EDITORIAL

Affording Medicines for Today's Patients and Sustaining Innovation for Tomorrow

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This is a time of unprecedented medical progress. Breakthrough science is transforming patient outcomes and enabling clinicians to treat—and sometimes cure—diseases that previously posed insurmountable challenges to people's health. However, many individuals in the United States are increasingly concerned about the out-of-pocket expenses they face in gaining access to the care they need. Escalating insurance premiums, co-insurance expenses, and co-payments can be financially devastating for individuals and families. Many patients with private insurance are shocked to learn that, even when they received care at a network facility, large balance bills—"surprise" medical bills for noncovered clinicians, ambulances, and other services—can amount to thousands of dollars.[1] But perhaps nothing has galvanized the current groundswell of populist outrage more than the money patients must pay for their prescription drugs in retail pharmacies. As a result, many patients skip doses because they simply cannot afford to pay for their medications or do not fill their prescriptions.[2,3] This should not be.

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The proportion of health care expenditures attributable to prescription drugs has been relatively constant, but the proportion patients pay is increasing.[4] Furthermore, many more people take prescription drugs than need expensive inpatient services, so out-of-pocket drug affordability has emerged as a central focus of the overall health care affordability debate, one that cuts across political parties at the federal, state, and community levels and is likely to intensify in the coming months. This issue of *JAMA* includes important and timely updates on 3 dimensions of drug affordability: the costs of discovering and developing innovative drugs, trends in drug pricing, and the profitability of biopharmaceutical companies.[5-7]

The report by Wouters et al[5] contributes new perspectives on the costs associated with drug research and development. The authors used audited financial disclosures from publicly traded companies between 2009-2018 to consider not only the costs of bringing a successful therapy to market, but also the costs of the many failures at various stages of development that typically precede the rare successes. However, their methodology excluded most products developed by larger companies, which usually report research expenses in aggregate form and not product-by-product. As a result, the subset of products included in the analyses was enriched with niche drugs that are dissimilar from the broader population of drugs approved by the US Food and Drug Administration (FDA) during the last decade. Specifically, the study sample has a higher proportion of orphan drugs and drugs that received accelerated approvals, and those characteristics often reduce clinical development costs, compared with costs associated with large-scale and long-term outcome studies of primary care or neurodegenerative disease treatments or studies of drugs with multiple indications.

In addition, the costs of failure were derived by dividing the costs associated with each phase of development by the estimated probability of success (POS) of that phase. This analysis was quite sensitive to small changes in assumed POS, which produce large variances in the median expenses associated with approved agents (as shown in Table 2 of the article).[5] Regardless of the precision of numerical estimates, one conclusion is clear: drug development is fraught with the risk of failure and ever-increasing development costs; these factors contribute to disturbing projections of further declines in research and development productivity across the industry and the influence that could have on the innovation ecosystem.[8]

In another report in this issue, Hernandez et al[6] evaluated trends in drug list prices and net prices (after discounts, rebates, co-payment cards, 340B discounts, and other price concessions provided by manufacturers) in the United States between 2007-2018. Inclusion of net prices in this assessment is important because list prices generally do not reflect what is actually paid for prescription drugs in the marketplace. Even though net prices are confidential, the SSR Health methodology used in their analysis does provide a reasonable overall approximation of net pricing trends. Yet the study does not include assessment of the most critical pricing issue—the actual out-of-pocket costs incurred by patients. Manufacturer discounts from list prices are generally not passed on to patients, and many patients are exposed to the full list price of drugs before they reach their deductibles, out-of-pocket spending caps (if they have one), or both. In fact, about 50% of the total amount spent on branded prescription drugs is retained by payers, hospitals, distributors, and others in the supply chain, not the manufacturer.[9]

In the third article in this issue, Ledley et al[7] used robust regression models to assess the median profitability of pharmaceutical companies listed in the 2018 S&P 500 compared with other large companies in that index over the years 2000-2018, using publicly reported measures of annual profit: gross profit, earnings before interest, taxes, depreciation, and amortization (EBITDA), and net income. Given the vastly different business models across the industries included in this study, comparing gross profit and EBITDA across companies is problematic, and net profit is probably the most useful margin ratio to consider. In addition,

measures of actual financial return (return on invested capital, return on equity, return on assets) are missing from this report. These measures are also important parameters for comparison, especially because many biopharmaceutical companies are research-intensive and funded by investors who deploy capital at fairly high risk over long periods of time and, consequently, demand higher returns. Given the "apples to oranges" nature of the comparisons across the highly variable set of S&P 500 companies, additional assessment of returns and cash flows could be enlightening.

