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MERGERS AND ACQUISITIONS (M&AS) IN PHARMACEUTICAL MARKETS: ASSOCIATIONS WITH MARKET CONCENTRATION, PRICES, DRUG QUANTITY SOLD, AND SHORTAGES

FINAL

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GLOSSARY

Acquiring company. In a merger, the company that is subsuming the assets of a target company being merged. In an acquisition, the company buying or otherwise acquiring the assets of the target company**.**

Acquirer drug. A drug involved in a merger or acquisition and owned by the acquiring company.

Biologic. Also referred to as a biological product. A therapeutic product derived from living human or animal tissue, either through genetic engineering or processing of products such as blood or plasma. Includes both biosimilar biologics approved through the 351(k) pathway (also called "biosimilars") as well as original biologics approved through the 351(a) pathway.

Brand drug. A drug that is marketed under a brand name or trade name, including both branded small molecule drugs and branded biologic products.

Competitive market (or low-concentration market). A market with an HHI score below 1,000.

Development stages. The major steps in the lifecycle of a new drug, including drug discovery, preclinical testing, phase I clinical trials, phase II clinical trials, phase III clinical trials, and marketing once approved.

Drug technology. The branch of pharmaceutical manufacturing of the primary asset in the M&A deal. We aggregated the drug technology variable in DealForma, and options include small molecules, biologics, dosage form technology, or other (e.g., genomics, microarrays, compound libraries).

Drug quantity sold. Also referred to as volume sales. We measured the quantity of drug sold using total mass in kilograms (kg) or total activity in International Units (IU) of the API in the finished drug product.

Drugs involved in an M&A transaction. In this report, marketed drugs are identified as being "involved" in an M&A if they (a) were owned by the target company and transferred to the acquirer, (b) were brand drugs owned by the acquirer with a shared therapeutic area as one of the target drugs, (c) they were generic drugs owned by the acquirer with a shared dosage form as one of the target drugs.

Essential medicines. Medicines listed on the Advanced Regenerative Manufacturing Institute (ARMI) Essential Medicine List (EML) or the Executive Order Essential Medicines List published by FDA.

Generic drug. A small molecule drug approved through an Abbreviated New Drug Application that is bioequivalent to a reference product, i.e., a brand drug.

HHI. Herfindahl-Hirschman Index, which measures market concentration and is calculated by summing the squared market shares of each company competing in the market.

Highly concentrated market. A market with an HHI score greater than 1,800.

Mergers and acquisitions. Technically, mergers are defined as two companies joining together by mutual agreement to form a new, third company. In practice, mergers often comprise a large company merging with a smaller one to gain one or more desirable assets, obtain new expertise or production capabilities, or facilitate expansion. Acquisitions are usually more direct purchases of another company, either through stock acquisition, bankruptcy auction, partnership buyouts, or other mechanism.

Moderately concentrated market. A market with an HHI score between 1,000 and 1,800.

Target company. The business entity that a (usually larger) pharmaceutical company wants to acquire or merge with in order to obtain the target company's assets or expand its own capabilities.

Target drug. A drug involved in a merger or acquisition and owned by the target company.

Therapeutic area. For this document, therapeutic area is used as an umbrella term to include some therapeutic classes of drugs—e.g., anti-infectives, immunomodulators—as well as representing specific fields of medicine that focus on particular diseases, body systems, or groups of organs, e.g., cardiology, oncology, pulmonology, genitourinary, etc.

Transaction value. The total value of cash and all other forms of payment made to the target company plus the value of the target's outstanding net debt if applicable. This typically includes payments of cash and/or stock but can also include notes, convertible debt, preferred stock, etc.

ABBREVIATIONS

Abbreviations	Definitions
ANDA	Abbreviated new drug application
API	Active pharmaceutical ingredient
ARMI	Advanced Regenerative Manufacturing Institute
ASPR	Administration for Strategic Preparedness and Response
BLA	Biologics license application
CBER	Center for Biologics Evaluation and Research
CDER	Center for Drug Evaluation and Research
CMH	Cochran-Mantel-Haenszel
CUSIP	Committee on Uniform Securities Identification Procedures
DOJ	Department of Justice
EBITDA	Earnings before interest, taxes, depreciation, and amortization
EML	Essential medicines list
EO	Executive Order
FDA	U.S. Food & Drug Administration
FDF	Finished dosage form
HHI	Herfindahl-Hirschman Index
IQR	Interquartile range
M&A	Merger and acquisition
NAICS	North American Industry Classification System
NDA	New drug application
NDC	National Drug Code
NSP	National Sales Perspective
OTC	Over-the-counter
PBM	Pharmacy benefit manager
SD	Standard deviation
USD	U.S. dollars
WAC	Wholesale acquisition cost

EXECUTIVE SUMMARY

In recent decades, the pharmaceutical industry has become increasingly concentrated in the United States, in part due to mergers and acquisitions (M&As) between drug manufacturers. This consolidation from M&As has been cited as a key factor affecting drug prices and drug shortages (U.S. Federal Trade Commission, 2022). In this study, we assessed trends in pharmaceutical M&As during 2010–2023 and evaluated the characteristics of drugs and companies involved in those M&As. We considered the effects of M&As on market concentration, drug prices, drug quantity sold, and drug shortages. We also considered how these associations vary by drug characteristics, including brand drugs versus generics, small molecule (i.e., chemical) drugs versus biological products, and essential medicines versus drugs not on essential medicines lists (EMLs). We used a combination of public and proprietary data sources on M&As, drug sales, drug shortages, and essential medicines. To establish drug ownership at the time of an M&A, we accessed historical archives of various U.S. Food & Drug Administration (FDA) datasets containing drug sponsor and application information, including Approved Drug Products with Therapeutic Equivalence Evaluations (commonly known as the Orange Book), the Purple Book, and the National Drug Code (NDC) Directory, among others. Figure ES-1 presents the main results of our study, which are discussed below.

From 2010–2016, the annual number of M&As in the pharmaceutical sector increased from just under 200 to 267. Thereafter, the numbers began to decline, going from 214 M&As in 2017 to 182 in 2023.[1] (See Figure ES-1A.) The years 2015 and 2016 were particularly active, with 2015 having the highest total transaction value ($314 billion)[2] and 2016 having the highest number of M&As (n=267). While there was no change, on average, in the annual number of pharmaceutical M&As across the full study period, the annual number of very high-value M&As of over $1 billion nearly doubled from 2010 to 2023 and accounted for 92.2 percent of the total M&A transaction value in 2023. The growing number of these high-value M&As is notable because drugs involved in transactions valued over $1 billion had higher odds of going into shortage within two years of the M&A date compared to similar drugs not involved in M&As ($p = 0.0198$).[3]

The therapeutic areas most frequently targeted for M&As were oncology (n=207 M&As or 24.8 percent[4]), followed by central nervous system disorders (n=127 or 15.2 percent) and anti-infectives (n=123 or 14.7 percent). Together, these three therapeutic areas accounted

[1] It should be noted that we excluded M&As involving cell and gene therapies, diagnostics, and medical devices.
[2] All monetary values are expressed in 2023 U.S. dollars. The sample estimate of $314 billion was calculated from M&As with known transaction values, which made up 60.8 percent of all M&As in 2015. Across all study years, 59.7 percent of M&As had known transaction values, and the annual rates of missing transaction values varied little.
[3] We define drugs "involved" in a transaction to include drugs owned by the target company and transferred to the acquirer, brand drugs owned by the acquirer with a shared therapeutic area as one of the target drugs, and generic drugs owned by the acquirer with a shared dosage form as one of the target drugs.
[4] In total, 835 M&As in our sample had a known and applicable therapeutic area, as reported in DealForma.

for over half of all M&As from 2010 to 2023 (see Figure ES-1B).[5] The relative frequency of oncology drug companies among M&A targets grew steadily, from 20.4 percent of M&As in 2010 to a peak of 34.8 percent in 2021. Anti-infective and vaccine-related M&As decreased from 2014 to 2019 but then increased from 2019 to 2023. This increase was driven in part by an increase in vaccine target companies during the same period—possibly a result of the COVID-19 pandemic.[6] Companies that make approved drugs were the most frequent M&A targets at the beginning of the study period, but their frequency dropped from 46.8 percent of M&As completed in 2010–2015 to only 28.6 percent of M&As in 2016–2021, when the leading asset's development stage was known. Preclinical drugs were the primary targets in just 8.7 percent of M&As occurring in 2010–2021, but rose to 16.2 percent in 2022–2023.

In the 12 months following an M&A, the market concentration increased by 5.9 percent, on average, when defining markets by therapeutic area. We divided the pharmaceutical sector into 14 markets based on therapeutic areas and evaluated each market's concentration using the Herfindahl-Hirschman Index (HHI). For each market, we calculated the average HHI over the study period and classified the market as highly concentrated, moderately concentrated, or competitive, according to U.S. Department of Justice guidelines (U.S. Department of Justice, 2024). Genitourinary drugs experienced the largest average increase in HHI of 27.6 percent in the year following an M&A, followed by gastrointestinal drugs (15.9 percent increase per M&A) and hematology drugs (13.5 percent increase per M&A). M&As in markets with high average concentration tended to produce larger increases in HHI (average increase of 171 points) than markets with moderate average concentration (average increase of 101 points) or markets that were competitive on average (average increase of only 9 points). Interestingly, M&As were associated with lower odds of drug shortage in highly concentrated markets ($p = 0.0465$) but were associated with elevated odds of drug shortage in competitive markets with low concentration ($p = 0.0055$).

Following an M&A, there was a decrease in the drug quantity sold, which we measured by the amount of active pharmaceutical ingredient (API) in the finished drug product that was sold, both for drugs involved in M&As and comparable drugs not involved in M&As. Generic drugs involved in M&As, however, experienced a more rapid decline in quantity sold than comparable non-M&A generics (see Figure ES-1C). Decreasing supply is a precursor to many (though not all) drug shortages. The accelerated declines that we observed in quantity sold are consistent with our finding that generic drugs involved in M&As have increased odds of going into shortage compared to similar non-M&A generics ($p = 0.0202$). Within the sample, M&As were associated with a more gradual decline in brand drugs' quantity sold, but the association was weak.

Price trends following an M&A differed between generic and brand drugs, based on our analysis of the IQVIA National Sales Perspective (NSP) invoice price and the wholesale

[5] Statistics are based on M&As for which there is an applicable and known therapeutic area. Therapeutic area was identified using DealForma data and is assigned to companies based on the therapeutic area of their leading asset.
[6] We included vaccines in the anti-infective therapeutic area, consistent with the Anatomical Therapeutic Chemical (ATC) classification system (WHO Collaborating Centre for Drug Statistics Methodology, 2024).

acquisition cost (WAC). For generics, the NSP invoice price and the WAC decreased both for M&A drugs and for comparable non-M&A drugs, but the average NSP invoice price declined more slowly for generics involved in M&As. This was a relatively small and short-term effect that lasted for one year after the transaction but had dissipated by the end of the second year after the M&A. In contrast, brand drugs experienced increasing NSP prices and WACs after an M&A. Brands involved in M&As had higher WAC growth in the six months immediately after the transaction, rising by 3.7 percent on average, compared to only 2.1 percent for similar non-M&A brand drugs ($p = 0.0032$).

Drugs involved in an M&A had 24.3 percent higher odds of going into shortage within two years of the transaction date compared to similar drugs not involved in M&As during the same time ($p = 0.0249$). Among generic drugs specifically, there was a 26.4 percent increase in the odds of a drug going into shortage if the company was involved in an M&A, compared to similar drugs not involved in M&As ($p = 0.0202$) (see Figure ES-1D). This finding is particularly salient as generic drugs already have the highest baseline risk of going into shortage (Schweitzer, 2013; U.S. Food and Drug Administration, 2020; The White House, 2021; Gagnon & Volesky, 2017). Our study did not find evidence that brand drugs involved in M&As go into shortage at higher rates than brands not involved in M&As (odds ratio = 1.02, $p = 0.9453$).

When analyzing generic and brand drugs collectively, M&As were associated with significantly higher shortage risk for the target company's drugs, but not for the acquiring company's drugs. We also found that essential medicines had 13.6 percent higher odds of going into shortage within two years if they had been involved in an M&A, though this association was weak ($p = 0.5528$). Essential medicines listed on the Advanced Regenerative Manufacturing Institute (ARMI) EML had 11.6 percent higher odds of being involved in an M&A than drugs not included on the ARMI EML ($p = 0.0307$).[7] Many of these essential drugs already have high baseline shortage risks and histories of drug shortage, and the possibility that this risk may increase further when involved in an M&A is notable.

