Additional Results

for

Resilience of Global Supply Chains and Generic Drug Shortages

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S1. Institutional Background

S1.1. Purchasing Organizations and Shared Capacity

Hospitals can belong to more than one GPO while concentrating most purchases through a principal organization. Burns and Lee (2008) report that 41 percent of the hospital providers surveyed had multiple GPO affiliations, with secondary organizations used for particular purchases. Sole sourcing for a particular product can therefore coexist with multiple purchasing relationships across a hospital's portfolio. Online Appendix D.1 describes how GPOs negotiate contracts with labelers.

Decentralized purchasing can also weaken incentives to finance reliable production. Several buyers may depend on the same supplier or production line. A buyer's payment for redundancy can then benefit other purchasers, while that buyer bears the cost of the payment. Similarly, losing one contract need not remove a supplier from the national market if it can sell through another purchasing organization. These are possible common-agency mechanisms, not separate effects identified by the aggregate sales data. The evidence on suppliers' subsequent national presence and market shares is reported in Online Appendix D.4.

S1.2. Generic Approval and Market Participation

The Hatch–Waxman Amendments established an abbreviated approval pathway for generic versions of existing drugs. An ANDA relies on the FDA's prior assessment of the reference drug's safety and efficacy, while requiring equivalence and compliance with manufacturing standards. FDA therapeutic-equivalence ratings support substitution among approved products (FDA, 2016).

Approval, listing, and production are distinct. A product can hold marketing approval without recording positive sales, and a registered establishment need not produce every drug to which it is linked in every year. The NDC Directory and Orange Book identify products and approvals; sales records identify active market participation; establishment and shipment records locate production. The model conditions on the set of suppliers in a market rather than modeling the application process.

Entry also carries regulatory costs. A labeler needs an approved ANDA, whose estimated cost is \$1-\$5 million (Berndt and Aitken, 2011), and since 2012 generic manufacturers pay user fees under the Generic Drug User Fee Amendments (GDUFA): in fiscal year 2019, \$178,799 for each new ANDA, plus annual fees for each manufacturing facility and each ANDA holder.

Previous work documents substantial price declines following generic entry, including for physician-administered injectable drugs (Conti and Berndt, 2016; Conrad and Lutter, 2019). This price competition coexists with the costs of maintaining specialized production facilities and spare capacity. Obtaining marketing approval, competing for procurement contracts, and investing in manufacturing capacity are therefore distinct decisions.

S1.3. FDA Inspections and Manufacturing Oversight

The FDA classifies inspection findings as No Action Indicated (NAI), Voluntary Action Indicated (VAI), or Official Action Indicated (OAI). NAI indicates that no objectionable conditions warranting action were found. VAI records objectionable conditions for which the agency is not recommending administrative or regulatory action. OAI indicates that such action is recommended (FDA, 2026). Warning letters document findings requiring correction, and regulatory responses can include import alerts, injunctions, and seizures.

The inspection frequencies reported in Section 2 are calculated from the FDA records linked to the plant panel over 2004–2019. They summarize observed inspection exposure across production locations, rather than a legally required schedule. Domestic and foreign plants face the same manufacturing standards; overseas inspections involve additional travel and access constraints (FDA, 2019b). Inspection classifications and warning letters record findings conditional on inspection. Comparisons of their incidence must therefore account for the number of plants inspected and the selection of sites for inspection.

S1.4. Collusion and Contestability in Generic Injectable Drug Markets

Even though generic drug markets are no longer protected by patents, many may not be large enough to attract the number of competitors needed to achieve marginal cost pricing (Berndt, Conti, and Murphy, 2017). Some suppliers have deviated from low prices: between 2010 and 2015, about a fifth of established generic drugs had at least one price increase of 100% or more (GAO, 2016). The generic drugs under scrutiny for collusive agreements, however, are rarely the sterile injectables that go short. Cuddy (2020) uses firm and supply-contract identities from the District Court case files of a 2019 indictment, and estimates that among the hundreds of generic drugs accused of collusive conduct, no more than two or three are injectable drugs. Collusion concerns mostly newer and more profitable generic drugs.

