

An Evaluation of Oncology Drug Shortage: A Means of Strengthening the Supply Chain of Active Pharmaceutical Ingredients in United States

ABSTRACT

Aims: This study seeks to identify the root causes of these shortages and evaluate the fragilities within the oncology supply chain that obstruct efforts to enhance drug availability. The United States is experiencing significant drug shortages that critically impact patient care, especially for oncology patients.

Study design: We utilized publicly accessible cross-sectional data on drug shortages documented by the US Food and Drug Administration between 2023 and 2024.

Methodology: Descriptive statistics were employed to examine drug availability across multiple influencing factors. Additionally, a bivariate correlational analysis explored the relationships between drug availability levels and various elements, including the rationale behind shortages, their current status, updates, and therapeutic classifications.

Results: The most common reason for drug shortages is the increase in demand for the Drug (12.1%), followed by a shortage of an active ingredient. Among the drugs impacted by shortages, 90.8% are non-oncology therapies, and only 9.2% are oncology therapies. The descriptive statistics indicate that complying with Good Manufacturing Practices (GMP) led to 92.3% of cases being unavailable. The shortage of an API contributed to 54.4% limited availability/supply and 39.2% unavailability. The oncology drugs are less likely to be with reported shortage causes. However, there is a moderate correlation to unresolved statuses ($r = 0.358$, $p < 0.001$), as seen in the bivariate correlation.

Conclusion: The persistent unavailability and limited supply of certain drug products underscore the systemic inefficiencies in the supply chain that necessitate targeted interventions. While oncology drugs comprise a smaller fraction of the overall drug shortages, their availability is crucial, given their clinical importance. Key supply chain challenges persist specifically for oncology therapies. Although surges in demand are a primary driver of these shortages, factors such as the shortage of active pharmaceutical ingredients and adherence to Good Manufacturing Practices significantly exacerbate the issue of drug unavailability.

Keywords: [Drug Shortage, Supply Chain, Pharmaceutical Active Ingredients, Availability Information, Oncology Therapies]

1. INTRODUCTION

In 2023, drug shortages in the United States (US) have reached an alarming point with remarkable effects on patient care and therapeutic outcomes, particularly among patients diagnosed with cancer.[1], [2] The recent shortages of essential drugs may underscore vulnerabilities in the logistic supply of active pharmaceutical ingredients, necessitating strategic interventions to promote the consistent availability of different categories of therapeutic medications.[3] According to the US Food and Drug Administration (FDA), a drug shortage occurs when the total supply of drugs is less than the current demand for commercially available drug products nationally. Reasons attributed to the shortage vary from manufacturing disruptions, competitive market landscape, issues with quality control, and delays in regulatory affairs to discontinuations.[4], [5], [6]

Drug shortages, amongst other factors like regulatory processes and off-label usage practices, influence the availability of oncology and non-oncology therapies in the US healthcare market.[7], [8] For instance, approximately 63% of oncology drugs evaluated in recent trials were available as off-protocol therapy at trial initiation.[9] Additionally, the oncology market was projected to exceed \$32 billion by 2005, driven by high demand exceeding the bioactive ingredient supply for almost a decade.[10] Furthermore, the limited approval of oncology drugs has created challenges in bringing new therapies to market.[11]

However, increasing localized production of active pharmaceutical ingredients (APIs) in the US significantly benefits the pharmaceutical supply chain and overall patient care. The positive outcomes of enhancing local manufacturing of these therapeutic compounds are eliminating the dependency on suppliers overseas, fostering advanced technologies for precision medicine, and stimulating local economies coupled with job creation.[12], [13], [14] The overall consequences involve mitigating the risk of drug logistics interruption,[14] enhancing healthcare and ensuring an uninterrupted supply of bioactive compounds for disease eradication to strengthen national drug logistics systems.[15]