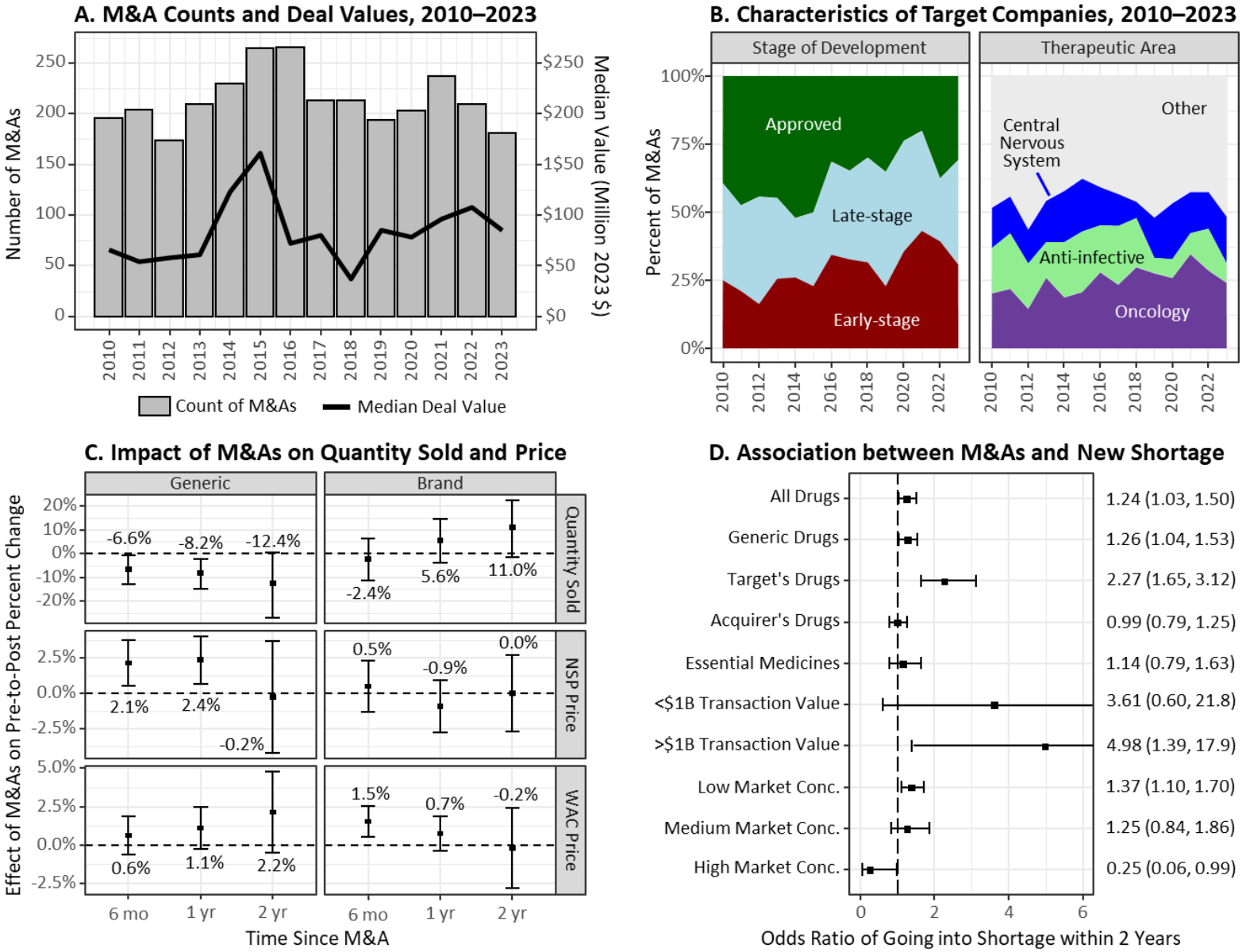
This study has several limitations. First, we did not account for parent companies, subsidiaries, or other corporate structures when assessing drug ownership. In our drug-level analysis, we only included M&As in which the target company or acquiring company was a sponsor of a U.S. drug application at the time of the transaction. Second, we relied on the North American Industry Classification System (NAICS) to identify pharmaceutical companies, which relies on self-reporting and may contain errors. The intended focus of the study was on U.S. markets, but the pharmaceutical industry is global by nature, and our analysis of M&As from 2010–2023 was not limited to transactions between companies headquartered in the United States. This may have led to the inclusion of some M&As focused on non-U.S. markets. Any such M&As, however, were excluded from the drug analysis, which only covered prescription drugs marketed in the United States.

[7] The ARMI EML was funded by the Department of Health & Human Services' (HHS) Office of the Assistant Secretary for Preparedness and Response (ASPR).

While our drug analysis was intended to include all prescription drugs marketed in the United States from 2018 to 2023, some drugs were likely omitted due to incomplete coverage in the underlying data and records failing to match across datasets, which could have affected our HHI calculations. Additionally, we used FDA's drug shortage list, which includes national shortages only. Our analysis does not capture the extent to which M&As affect availability of drugs at local or regional levels. It should also be noted that our drug-level analysis was performed for the period 2018–2023, which included the COVID-19 pandemic and two years of relatively high inflation. Temporary effects of the pandemic on drug prices, drug quantity sold, supply, and shortages may affect our findings. Finally, while our drug-level analysis aimed to reduce imbalances between a cohort of M&A drugs and a cohort of non-M&A drugs, additional evidence and analysis may be needed before the associations presented in this report can be interpreted as causal relationships. M&As are one of a variety of factors that can influence drug prices, drug quantities sold, shortages, or market concentration, and our study accounts for some but not all possible confounders.

Future research should investigate how M&As affect the number of manufacturers in pharmaceutical markets and the geographical dispersion of manufacturers. These changes could contribute to a less diversified pharmaceutical supply chain and negatively affect manufacturers' ability to respond to sudden changes in supply or demand. Additionally, the pharmaceutical supply chains are typically complex, and M&As involving supply chain intermediaries also likely impact drug shortage risks. Our study was focused on drug manufacturers, but medical device companies, wholesalers, pharmacies, pharmacy benefit managers (PBMs), and insurance companies can often affect the resiliency of the pharmaceutical supply chain. PBMs often negotiate exclusive contracts with a single drug manufacturer in exchange for lower prices of a drug, which could tend to reduce the number of suppliers for that drug—particularly given that the PBM sector is highly concentrated in the United States. Evaluating changes in formularies and in the number of suppliers may provide additional insights into drug shortage risk. Wholesalers, which are also highly concentrated in the U.S. pharmaceutical supply chains, often act as price setters in generic drug markets and can negotiate lower prices when there are multiple generic suppliers of a drug. Evaluating the impact of M&As with or between other supply chain intermediaries is a useful area for further study.

Figure ES-1. Overview of Results



1 INTRODUCTION

In the last two decades, there has been much consolidation in the U.S. pharmaceutical industry (Richman, et al., 2017), largely due to mergers and acquisitions (M&As). Pharmaceutical M&As and drug shortages have been important focus areas for researchers, the healthcare industry, and federal agencies in recent years. For example, in a 2022 workshop jointly organized by the Federal Trade Commission (FTC) and Department of Justice (DOJ), it was noted "that the median list price for new drugs has been increasing in recent years, that 'killer' acquisitions shut down potential competitors, and that lawsuits have been alleging illegal bundling and tying practices in the industry" (U.S. Federal Trade Commission, 2022). In healthcare markets, the stakes are often life-or-death, with many millions of people relying on pharmaceuticals to treat or manage diseases and health conditions, or for preventative care. There is potential for pharmaceutical M&As to be followed by drug price increases, lower patent output (a potential sign of diminished innovation), issues with manufacturing quality, and diminished drug availability (U.S. Federal Trade Commission, 2022).

Recent studies have reported mixed findings about the effects of M&As on pharmaceutical markets, including on drug prices and the quantities of drug sold. Hammoudeh and Nain (2024) found that M&As in the pharmaceutical sector have a negligible effect on drug prices, but other studies concluded that M&As are associated with price increases (Gupta, et al., 2019; Schutz, 2023; Bonaime & Wang, 2024). Several authors identify specific market characteristics that relate to different pricing effects in the wake of M&As, including drug type (Fein, 2024; Schutz, 2023; Hammoudeh & Nain, 2024), level of market concentration (Chintan, et al., 2017; Schutz, 2023; Bonaime & Wang, 2024; Gagnon & Volesky, 2017; Gupta, et al., 2019), and overlapping therapeutic areas between the target and acquirer's drug portfolios (Schutz, 2023; Bonaime & Wang, 2024; Hammoudeh & Nain, 2024).

Few studies have examined the effect of M&As on supply chain vulnerabilities and drug shortages, although these are areas of serious concern to policymakers. Gagnon (2012) concluded that M&As often lead to decisions that affect drug supply chains, such as reducing product lines, discontinuing products altogether, or changing manufacturing practices. Any of these can result in supply shortages. Most drug shortages in the United States affect generics (The White House, 2021), and a 2017 study found M&As to be steadily rising in the generic drug industry since 1995, with a surge in 2015 (Gagnon & Volesky, 2017). It is therefore of interest to understand whether and how M&As are associated with risks of drug shortages, supply disruptions, and price changes. The nature and extent of such associations are likely to be highly relevant to the U.S. drug market given their potential effects on national drug expenditures and patient health.

2 STUDY OBJECTIVES

The primary objectives of this study are to (1) assess trends in pharmaceutical M&As over the 2010–2023 period, (2) evaluate characteristics of drugs involved in M&As, and (3) examine the effects of M&As on the pharmaceutical supply chain. The primary metrics we apply to measure these effects are price, volume (or quantity) of the drug sold, market

concentration (using Herfindahl-Hirschman Index scores), and a drug's odds of going into shortage. Specifically, we aim to answer the following research questions:

1. How many pharmaceutical M&As occurred between 2010–2023? Has the frequency of M&As shown an identifiable trend during these years?

2. What are the characteristics of the companies and products involved in pharmaceutical M&As? What are the main therapeutic areas, drug technologies[8], and development stages[9] of the drug assets targeted by M&As? What types of drugs, company ownership structures (publicly held or private), and sizes of companies are typical of M&A acquiring companies and target companies?

3. Are M&As associated with a change in drug prices or the quantity of drugs sold (as measured through the quantity of active pharmaceutical ingredient in the finished drug product that is sold)?

4. How do M&As affect the pharmaceutical supply chain?
    a. Are M&As followed by changes in market concentration, as measured by the Herfindahl-Hirschman Index (HHI)?
    b. Do M&As increase the odds of a drug going into shortage?

This study advances the literature in several ways. We identified a total of 3,006 pharmaceutical M&As across the 14-year period 2010–2023, and 31,837 unique drugs that were marketed in the United States between 2018–2023. In addition to providing new findings about the associations between M&As and drugs prices and quantities sold, we also present a stratified cohort analysis of the effects of M&As on a drug's odds of going into shortage within two years of the M&A date, with subgroup analyses for particularly high-risk drug groups, such as generics and essential medicines. To our knowledge, this is the first study designed to quantify the association between M&As and drug shortages.

3 EXISTING RESEARCH ON M&As IN THE PHARMACEUTICAL SECTOR

3.1 Trends in M&As

Gagnon and Volesky (2017) studied the rise of M&As in generic drug markets from 1995 to 2016. Using data from Bloomberg Finance L.P., they found 345 M&As completed in those years that had a target company classified as a "generic medical drug company."[10] Of these

[8] Drug technologies were identified using the corresponding variable in the DealForma database, which defines drug technology as the branch of pharmaceutical manufacturing of the primary asset in the M&A deal. We aggregated this variable and options include small molecules, biologics, dosage form technology, or other (e.g., genomics, microarrays, compound libraries).

[9] Development stages refer to the major steps in bringing a new drug to market, including drug discovery, preclinical testing, phase I testing, phase II testing, phase III testing, and marketing after receiving approval.

[10] This likely excludes many companies that make brand drugs. Many companies that make both brands and generics would be classified as brand drug companies because brand drug sales generally surpass generic drug sales.

M&As, 122 (35.3 percent) involved target companies based in the United States. Among the deals targeting companies based in the United States, M&A activity increased after 1995 and spiked in 2014 and 2015. They found no M&As targeting U.S. generic drug companies in 1995, and only seven such M&As in 2014 (with a total announced value of $0.89 billion). By 2015, there were 16 such M&As totaling $26.66 billion, and in 2016 there were 17 M&As totaling $42.95 billion. These high transaction prices suggest that many of those generic drug company targets are relatively large, making M&As a strategy for substantial growth among acquiring companies that market generic drugs or are entering these markets. The high dollar value of M&As between 2015 and 2016 was in part due to Teva's acquisition of Allergan's generic drug business for $40.5 billion, accounting for 89.8 percent of the total M&A value in 2016 involving U.S. target companies (Teva Pharmaceuticals, 2015; Gagnon & Volesky, 2017). Bansal et al. (2018) attribute another spike in pharmaceutical M&A activity in 2018 to U.S. tax reform that went into effect in late 2017, which provided tax cuts to targets of M&A. Bansal et al. found that pharmaceutical transactions increased from 151 M&As in 2017 to 212 M&As in the first six months of 2018 alone, totaling over $200 billion in transaction value.

Several authors have concluded that the characteristics of companies' drug portfolios affect the incidence of M&A transactions. Hammoudeh and Nain (2024) found that companies with portfolios of drugs in the same therapeutic area(s) are more likely to merge. Similarly, Bena and Li (2014) reported that companies with "technological overlap," including companies having comparable patent portfolios and technical knowledge bases, are more likely to merge. In contrast, Feng et al. (2023) studied M&As in the United States involving on-patent drugs between 2007 to 2019 and found that just 25 percent of deals in their sample involved companies that made drugs in the same therapeutic area. It was far more common during their period of analysis for acquisitions to involve companies whose drugs did not compete in the same therapeutic area.