Generic injectable markets are instead highly contestable. Since the Generic Drug User Fee Amendments of 2012, every plant that manufactures generic drugs for the U.S. market must identify itself to the FDA each year and pay an annual fee. An approved ANDA, however, does not lapse when its holder stops producing, so that a labeler that exits a market keeps the option to re-enter it. In a contestable market, prices may look like those of a highly competitive market even when few firms produce, because the threat of (re)entry disciplines incumbents.

Low profit margins of generic drugs may also be related to contracting practices. In its *Drug Shortages Report* (FDA, 2019a), the FDA relays stakeholders' view that contracts generally do not guarantee that a certain volume will be purchased at an agreed price, and leave manufacturers exposed to competitors willing to undercut them to gain market share, even at unsustainable prices; generic sponsors may then lack the resources to invest in manufacturing quality or redundant capacity. It is also hard to purchase for quality upstream. Many U.S. labelers are foreign-owned companies,[1] and buyers do not

[1] ANDA holders manufacture generic drugs in very different ways: in-house for both the active ingredient and the finished dosage form, in-house for the finished form with an outsourced active ingredient, or fully outsourced, while some firms only

generally observe which facilities produce a particular drug or their histories of supply disruptions. The FDA makes warning letters public, but the names of drugs are redacted, and no rule requires disclosing which company or plant actually makes a product.

S2. Descriptive Facts on Injectable Drug Markets

S2.1. Drug Age

Figure S2.1 reports the age distribution of injectable drugs in the Orange Book data. Age is measured from the first recorded marketing application for a drug. Many injectable drugs have long approval histories. Online Appendix D.2 reports the proportion of drugs ever listed in shortage by category and the distribution of reported shortage causes.

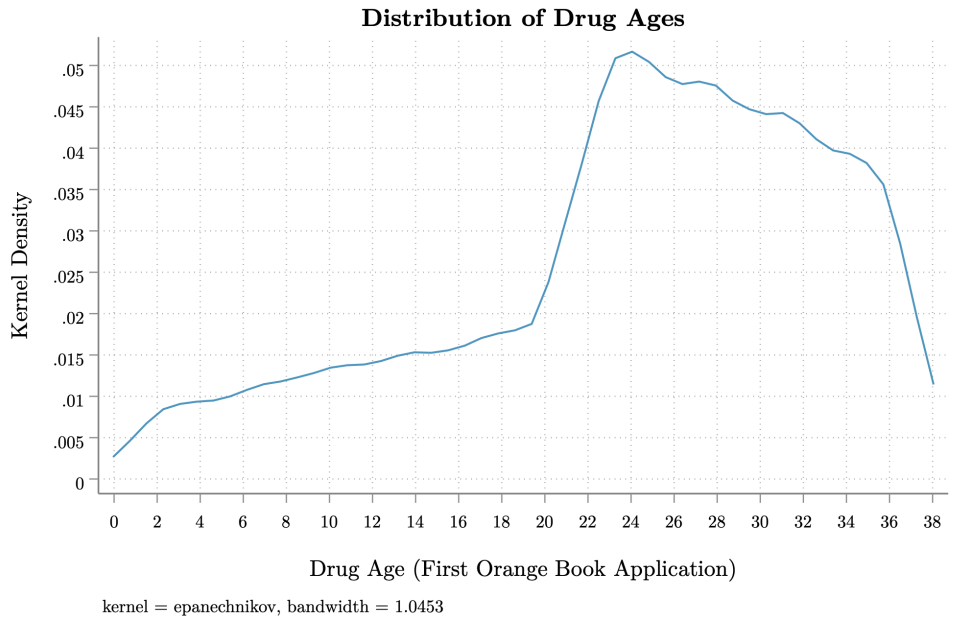


Figure S2.1: Distribution of Injectable Drug Ages

Notes: This figure plots the distribution of sterile injectable drug ages. Drug age is measured as the number of years since the first marketing application for a drug in the FDA's Orange Book. In the U.S. branded-drug patents generally have limited life-span (typically twenty years, but most drugs lose their exclusivity after 7 years, and the first approved generic drug receives 180 days of exclusivity against additional generic entry). This plot shows that most injectable products are old, off-patents products. Older generic drugs are generally less profitable than newer, more innovative products.

manufacture under contract for ANDA holders.

