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*World Journal of Clinical Oncology* (*World J Clin Oncol*, *WJCO*, online ISSN 2218-4333, DOI: 10.5306) is a peer-reviewed open access academic journal that aims to guide clinical practice and improve diagnostic and therapeutic skills of clinicians.

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Retrospective Study

# Physician approaches to drug shortages: Results of a national survey of pediatric hematologist/oncologists

Jill C Beck, Baojiang Chen, Bruce G Gordon

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**Author contributions:** Beck JC designed the study and gathered data; Chen B provided statistical analysis of results; Beck JC and Gordon BG wrote the manuscript.

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## Abstract

### AIM

To evaluate personnel involved in scarce drug prioritization and distribution and the criteria used to inform drug distribution during times of shortage among pediatric hematologists/oncologists.

### METHODS

Using the American Society of Pediatric Hematology/Oncology (ASPHO) membership list, a 20 question survey of pediatric hematologists/oncologists was conducted *via* email to evaluate personnel involved in scarce drug prioritization and distribution and criteria used to inform scarce drug distribution.

### RESULTS

Nearly 65% of the 191 study respondents had patients directly affected by drug shortages. Most physicians find out about shortages from the pharmacist ( $n = 179$ , 98%) or other doctors ( $n = 75$ , 41%). One third of respondents do not know if there is a program or policy for handling drug shortages at their institution. The pharmacist was the most commonly cited decision maker for shortage drug distribution ( $n = 128$ , 70%), followed by physicians ( $n = 109$ , 60%). One fourth of respondents did not know who makes decisions about shortage drug distribution at their institution. The highest priority criterion among respondents was use of the shortage drug for curative, rather than palliative intent and lowest priority criterion was order of arrival or first-come first-served.

### CONCLUSION

Despite pediatric hematology/oncology physicians and patients being heavily impacted by drug shortages, institutional processes for handling shortages are lacking. There is significant disparity between how decisions for distribution of shortage drugs are currently made and how study respondents felt those decisions should be made. An institution-based, and more importantly, a societal

approach to drug shortages is necessary to reconcile these disparities.

**Key words:** Pediatric hematology/oncology; Chemotherapy; Ethics

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**Core tip:** The frequency of drug shortages are increasing and heavily impact physicians and patients. However, processes for handling drug shortages are lacking. An institution-based, and more importantly, a societal approach to drug shortages are necessary to reconcile these disparities.

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## INTRODUCTION

Drug shortages occur whenever demand for a medication is greater than the available supply. The frequency of drug shortages has increased considerably over the last decade due to decreased availability of raw materials, disruptions along the supply chain, economic decisions by drug companies and health care systems, and increased demand<sup>[1-5]</sup>. Although drug shortages are a global issue, they have significantly impacted the United States due to low pharmaceutical company reimbursement rates for generic drugs with narrow cost margins<sup>[4,5]</sup>.

Important ethical issues arise whenever the supply of an effective drug is insufficient to meet demand. The principles of beneficence, non-maleficence, and justice can guide prioritization of scarce drug distribution, but an individual's application of those principles may vary widely. The ethical principle of autonomy, which so commonly drives ethical decision making, is not relevant to drug shortages, perhaps making these decisions more difficult.

Several reports have evaluated the impact of drug shortages and ethical frameworks have been proposed for handling shortages, however, no studies have evaluated the key factors physicians use to determine drug distribution during times of shortage<sup>[3,6-13]</sup>. A more thorough understanding of the decision-making processes physicians are using will assist in developing frameworks and policies to more effectively manage drug shortages.

## MATERIALS AND METHODS

### Study review

The Institutional Review Board at University of Nebraska

Medical Center (UNMC) in Omaha, Nebraska reviewed and approved the study.

### Study population

The online membership directory from the American Society of Pediatric Hematology/Oncology (ASPHO) was used to identify pediatric hematology/oncology physicians in the United States.

