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High Generic Drug Prices and Market Competition

A Retrospective Cohort Study

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Background: Prices for some generic drugs have increased in recent years, adversely affecting patients who rely on them.

Objective: To determine the association between market competition levels and the change in generic drug prices in the United States.

Design: Retrospective cohort study.

Setting: Prescription claims from commercial health plans between 2008 and 2013.

Measurements: The 5.5 years of data were divided into 11 study periods of 6 months each. The Herfindahl–Hirschman Index (HHI)—calculated by summing the squares of individual manufacturers' market shares, with higher values indicating a less competitive market—and average drug prices were estimated for the generic drugs in each period. The HHI value estimated in the baseline period (first half of 2008) was modeled as a fixed covariate. Models estimated price changes over time by level of competition, adjusting for drug shortages, market size, and dosage forms.

Results: From 1.08 billion prescription claims, a cohort of 1120 generic drugs was identified. After adjustment, drugs with quadropoly (HHI value of 2500, indicating relatively high levels of competition), duopoly (HHI value of 5000), near-monopoly (HHI value of 8000), and monopoly (HHI value of 10 000) levels of baseline competition were associated with price changes of −31.7% (95% CI, −34.4% to −28.9%), −11.8% (CI, −18.6% to −4.4%), 20.1% (CI, 5.5% to 36.6%), and 47.4% (CI, 25.4% to 73.2%), respectively, over the study period.

Limitation: Study findings may not be generalizable to drugs that became generic after 2008.

Conclusion: Market competition levels were associated with a change in generic drug prices. Such measurements may be helpful in identifying older prescription drugs at higher risk for price change in the future.

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Use of generic drugs as a percentage of total dispensed prescriptions has increased in recent years, from 57% in 2004 to 86% in 2013 (1). The U.S. Government Accountability Office estimates that this increased use has saved the U.S. health care system $1 trillion over the past decade, with $157 billion in savings from 2010 alone (2). Patients also realize these savings in the form of lower copayments, leading to increased medication adherence and improved health outcomes (3–5).

In recent years, rising prices have been reported for several generic medications (6). One review found that the price of digoxin increased by 637% in a single year (7). Concern over rising generic drug prices has garnered much attention from policymakers, physicians, and patients (8, 9). Many factors have been linked to these price increases, including shortages in the manufacturing supply chain (leading to reduced production) (10) and a reduction in the number of manufacturers of a drug (resulting in insufficient competition). In the most problematic cases, companies like Turing and Valeant have purchased older drugs, such as pyrimethamine (Daraprim [Turing]) and isoproterenol (Isuprel [Valeant]), that are produced by a single manufacturer and have raised prices by thousands of percent.

Although increases in generic drug prices are thought to be the result of insufficient competition, no study has examined the relationship between price increases and market competition levels. Understanding how prices relate to market changes may help identify drugs at risk for price changes so that interventions may occur before patient care is affected. Therefore, we sought to examine the association between market competition levels and changes in generic drug prices for a large cohort of generic drugs in the United States.

METHODS

The study was approved by the Institutional Review Board at the University of Florida.

Study Cohort and Data Sources

We used MarketScan Commercial Claims and Encounters data from January 2008 to June 2013. MarketScan, an employer- and health-plan–sourced drug database, collects information on approximately 30 million patients annually from 130 commercial health plans. The outpatient pharmacy files contain patient-level data for pharmacy services, including price information on patient copayments and third-party payments for each dispensed prescription. In addition, they provide information on drug fill dates, quantity of drug supplied, and National Drug Code (NDC) numbers. The NDC numbers were used to link the outpa-

See also:

Web-Only
Supplement

Table 1. Descriptive Characteristics of the Baseline Competition Groups*

Characteristic	High-Competition Group (*n* = 574)	Medium-Competition Group (*n* = 341)	Low-Competition Group (*n* = 205)
Mean HHI value (SD)			
At baseline	3600 (834)	5900 (750)	9600 (549)
At end of follow-up	4100 (1609)	5700 (2148)	7400 (2644)
Change in competition levels during follow-up, *n (%)*†			
Increase	163 (28.4)	91 (26.7)	6 (2.9)
No change	331 (57.7)	109 (32.0)	97 (47.4)
Decrease	80 (13.9)	141 (41.4)	102 (49.7)
Median manufacturers at baseline (range), *n*‡	4 (2–16)	2 (1–11)	1 (1–5)
Drug shortages			
Shortages, *n (%)*	99 (17.2)	55 (16.1)	30 (14.6)
Median duration (range), *mo*	9.4 (0.3–38.9)	10.0 (1.5–25.5)	9.8 (1.5–31.2)
Market size, *n (%)*§			
Small	68 (11.8)	84 (24.6)	59 (28.8)
Medium	149 (26.0)	119 (34.9)	68 (33.1)
Large	357 (62.2)	138 (40.5)	78 (38.1)

HHI = Herfindahl–Hirschman Index.
* For descriptive purposes, using baseline HHI thresholds of duopoly (HHI value, 5000) and near-monopoly (HHI value, 8000), drugs were grouped into high-competition (HHI value, <5000), medium-competition (HHI value, 5000 to <8000), and low-competition (HHI value, ≥8000) groups. The HHI value was rounded to the nearest 100 to facilitate interpretability. Percentages may not sum to 100 due to rounding.
† Estimated by examining the difference in HHI value during the last study period (first half of 2013) and the baseline period (first half of 2008); a threshold of 1000 was used to designate a change in competition levels.
‡ Only manufacturers with a minimum of 100 dispensings for a study drug during the baseline period were included in this calculation.
§ Defined as the percentage of the total generic drug market held by a study drug during the baseline period (see text for details). Terciles were used to group drugs into 1 of the 3 market categories.

tient pharmacy data files to Red Book (11), a drug information database of more than 200 000 prescription and over-the-counter health care items. Red Book provides information on active ingredients, dosage forms, drug strength, manufacturer name, and whether the dispensed NDC was a generic or brand-name medication. We considered distinct combinations of active ingredients, dosage forms, and drug strength as individual study drugs. For example, diazepam 2-mg tablets, 5-mg tablets, and rectal gel were considered as individual study drugs. Only drugs classified by Red Book as either single-source or multisource generic for the entire study period were included in the study.

Outcome

We summed the patient out-of-pocket costs (copayments, coinsurance, and deductibles) and the amount paid by the third-party payer to estimate the overall price of a dispensed prescription. We combined these costs to account for any cost shifting from third-party payers to patients over time. To ensure valid comparisons, this overall price was standardized by the metric quantity of the drug dispensed. Depending on the dosage form, this metric quantity might be the number of tablets, grams of ointment, or milliliters of solution dispensed.

The 5.5 years of data were divided into 11 periods of 6 months each, and the first 6-month period (first half of 2008) was designated as the baseline period. Average prices were calculated for each drug in the 11 periods. Prices calculated during the baseline period were adjusted as a covariate, and prices estimated in the 10 subsequent study periods were modeled as the dependent variable. In other words, the outcome of the study was the change in drug price from its baseline value (measured in the first half of 2008).

Independent Variables

We used the Herfindahl–Hirschman Index (HHI) to estimate market competition levels for each drug. The HHI is the U.S. Department of Justice's preferred method of quantifying market competition (12) and is calculated by summing the squares of the market shares of individual firms (generic manufacturers) (13). Index values range from approaching 0 (a large number of small generic drug manufacturers) to 10 000 (a monopoly, or 1 generic drug manufacturer). Because the HHI is calculated by squaring the market share of individual generic drug manufacturers, it gives disproportionately higher weights to a larger market share. For example, a generic drug that is produced by 4 manufacturers with market shares of 10%, 20%, 30%, and 40% has an HHI value of $10^2 + 20^2 + 30^2 + 40^2$, or 3000; higher HHI values indicate a less competitive market. We estimated the market share of a manufacturer by dividing the number of prescriptions attributable to that manufacturer by the number of prescriptions dispensed for a given study drug in that period.

