for biosimilars to reach the market, they still face at least two significant hurdles relative to generic drugs: First, biosimilars cannot take advantage of regulations that promote the use of generic products, such as mandatory substitution laws. As a result, switching existing patients from biologics to biosimilars may be difficult. Second, the cost of developing a biosimilar is still much higher than developing a generic. Informal estimates place the cost of bringing a biosimilar drug to market between $100 million and $250 million, which—while much lower than the cost to bring a new drug to market—far surpass the development cost of a generic small-molecule drug (about $2–$5 million) (Grabowski et al., 2014).[7] This cost difference stems from both the complicated nature of biologic drugs and the clinical trial requirement noted above.

Moreover, biosimilars face much higher risks of litigation from the incumbent biologic manufacturers, which also contributes to higher expected entry costs. Biologic drugs are protected by a much larger number of patents relative to small molecule drugs, and infringement of any of these patents is enough to prevent a biosimilar from entering (Chen et al., 2017). As a result, we would expect fewer biosimilar than generic entrants even holding market size fixed.

Taken together, these limitations imply that potential competition from biosimilar competitors might have different implications for biologic originators than for small-molecule brands that face generic entry.

3 A Model of Strategic Responses to Copycat Entry

We model competition between an originator and a fringe of $N - 1$ copycat competitors over two consumer segments. Our approach is in the spirit of Frank and Salkever (1992), who first used this approach to model the effect of generic entry.

We model the market as a measure 1 set of consumers, divided into a measure γ

[7] See the remarks made by FDA Commissioner Scott Gottlieb to the America's Health Insurance Plans' National Health Policy Conference on March 7, 2018 (https://www.fda.gov/news-events/speeches-fda-officials/capturing-benefits-competition-patients-03072018, retrieved November 3, 2020). Estimates place the cost of developing a new drug at around $2.87 billion (DiMasi et al., 2016).

of "loyal" consumers, and a measure $1-\gamma$ of price-sensitive consumers. The utility of consumers in the price-sensitive segment follows the standard "logit" random utility choice model:

$$u_{ij} = \delta_j - \alpha p_j + \varepsilon_{ij} \tag{1}$$

where i and j index consumers and products respectively; δ_j represents the vertical quality; p_j represents the price; and ε_{ij} is a mean-zero, unit-variance shock that follows a Type 1 extreme value distribution. We assume that these consumers also consider an outside option $j = 0$ whose quality and price are normalized to zero. We denote the incumbent as $j = 1$, with copycat entrants' numbers $j = 2, \ldots, N$. Consumers in the loyal segment do not consider copycat products and have a willingness to pay $\bar{p}$ for the originator product.

We assume that the originator and copycats play a sequential pricing game: The originator moves first, and then entrants play a simultaneous Bertrand-Nash pricing game.[8] The initial price that is set by the originator determines whether it will compete for consumers in both segments, or will choose simply to extract the maximum surplus from loyal consumers.[9] We choose a sequential game to avoid the possibility of mixed strategy equilibria, which can occur in a model with two consumer segments when the originator chooses prices at the same time as the copycat entrants.[10] The originator chooses the price that maximizes its own profits, taking into account subsequent play by the copycat entrants:

$$\max_{p_1} p_1 \times [\gamma \times \mathbb{I}_{p_1 \leqslant \bar{p}} + (1-\gamma) \times s_1(\mathbf{p})] \tag{2}$$

where $s_1(\mathbf{p})$ is the market share of the originator as a function of its own price and the price of the copycat competitors $\mathbf{p} = \{p_1, \ldots, p_N\}$, which is given by the standard logit

[8] We rule out price discrimination from the set of possible strategies. In theory, price discrimination is possible in pharmaceutical markets. In practice, doing so on the basis of "loyalty" is very difficult because manufacturers do not sell to specific patients, but rather to large intermediaries: either pharmacy benefit managers (PBMs) that operate on behalf of health insurance plans, or group-purchasing organizations that operate on behalf of hospitals. These organizations then serve both loyal and non-loyal consumers. Second-degree price discrimination is also difficult, because product quality is fixed, and contracts usually specify a fixed unit-price.

[9] Because of the logit error, the originator will always get a non-zero share of the remaining consumers.

[10] The presence of mixed strategy equilibria does not significantly alter the predictions of the model, but it complicates the illustration of our results.

expression:

$$s_1(\mathbf{p}) = \frac{\exp(\delta_1 - \alpha p_1)}{1 + \sum_{j=1}^{N} \exp(\delta_j - \alpha p_j)} \tag{3}$$

Once the originator sets p_1, copycats simultaneously set prices to maximize

$$\max_{p_j} p_j \times (1 - \gamma) \times s_j(\mathbf{p}). \tag{4}$$

3.1 Equilibrium Predictions

To illustrate the key predictions of our model, we show how the response of the originator to copycat entry varies with:

1. the number of entrants;
2. the quality of entrants; and
3. the size of the loyal segment.

These comparative statics correspond to variation in our data. To test the first comparative static we will show how the incumbent's prices change after the entry of each new biosimilar. To test the second comparative statics prediction we will compare how price, volume, and coverage of the incumbent product respond to: (i) biosimilar entrants that followed different marketing approval processes; and (ii) biosimilar entrants versus generic entrants. To test the third comparative static, we will compare outcomes in biologic markets with varying flows of new patients, under the assumption that newer patients are more likely to be "loyal" to the originator biologic because of history-dependence in drug demand (Feng, 2024).

Because logit demand leads to non-linear equations in price, we do not provide closed-form solutions. Instead, we compute the equilibrium of the game that we described above under specific parameters—$\bar{p} = 25$, $\delta_1 = 2$, $\alpha = 0.1$—and vary the quality of the entrants δ_j and the size of the loyal segment γ. The qualitative implications discussed below are stable with respect to changes in any of the parameters.

Figure 1 shows the price response of the originator as a function of the entrant's quality and the size of the loyal segment. The top panel plots the change in the originator's price after the first copycat enters. We find that when the size of the loyal segment increases—when we move from left to right along the x-axis—the originator is less likely to compete with the copycat entrant by reducing its price. When the quality

of the entrant increases—when we move up the y-axis—the originator can respond in two ways: If the size of the loyal segment is small, a higher-quality entrant can induce a stronger competitive response, as in standard models. However, for a sufficiently large loyal segment, a higher-quality entrant leads to higher originator prices as the originator focuses on extracting the maximum surplus from consumers in the loyal segment.

The second panel shows the change in price (again, relative to the baseline monopoly case) after two identical copycats enter the market. The larger number of copycat entrants does not alter the qualitative implications that are shown in the first panel, but amplifies the response of the originator. A second entrant expands the values of γ and δ_j for which the originator ceases competing in the price-sensitive segment and focuses on extracting the highest possible surplus from the loyal segment. At the same time, an additional entrant leads to lower equilibrium prices for values of γ and δ_j where the competitor chooses to compete in the price-sensitive segment as well.

Figure 2 shows the change in the incumbent's market share. Although the market share of the incumbent always falls (and more so with a larger number of entrants), the largest drops occur for high-quality entrants. The size of the loyal market has a small effect on market share. When the loyal market is large enough that the incumbent prefers to not compete on price, there is an additional small decline in the incumbent's market share. However, as the size of the loyal market keeps increasing, the incumbent's market share recovers since the dominant effect is that the entrants have fewer consumers that they can potentially capture.[11]

These comparative statics illustrate the potential differences that one might expect when comparing the competitive effects generated by generic and biosimilar entrants, or by biosimilar entrants with different characteristics. First, because entry costs are higher for biosimilars, originator biologics can expect to face fewer entrants than do small molecule originators. This suggests that a smaller fraction of originator biologics should respond to biosimilar entry by "retreating" to the loyal segment of the market.

Second, we expect biosimilar products to be more differentiated than are generics, because entrants cannot exactly replicate the originator's molecule. In turn, these differences may translate into lower perceived quality. This would also make it easier for originators to compete in the non-loyal segment, and reduce the likelihood of "retreating" to the loyal segment of the market.

[11] Although our model does not explicitly incorporate insurance coverage, we expect coverage of the incumbent's product to follow a pattern that is similar to volume with larger declines when the incumbent decides not to compete on price.

