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Impacts of a Nonprofit Membership-Based Pharmaceutical Company on Volume of Generic Drugs Sold and Drug Prices: A Case Study

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KEY FINDINGS

- Drug shortages, especially for generic drugs, are a persistent public health issue. The COVID-19 pandemic highlighted the need to enhance the resilience of the U.S. pharmaceutical supply chain to ensure medicines are affordable and accessible to those who need them. Non-traditional pharmaceutical business models have been increasingly touted as a potential solution to address drug shortages.
- We conducted a case study of Civica Rx, a U.S. nonprofit pharmaceutical company whose model is based on long-term hospital membership agreements with minimum volume commitments and buffer stock requirements. These features may be attractive to hospitals and health systems that are willing to trade-off procurement agility for more reliability in drug supply.
- Between 2020 and 2022, the non-traditional pharmaceutical model sold 64 drugs, which were all generic sterile injectables. The non-traditional model sold 350.2 million units for total sales worth $255.9 million.
- We found that the non-traditional model sold similar, or in some cases larger, quantities of drugs, including drugs in shortage and essential medicines, as the average traditional competitor. The product mix for the non-traditional model leaned toward production of drugs in shortage and essential medicines, which may reflect the needs of their membership.
- In some cases, the average price for the products was roughly equal between the non-traditional and traditional model, and in some cases the non-traditional model's price was much lower. However, in other cases, the relative price of certain generic drugs in the non-traditional model was up to 2.15 times higher than the price of drugs in the traditional model; further research is needed to understand the factors that could explain these differences, while noting the non-traditional model may promote reliability of the generic drug supply.

Introduction

Generic drug shortages threaten access to lifesaving therapeutics and pose a risk to the capacity of the U.S. healthcare system to mitigate and respond to public health emergencies and ongoing public health issues.[1] The COVID-19 pandemic highlighted the necessity of enhancing resiliency and reducing vulnerability risks in the supply chain, particularly with respect to drug shortages, and ensuring

[1] Bosworth, A, Sheingold, S, Finegold K, De Lew, N, Sommers, B.D. (2022). Issue Brief No. HP-2022-27. Washington, DC: Office of the Assistant Secretary for Planning and Evaluation, U.S. Department of Health and Human Services. https://aspe.hhs.gov/reports/prescription-drug-price-increases

medicines are affordable and accessible.[2] Even before the COVID-19 pandemic, nearly two-thirds of hospitals (64 percent) reported more than 20 medical product shortages at any one time, including antibiotics used to treat severe bacterial infections, controlled substances, local anesthetics, and crash cart drugs required to stabilize and resuscitate critically ill adults.[3] The frequency and severity of these supply disruptions have been exacerbated over the last few years. The problem of drug shortages is particularly critical for medicines that are medically necessary to have available at all times and in an amount adequate to serve patient needs in the appropriate dosage forms.

Drug shortages have numerous causes, including manufacturing quality issues, an increase in demand, supply chain disruptions from natural disasters or other unexpected events, or product discontinuations. Some have noted that old generic drugs are particularly vulnerable to shortage because of low margins, which represent a high-risk and low-reward financial outlook for manufacturers.[4,5] Thus, manufacturers may be disincentivized to make investments such as upgrading existing or building new manufacturing facilities, adopting practices that promote proactive detection of vulnerabilities, and preventing manufacturing problems.[6,7] Furthermore, uncertainty about future demand by purchasers can drive market exits. Given these challenges and the increasing incidence of drug shortages, ensuring the resiliency of the generic drug supply chain is a public health priority.[8] Many solutions have been proposed to mitigate drug shortages.[9] These solutions include domestic manufacturing, buffer stocks (e.g., requiring that excess inventory be held and maintained to facilitate availability of certain products in case of unexpected supply disruptions, long-term contracts with guaranteed volume purchasing, and price guarantees. However, there is a literature gap on the prevalence of these practices in the United States.

We use a case study approach to examine one pharmaceutical company, Civica Rx (henceforth Civica or non-traditional model), that uses a membership-based and long-term contracting model for the U.S. market. Civica was created as a nonprofit pharmaceutical company[10] in 2018 by seven health systems and three philanthropic organizations with a mission "to reduce and prevent drug shortages and the price spikes that can accompany them…to make quality generic medicines accessible and affordable."[11]

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[2] The White House. (2021). Building Resilient Supply Chains, Revitalizing American Manufacturing, and Fostering Broad-Based Growth: 100-Day Reviews under Executive Order 14017. A Report by The White House. https://www.whitehouse.gov/wp-content/uploads/2021/06/100-day-supply-chain-review-report.pdf

[3] Vizient, *Drug Shortages and Labor Costs: Measuring the Hidden Costs of Drug Shortages on U.S. Hospitals*, June 2019: https://wieck-vizient-production.s3.us-west-1.amazonaws.com/page-Brum/attachment/c9dba646f40b9b5def8032480ea51e1e85194129

[4] U.S. Food and Drug Administration, Drug Shortages: Root Causes and Potential Solutions (Revised) (2020). https://www.fda.gov/media/131130/download

[5] IQVIA. (2023). Drug Shortages in the U.S. 2023. https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/drug-shortages-in-the-us-2023

[6] Frank, R. G., McGuire, T. G., & Nason, I. (2021). The evolution of supply and demand in markets for generic drugs. *The Milbank Quarterly*, *99*(3), 828-852.

[7] Sivashanker, K., Fanikos, J., & Kachalia, A. (2018). Addressing the lack of competition in generic drugs to improve healthcare quality and safety. *Journal of general internal medicine*, *33*, 2005-2007.

