A novel prescription to combat drug shortages

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The generic drug trilemma, depicted above with related policy reforms. A better understanding of the policy trade-offs could help ease supply shortages, SIEPR scholar Lisa Ouellette says. Credit: Stanford University

Prescription drug shortages, a longstanding issue for patient care in the United States, are reportedly reaching all-time highs. Safety lapses at

manufacturing sites, razor-thin profit margins, and stiff competition have all been blamed in recent months as doctors scramble to find chemotherapy drugs, antibiotics, and other potentially life-saving therapies now in short supply.

As the Biden administration and members of Congress weigh what to do, Lisa Larrimore Ouellette, a Stanford Law School professor, argues that policymakers need to think differently about solutions to the crisis. In a recently published analysis, she details a new approach to understanding the underlying problems—and makes the case for how it supports new forms of drug manufacturing and a crackdown on deceptive practices within the industry.

The analysis—by Ouellette, who is also a senior fellow at the Stanford Institute for Economic Policy Research (SIEPR), and Daniel Hemel of New York University School of Law—comes amid calls for government-mandated reforms that get to the root of the country's persistent drug shortages. Earlier this year, Robert Califf, the commissioner of the Food and Drug Administration, told federal lawmakers measures that stop short of fixing the "core economics" of the prescription drug market ultimately won't work.

One strategy is to tackle what Ouellette and Hemel call the generic drug trilemma—a situation that pits the dynamics of costs, supply, and quality against each other.

"There's no perfect solution to the problem of drug shortages, but we think our framework will help policymakers avoid Band-Aid fixes that merely create different problems for other parts of the drug supply," says Ouellette, the Deane F. Johnson Professor of Law, whose research looks at the interplay between innovation policy and intellectual property law.

Ouellette and Hemel say that drug shortages stem from a common misconception of what makes for effective policies when it comes to prescription medicines. Much of the attention in policy circles and in research around prescription drugs focuses on brand-name medications that are protected by patents, they write. Yet it's generic medicines —alternatives to brand-name drugs whose patents have expired—that comprise more than 90 percent of prescription medications dispensed in the United States.

And the policy objectives for regulating patented medications versus their generic versions are not the same, Ouellette says.

"Designing policies for the prescription drug market entails trade-offs that are different for patented drugs than for off-patent medications, or what we think of as generic drugs," says Ouellette. "Our analysis suggests that you can reduce the severity of drug shortages through policies that better account for these differences in trade-offs."

Ouellette's and Hemel's paper was published in Entrepreneurship and Innovation Policy and the Economy.

The 'unintended consequences' of existing policies

Consider, the authors say, the chief goals of patented drug policy. One is to encourage the development of new medications by rewarding the scientists and companies who discover them with a patent, which essentially establishes a 20-year monopoly that can lead to higher prices. The other is to try to ensure that patients can pay for the new drug treatment. The best policies strike a balance between the two, often called the "innovation-access dilemma."

Generic drug policymaking, in contrast, aims to serve three primary purposes: to keep prices down, encourage sufficient supplies, and ensure

that off-patent medicines are safe and effective.

Ouellette and Hemel argue that generic drug policy faces a "trilemma" in that it can never meet all three objectives at once. Policymakers can achieve one or two goals, but always at the expense of the third. For example, they can guarantee higher prices, which would likely reduce shortages, and maintain rigorous safety standards, but these policies necessarily increase prices. Or they could cap prices without addressing manufacturing costs, but that would come at the expense of supply.

For a real-world example of the price-quantity-quality trilemma, Ouellette and Hemel point to a program that Congress created 30 years ago that offers vaccines to more than half of U.S. children at no cost to their families. In designing the policy, lawmakers capped prices without addressing quality costs. This hurt manufacturers' profit margins so they cut supplies. A decade later, routine pediatric vaccines were in such short supply that 35 states lowered their immunization requirements for school-age children.

Congress made a mistake, Ouellette says, in overlooking the role of pricing. Vaccines had been around for so long that lawmakers were no longer concerned about rewarding manufacturers for supplying them.

"The Vaccines for Children program illustrates how policies that don't account for the trilemma can have unintended consequences, creating more problems down the road," says Ouellette, whose recent work with Hemel also includes an examination of flaws in drug pricing.

Reforms under the 'trilemma' approach

Using the trilemma framework allows policymakers and researchers to better understand the trade-offs in addressing drug shortages—and to respond more effectively, according to Ouellette and Hemel. The key is

to recognize that fixing two sides of the trilemma will negatively affect the third, but that the harm can be less than the overall benefit.

The authors explore three possible policy moves. One is to step up antitrust enforcement, and they detail the many ways that brand-name and generic manufacturers game the system. Brand-name manufacturers, for example, exploit the fact that prices for off-patent drugs are unregulated and that generic manufacturers have to clear high government hurdles to market a drug.

Another possibility is for government to play a larger role in supplying medicines—as it has done during the COVID-19 pandemic by contracting with vaccine makers to provide free immunizations. Ouellette and Hemel say that the federal government could become an additional source of medicines by manufacturing generic drugs itself or contracting with other producers to do so.

A third option proposed by the authors is to dramatically cut the amount of time it takes to make a medication, without compromising on safety or quality. Currently, the vast majority of medicines are produced in batches and follow a sequence of time-consuming steps. By contrast, a process known as "continuous" manufacturing operates like an assembly line: at any given time, medicines are in different stages of production. As of early 2022, the FDA had approved six drugs that are produced by continuous production, but policymakers could provide incentives for all manufacturers to invest in the process, according to Ouellette and Hemel.

The major downside to these reforms—or any that are likely to significantly reduce drug shortages—is that they are costly, notes Ouellette.

"And none of these policies in and of themselves can eliminate the

trilemma," Ouellette says. "But they could do a lot to alleviate the persistent problem of scarcity in the pharmaceutical drug supply."

More information: Daniel J. Hemel et al, The Generic Drug Trilemma, *Entrepreneurship and Innovation Policy and the Economy* (2023). DOI: 10.1086/723235

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