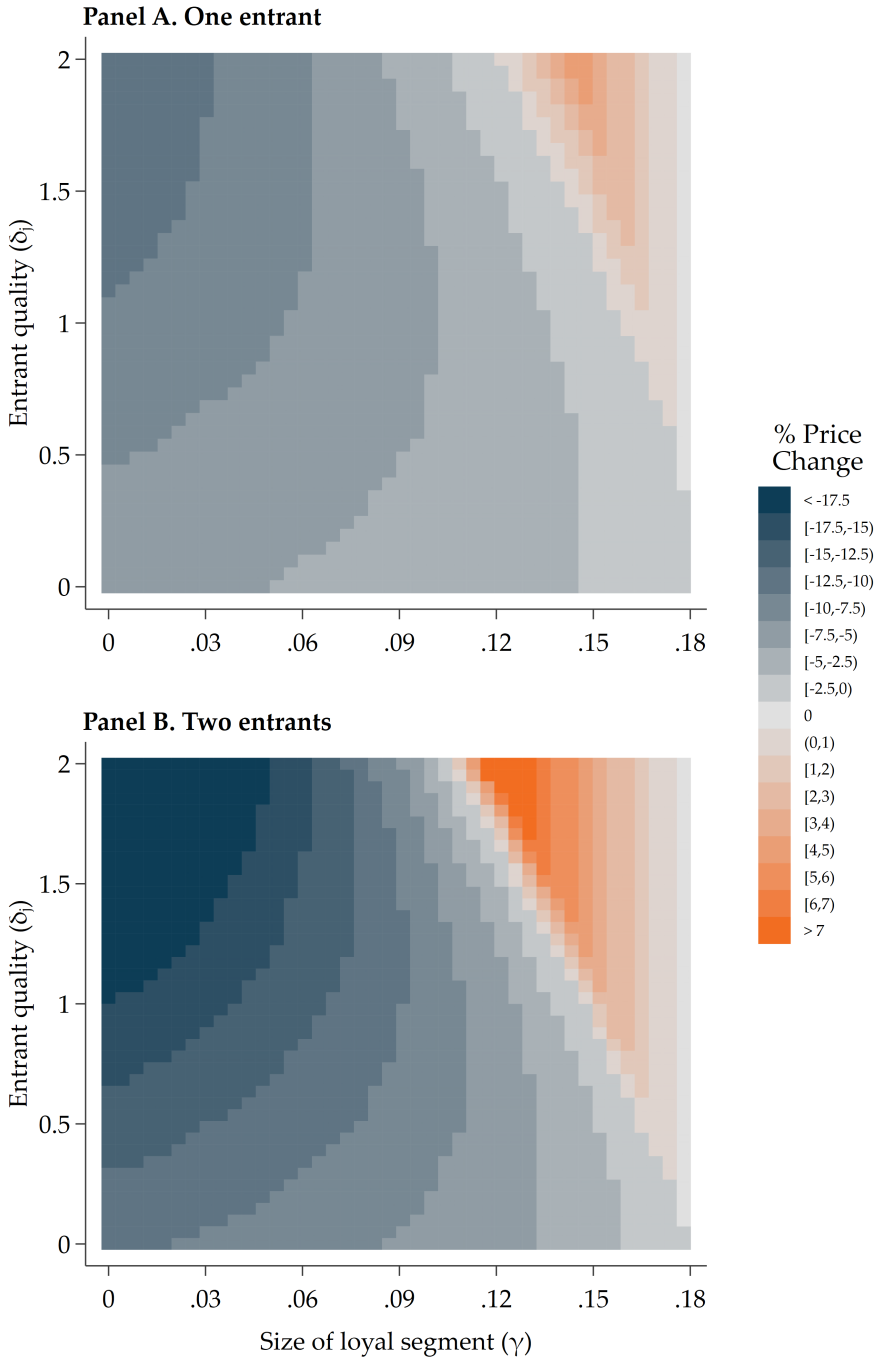


Figure 1: Change in originator price after copycat entry

Notes: Figures plot the originator's change in price in response to the first and second copycat entrant. The orange region reflects parts of the parameter space where the incumbent acquiesces to the copycats. The darker blue region reflects the part of the parameter space where the incumbent reduces price to compete in the price-sensitive segment.

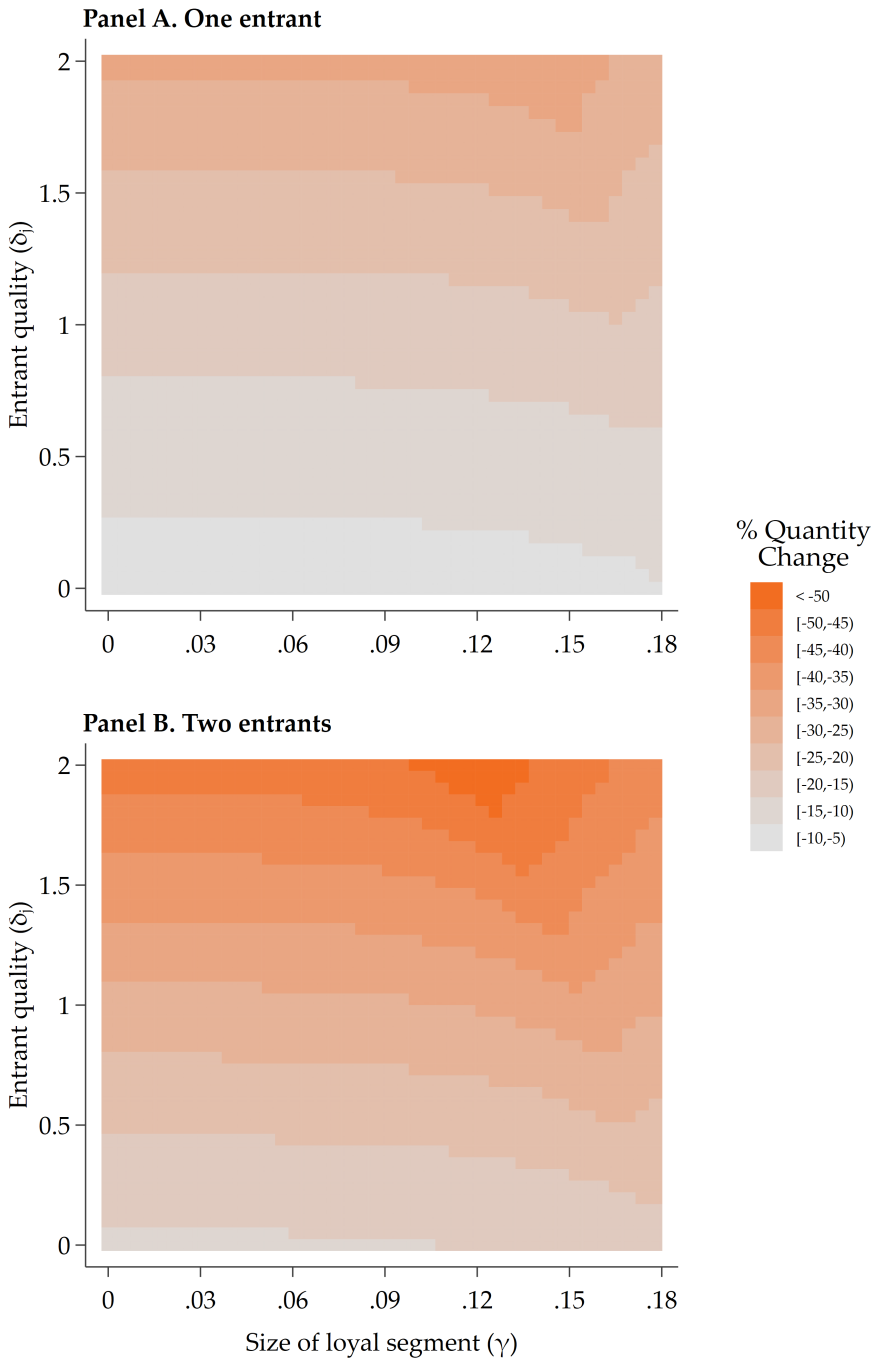


Figure 2: Change in originator market share after copycat entry

Notes: Figures plot the originator's change in market share after the first and second copycat entrant.

Finally, we expect originators with a larger "loyal" segment to be less likely to compete on price.

4 Empirical Approach

4.1 Sample and Data

Our main analysis focuses on a set of ten molecules that experienced at least one biosimilar competitor that launched prior to June 2020. Table A1 in Appendix A.1 lists all of the originator biologics and biosimilars in the U.S. and their approval and launch dates, which we collected from the FDA's website and from public announcements by pharmaceutical companies. Four of the products that we include are effectively biosimilars but were not approved through the abbreviated pathway introduced by the BPCI Act. These are: Admelog (biosimilar of Humalog); Basaglar (Lantus); Extavia (Betaseron); and Granix (Neupogen). Extavia and Granix applied for marketing approval before the abbreviated pathway was introduced.[12] Admelog and Basaglar are insulin products, which the FDA did not consider to be biologics until 2020 and therefore were ineligible for the abbreviated entry pathway.[13] As a result, these two drugs were approved through the "505(b)(2) pathway" that is usually reserved for follow-on products of existing brands.

To perform our analysis, we rely on price and revenue data from SSR Health and the Centers for Medicare and Medicaid Services (CMS). The SSR Health database covers roughly 1,000 branded drugs and contains quarterly data from 2007Q1 to 2020Q2 on: wholesale acquisition cost (WAC); estimated net price; units sold; and net sales.[14] CMS reports quarterly data on Average Sales Price (ASP) for physician-administered drugs.

[12] Extavia was approved in 2009. Granix was approved in 2012, but submitted its first application to the FDA in 2009 (see https://www.drugs.com/nda/xm02_091202.html, retrieved November 10, 2020).

[13] Although insulin is a biologic drug, it was first marketed in the U.S. before the word "biologic" entered the official U.S. regulation terminology. The FDA closed this loophole in February 2020; it published a rule that included insulins among the products eligible for approval under the abbreviated BPCI Act pathway (see https://www.fda.gov/news-events/press-announcements/fda-works-ensure-smooth-regulatory-transition-insulin-and-other-biological-products, retrieved November 10, 2020).

[14] SSR Health derives its estimates by comparing data on invoice sales and units sold from Symphony Health to net sales figures collected from SEC filings and other disclosures of publicly-traded companies. This estimate reflects the average revenue earned by the manufacturer for each unit of drug sold. See also Ippolito and Levy (2022) for a thorough discussion of the SSR Health data. The amount corresponding to the unit measure varies across drugs; but this does not matter for our regression because we analyze percentage effects and also control for drug fixed-effects. In one case, the unit of a product (Herceptin) changed in the middle of our sample; we adjust units by a $44/15$ factor in all years following the change.

There are advantages to each of our price measures. Relative to the measure of net price in the SSR Health data, ASP has the advantage of being calculated using proprietary data that are provided directly from manufacturer to the federal government. However, the ASP measure has three drawbacks: First, ASP excludes rebates that are paid to "340B hospitals."[15] This is an important omission, as a growing share of all U.S. hospitals have become eligible for this program in recent years, and evidence shows that these hospitals are more likely to prescribe originator biologics (Bond et al., 2023).

Second, CMS publishes ASP only for drugs covered by Medicare Part B. As a result, we do not have ASP for drugs that are available only through retail pharmacies.

Third, CMS aggregates ASP at the level of a "healthcare common procedure coding system" (HCPCS), which for drugs usually means a molecule. This aggregation has a minimal effect on our sample, which is made up of biologics and on-patent branded drugs. The only exception is insulin, which has a single HCPCS code. As a result, we must exclude from the ASP analysis the two insulin products that experience biosimilar entry in our data.

We combine our price data with insurance coverage data from MMIT Analytics. The MMIT data contain quarterly snapshots of insurance coverage from 2011Q1 to 2020Q2 at the drug-health-insurance-plan level.[16] The data span all health insurance plans in the U.S. across: commercial insurance; Medicare; Medicaid; and the ACA health exchanges. This yields a total of over 300 million covered lives in 2020. Using the MMIT data, we construct three measures of coverage at the drug-year level: the fraction of insured individuals whose health plan offers: (i) any coverage; (ii) unrestricted coverage; or (iii) preferred coverage of a given drug.