The HHI has some important thresholds. An HHI value of 2500 represents quadropoly-like competition levels, at which a generic drug is produced by 4 manufacturers with equal market shares (that is, $25^2 + 25^2 + 25^2 + 25^2$). Similarly, an HHI value of 5000 represents a duopoly-like competition level, at which a generic drug is produced by 2 manufacturers with equal market shares (that is, $50^2 + 50^2$). An HHI value of 8000, indicating a near-monopoly–like competition level, is achieved when 1 manufacturer controls nearly

90% of the generic drug market (that is, 90^2). As previously stated, an HHI value of 10 000 represents a monopoly, in which a single manufacturer produces the generic drug.

The primary association of interest was between competition levels (HHI) and changes in drug prices. Prices may increase faster for drugs with low baseline competition levels (time-stable component of HHI) or for those that become less competitive over time (time-varying component of HHI). The index value measured during the baseline period was designated as the baseline HHI value. Change in HHI from its baseline value was estimated by calculating the difference between the HHI in the previous study period and its baseline value. We used lagged values of HHI to ensure that a change in HHI preceded a change in price.

Although we modeled HHI as a continuous variable (see the Statistical Analysis section), for descriptive purposes, by using HHI thresholds of duopoly (HHI value, 5000) and near-monopoly (HHI value, 8000), we categorized drugs into high–baseline competition (HHI value, <5000), medium–baseline competition (HHI value, 5000 to <8000), and low–baseline competition (HHI value, ≥8000) groups.

Covariates

We controlled for baseline market size, because it could be associated with both HHI and drug prices. The baseline market size, defined as the percentage of the total generic drug market held by a drug, was calculated by dividing the number of fills for each drug (for example, diazepam 2-mg tablets) by the number of fills for the entire cohort of generic drugs in the baseline period. Using tertiles of market size, we grouped the study drugs into small, medium, and large markets. We also adjusted for dosage forms by creating dummy variables to classify the drugs into 7 categories: tablets; extended-release tablets; capsules; extended-release capsules; cream, lotion, or gel; solution; and miscellaneous.

We used the University of Utah Drug Information Services (UUDIS) database to collect information on drug shortage status (14). The UUDIS database, considered one of the most reliable and comprehensive sources on drug shortages in the United States (15), contains information on active ingredients, dosage forms, drug strengths, and shortage start and end dates. We linked the study drugs to the UUDIS database and modeled the number of months that a drug was in shortage as a lagged, time-varying, cumulative, continuous variable.

Statistical Analysis

Within the data were 3 sources of correlation nested within one another. Prices measured repeatedly for the same drug constituted the first level of data. The second and third levels were related to manufacturing efficiencies and cross-price elasticity of demand. Although not always the case, owing to overlap in manufacturing processes, drugs with the same active ingredients and dosage forms may be easier to produce. For example, manufacturers that produce diazepam 2-mg tablets may also produce diazepam 5-mg tablets, and their prices may be correlated. Therefore, we modeled the combinations of active ingredients and dosage forms (for example, diazepam tablets) as the second hierarchical level. Cross-price elasticity of demand means that prices for substitutable generic drugs may be similar to one another. Prices for a generic statin may be more like those for another generic statin than those for a generic antibiotic. We used American Hospital Formulary Service Drug Information and classified

Table 2. Change in Drug Prices and Competition Levels for the Cohort of Generic Drugs*

Variable	First Half of 2008	Second Half of 2010	First Half of 2013	Overall Change, %†
Overall trends				
Prices, %				
Mean	–	–2.6	33.4	30.0
Median	–	–12.9	–3.8	–16.3
Weighted‡	–	–14.3	0.1	–14.2
HHI value				
Average	5400	5400	5200	–3.7
Weighted‡	4200	4200	3800	–9.5
Trends, by baseline market competition group				
High				
Standardized prices§	–	–14.3	28.0	9.7
Average HHI value	3600	4100	4100	13.8
Medium				
Standardized prices§	–	9.6	31.2	43.8
Average HHI value	5900	5900	5700	–3.4
Low				
Standardized prices§	–	9.8	49.1	63.8
Average HHI value	9700	8400	7400	–23.7

HHI = Herfindahl–Hirschman Index.
* See text for details on standardized prices. HHI value was rounded to the nearest 100 to facilitate interpretability.
† Change in prices calculated by using the baseline prices (first half of 2008) as reference.
‡ Weighted by the percentage of the total generic drug market held by a study drug during the baseline period (market size) as a continuous variable.
§ Percentage change in mean standardized prices is reported.