S2.2. Size of the Impacted Market

Table S2.1: **Share of Generics and Sterile Injectables in the FDA's Orange Book Data**

Generic	**Sterile Injectable**					
	No		Yes		*Total*	
	Freq.	Percent	Freq.	Percent	Freq.	Percent
No	3,584.0	19.7	1,642.0	30.3	5,226.0	22.1
Yes	14,653.0	80.3	3,772.0	69.7	18,425.0	77.9
Total	18,237.0	100.0	5,414.0	100.0	23,651.0	100.0

Notes: This table records the share of generic and sterile injectable drugs among all U.S.-marketed drugs, as recorded by the FDA's Orange Book (FDA's list of approved drug products with therapeutic equivalence evaluations). I use both the January 2020 version of the Orange Book and historical Orange Book records to get the list of marketed drugs in each year over the period 2004-2019. The first row reports the frequency and percentage of branded (non-generic) drugs, while the second row reports generic drugs. The first two columns are for non-sterile injectable drugs, and the second two for sterile injectable drugs. The last two columns report the total frequency and share of generic and non-generic drugs, over all form-types.

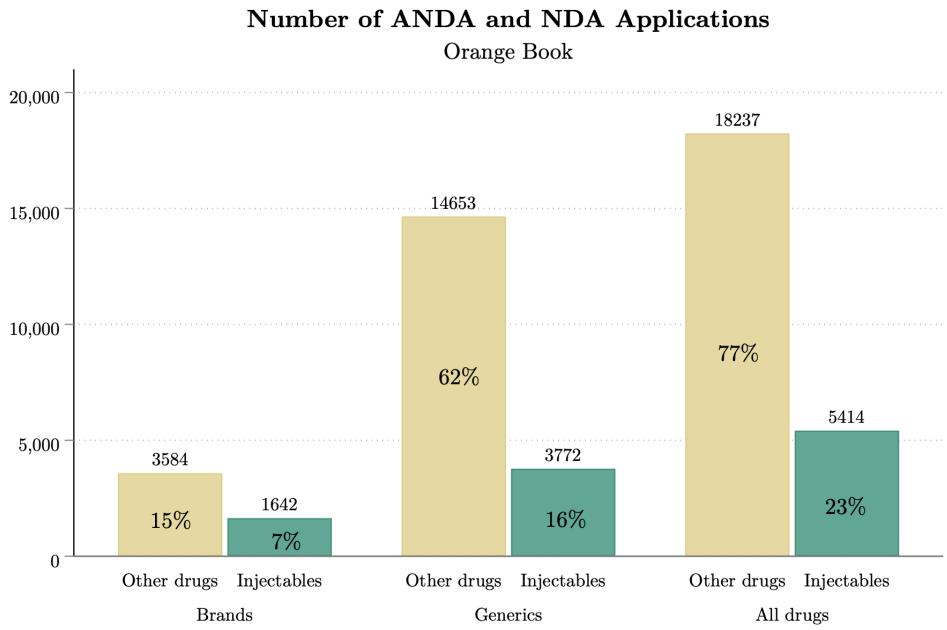


Figure S2.2: Impacted market size

Notes: This figure plots the frequency (number above each bar plot) and share of all U.S.-marketed drugs, by drug type. The list of all U.S.-marketed drugs is from the FDA's Orange Book (FDA's list of approved drug products with therapeutic equivalence evaluations). I use both the January 2020 version of the Orange Book and historical Orange Book records to get the list of marketed drugs in each year over the period 2004-2019. The first four bar-plots sum to one-hundred, and split U.S.-marketed drugs between brand, generic and injectables versus non-injectables. Within the Orange Book, 15% of drugs are non-injectable branded drugs, while only 7% of branded drugs are injectables. 62% of drugs in the Orange Book are generic, non-injectable drugs, while generic injectables represent 16% of all U.S.-marketed drugs. The last two bars sum to one hundred, and simply report that 23% of all U.S.-marketed drugs are injectable formulations.

