Chemotherapeutic Shortages: How Do We Prioritize?

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Knowing that curative treatments exist but being unable to provide them is perhaps one of the most devastating experiences for an oncology provider. Drug shortages represent a public health crisis that predates but has been exacerbated by the COVID-19 pandemic. Drug shortages are a systematic problem: a manifestation of perverse incentives for pharmaceutical companies and other stakeholders, and of the fundamentally broken healthcare system in which we work. Drug shortages are often a result of decreased production and supply. Pharmaceutical companies often prioritize manufacturing of profitable drugs at the expense of older, generic (but still quite useful) drugs. The COVID-19 pandemic has worsened this problem by leading to increased demand for medications, with a rapid influx of patients with COVID-19, and by causing interruptions in domestic and international supply chains. Drug shortages significantly impact patient care and can increase the risk of medication errors, adverse drug interactions, inferior treatment, and mortality. Data-driven guidance on how clinicians can best respond in real-time to such calamities is thus critical.

Chemotherapeutic shortages represent an especially pressing problem given their complexity and direct implications for patients with curable malignancies. For example, a shortage of vincristine in 2019 led to delays in treatment and uncertainty regarding how to approach patient prioritization strategies. This was in part due to a business decision by one pharmaceutical company to decrease production, leaving one other company to keep up with demand. Subsequent manufacturing delays led to a national shortage of vincristine, underscoring the importance of developing recommendations to guide allocation of scarce medical resources.

Recommendations to guide rationing of scarce medical resources, including drugs, during the COVID-19 pandemic have often emphasized the utilitarian principle of maximizing benefits for society by saving the most lives or life-years, based on prognosis. For example, the United Kingdom’s National Institute for Health and Care Excellence issued recommendations for prioritization of patients requiring systemic cancer treatments, radiotherapy, and bone marrow transplants. Canadian triage guidelines for patients with cancer recommend giving top priority to patients who will benefit the most from immediate treatment, deprioritizing patients who can reasonably wait for medical care until it is more accessible. Although ethically sound consensus recommendations exist to guide some aspects of scarce resource allocation, the potential real-world outcomes of allocation strategies remain largely unknown.

In this issue of JNCCN, Hantel et al describe a hospital-level model constructed to compare effects of different chemotherapy allocation strategies on patient survival using vincristine as an example. Using an institutional database and survival probabilities from NCCN Guidelines, a model was constructed and validated to determine survival outcomes across varying levels of vincristine shortages, testing different prioritization strategies. Hantel et al found that an efficacy-per-volume prioritization strategy significantly improved projected survival. The model operates on the principle of maximizing survival and was successful in testing different allocation strategies and demonstrating that the choice of allocation strategy can impact patient survival based on real-world data.

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These authors’ approach is novel and laudable. Knowing how such choices actually impact patients downstream is critical to making these wrenching decisions. But a purely utilitarian calculus is not necessarily the right answer. A Rawlsian approach may work in the halls of a philosophy department, but it does not apply neatly in an infusion center. Making decisions that are purely utilitarian may inadvertently deprioritize certain vulnerable patients. For example, prioritization strategies based on maximizing quality-adjusted life-years could put patients with disabilities or advanced age at a disadvantage. Additionally, patients whose diagnosis was delayed as well as certain racial or ethnic minority groups may be inadvertently deprioritized. For example, we know that Black and Hispanic patients with acute myeloid leukemia have higher mortality rates that are reliably predicted by census tract measures and treatment patterns. A strictly utilitarian approach to allocation of vincristine based only on estimated survival may fail to account for these factors, including those due to systemic racism, which could further exacerbate existing health disparities. Drug allocation schemes must be designed to mitigate bias in prioritization.

Unpredictable and potentially devastating drug shortages will likely remain a problem in cancer care in the near future. Although paradigms such as the proposed vincristine model described by Hantel et al’ are helpful in considering allocation schemas, we know that drug shortages are often sudden and unpredictable, leaving pharmacists and providers to make real-time allocation decisions without the benefit of an established model. In addition, the Hantel et al study is based on a projected 9-month shortage; another challenge with creating and interpreting these data is the uncertain duration of shortages, which may wax and wane. With this in mind, scarce resource allocation committees might better prioritize rationing criteria based on a modified utilitarian approach.

Aside from medication allocation strategies, multiple potential solutions exist to lessen the impact of drug shortages that occur due to decreased production. Communication between healthcare systems in the same region is crucial to ensure awareness of potential drug shortages as they arise, potentially allowing shifting of drugs or patients between hospitals based on need. Ultimately, federal legislation to control drug pricing and supply chains may be the most effective way to prevent drug shortages. Potential solutions to reduce the impact of drug shortages demand further attention and action, from the bedside to pharmaceutical companies to Congress.

The COVID-19 pandemic has led to previously unthought of challenges in healthcare delivery and has exposed how medical resource shortages across innumerable facets of healthcare can affect patients. Workforce shortages have been attributable to redeployment, quarantine, illness, and job vacancies in the setting of staff departures. Patients are experiencing longer wait times for cancer-related diagnosis and treatment. Oncologists have reported ubiquitous uncertainty and fear related to adverse impacts on patient care from the pandemic. And even when the personnel and drugs are available, the supply of equipment necessary to deliver life-saving chemotherapy has been strained; the lack of infusion pumps prompted a specific FDA guideline to improve manufacturing efficiency.

There is an urgent need for practical recommendations to guide healthcare systems faced with shortages to ensure that resources are allocated to maximize benefits while ensuring equitable distribution. Prioritizing the development of thoughtful and comprehensive data-driven strategies for scarce drug allocation is a step toward addressing drug shortages and minimizing harm to patients.

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