Table 3. Drugs With the Highest Percentage Increase in Price*

Variable	First Half of 2008	Second Half of 2010	First Half of 2013	Overall Change, %
Hydrocortisone acetate–lidocaine hydrochloride 0.5%/3% cream				
Price per application, $	0.92	0.54	42.27	4494.6
HHI value	3500	9300	9900	182.9
Mesalamine 4 g/60 mL enema				
Price per enema, $	3.34	39.08	82.47	2369.1
HHI value	4800	5200	6400	33.3
Erythromycin 2% solution†				
Price per milliliter, $	0.16	0.25	3.12	1850.0
HHI value	5000	5700	5800	16.0
Fluocinolone acetonide 0.01% solution				
Price per milliliter, $	0.24	0.34	2.88	1100.0
HHI value	10 000	10 000	8900	−11.0
Nystatin–triamcinolone acetonide 100 000 U per g/0.1% cream				
Price per gram, $	0.24	0.21	2.68	1016.7
HHI value	6000	8000	9600	60.0

HHI = Herfindahl–Hirschman Index.
* HHI value was rounded to the nearest 100 to facilitate interpretability. Standardized prices were calculated by dividing the overall price of a dispensed prescription by the metric quantity of the drug supplied (see text for explanation).
† Drug was in shortage during the study period.

all active ingredients into drug classes, as a surrogate for this effect, and accordingly modeled drug classes (for example, statins) as the third hierarchical level.

Because drug prices were highly skewed and nonnormal, we log transformed them and used a linear mixed-effects model (see section 1.5 of the **Supplement** [available at Annals.org] for complete model specifications). We modeled time as a categorical factor to avoid assumptions of linear trends. Parametric specifications of time also were considered (section 1.4 of the **Supplement**). We computed SEs using the Kenward–Roger degrees-of-freedom approximation (16). To account for the correlation within the data, we fit an unstructured covariance matrix for the residuals while accounting for the nested nature of the data (section 1.3 of the **Supplement**). We also attempted to fit a generalized linear mixed model but could not get the model to converge (section 1.2 of the **Supplement**). Data were analyzed by using the MIXED procedure in SAS, version 9.4 (SAS Institute).

Baseline HHI and change in HHI were modeled as continuous variables. To illustrate the trajectory of price change over time as a function of baseline competition levels, we used 4 competition levels: quadropoly (HHI value, 2500), duopoly (HHI value, 5000), near-monopoly (HHI value, 8000), and monopoly (HHI value, 10 000).

Effect Modification by Baseline Price

Because manufacturers may have greater leeway in raising prices of lower-priced drugs, we tested for the presence of effect modification by baseline price. Using percentiles of baseline price within each dosage form, we grouped drugs into low–, medium–, and high–baseline price groups (**Supplement Table 1** [all supplement tables available at Annals.org]) and estimated slopes for baseline HHI and change in HHI within each of the 3 groups (while also interacting all covariates with the 3 baseline price groups [see the **Supplement** for full model specifications]).

Role of the Funding Source

The study was not funded.

RESULTS

Descriptive Findings

We analyzed 1.08 billion prescription drug claims for 57.3 million patients and identified a cohort of 1120 drugs that were generic throughout the study period. We classified drugs into 90 drug classes and 1 miscellaneous drug class (**Supplement Table 2**). Examples of therapeutic classes represented in the cohort were amphetamines, angiotensin-converting enzyme inhibitors, benzodiazepines, statins, macrolides, and quinolones.

We found that nearly half the drugs in the baseline period had duopoly-like competition levels (**Supplement Table 3**) and several had near-monopoly competition levels, including bacitracin 500-U/g ointment, erythromycin 400-mg tablets, and fluoxetine 20-mg tablets. Drugs in the lower–baseline competition groups generally had smaller market sizes (**Table 1**).

During the study period, the average drug price increased by 30.0%, whereas the weighted price (weighted by baseline market size as a continuous variable) decreased by 14.2% (**Table 2**), indicating that the prices for less commonly used drugs increased disproportionately. The median price decreased by 16.3% during the study period, implying that prices for most generic drugs decreased during this time.