In addition, the companies in the 2018 S&P 500 are by definition "winners" at the point in time the cohort was selected. What is not addressed in this report are the "losers," ie, companies that at one time qualified for the index but were removed, acquired, or went out of business during the look-back study period. Given the inherent risk of failure in the search for breakthroughs, the long time horizon of returns, and the resultant consolidation across the biopharmaceutical industry, comparing profitability with other industries over time may not represent an accurate comparison of industry profitability.

Collectively, the 3 reports in this issue of *JAMA* make one overarching point that should not be overlooked: the biopharmaceutical industry is adjusting its business model in response to concerns about affordable access to medicines and is still making substantial research and development investments to sustain the innovation ecosystem. In a departure from earlier trends, Hernandez et al[6] found that from 2015 to 2018, net drug prices in the United States have been stable. As the authors point out in their sensitivity analysis, if new drugs are included, net prices have actually been decreasing since 2015. Likewise, Ledley et al[7] report that over the past 5 years, between 2014-2018, pharmaceutical net income was markedly lower than in earlier years, and there was no significant difference between the net income margin of pharmaceutical companies compared with other S&P 500 companies during this period. Nevertheless, pharmaceutical companies continue to make large investments in research and development in the pursuit of treatments and cures for the still-significant unmet medical needs of patients across the globe.[5,8]

These trends—declining net prices and growing discovery and development expenses, coupled with reimbursement policy uncertainties in virtually every market—create unprecedented challenges for the biopharmaceutical industry and threaten future investments in innovation. At the same time, the scientific prospects for breakthrough medicines and vaccines have never been more promising. To fulfill that promise, all sectors of the health care system need to work together to solve the affordability challenges encountered by patients without jeopardizing the hopes of those waiting for tomorrow's cures. Even though the price of medicines overall may be increasing at the slowest rate in years, the system is still not working for patients who are paying more out-of-pocket due to the complex system of pricing, distribution, and above all, the regressive insurance benefit designs in which most patients are enrolled. This is true irrespective of the actual price of the medication. Solving this will take effort on the part of pharmacy benefit managers, insurers, government, industry, and other partners, and the biopharmaceutical sector must do its part to help patients now.

First, the biopharmaceutical industry has a duty to be responsible in pricing practices and to contribute to solutions that address patient affordability. Responsible pricing includes publishing useful information about prices and the aggregate rebates and discounts provided to payers within an appropriate context. For instance, for Merck, this includes pledging to not increase average net prices for the company's portfolio by more than the rate of inflation annually. It also includes supporting policies and other strategies for ending price gouging by those who excessively increase off-patent drug prices with no alternative suppliers[10]—a practice that is especially harmful to vulnerable patients and an egregious violation of what Merck views as the "social contract" between biopharmaceutical companies and society.

Second, the drug rebate system must be reformed so that patients benefit directly from the discounts and other pricing concessions that currently benefit the insurers and pharmacy benefit managers. The current system perversely creates incentives that favor choosing products with higher list prices, a practice that further penalizes patients with high deductibles or high co-insurance plans.

Third, the biopharmaceutical industry must respect the intent of the patent protections it enjoys and encourage generic competition when the period of patent protection ends, without inappropriately gaming the system. For instance, to encourage uptake of generic medications, Merck does not provide coupons for its medications once a generic version of the medication enters the market. Likewise, the industry and government must work to encourage a robust biosimilars market in the United States and elsewhere and advocate for uptake of biosimilars to reduce spending for patients and health systems.

Fourth, the biopharmaceutical industry needs to collaborate across the health system to accelerate effective advocacy for the policy changes that will allow companies to more readily negotiate value-based contracts (ie, innovative arrangements that base reimbursement on the benefits of a drug to patients and society). Likewise, industry needs to join with other stakeholders (such as patients, clinicians, payers, and government) to achieve reforms to ensure that Medicare Part D beneficiaries are protected by a cap on out-of-pocket expenses.

Finally, the biopharmaceutical industry must align with the other segments of the health care system, whether for-profit or not-for-profit, to ensure that the vital health care businesses on which patients and society depend remain sustainable. This includes affirming patients as central to the fundamental mission of the biopharmaceutical industry and collaborating across system stakeholders to reduce the cost and complexity of health care. Only by working together can health security for patients be achieved. Patients deserve to have confidence that they will be able to access the medicines, vaccines, and health services they need to prevent, treat, and hopefully cure diseases that today all too often threaten their health and financial future. After all, achieving better health and curing disease is the best solution to rising health care costs.

ARTICLE INFORMATION

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