

By Inmaculada Hernandez, Chester B. Good, David M. Cutler, Walid F. Gellad, Natasha Parekh, and William H. Shrank

DOI: 10.1377/hlthaff.2018.05147
HEALTH AFFAIRS 38,
NO. 1 (2019): 76–83
©2019 Project HOPE—
The People-to-People Health
Foundation, Inc.

CONSIDERING HEALTH SPENDING

The Contribution Of New Product Entry Versus Existing Product Inflation In The Rising Costs Of Drugs

Inmaculada Hernandez (inh3@pitt.edu) is an assistant professor of pharmacy and therapeutics at the University of Pittsburgh, in Pennsylvania.

Chester B. Good is the senior medical director for Value-based Pharmacy Initiatives at the University of Pittsburgh Medical Center (UPMC) Center for High-Value Health Care, within the Insurance Services Division of UPMC.

David M. Cutler is the Otto Eckstein Professor of Applied Economics in the Department of Economics at Harvard University and a research associate at the National Bureau of Economic Research, both in Cambridge, Massachusetts.

Walid F. Gellad is a core investigator at the Center for Health Equity Research and Promotion, Veterans Affairs Pittsburgh Healthcare System, and an associate professor of medicine at the University of Pittsburgh School of Medicine.

Natasha Parekh is a senior adviser in the UPMC Insurance Services Division.

William H. Shrank is the chief medical officer at UPMC Health Plan.

ABSTRACT It is unknown to what extent rising drug costs are due to inflation in the prices of existing drugs versus the entry of new products. We used pricing data from First Databank and pharmacy claims from UPMC Health Plan to quantify the contribution of new versus existing drugs to the changes in costs of oral and injectable drugs used in the outpatient setting in 2008–16. The costs of oral and injectable brand-name drugs increased annually by 9.2 percent and 15.1 percent, respectively, largely driven by existing drugs. For oral and injectable specialty drugs, costs increased 20.6 percent and 12.5 percent, respectively, with 71.1 percent and 52.4 percent of these increases attributable to new drugs. Costs of oral and injectable generics increased by 4.4 percent and 7.3 percent, respectively, driven by new drug entry. The rising costs of generic and specialty drugs were mostly driven by new product entry, whereas the rising costs of brand-name drugs were due to existing drug price inflation.

Rising drug costs are a pressing concern for the US health care system. Annual increases in drug costs have consistently exceeded general inflation in the past ten years.¹ Drug prices increased annually by nearly 10 percent in the period 2013–15—over six times the rate of general inflation.^{1,2}

Several studies have evaluated cost increases for different drug classes, finding that specialty drugs experienced the largest inflation, followed by brand-name drugs.^{1,3,4} However, these studies examined inflation only within existing pharmaceuticals—that is, for each time period they estimated the average change in prices for drugs that were already in the market at the beginning of the period.^{1,3,4} Although this approach is appropriate for estimating inflation, it does not address a broader question: To what

extent are rising drug costs due to inflation in the prices of existing products versus the market entry of new, more expensive drug products? Answering this question is critical in the development of policies to improve the affordability of medications in the US.

In this study we used pricing data from First Databank and pharmacy claims from UPMC Health Plan for the period 2005–16 to quantify the contribution of new versus existing drug products in the rising costs of prescription drugs used in the outpatient setting in the US.

Study Data And Methods

DATA SOURCES AND STUDY SAMPLE We obtained monthly wholesale acquisition costs for all National Drug Codes available in 2005–16 from AnalySource (used with the permission of First

Databank) and selected those drugs whose dosage form was capsules or tablets (“oral drugs”) or vials, ampules, syringes, intravenous solutions, injector pens, or infusion bottles (“injectable drugs”). Our sample included 24,877 National Drug Codes for oral drugs and 3,049 for injectable drugs. We extracted the wholesale acquisition costs in December of each year for each unit of administration (tablets, capsules, vials, or milliliters) and multiplied them by the number of units included in each code. We used the number of units included in each code as a proxy for the average number of units dispensed in a claim, because this information was not available in our data. Wholesale acquisition costs were then reported as US dollars per the average number of units included in a code.