Despite the FDA's efforts to mitigate supply disruptions, drug shortages remain a significant drawback in the US healthcare system. Disparities in availability across oncology and non-oncology therapeutics highlight a need for more resolution to systemic issues.[3], [14] The FDA monitors the ongoing status of drug shortages and provides updates on the market covered when local manufacturers can meet the demand.[4] However, gaps persist due to the limited availability of API from production within the US. This inconsistency in supply reinforces a critical research gap in interpreting the factors contributing to these shortages and the effectiveness of current mitigation strategies. The primary issue is the lack of targeted approaches to address therapeutic-specific shortages, such as those anticancer medications, resulting in unequal access to safe and effective medications. This study aims to investigate the underlying causes of drug shortages to evaluate the weaknesses in the supply chain that undermine the existing interventions in drug availability. The mainstay of this study would inform the development of more robust and equitable strategies to address the ongoing problem of the drug supply chain system.

2. METHODS

Data Description

The publicly available cross-sectional data were obtained from all drug shortages recorded between 2023 and 2024 and were extracted from the US Food and Drug Administration (FDA) drug shortage list (<https://dps.fda.gov/drugshortages>). This study did not involve direct human subjects' investigation; therefore, approval from the institutional review board (IRB) was not required.

Dependent and Independent Variables.

The dependent variable utilized in this analysis is the availability of information regarding drug shortages. Categories of information available about drugs include available or estimated

availability, limited availability, limited supply, unavailable, discontinued, and others (out of stock, pending approval). The different levels of independent variables utilized in this study include reasons for drug shortage (delayed shipping, demand increase for the drug, discontinuation of the manufactured drugs, regulatory delay, requirements related to complying with GMP, and shortage of an active ingredient), Type of update on drug shortage (new, reverified, and revised), status of shortage(resolved and unresolved), therapeutic categories (Oncology and non-oncology therapeutics)

Statistical Analysis

The frequency distribution of variables was employed to examine the number of occurrences of the levels of factors used to assess drug shortages. Descriptive Statistics were used to investigate drug availability information outcomes across different levels of factors used to evaluate drug shortages. Chi-square tests were performed to determine differences in the characteristics of the dependent variables across each category of independent variables. A 2-tailed t-test and χ^2 tests were implemented using IBM SPSS, version 29, and the significance level was set at 2-sided $P < .05$. The correlational analysis examines the relationship between different levels of drug availability information and various reasons for drug shortage, status of drug shortage, updates on drug shortage, and therapeutic categories.

3. RESULTS AND DISCUSSION

Table 1 and Figure 1 show the pattern of drug shortages with combined percentages of unavailable and limited availability/supply (26.8%). 12.6% of drugs are reported as having limited Availability/Supply, while a proportion, 14.2%, of drugs are entirely unavailable. The most common reason for drug shortages is the increase in demand for the Drug (12.1%), followed by a shortage of an active ingredient. More than half (54.2%) of the updates regarding drug shortages are currently at a re-verification stage. Updates indicate that approximately 30% of these shortages fall under revision, reflecting ongoing changes to updates on drug availability due to supply disruptions or shortages. Almost all of the ongoing shortages—about 93.6%—are unresolved, while just a small portion, only 6.4%, have been resolved. Among the drugs impacted by shortages, 90.8% are non-oncology therapies, and only 9.2% are oncology therapies.

Table 1

Description of Variables for Assessing Drug Shortage		
Variables	Number of Occurrence	Percent Occurrence
Drug Availability Information		
Available/Estimated Availability	923	48.30%
Discontinued	9	0.50%
Limited Availability/supply	240	12.60%
Unavailable	272	14.20%
Others	466	24.40%
Reasons for Shortage		
Delay In Shipping Of The Drug	59	3.10%
Demand Increase For The Drug	232	12.10%
Discontinuation Of The Manufacture Of The Drug	31	1.60%
Other	130	6.80%
Regulatory Delay	3	0.20%
Requirements Related To Complying With Good Manufacturing Practices	13	0.70%
Shortage Of An Active Ingredient	125	6.50%
Update on Shortage		
New	329	17.20%
Reverified	1036	54.20%
Revised	545	28.50%
Status of Shortage		
Unresolved	1787	93.60%
Resolved	123	6.40%
Therapeutic Categories		
Non-Oncology therapies	1735	90.80%
Oncology therapies	175	9.20%