[8] United States Senate Committee on Homeland Security and Governmental Affairs. (2023). Short Supply: The Health and National Security Risks of Drugs Shortages. https://www.hsgac.senate.gov/wp-content/uploads/2023-06-06-HSGAC-Majority-Draft-Drug-Shortages-Report.-FINAL-CORRECTED.pdf

[9] Wosińska, M. & Frank, R. (2023). Federal Policies to Address Persistent Generic Drug Shortages. https://www.hamiltonproject.org/publication/policy-proposal/federal-policies-to-address-persistent-generic-drug-shortages/

[10] Classified as a 501(c)(4) social welfare organization. Civica is a nonstock company funded by its members and governed by a board.

[11] Civica RX. Why Civica? https://civicarx.org/#talking_points

Civica's members are hospitals or health systems, and it focuses on generic sterile injectables that are administered in a hospital setting. The non-traditional model includes guaranteed delivery, the same price per drug for all members regardless of volume, and a six-month buffer stock to supply drugs to its members. The members commit to purchase approximately 50 percent of their expected volume for specific drugs for a minimum duration that ranges from 3 to 10 years.[12] Civica's membership strategy and nonprofit status is different from other U.S. pharmaceutical companies; hence we refer to Civica as the non-traditional model. While products typically flow from manufacturers to health systems or hospitals through wholesalers and group purchasing organizations (GPOs) in the traditional model, Civica sells directly to health systems or hospitals that are its members without these intermediaries. Further, Civica entered the market by utilizing contracting manufacturing organizations (CMOs) to manufacture its products. These CMOs had excess capacity and the Abbreviated New Drug Applications (ANDAs) required to market generic drugs in the United States. However, the use of CMOs is not a unique feature of the non-traditional model because companies in the traditional model also use CMOs to produce their products. Recent research reported that the non-traditional model fulfilled its contractually guaranteed volume at 96 percent, while wholesaler orders were fulfilled at 86 percent.[13] However, that analysis did not compare the same sample of drugs, which limits the generalizability of the results.

We use U.S. national sales and volume data of the sample of drugs sold by Civica and compare the volume and price with other pharmaceutical companies in the market. The results of our study have implications for understanding whether non-traditional business models are able to fill certain market gaps, particularly when it comes to shortages of critical medicines.

Methods

Data

We used IQVIA National Sales Perspective (NSP) data from January 2017 through December 2022. IQVIA NSP captures approximately 88 percent of U.S. drug sales across all payers and distribution channels.[14] IQVIA NSP includes information such as sales revenue, volume, National Drug Code (NDC), molecule, strength, form, and manufacturer name. We calculated price per unit by dividing total sales revenue by total volume of extended units.

The non-traditional model: We identified our sample by searching for "CIVICA RX" in the company name variable. Next, we defined Civica's list of products by combining a drug's molecule (i.e., the active ingredient), dosage form (e.g., injectable drug), and strength information.

The traditional model: We identified our comparison group as all other companies making drugs with the same molecule-form-strength combination (i.e., "product") that Civica sold. The comparators were for-profit pharmaceutical companies without a membership-based model, i.e., "traditional model". The sample of drugs included all drugs marketed by Civica and a matched list of any equivalent drug product

[12] Dredge C, Scholtes S. The health care utility model: a novel approach to doing business. NEJM Catalyst Innovations in Care Delivery. 2021 Jul 8;2(4).
[13] Dredge, C., & Scholtes, S. (2023). Vaccinating Health Care Supply Chains Against Market Failure: The Case of Civica Rx. *NEJM Catalyst Innovations in Care Delivery*, *4*(5), CAT-23.
[14] IQVIA. U.S. National Data. <https://www.iqvia.com/insights/the-iqvia-institute/available-iqvia-data>.

from the traditional competitors.[15] We retained distinctions on strength (5GM, 10GM, etc.) because these can impact the cost and utilization of a drug.

In order to identify drug shortages, we used the US Food and Drug Administration (FDA) Drug Shortages Database downloaded on February 15, 2023.[16] This database includes information such as the shortage posting date, reason for the shortage, and status of the shortage (current, resolved, or discontinued). FDA's Drug Shortage Database defines a shortage at the molecule-level, but also provides information on the NDCs associated with the shortage.

To identify essential medicines, we used the Executive Order 13944 List of Essential Medicines, Medical Countermeasures, and Critical Inputs (hereinafter referred to as the "EO 13944 List", as developed by the FDA.[17] The list defines "essential medicines" as those medical products that have the greatest potential impact on public health and are most needed by patients in medical facilities for acute and urgent medical conditions. The essential medicines list provides medicines by drug name and dosage form.

We merged the IQVIA NSP data and FDA Drug Shortages Database by NDC. Then we matched this dataset to the essential medicine list at the molecule-form level, in consultation with a clinical pharmacist. The final database's unit of analysis was at the year-month-combined molecule-form-strength level. To create a shortage indicator, we assigned a shortage start and end date to the entire combination of molecule-form-strength if one or more NDCs were in shortage for that combination. The earliest shortage date among all NDCs for a combination was listed as the shortage start date and the latest shortage date among all NDCs for a combination was listed as the shortage end date.

Analytical Approach

The goal of our analyses was to identify whether there are differences in market performance, measured by the sales revenue, volume of extended units sold, and price per unit for the same cohort of drugs, between the traditional and non-traditional models. Specifically, we examined changes between 2017 and 2022, to capture the time before and after the non-traditional model first began marketing drugs in 2020. For purposes of this analysis, we define "market" to be the total volume and sales of drugs sold by the traditional and non-traditional models among those drugs that the non-traditional model produces at any point during the period of analysis, which may not be generalizable to all hospital-based drugs.