We obtained annual counts of pharmacy claims for each code in the period 2005–16 from UPMC Health Plan. The plan is a health insurer offering self-insured and fully insured commercial, Medicare, special needs, Children’s Health Insurance Program, Medicaid, Marketplace, and behavioral health insurance to over 3.2 million members in Pennsylvania and parts of Ohio, West Virginia, and Maryland. We believe that the plan provides a generally representative indication of medication use in an insured population. We calculated annual counts of pharmacy claims for each National Drug Code, standardized as if the total number of UPMC Health Plan beneficiaries had remained constant since 2005.

DRUG CLASSES For each year we categorized drugs into new and existing products and into brand-name, specialty, and generic drugs. For each year new drug products were defined as combinations of active ingredients, dosage forms, and drug denominations (brand-name, generic, or specialty) that became available within the past three calendar years, and existing drug products were defined as those available before then. For instance, the first National Drug Code for a brand-name version of lisdexamfetamine capsules became available in 2007. All codes for brand-name versions of the capsules would be considered new drugs in 2007, 2008, and 2009, but existing drugs from 2010 onward. Similarly, the first code for a generic version of escitalopram tablets became available in 2012. All codes for generic versions of the tablets would be considered new drugs in 2012, 2013, and 2014, but existing drugs from 2015 onward.

We used this definition because previous literature has estimated that adoption of new drugs takes two to three years, on average.^{5,6} To identify specialty medications, we used a list of specialty medications obtained from a national pharmacy benefit manager,⁷ as the Department of Human and Health Services previously used such a list to

study pharmaceutical pricing.⁸ All drug products were identified at the National Drug Code level.

ANALYSIS We calculated the average weighted wholesale acquisition cost in December of every year for all drug products and stratified for new and existing drug products. This cost, which we refer to as “average weighted cost,” is the average wholesale acquisition cost of all National Drug Codes, weighted by the standardized counts of pharmacy claims for each code in the respective year.^{1,9} Then, for every year we calculated the increase in average weighted cost as the difference between the average weighted cost in December of the given year and the cost in December of the previous year, divided by the cost in December of the previous year.^{1,8,9} For example, the average weighted cost of all oral generic drugs was \$79.92 in December 2010 and \$92.06 in December 2011, so the annual change was 15.2 percent (\$92.06 minus \$79.92, or \$12.14, divided by \$79.92).

To quantify annual changes in average weighted costs that were due to existing versus new drug products, we performed a similar calculation, using the estimates for the weighted average wholesale acquisition costs for existing or for new drug products. The specific steps involved in this calculation are described and illustrated in the online appendix.¹⁰

Analyses were stratified by brand-name, specialty, and generic medications and by oral and injectable drugs, and they were conducted with the statistical software SAS, version 9.4.

LIMITATIONS Our study was subject to several limitations. First, because the US health care system is market based, data on actual transaction prices or on proprietary rebates are not accessible. As a result, we used wholesale acquisition costs as cost estimates; they represent manufacturers’ list prices for a drug to wholesalers but do not capture rebates or other types of discounts. Because rebates are often greater once several exchangeable products within the same therapeutic class have reached the market, our estimates for the relative contribution of existing drugs to the rising costs of brand-name drugs may be upward biased. In other words, after rebates are accounted for, the contribution of existing drugs may have been lower than we estimated. Additionally, because the magnitude of rebates has increased in the past decade,^{11–13} our findings likely overestimated cost increases for brand-name drugs. Nonetheless, list prices are commonly used to provide key directional information about medication prices, and patients without insurance or those with coinsurance or in high-deductible plans are exposed to those prices.

Second, in calculating average costs and annu-

al changes in those costs, we weighted each National Drug Code by the counts of use in UPMC Health Plan, because otherwise large increases in costs of drugs used by a small number of patients would have had a misleadingly large impact on our results. Although the use of weights that represent the relative use of each code is a strength of our study, the use of data from only one insurer for their calculation limited the generalizability of our results. Nevertheless, because UPMC Health Plan offers a wide range of insurance products, its use was preferred over that of other data sources that captured only one type of insurance.