### Survey

A twenty question survey of pediatric hematologists/oncologists was conducted *via* email to evaluate demographics of study respondents, personnel involved in scarce drug prioritization and distribution, and criteria used to inform scarce drug distribution (Appendix I ). The survey was developed and piloted by the authors. The questions evaluating demographics and personnel involved in prioritization were multiple-choice closed-ended questions. Demographic information included current position, type of patients seen, practice type, and years since completing fellowship. Survey questions regarding experiences with drug shortages included whether drug shortages had directly affected the provider's patients and whether the provider knew of drug shortages at the institution but the shortage had not resulted in the provider's patient not receiving a needed medication. In addition, respondents were asked to identify whether the shortage drugs were chemotherapy or non-chemotherapy, however further specifics were not requested. Questions also addressed whether the respondent's institution has a program or policy to handle drug shortages, whether the provider felt a program or policy was necessary, who makes decisions about shortage drug distribution at their institution, and who should make decisions about shortage drug distribution. Respondents were asked to choose all decision makers with no limit on the number of answers and were asked to specify with an open-ended response if they chose other. The criteria for scarce drug distribution provided eight statements which were evaluated using a Likert scale ranging from 0 (strongly disagree) to 100 (strongly agree).

Survey questions did not specify definitions for relative terms such as length of survival, age, type or length of therapy, or dose. Study data was collected and managed using REDCap electronic data capture tools hosted at UNMC. REDCap is a secure, web-based application designed to support data capture for research studies. The invitation email provided an explanation of and electronic link to the voluntary survey. Participants entered responses directly into the online REDCap survey and responses were de-identified.

### Survey population

At the time of this study, 1259 physicians in the United States had available email addresses in the ASPHO online membership roster and were emailed survey invitations. Twenty-nine addresses were undeliverable.

**Table 1** Demographics

Characteristic	n (%)
Current position	
Attending physician	161 (84.7)
Fellow	23 (12.1)
Non-practicing physician	2 (1.1)
Type of patients	
Oncology	162 (85.7)
Hematology	145 (76.7)
Stem cell transplant	54 (28.6)
Do not see patients	2 (1.1)
Type of practice	
Academic medical center	160 (83.8)
Community/private institution	39 (15.7)
Years since completing fellowship	
Less than 5	64 (34.4)
5-10	44 (23.7)
11-20	33 (17.7)
More than 20	45 (24.2)
Gender	
Female	104 (55)
Male	85 (45)

Of the 1230 remaining physicians, 191 (15.5%) responded and were included in the study analysis.

The majority of respondents were attending pediatric hematologist/oncologists currently practicing ( $n = 161$ , 84.7%) and 12.1% ( $n = 23$ ) were fellows in pediatric hematology/oncology (Table 1). The types of patients seen by the surveyed physicians were mostly oncology ( $n = 162$ ) and hematology ( $n = 145$ ), with 54 physicians seeing stem cell transplant patients. Sixty-seven percent of physicians saw multiple patient types. Most respondents practice in an academic medical center ( $n = 160$ , 83.8%) with the remainder practicing in a community or private institution ( $n = 30$ , 15.7%). The number of years since completing pediatric hematology/oncology fellowship was nearly evenly divided among respondents.

### Statistical analysis

$\chi^2$  or Fisher's Exact test was used to obtain  $P$ -values to evaluate association among categorical responses. A  $P$ -value less than 0.05 indicates statistical significance. Logistic regression was used to determine the odds ratios to study the association of the outcomes with all variables simultaneously. Responses to scaled questions were reported as means and compared using analysis of variance.

## RESULTS

Nearly 65% of study respondents had patients directly affected by drug shortages where the provider was not able to prescribe a needed medication for his/her patient due to a shortage and 79% of study respondents knew of drug shortages at their institution, but the shortage did not result in a patient under the provider's care not receiving a needed drug. Physicians

**Table 2** Decision makers for shortage drug distribution

	Who makes the decision about distribution of shortage drugs at your institution?	%	Who should make the decision about distribution of shortage drugs at your institution?	%
Pharmacist	128	70.3	147	80.3
Physician	109	59.9	152	83.1
Hospital administration	41	22.5	35	19.1
Panel/group	32	17.6	77	42.1
Ethics committee	8	4.4	35	19.1
Nurse	1	0.5	8	4.4
Parent	1	0.5	6	3.3
Do not know	46	25.3	13	7.1
Total responses	366		473	

practicing in an academic medical center were more likely to have patients directly affected than physicians practicing in a community or private institution (OR = 2.61, 95%CI: 1.10-6.21). The physician's type of patients (hematology, oncology and/or stem cell transplant) did not impact the rate of patients directly affected by shortages.