Drugs in the low-competition group exhibited the largest increase in average price (63.8%), followed by the medium-competition (43.8%) and high-competition (9.7%) groups. Most of this price increase occurred in the second half of the study. (**Supplement Table 4** shows the changes in drug prices, by administration form and HHI group.)

Table 3 and Supplement Table 5 show prices and competition levels for drugs that had the largest price increases during the study. Although most of these drugs also exhibited low levels of competition, this was not always the case. For example, the price of erythromycin 2% solution may have increased as a direct response to drug shortages.

Supplement Table 6 shows prices and competition levels for drugs with the greatest increase in HHI (that is, those that became less competitive) during the study. Hydrocortisone acetate–lidocaine hydrochloride 0.5%/3% cream and nystatin–triamcinolone acetonide ointment had an HHI increase from 3400 and 4400, respectively, to 9900 during the study period. In most instances, a decrease in competition level was followed by an increase in drug price.

Primary Analysis and Effect Modification

We found that baseline competition levels (measured during the first half of 2008) were associated with price changes from baseline values (also measured during the first half of 2008 [Table 4]); here, we focus on the price changes in the last study period (first half of 2013). After adjustment, drugs with quadropoly, duopoly, near-monopoly, and monopoly levels of baseline competition were associated with price changes of −31.7% (95% CI, −34.4% to −28.9%), −11.8% (CI, −18.6% to −4.4%), 20.1% (CI, 5.5% to 36.6%), and 47.4% (CI, 25.4% to 73.2%), respectively, during the study period. With quadropoly used as the reference group, these changes correspond to a relative price difference of 29.2%, 75.8%, and 115.9% for duopoly, near-monopoly, and monopoly, respectively.

Previous results reflect the association between price changes and baseline competition levels; we then examined the association between changes in price and changes in competition levels over time. Change in competition levels over time also was associated with price changes (Supplement Table 7); however, the magnitude of this association was smaller than similar differences in baseline HHI. For example, a duopoly at baseline was associated with a price change of −11.8% (CI, −18.6% to −4.4%) over the study period, assuming no change in competition level. However, if that duopoly were to transition to a monopoly (become less competitive over time), then instead of the expected price decrease of 11.8%, we would expect a price increase of 7.4% (CI, −5.6% to 22.2%). Compared with a 7.4% price increase for a drug that transitioned from a duopoly to a monopoly, a monopoly at baseline was associated with a greater price increase of 47.4%.

Finally, we examined how baseline prices modify the relationship between baseline competition levels and changes in drug prices, focusing on quadropoly and monopoly levels of baseline competition and the last study period (first half of 2013). We found that low baseline levels of market competition had a more pronounced effect on price for lower- than higher-priced drugs (Figure and Supplement Table 8). For instance, a quadropoly was associated with a price change of −40.3% (CI, −44.0% to −36.3%) in the high–baseline price group, compared with −24.0% (CI, −29.4% to −18.2%) in the low–baseline price group. Similarly, a monopoly was associated with a price increase of 21.6% (CI, −6.0% to 57.2%) in the high–baseline price group, compared with 91.9% (CI, 43.1% to 157.2%) in the low–baseline price group, a greater than 4-fold rate of increase.

Although we could not model drug prices directly, we could approximate the percentage increases in drug prices into dollar amounts. For instance, assume tablet A and tablet B were both priced at $1.07 per pill in the first half of 2008 (overall mean price for tablets in the baseline period [Supplement Table 1]) and that tablet A was a quadropoly and tablet B a monopoly. Holding other factors constant, we would predict tablet A and tablet B to be priced at $0.73 and $1.57, respectively, by the first half of 2013 (Table 4, first half of 2013; quadropoly, −31.7%, and monopoly, +47.4%, from $1.07), which translates to an incremental difference of $25.20 for a standard 30-day supply.