Third, because we used pharmacy claims as the source of weights, our study sample was more representative of drugs commonly used in the outpatient setting than of those used in the inpatient setting. However, pharmacy claims represent 80 percent of claims for prescription drugs and account for two-thirds of total pharmaceutical spending.¹⁴

Fourth, our analyses were stratified by route of administration because our methods required the use of comparable drug market baskets. Nevertheless, drugs might not have been completely comparable across years, because the days' supply provided by an average claim could have changed across the study period. Evaluating changes in average costs per month or year of treatment could have mitigated this issue. However, this was not feasible because of the large numbers of drugs included in the study, and because many drugs are approved for several

indications that require different dosing.

Fifth, our analyses did not include drugs with dosage forms other than tablets and capsules or injectable preparations. Nevertheless, the dosage forms included in our analyses accounted for 80 percent of all National Drug Codes captured in pharmacy claims.

Finally, we did not conduct analyses that combined brand-name, specialty, and generic drugs because there was a shift from brand-name to generic drug use across our study period, and our methods required the use of comparable drug market baskets. Consequently, our study did not examine how the expiration of brand-name drug patents and those drugs' subsequent replacement with generics affected pharmaceutical spending, which has been previously described in the literature.¹⁵

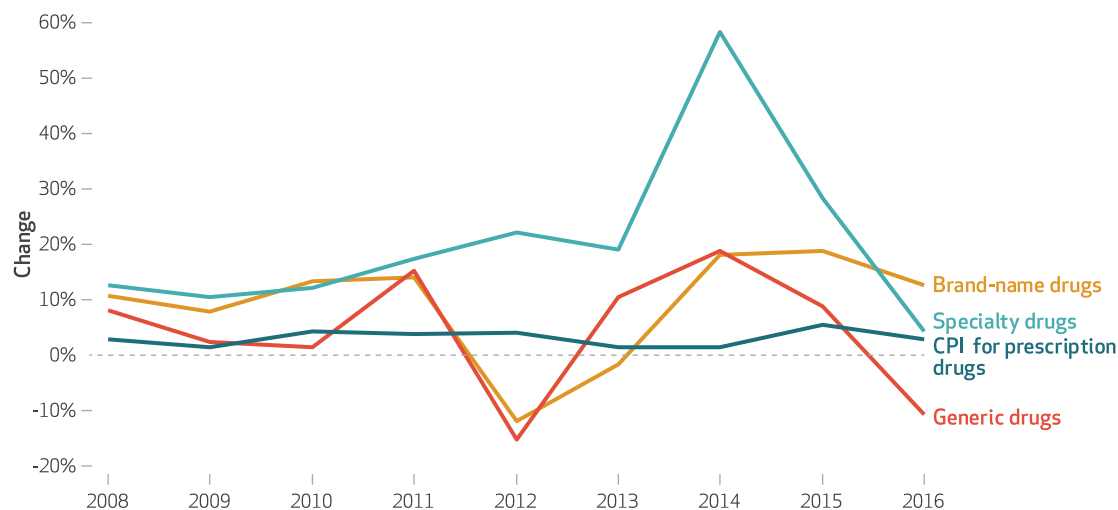
Study Results

In the period 2008–16 the number of National Drug Codes included in the study sample increased from 11,201 to 24,825 for oral drugs and from 1,708 to 3,047 for injectable drugs. Average weighted costs increased across the study period for all drug classes. For instance, for oral brand-name drugs they increased by 92 percent, from \$240.36 to \$461.34. (For the number of codes and the average weighted costs for oral and injectable drugs available in every year, see appendix exhibits A1 and A2.)¹⁰

ANNUAL CHANGES IN AVERAGE COSTS Exhibits 1 and 2 show annual percentage changes in