Most physicians find out about drug shortages from the pharmacist ( $n = 179$ , 98%) or other doctors ( $n = 75$ , 41%). Other sources of information about drug shortages include a list or website ( $n = 69$ , 38%) and nurses ( $n = 13$ , 7%). Three respondents receive information from the Pharmacy and Therapeutics Committee or a drug shortage task force. Sixty-six percent found out from more than one of the above sources. One respondent stated they do not find out about drug shortages.

Sixty-two percent of respondents work at institutions that have a program or policy to handle drug shortages and 4% of institutions do not have a program or policy. One third of respondents do not know if there is a program or policy for handling drug shortages at their institution. However, 95% of respondents felt that a program or policy is necessary.

The pharmacist was the most commonly cited decision maker for shortage drug distribution ( $n = 128$ , 70%), followed by physicians ( $n = 109$ , 60%), hospital administration ( $n = 41$ , 23%), a panel or group ( $n = 32$ , 18%), ethics committee ( $n = 8$ , 4%), parent ( $n = 1$ , 0.5%), and nurse ( $n = 1$ , 0.5%) (Table 2). Sixty-six percent reported multiple decision makers. One fourth of respondents did not know who makes decisions about shortage drug distribution at their institution. In contrast, respondents felt that the physician ( $n = 152$ , 83%) and pharmacist ( $n = 147$ , 80%) should be the decision maker for shortage drug distribution. Other responses included a panel or group ( $n = 77$ , 42%), ethics committee ( $n = 35$ , 19%), hospital administration ( $n = 35$ , 19%), nurse ( $n = 8$ , 4%), and parent ( $n = 6$ , 3%). Seven percent of respondents did not know who should make the decision about distribution of shortage

**Table 3** Prioritization of distribution criteria

	Mean	Criteria	Ethical Framework
Strongly disagree	0.0		
	37.1	Order of arrival should impact the priority given to a patient	First-come first-served
	41.8	A patient with fewer co-morbidities should be given priority over a patient who has more co-morbidities	Sickest first
	44.3	Younger patients should receive priority over older patients	Fair innings
	47.3	A patient with longer anticipated survival should be given priority over a patient with shorter anticipated survival	Saving the most
	51.8	A patient needing a small dose of a shortage drug should be prioritized over a patient needing a larger dose	Saving the most
	57.2	A patient using a drug for an approved indication should have priority over a patient using the drug for off-label use	Saving the most
	61.0	A patient who is starting therapy should be prioritized over a patient who has nearly completed therapy	Saving the most
	74.3	A patient using the shortage drug for curative intent should be prioritized over a patient using the drug for palliation	Saving the most
Strongly agree	100.0		

drugs.

Respondents ranked criteria for prioritizing scarce drug distribution on a scale of 0 (strongly disagree, low priority) to 100 (strongly agree, high priority) (Table 3). Respondents prioritized use of the shortage drug for curative, rather than palliative intent (a patient using the shortage drug for curative intent should be prioritized over a patient using the shortage drug for palliation, mean 74) as the most important criteria in determining which patient should receive a shortage drug.

Prioritization of patients starting vs completing therapy (a patient who is starting therapy should be prioritized over a patient who has nearly completed therapy, mean 61), using a drug for an approved indication (a patient using a drug for an approved indication should have priority over a patient using the drug for off-label use, mean 57), dose (a patient needing a small dose of a shortage drug should be prioritized over a patient needing a larger dose, mean 52), anticipated survival (a patient with longer anticipated survival should be given priority over a patient with shorter anticipated survival, mean 47), patient age (younger patients should receive

priority over older patients, mean 44), and number of comorbidities (a patient with fewer co-morbidities should be given priority over a patient who has more comorbidities, mean 42) had closely ranked means. The priority ranking for anticipated survival (mean 44 vs 58,  $P = 0.005$ ) and patient age (mean 40 vs 58,  $P = 0.008$ ) was lower for physicians practicing at academic medical centers compared to community or private institutions. The priority ranking for using a drug for an approved indication was higher for fellows than attendings (mean 72 vs 54,  $P = 0.02$ ). As the years after fellowship increased, the priority of mean rank of prioritizing patients starting vs completing therapy also increased (< 5 years mean 53, 5-10 years mean 63, 11-20 years mean 64, > 20 years mean 66,  $P = 0.04$ ).