One way authors assess the types of drugs transferred in M&As is by evaluating the proportion of total M&A transaction value associated with certain drug types. A report released by GlobalData (2024) found that orphan drugs for rare diseases accounted for 36 of the announced M&As in the first quarter of 2024, accounting for $17 billion out of $65 billion (26.2 percent) total value of pharmaceutical M&As. Using a similar method, Gagnon and Volesky (2017) found that generic drug target companies accounted for 9.8 percent and 8.6 percent of all completed M&As with pharmaceutical targets based inside the United States and outside the United States, respectively, between 1995 to 2016.

3.2 Effects of M&As on Drug Prices and Quantity Sold

According to the literature, the impacts of pharmaceutical M&As on drug prices and quantity sold depend on the price metric being used and the drug's characteristics—including whether the acquirer and target have drugs that compete with each other (e.g., as indicated by the drugs treating the same indications or having the same therapeutic areas). Bonaime and Wang (2024) studied Medicaid-covered outpatient drug products using prices reported in the National Average Drug Acquisition Cost (NADAC) survey. They found that, when the target and acquirers' drugs had similar therapeutic areas, the M&A was followed by an average increase of

2.2 percent in the NADAC price of the acquirer's drugs. This effect, however, lasted for about one year. Feng et al. (2023) analyzed 151 M&As between 2007 and 2019 and observed much larger changes in manufacturers' net prices when the M&A was not required to be disclosed to DOJ or FTC because the deal valuation was below $200 million. These undisclosed M&As were associated with large average increases in the net price of drugs with indications common to both the acquirer and the target. The average increases were 270 percent for the target company's drugs and 63 percent for the acquiring company's drugs.

In contrast, similar M&As above the reporting threshold were associated with a more modest average price increase of 11 percent shortly after the transaction. No price increase was observed, on average, for "diversifying" acquisitions by large pharmaceutical companies that were acquiring drugs in nonoverlapping therapeutic areas. The authors concluded that regulatory review and government oversight help maintain competition in U.S. drug markets.

Schutz (2023) analyzed branded drug companies and found that M&As led to net price increases of 19 percent after the transaction. They also found that a net price increase was most common when the target and acquiring companies had overlapping therapeutics portfolios. Hammoudeh and Nain (2024) similarly found that brand drugs' pre-rebate prices increased after a merger.

According to the literature, M&As may also affect drug prices because of their role in market consolidation. Several authors found reduced market competition to be a factor in rising drug prices and supply shortages. Gagnon and Volesky (2017) argue that, by nature, M&As tend to decrease the number of competing firms. Gupta et al. (2019) agreed; their analysis of generic drugs suggests that a decrease in the number of generic suppliers—and thus a decrease in the number of available generic substitutes for a given brand drug—is associated with increasing prices of generic drugs. Schutz (2023) found that M&As lead to price increases for brand drugs as well; this was true for brand drugs with overlapping therapeutic areas between the two parties in the M&A, and it was also true regardless of market concentration, i.e., whether there was a single product dominating the market. Hammoudeh and Nain (2024) similarly found that, after an M&A, highly innovative companies (defined as those generating the majority of their revenue from novel, first-in-class drugs) tended to raise pre-Medicaid-rebate prices of drugs with therapeutic areas shared by both M&A parties, especially in the case of first-in-class patented brands.

However, different patterns have been observed for other drug groups. Hammoudeh and Nain (2024) found that generic drugs tend to experience declining prices after an M&A due to gains in efficiency, reductions in cost, and reallocating research and development (R&D) spending to cheaper, lower-risk products. While this differs from the findings of Gupta et al. (2019), the study by Hammoudeh and Nain (2024) was based on pre-Medicaid-rebate drug prices paid by state Medicaid agencies, which they calculated using CMS's State Drug Utilization Data.

3.3 Impact of M&As on Drug Shortages

Based on a 2023 analysis by the U.S. Food & Drug Administration (FDA), new drug shortages peaked in 2011 and then rapidly declined over the next few years, but since 2015, the number of new drug shortages per year has steadily increased (U.S. Food & Drug Administration, 2023). The same analysis found that, between 2017 and 2023, the number of annual ongoing drug shortages also increased. Sterile injectables make up the majority of shortages. FDA analyzed a sample of 127 drug shortages in 2010 and 2011 and found that 80 percent were sterile injectables (U.S. Food & Drug Administration, 2011). In another analysis from 2020, FDA sampled 163 drugs that went into shortage between 2013 and 2017 and found that 63 percent were sterile injectables (U.S. Food and Drug Administration, 2020).

While there is limited research on the impact of M&As on drug shortages, two main contributing factors are often identified—vulnerabilities in the pharmaceutical supply chain and limited domestic manufacturing capacities. There is debate among authors, however, about whether growing market concentration increases supply chain vulnerabilities. Gagnon and Volesky (2017) note that market competition tends to decrease following an M&A, which may partially explain the increasing number of shortages during their study period from 1995 to 2016. While a causal analysis is beyond the scope of Gagnon and Volesky's study, a possible explanation for their observations is that undiversified supply chains have increased risk for drug shortages, and reduced competition from M&As heightens this risk (U.S. Department of Health and Human Services, 2024). In the United States, most of the injectable generic drugs on the market were supplied by only seven manufacturers as of 2016 (World Health Organization, 2016). The high degree of consolidation may be partly responsible for recent shortages in injectable generic oncology drugs, which have an especially high public health impact due to the heavy reliance of cancer patients undergoing chemotherapy on those drugs (U.S. Food and Drug Administration, 2020).

Haninger et al. (2011), however, offer an alternative view. They found that market consolidation in the sterile injectable industry was relatively rare between 2005 and 2011. They concluded that M&As were not a factor in shortages of sterile injectable drugs during that time and suggested instead that manufacturing capacities were misaligned with demand. Specifically, they pointed to a sudden increase in use of chemotherapy, driven in part by expiration of numerous chemotherapy drug patents expiring between 2008–2010.

Generic drugs are especially vulnerable to supply shortages and experienced high-profile shortages in the early 2010s (Schweitzer, 2013), which have continued in recent years (Joyce, 2023). Generic drugs often have low profit margins, and sterile injectables generally require large financial investments due to complex and highly specialized production technologies. This limits manufacturers' profitability and disincentivizes market entry, leading to fewer suppliers in those drug markets (U.S. Department of Health and Human Services, 2024). Additionally, there are periods of extreme concentration in the U.S. generic drug markets. In 2020, FDA reported that 40 percent of generic drug markets had only a single manufacturer supplying the market (U.S. Food and Drug Administration, 2020). Without other suppliers to help meet unexpected supply shortfalls or demand surges, a single disruption may be sufficient to trigger a shortage.

We did not identify any studies that quantify the effects of M&As on drug shortages, but there is significant literature on how shortages are caused by supply chain vulnerabilities, which M&As may precipitate. For example, some authors have suggested that M&As impact manufacturing practices, leading to consolidation of product lines, product discontinuations, or relocation of manufacturing facilities abroad—all of which can reduce supply chain resiliency and increase the risk of drug shortages (The Multi-Stakeholder Steering Committee On Drug Shortages In Canada, 2017; Gagnon, 2012; Gagnon & Volesky, 2017). A report by FDA (2020) points to manufacturing and product quality problems as the primary reasons for disruptions in production and supply, accounting for 62 percent of all drug shortages. While M&As were not the focus of this FDA report, some of the quality problems may have followed an M&A (e.g., brought on by a product discontinuation or product line consolidation). Additionally, over the past three decades, pharmaceutical manufacturing has become increasingly global. This limits the nation's options in responding to some supply chain disruptions and the timeliness of responses, because changes that increase manufacturing output (e.g., repurposing a facility to make the drug in shortage) may trigger regulatory review by multiple other governments. As of August 2024, 52 percent of all FDA-registered finished dosage form (FDF) manufacturing facilities and 76 percent of all FDA-registered active pharmaceutical ingredients (API) manufacturing facilities were outside the United States (National Economic Council, National Security Council, 2024). The percentage of FDA-registered manufacturers making FDFs and APIs is even higher among generics, with 54 percent of generic FDF manufacturers and 82 percent of generic API manufacturers being located internationally. While global manufacturing does offer economic benefits, it also increases the complexity of supply chains, which may limit the United States' ability to respond to supply chain risks and disruptions.

4 METHODOLOGY

We constructed three distinct analytic datasets by linking the data sources described in Section 4.1. Section 4.2 describes the inclusion criteria for our study, and Section 4.3 presents the analytic methods we used to answer the research questions.

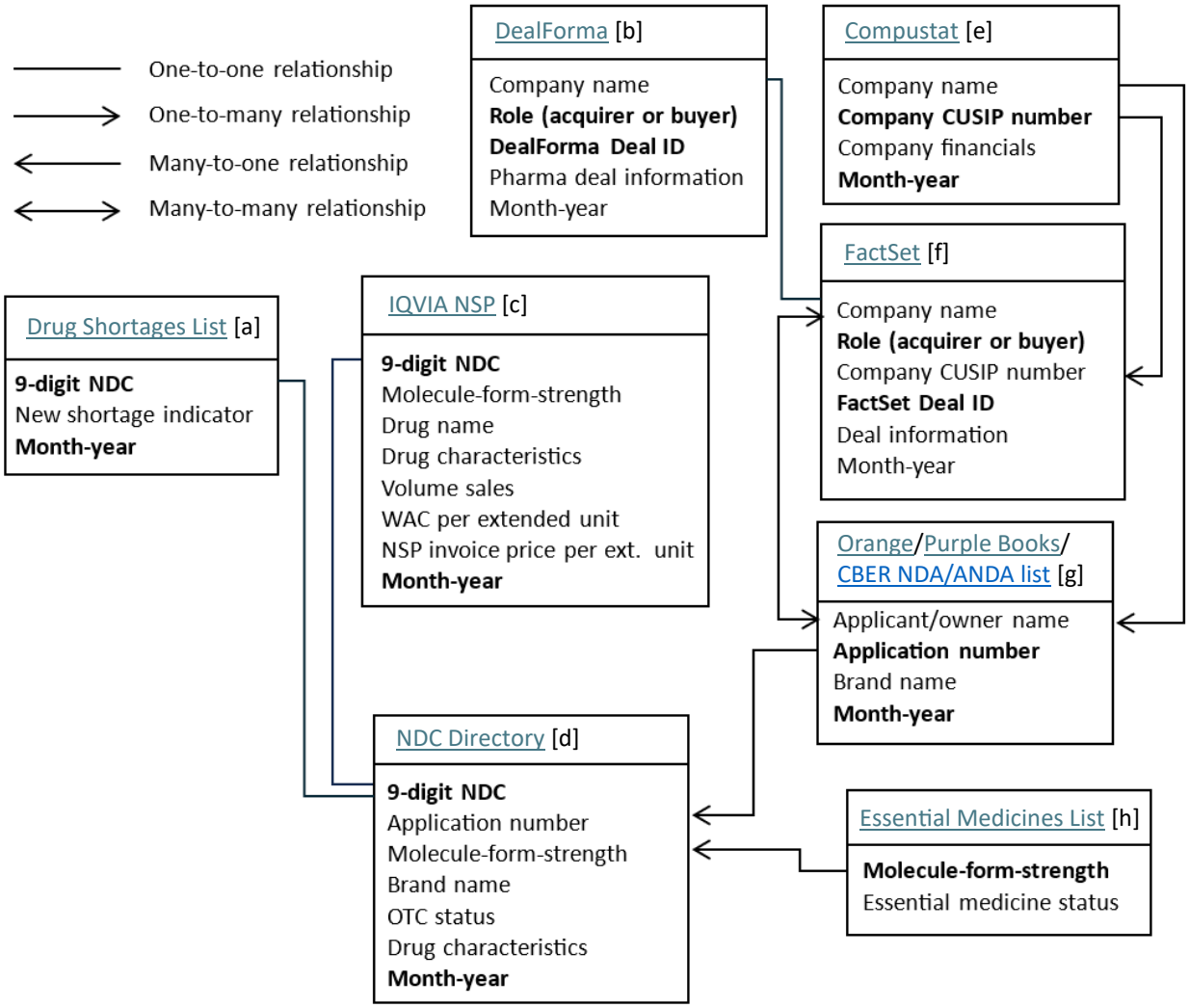
4.1 Data Sources

Figure 1 provides an overview of the data sources we used in the analysis. A detailed description of each data source and the methods of assembling the analytic datasets appears in Appendices A.1 and A.2. Variables in bold indicate primary keys that uniquely identify rows of each dataset. The arrows represent the parent-child relationships, which correspond to the type of matching when joining datasets. For datasets that are periodically updated—including the Drug Shortages list, the National Drug Code (NDC) Directory, and the Orange and Purple Books—we used the Internet Archives to construct historical records (Internet Archive, 2024). This allowed us to (a) identify the complete list of drugs that went into shortage even if they have since been removed from the shortage list; (b) establish the correct ownership of drug applications at the time of the M&A; and (c) identify the full list of drugs (i.e., 9-digit NDCs) that were marketed under a drug application when the drug sponsor/applicant was involved in an M&A.