DISCUSSION

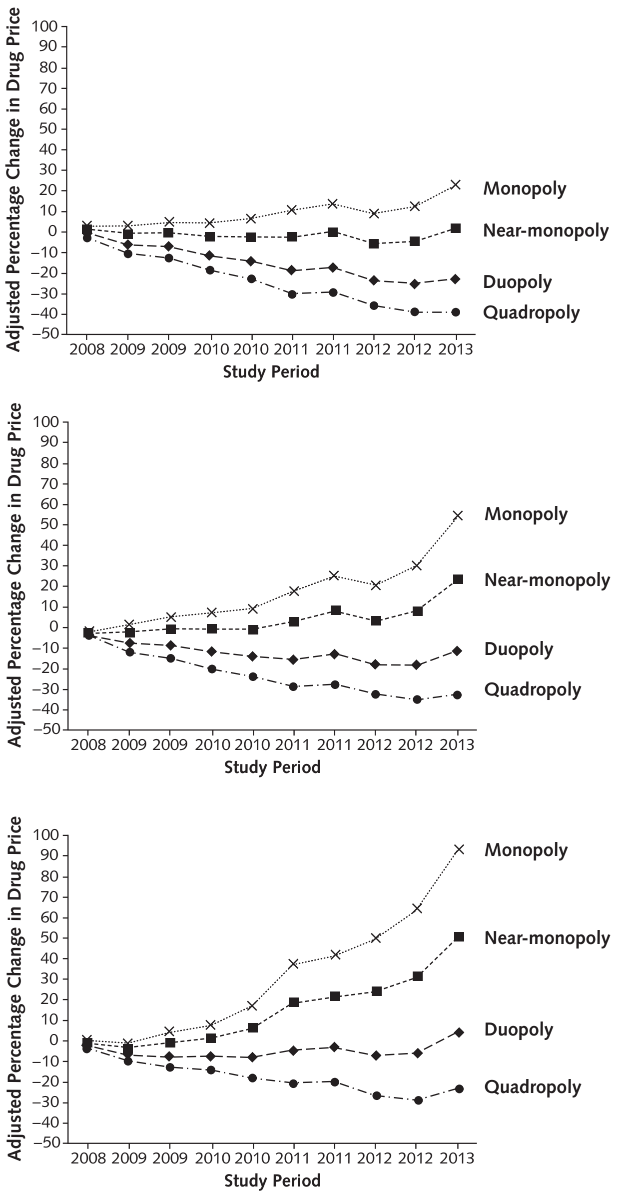
We found that low baseline levels of market competition (measured during the first half of 2008) were associated with a change in drug price. This association was modified by baseline price; low competition levels had a more pronounced effect on price in lower- than higher-priced drugs. A decrease in market competition level over time (an increase in HHI from its baseline value) did not have as strong an effect on drug prices,

Table 4. Adjusted Percentage Change in Drug Prices From Their Baseline Value for Selected Baseline Competition Levels*

Period†	Quadropoly (HHI Value, 2500)	Duopoly (HHI Value, 5000)	Near-Monopoly (HHI Value, 8000)	Monopoly (HHI Value, 10 000)
2009	–11.6 (–12.6 to –10.6)	–8.0 (–10.0 to –5.8)	–3.4 (–6.9 to 0.1)	–0.3 (–4.7 to 4.3)
2010	–18.3 (–19.7 to –16.8)	–11.4 (–14.5 to –8.1)	–2.4 (–7.8 to 3.4)	4.2 (–3.1 to 11.9)
2011	–26.8 (–28.8 to –24.8)	–14.4 (–18.9 to –9.6)	3.3 (–5.3 to 12.7)	17.1 (5.0 to 30.6)
2012	–31.7 (–34.0 to –29.3)	–17.4 (–22.9 to –11.5)	3.7 (–7.1 to 15.8)	20.7 (5.2 to 38.5)
2013	–31.7 (–34.4 to –28.9)	–11.8 (–18.6 to –4.4)	20.1 (5.5 to 36.6)	47.4 (25.4 to 73.2)

HHI = Herfindahl–Hirschman Index.
* Model adjusted for study period, drug shortages, market size, and dosage forms while accounting for all clustering effects. All covariates were included in the model without selection. Values are adjusted percentage changes in price (95% CIs).
† Data for the first half of each year are presented.

Figure. Adjusted percentage change in drug prices, within baseline price groups, for select baseline competition levels.