S3. Additional Reduced-Form Results

S3.1. Offshoring and Shortages: Correlations

S3.1.1. Sterile injectable drugs in shortage are heavily exported by Indian firms

In Figure S3.1, I use detailed descriptions of shipments from digitized Indian Customs Data to plot the evolution of Indian exports of sterile injectable drugs over years 2008-2019. I exploit similar text mining techniques already used to identify drugs in the U.S. custom manifests to look for text strings that match the list of sterile injectable drugs sold in the U.S. inside Indian imports and exports of pharmaceutical products.[2] Figure S3.1 plots the evolution of imported quantities and imported drug values over time. I then further split the sterile injectable drugs I capture in the Indian Customs Data by their shortage status in Figure S3.1 (a drug is labeled as "shortage" if it appears on the U.S. shortage list at some point).

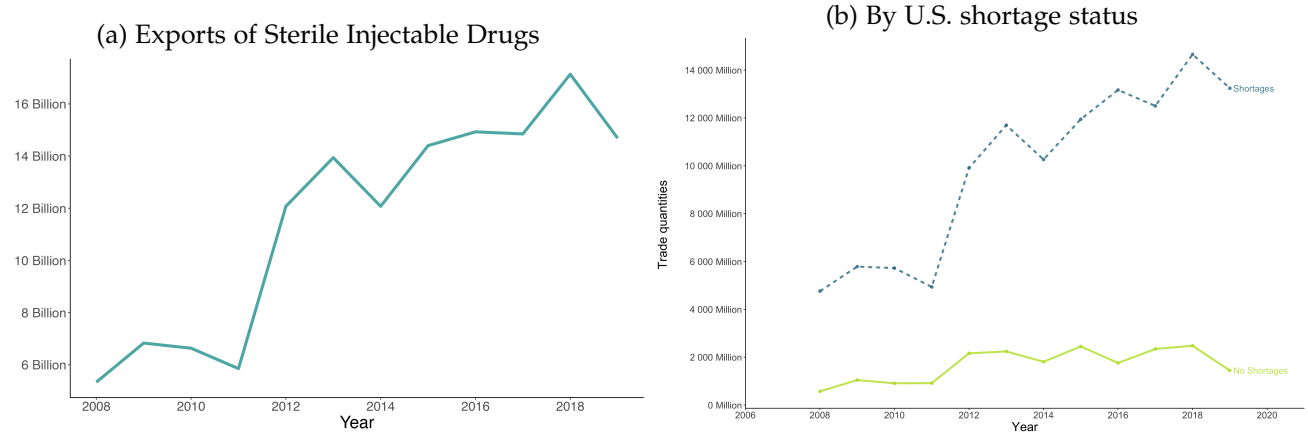


Figure S3.1: **Global Exports of Sterile Injectable Drugs, India**

Notes: This figure exploits detailed descriptions of shipments from digitized Indian Customs to plot the evolution of Indian exports of sterile injectable drugs over years 2008-2019. Panel (b) split the sterile injectable drugs I capture in the Indian Customs Data by their shortage status. A drug is labeled as in "shortage" if it appears on the U.S. shortage list at some point. I have approximately the same number of drugs in both groups (250 drugs categorized as "shortage" drugs and 260 drugs without U.S. shortages). Sterile injectable drugs that went into shortage at some point over the last 15 years are those that are the most heavily exported by Indian firms.

S3.1.2. An increase in offshoring is correlated with a higher probability of shortage *ex-post*

Figure S3.2 then reports the coefficients of a fixed-effects panel regression of shortage on offshoring, with the purpose of assessing one question: is a marginal increase in the share of foreign-based manufacturers for a drug correlated with a higher probability of this drug going short in the *subsequent* period? To answer, I calculate annual variations in each drug's foreign manufacturer share and categorize it using a dummy variable: 1 signifies an at least 10% increase; 0 signifies a decrease or no change. I then evaluate changes between $t-(n+1)$ and $t-n$ for $n \in \{1,2,3\}$, just prior to a shortage.

