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Perspective

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Addressing Generic-Drug Market Failures — The Case for Establishing a Nonprofit Manufacturer

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Robust competition usually keeps the price of generic drugs well below that of brand-name drugs. When there is little or no competition, however, generic-drug manufacturers can substantially increase prices, and drug shortages may occur. Such market failures can compromise care and negatively affect patients, health care providers, government insurance programs, and private health plans.[1,2]

One strategy for generic-drug manufacturers seeking to maximize profit is to enter a market where they have the capacity to produce enough of a drug to meet market demand and the power to dictate the drug's price. In 2010, for example, Valeant acquired the rights to Syprine (trientine hydrochloride), a drug invented in the 1960s to treat Wilson's disease, a rare condition, and subsequently raised its price by more than 3000% for a monthly supply, from $652 to $21,267. Similarly, in 2015 Turing acquired the rights to Daraprim (pyrimethamine), a drug used to treat toxoplasmosis, which has a market of only 6000 patients in the United States, so that one manufacturer could supply the entire market. Turing then raised the price of Daraprim by more than 5000% for one tablet, from $13.50 to $750. In these and other cases, policymakers and economists have asked, "Why don't other manufacturers enter this seemingly lucrative market?"

One reason is that the start-up costs for entering generic-drug markets can be substantial relative to the size of the market for a particular drug because of the initial investment required and the cost of obtaining Food and Drug Administration (FDA) approval. More important, however, is the threat that the current manufacturer (Valeant, in the case of Syprine, or Turing, in the case of Daraprim) will drastically reduce the price of its product once the FDA grants approval for the new entrant. The threat of a price collapse imposes a substantial financial risk for prospective for-profit entrants. Although the FDA and Congress have taken steps to foster greater competition in generic-drug markets,[3] such as offering expedited review and restricting the use of limited-distribution networks (in which a manufacturer allows only a certain number of pharmacies to distribute a specialty drug), many generic drugs are still supplied by a small number of manufacturers. Using limited-distribution networks can obstruct access to drug samples that competing manufacturers are seeking in order to conduct testing to submit a generic or biosimilar drug application to the FDA.[4]

We believe that market-based solutions are an important alternative approach to stimulating

competition in generic-drug markets. One such solution is to establish a nonprofit generic-drug manufacturer with the explicit mission of producing affordable versions of essential drugs and ensuring a stable supply of such products. A consortium of hospitals and health plans, including Intermountain Healthcare, Trinity Health, SSM Health, and Ascension, in collaboration with the Department of Veterans Affairs and philanthropists, is following this approach and developing a nonprofit generic-drug manufacturer code-named Project Rx.

A nonprofit generic-drug manufacturer, which cannot sell equity shares, can initially be funded by philanthropic contributions. It can contract with existing manufacturing facilities or, if necessary, establish its own facilities and rely on guaranteed purchases by institutional partners, such as hospitals, health plans, and government agencies. These institutions, which need uninterrupted access to generic drugs and have a financial incentive to purchase them at reasonable prices, will provide a stable revenue source for the manufacturer.

Hospitals and other institutional partners know which drugs they need (and in what quantities), the price and shortage histories for various drugs, and the competitiveness of each market and its vulnerability to market failures. Before a nonprofit manufacturer begins finding investors and initiating production, it can enter into agreements to sell generic drugs directly to these institutional partners at predetermined low prices and with a contracted minimum volume. Such purchasing agreements protect the manufacturer from being forced out of the market by a for-profit manufacturer that reduces the price of a competing product. Donations from philanthropists and institutional partners can be used to finance a nonprofit manufacturer's start-up costs (usually about $200,000 per drug, which covers the FDA Abbreviated New Drug Application filing fee and bioequivalence testing).[5] With its distinctive nonprofit orientation, capital structure, and marketing strategy, such a manufacturer might overcome entry barriers that deter potential for-profit entrants from competing in some generic-drug markets, since it cannot be forced out because of price changes in the market. If an existing for-profit manufacturer reduces the price of its product to compete with the nonprofit manufacturer, patients and payers will benefit from greater access to cheaper drugs.

Once a nonprofit manufacturer enters the market, it will have the potential to provide a stable supply of generic drugs at an affordable price. Its cost of capital will be low because it doesn't need to pursue a certain level of profit to attract equity investors. The legal constraint that it cannot distribute earnings and the relationship it maintains with its institutional purchasers ensure that the manufacturer will pursue a cost-plus strategy — generating only enough revenue to cover costs and maintain a limited surplus for financial viability — rather than a profit-maximization strategy. Furthermore, the manufacturer's tax-exempt status will allow it to rely on charitable contributions as well as patent donations from brand-name drug manufacturers to bring generic drugs to the market, thereby lowering its cost of operation.