With the use of percentiles of baseline prices (measured during the first half of 2008), drugs were grouped into high-, medium-, and low-baseline price groups (top, middle, and bottom panels, respectively). Adjusted percentage changes in drug price are shown for the following baseline HHI levels: quadropoly (HHI value, 2500), duopoly (HHI value, 5000), near-monopoly (HHI value, 8000), and monopoly (HHI value, 10 000). HHI = Herfindahl–Hirschman Index.

implying that prices do not change immediately after a shift in market competition levels.

Drug prices may increase in low-competition markets for several reasons. Manufacturers that produce generic drugs to serve such markets—especially for agents without close therapeutic substitutes—may have more leeway in raising drug prices. Generic drug manufacturers with multiple-drug portfolios may increase prices in noncompetitive markets to offset lower profits in more competitive ones. Also, only in a highly noncompetitive drug market is it possible for an opportunistic pharmaceutical firm to buy the rights to a generic drug and subsequently raise the price, as seen with the Turing and Valeant cases.

Although rapidly increasing prices for a generic drug should encourage other manufacturers to produce that drug, several potential deterrents may prevent them from entering the market. Our findings indicate that low levels of competition are common in smaller markets that other manufacturers may not find financially lucrative to enter. Other reasons may be a lack of knowledge about the opportunities presented by rapid changes in certain generic markets, an inability to procure raw materials at competitive prices, and a lack of capacity to scale up manufacturing for a new generic drug in a timely manner (17).

The time required to gain regulatory approval for a generic drug may have been another factor underlying generic drug price increases. The review times for new generic drug applications at the U.S. Food and Drug Administration's Office of Generic Drugs (OGD) increased to more than 3 years during the study period. However, an influx of user fees from generic drug manufacturers after 2012 has reduced review times to 1 year. Through legislative action, the OGD recently announced that it would grant expedited reviews to generic drugs produced by a single manufacturer (18). Although this development is positive, it addresses a special case of low competition, namely a monopoly (HHI value, 10 000). The HHI may provide a more flexible approach in identifying drugs that might benefit from an expedited review.

In recent years, some generic drug manufacturers have sought to consolidate their market power by merging with rivals (19). For instance, Teva, the world's largest generic drug manufacturer, recently acquired Allergan, the third-largest manufacturer (20). Such mergers carry a risk for decreasing competition in parts of the U.S. generic drug market. Our finding that nearly half the generic drugs in the first half of 2008 had an HHI value exceeding 5000 (duopoly-like competition levels) should be a concern for regulators and policymakers. It is estimated that a generic market with 7 or more manufacturers leads to drug prices that approach the cost of manufacturing them (21).

Our study has limitations. Because we included only drugs that were available as generic products during the study period, our findings may not be generalizable to drugs that became generic after 2008. Although we did not find any signs of an increase in market consolidation over time, our study ended after the first half of 2013. Therefore, after this period, different mechanisms—even one possibly related to an increase in market consolidation—may have played a role in increasing generic drug prices. Most of the widely publicized cases of price increases occurred during or after 2013. Although we note a sharp increase in generic drug prices in the second half of the study, we cannot extrapolate this trend to later years, after the study ended.

Although we were able to combine different databases to capture variables related to drug prices, competition levels, and drug shortages, we could not control for the loss of market exclusivity for therapeutically comparable brand-name medications, which could theoretically decrease the price of some generic medications by increasing competition within that therapeutic class. For example, we excluded atorvastatin (Lipitor [Pfizer]), which became generic after our study began, but it could serve as a viable substitute for other drugs within the statin therapeutic class. The inability to control for this effect may lead to a decrease in drug prices that is unrelated to competition levels and might bias the study results toward no difference. However, we sought to mitigate this effect by clustering the study drugs in therapeutic classes.

We found that increases in generic drug prices were strongly associated with market competition levels. Unless policies are enacted to stabilize generic drug markets in response to a decrease in competition, we may continue to see cases of generic drugs subject to large price increases.

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Reproducible Research Statement: *Study protocol and statistical code:* Not available. *Data set:* Analytic data set is available from Dr. Dave (e-mail, chintandave19@gmail.com).

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Current author addresses and author contributions are available at Annals.org.

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