[2] I match 65% of sterile injectable drugs present in my data for the U.S. based on a matching of exact drug names. I did not use here such a comprehensive pre-cleaning of shipment descriptions and fuzzy-matching techniques as performed for the main U.S. customs data

Looking at the probability a drug goes into shortage at time t conditional on changes in offshoring rates in years just prior to the shortage allows testing whether variations are influenced by the 2011 peak of offshoring. Because the timing and length of offshoring events vary across drugs, regression coefficients in panel data models can indeed be contaminated by effects from other periods, and correlations can arise solely from heterogeneity in the timing of offshoring (see Section 3.2 of the paper for a further resolution of these issues). In each case, I regress a shortage dummy on an offshoring dummy, covariates, drug, and time fixed-effects, first using data from 2004 to 2019, then only from 2013 to 2019. The fixed-effects panel regression equivalent is given by the equation:

$$\text{Shortage}_{jt} = \beta \, \text{Offshored}_{jt} + \alpha_j + \xi_t + x'_{jt}\gamma + \omega_{it} \tag{1}$$

where the dependent variable is an indicator variable equal to 1 if a given drug j is in shortage at time t, Offshored_{jt} is an indicator variable equal to 1 if the drug offshoring rate increases between time $t-n$ and t. x_{jt} are time-varying drug-level covariates (log mean unit price for a drug as measured by average wholesale price, age of the drug, average number of manufacturers), ξ_t are time fixed-effects, α_j are drug fixed-effect. Drug products are defined at the molecule-form level here (not at the manufacturer level).

Figure S3.2 plots the β coefficients from regression 1. Taking all foreign-based facilities, an increase in the share of foreign manufacturers in the last 1 to 3 years is strongly correlated with a higher probability of the drug being in shortage at time t. The share of facilities located in Asia is overall higher than when taking all foreign facilities together, suggesting a higher correlation when manufacturers choose locations with lower marginal costs of production. Regression coefficients are reported in the appendix Tables S3.2 and S3.1.

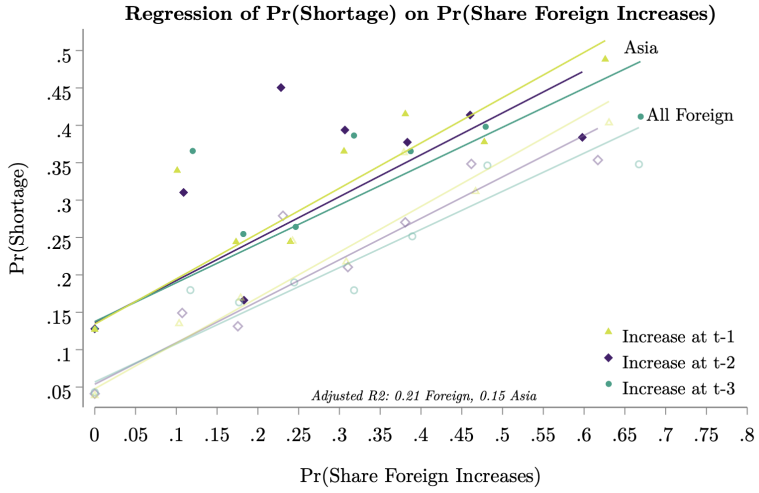


Figure S3.2: **Shortage events are correlated with offshoring increase**

Notes: This figure plots the β coefficients from regression 1. Taking all foreign-based facilities, an increase in the share of foreign manufacturers in the last 1 to 3 years is strongly correlated with a higher probability of the drug being in shortage at time t. The share of facilities located in Asia is overall higher than when taking all foreign facilities together, suggesting a higher correlation when manufacturers choose locations with lower marginal costs of production. Regression coefficients are reported in the appendix Tables S3.2 and S3.1

Table S3.1: **Impact of an increase in the share of foreign manufacturers of a drug on its future shortage probability**