The lowest priority criterion was order of arrival [order of arrival (first come-first served) should impact the priority given to a patient, mean 37]. The priority ranking for order of arrival for physicians practicing at academic medical centers was significantly lower than physicians in community or private institutions (mean 34 vs 45,  $P = 0.03$ ). Physicians whose patients were directly affected by drug shortages gave lower priority to order of arrival than physicians who did not have patients directly affected by shortages (mean 33 vs 42,  $P = 0.01$ ).

## DISCUSSION

While numerous reports have detailed the impact of drug shortages and several ethical frameworks have been proposed for handling shortages, this is the first survey of physicians evaluating individual approaches to prioritization<sup>[3,6-13]</sup>. The frequency of drug shortages have increased over the last decade and have disproportionately affected oncology due to quality issues, limited manufacturers, and complex production processes with specialized equipment<sup>[3,4]</sup>. In addition, chemotherapy medications often have no equivalent for substitution, whereas other drugs may have several alternatives within a medication class<sup>[5]</sup>. Unique issues arise when dealing with drug shortages in pediatric oncology due to the increased use of off-label drugs in pediatrics compared to adult medicine and dosing based on weight and size<sup>[2,3,7,14]</sup>. In addition, pediatric patients have surrogate decision makers, usually parents, determining the child's best interest in a situation in which no alternative may be ideal.

In this study, nearly 65% of respondents had patients unable to receive a needed drug due to shortages and 79% knew of drug shortages at their institution that had not directly affected their patients. Overall, physicians report they are informed about drug shortages from a variety of sources, most commonly pharmacists, other doctors, and/or a list or website. Despite being heavily impacted by and well informed about drug shortages,

institutional processes for handling shortages are lacking, or at least are not well known to the physicians caring for the patients: One third of respondents did not know if there is a program or policy for handling drug shortages at their institution.

There is significant disparity between how decisions for distribution of shortage drugs are made and how study respondents felt those decisions should be made. Currently, the pharmacist was the most commonly cited decision maker for shortage drug distribution, followed by physicians. Although respondents felt that physicians and pharmacists should be included in decisions regarding shortage drugs, many believed that a panel, group, or ethics committee should also be involved. This is not currently the practice at most institutions surveyed and may reflect the need to systematically involve more members of the health care team.

Physicians in academic medical centers were more likely to have patients directly affected by shortages than those in community or private institutions. It is not clear why this is the case, however, a report of adult oncologists found private practice providers were more likely to use brand name rather than generic drugs which more frequently have shortages<sup>[5]</sup>. The criteria of using a drug for an approved indication was given higher priority by fellows than attendings, likely reflecting increased comfort with using off-label medications as experience increased.

Important ethical issues arise whenever the supply of an effective drug is insufficient to meet demand. The principles of beneficence, non-maleficence, and justice can guide prioritization of scarce drug distribution, but as is demonstrated in this study, an individual's application of those principles may vary widely. The ethical principle of autonomy, which so commonly drives ethical decision making, is not relevant to drug shortages perhaps making these decisions even more difficult. Beneficence encourages safe and effective care such as utilizing evidence-based medicine and optimizing resource utilization. Non-maleficence promotes minimizing pain and suffering, a major potential effect on a patient unable to obtain a needed medication. Justice demands reasonable access to resources and is threatened by the many causes of shortages as well as institutional stockpiling of shortage drugs.

Prioritization frameworks have been proposed, some of which include "sickest first", "fair innings", "first-come first-served", and "saving the most", among others (Table 3)<sup>[3,13,15]</sup>. Sickest first prioritizes patients based on degree of illness. Therefore, using the sickest first criteria to distribute shortage drugs, patients with the worst disease and the most co-morbidities would have highest priority. The fair innings approach argues that each person should have an equal opportunity to live a normal lifespan. The prioritization criterion of patient

age relies on the fair innings approach. "First-come first-served" distributes shortage drug based on order of arrival. Finally, the goal of saving the most is to provide the most good to the most patients. In the case of drug shortages, this method focuses on the indication of the drug and goals of care while balancing risks and benefits<sup>[3]</sup>.

In this survey, the highest priority criterion was use of the shortage drug for curative, rather than palliative, intent, which evokes the ethical framework of saving the most. The criteria of starting vs completing therapy, using a drug for an approved indication, dose, and anticipated survival completed the top five highest ranked criteria and all rely on the concept of saving the most. Therefore, the ethical framework of saving the most is used most often by pediatric hematologist/oncologists in the United States when considering shortage drug distribution.