Our main analysis compares the 10 originator biologics that experienced biosimilar entry prior to June 2020 to 159 other biologic drugs that did not experience biosimilar entry. In a secondary analysis we compare 204 small-molecule brands that experienced loss of exclusivity (LOE) between 2007 and 2019 to a set of 626 other small-molecule brands that did not.[17]

[15] "340B hospitals" are a category of hospitals created by the Veterans Health Care Act of 1992. ASP also excludes rebates to Medicare Part D plans, Medicaid, the Veteran Affairs, and a few other smaller federal programs. See the *Code of Federal Regulations* (42 CFR §414.804 (a)(4)(i)).

[16] This includes both physician-administered drugs covered under medical benefits as well as drugs sold through retail pharmacies covered under prescription drug benefits. Some drugs have missing data because of small gaps in MMIT's historical coverage.

[17] Our sample includes all products in the SSR Health and MMIT data with one exception. The volume of some of the drugs in the SSR Health data is underreported, which can lead to some net prices being systematically higher than list prices (this is a known issue, noted also in Ippolito and Levy 2022; Feng et al. 2023, 2026). While this does not affect our results (since our analysis relies on within-drug changes

4.2 Empirical Strategy and Summary Statistics

We analyze the impact of copycat entry using a two-way fixed effects (TWFE) approach:

$$Y_{it} = \alpha_i + \delta_t + \beta \times \text{EventCounter}_{it} + \varepsilon_{it} \tag{5}$$

In our main specification, our core sample is the set of all biologic drugs, and the "Event Counter" increases by one step for the originator biologic every time a biosimilar enters. Our dependent variables are measures of: list and net price; volume of sales; and coverage. We control for drug fixed-effects in all regressions. When the dependent variable measures price or coverage, we also control for year fixed-effects. When the dependent variable measures volume, we control for age fixed-effects instead.[18] We cluster standard errors at the drug level in all specifications.

Recent work in the econometrics literature has highlighted several limitations of TWFE methods (see e.g. Callaway and SantAnna, 2020; Sun and Abraham, 2020; Goodman-Bacon, 2021; Borusyak et al., 2024). In our setting, a primary concern is treatment effect heterogeneity: especially responses that change over time as markets evolve. Because our entry events do not occur simultaneously and markets may take time to adjust, this can mean that earlier treated observations contaminate the control group for subsequent observations.

In practice, the number of untreated observations in our sample is much larger than the number of treated observations, which limits the scope of potential issues. However, we still provide results from three additional specifications: (i) time-varying estimates; (ii) using the never-treated correction suggested by Sun and Abraham (2020); and (iii) matching "treated" drugs to control groups with similar age, broad therapeutic area, and revenue.

Our regressions include ten biologic drugs that experienced biosimilar entry at some point between 2007Q1 and 2020Q2, and 159 other drugs. Table 1 displays basic summary statistics for these two groups. Biologics that experience biosimilar entry tend to have higher average invoice sales and net sales, and slightly better coverage. This is not surprising, as biosimilars are more likely to challenge successful products

in prices), it can create large fluctuations in prices for drugs with low sales. Hence, to improve precision of our estimates, we exclude a small number of drugs (less than 10) whose net prices fluctuate too much relative to list prices. This filter does not alter the qualitative implications of the results.

[18] We measure age as years since U.S. launch date. Although controlling for both age and year FE may be preferable, the two sets are highly collinear. Prices tend to increase over time, whereas coverage tends to decrease over time, regardless of age. Conversely, volume follows an inverted-U shape, which makes it more important to control flexibly for age effects.

Table 1: Summary statistics for treatment and control groups

	Biologics w/ Biosimilar				Control Group			
	Mean	Median	Min	Max	Mean	Median	Min	Max
Yearly Invoice Sales (million USD)	3,277.76	2,905.79	137.27	10,497.13	760.55	225.62	0.08	23,222.96
Yearly Net Sales (million USD)	2,215.65	2,291.00	73.00	5,596.57	599.78	233.43	0.05	14,864.00
WAC	1,298.54	188.75	7.22	10,385.00	3,412.41	326.74	0.90	850,000.00
Estimated net price	911.23	160.94	3.72	6,060.49	3,809.20	368.73	0.81	750,933.44
ASP	396.25	56.93	0.23	4,686.46	110.66	31.11	0.23	2,763.34
Units	64.06	7.12	0.25	431.64	13.23	0.82	0.00	327.52
# of Drugs (sales data)	10				159			
Fraction Covered	0.90	0.92	0.71	0.99	0.82	0.85	0.00	1.00
Fraction Unrestricted	0.52	0.50	0.18	0.98	0.48	0.51	0.00	0.94
Fraction Preferred	0.28	0.15	0.03	0.93	0.14	0.10	0.00	0.87
# of Drugs (coverage data)	10				147			

Notes: Figures refer to the average value over the years 2007 through 2019. The sales figures come from SSR Health, and are based on public company financial filings (10-K and 10-Q). The coverage numbers are derived from MMIT data, by taking plan-level coverage information for each drug and taking a weighted average based on plan enrollment across all plans.

that have large markets.

5 The Impact of Biosimilar Entry on Originator Price, Volume, and Coverage

5.1 Average Impact of Biosimilar Entry

Table 2 displays estimates of Equation 5, estimated on our sample of biologic drugs. In Panel A, we find that biosimilar entry is associated with no response in WAC, but a statistically significant 0.133 decrease in log net price (which is equivalent to a 12.5% decline). [19] ASP also decreases, but by a smaller percentage, which mirrors the results that were obtained by Frank et al. (2021); however, our estimate is noisy. As we noted above, the discrepancy between net price and ASP estimates are likely due to the exclusion of 340B discounts from ASP. We also find some noisy evidence that biosimilar entry leads to a decrease in the volume of sales.

Panel B reports estimates of the effect of biosimilar entry on originators' coverage. We find that biosimilar entry leads to worse coverage for the originator, but that the

[19] The phenomenon of WAC, or list price, not falling after a biosimilar enters has been widely reported in the media and may have contributed to skepticism about biosimilars. For example, Atteberry et al. (2019) use the absence of response in WAC after the entry of a filgrastim biosimilar as evidence that biosimilars are ineffective.

Table 2: Impact of biosimilar entry on price and volume of biologics

Panel A: Price and Volume

	Log(WAC)	Log(Net)	Log(ASP)	Log(Units)
Biosimilar Entry Counter	0.0123	-0.133*	-0.0590	-0.0650
	(0.0465)	(0.0558)	(0.0568)	(0.128)
Drug FE	x	x	x	x
Year FE	x	x	x	
Age FE				x
N	1,324	1,324	765	1,320
Adjusted R^2	0.988	0.978	0.993	0.952

Panel B: Coverage

	Frac. Cov.	Frac. Unrestr.	Frac. Pref.
Biosimilar Entry Counter	-0.0423*	-0.0335**	-0.0602**
	(0.0191)	(0.0105)	(0.0158)
Drug FE	x	x	x
Year FE	x	x	x
N	971	971	971
Adjusted R^2	0.713	0.862	0.829

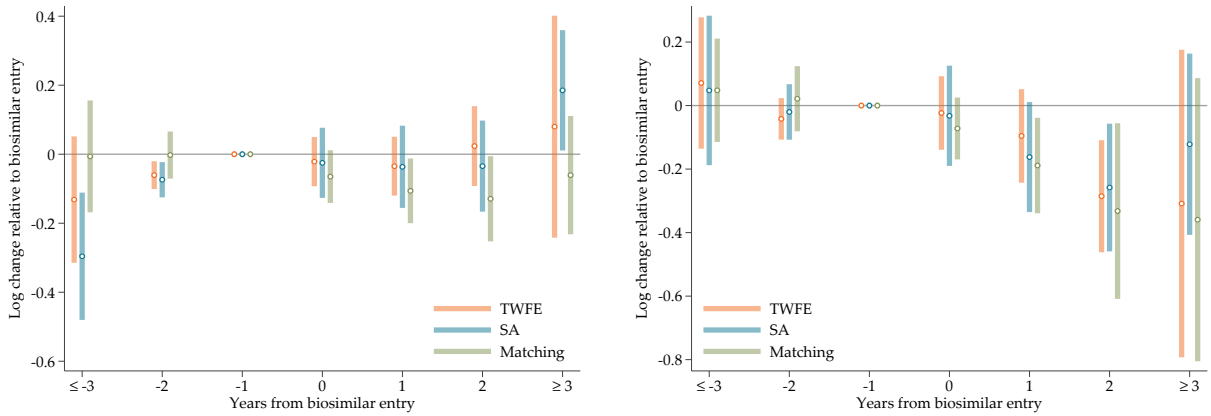
Notes: Estimates of Equation 5 using SSR Health and MMIT data. Standard errors are clustered at the drug level. *p $<$ 0.05, ** p $<$ 0.01. Four observations are dropped by the STATA command reghdfe in the log units analysis because they are singletons once the age effect is taken out.

effects are relatively small. The biggest change is to the preferred coverage rate, which falls by 6.0% points from a baseline of 28% points in the treated sample. Unrestricted coverage falls by 3.4pp from a baseline of 52%, and coverage rate falls by 4.2pp from a baseline of 90%.[20] All three estimates are statistically significant from zero.

Our results from more flexible specifications that address potential TWFE issues replicate the findings of the "naive" analysis (Figure 3). Across all three alternative estimation approaches we find: no change in WAC; consistent evidence of a large decline in net price; a smaller possibly non-significant decline in ASP; and noisy evidence of a decline in volume. All methods yield similar estimates (with a few minor discrepancies); and the estimates increase slightly in magnitude over time.

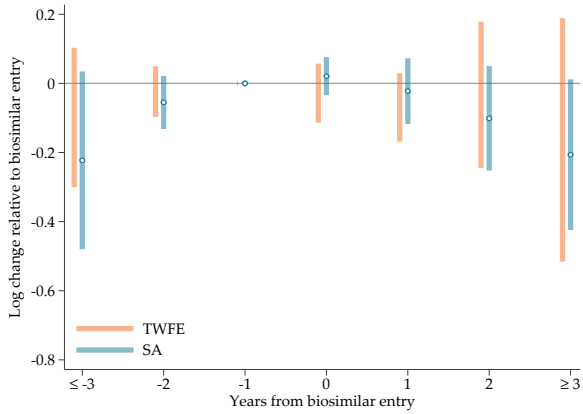
Finally, we note that all estimators suggest minimal pre-trends in the years leading

[20] We note that, because our coverage data begins in 2011, the results do not reflect the effect of early biosimilar entry.