We used FactSet to identify in-scope M&As between pharmaceutical companies, DealForma for deal-related information, and Compustat for company financial information. We used IQVIA National Sales Perspective (NSP) for the quantity of drugs sold and prices. We used FDA Drug Shortage lists to identify drugs that went into shortage and shortage start dates, and the FDA NDC Directory to link NDC numbers to drug application numbers. We identified essential medicines based on both the Executive Order Essential Medicines List (EML) published by FDA and the EML published by the Department of Health & Human Services' (HHS) Office of the Assistant Secretary for Preparedness and Response (ASPR) and the Next Foundry for American Biotechnology at Advanced Regenerative Manufacturing Institute (ARMI). To determine the owner of the drug application (i.e., "sponsor" or "applicant"), we combined the FDA Orange Book, the FDA Purple Book, and the Center for Biologics Evaluation and Research (CBER) list of New Drug Applications (NDAs) and Abbreviated New Drug Applications (ANDAs).

Where possible, datasets were merged on unique identifiers, such as NDC numbers, drug application numbers, and company Committee on Uniform Securities Identification Procedures (CUSIP) numbers. If a unique identifier was not available, we used name-based matching (e.g., product names, drug ingredient lists, company names). We did name-based matching using a combination of automated methods (e.g., exact matching, fuzzy matching, regex matching) followed by manual review.

Figure 1. Analytic Dataset Architecture (Entity-Relationship Diagram)



Variables in bold indicate primary keys, which uniquely identify rows of dataset.
[a] We pre-processed the drug shortage data to collapse from 11-digit NDC to 9-digit NDC, see Table A - 2.
[b] For full list of deal information, see Table A - 8.
[c] To aggregate across sales channels, we calculated total volume sales and weighted average prices per API unit and per extended unit, both in WAC dollars and in NSP invoice price dollars. For the full list of IQVIA-NSP drug characteristic variables, see Table A - 1.
[d] We de-duplicated cases where a single NDC had multiple entries in a given month-year. For the full list of drug characteristic variables, see Table A - 4.
[e] For full list of company financial variables, see Table A - 7.
[f] For full list of deal information, see Table A - 6.
[g] To acquire a single row per application number and month-year, we removed extraneous information relating to product number, supplements, etc., see Table A - 3.
[h] We merged the Executive Order EML with the ARMI EML and added an indicator for the EML source (EO, ARMI, or both) (see Table A - 5).

To perform the analysis, we developed three distinct datasets.

- **M&A dataset (2010–2023).** We identified 3,006 pharmaceutical M&As that were completed from 2010–2023 between companies that manufacture or develop drugs. We used this dataset to evaluate the frequency and type of pharmaceutical M&As, the value of these transactions, and the types of companies involved in these M&As.

- **Drug dataset (2018–2023).** We developed a dataset of 31,837 unique 9-digit NDCs, which we refer to hereafter as "drugs." We analyzed these drugs from 2018–2023, linking historical records of drug ownership, historical sales data, historical records of drug shortage announcements (including the specific drugs that went into shortage[11]), and essential medicine lists, which allowed us to assess trends in individual drugs before and after M&As. We used this dataset to evaluate the types of drugs involved in M&As (including whether they are designated as essential), the frequency and rate at which they went into shortage, and the effects of M&As on market concentration.

- **Drug cohort study dataset (2018–2023).** We assigned 27,583 of the 31,837 drugs to one of two cohorts: a "treated" cohort of drugs that were involved in an M&A (n = 2,124) and a "control" cohort of drugs not involved in an M&A (n = 25,459). To assign drugs to their proper cohort, we used an exact matching algorithm. First, we partitioned the drug dataset (i.e., all 2,288,966 observations of the 31,837 drugs) into strata based on the month-year, price quintile, dosage form, brand/generic status,[12] and molecule type (small molecule versus biologic). Then we identified strata that contained at least one drug that was involved in an M&A in the listed month-year and at least one drug that was marketed in that same month-year and had no M&As during the study period. We selected strata with at least one M&A drug and at least one non-M&A drug and included all observations in the selected strata. The resulting observations formed our drug cohort study dataset. We used this dataset to assess whether a drug's price and quantity sold were different after an M&A compared to similar drugs not involved in an M&A. We also used the drug cohort study dataset to evaluate whether drugs involved in M&As had higher odds of going into shortage within two years of the M&A date. By matching on month and year, we were able to compare the M&A drugs to similar non-M&A drugs over the same periods of time. Matching on the other variables removed imbalances between the M&A drugs and the non-M&A drugs.

[11] We note that, in this study, the definition of a "drug in shortage" is different from FDA's definition of a shortage. Specifically, FDA lists a shortage by active ingredient; a single active ingredient may cover several NDCs accounting for different dosage forms. Consequently, the number of shortages as reported by FDA will differ from the number of shortages reported in this study.

[12] We used IQVIA NSP to identify the brand/generic status of each drug. In general, drugs are marked as brands if they are sold under a brand name, which includes original biologics and biosimilars sold under brand names. Drugs are marked as generic if they are not sold under a brand name, which could include drugs like "water for injection."

For our final dataset of in-scope pharmaceutical M&As, we merged FactSet, DealForma, and Compustat. For our final drug dataset, we merged all data sources in Figure 1 for the period 2018–2023. The drug cohort study dataset was selected from the drug dataset. Table 1 presents the characteristics of the drug dataset and the drug cohort study dataset.

Table 1. Sample Sizes of Drug Datasets [a]

	Drug Dataset (2018–2023)		Drug Cohort Study Dataset (2018–2023) [b]	
	Involved in M&A	Not Involved in M&A	Involved in M&A	Not Involved in M&A
Number of Observations [c]	4,142 [d]	2,284,824	2,506	168,511
Number of Drugs	3,595	28,242	2,124	25,459
Number of M&As	91		61	

N/A = not applicable.
[a] The full M&A dataset contained 3,006 M&As from 2010 to 2023. We matched 91 of these M&As to the prescription drugs marketed in the United States from 2018 to 2023.
[b] The 171,017 observations in the cohort study dataset were selected from the 2,288,966 observations in the full drug dataset.
[c] Shows the count of month-drug combinations involved in an M&A or not involved in an M&A. In the drug dataset, a single drug can be counted in both columns if it has data in a month when it was involved in an M&A and data in months when it was not involved in an M&A.
[d] There are more observations of M&As (4,142) than drugs involved in M&As (3,595) because a small percentage of drugs were involved in more than one M&A.

4.2 Inclusion Criteria

For the M&A dataset, we applied the following inclusion criteria:

- The transaction event was completed between January 1, 2010, and December 31, 2023.
- The transaction event is categorized as a merger, an acquisition of assets, or an acquisition of majority interest. We refer to all of these—mergers, acquisitions, asset transfers, divestitures—as M&As.
- The acquiring company owned less than 50 percent of the target company before the transaction and at least 90 percent afterwards. The acquirer ownership percentage was reported in FactSet and served as the basis for this inclusion criterion.
- The acquiring company had a primay or secondary North American Industry Classification System (NAICS) code of 325412, Pharmaceutical Manufacturing, or 325414, Biological Product (except Diagnostic) Manufacturing.
- The target company had one or more of the following primary or secondary NAICS codes:
  - 325412—Pharmaceutical Manufacturing

- 325414—Biological Product (except Diagnostic) Manufacturing
- 325411—Medicinal and Botanical Manufacturing
- 541714—Research and Development in Biotechnology (except Nanobiotechnology)

- The target company in the transaction was not focused on cell/gene therapies, medical devices, or diagnostics. We identified these companies using the DealForma data.

For the drug dataset, we included prescription drugs marketed in the United States at any time between January 1, 2018, and December 31, 2023. When matching M&As to the drug-level data, we only included the M&As meeting the inclusion criteria above. While we did not exclude M&As based on company location,[13] we only analyzed drugs marketed in the United States.

4.3 Analytic Methods

To answer the research questions, our study performed several analyses, which used different time periods based on data availability. The methods are described briefly below and are discussed in depth in Appendix A.3.

We used the dataset of 3,006 pharmaceutical M&As from January 2010 through December 2023 to analyze M&As by transaction value, type of deal, therapeutic area, technology, phase of development, drug type, company type, and company NAICS. Based on company type and NAICS, we evaluated trends in the specific pharmaceutical industries of the acquiring company and target company. We used the full drug dataset of 31,837 drugs from 2018–2023 to calculate descriptive statistics on the types of drugs involved in M&As, their annual sales, and their therapeutic areas. The full drug dataset also allowed us to calculate the HHI in the 12 months preceding and following each M&A, in order to assess changes in market concentration within markets defined by aggregate therapeutic areas.[14] As part of our analysis of drug shortages, we used the full drug dataset to compare shortage rates within various drug subgroups (e.g., type of drug, therapeutic area). We also evaluated whether essential medicines are involved in M&As more frequently than drugs that are not listed in the EMLs, which we refer to as "non-essential medicines." In our drug-level analysis, we define a drug at the level of the 9-digit NDC, which uniquely identifies the molecule, strength, dosage form, and labeler. Unless stated otherwise, all references to "drugs" refer to distinct 9-digit NDCs.

We used the drug cohort analysis dataset of 27,583 drugs from 2018 to 2023 to perform two retrospective cohort analyses comparing a cohort of drugs involved in M&As to a similar cohort of control drugs not involved in M&As. The two cohorts were matched on month and

[13] The pharmaceutical industry is highly global and excluding companies on the basis of geographic location would have been too restrictive given that many non-U.S. companies operate in the U.S. drug market.

[14] HHI is a measure of market concentration. We used it to assess consolidation and levels of competition before and after an M&A. We defined drug markets by therapeutic area. See Appendix A.3.5 for how HHI is calculated.

year so that they could be compared over the same calendar time. (See Appendix A.3 for a full description of all matching criteria.) In the first cohort analysis, we evaluated changes in price and quantity sold after the M&A date between the two cohorts. We considered two main price metrics, the NSP invoice price and the wholesale acquisition cost (WAC), both of which we calculated per extended unit, weighted by the quantity of drug sold. We measured the quantity of drug sold using total mass in kilograms (kg) or total activity in International Units (IU) of the API in the finished drug product. The NSP price provides insight into drug manufacturers' sales price before accounting for off-invoice discounts. The WAC is the manufacturer's list price, which often serves as a basis of negotiation for reimbursements paid by the payer or healthcare plan and therefore provides insight into how M&As are associated with changes in the cost to beneficiaries and plan sponsors.

In the second cohort analysis, we compared the two cohorts' odds of going into shortage within two years of the M&A date. We selected a two-year period because an analysis by the Government Accountability Office (GAO) found that drugs that experienced a decrease in the number of suppliers in the prior two years were more likely to go into shortage (U.S. Government Accountability Office, 2016). This provides at least one theoretical mechanism that might explain associations found in this study, i.e., shortages occurring in the two-year period could plausibly be attributed to consolidating M&As. When identifying the drugs that went into shortage in a given month, we included any drugs listed in the FDA shortage announcement as well as any other drugs marketed at that time that had the same molecule-form-strength, since FDA declares shortages for the entire drug market.

All monetary values were inflated to 2023 dollars using the seasonally adjusted consumer price index for medical care (U.S. Bureau of Labor Statistics, 2024), including drug prices, drug sales data, M&A transaction values, and company financial information. Any values that were reported in foreign currency were converted to U.S. dollars using an exchange rate for the month when the data were reported (International Monteary Fund, 2024) before being inflated to 2023 dollars.

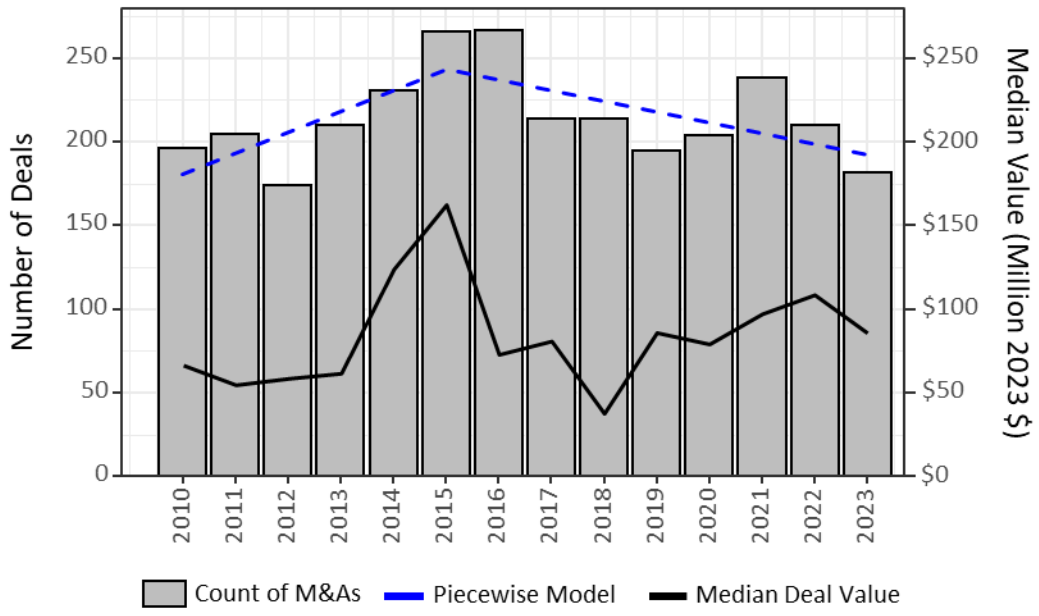
5 RESULTS

5.1 Frequency and Type of Pharmaceutical M&As

5.1.1 Overall Trends

The number of pharmaceutical M&As per year ranged from a minimum of 174 in 2012 to a maximum of 267 in 2016 (see Figure 2). The annual M&A frequency varied widely and did not show a clear trend over the study period, though there was a decline in the number of M&As over the last three years analyzed, 2021–2023. The median and average transaction values both contained high variation but had a peak in 2015, which coincided with high M&A activity. In 2015, total M&A transaction value was $314 billion (not shown). In comparison, total transaction value was $74.9 billion in 2010, the first year of the study, and $143 billion at the end of the study time period (in 2023). Over the study period, the median value per M&A grew by 2.4 percent annually, and the mean M&A deal value grew by 5.8 percent annually, but these trends were not strongly distinguishable from year-to-year variation ($p = 0.3387$ and $p = 0.1189$, respectively).