EXHIBIT 1

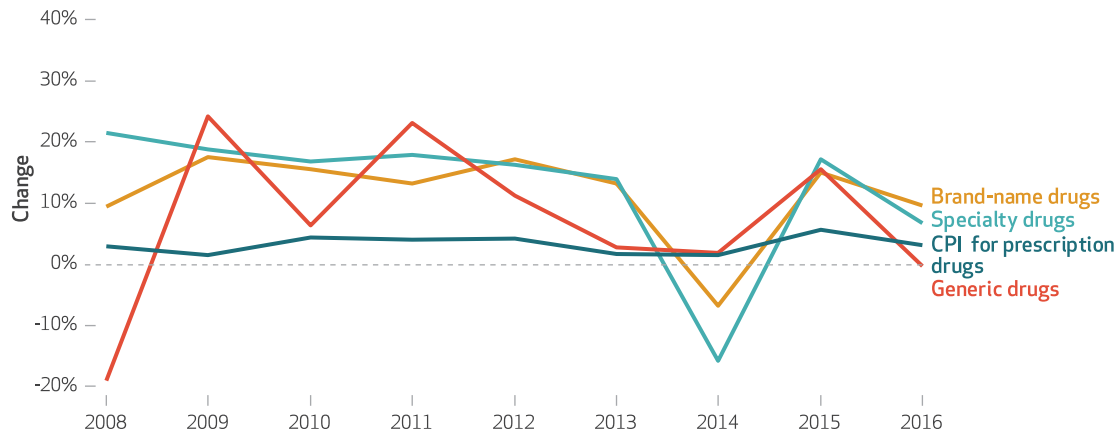
Annual percent change in the average weighted costs of oral brand-name, generic, and specialty prescription drugs, 2008–16



SOURCE Authors' analysis of pricing data from First Databank and pharmacy claims from UPMC Health Plan for the period 2005–16.
NOTES The point estimates for these annual changes are shown in exhibit 4. CPI is Consumer Price Index.

EXHIBIT 2

Annual percent change in the average weighted costs of injectable brand-name, generic, and specialty prescription drugs, 2008–16



SOURCE Authors’ analysis of pricing data from First Databank and pharmacy claims from UPMC Health Plan for the period 2005–16. **NOTES** The point estimates for these annual changes are shown in exhibit 4. CPI is Consumer Price Index.

the average weighted costs of brand-name, specialty, and generic drugs (new and existing combined) in 2008–16, and exhibit 3 shows average changes across the study period.

► **BRAND-NAME DRUGS:** Annual increases in average weighted costs of oral brand-name drugs averaged 9.2 percent across the study period. They were particularly high in 2010–11 and 2014–16, when they exceeded 10 percent (exhibit 1). Average weighted costs of injectable brand-name drugs also increased by over 10 percent in the period 2009–13 (exhibit 2). Across the study period, annual changes in average weighted costs of injectable brand-name drugs averaged 15.1 percent.

► **SPECIALTY DRUGS:** With an annual average increase of 20.6 percent, oral specialty drugs showed the largest cost increases and presented an abrupt increase in 2014 following the approval of sofosbuvir (Solvaldi) and ledipasvir/sofosbuvir (Harvoni) (exhibit 1). Annual increases in average weighted costs of injectable specialty medications exceeded 15 percent in 2008–12 (exhibit 2) and averaged 12.5 percent across the study period.

► **GENERIC DRUGS:** Average weighted costs of oral generic drugs increased in all years of the study period except for 2012 and 2016, when they decreased by more than 10 percent (exhibit 1). Across the study period, average weighted costs of oral generics increased by an average of 4.4 percent. Annual changes in average weighted costs of injectable generic drugs averaged 7.3 percent across the study period. They were particularly high in 2009, 2011, 2012, and 2015, when they exceeded 10 percent (exhibit 2).

NEW VERSUS EXISTING DRUG PRODUCTS Exhibit 4 shows the relative contributions of existing and new drug products in the annual changes in average weighted costs of oral and injectable drugs in 2008–16, and appendix exhibits A3 and A4 present these results in a visual manner.¹⁰ Exhibit 3 summarizes the relative contributions of existing and new drug products across the study period.

► **ORAL BRAND-NAME DRUGS:** Across the study period, 87.3 percent of the annual in-

EXHIBIT 3

Relative contributions of new and existing drugs to the average annual percent change in average weighted costs of oral and injectable drugs, by drug class, 2008–16

Drug class	Oral drugs (%)	Injectable drugs (%)
BRAND-NAME DRUGS		
Average annual change	9.2	15.1
Relative contribution		
Existing drugs	87.3	104.3
New drugs	12.7	-4.3
SPECIALTY DRUGS		
Average annual change	20.6	12.5
Relative contribution		
Existing drugs	28.9	47.6
New drugs	71.1	52.4
GENERIC DRUGS		
Average annual change	4.4	7.3
Relative contribution		
Existing drugs	-68.2	-30.0
New drugs	168.2	130.0