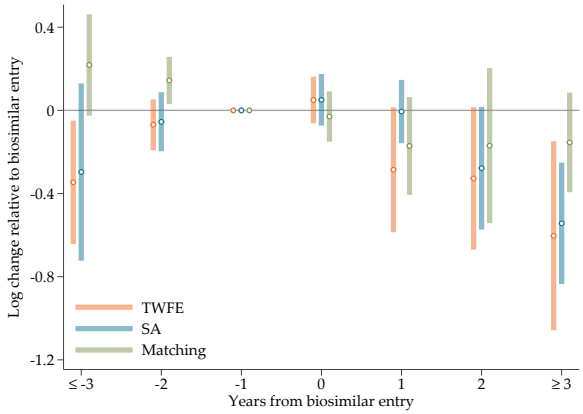


(a) Log(WAC)

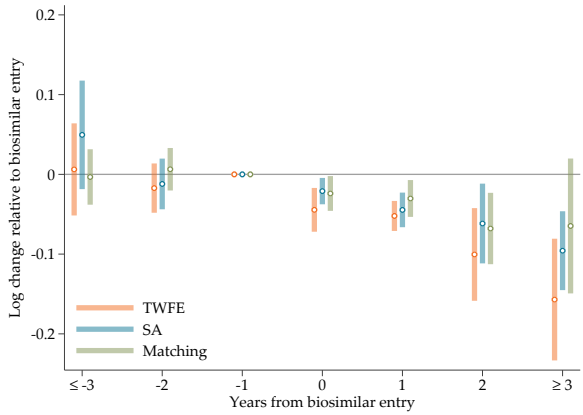
(b) Log(Net)



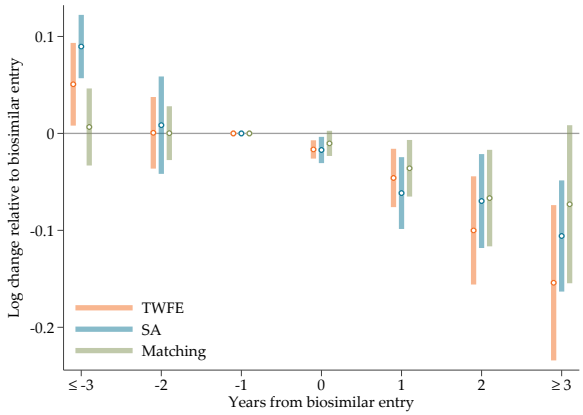
(c) Log(ASP)



(d) Log(Units) SA



(e) Fraction covered



(f) Fraction preferred

Figure 3: Time-Varying Coefficient Estimates (Price and Units)

Notes: Estimates of Equation 5 with time-varying coefficients using: (i) TWFE, (ii) Sun and Abraham (2020), and (iii) matching. The matching approach uses only three years before and after biosimilar entry. Bars reflect 95 percent confidence intervals with clustering at the drug level. There is no matching estimator for ASP due to an inability to identify a matched control group for most of the treated drugs.

up to entry. Pre-trends are potentially problematic in our setting because biosimilars are more likely to enter markets with higher and faster-growing sales. Our estimates can partially control for the level of sales with the use of drug fixed-effects, but cannot adequately control for future growth. Therefore, any negative effect of biosimilars on the originator biologic's volume and price will be attenuated by the growing path of the market for that molecule, which generates a downward bias in our estimated coefficients.

To confirm that our estimates are not driven by market trends, we conduct a placebo test that involves originator biologic responses to biosimilar approval. This test exploits the long lag between approval and entry that we noted in the background section. In particular, we include in the "treated" group biologics with approved biosimilars that had not yet launched by the end of our sample period. We find that approval has no negative effects on any of our outcomes of interest (see Appendix B.1).

5.2 Evidence of Heterogeneous Responses to Copycat Entry

Our main analysis shows that the average response of originator biologics to biosimilar entrants is to compete on price. We also find that by competing on price, originators are able to minimize loss of volume and coverage. In this section, we compare this response to the response of small molecule brands to generic entrants, and we examine more closely the average response of originator biologics so as to examine underlying heterogeneity.

Differential responses across generic and biosimilar entrants

Conventional wisdom suggests that small-molecule brands do not compete on price with generic entrants (Grabowski and Vernon, 1992; Berndt and Aitken, 2011; Grabowski et al., 2016). However, the available evidence uses relatively old data, and examines only list prices. We update this evidence with our data on: estimated net prices, changes in volume, and list prices after small-molecule brands experience loss of exclusivity.[21]

Our analysis comes with an important caveat: Estimated net prices rely on self reported data on revenues from drug manufacturers. Because most small-molecule brands lose most of their revenue after generic entry, it is very common for companies to stop reporting these numbers shortly after generics enter. In our data, revenue

[21]The SSR Health data report the date that a product loses exclusivity. Although this generally corresponds to the date of the first generic entry, we do not have actual data on generic entry or on the number of generic competitors.

Table 3: Summary statistics for treatment and control groups, generic entry

	Brands w/ Generics				Control Group			
	Mean	Median	Min	Max	Mean	Median	Min	Max
Yearly Invoice Sales (million USD)	563.38	203.93	0.02	8,933.02	428.97	102.70	0.00	16,973.48
Yearly Net Sales (million USD)	380.29	131.40	0.00	7,195.00	283.37	79.24	0.00	10,090.00
WAC	46.78	7.71	0.05	964.56	401.60	24.61	0.13	35,616.73
Estimated net price	34.48	5.14	0.05	2,486.89	551.43	16.53	0.02	128,244.57
ASP	32.74	4.32	0.04	539.55	44.84	31.54	0.03	36,643.61
Units	116.14	17.19	0.00	2,865.75	46.12	2.21	0.00	1,805.57
# of Drugs (sales data)	204				626			
Fraction Covered	0.86	0.86	0.46	1.00	0.85	0.86	0.01	1.00
Fraction Unrestricted	0.61	0.63	0.07	0.98	0.58	0.61	0.00	0.99
Fraction Preferred	0.23	0.15	0.01	0.89	0.20	0.13	0.00	0.95
# of Drugs (coverage data)	192				578			

Notes: Figures refer to the average value over the years 2007 through 2019. The sales figures come from SSR Health, and are based on public company financial filings (10-K and 10-Q). The coverage numbers are derived from MMIT data, by taking plan-level coverage information for each drug and taking a weighted average based on plan enrollment across all plans.

data are available for only 60% of products three years after generic entry. Given reporting incentives, we expect products that still report revenue to be relatively more successful, which may select for products that are more likely to attempt to compete on price with generic entrants.

Table 3 provides the summary statistics for the small-molecule data, and Table 4 replicates the results of Table 2 for small-molecule brands. Because our data does not include generic drugs, we include a simple indicator for being past the loss of exclusivity date.

The results are consistent with our model: Small-molecule brands experience only a small decline in net price and a dramatic loss of volume after loss of exclusivity. ASP falls dramatically, because, for small-molecule brands, ASP is calculated at the molecule level and includes the much-cheaper generic products. Coverage also declines by about twice as much as for originator biologics. Appendix B.2 presents the associated time-varying coefficients, which are consistent with the basic regression results.

Differential responses by type of biosimilar entrant and type of originator biologic

As a second test of our model, we try to identify variation across markets defined by biologic molecules so as to match the comparative statics in entrant quality and size of

Table 4: Impact of generic entry on price and volume of small-molecule brands

Panel A: Price and Volume

	Log(WAC)	Log(Net)	Log(ASP)	Log(Units)
Post-LOE Indicator	-0.0255	0.00182	-0.827**	-1.681**
	(0.0173)	(0.0249)	(0.0425)	(0.0503)
Drug FE	x	x	x	x
Year FE	x	x	x	
Age FE				x
N	6,311	6,311	1,323	6,309
Adjusted R^2	0.979	0.962	0.981	0.922

Panel B: Coverage

	Frac. Cov.	Frac. Unrestr.	Frac. Pref.
Biosimilar Entry Counter	-0.0955**	-0.0631**	-0.175**
	(0.00467)	(0.00576)	(0.00636)
Drug FE	x	x	x
Year FE	x	x	x
N	4,529	4,529	4,529
Adjusted R^2	0.638	0.839	0.801

Notes: Estimates of Equation 5 using SSR Health and MMIT data. Standard errors are clustered at the drug level. *p $<$ 0.05, ** p $<$ 0.01. Two observations are dropped by the STATA command reghdfe in the log units analysis because they are singletons once the age effect is taken out.

the loyal market that were presented in Figure 1.

Entrant quality. To find variation in entrant quality, we exploit differences in the approval mechanisms that are used by biosimilar entrants that result in some biosimilars that come to market with a larger body of clinical evidence.

Of all of the biologics that experienced biosimilar entry, six competed against biosimilar products that were approved through the abbreviated channel that was introduced by the BPCI Act; but four competed against products that used more traditional avenues for approval: Betaseron, Lantus, Humalog, and Neupogen.[22] Our assumption is that patients and providers might perceive these four products to be closer in quality to their biosimilars, given the aforementioned evidence in Alsan et al. (2024).

[22]Neupogen competed initially against a biosimilar approved through a regular Biologic License Application (Granix), but it also later competed against additional biosimilars approved through the abbreviated procedure. We account for this in our analysis.

We note that the comparison is not just a temporal one. Although the abbreviated entrants necessarily come after the BPCI Act, the other entrants are more idiosyncratic. As noted earlier, insulins were not considered biologics until 2020, and were therefore excluded from the BPCI Act. The two insulin biosimilars entered during the same time period as the other abbreviated entrants in our sample.