Figure 2. M&A Counts and Median M&A Deal Values, 2010–2023

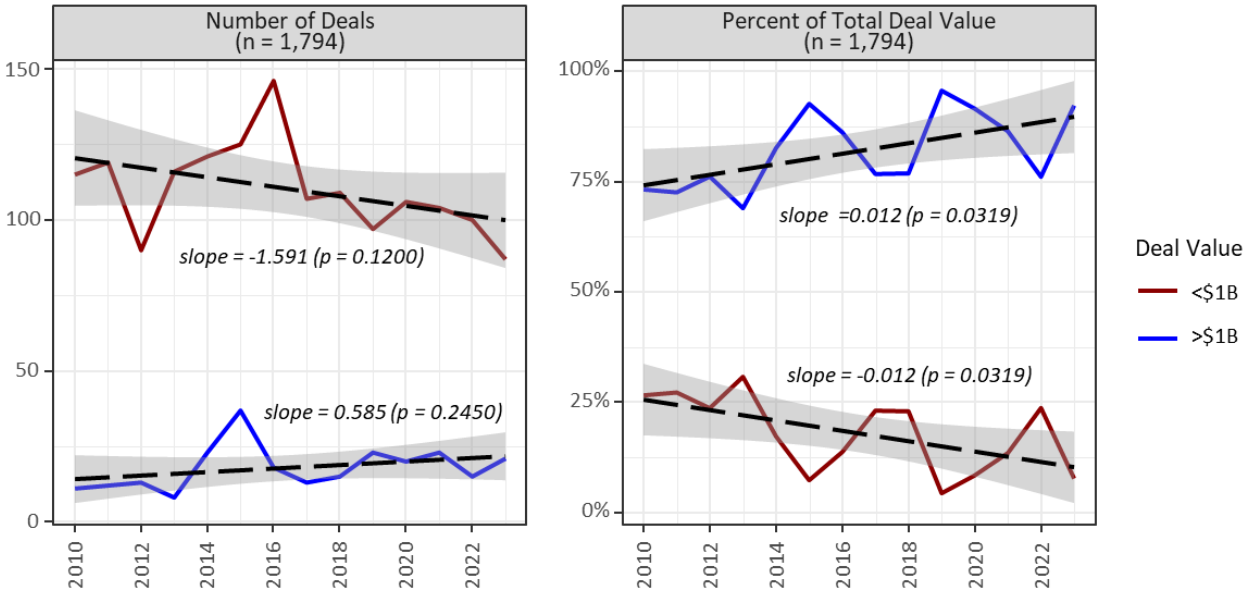


Data Source: 3,006 in-scope M&As identified in FactSet, of which 1,794 (59.7%) had a known transaction value. Transaction values were inflated to 2023 dollars using the consumer price index for medical care, seasonally adjusted (U.S. Bureau of Labor Statistics, 2024). The piecewise linear model identified the year 2015 as a break point when the trend in annual number of M&As changed ($p = 0.0716$ using Davies' test). These counts represent the universe of M&As for 2010–2023 that met our inclusion criteria.

Transaction values were heavily right-skewed, with some M&As having significantly higher transaction values. In the sample, these highest-value M&A deals exhibited some

distinct trends (see Figure 3). Among M&As with a known transaction value,[15] there was a slight decline in M&As valued below $1 billion, and a slight rise in M&As valued over $1 billion, though these trends were not easy to distinguish from year-to-year variation (p = 0.1200 and p = 0.2450, respectively). M&As valued at over $1 billion, however, made up a growing share of total annual transaction dollars, and this trend was statistically significant (p = 0.0320). In 2023, M&As valued over $1 billion made up 92.2 percent of the total M&A transaction value. While the number of M&As valued below $1 billion may be decreasing, the observed growth in median transaction values in our sample suggests mid-value M&As may also be rising in value. Within the lower-valued M&As, trends were highly similar between M&As valued at <$500 million and M&As valued at $500 million to $1 billion.

Figure 3. Trends in High-Value M&A Deals, 2010–2023



Data Source: FactSet (2010–2023). Note: Black line shows fitted linear trend. Gray area shows standard error in fitted trend. Prior to fitting linear trends, we checked for homoscedasticity,[16] normality, and independence. The slope of the left graph is the average change in number of M&A deals per year. The slope of the right graph is the average change in percentage of total deal value per year (e.g., an increase of 1.2 percentage points per year for M&As over $1 billion).

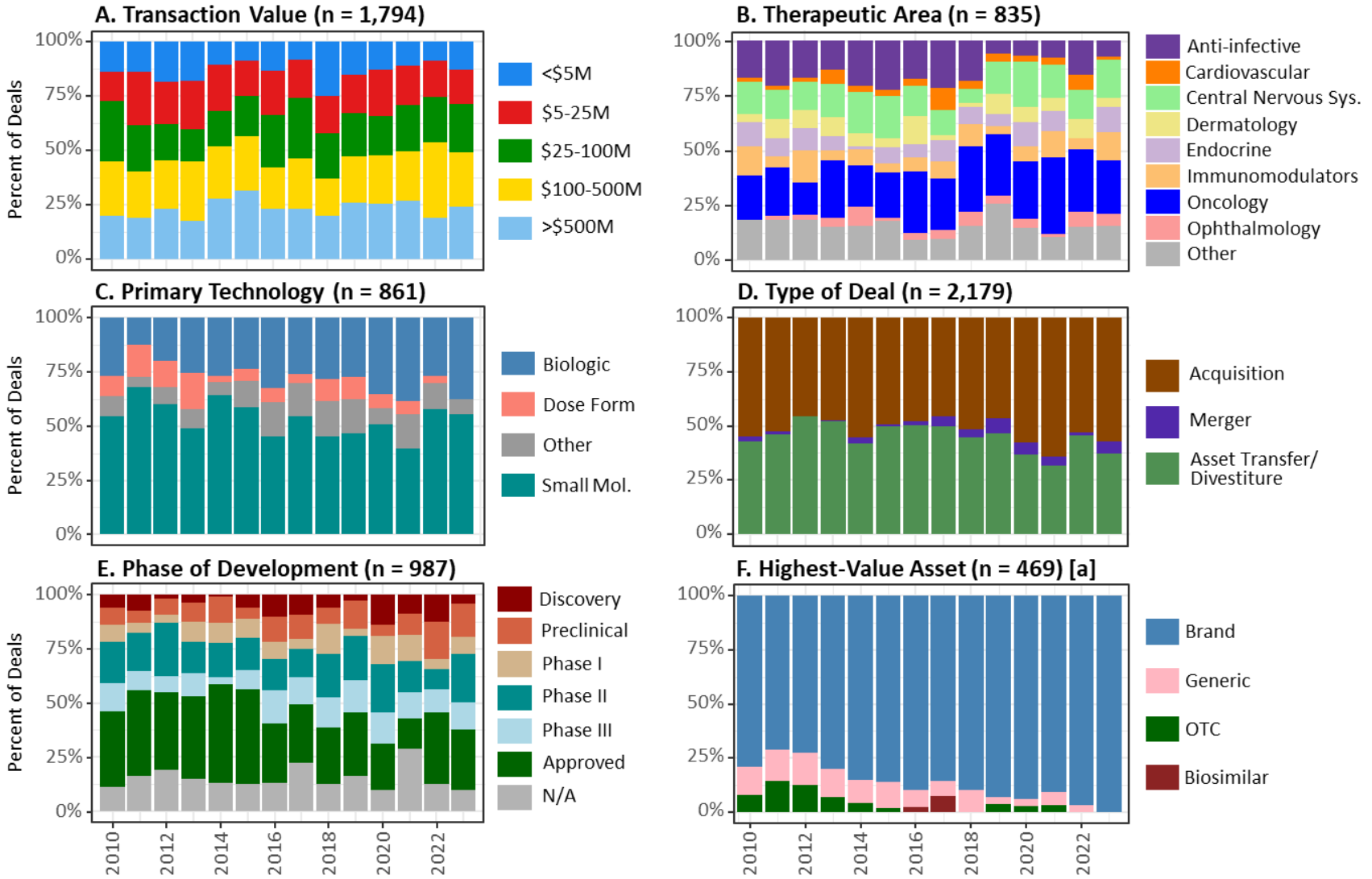
Transactions valued at over $500 million or from $100–$500 million accounted for the largest shares of M&As, with each comprising 23.6 percent of M&As from 2010–2023 (see Figure 4A, below). Mid-sized M&As of $25–$100 million made up 20.7 percent of M&As. Small M&As of $5–$25 million and less than $5 million accounted for 18.7 percent and 13.4 percent of all M&As, respectively. The two lowest-value M&A groups (<$5 million and $5–$25 million)

[15] Of the 3,006 in-scope M&As in our 2010-2023 dataset, 1,794 (59.7 percent) had known transaction values. The annual rate of missing values ranged from 35.7 percent (in 2010) to 46.6 percent (in 2021), with a standard deviation of 3.3 percent.

[16] "Homoscedasticity describes a situation in which the error term (that is, the "noise" or random disturbance in the relationship between the independent variables and the dependent variable) is the same across all values of the independent variables." (Statistics Solutions, 2025)

are the most likely to include failed ventures in which the company's assets were acquired during liquidation.

Figure 4. Characteristics of M&As and Target Companies, 2010–2023



Data Sources: FactSet (2010–2023) and DealForma (2010–2023). N/A = not applicable. For additional numerical tabulations, see Table B - 3.
[a] Target companies that make both brand drugs and generic drugs are classified by DealForma according to the highest-selling product, which would typically be a brand drug and not a generic drug.

For most therapeutic areas, the acquisition rate did not show major trends (see Figure 4B). In our sample, target companies that focused on oncology drugs, however, saw a substantial increase in relative M&A activity, rising from 20.4 percent of M&As in 2010 to a peak of 34.8 percent in 2021. M&As targeting companies with infectious disease drugs were decreasing from 2014–2019, but then began increasing after 2019—possibly a result of the COVID-19 pandemic. In our sample, 835 M&As had a known and applicable therapeutic area, and the most common M&A targets were oncology (n=207 M&As or 24.8 percent), followed by central nervous system (n=127 or 15.2 percent) and anti-infective (n=123 or 14.7 percent).

The leading technology of the target company in M&A was dominated by small molecule drugs, which made up roughly half of all M&As from 2018–2023 with known technology (see Figure 4C). Biological products grew as a target from 2010–2023, partly fueled by an increase in acquisitions involving antibody technology, which tripled from 7.3 percent of M&As in 2010 to 21.7 percent of M&As in 2023. M&As with vaccine technologies made up a relatively small share and were decreasing before 2019, but have been increasing since then, which may partly explain the similar trend seen in infectious disease targets.

Only 2.9 percent of M&As qualified as mergers (see Figure 4D). The other 97.1 percent of M&As were divided roughly equally between acquisitions (52.1 percent) and asset transfers/ divestitures (45.0 percent). Acquisitions, however, have become more frequent since 2019. From 2010–2019, acquisitions showed little trend and composed 49.7 percent of all M&As. From 2020–2023, they rose to 58.4 percent of all M&As. In 2021, the relative frequency of acquisitions reached a peak, when they made up 64.3 percent of M&As.