We then performed two subgroup analyses focusing on drugs in shortage and essential medicines to understand whether there are differences between the traditional and non-traditional models in supplying these types of drugs to the market. For these drugs, we compared the percent of total sales, the percent of total volume, and price per unit between the traditional and non-traditional models.

[15] Matching non-traditional and traditional company drugs: Only 4 of these unique combinations did not have an initial exact match, 3 due to differences in form and 1 due to difference in strength. For the 3 with differences in form, matches were identified by matching the NDC specifying text. For the 1 with difference in strength, matches were identified after correcting strength information from 20/MG/10ML to 2MG/ML. After manual corrections for the 4 unique combinations, there was a 100 percent match rate between non-traditional drugs and traditional alternatives.
[16] U.S. Food and Drug Administration. FDA Drug Shortages. https://www.accessdata.fda.gov/scripts/drugshortages/default.cfm
[17] U.S. Food and Drug Administration. (2020). Drug and Biologic Essential Medicines, Medical Countermeasures, and Critical Inputs for the List Described in Section 3 of the Executive Order 13944. https://www.fda.gov/media/143406/download

Although we have a cohort of drugs that is selected over the entire period of analysis, the mix of products changes over time, which may be an omitted variable in our primary analysis. For example, as the non-traditional model introduced more drugs to market across the sample period, the number and types of products changed, some products had larger (and differentially growing) markets than others in terms of volume, sales, or number of traditional manufacturers. Moreover, since each drug treats different conditions and faces different market conditions, the equilibrium price of some products (all else equal) may be naturally greater than others. Hence, to examine the robustness of our aggregate estimates, we conducted a sensitivity analysis in which we calculated, for each drug in the sample, the volume share and relative price of the non-traditional model vis-à-vis the traditional model. By examining the distribution of price and volume for exactly equivalent drug products between the two models, we can test the robustness of our primary results to any potential impacts of the changing drug mix through time. (For additional details, see the Appendix.)

Limitations

As noted above, the non-traditional model has two distinguishing characteristics – its nonprofit, social welfare status and its membership-based model with long-term minimum volume purchase agreements. While there are a few other nonprofit pharmaceutical companies in the United States, none had directly launched their own drugs onto the market during the period examined in this study. We are unaware of any other pharmaceutical companies adopting a membership model; thus, we cannot disentangle the individual impact of being a nonprofit drug company compared to having a membership model for any differences we observe between the non-traditional model and its more traditional competitors. As a result, our analyses may not be generalizable to other nonprofit companies that enter the market at a later date and other companies utilizing membership models.

Another limitation is that our period of analysis includes about two years of post-marketing data for the non-traditional model. This limits our understanding of long-term impacts. Nonetheless, understanding the short-term impacts of the non-traditional model is a critical first step to understanding overall impacts of non-traditional models.

There are also a few limitations specific to the FDA Drug Shortages Database. First, it is based on information that is self-reported by manufacturers and has missing information on some variables. For example, almost 70 percent of drugs in our sample do not have an identified or known cause of the shortage. This can be because the information is not known, because release of this information would exacerbate a shortage, or because the information is not allowed to be released because it has been designated as commercially confidential information. FDA uses the self-reported information submitted as the starting point to assess the nature of the shortage and the underlying reason for it, however the publicly available database may not reflect all the information that FDA uses. For example, it is possible for a manufacturer to select “Other” as the cause of the shortage and then FDA may learn during its assessment that the underlying reason is due to manufacturing delays.

Results

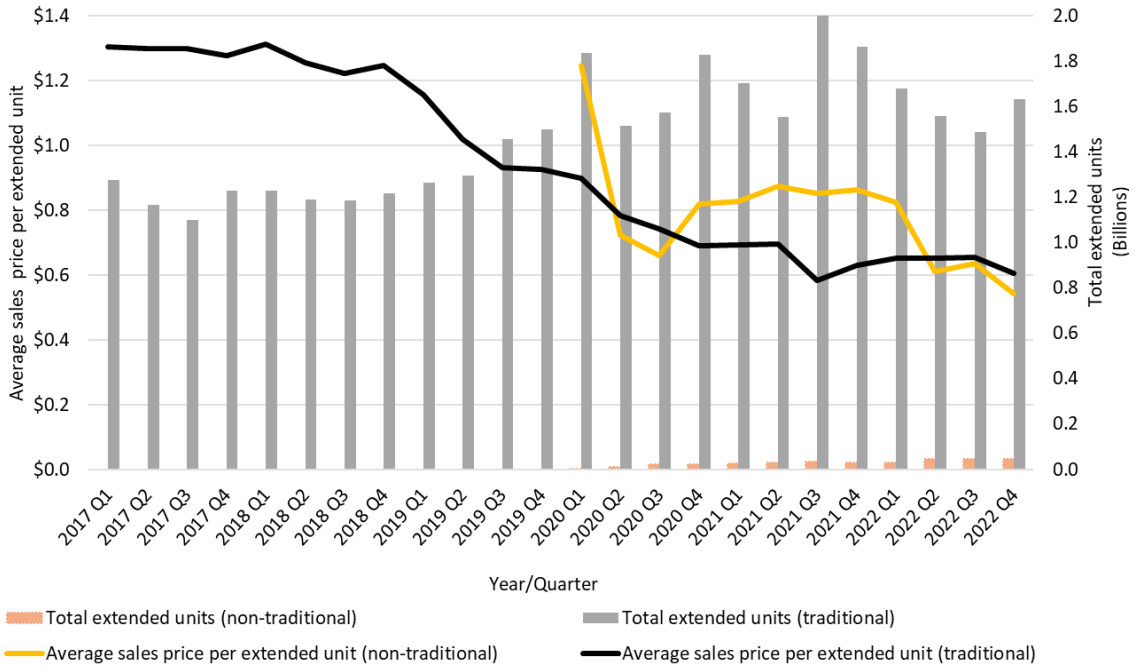
Between 2020 and 2022, there were 64 unique drug products (defined at the molecule-form-strength level) marketed by the non-traditional model (see Appendix Exhibit 1 for a list of these drugs), which were also marketed by 88 traditional competitors. In the same period, the non-traditional model sold 350.2 million units for total sales worth $255.9 million. This represented one percent of total sales and volume for these drugs when including the drugs marketed by the traditional model, which sold 20.2 billion units for total sales of $7.5 billion. Because the aggregate for the traditional model includes many

companies, we standardized the average units sold per company – on average, each traditional company produced 230.1 million units worth $158.9 million in sales, which is less than the non-traditional model.