SOURCE Authors’ analysis of pricing data from First Databank and pharmacy claims from UPMC Health Plan for 2005–16. **NOTES** The table shows averages across 2008–16. Existing and new drugs are explained in the text.

creases in average weighted costs of brand-name drugs was attributable to existing drugs and 12.7 percent to new drug products (exhibit 3). The average weighted costs of oral brand-name drugs decreased by over 10 percent in 2012 (exhibit 4), coinciding with the patent expirations of several widely used brand-name drugs—including atorvastatin, clopidogrel, olanzapine, quetiapine, escitalopram, montelukast, esomeprazole, and methylphenidate.

► **INJECTABLE BRAND-NAME DRUGS:** Across the study period, increases in the average weighted costs of injectable brand-name drugs were mostly driven by existing drugs (exhibit 3). However, in 2010 and 2011, following the approval of paliperidone (Invega Sustenna), 60.5 percent and 80.2 percent, respectively, of the increases in average weighted costs of injectable brand-name drugs were attributed to new drug products (exhibit 4 and appendix exhibit A4).¹⁰ In

2012–16 cost increases were due to inflation in the prices of existing drugs, particularly insulins. In this period, new brand-name drugs had a negative contribution to the annual changes in average weighted costs. This was driven by influenza vaccines, which were cheaper than average brand-name injectable drugs and were continuously considered new medications because their formulations were registered as new active ingredients every year.

► **ORAL SPECIALTY DRUGS:** Costs of oral specialty drugs showed the largest annual increases, 71.1 percent of which were due to market entry of new drug products and 28.9 percent to existing drug price inflation (exhibit 3). The contribution of new drug products to these increases was particularly high in 2014, following the approval of sofosbuvir (Sovaldi) and ledipasvir/sofosbuvir (Harvoni) (exhibit 4 and appendix exhibit A3).¹⁰ In 2010–12 annual changes in the average

EXHIBIT 4

Relative contributions of new and existing drugs to the annual percent change in average weighted costs of oral and injectable drugs, by drug class, 2008–16

	2008	2009	2010	2011	2012	2013	2014	2015	2016
ORAL DRUGS									
Brand-name									
Average annual change	10.7%	8.0%	13.3%	14.0%	-11.9%	-1.5%	18.2%	18.9%	12.8%
Relative contribution									
Existing drugs	102.3	103.6	102.5	98.3	117.2	250.7	87.2	87.3	83.3
New drugs	-2.3	-3.6	-2.5	1.7	-17.3	-150.6	12.8	12.7	16.7
Specialty									
Average annual change	12.8	10.7	12.3	17.4	22.2	19.2	58.3	28.5	4.4
Relative contribution									
Existing drugs	54.9	77.4	80.0	94.7	97.1	53.8	8.0	-46.9	-251.0
New drugs	45.1	22.6	20.0	5.3	2.9	46.2	92.0	146.9	351.0
Generic									
Average annual change	8.2	2.5	1.4	15.2	-15.1	10.5	18.8	8.8	-10.5
Relative contribution									
Existing drugs	36.6	-216.6	-404.2	29.5	136.1	6.4	53.4	8.7	136.9
New drugs	63.3	316.4	504.2	70.6	-36.1	93.6	46.6	91.3	-36.9
INJECTABLE DRUGS									
Brand-name									
Average annual change	15.5%	6.7%	19.6%	25.3%	17.3%	11.9%	27.4%	5.3%	6.8%
Relative contribution									
Existing drugs	75.7	78.4	39.5	19.8	133.4	153.4	129.7	299.8	280.4
New drugs	24.3	21.6	60.5	80.2	-33.4	-53.4	-29.7	-199.8	-180.3
Specialty									
Average annual change	21.5	18.8	16.7	17.9	16.2	13.9	-15.9	17.2	6.8
Relative contribution									
Existing drugs	70.6	-1.3	-40.4	70.7	85.1	106.6	98.5	91.6	64.4
New drugs	29.4	101.3	140.4	29.3	14.9	-6.5	1.5	8.4	35.6
Generic									
Average annual change	-19.0	24.1	6.4	23.0	11.1	2.7	1.9	15.6	-0.4
Relative contribution									
Existing drugs	102.9	39.5	-133.4	41.8	15.9	-379.8	-521.2	52.7	165.8
New drugs	-2.9	60.5	233.4	58.2	84.0	479.6	621.9	47.4	-65.8

SOURCE Authors' analysis of pricing data from First Databank and pharmacy claims from UPMC Health Plan for 2005–16. NOTE Existing and new drugs are explained in the text.

weighted costs of oral specialty medications were largely accounted for by existing drugs.