	P(Shortage=1)					P(New Shortage=1)				
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)
Share Foreign Up at t-1 (t-1 - t-2)	0.1817***			0.1946***	0.1945***	0.04698***			0.04584***	0.03631***
	[0.01354]			[0.01583]	[0.01876]	[0.00848]			[0.01005]	[0.01198]
Share Foreign Up at t-2 (t-2 - t-3)		0.166***		0.153***	0.165***		0.05554***		0.04974***	0.04921***
		[0.01444]		[0.01546]	[0.01856]		[0.00918]		[0.00982]	[0.01185]
Share Foreign Up at t-3 (t-3 - t-4)			0.1802***		0.1538***			0.05141***		0.04384***
			[0.01515]		[0.01768]			[0.00967]		[0.01129]
Constant	0.1605***	0.1734***	0.1767***	0.1457***	0.1298***	0.0552***	0.05903***	0.06148***	0.0505***	0.04627***
	[0.00577]	[0.00623]	[0.0067]	[0.00722]	[0.00927]	[0.00361]	[0.00396]	[0.00428]	[0.00459]	[0.00592]
Year & Drug Fixed Effects	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
R^2	0.031	0.026	0.031	0.060	0.093	0.005	0.007	0.006	0.012	0.016
Observations	5555	5017	4488	4245	3077	5555	5017	4488	4245	3077

Notes: * p<0.1, ** p<0.05, *** p<0.01. Robust standard errors are clustered at the drug (molecule-form) level (in brackets). The data is a balanced panel of sterile injectable drugs matched to their production plants, over the period 2004 to 2019. All regressions include drug and year fixed effects. The dependent variables are dummies equal to 1 if a (new) shortage is notified at t; averages thus provides the probability of a (new) shortage. Independent variables are dummies equal to 1 if the share of foreign producers increases between two periods.

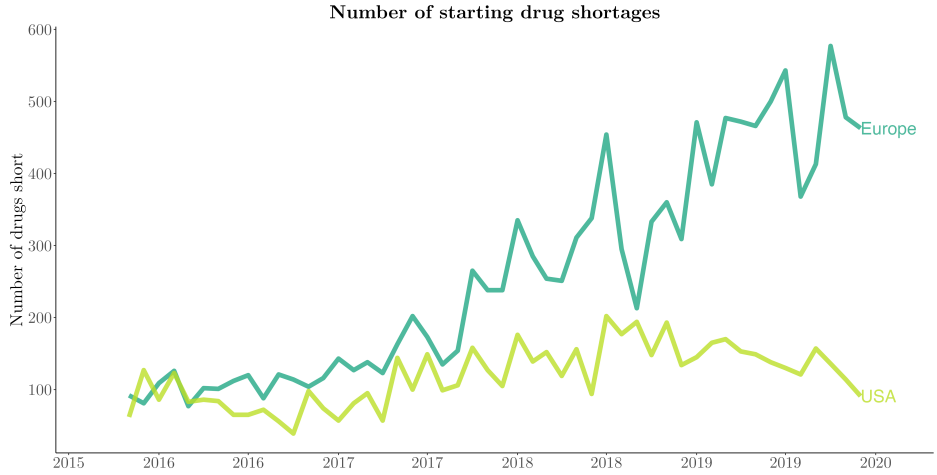
Table S3.2: **Impact of an increase in the share of foreign manufacturers of a drug on its shortage probability**

	P(Shortage=1)					P(New Shortage=1)				
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)
Share Foreign Up (t - t-1)	0.17***			0.1373***	0.1453***	0.04651***			0.03926***	0.05064***
	[0.01284]			[0.01835]	[0.02172]	[0.00796]			[0.01126]	[0.01345]
Share Foreign Up (t - t-2)		0.1744***		0.09552***	0.09518***		0.05276***		0.02154**	-0.00379
		[0.01328]		[0.01682]	[0.02294]		[0.00832]		[0.01032]	[0.01421]
Share Foreign Up (t - t-3)			0.1799***		0.04401**			0.0637***		0.03387***
			[0.01467]		[0.02044]			[0.00923]		[0.01266]
Constant	0.1553***	0.1645***	0.1816***	0.1552***	0.1629***	0.0521***	0.05466***	0.05713***	0.05048***	0.05113***
	[0.00543]	[0.00627]	[0.00735]	[0.00654]	[0.00798]	[0.00336]	[0.00393]	[0.00463]	[0.00401]	[0.00495]
Year & Drug Fixed Effects	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
R^2	0.028	0.033	0.035	0.042	0.055	0.006	0.008	0.011	0.008	0.013
Observations	6075	5133	4184	4757	3570	6075	5133	4184	4757	3570