Over the three-year period of interest, there was an increase in production by the non-traditional model. In the first quarter (Q1) of 2020, the total units sold in the traditional model equaled 1.8 million units for $2.2 million, both of which represented 1% of the total market size (i.e., the sample of drugs produced by the non-traditional model and its traditional competitors). The drugs sold by the traditional model increased to 47.7 million units in the fourth quarter (Q4) of 2022 for total sales of $25.9 million, or 2.6 percent of the market. After standardizing the 2022 production to a per company basis, on average, each traditional company produced 23.7 million units.

Figure 1 shows the total units sold and average sales price for all drugs in our sample, comparing the non-traditional and traditional models. In Q1 of 2020, the average sales price for the traditional model was $1.25 per unit while the price for the traditional model was $0.90 per unit. From Q4 of 2020 to Q4 of 2022, the average sales price of the non-traditional model was higher than the traditional competitor, with the largest difference (46 percent, $0.85/$0.58) occurring in the third quarter (Q3) of 2021. By the second quarter (Q2) of 2022, the average sales price was approximately $0.60 per unit for both the traditional and non-traditional competitors and remained relatively unchanged through the end of 2022.

Figure 1. Total Units and Average Sales, Non-traditional versus Traditional Models, 2017-2022



Source: ASPE analysis of IQVIA National Sales Perspective Data

Drug Shortages

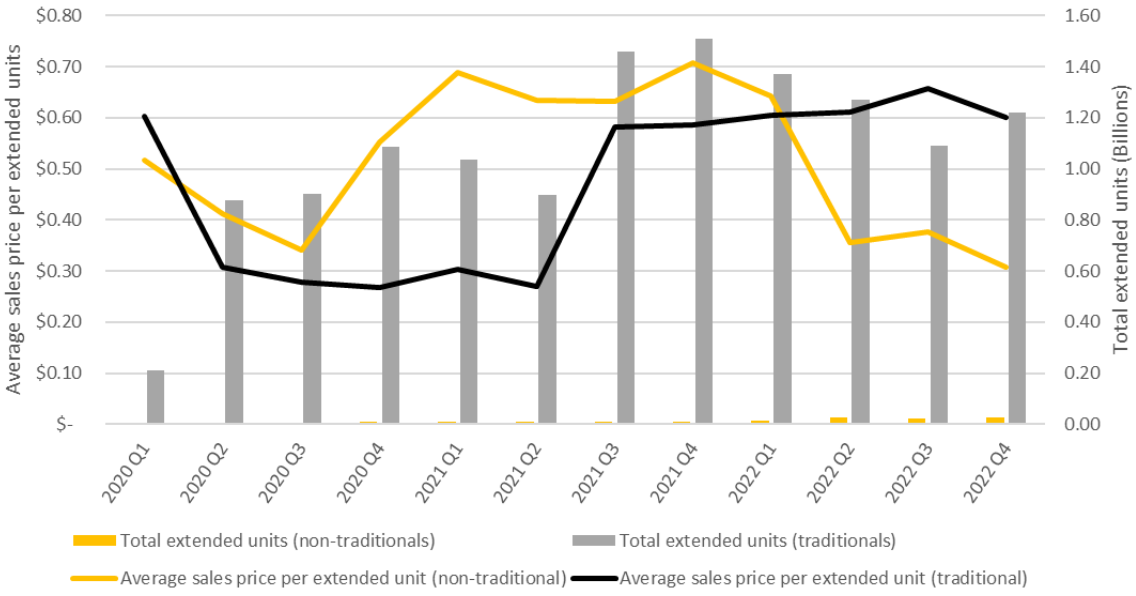
Of the 64 unique drug products in the sample, 28 drugs (44 percent) were in shortage (see Appendix Table 1 for more details). Similar to the findings in the previous section, total sales revenue for the non-traditional model represented a small percentage of the total market, peaking at 2.2 percent in Q4 2022. In Q1 2020, there were nine drugs manufactured by the non-traditional model that FDA listed as in

shortage. For these nine drugs, the non-traditional model sold 652,350 units corresponding with $337,018 in sales, both of which represented 0.3 percent of the total market, the lowest percentage over the period of analysis.

Over time, the number of drugs in shortage sold increased as did the share of drugs in shortage sold by the non-traditional model; production increased to 27.4 million units in Q4 2022 compared with 1.2 billion units for the traditional model. However, the non-traditional model's share of sales, $8.4 million relative to $736.7 million for the traditional model, was only 1.1 percent of the total market in Q4 2022. After standardizing volumes per company, we observed they were nearly equal – the non-traditional model produced 27.4 million units compared to 27.7 million units per traditional competitor.

As shown in Figure 2, in Q1 2020, the average sales price per unit of drugs in shortage sold by the non-traditional model was $0.10 lower than the average price of the competitors ($0.60 versus $0.50 per drug). Over the next eight quarters, the average price of drugs sold in the traditional model was lower than that of the non-traditional model. The price of drugs sold in the non-traditional model began to drop in Q1 2022; in Q2 2024, the average price was $0.60, or about half the price of traditional model competitors ($1.20). Notably, while the volume remained relatively unchanged for the non-traditional and traditional competitors, the price drop resulted in a lower share of total sales.

