CORRESPONDENCE

Prices of Generic Drugs Associated with Numbers of Manufacturers

TO THE EDITOR: Low-cost generic drugs have improved outcomes in patients while saving the health care system more than $1 trillion in the past decade. However, the prices of some generic drugs, such as captopril (Capoten)[1] and pyrimethamine (Daraprim),[2] have risen substantially in recent years, threatening these gains. Effective competition can ensure low prices of generic drugs, but how much is needed remains an open question.[3]

We examined the relative prices of generic and brand-name drugs using MarketScan commercial claims data from the period 2008–2014. To ensure stable price estimates, we required a drug to have a minimum of 100 dispensings as a brand-name version and as a generic version in each calendar year. Drugs with a narrow therapeutic index (e.g., levothyroxine) were excluded.

For brand-name and generic versions of an eligible drug, the average yearly prices per dose were estimated. The outcome was the relative price of the generic version to the brand-name version. Competition levels were represented by the number of manufacturers of the generic drug in that year; the subgroup analysis included stratification according to market size.

With 1.9 billion prescription claims, the number of manufacturers of the generic drug was strongly associated with relative price ($P<0.001$ for trend) (Fig. 1). For drugs with one manufacturer of the generic version, the prices of the generic drug and the brand-name drug were similar (relative price of the generic version to the brand-name version, 87%). For drugs with a second manufacturer, the corresponding relative price decreased by 10 percentage points (relative price, 77%), and the relative price for drugs with three manufacturers decreased a further 17 percentage points (relative price, 60%). With each additional manufacturer, the relative prices decreased at a slower rate. Our findings were largely similar across the study years. Larger drug markets saw a steeper decline in the relative prices for the first four manufacturers than did their smaller counterparts.

A similar analysis that was published by the Food and Drug Administration (FDA) covering the period 1999–2004, which predates the current controversies surrounding high-cost generic drugs, showed that drug prices fell by only 6% with one manufacturer of the generic version in a market and reached 52% of the price of the brand-name version with two manufacturers.[4] By contrast, we found that the second manufacturer of a generic drug resulted in a smaller decrease in the relative price, signifying a shift in the relationship between the number of manufacturers and drug prices in the past decade.

The FDA recently announced that drugs with fewer than three manufacturers of the generic version would be eligible for expedited review as additional entrants into the generic-drug market, as previously recommended.[5] We observed that

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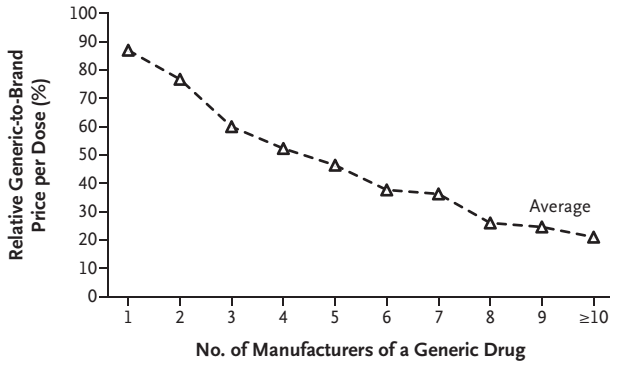

Relative Price per Dose, According to Subgroup (%)										
Average	87	77	60	52	46	38	36	26	25	21
Year										
2008	81	73	57	54	50	39	47	29	34	29
2009	78	77	50	52	49	41	39	36	23	27
2010	86	77	52	47	47	43	30	27	37	21
2011	89	69	58	50	46	37	40	23	23	21
2012	77	78	56	47	40	41	38	22	21	18
2013	109	86	78	62	42	26	29	25	18	17
2014	88	77	68	54	51	37	31	19	15	14
Market										
Small	87	77	63	56	47	38	39	27	23	28
Large	84	74	54	47	46	40	35	25	24	19

Figure 1. Relationship between the Number of Generic-Drug Manufacturers and Relative Prices of Generic Drugs to Brand-Name Drugs.

The relative prices of the generic and brand-name versions of drugs were estimated by the calculating the average relative price of a generic drug in a calendar year and comparing it with its brand-name counterpart. For the subgroup analysis, the market size was estimated by dividing the number of dispensings of an individual drug by the total number of dispensings of all generic drugs in a given calendar year; the estimated median market size was used for grouping the drugs into small and large markets.

the effect on prices by the market entry of a generic-drug manufacturer was most pronounced for the first three manufacturers, which provides empirical support for this threshold. However, other initiatives, including importation from trusted sources, should be considered to ensure the maximal amount of competition in the generic-drug market.

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Trials of Patent Foramen Ovale Closure

TO THE EDITOR: Three randomized, open-label trials — Gore REDUCE,[1] CLOSE (Patent Foramen Ovale Closure or Anticoagulants versus Antiplatelet Therapy to Prevent Stroke Recurrence),[2] and RESPECT (Randomized Evaluation of Recurrent Stroke Comparing PFO Closure to Established Current Standard of Care Treatment)[3] — the results of which were published in the *Journal* (Sept. 14 issue), showed that the risk of stroke was lower with patent foramen ovale (PFO) closure than with medical therapy alone. We have two comments. First, the trials were open-label with blinded adjudication of end-point events and did not use a sham procedure as a control. The SYMPLICITY HTN-3 study on renal denervation has shown the importance of including a sham control.[4] Second, the underlying mechanism of stroke in patients with PFO is presumably paradoxical embolism of a venous clot, and treatment is with anticoagulants, not with antiplatelet drugs. Only 25.2% of patients in the RESPECT extended trial received warfarin.[3]

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