► **INJECTABLE SPECIALTY DRUGS:** Across the study period, 52.4 percent of the increases in costs of injectable specialty medications were due to the entry of new drugs and 47.6 percent to existing drug price inflation (exhibit 3). In 2009 and 2010, following the approval of ustekinumab (Stelara) and golimumab (Simponi), new drugs were the main contributors to cost increases (exhibit 4 and appendix exhibit A4).¹⁰ However, in 2011–15 over 70 percent of the cost increases were due to existing drugs. In 2014 the average weighted costs of injectable specialty medications decreased because of an abrupt decrease in the price of glatiramer acetate.

► **ORAL GENERIC DRUGS:** Across the study period, existing generic drugs had a negative contribution to the annual change in the average weighted costs of oral generics (exhibit 3). However, new generic products were more expensive than those already on the market (appendix exhibit A1)¹⁰ and tended to increase the average weighted costs. The average weighted costs of oral generics decreased by over 15 percent in 2012 (exhibit 1), following strong decreases in the prices of widely used existing generic products, including omeprazole, simvastatin, and lisinopril.

► **INJECTABLE GENERIC DRUGS:** Similarly, increases in the costs of injectable generics were driven by the entry of new generic products (exhibit 3). Existing generics had a negative contribution to average weighted costs in most years, particularly in 2010, 2013, and 2014, when prices decreased abruptly. The contribution of new generic products was particularly high in 2009–14, following the market entry of generics for enoxaparin, sumatriptan, oxaliplatin, and zoledronic acid.

Discussion

To our knowledge, our study is the first to quantify the contributions of new versus existing drug products to the rising costs of outpatient prescription drugs observed in the past decade. Our analyses yielded three main findings. First, costs increased considerably faster than inflation across all drug classes, and increases were highest for oral specialty drugs and lowest for oral generics. Second, rising costs of brand-name drugs were driven by inflation in the prices of widely used existing drugs, and rising costs of specialty drugs were due to a combination of new product entry and existing product price inflation, with new drug product entry accounting for a larger proportion of rising costs. Finally, existing generics tended to decrease the average costs

of generic drugs. However, new generic products were more expensive than those already in the market, which drove the annual increases in average costs that we observed.

Our results are consistent with those of previous reports showing that specialty drugs had the largest cost increases (about 12.5 percent every year), followed by brand-name drugs (with average annual increases of 5–10 percent).¹ Our observation that new and existing drug products contribute in opposite directions to the annual changes in average costs of generics explains the apparently contradictory results in previous studies.^{1,3} Whereas those that quantified inflation for a fixed basket of generics found that costs decreased annually by 7.5 percent,¹ studies that factored in new generics estimated that costs increased by 3 percent.³ However, our estimates for the annual changes in average costs are considerably higher than those reported by the Consumer Price Index (CPI) for prescription drugs,¹⁶ which likely reflects the different methods used in the calculation of these estimates. Because inclusion in the basket of drugs measured by the CPI is dependent on popularity, new drugs are less likely to be included in the CPI.¹⁷ Moreover, when new products are introduced into the basket, their prices are not compared to those of existing products.^{18,19} Because most of the price increases related to the appearance of new drugs is experienced at market entry, the CPI does not capture increases in drug prices due to the entry of new products that are more expensive than existing ones.²⁰ Another important methodological difference is the calculation of weights: Whereas we used annual counts of pharmacy claims as weights, the weight of each drug in the CPI is calculated as a series of probabilities that represent the probability that a specific outlet within a region will be included in the sample, and the relative use of every drug is calculated from the Consumer Expenditure Survey, which is updated every two years.¹⁹ In fact, a prior study found that when CPI methodology was followed but IQVIA National Prescription Audit data and monthly pharmacy sales data were used as weights, estimates for price indexes for prescription drugs were larger than those reported by the CPI.¹⁹

Our study has important implications. First, costs increased faster than general inflation across all drug categories. Even for oral generics, the class with the smallest changes, annual increases were more than double rates of general inflation in the same time period. In the case of specialty drugs, average costs increased thirteen times faster than general inflation. These increases threaten the affordability of pharmaceutical benefits coverage by US public payers and

warrant consideration of more potent policies to control drug prices, in particular for government payers.