A nonprofit manufacturer can make some generic drugs substantially more affordable. For example, the cost of manufacturing one Daraprim tablet through outsourcing contracts is less than 10 cents. Assuming that a $200,000 one-time cost of entering the market for Daraprim is to be paid off within 1 year, the cost for each tablet would be approximately 35 cents (10 cents of manufacturing cost plus 25 cents of average one-time cost). Even allowing for a 10-fold markup to cover administrative and other expenses, the nonprofit manufacturer can set a price of $3.50 per tablet — less than 0.5% of the price of Daraprim after it was acquired by Turing ($750) and roughly one quarter of the price before the acquisition ($13.75).

To ensure that a nonprofit manufacturer's operations are aligned with its core mission, its institutional partners and major donors can serve on its board of trustees. Participation on the board by institutional partners, who have a financial interest in keeping prices low, will strengthen the board's fiduciary responsibility and further constrain the manufacturer from engaging in price-gouging behaviors. The manufacturer's portfolio of products might initially be limited to drugs with the most severe price distortion and supply shortages as well as drugs that are in high demand among its institutional partners. One place to start could be generic injectable drugs, which are used primarily for hospital inpatients, account for most of the drugs on the FDA's list of current drug shortages, and have experienced substantial price increases in recent years. As the capacity of the nonprofit manufacturer expands, its product portfolio can be diversified to include a broader range of generic drugs, and its distribution channels can be expanded to include group purchasing organizations and pharmacy benefit managers. Eventually, the

presence of nonprofit manufacturers will bring increased competition to areas of the generic-drug market where market failure is prevalent, which will motivate for-profit manufacturers to reduce prices and stabilize supply.

An audio interview with Mr. Liljenquist is available at NEJM.org

The complex nature of market failures for generic drugs implies that a single alternative business model cannot address all aspects of this problem. We believe that Project Rx may drive other nonprofit and for-profit manufacturers to enter generic-drug markets, compete among themselves, and collectively improve market efficiency and broaden access to generic drugs.

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HIV Population Surveys — Bringing Precision to the Global Response

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The past two decades have seen extraordinary advances in our understanding of human immunodeficiency virus (HIV). The global scale-up of access to antiretroviral therapy (ART) for people living with HIV is perhaps the greatest of these advances. As of the end of 2017, more than 20 million of the world's 37 million people with HIV were taking ART, often in the form of a single pill a day. Despite this major public health achievement, almost 2 million new infections continue to occur each year,[1] leaving many countries, primarily in sub-Saharan Africa, with a daunting epidemic.

In order to make further progress, countries need to answer some fundamental questions: How well are they faring in responding to their national epidemics? Where have they succeeded and where have they fallen short? What would be the best focus for future resources and efforts?

Until now, the information needed to answer these questions has come largely from health facility data and mathematical modeling. Each of these sources has its limits. Health facility HIV data vary in quality and include information only from people who have already tested HIV-positive. Key groups are missing: those who have not had an HIV test and are unaware of their HIV-positive status, those who may be aware of their HIV-positive status but have yet to present at health facilities and engage in care, and those who've been lost to follow-up. Projections from mathematical models are useful in understanding the trajectory of an epidemic but often depend on health facility data and on a series of assumptions.

These limitations highlight the need for population-based, directly measured estimates. Such data provide a more complete picture of an epidemic, including the gaps in the response, and point the way to focused approaches and efficient use of resources. Some population measures of the HIV epidemic have been available through the Demographic and Health Surveys and AIDS Indicator Surveys, but these surveys have not provided direct estimates of critically important measures, such as HIV incidence, population-level viral load suppression (defined as HIV RNA <1000 copies per milliliter) as well as other essential biomarkers needed to measure progress.

To address the need for detailed population HIV measures, the Population-based HIV Impact Assessment (PHIA) Project was launched in 2014 (http://phia.icap.columbia.edu/) to conduct HIV-focused, household-based, nationally representative surveys of adults and children in 14 high-burden countries. These surveys, funded by the President's Emergency Plan for AIDS Relief and conducted by ICAP at Columbia University in partnership with ministries of health and the Centers for Disease Control and Prevention, go beyond measuring HIV prevalence.