Drug shortages require the physician to consider both the good of an individual patient and society at large. Using the framework of saving the most necessitates physicians to prioritize their patient within the larger context of the population. An institution-based, and more importantly, a societal approach to drug shortages is necessary to reconcile the physician-patient relationship with that of the larger population. Cooperative groups and medical societies can play an important role in this process.

Several groups have begun to address drug shortages in pediatric oncology. The Working Group on Drug Shortages in Pediatric Oncology has created recommendations for responding to drug shortages, COG gives guidelines for management of shortages within treatment protocols, the American Society of Health-System Pharmacists has provided guidelines and recommendations, and the American Board of Pediatrics, American Society of Clinical Oncology, and American Society of Pediatric Hematology/Oncology have provided commentary and position statements<sup>[6,7,11,16]</sup>. However, given the continued prevalence of drug shortages and their widespread impact, a continued coordinated effort is needed to ensure consistency and provide guidance for implementation. The recently published follow-up recommendations to the Working Group on Drug Shortages in Pediatric Oncology by Unguru *et al.*<sup>[13]</sup> provides much needed concrete methods for shortage drug distribution in pediatric oncology that can ideally be adopted within and across institutions. Pediatric oncology is a prime subspecialty to formulate this coordinated endeavor given its established history of collaboration and could potentially set the stage as a model for other subspecialties impacted by drug shortages.

The lowest priority criterion in this survey was first-come first-served. Interestingly, this criterion may actually be used frequently in practice. One third of respondents did not know if there is a program or

policy for handling drug shortages at their institution. In addition, respondents who had patients directly affected by drug shortages gave first-come first-served lower priority than physicians who did not have patients directly affected by shortages. At those institutions, shortage drugs are rationed at the bedside and priority for shortage drug distribution is likely first-come first-served by default. If a program or policy for handling drug shortages is not in place, advance decision-making is unlikely to occur resulting in a process that may not be reasonable or transparent. This discrepancy between aims and reality highlights the need for clear institutional and ideally national guidelines developed prior to a drug shortage.

Limitations to this study include the limited sample size and voluntary nature of the survey resulting in possible selection bias. The small sample size offers trends in approaches to prioritization of shortage drug distribution. Non-practicing physicians were included because the decision processes are not limited to practicing providers. The survey statements were left purposefully broad to allow respondent interpretation, as is the case in clinical practice, however this approach may impact validity. However, this is the first national survey of physicians on the topic of physician prioritization criteria used for shortage drugs. The crucial finding of this study is the disparity between how decisions are made and how respondents feel they should occur, reinforcing the need for continued attention to organizational frameworks and policy development. Perspectives of other physician subspecialty groups, health professionals, patients, or family members are an important area for follow-up and such studies are underway by the authors.

## COMMENTS

### Background

The frequency of drug shortages is increasing. Important ethical issues arise whenever the supply of an effective drug is insufficient to meet demand. The principles of beneficence, non-maleficence, and justice can guide prioritization of scarce drug distribution, but an individual's application of those principles may vary widely. The ethical principle of autonomy, which so commonly drives ethical decision making, is not relevant to drug shortages, perhaps making these decisions more difficult.

### Research frontiers

Little data is available evaluating the key factors physicians use to determine drug distribution in times of shortage. A more thorough understanding of the decision-making processes physicians are using will assist in developing frameworks and policies to more effectively manage drug shortages.

### Innovations and breakthroughs

The frequency of drug shortages are increasing and heavily impact physicians and patients. However, processes for handling drug shortages are lacking. An institution-based, and more importantly, a societal approach to drug shortages is necessary to reconcile these disparities.

### Applications

While numerous reports have detailed the impact of drug shortages and

several ethical frameworks have been proposed for handling shortages, this is the first survey of physicians evaluating individual approaches to prioritization. Unique issues arise when dealing with drug shortages in pediatric oncology due to the increased use of off-label drugs in pediatrics compared to adult medicine and dosing based on weight and size. Given the continued prevalence of drug shortages and their widespread impact, a continued coordinated effort is needed to ensure consistency and provide guidance for distribution of shortage drugs. Pediatric oncology is a prime subspecialty to formulate this coordinated endeavor given its established history of collaboration and could potentially set the stage as a model for other subspecialties impacted by drug shortages.

### Peer-review

The manuscript is well written and the topic is quite relevant.

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