To test the hypothesis we run another set of regressions that use time-varying coefficients that distinguish between originator biologics that competed against biosimilars approved through the abbreviated procedure, and originator biologics that competed against biosimilars that were approved through other procedures. Formally, we allow for an additional effect for originators' responses to biosimilars that entered through non-abbreviated pathways:

$$Y_{it} = \alpha_i + \delta_t + \beta_1 \times EventCounter_{it} + \beta_2 \times EventCounter_{it} \times Nonabbr_i + \varepsilon_{it} \quad (6)$$

Table 5 shows price, volume, and coverage trends for biologics in the two groups. Consistent with the predictions of the model, we find evidence of different responses by originators that faced drugs that were approved through non-abbreviated channels. The baseline effect, which captures the response to abbreviated entry, shows negative net price and ASP responses, with noisy estimates for units and coverage. The additional effect of non-abbreviated entry is highly positive for ASP and strongly negative for coverage, which is consistent with originators' yielding volume. These results are suggestive of incumbents' yielding to copycats that enter through traditional channels—at least relative to how they respond to copycats that enter through abbreviated channels. However, we note that the net price and units differences are small in magnitude and statistically insignificant, whereas our model would predict positive and negative interaction estimates, respectively.

Appendix B.3 reports time-varying coefficients and results that are based on the Sun and Abraham (2020) correction. The estimates support the core findings on ASP and coverage.

Size of the loyal segment. To test whether the size of the loyal segment matters for originators' pricing strategy, we split originators into two groups by whether they were experiencing volume growth in the years that preceded the entry of their first biosimilar competitor (year $t-1$ versus year $t-2$) versus not. This empirical strategy is based on the idea that demand for drugs exhibits history-dependence (Feng, 2024): The existing users of a drug are much more likely to continue using it than are new

Table 5: Responses to Abbreviated Versus Non-Abbreviated Entry

	Log(Net)	Log(ASP)	Log(Units)	Covered
Response to Entry	-0.115+	-0.180**	-0.0703	-0.0244
	(0.0623)	(0.0493)	(0.162)	(0.0171)
Response to Entry	-0.0748	0.555**	0.0225	-0.101**
×Non-abbreviated Launch	(0.215)	(0.155)	(0.306)	(0.0339)
Drug FE	x	x	x	x
Year FE	x	x		x
Age FE			x	
N	1,324	765	1,320	971
Adjusted R^2	0.940	0.995	0.931	0.769

Notes: Estimates of Equation 6 using SSR Health and MMIT data. Standard errors are clustered at the drug level. + $p < 0.10$ *$p < 0.05$, ** $p < 0.01$. Four observations are dropped by the STATA command reghdfe in the log units analysis because they are singletons once the age effect is taken out.

patients. Drugs that experience volume growth are more likely to have new patients who are starting treatment. New patients are less likely to be loyal, so drugs that experience volume growth are more likely to have a small loyal segment. We note that, unfortunately, defining treatment based on volume growth introduces selection in the treatment (and control) groups, which generates bias that cannot easily be controlled for. We discuss how this affects our estimates below.[23]

Formally, we estimate the following specification

$$Y_{it} = \alpha_i + \delta_t + \beta_1 \times \mathrm{EventCounter}_{it} + \beta_2 \times \mathrm{EventCounter}_{it} \times \mathrm{UnitGrowth}_i + \varepsilon_{it} \quad (7)$$

where $\mathrm{UnitGrowth}_i$ is an indicator for whether the originator drug had positive volume growth in the year before entry.

Table 6 presents the estimates: Consistent with our model's predictions, we find that originators with units growth seem to compete on price and maintain units sold, although the difference for both price measures is statistically insignificant. We also find that the average coverage response is negative, but the high-growth originators fully offset the decrease. Although the units response difference is large and in the expected direction, the estimates are partly capturing pre-trends (given the way that we split the sample). We provide time-varying estimates—which generally support the main findings—in Appendix B.3. In particular, the price response difference is statisti-

[23]The ideal test would use claims data to measure the rate of new patients relative to existing patients. Unfortunately, we do not have access to claims data for this project.

Table 6: High vs. Low Market Size Growth Drugs

	Log(Net)	Log(ASP)	Log(Units)	Covered
Response to Entry	-0.129	0.0462	-0.149	-0.0948**
	(0.123)	(0.156)	(0.159)	(0.0242)
Response to Entry	-0.164	-0.248	0.597+	0.108**
×Positive Unit Growth	(0.173)	(0.181)	(0.311)	(0.0299)
Drug FE	x	x	x	x
Year FE	x	x		x
Age FE			x	
N	1,324	765	1,320	971
Adjusted R^2	0.978	0.993	0.952	0.715

Notes: Estimates of Equation 7 using SSR Health and MMIT data. Standard errors are clustered at the drug level. + $p < 0.10$ *$p < 0.05$, ** $p < 0.01$. Four observations are dropped by the STATA command reghdfe in the log units analysis because they are singletons once the age effect is taken out.

cally significant in later periods. In addition, the units pre-trend differences are much smaller than the difference in the trends that are observed for the post-entry coefficients: very negative for low-growth incumbents, and flat for high-growth incumbents.

We conclude by cautioning that both sets of heterogeneity results cannot be interpreted as more than suggestive evidence, given: (i) the small sample sizes; and (ii) the lack of long-term data (especially for the abbreviated pathway products). As more biosimilars are approved, more evidence should be gathered to confirm this initial analysis.

6 Conclusion and Policy Implications

In this article, we examine how manufacturers of biologic drugs react to the entry of biosimilar competitors. We find that the average reaction has been to compete on price with these new entrants. By cutting prices, originator biologics limit losses in volume and coverage; in turn, this contributes to the slow uptake of biosimilars that has been highlighted by many contemporaneous reports (see, e.g., IQVIA Institute for Human Data Science, 2020). This response stands in contrast to the behavior of small-molecule brand drugs, which our evidence shows rarely compete on price with generic drugs, and instead accept large losses in volume and coverage.

We hypothesize that the divergence in these responses may be driven by strategic considerations when a firm faces a market where a fraction of consumers are loyal

and can be counted on to provide a reliable (albeit smaller) stream of revenue even at higher prices. Our model highlights three key factors that influence an incumbent's choice to compete or not compete on prices: (i) the number of entrants; (ii) their quality; and (iii) the size of the loyal segment. In addition to comparing originator biologic and small-molecule brands, we also provide suggestive evidence that is consistent with the model's predictions by exploiting variation within the small number of biosimilar entrants that were approved before 2020.

Our model provides a different perspective on the current and future outlook of markets for biologics and biosimilars. In terms of current outlook, we show that even when biosimilars have faced difficulty in gaining market share, this does not necessarily imply that competition in the biosimilars market has failed (as suggested, e.g., in Atteberry et al., 2019), because they have induced meaningful net price reductions from originators.

In terms of future outlook, we highlight how the two main challenges that face biosimilars—lingering uncertainty about their effectiveness and quality and high development costs that limit the number of entrants—interact to create an environment where originator biologics can maintain a dominant position by competing on prices. Interestingly, this phenomenon matches early trends in the generic markets, when generics were occasionally slow to gain market share (Berndt and Aitken, 2011).[24] One interpretation of our results is that the same patterns are present for biosimilars, which may benefit from physicians' and patients' becoming more familiar with biosimilars over time, even absent further policy. Stern et al. 2021 provides suggestive evidence that is consistent with this idea.

Our results are also relevant to the direction of innovation in the pharmaceutical industry. Branstetter et al. (2022) show that the presence of generics can influence manufacturers to invest more in developing biologics rather than small molecule drugs. The evolution of competition between biosimilars and originator biologics will likely alter the balance of incentives between the two types of drug products.

Finally, our work can inform the understanding of how different types of policies affect competition between originators and biosimilars. Recent policies that boost the perception of biosimilars or monetary incentives associated with biosimilar prescribing by physicians will likely shrink the effective quality gap and increase the chances that originators acquiesce. Reducing entry costs through patent policy would likely

[24] Some theoretical and empirical evidence suggests that branded drugs originally set lower prices so as to compete with generics on volume, and, by doing so, limit consumer learning (Ching, 2010a,b).

increase the number of competitors, which would have similar effects.

Our model makes more ambiguous predictions about the FDA's new "interchangeability" designation. On the one hand, interchangeability could reduce the size of the loyal segment, which would increase the chances that the originator competes. On the other hand, interchangeable biosimilars could also be perceived as being higher quality (and thus more similar to a generic competitor), which could increase the chances of acquiescing.

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Appendix

A Data

We describe the coverage data we obtained from MMIT Analytics, and explain how we constructed the coverage variables from that data. For a description of the SSR Health data, see instead Online Appendix A to Feng et al. (2023), particularly Section A.1.

A.1 List of biologic and biosimilar products

Table A1 reports information on biosimilar products, including the reference biologic, approval date, and launch date.

A.2 Coverage Data

MMIT Analytics collects monthly data on coverage from health plans. This data includes information about the coverage tier of a specific drug, as well as the plan sponsor, and the number of lives it covers.

We have data on over 800 drugs—including all biosimilars and originator biologics—from January of 2011 until December of 2019. Throughout this period, MMIT's coverage grew from around 100 million lives to over 300 million lives, representing almost the entirety of the insured U.S. population. The data includes health plans across all possible channels: commercial plans, Medicare, Medicaid (both State-sponsored and Managed Medicaid), as well as the ACA health exchanges (Figure A1).[25]

A.3 Construction of coverage variables

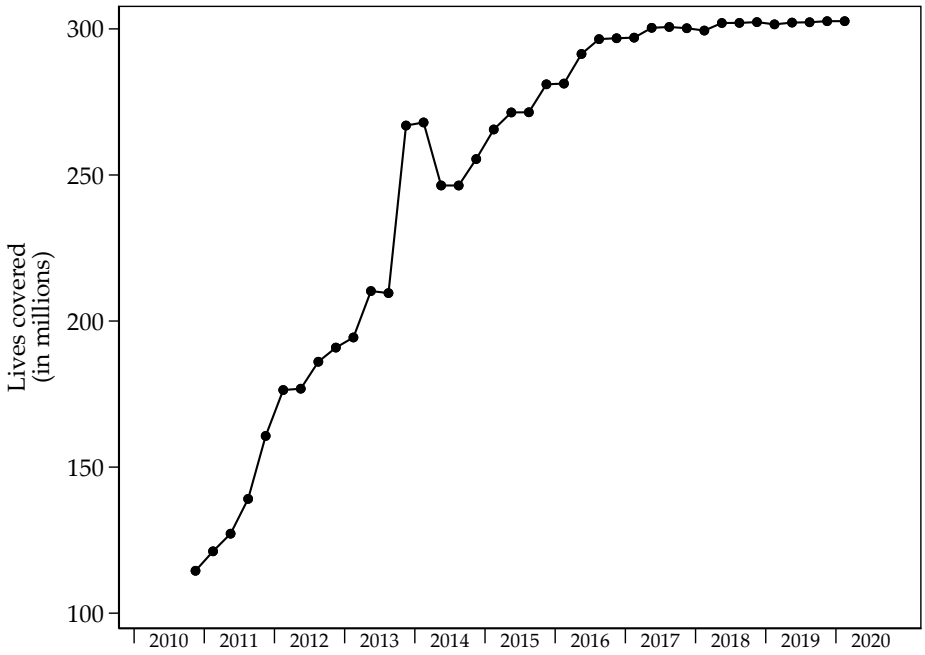
MMIT Analytics processes the tier information for all formularies to create a harmonized "universal status" variable that makes coverage comparable across plans and years. Moreover, each drug is flagged for three possible non-monetary restrictions: Prior Authorization (PA), Step Therapy (ST), and Quantity Limit (QL). Of these three,

[25]The spike in 2014Q1 and 2014Q2 is caused by double-counting of lives in certain (unidentifiable) commercial plans. The issue does not affect other quarters.