Figure 2. Total Units and Average Sales for Drugs in Shortage, Non-traditional versus Traditional Models, United States, 2017-2022



Source: ASPE analysis of IQVIA National Sales Perspective Data

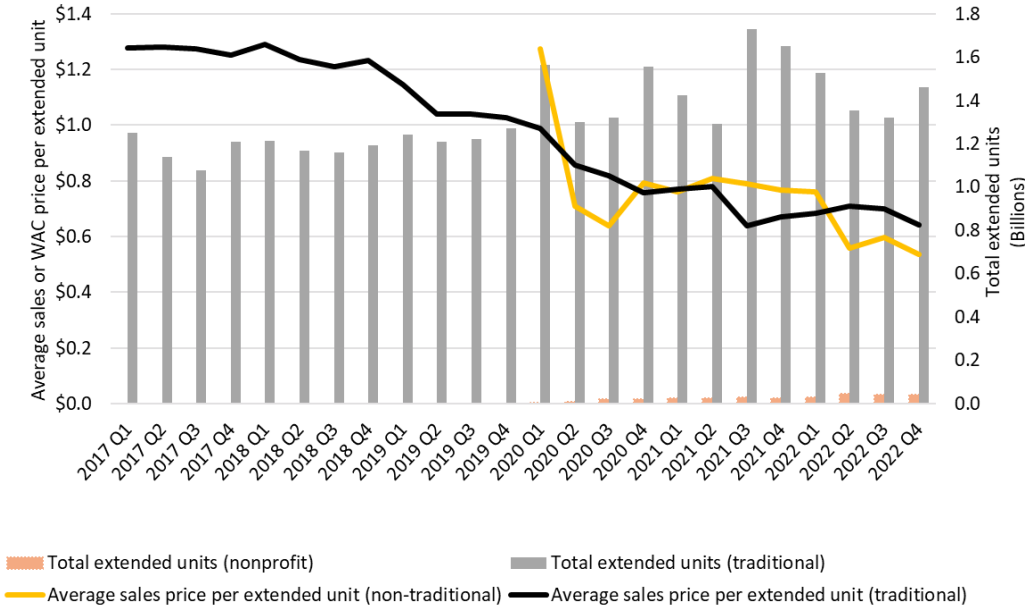
Essential Medicines

The majority of the drugs in the sample, 53 out of 64 drugs (83 percent), were identified as essential medicines (see Appendix Exhibit 1 for more details). The non-traditional model sold 1.6 million units for sales of $2.1 million, which represented 1 percent of the market. By Q4 2022, the non-traditional model was supplying 41.6 million units, which represented 3 percent of the market while the traditional model competitors produced 1.4 billion units. With respect to sales, the non-traditional model had sales of $22.3 million which made up 2 percent of the market ($962.7 million). Standardizing volumes per

company, the non-traditional model supplied 1.9 times as much as a traditional model competitor in Q4 2022 (41.6 million units compared to 21.5 million units per traditional model competitor).

As shown in Figure 3, in Q1 2020, the average sale price for drugs sold under the non-traditional model was $1.27 per unit, which decreased to $0.54 per unit in Q4 2022. When output peaked for the non-traditional model in Q2 2022, prices were $0.56 per unit. In contrast, the average sales price for drugs sold under the traditional model was $1.24 in Q1 2020 and $0.64 by Q4 2022. This translates to prices for the non-traditional model being 3 percent higher than the price for the traditional model competitors in Q1 2020, and 17 percent lower in Q4 2022.

Figure 3. Total Units and Average Sales of Essential Medicines, Non-traditional versus Traditional Models, United States, 2017-2022



Source: ASPE analysis of IQVIA National Sales Perspective Data

Sensitivity Analysis

Our analysis has shown that the sales, volume, and price of the drugs sold by the non-traditional model vary across time. These trends could reflect changes in market share or in the mix of products that are sold across time. We conduct two analyses to examine these issues further (see Appendix for additional information on the methods). First, we examined the share of market in terms of volume across time and key percentiles (Appendix Exhibit 2). We found wide variation in that market share. For example, the shares of market volume by the non-traditional model at 10th and 90th percentiles were two percent and 100 percent, respectively, which suggests that the non-traditional model may have more market power in certain product markets.

Second, to examine the robustness of our results with respect to changes in the product mix, for each drug in our sample we calculated the relative price of the non-traditional model, defined as the price for a given drug sold in the non-traditional model relative to the price of the same drug sold by the traditional model (Appendix Exhibit 2). We found that the relative pricing of the non-traditional model varied across time and key percentiles. For example, the relative prices across the 10^{th} to 90^{th} percentile were 0.38 to 2.15, respectively, which indicates that the prices for drugs sold under the non-traditional

model ranged from being close to two-thirds cheaper to being more than twice as expensive as the traditional competitors.

Discussion

This study found that as of 2022, the one example of a non-traditional model was a relatively small player in the pharmaceutical drug market with regard to their total market share. However, the results suggest that the non-traditional model may be able to produce volumes of drugs that are as large, and in some cases larger, than each traditional model competitor. This was most salient in the case of essential medicines, where the non-traditional model's volume was significantly larger than the traditional model's volume. The variation in market share across different drugs by the non-traditional model suggests that the non-traditional company spreads its risk across a large portfolio of drugs. This means that as the market changes (for example, drug shortages and new generic entrants) the non-traditional model has the ability to adapt its portfolio to ensure its longer-term viability, possibly considering factors such as demand of its membership or underlying profitability of certain drugs. In this way, non-traditional model companies have the potential to distinguish themselves, create a niche market, and leverage economies of scale and other efficiencies that may be associated with product specialization.