The descriptive analysis summarizing the drug availability information and other variables of drug shortages from Table 2 underscores the critical role of demand surges as the leading cause of shortages. Manufacturing and supply chain issues also contribute to significant unavailability. For instance, requirements related to complying with Good Manufacturing Practices (GMP) led to 92.3% of cases being unavailable. A shortage of an API contributed to 54.4% limited availability/supply and 39.2% unavailability. Delays in drug shipping accounted for 45.8% of cases with limited availability/supply, and 50.8% of cases were classified as unavailable. Updates on reverified drugs: 71.2% were reported as available, 11.4% had limited availability, and 16.1% were unavailable.

The unresolved status of shortages accounted for 63.6% of available drugs and was disproportionately represented in cases with limited availability (16.5%) and unavailability (18.7%). Notably, no resolved shortages were reported across all availability categories, highlighting the persistent challenges in addressing shortages. Therapeutic non-oncology agents have more issues with availability, with about 13.1% being only limited availability and 14.9% not available at all. Conversely, the availability of oncology therapies is relatively high, with approximately 7.4% partially available and 8% completely unavailable. A substantial proportion of cancer therapies, approximately 34.9%, are classified into other categories based on their availability of information. Overall, all analyses from the Chi-Square test revealed significant differences across the variables in the descriptive analysis.

Table 2

Descriptive Analysis of Drug Availability Information to Estimate Characteristic Drug Shortages

Variables	Categories of Variables	Available/Estimated Availability(%)	Discontinued(%)	Limited Availability&supply(%)	Unavailable(%)	Others(%)	Pearson Chi-Square Tests Value(P-Value)
Reasons for Shortage	Delay In Shipping Of The Drug	1.7	0	45.8	50.8	1.7	266.22 (<.001)
	Increase For Demand The Drug	22	0	34.5	42.2	1.3	
	Discontinuation Of The Manufacture Of The Drug	0	29	35.5	22.6	12.9	
	Other	3.1	0	39.2	56.9	0.8	
	Regulatory Delay	0	0	33.3	66.7	0	
	Requirements Related To Complying With Good Manufacturing Practices	0	0	7.7	92.3	0	
	Shortage Of An Active Ingredient	6.4	0	54.4	39.2	0	
	%Total	10.8	1.5	40.3	45.9	1.5	
Update on Shortage	New	2.7	0	2.4	0	94.8	1314.569 (<.001)
	Reverified	71.2	0.7	11.4	16.1	0.6	
	Revised	32.3	0.4	20.9	19.3	27.2	
	%Total	48.3	0.5	12.6	14.2	24.4	
Status of Shortage	Unresolved	63.6	0.5	16.5	18.7	0.7	1848.48 (<.001)
	Resolved	0	0	0	0	0	
	%Total	48.3	0.5	12.6	14.2	24.4	
Therapeutic Categories	Non-Oncology therapies	48.3	0.4	13.1	14.9	23.3	19.8(<.001)
	Oncology therapies	48.6	1.1	7.4	8	34.9	
	%Total	48.3	0.5	12.6	14.2	24.4	

The correlational analysis in Table 3 uncovers a compelling trend: drugs with unresolved shortages are more likely to face limited availability or complete unavailability. Even oncology drugs, less associated with reported shortage causes, show a moderate link to unresolved statuses ($r = 0.358$, $p < 0.001$). However, there is no significant association between different categories of drug availability information and oncology therapies ($r = 0.025$, $p = 0.274$). The result shows that reasons for shortages have minimal impact on information on drug availability trends, with a slight but statistically significant relationship ($r = 0.081$, $p = 0.049$).

95% Confidence Interval 0.000, 0.160). Demand fluctuations or manufacturing delays may significantly be linked to different categories of information on drug availability.