Table A1: List of biologic and biosimilar products approved before June 2020

Drug	Molecule	Product	Approval Date	Launch Date
Abrilada	adalimumab	Humira	11/1/2019	11/1/2023
Amjevita			9/23/2016	1/31/2023
Cyltezo			8/25/2017	7/1/2023
Hadlima			7/1/2019	6/30/2023
Hyrimoz			10/1/2018	9/1/2023
Mvasi	bevacizumab	Avastin	9/14/2017	7/18/2019
Zirabev			6/1/2019	12/31/2019
Retacrit	epoetin alfa	epogen	5/1/2018	11/12/2018
Erelzi	etanercept	enbrel	8/30/2016	
Eticovo			4/26/2019	
Granix	filgrastim	neupogen	8/29/2012	11/11/2013
Nivestym			7/1/2018	10/1/2018
Zarxio			3/6/2015	9/3/2015
Avsola	infliximab	remicade	12/1/2019	7/1/2020
Inflectra			4/5/2016	11/30/2016
Ixifi			12/13/2017	
Renflexis			4/21/2017	7/24/2017
Extavia	interferon beta-1B	betaseron	8/14/2009	8/14/2009
Fulphila	pegfilgrastim	neulasta	6/1/2018	7/30/2018
Udenyca			11/1/2018	1/3/2019
Ziextenzo			11/1/2019	11/15/2019
Ruxience	rituximab	rituxan	7/1/2019	1/23/2020
Truxima			11/1/2018	11/11/2019
Herzuma	trastuzumab	herceptin	12/1/2018	3/1/2020
Kanjinti			6/1/2019	7/18/2019
Ogivri			12/1/2017	12/2/2019
Ontruzant			1/1/2019	4/15/2020
Trazimera			3/1/2019	2/15/2020
Basaglar	insulin glargine	lantus	8/1/2014	12/15/2016
Admelog	Insulin lispro	humalog	12/1/2017	4/1/2018

Figure A1: MMIT lives covered



only the first two represent meaningful obstacles to the prescription of a drug.[26] We use these two variables to create indicators for three levels of coverage: any coverage, unrestricted coverage, and preferred coverage. Table A2 shows how we map the universal status variable to our indicators for any coverage and preferred coverage. Additionally, we consider all drugs that are flagged for PA or ST as "restricted", which in turn defines our unrestricted variable.[27]

The dependent variables in our coverage regressions are weighted averages (using number of lives covered as weights) of these three indicators for each drug and year, across all health plans. Another way to interpret them is as the percentage of lives with a certain level of coverage for a given drug.

[26] Quantity limit refers to the maximum number of doses that can be prescribed, and is used to prevent abuse of medications like opioids—e.g Vicodin or Oxycontin —or amphetamines—e.g. Adderall or Ritalin.

[27] In the rare cases when a "preferred" drug is flagged for PA or ST, we set the preferred coverage indicator to 0. Missing values (also rare) are considered not covered.

Table A2: Drug tiers assignment

Universal Status	Any coverage	Preferred coverage
Not Covered Drugs Tier	0	0
Unknown Coverage	0	0
Medical	1	0
Injectable Drugs Tier	1	0
Non-Preferred Specialty Drugs Tier	1	0
Specialty Drugs Tier	1	0
Covered Drugs Tier	1	0
Non-Preferred Brand Drugs Tier	1	0
Non-Preferred Generics and Non-Preferred Brands	1	0
Preferred Specialty Drugs Tier	1	1
Generic Drugs Tier	1	1
Non-Preferred Generic Drugs Tier	1	1
Non-Preferred Generics and Preferred Brands	1	1
Preferred Brand Drugs Tier	1	1
Preferred Generic Drugs Tier	1	1
Preferred Generics and Preferred Brands	1	1
Value Brand Drugs Tier	1	1
Value Generic Drugs Tier	1	1
Zero Co-pay Tier	1	1

Table A3: Approval placebo test results

	Log(WAC)	Log(Net)	Log(ASP)	Log(Units)	Frac. Cov.
Biosimilar Entry Counter	-0.112*	-0.263**	-0.0764	-0.252*	-0.0484*
	(0.0470)	(0.0563)	(0.0608)	(0.125)	(0.0197)
Biosimilar Approval Counter	0.121**	0.127**	0.0166	0.188**	0.00607
	(0.0387)	(0.0344)	(0.0399)	(0.0416)	(0.00630)
Drug FE	x	x	x	x	x
Year FE	x	x	x		x
Age FE				x	
N	1,324	1,324	765	1,320	971
Adjusted R^2	0.988	0.978	0.993	0.953	0.713

Notes: Standard errors are clustered at the drug level. *p $<$ 0.05, ** p $<$ 0.01

B Robustness Checks and Additional Results

B.1 Response to Biosimilar Approval

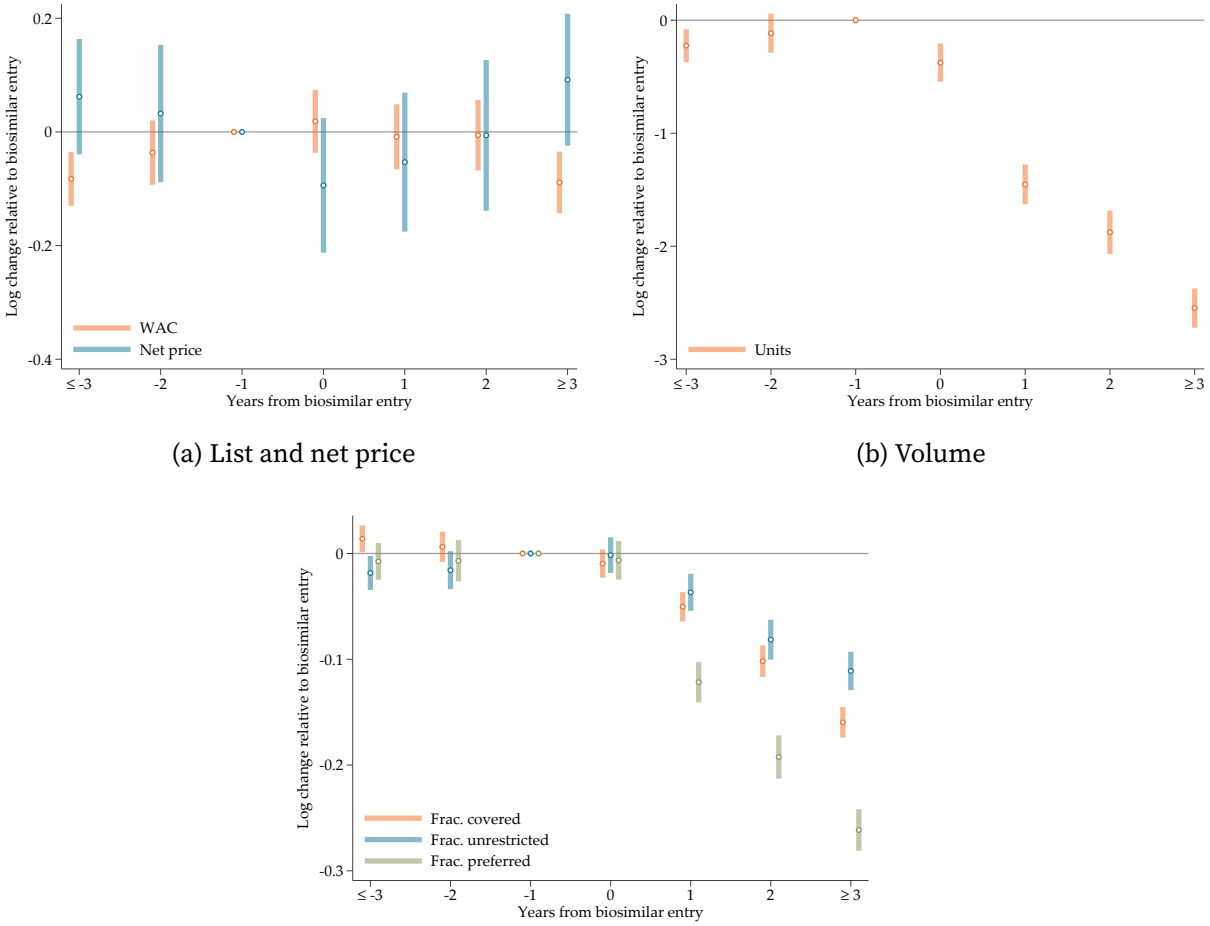
As noted in the main text, there are often significant delays from approval to launch of biosimilars. In Table A3, we include an indicator for whether the biosimilar has been approved, in order to test whether incumbents respond to the approval of biosimilars. Focusing on net price, we find an increase of 10 percent in net price after approval, followed by a decrease of 28 percent after biosimilar entry. Potentially, this could reflect some anticipation by the incumbent.

B.2 Response to generic entry

Here, we provide the time-varying coefficient estimates related to the estimates presented in Table 4 of the main text. The graphs confirm that there are no significant pre-trends leading up to LOE in any of our outcomes of interest (WAC and volume exhibit some sign of increasing pre-trends, but those effects generate bias that goes against our results).