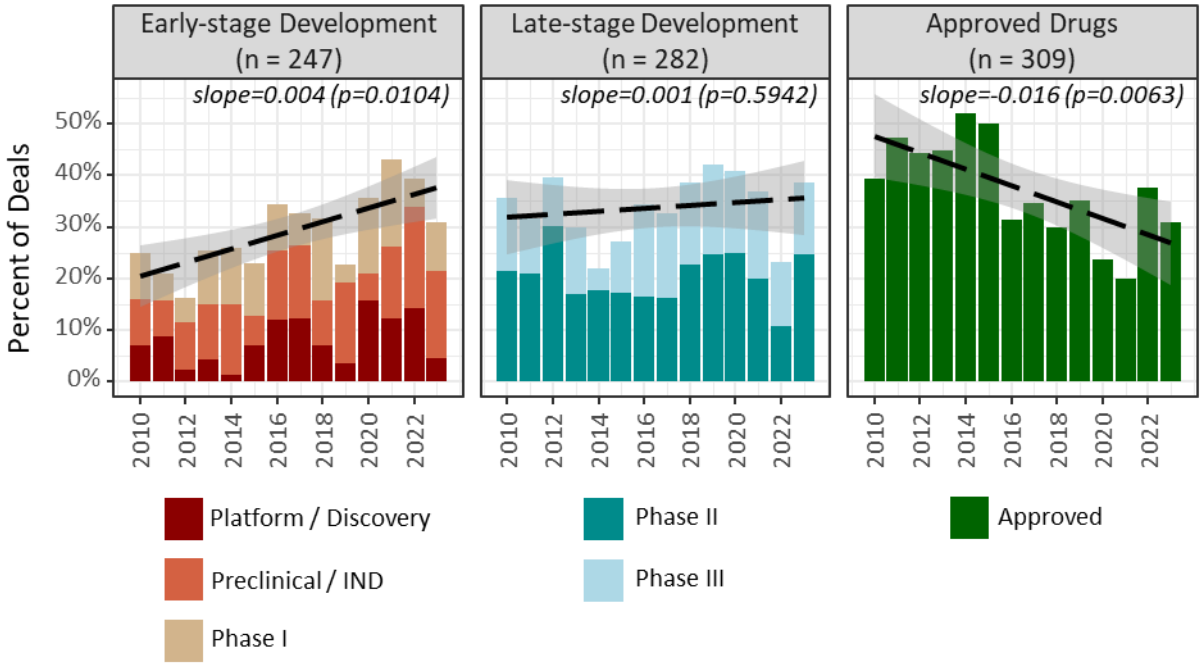
As Figure 4F shows, the target company's leading asset was a brand drug in 85.3 percent of the M&As from 2018 to 2023 (when known). However, this may create a false impression that most M&As are focused on brand drugs. Many of these "brand drug companies" likely also marketed generics.[17] In fact, generic drugs are far more common in the 2018–2023 drug sample (discussed below) than Figure 4F might suggest. In our drug sample, the number of generic drugs that we identified as being involved in an M&A was more than twice the number of brand drugs (see Table 2). While Figure 4F shows that the majority of companies are classified as brand drug manufacturers, many of these likely also make generic drugs.

Figure 4E and Figure 5 (below) display a steady decrease in M&As targeting companies with approved drugs, which historically were the most frequent targets. From 2010–2015, approved drug companies were involved in 46.8 percent of M&As in which the leading asset's development stage was known and applicable. This dropped to only 28.6 percent in the period from 2016–2021. Companies with leading assets in late-stage clinical development (phases II and III) and companies with leading assets in early-stage development saw the reverse trend.

[17] DealForma classifies companies according to their highest-selling product. Target companies that make both brand drugs and generic drugs typically would be classified as brand drug companies, since generic drugs usually earn lower sales than brand drugs.

M&As involving preclinical drugs, in particular, increased substantially, from 10.5 percent of all M&As in the period 2010–2021 to 18.2 percent in 2022–2023.

Figure 5. Trends in Development Stage of Target Company, 2010–2023



Data Source: FactSet (2010–2023) and DealForma (2010–2023). Note: Black line shows fitted linear trend. Gray area shows standard error in fitted trend. Prior to fitting linear trends, we checked for sufficient homoscedasticity, normality, and independence. Graphs exclude M&As for which the stage of development is not relevant or unknown.

5.1.2 Industry, Ownership, and Size of Acquirer and Target Companies

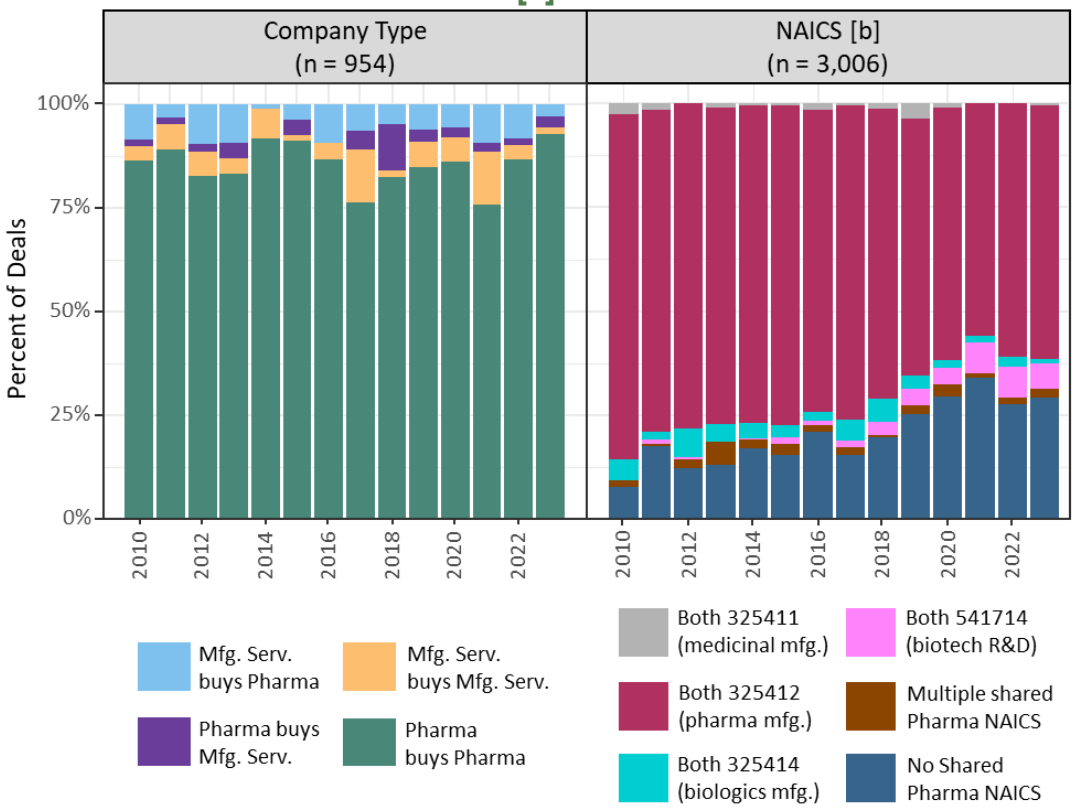
A large majority of M&As—77.6 percent—between 2010–2023 involved companies that shared at least one of the four relevant pharmaceutical NAICS codes (see Figure 6).[18] However, there was also an increase in M&As between pharmaceutical companies that have no overlapping pharmaceutical NAICS codes, as shown in Figure 6.

Most M&As were between two companies that both held the 325412 NAICS designation, i.e., Pharmaceutical Manufacturing, though this percentage has declined from 83.2 percent in 2010 to 61.0 percent in 2023. In contrast, M&As between companies that did not have a mutual NAICS code increased from 7.7 percent in 2010 to 29.1 percent in 2023—almost a 300 percent increase.

This increase in expanding in-house capabilities was focused on acquiring companies in NAICS 541714, Research and Development in Biotechnology (except Nanobiotechnology). In 2010, companies with this biotech R&D NAICS (541714) were involved in less than 1 percent of M&As between companies with nonoverlapping pharmaceutical NAICS codes. By 2023, this had risen to 67.9 percent. This dramatic increase reflects potential consolidation of pharmaceutical manufacturers with pharmaceutical R&D companies.

[18] The relevant NAICS codes include:
NAICS 325411–Medicinal and Botanical Manufacturing
NAICS 325412–Pharmaceutical Manufacturing
NAICS 325414–Biological Product (except Diagnostic) Manufacturing
NAICS 541714–Research and Development in Biotechnology (except Nanobiotechnology)

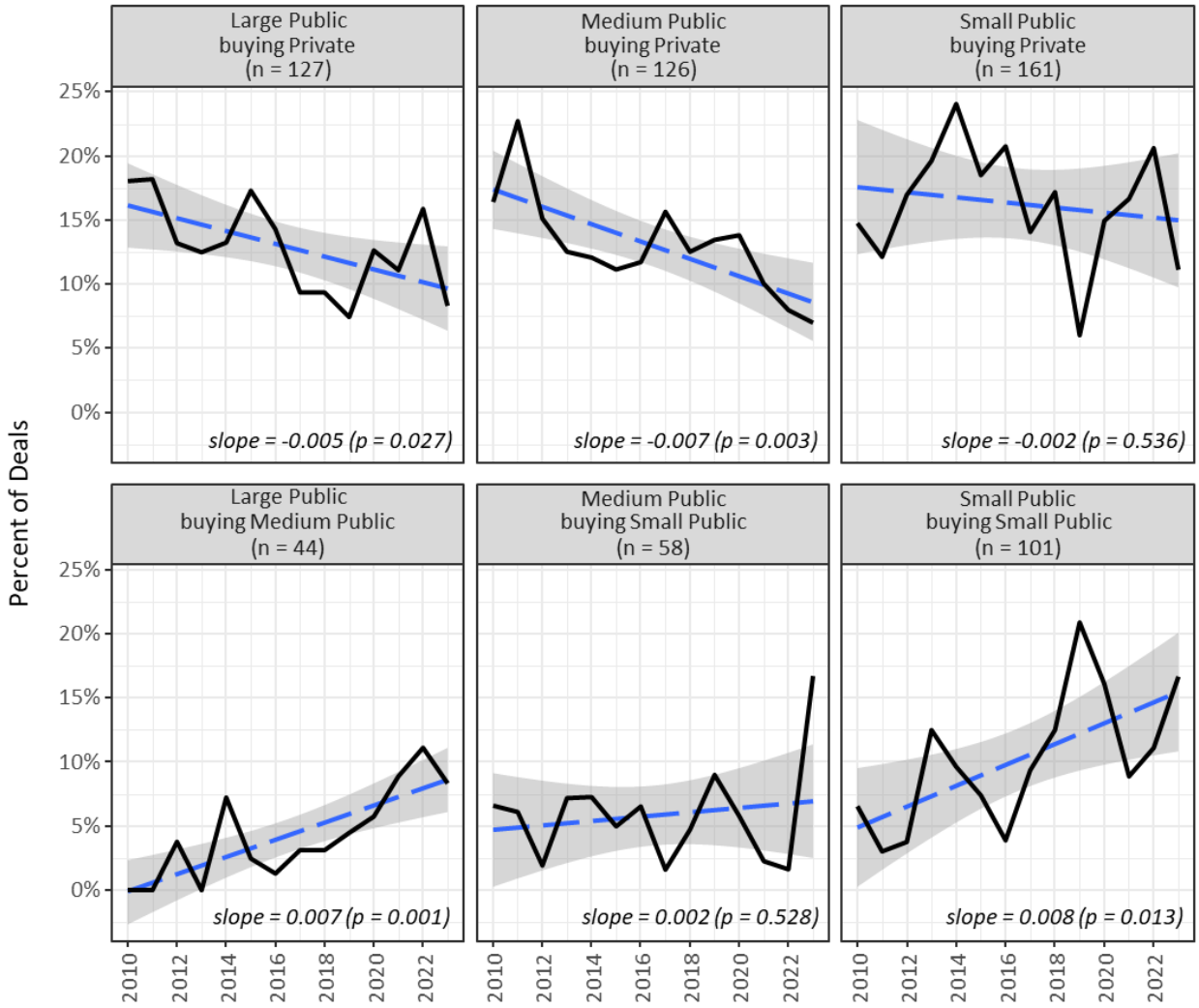
Figure 6. Company Types and Industries Involved in Pharmaceutical M&As [a]



Data Source: FactSet and DealForma data on M&As from 2010–2023. Using DealForma, company type could be determined for 954 of the M&As that matched to FactSet.
Note: mfg. serv. = manufacturing services.
[a] Additional information on industry inclusion criteria can be found in Section 4.2. Categorizations account for companies with relevant primary or secondary NAICS.
[b] NAICS 325411 is Medicinal and Botanical Manufacturing; NAICS 325412 is Pharmaceutical Manufacturing; NAICS 325414 is Biological Product (except Diagnostic) Manufacturing; NAICS 541714 is Research and Development in Biotechnology (except Nanobiotechnology).

Figure 7 shows select trends among the "pharma buys pharma" group. In our sample, large, medium, and small publicly traded companies all shifted away from buying private companies, as indicated by the downward trend in the top three panels of Figure 7. Instead, publicly traded acquirers focused more on buying smaller public companies, as the bottom three panels show.

Figure 7. Select Trends in Publicly Traded Pharmaceutical Companies Buying Other Pharmaceutical Companies



Data Source: FactSet and DealForma data on M&As from 2010–2023.
Note: Blue line shows fitted linear trend. Gray area shows standard error in fitted trend. Before fitting linear trends, we checked for homoscedasticity, normality, and independence. Company size is based on market capitalization; small publicly traded companies have less than $1 billion, medium publicly traded companies have $1 billion to $50 billion, and large publicly traded companies have more than $50 billion. Graphs are only shown for groups with evidence of a trend. For other types of acquisitions (e.g., large public pharma buying small public pharma), there were no substantial trends over the study period.