Second, rising generic costs were largely driven by the entry of new products, which is not unexpected because in 2008–16 numerous blockbuster brand-name medications lost patent protection.²¹ This strong contribution of new generics explains why average costs of generics increase over time,³ even though competition inherent in the generic market should theoretically drive prices down.

Third, whereas the increasing costs of specialty drugs were largely driven by new products, the rising costs of brand-name drugs were mostly due to existing drug price inflation. These results illustrate how the distinction between specialty and nonspecialty drugs, often defined based on price, affects the measurement of drug price inflation and new drug spending: New and expensive brand-name drugs are often considered specialty medications.

Finally, despite few new blockbuster entrants, the average costs of oral and injectable brand-name drugs increased 9.2 percent and 15.1 percent, respectively, on average, every year, with

most of these increases being attributed to cost increases in existing drug prices. Specifically, inflation in prices for oral and injectable brand-name drugs averaged 8 percent and 16 percent, respectively, which is five to eight times the general rate of inflation in the same time period. These estimates demonstrate the important contribution of existing product price inflation on the rising cost of drugs and lend support to policy efforts aimed at controlling price inflation. This is particularly important because in the current value-based landscape, increasing drug costs attributable to new products can sometimes be justified on the basis of improved outcomes. However, rising costs due to inflation do not reflect improved value for patients.

Conclusion

In this retrospective study of pharmaceutical pricing data for 2005–16, we found that increases in the costs of specialty and generic drugs were driven by the entry of new drug products, but rising costs of brand-name drugs were largely due to inflation in existing medication prices. ■

Chester Good, Natasha Parekh, and William Shrank are employees of the Insurance Services Division, University

of Pittsburgh Medical Center (UPMC). The authors thank Angela Merrell from UPMC Health Plan for her help in

extracting pharmacy claims for the study sample.

NOTES

- Schondelmeyer SW, Purvis L. Trends in retail prices of prescription drugs widely used by older Americans, 2006 to 2013 [Internet]. Washington (DC): AARP Public Policy Institute; 2016 Feb [cited 2018 Nov 13]. Available from: <https://www.aarp.org/content/dam/aarp/ppi/2016-02/RX-Price-Watch-Trends-in-Retail-Prices-Prescription-Drugs-Widely-Used-by-Older-Americans.pdf>
- Walker J. Drugmakers' pricing power remains strong. *Wall Street Journal* [serial on the Internet]. 2016 Jul 14 [cited 2018 Nov 13]. Available from: <https://www.wsj.com/articles/drugmakers-pricing-power-remains-strong-1468488601>
- Dennis B. Prescription drug prices jumped more than 10 percent in 2015, analysis finds. *Washington Post* [serial on the Internet]. 2016 Jan 11 [cited 2018 Nov 1]. Available from: <https://www.washingtonpost.com/news/to-your-health/wp/2016/01/11/prescription-drug-prices-jumped-more-than-10-percent-in-2015/>
- Penington R, Stubbings JA. Evaluation of specialty drug price trends using data from retrospective pharmacy sales transactions. *J Manag Care Spec Pharm*. 2016;22(9):1010–7.
- Hernandez I, Zhang Y. Comparing adoption of breakthrough and “me-too” drugs among Medicare beneficiaries: a case study of dipeptidyl peptidase-4 inhibitors. *J Pharm Innov*. 2017;12(2):105–9.
- Garjón FJ, Azparren A, Vergara I, Azaola B, Loayssa JR. Adoption of new drugs by physicians: a survival analysis. *BMC Health Serv Res*. 2012;12:56.
- CVS Specialty. CVS specialty pharmacy distribution drug list [Internet]. Woonsocket (RI): CVS Specialty; 2018 Oct [cited 2018 Nov 28]. Available from: <https://www.cvsspecialty.com/education-center/downloads/SpecialtyDrugs.pdf>
- Department of Health and Human Services, Office of the Assistant Secretary for Planning and Evaluation. Observations on trends in prescription drug spending [Internet]. Washington (DC): HHS; 2016 Mar 8 [cited 2018 Nov 13]. (ASPE Issue Brief). Available from: <https://aspe.hhs.gov/system/files/pdf/187586/Drugspending.pdf>
- Department of Health and Human Services, Office of Inspector General. Calculation of volume-weighted average sales price for Medicare Part B prescription drugs [Internet]. Washington (DC): HHS; 2006 Feb [cited 2018 Nov 13]. Available from: <https://oig.hhs.gov/oei/reports/oei-03-05-00310.pdf>
- To access the appendix, click on the Details tab of the article online.
- Boards of Trustees, Federal Hospital Insurance and Federal Supplementary Medical Insurance Trust Funds. 2017 annual report of the Boards of Trustees of the Federal Hospital Insurance and Federal Supplementary Medical Insurance Trust Funds [Internet]. Baltimore (MD): Centers for Medicare and Medicaid Services; 2017 Jul 13 [cited 2018 Nov 1]. Available from: <https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/ReportsTrustFunds/Downloads/TR2017.pdf>
- IQVIA. Medicines use and spending in the U.S.: a review of 2016 and outlook to 2021 [Internet]. Parsippany (NJ): IQVIA; 2017 May 4 [cited 2018 Nov 13]. Available (registration required) from: <https://www.iqvia.com/institute/reports/medicines-use-and-spending-in-the-us-a-review-of-2016>
- Bai G, Sen AP, Anderson GF. Pharmaceutical benefit managers, brand-