B.3 Additional Heterogeneity Results

This section contains additional results related to the heterogeneity analysis, primarily providing time-varying estimates related to the results presented in the main text.



(a) List and net price

(b) Volume

(c) Coverage

Figure A2: Time-Varying Coefficient Estimates for Generic Entry

Notes: Time-varying coefficients corresponding to the basic estimates presented in Table 4. Confidence bars reflect 95 percent confidence intervals with clustering at the drug level.

First, we provide results comparing originators' responses to abbreviated and non-abbreviated entrants, corresponding to the estimates in Table 5. We report the associated p-values for testing whether the abbreviated and non-abbreviated responses are equal in each relative year in Table A4.

The net price response differences are imprecisely estimated, but the results do show a precisely estimated decreasing response to abbreviated entry, whereas the response to non-abbreviated entry is flat and very imprecisely estimated. There are no clear pre-trend differences across the two groups. The ASP responses are statistically significantly different in most years in both the TWFE and SA approaches, with abbreviated entrants eliciting a decline in incumbents' ASP and non-abbreviated eliciting a

Table A4: P-value of F-test

	Log Net		Log ASP		Log Units		Frac. Covered	
Period	TWFE	SA	TWFE	SA	TWFE	SA	TWFE	SA
<-2	**0.044**	0.819	**0.000**	**0.000**	0.144	**0.068**	**0.036**	0.888
-2	0.487	0.911	**0.048**	0.102	0.749	0.975	0.879	0.242
0	0.683	0.613	**0.049**	0.275	0.943	0.782	0.269	0.284
1	0.755	0.526	**0.010**	**0.057**	0.115	0.310	**0.054**	**0.001**
2	0.256	0.407	**0.033**	**0.047**	0.349	0.518	0.297	0.658
>2	0.151	**0.007**	0.382	**0.028**	0.325	**0.091**	0.530	0.160

Notes: Reports the p-values of the F-test of whether the coefficients in period t for abbreviated and non-abbreviated entry events are equal, based on the TWFE and SA estimates in Figures A3 and A4. Bold values indicate statistical significance at the 10 percent level.

flat response. However, there are significant pre-trends.

Volume estimates are imprecise for both event types, and the difference is also imprecisely estimated. Finally, we see differences in the coverage responses in some periods, with incumbents losing more coverage when facing a non-abbreviated entrant. All of these findings are broadly consistent with the average estimates shown in Table 5 of the main text.

Finally, we discuss the time-varying estimates related to low and high growth incumbents. Figures A5 and A6 present time-varying estimates corresponding to the simple estimates presented in Table 6. Table A5 presents the p-values associated with testing whether the response coefficients in each period are equal across high and low growth incumbents.

In terms of price, we see more negative responses for the high-growth group versus the low-growth group, consistent with the predictions of the model. However, the difference is generally imprecisely estimated, with the exception of the long-term net price estimate under the SA correction and the long-term ASP estimate under both methods. Throughout, we see minimal pre-trend differences across the two groups. In general, the results reflect the coefficients in Table 6: a negative but imprecisely estimated additional effect for high-growth incumbents.

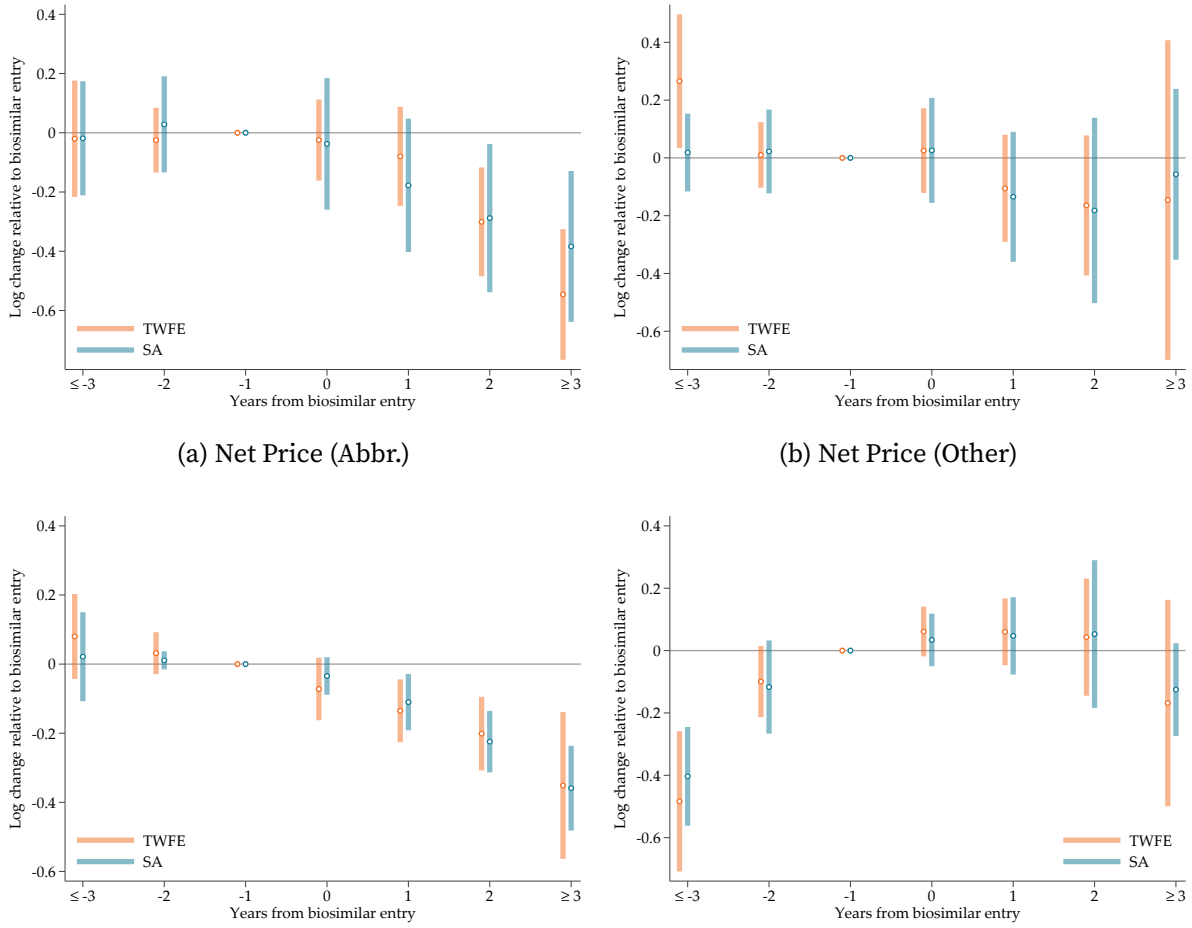
In terms of volume and coverage, we see clearer differences, consistent with Table 6. High-growth incumbents generally maintain volume, whereas low-growth incumbents lose volume, especially in the long-run. As noted in the main text, the classification approach necessarily means that there are differential pre-trends. In terms of coverage, we see that high-growth incumbents generally maintain coverage, whereas

Table A5: P-value of F-test

	Log Net		Log ASP		Log Units		Frac. Covered	
Period	TWFE	SA	TWFE	SA	TWFE	SA	TWFE	SA
<-2	0.543	0.150	0.211	**0.019**	0.191	0.366	**0.003**	**0.000**
-2	0.454	0.212	0.661	**0.051**	0.824	0.148	**0.001**	**0.004**
0	0.960	0.827	0.577	0.354	0.742	**0.067**	0.918	0.479
1	0.919	0.888	0.536	0.948	0.854	**0.003**	0.819	0.494
2	0.438	0.644	0.214	0.549	**0.000**	**0.000**	**0.001**	**0.075**
>2	0.236	**0.004**	**0.023**	**0.000**	**0.000**	**0.000**	**0.001**	0.703

Notes: Reports the p-values of the F-test of whether the coefficients in period t for abbreviated and non-abbreviated entry events are equal, based on the TWFE and SA estimates in Figures A5 and A6. Bold values indicate statistical significance at the 10 percent level.

low-growth incumbents exhibit large losses in coverage.



(a) Net Price (Abbr.)

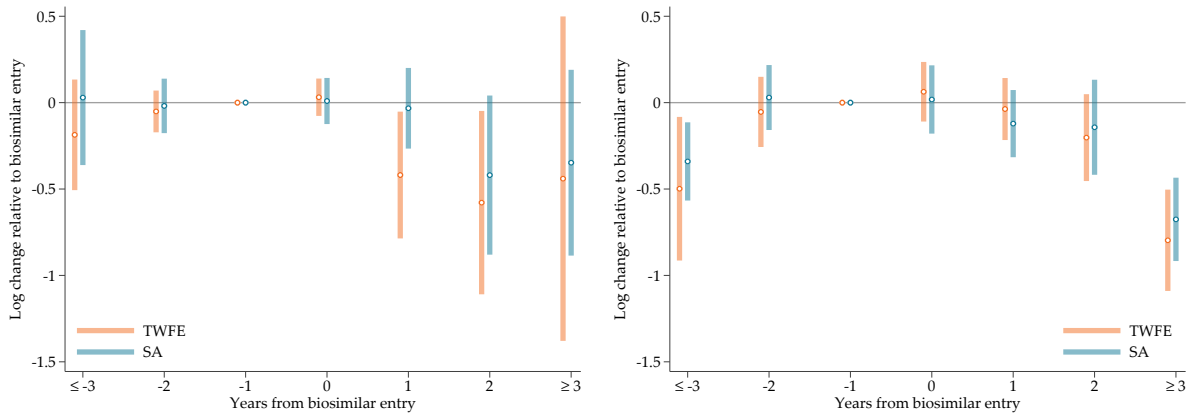
(b) Net Price (Other)

(c) Log ASP (Abbr.)