5.1.3 Types of Drugs Involved in M&As

For the subset of M&As from 2018–2023, we matched the acquiring and target companies to the sponsor names in the drug-level data. We then analyzed the characteristics of

individual marketed prescription drugs involved in M&As.[19] Table 2 presents the characteristics of the drugs in the sample that were involved in M&As, using IQVIA data. Most of the target drugs (i.e., those owned by the target company in the M&A) in the sample were generic small molecules (65.0 percent), followed by brand small molecules (30.0 percent) and original biologics (5.0 percent).[20,21] Among target drugs involved in M&As, most (29.0 percent) had annual IQVIA NSP invoice sales of under $0.5 million, followed by drugs with annual sales between $1 million–$5 million (20.1 percent). Drugs involving the central nervous system were most common in the sample (22.5 percent), followed by dermatology medication (12.1 percent) and pain medication (11.1 percent). Among acquirer drugs involved in M&As, 90.8 percent (n=2,407) were small molecule generics, and 42.5 percent of these had annual sales under $0.5 million. As stated previously, these drug-level statistics refer to an individual 9-digit NDC.

Table 2. Characteristics of Drugs Involved in M&As, 2018–2023 [a]

	Number of Target Company Drugs (Percent of All Target Company Drugs)	Number of Acquiring Company Drugs (Percent of All Acquiring Company Drugs)
Type of Compound		
Small molecule, generic	970 (65.0%)	2,407 (90.8%)
Small molecule, brand	447 (30.0%)	189 (7.1%)
Original biologic, 351(a)	75 (5.0%)	40 (1.5%)
Biosimilar, 351(k)	0 (0.0%)	14 (0.5%)
Drug's Annual IQVIA NSP Invoice Sales [b]		
<$0.5 million	305 (29.0%)	785 (42.5%)
$0.5–1 million	160 (15.2%)	354 (19.1%)
$1–5 million	211 (20.1%)	399 (21.6%)
$5–20 million	179 (17.0%)	191 (10.3%)
$20–100 million	110 (10.5%)	70 (3.8%)
>$100 million	85 (8.1%)	50 (2.7%)
Therapeutic Area		
Central Nervous System	335 (22.5%)	485 (18.3%)
Dermatology	181 (12.1%)	8 (0.3%)
Pain Medication	165 (11.1%)	330 (12.5%)
Endocrine	127 (8.5%)	229 (8.6%)
Anti-infective	117 (7.8%)	296 (11.2%)
Cardiovascular	116 (7.8%)	423 (16.0%)
Gastrointestinal	101 (6.8%)	180 (6.8%)
Oncology	88 (5.9%)	306 (11.5%)
Hematology	81 (5.4%)	211 (8.0%)

[19] As stated above, marketed drugs were identified as being "involved" in the M&A if (a) they were owned by the target and transferred to the acquirer; (b) they were brand drugs owned by the acquirer with a shared therapeutic area as one of the target drugs; or (c) they were generic drugs owned by the acquirer with a shared dosage form as one of the target drugs.

[20] We use the term "biologics" to refer to both original biological products approved through the 351(a) pathway, and biosimilar biological products (also referred to as biosimilars) approved through the 351(k) pathway.

[21] These findings differ from those in Figure 4F because DealForma categorizes a company with both brand and generic drugs on the market as brand if their asset with the highest dollar sales is a brand drug and generic if their highest revenue drug is generic.

	Number of Target Company Drugs (Percent of All Target Company Drugs)	Number of Acquiring Company Drugs (Percent of All Acquiring Company Drugs)
Genitourinary	42 (2.8%)	55 (2.1%)
Immunomodulators	39 (2.6%)	28 (1.1%)
Other	38 (2.5%)	55 (2.1%)
Respiratory	28 (1.9%)	29 (1.1%)
Ophthalmology	23 (1.5%)	13 (0.5%)
Vaccines [c]	11 (0.7%)	2 (0.1%)

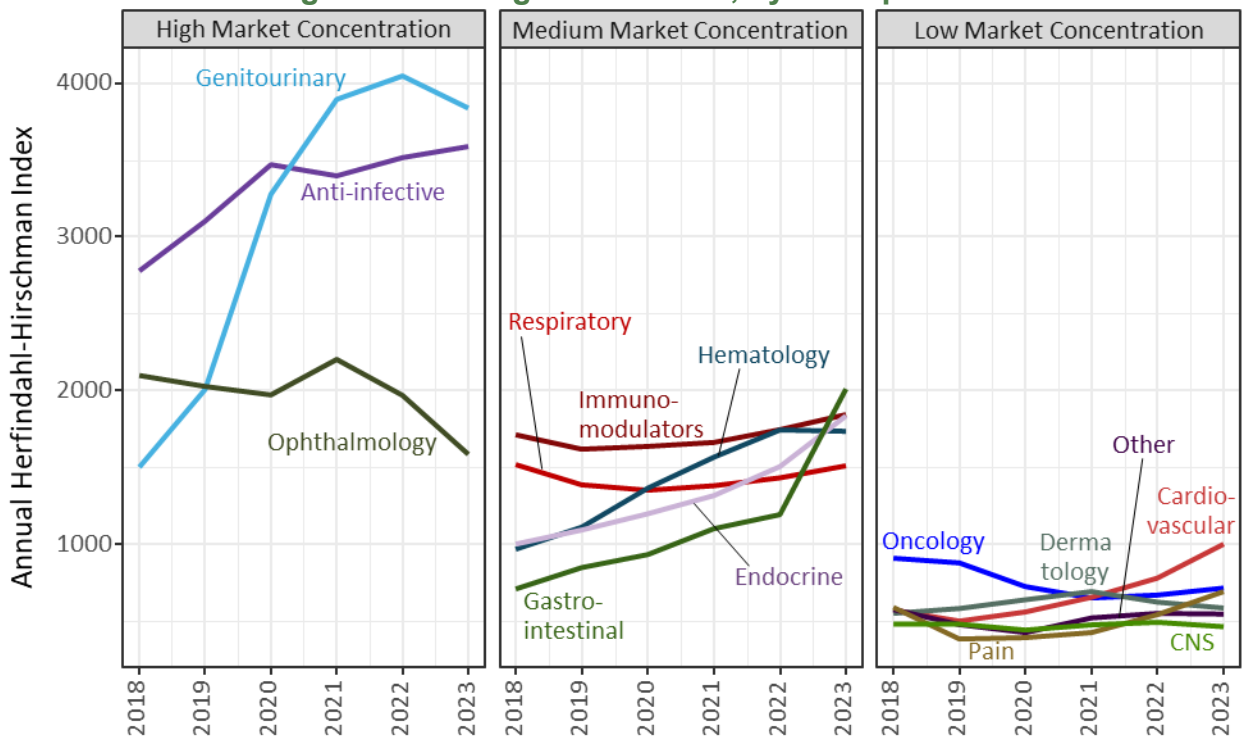
[a] Whereas Figure 4 presents company-level and M&A-level statistics covering all drugs and drug candidates from 2010–2023, this table presents drug-level statistics for prescription drugs marketed between 2018–2023 in our final drug sample. See Table B - 4 for cross tabulation of therapeutic area and brand status for all drugs in our dataset.
[b] Calculated based on all available IQVIA NSP sales in the year before the M&A.
[c] Coverage of vaccines is lower because many vaccine products are not sold through typical distribution channels (e.g., those purchased by the national stockpile) and may be missing at a higher rate. Vaccines are excluded from some analyses below, where explicitly noted.
Data source: IQVIA NSP

5.2 Change in Herfindahl-Hirschman Index

Figure 8 shows the change in annual HHI per therapeutic area[22] over the study period, using harmonized company identifiers derived from historical records of drug ownership[23]. According to DOJ standards (U.S. Department of Justice, 2024), markets with HHIs over 1,800 are considered highly concentrated, markets with HHIs between 1,000 and 1,800 are considered moderately concentrated, and markets with HHIs below 1,000 are considered competitive (i.e., low concentration markets).[24] Overall, we found that three markets were highly concentrated on average—anti-infectives, genitourinary, and ophthalmology. Five markets were moderately concentrated on average—immunomodulators, hematology, respiratory, endocrine, and gastrointestinal. Six markets were competitive on average—oncology, cardiovascular, dermatology, "other," central nervous system, and pain medication.

[22] Therapeutic class may be too broad or too narrow for defining a market, depending on the circumstances. When assessing mergers, DOJ and FTC use product substitutability to define markets of products that compete with each other (U.S. Department of Justice and the Federal Trade Commission, 2023). We use therapeutic class as an approximate definition of a pharmaceutical market given that the study is not focused on any one specific product. For more information on the challenges associated with defining pharmaceutical markets—including lack of product interchangeability, volume rebating, and product bundling—see Feldman et al. (2022).
[23] In Figure 8, HHI was calculated for each calendar year, defining markets by their aggregate therapeutic classes. We used harmonized company identifiers because HHI involves calculating each company's market share, which required harmonizing different versions of a single company name in the drug dataset.
[24] HHI can be affected by factors other than consolidation of suppliers, including entry or emergence of high-selling products in an existing market. HHI may also depend on the total size of a therapeutic market. For example, a $10 billion market evenly divided across 10 suppliers has twice the HHI as a $20 billion market evenly divided across 20 suppliers.

Figure 8. Average Annual HHI, by Therapeutic Area



Note: Vaccines not shown because sales data are missing at a higher rate. The steep rise in genitourinary HHI is primarily due to large growth in sales of the drug Myrbetriq, manufactured by Astellas Pharma.

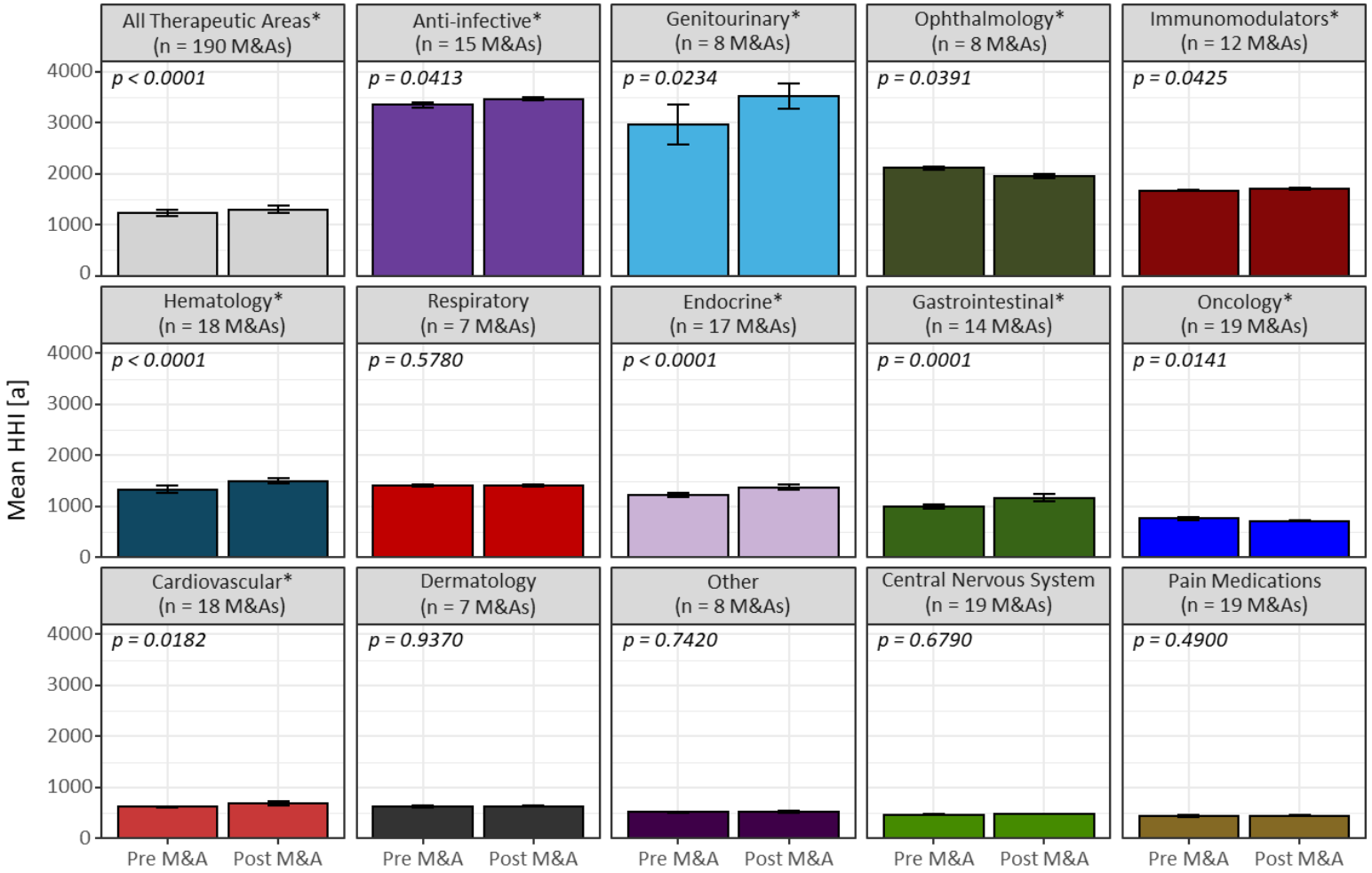
Figure 9 shows how M&As during the study period are associated with market concentration one year after the merger or acquisition when defining markets by the 14 therapeutic areas.[25] Across all M&As, the average change in HHI in the year following the M&A was +73 points (5.9 percent). Although we generally found greater market concentration after an M&A, this analysis does not account for other factors that may have occurred in the year following the M&A, including entry of new companies and products, changes in demand and patient population, and subsequent M&As. By far, the market that experienced the greatest consolidation was the market for genitourinary drugs, with an average HHI increase of 27.6 percent after an M&A ($p = 0.0234$). We also observed large HHI changes following an M&A in the market for gastrointestinal drugs (15.9 percent increase in HHI, on average, $p = 0.0001$), endocrine system drugs (12.2 percent increase, $p < 0.0001$), hematology drugs (13.5 percent increase, $p < 0.0001$), and cardiovascular drugs (11.4 percent increase, $p = 0.0182$). In two markets, oncology and ophthalmology medications, HHI was lower after the M&A, on average. Reductions in HHI could have occurred if drug companies used M&As to acquire approved drugs and enter those markets. Additionally, if new companies are also entering those markets, then this would tend to counteract the consolidating effects M&As may have.