Notes: * p<0.1, ** p<0.05, *** p<0.01. Robust standard errors are clustered at the drug (molecule-form) level (in brackets). The data is a balanced panel of sterile injectable drugs matched to their production plants, over the period 2004 to 2019. All regressions include drug and year fixed effects. The dependent variables are dummies equal to 1 if a (new) shortage is notified at t; averages thus provides the probability of a (new) shortage. Independent variables are dummies equal to 1 if the share of foreign producers increases between two periods.

S3.2. European Shortages

(a) **European Shortages: U.S. vs Europe, 2016-2020**



(b) **European Shortages: European countries vs U.S., 2016-2020**

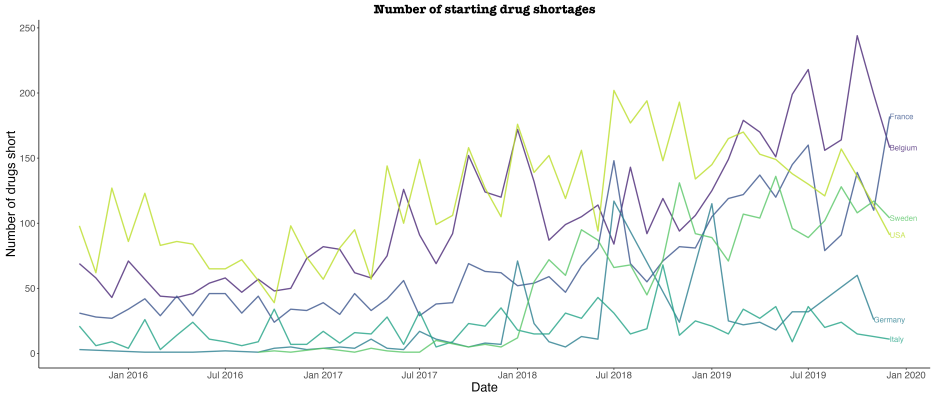


Figure S3.3: **European shortages**

Notes: These plots compare drug shortages in the U.S. and in Europe over the period 2016-2020, as recorded by national health agencies. Most European countries do not have consistent historical records of shortages before 2014-2015. The exact stringency of the drug shortages definition may also vary across countries (some record drugs in their shortage list as soon as the drug's supply is under "tension"; others only record shortages of critical medical products and do not report stock-outs of routine, non-essential medications). Comparisons of shortages across countries are thus to be interpreted with caution. The bottom panel compares the U.S. (in light green) with 5 European countries: France, Belgium, Germany, Sweden and Italy. The top panel aggregates all these European countries and compares them to the U.S. The trend of shortages in Belgium is the most closely similar to the U.S. Many spikes of shortages are correlated over time across countries. Aggregating all European countries, the amplitude of medication shortages is larger than in the U.S., especially since 2018.

S3.3. Additional Tables: Instrumental Variable Analysis

Table S3.3 reproduces the regressions of Online Appendix Table E.6 without controls, on the same drug-years. The coefficients are of similar magnitude with and without controls; only the effect of Asian production on the fraction of the year in shortage is larger once the controls are added.