- name drug prices, and patient cost sharing. *Ann Intern Med.* 2018; 168(6):436–7.
- 14 Minnesota Department of Health All Payer Claims Database. Pharmaceutical spending and use in Minnesota: 2009–2013 [Internet]. Saint Paul (MN): The Department; 2016 Nov [cited 2018 Nov 13]. (Issue Brief). Available from: <http://www.health.state.mn.us/healthreform/allpayer/RxIssueBriefProof20161102.pdf>
 - 15 Aitken M, Berndt ER, Cutler D, Kleinrock M, Maini L. Has the era of slow growth for prescription drug spending ended? *Health Aff (Millwood)*. 2016;35(9):1595–603.
 - 16 Bureau of Labor Statistics. Databases, tables, and calculators by subject: prescription drugs in U.S. city average, all urban consumers, seasonally adjusted [Internet]. Washington (DC): BLS; 2018 [cited 2018 Nov 13]. Available from: https://data.bls.gov/timeseries/CUSR0000SEMF01?output_view=pct_3mths
 - 17 Griliches Z, Cockburn I. Generics and new goods in pharmaceutical price indexes [Internet]. Cambridge (MA): National Bureau of Economic Research; 1993 Feb [cited 2018 Nov 13]. (NBER Working Paper No. 4272). Available from: <http://www.nber.org/papers/w4272.pdf>
 - 18 Bureau of Labor Statistics. Handbook of methods [Internet]. Washington (DC): BLS. Chapter 17, The Consumer Price Index [last updated 2018 Feb 14; cited 2018 Nov 13]. Available from: <https://www.bls.gov/opub/hom/pdf/homch17.pdf>
 - 19 Bosworth B, Bieler J, Kleinrock M, Koepcke E, Berndt ER. An evaluation of the CPI indexes for prescription drugs [Internet]. Washington (DC): Brookings Institution; 2018 Jan 22 [cited 2018 Nov 13]. Available from: https://www.brookings.edu/wp-content/uploads/2018/01/es_20180103_bosworthcpiindexes_final.pdf
 - 20 Armknecht PA, Lane WF, Stewart KJ. New products and the U.S. Consumer Price Index. In: Bresnahan TF, Gordon RJ, editors. *The economics of new goods*. Chicago (IL): University of Chicago Press; 1997. p. 373–96.
 - 21 Harrison C. Patent watch: the patent cliff steepens. *Nat Rev Drug Discov.* 2011;10(1):12–3.