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regarding the optimal choice for this vulnerable population.

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## Medication Shortages: A Matter of National Security—Time for Action



**To the Editor:** As noted by Choo and Rajkumar<sup>1</sup> in the June 2020 issue of *Mayo Clinic Proceedings*, the COVID-19 (coronavirus disease 19) pandemic has exposed extreme vulnerabilities in our nation's drug supply chain. The fragility of the drug supply chain was not created overnight and has been brewing for over a decade. Frequent generic drug shortages and quality deficiencies are compromising standard of care, producing waste, and increasing costs. For example, antibiotic shortages contribute to

resistance, when clinicians are forced to use broad-spectrum agents. Today, 80% of active product ingredient (API) manufacturers are located overseas,<sup>2</sup> with the majority being obtained from India and China. India, a large manufacturer of finished products, obtains 70% of APIs from China.<sup>3</sup> China has a virtual monopoly on the APIs required to make critical drugs such as antibiotics, antihypertensives, and many others. Although the United States remains a global leader in drug discovery, we have almost completely transitioned manufacturing abilities to overseas because of lower production and labor costs. The United States' overreliance on importing APIs from overseas has created a devastating impact on our public health with a potential for catastrophic events in the event of a war, trade conflict, or pandemic such as COVID-19 and impacting our national security. As expected, the United States is waiting in line with every other country for essential drugs during the current pandemic.

Although there are no easy or fast solutions to this problem, we must act now. In addition to Choo and Rajkumar's recommendations, the following steps may be considered with the ultimate goal of domestic manufacturing of most of the essential lifesaving drugs to protect our patients from harm.

- Designate the pharmaceutical industry as a high-priority infrastructure critical to national security (like the aviation and energy sectors) to allow the federal government to coordinate efforts during shortages or national crises.
- Develop an essential national security drug supply list that includes medications for which a supply interruption could cause an immediate risk to public health.

- Create a national agency to monitor, plan, and identify potential manufacturers in the event of a shortage.
- Manufacture products in multiple locations to protect the supply chain in the event of a natural disaster or other threats.
- Strengthen federal oversight of manufacturers to ensure the highest product integrity and require manufacturers to provide transparency related to source of APIs and quality issues.
- Develop a partnership between the private and public sectors acting as a united cohort to uncover incentives to drive actions to ensure domestic production of essential drugs.
- Require manufacturers to report to the US Food and Drug Administration (FDA) immediately on discovery of an interruption, disclosing the reason and the expected time to resolution.
- Create a national database for tracking of essential drug supplies and use predictive analytics to identify surge, production problems, and future shortages.
- Allow outsourced 503B compounds to prepare drugs in short supply.
- Allow the FDA to prioritize and expedite generic drug approvals.
- Provide adequate FDA resources to allow frequent inspection of overseas facilities to ensure product integrity and quality.

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**Editor's Note:** When publishing a letter that comments on an article published previously in *Mayo Clinic Proceedings*, it is the journal's policy to invite the author(s) of the referenced article to publish a response. Drs Choo and Rajkumar were fully supportive of the letter by Guharoy and did not feel any response from them was necessary.

## Impactful Policy Action to Reduce Drug Costs in Managing Critically Ill Patients with COVID-19



**To the Editor:** We read the recent commentary *Medication Shortages During the COVID-19 Crisis* by Drs Choo and Rajkumar with great interest.<sup>1</sup> As supply chain management leaders at Mayo Clinic, we appreciate the attention these authors draw towards the issue of drug shortages and drug costs. One of the interesting observations we have made from the supply chain perspective while navigating the coronavirus disease 2019 (COVID-19) pandemic is that the impacts on drug cost from COVID-19 have been minimal in the retail segment and are more significant in the hospital sector. This phenomenon is a result of costly inpatient care for COVID-19 and there are currently no effective commercially available drug therapies that are being routinely used in the ambulatory setting.<sup>2</sup>

Due to the high cost of COVID-19 inpatient care within health care,

we project that the cost containment recommendations of Medicare price negotiations and controls of deductibles/rebates suggested by Drs Choo and Kumar will have minimal impact on drug costs at this time (there could be a benefit if new therapeutic agents emerge in the future or if brand name drugs are used for COVID-19 patients). One potentially highly impactful and easy to implement public policy solution we call attention to is the need to remedy unintended effects of the Drug Efficacy Study Implementation and Unapproved Drugs Initiative programs. These programs were implemented to provide review of drugs that have been available for decades and that had not completed formal Food and Drug Administration review. Because of these programs and abuses by manufacturers, dramatic escalation of cost and expense for certain older drugs that were once generic continue to occur.<sup>3,4</sup>

The most egregious example in the hospital sector over the past decade is the dramatic rise in the cost of vasopressin, a drug that has been around for over 80 years and that is now among the top 25 drugs expenditures in hospitals as of 2019 and has patent protection until 2032.<sup>5</sup> Because of the high use of vasopressin in critically ill COVID-19 patients and the greater than 6000% price increase that has occurred after completing the Unapproved Drugs Initiative process, vasopressin will likely become a top 10 drug expense within the hospital sector by the end of 2020. Inflation for vasopressin since undergoing approval through the Unapproved Drugs Initiative has been and continues to be dramatic. As result of COVID-19, the manufacturer Parr Pharmaceuticals will experience further massive windfall profits and inflict billions of dollars of

unreasonable costs for managing critically ill patients over the next decade.

Policy adjustments that address unintended consequences of the Drug Efficacy Study Implementation and Unapproved Drugs Initiative programs could prevent further economic harm related to vasopressin pricing and avoid similar abuses in the future.

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**Editor's Note:** When publishing a letter that comments on an article published previously in *Mayo Clinic Proceedings*, it is the journal's policy to invite the author(s) of the referenced article to publish a response. Drs Choo and Rajkumar were invited to respond,