Table 3

Bivariate Correlational Analysis to Determine Factors Associated with Drug Availability Information of Drug Shortages

		Reasons for Shortage	Status of Shortage	Types of Availability Information	Therapeutic Categories
Reasons for Shortage	Pearson Correlation	1	.a	.081*	-.088*
	Sig. (2-tailed)		.	0.049	0.031
	N	593	593	593	593
Status of Shortage	Pearson Correlation	.a	1	.358**	.235**
	Sig. (2-tailed)	.		<.001	<.001
	N	593	1910	1910	1910
Types of Availability Information	Pearson Correlation	.081*	.358**	1	0.025
	Sig. (2-tailed)	0.049	<.001		0.274
	N	593	1910	1910	1910
Therapeutic Categories	Pearson Correlation	-.088*	.235**	0.025	1
	Sig. (2-tailed)	0.031	<.001	0.274	
	N	593	1910	1910	1910

* Correlation is significant at the 0.05 level (2-tailed).
 ** Correlation is significant at the 0.01 level (2-tailed).
 a Cannot be computed because at least one of the variables is constant.

The unavailability, limited availability, or supply of drug products reflects persistent supply chain inefficiencies that require intervention. A previous investigation demonstrated a shortage of cisplatin and carboplatin, chemotherapeutic products while proposing importation and promoting local medication production to strengthen the US pharmaceutical supply chain.[7] Conversely, the correlational analysis in our study showed that reasons for shortages are less likely to be reported regarding oncology therapies. Although oncology therapies represent a smaller proportion of total shortages, their availability remains a high-priority concern due to their clinical importance.

Furthermore, there are chances of unresolved supply chain issues, specifically regarding oncology drugs. Effective resolution strategies are crucial, as medications with unresolved shortages are more likely to face limited availability or complete unavailability. Another drawback is the re-verification process of updating drug logistics, which may lead to shortages, signaling that active efforts are required to track and manage availability. However, many updates require revision, indicating ongoing instability in supply chains. There is a clear need for more decisive interventions to resolve shortages, as current measures are insufficient.

While spikes in drug demand are the leading cause, active ingredient shortages and GMP compliance are significant causes of drug unavailability. Reasons for drug shortages have minimal impact on availability trends, indicating that other factors, such as demand fluctuations, regulatory processes, or manufacturing delays, may play a more prominent role.

Overall, stabilizing availability for oncology and non-oncology therapies in the US presents a viable solution to reduce drug shortages through localized production of active pharmaceutical ingredients. One limitation of this study is the limited information on the specific reasons for API shortage, and sufficient information was unavailable to determine the resolution status of all the available drugs. However, this study reveals the post-pandemic trends of drug shortages, which was one of the limitations of a previous study.

4. CONCLUSION

Although surges in demand are the primary drivers of drug shortages, shortages of active pharmaceutical ingredients (APIs) and issues related to Good Manufacturing Practice (GMP) compliance also play critical roles. Current supply chain challenges are particularly concerning for oncology medications. Additionally, the factors contributing to shortages of oncology therapies are often underreported, complicating efforts to address these issues effectively.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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APPENDIX

Confidence Intervals				
Bivariate Correlation of Variables	Pearson Correlation	Sig. (2-tailed)	95% Confidence Intervals (2-tailed) ^b	
			Lower	Upper
Reasons for Shortage - Status of Shortage	.a	.	.	.
Reasons for Shortage - Availability Information	0.081	0.049	0	0.16
Reasons for Shortage - Therapeutic Categories	-0.088	0.031	-0.168	-0.008
Status of Shortage - Types_of_Availability	0.358	<.001	0.318	0.397
Status of Shortage- Therapeutic Categories	0.235	<.001	0.192	0.277
Availability Information -Therapeutic Categories	0.025	0.274	-0.02	0.07
a Cannot be computed because at least one of the variables is constant.				
b Estimation is based on Fisher's r-to-z transformation.				