The observed results show more heterogeneity in prices across the cohort of drugs sold by the traditional and non-traditional models. In general, the average price of drugs sold under the non-traditional model was higher than the prices of the same drugs sold by the traditional model, although there were some notable exceptions in which the non-traditional model's price was much lower. It is possible that the non-traditional model's strategy of long-term purchasing agreements with hospitals gives it more flexibility to set prices to ensure longer term supply, rather than focusing on the lowest price that may not guarantee future supply. As the non-traditional model increases its membership base, there may be higher predictability into its future stream of revenue and demand, allowing for more price stabilization.

An important caveat for the study findings is that there is only one non-traditional pharmaceutical company, so results may not be generalizable outside of this case study. This analysis suggests that non-traditional pharmaceutical companies could have impacts on volume, price, and resiliency across a broader set of products if they were to become more mature in the market. However, the slow ramp up of production and the variability in prices over time shows that it takes several years for new entrants to find their optimal pricing, product mix, and production levels. This case study of the non-traditional model included only one company that was able to ramp up production in a relative short timeframe. This might be due to multiple reasons. First, the non-nontraditional model launched only generic products that have a shorter timeframe and are less expensive to bring to market than new originator drugs. Second, the non-traditional model leveraged the large volume and long-term commitments from its membership to extend long-term purchasing agreements with CMOs. The long-term purchasing agreements with these CMOs, those capable of producing and marketing generic drugs, might have incentivized reentry and utilized excess capacity to ramp up production.[18]

An important context for the findings is that the non-traditional model ramped up operations during the COVID-19 pandemic, which was a period of unprecedented challenges for drug manufacturing. There

[18] Dredge C, Scholtes S. The health care utility model: a novel approach to doing business. NEJM Catalyst Innovations in Care Delivery. 2021 Jul 8;2(4).

was a significant increase in drug shortages triggered by unexpected sharp increases in demand, often exceeding a manufacturers' production capacities.[19] In addition, the international nature of the drug supply chains exacerbated shortages due to disruptions to the production and shipping of pharmaceutical ingredients caused by lockdowns, understaffing, and travel and export bans.[20] From a regulatory perspective, there were delays in FDA inspections due to travel restrictions that limited FDA's capacity to inspect drug-manufacturing plants overseas, in turn further reducing its ability to authorize new entrants for manufacturing medications. These challenges were not specific to the non-traditional business model, but the confounding effects make it difficult to generalize the non-traditional volume capacity with future non-traditional entrants. However, despite these challenges, the non-traditional model sold similar or larger volumes of drugs in shortage and essential medicines than traditional pharmaceutical models. This points to the distinguishing features of the non-traditional model: long-term contracts with its members, diversified purchasing, and maintaining 6-month buffer stock of its products, which may help to ensure that there is a reliable supply for the non-traditional model's products. These features may be attractive to hospitals and health systems that are willing to trade-off the lowest cost at any given time for more reliability in drug supply.

Future research should examine if the variability in prices between the two models could be capturing the cost to engage in practices that enhance supply chain resiliency, which may not be reflected in the pricing of competitors, who need to incorporate profit for shareholders in pricing and might forgo resiliency investments for products with low margins.

Conclusion

This study compared the sales and volume of a non-traditional pharmaceutical model, which utilizes long-term purchase volume guarantees from its members. This non-traditional model sold similar volumes of drugs as their traditional model competitors. The non-traditional model's product mix supplied drugs in shortage and essential medicines, which may reflect the needs of its membership. Further, the prices of the non-traditional model were not always lower than its traditional competitors. Non-traditional models may provide an opportunity to identify and address market gaps, but further research is needed to better understand long-term effects and implications.

[19] Socal, M. P., Sharfstein, J. M., & Greene, J. A. (2021). The pandemic and the supply chain: gaps in pharmaceutical production and distribution. *American journal of public health*, *111*(4), 635-639.

[20] Mulcahy, A. W., & Kareddy, V. (2021). Prescription Drug Supply Chains.. Washington, DC: Office of the Assistant Secretary for Planning and Evaluation, U.S. Department of Health and Human Services. https://aspe.hhs.gov/reports/prescription-drug-supply-chains

Appendix

Appendix Exhibit 1: Drugs Used in Analysis by Form, Strength, Shortage Status, and Essential Medicines Status