Table S3.3: **Probability of shortage on share foreign, with and without controls**

Dependent Variable:	**P(New Shortage=1)**		**Fraction of Year Short**	
	(1) Foreign	(2) Asia	(3) Foreign	(4) Asia
Panel A. With Controls†				
Production Share	**0.2366*****	**0.3039*****	**0.7395*****	**0.9497*****
	[0.0598]	[0.1040]	[0.1405]	[0.2738]
log(PDB), First Stage	0.4778***	0.3721***	0.4778***	0.3721***
	[0.1126]	[0.0621]	[0.1126]	[0.0621]
F-stat First-Stage‡	18.01	35.85	18.01	35.85
Wild cluster bootstrap p-value, second stage	0.035	0.035	0.026	0.026
Panel B. Without Controls				
Production Share	**0.2860*****	**0.2962*****	**0.6830*****	**0.7075*****
	[0.0442]	[0.0644]	[0.0675]	[0.1454]
log(PDB), First Stage	0.5964***	0.5758***	0.5964***	0.5758***
	[0.1315]	[0.0857]	[0.1315]	[0.0857]
F-stat First-Stage‡	20.58	45.16	20.58	45.16
Wild cluster bootstrap p-value, second stage	<0.001	<0.001	0.002	0.002
Drug Fixed Effects	✓	✓	✓	✓
Observations	21,502	21,502	21,502	21,502
Disease Clusters	39	39	39	39

Notes: * $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$. Standard errors clustered by disease in brackets. †Instrument: log predicted disease burden in India and China. ‡Kleibergen-Paap F statistic. Both panels use the same drug-years with drug fixed effects and differ only in the controls (price, number of labelers, off-patent status). The wild cluster bootstrap p-values are weak-instrument robust (Anderson-Rubin form, Webb weights).

Figure S3.4 drops one year at a time from the regressions of Online Appendix E.3. The reduced-form effect of predicted disease burden on both outcomes stays positive and close to its full-sample value whichever year is left out.

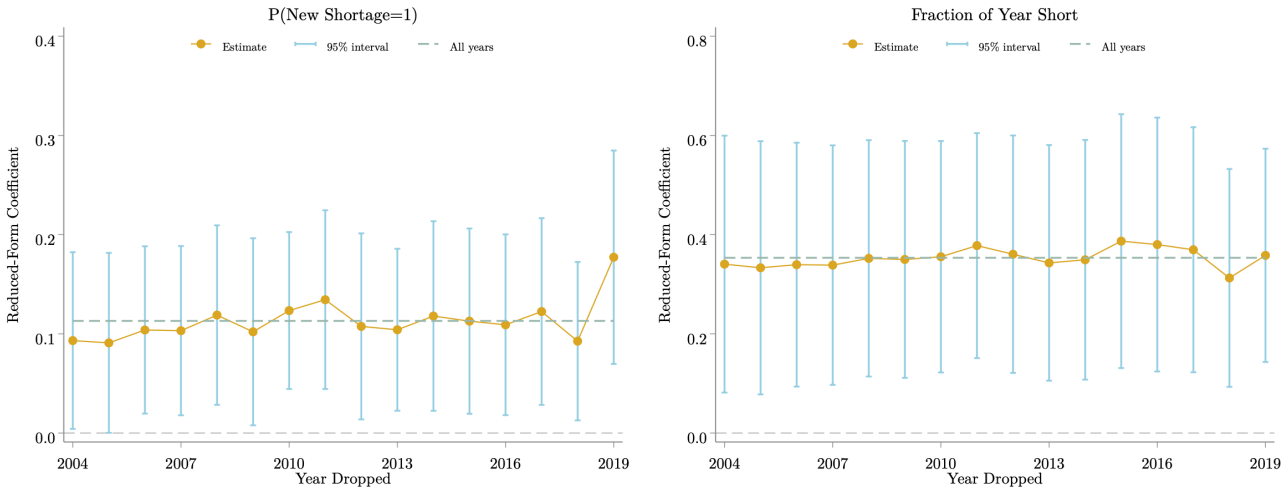


Figure S3.4: **Reduced-Form Effect of Predicted Disease Burden, Dropping One Year at a Time**

Notes: Each point drops one year, and then the NDCs left with a single year, and regresses the outcome on log predicted disease burden in India and China with drug fixed effects and the controls; the dashed line is the estimate on all years, the bars 95 percent intervals from standard errors clustered by disease. Across the sixteen drops, the second-stage effect of an entirely foreign production structure stays between 19 and 36 percentage points on the probability of a new shortage and between 67 and 84 percentage points on the fraction of the year in shortage.

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