(d) Log ASP (Other)

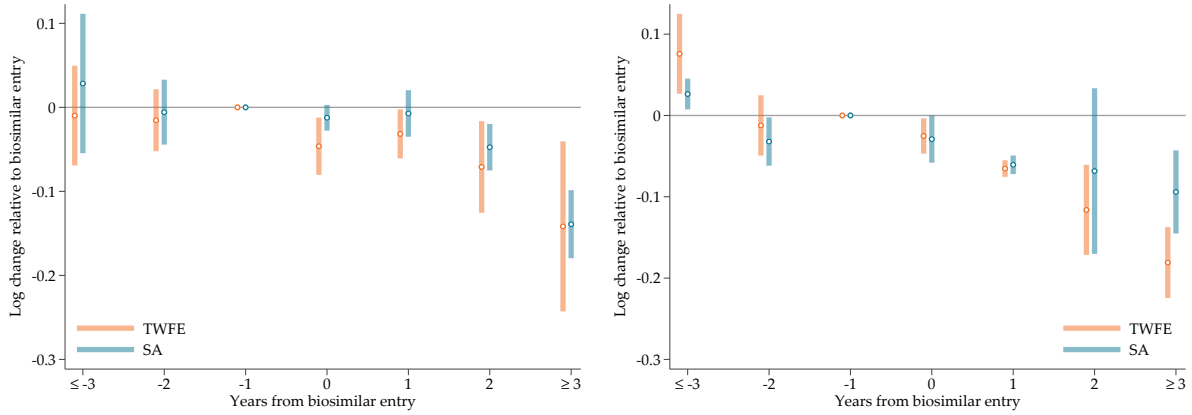
Figure A3: Comparison of originator biologics' price responses: abbreviated vs. non-abbreviated approval

Notes: Estimates of time-varying coefficients using TWFE and the Sun and Abraham (2020) correction (SA). "Abbr." refers to responses to biosimilars that entered through the abbreviated pathway. "Other" refers to responses to biosimilars that entered through non-abbreviated pathways. Standard errors are clustered at the drug level. Confidence bars reflect 95 percent confidence intervals.



(a) Volume (Abbr.)

(b) Volume (Other)

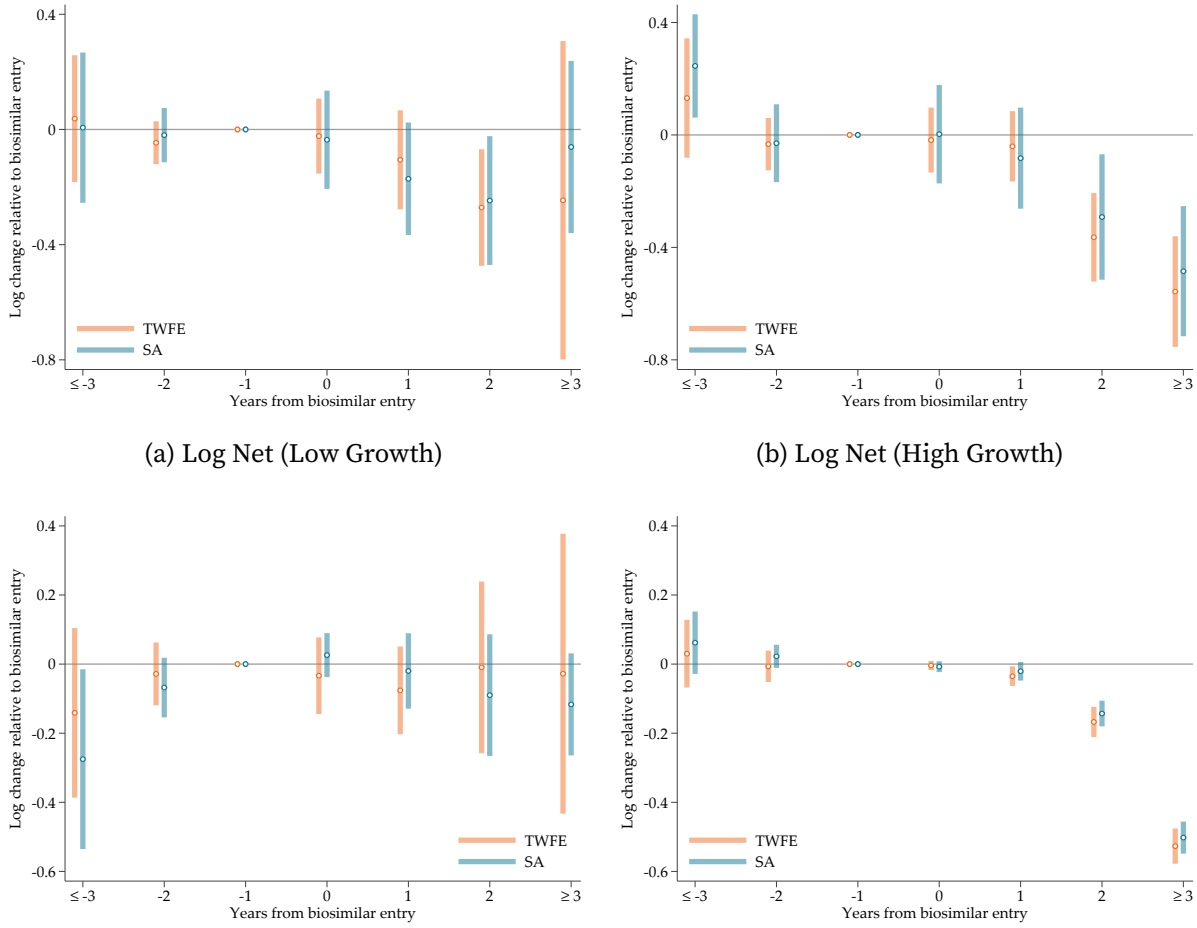


(c) Fraction Covered (Abbr.)

(d) Fraction Covered (Other)

Figure A4: Comparison of originator biologics' volume and coverage responses: abbreviated vs. non-abbreviated approval

Notes: Estimates of time-varying coefficients using TWFE and the Sun and Abraham (2020) correction (SA). "Abbr." refers to responses to biosimilars that entered through the abbreviated pathway. "Other" refers to responses to biosimilars that entered through non-abbreviated pathways. Standard errors are clustered at the drug level. Confidence bars reflect 95 percent confidence intervals.



(a) Log Net (Low Growth)

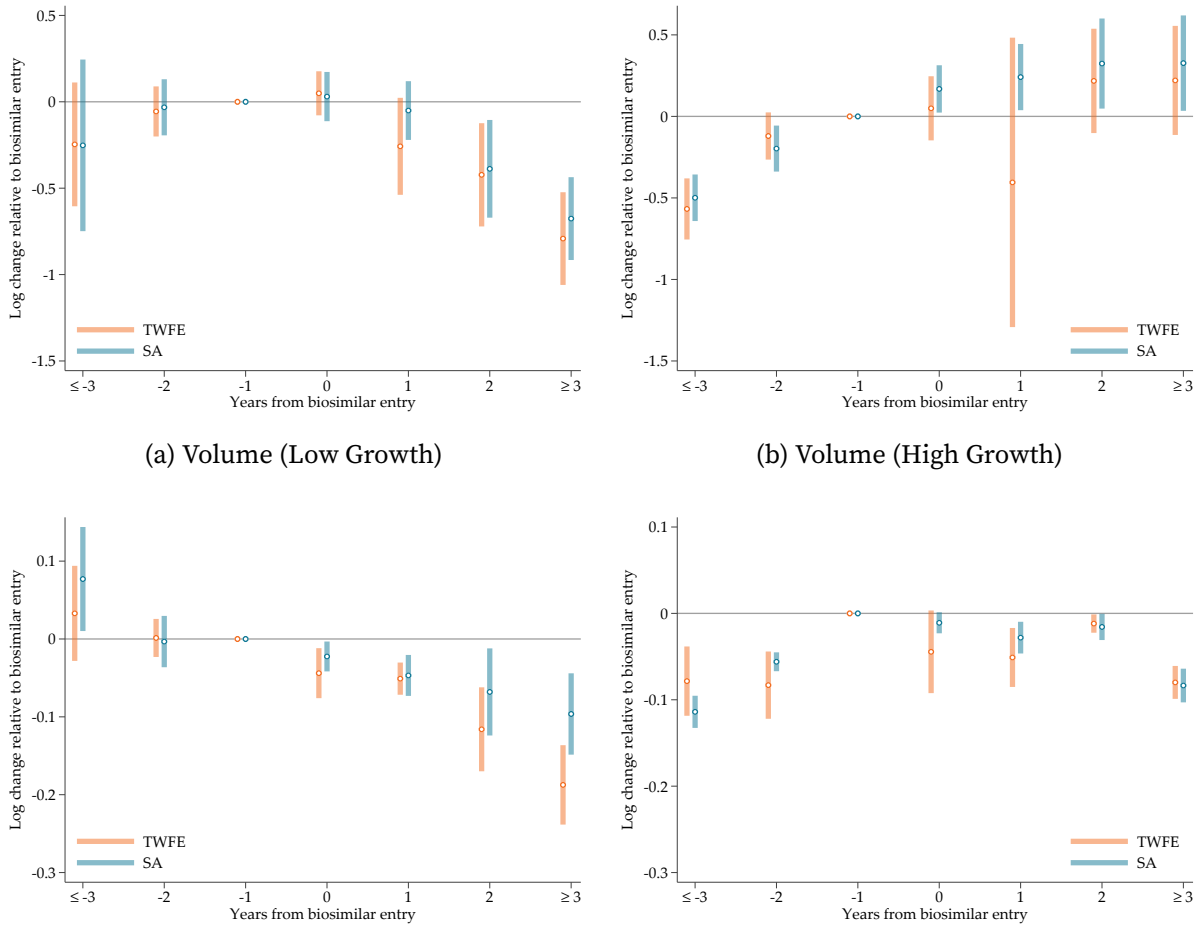
(b) Log Net (High Growth)

(c) Log ASP (Low Growth)

(d) Log ASP (High Growth)

Figure A5: Comparison of originator biologics' price responses: low vs. high volume growth

Notes: Estimates of time-varying coefficients using a basic TWFE approach. "Abbr." refers to responses to biosimilars that entered through the abbreviated pathway. "Other" refers to responses to biosimilars that entered through non-abbreviated pathways. Standard errors are clustered at the drug level. Confidence intervals reflect 95 percent confidence intervals.



(a) Volume (Low Growth)

(b) Volume (High Growth)

(c) Fraction Covered (Low Growth)

(d) Fraction Covered (High Growth)

Figure A6: Comparison of originator biologics' volume and coverage responses: low vs. high volume growth