Combined Molecule	Form	Strength	Drug in Shortage	Essential Medicines
Albuterol	Kc- Inhalant Aerosol Systmc	90MCG	2021-2022	Yes
Aminocaproic acid	Fdb Vial Regular I.V. Only	250MG/ML	-	-
Ampicillin	Fed Dry Vial Reg Im/Iv/Sc	1GM, 2GM	2022	Yes
Ampicillin sulbactam	Fed Dry Vial Reg Im/Iv/Sc	1.5GM, 3GM	-	Yes
Bacitracin	Fea Dry Vial Reg I.M. Only	50MU	-	-
Bivalirudin	Feb Dry Vial Reg I.V. Only	250MG	-	-
Bumetanide	Fdd Vial Regular Im/Iv/Sc	0.25MG/ML	2018-2022	-
Calcium	Fdb Vial Regular I.V. Only	100MG/ML	2021-2022	-
Ceftriaxone	Fed Dry Vial Reg Im/Iv/Sc	1GM, 2GM	-	Yes
Clindamycin	Fgb Piggy Back Reg I.V. Onl	600MG/50ML, 900MG/50ML	-	Yes
Daptomycin	Feb Dry Vial Reg I.V. Only	350MG, 500MG	2021-2022	Yes
Dexamethasone	Fdd Vial Regular Im/Iv/Sc	10MG/ML, 4MG/ML	-	Yes
Dexmedetomidine	Ffb Bottle Regular I.V.Only	200MCG/50ML, 400MCG/100ML	2019-2022	Yes
Diazepam	Fcd Disp Syr Reg Im/Iv/Sc	5MG/ML	-	Yes
Ephedrine	Fdd Vial Regular Im/Iv/Sc	50MG/ML	-	-
Etomidate	Fdb Vial Regular I.V. Only	2MG/ML	2022	Yes
Fentanyl	Fdd Vial Regular Im/Iv/Sc	0.1MG/2ML, 0.25MG/5ML, 2.5MG/50ML	-	Yes
Glycopyrrolate	Fdd Vial Regular Im/Iv/Sc	0.2MG/ML	-	Yes
Heparin	Fdd Vial Regular Im/Iv/Sc	1MU/ML, 5MU/ML	-	Yes
Hydralazine	Fdd Vial Regular Im/Iv/Sc	20MG/ML	2020-2021	Yes
Ketamine	Fdd Vial Regular Im/Iv/Sc	100MG/ML, 50MG/ML	2018-2022	Yes
Labetalol	Fdb Vial Regular I.V. Only	5MG/ML	-	Yes
Lidocaine	Fdd Vial Regular Im/Iv/Sc	1%, 2%	2018-2022	Yes
Lorazepam	Fdd Vial Regular Im/Iv/Sc	2MG/ML	2018-2022	Yes
Meropenem	Feb Dry Vial Reg I.V. Only	1GM, 500MG	-	Yes
Metoprolol	Fdb Vial Regular I.V. Only	5MG/5ML	-	Yes
Micafungin	Feb Dry Vial Reg I.V. Only	100MG	-	Yes
Midazolam	Fdd Vial Regular Im/Iv/Sc	2MG/2ML, 5MG/5ML	2020-2022	Yes
Morphine	Fdd Vial Regular Im/Iv/Sc	4MG/ML	2018-2022	Yes

Naloxone	Fdd Vial Regular Im/Iv/Sc	0.4MG/ML	-	Yes
Neostigmine	Fdb Vial Regular I.V. Only	0.5MG/ML, 1MG/ML	-	-
Nicardipine	Fdb Vial Regular I.V. Only	25MG/10ML	-	-
Norepinephrine	Fdf Vial Regular Infusion	1MG/ML	2022	Yes
Ondansetron	Fdb Vial Regular I.V. Only	4MG/2ML	2018-2022	Yes
Pantoprazole	Feb Dry Vial Reg I.V. Only	40MG	2019-2022	Yes
Phenylephrine	Fdb Vial Regular I.V. Only	10MG/ML	-	Yes
Piperacillin tazobactam	Fef Dry Vial Reg Infusion	3.375GM, 4.5GM	-	Yes
Prochlorperazine	Fdd Vial Regular Im/Iv/Sc	10MG/2ML	-	-
Propofol	Fdb Vial Regular I.V. Only	10MG/ML	2020-2022	Yes
Rocuronium	Fdb Vial Regular I.V. Only	10MG/ML	2018	Yes
Sodium	Fdb Vial Regular I.V. Only	1MEQ/ML	-	Yes
Succinylcholine	Fdd Vial Regular Im/Iv/Sc	20MG/ML	-	Yes
Tacrolimus	Aaa Caps Regular Ordinary	0.5MG, 1MG	2019-2022	Yes
Vancomycin	Feb Dry Vial Reg I.V. Only	10GM, 1GM, 5GM	-	Yes
Water for injection	Fdd Vial Regular Im/Iv/Sc	N/A	2021-2022	-

Sensitivity Analysis

Methods

We performed a sensitivity analysis that examined the variability of the relative price and production volume for each drug product marketed by the non-traditional and traditional model. In order to avoid the potential confounding effects of a differential (and changing) mix of drugs actively produced by the non-traditional sector compared to the traditional sector, we calculated the share of each product produced by the non-traditional sector versus the traditional companies at the drug level and then plotted quantiles of this distribution through time including, the median (i.e., 50th percentile), 25th and 75th percentiles, and the 10th and 90th percentiles.

We did this for two reasons. First, the non-traditional model's products were new to the market and introduced in a staggered fashion across the sample period. The methodology examined the changing distribution of relative price and production volumes as new products were being introduced onto the market. The goal was to provide insight into whether the non-traditional model's market performance was moving towards an equilibrium with regard to their relative pricing and sales revenue per drug. It also allowed us to examine the plausible range of market performance that non-traditional companies might produce once they move towards a stable market presence. Second, it allowed for disentangling the impacts of individual drugs, because a few outliers could affect the aggregate level findings.

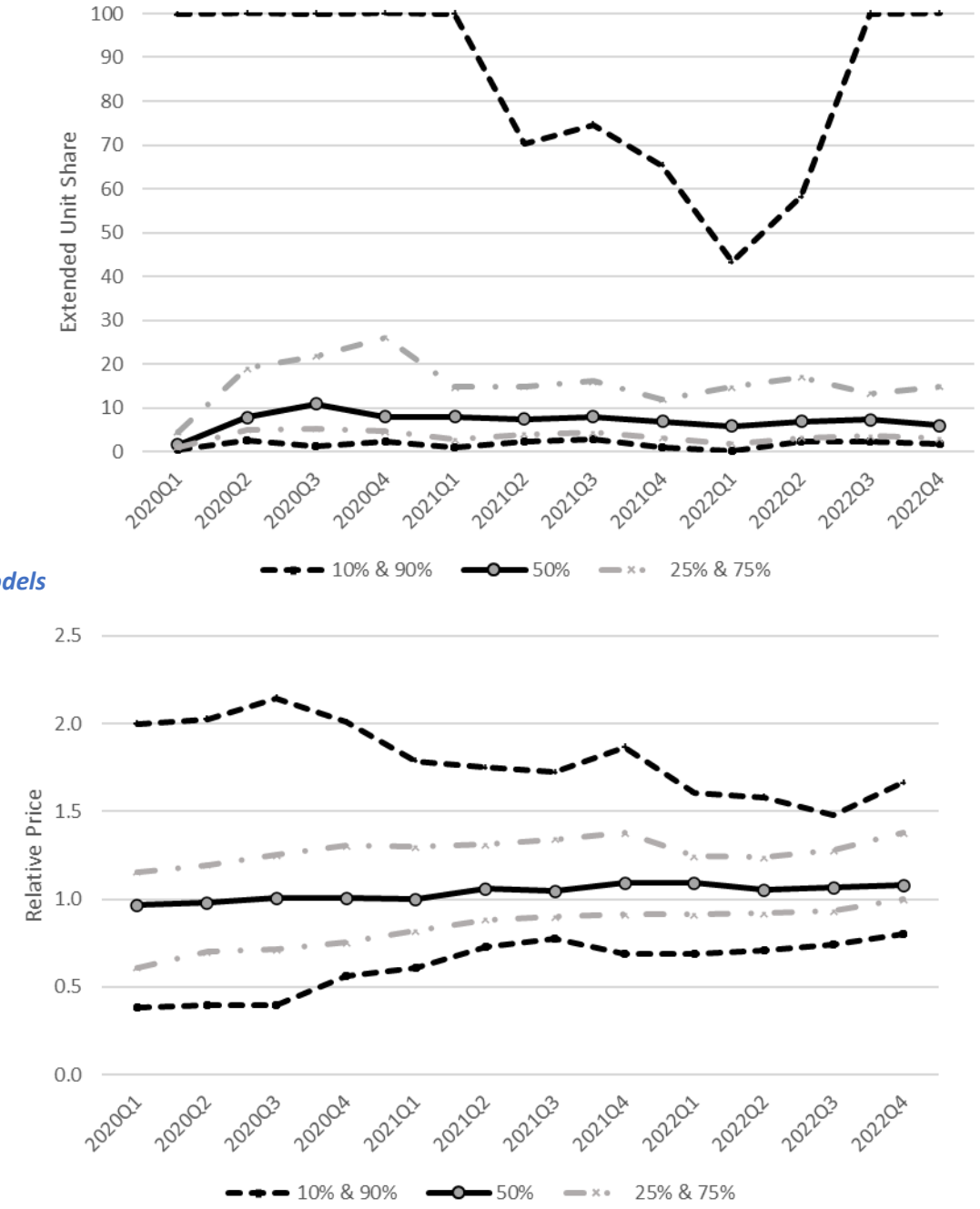
Results: Understanding Potential Future Impacts

The top graph in Appendix Exhibit 2 shows the distribution of the share of total *units* produced by the non-traditional model. Consistent with the primary findings, when the non-traditional model first launched, its median production share was approximately two percent. Production then increased quickly but had significant variation over time, between six and 11 percent. By taking the median of the individual drug market shares instead of the overall average, which the primary results did, this approach is more robust to potential changes in the mix of drug production over time. An additional

advantage of this approach is the ability to evaluate the heterogeneity in the non-traditional model's performance across the drug product markets through time as it becomes more established. These are represented by the trends in the 25th – 75th percentile range (marked with a dotted line), and the 10th – 90th percentile range (marked with a dashed line). At the 25th and 75th percentile, the non-traditional model's share of total units sold were between three and 16 percent of their drug portfolio, respectively. At the 10th and 90th percentile, there was significant variation as the non-traditional model represented as much as 100 percent of the market in some periods at the 90th percentile. This graph provides some evidence that while the non-traditional model is generally not yet a dominant player in the overall market, in some more narrow submarkets it has the ability to play a significant role in helping to fill production capacity for certain products and that over time non-traditional companies have the ability to significantly increase their production volume.

The bottom graph of Appendix Exhibit 2 shows an equivalent analysis applied to the distribution of the relative price of the non-traditional model compared with its traditional competitors. We observed a smooth and stable trend of modestly rising relative prices for the non-traditional model compared to traditional competitors. When the first products were launched by the non-traditional model, their median relative price was four percent lower than traditional competitors. Over time, the median relative price rose such that by the end of the sample, the price of the non-traditional model's drugs was eight percent higher than the traditional alternative. Examining the range at the 25th and 75th percentiles shows that relative pricing between the non-traditional and traditional companies narrowed over time. In 2020, the non-traditional model's relative prices ranged from 39 percent less than the traditional competitors to 16 percent more than the traditional sector. By the end of 2022, this narrowed to a range of the same price or 38 percent higher than the traditional sector. These results show that as non-traditional companies become more established, their relative pricing becomes less variable and closer to the traditional competitors. Moreover, we find a similar result when looking at the price distribution across the 10th – 90th percentile range; in 2020, relative prices for the non-traditional model were 62 percent less to 100 percent more than the traditional companies, but this range decreased to 20 percent less to 67 percent more than traditional companies in 2022. This range reduction of nearly 50 percent over a two-year time period reiterates that pricing is likely to be similar between the non-traditional and traditional competitors once the non-traditional model becomes more established.

Appendix Exhibit 2. Distribution of Relative Volume and Prices Comparing the Non-Traditional and Traditional Models



Source: ASPE analysis of IQVIA National Sales Perspective Data
Notes: The numbers in the legend represent the percentile of the share of units produced by the non-traditional model or the percentile of the relative price of the non-traditional model measured against its traditional competitors.

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