M&As in highly concentrated markets such as genitourinary tended to produce larger increases in HHI (simple average increase of 171 points across highly concentrated markets)

[25] See Table B - 6 for data values.

than moderately concentrated markets (average increase of 101 points) or competitive markets (average increase of 9 points). In percentage terms, however, the average increase was similar for high-concentration and medium-concentration markets (8.1 percent increase and 8.4 percent increase, respectively), but smaller for low-concentration markets (2.2 percent increase).

Figure 9. Mean HHI One Year Before and After M&A, by Therapeutic Area, 2018–2023 [a]



[a] Higher HHI indicates greater market concentration. Error bars show one standard error in the mean, calculated as (standard deviation)/$\sqrt{n}$. A star indicates that the difference from pre to post is statistically significantly different from 0 (using a significance level of 0.05), according to the one-sample Wilcoxon test (p value shown on graph). Vaccines are not presented separately because there was only a single vaccine M&A in our drug-level sample. M&As between 2019–2022 were analyzed to ensure one full year of data when calculating HHI before and after the M&A. "Other" includes dietetics, vitamins and minerals, allergen tests, hospital solutions, and other categories classified by IQVIA as "other therapeutic class." For data values, see Table B - 6.

5.3 Effects of M&As on Prices and Quantity Sold

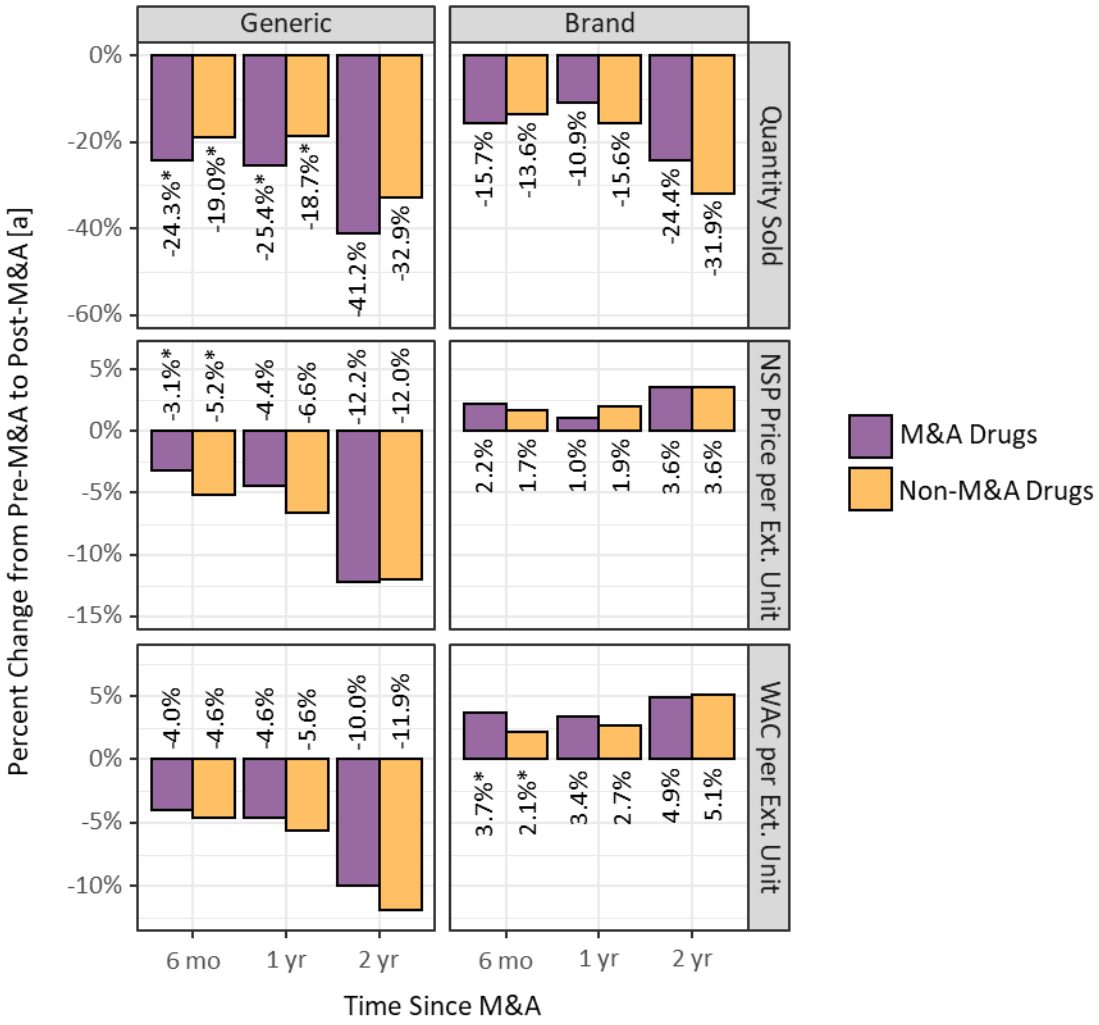
We found that, after the M&A date, quantity sold decreased on average, both for drugs involved in an M&A and drugs not involved in an M&A.[26] Generic drugs, however, experienced a greater decrease in quantity sold if they were involved in an M&A (see Figure 10).[27] This downward effect became stronger over the two-year period we analyzed. In contrast, M&As were associated with slowing the decrease in quantity sold of brand drugs involved in the M&A, which was discernible both one year ($p = 0.2445$) and two years after the M&A ($p = 0.0822$) (see Figure 11 and Table B - 5).

In terms of price, brand drug prices increased after the M&A date, while generic drug prices decreased after the M&A date. At a high level, this trend was visible both for the WAC and the NSP price, and the direction of change was the same for M&A drugs and non-M&A drugs. For generics, though, prices dropped more slowly if the drug was involved in an M&A. This effect was visible for the NSP price at six months ($p = 0.0097$) and one year ($p = 0.0069$) but had dissipated by two years. Brand drugs showed less evidence of price changes. The WAC, though, had increased 1.5 percent faster for brands involved in M&As than for brands not involved in M&As at six months post-transaction ($p = 0.0032$).

[26] The quantity sold refers to the total mass in kg or total activity in IU of the active ingredient in the finished drug product that was sold.

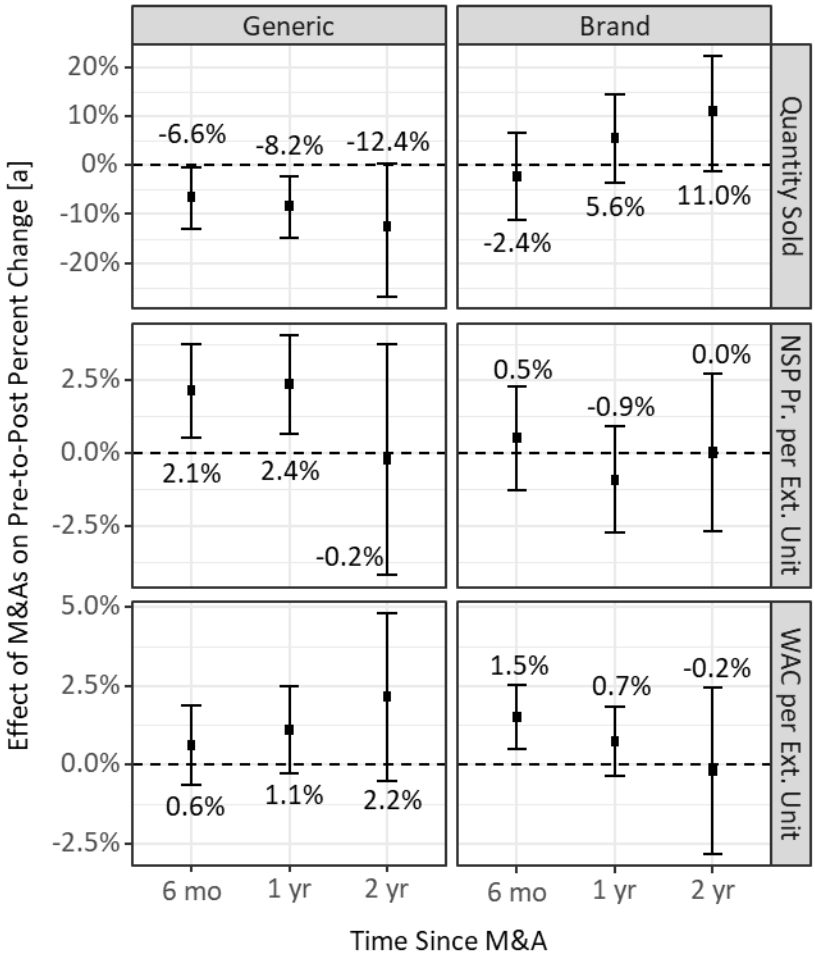
[27] The price of the drug after the M&A was calculated using the specified period of time. The price before the M&A was calculated using a one-year period. Only drugs with at least one full year of pre-M&A data were included in the sample.

Figure 10. Percent Change in Quantity Sold and Price for M&A vs. Non-M&A Drugs



[a] Brand drugs refer to any drug with a brand name, including original biologics and biosimilars.
[b] Pre-M&A values were measured over a one-year period that excluded the month of the M&A. A star indicates a strong statistical association, with significant difference between M&A and non-M&A drugs at a significance level of 0.05. See Table B - 5.

Figure 11. Effect of M&As on Changes in Quantity Sold and Price



[a] Brand drugs refer to any drug with a brand name, including original biologics and biosimilars.
[b] The effect is measured as (pre-to-post percent change for M&A drugs)/(pre-to-post percent change for non-M&A drugs) – 1, expressed as a percentage. Error bars show 95 percent confidence intervals, calculated using robust standard errors.

5.4 M&As and Market Dynamics

5.4.1 Drugs in Shortage and M&As

As Table 3 shows, small molecule generics made up 81.5 percent of our sample (25,968 out of 31,873 total drugs) but 86.5 percent of the drugs that went into shortage (3,263 out of 3,772 total drugs). These drugs went into shortage more frequently between 2018–2023, with 12.6 percent of sampled small molecule generics going into shortage at some point during this period, compared to 6.8 percent of sampled original biologics and 9.2 percent of sampled small molecule brands. The number of new shortages of small molecules was highest in 2018 and 2019, when 1,207 and 1,000 of these drugs (i.e., 9-digit NDCs) went in shortage, respectively. Overall, though, there were more unique shortage events in 2018 (n=160) and 2023 (n=129) than in any other years in the study period.

Table 3. Shortage Frequency by Type of Drug, 2018–2023

Year	Number of Drugs in Sample that Went into Shortage, 2018–2023 [a]				Number of Unique Shortage Events [c]
	Original Biologics, Brand [b]	Small Molecule, Brand	Small Molecule, Generic	Total	
2018	7	101	1,207	1,315	160
2019	20	120	1,000	1,140	106
2020	1	103	614	718	103
2021	5	71	248	324	77
2022	13	74	362	449	91
2023	27	115	748	890	129
Total number of unique drugs that went into shortage between 2018–2023 [d]	73	436	3,262	3,771	666
Total number of drugs marketed between 2018–2023	1,081	4,742	25,968	31,869 [e]	N/A
Percent of marketed drugs that went into shortage between 2018–2023	6.8%	9.2%	12.6%	11.8%	N/A

N/A = not applicable.
[a] A drug is defined as a unique 9-digit NDC number.
[b] Original biologics include products approved through the 351(a) pathway, which excludes biosimilars. A column is not provided for biosimilars because no biosimilars in our sample went into shortage in 2018–2023.
[c] Defined as number of unique instances of a molecule-form-strength combination going into shortage.
[d] Total may be less than column sum because some drugs went into shortage in more than one year.
[e] The total number of drugs is 78 higher than the row sum because there were 78 biosimilars in our sample, none of which went into shortage.

Table 4 shows the proportion of drugs that went into shortage from 2018–2023, by therapeutic area. Drugs classified as "other" had the highest shortage rate, at 21.9 percent, followed by ophthalmology drugs (19.4 percent of drugs went into shortage from 2018–2023), gastrointestinal drugs (19.4 percent), pain medication (17.7 percent), and central nervous system drugs (15.6 percent). Among oncology drugs, 11.3 percent went into shortage at some point during the study period.

Table 4. Proportion with New Shortage, by Therapeutic Area and Related Characteristics, 2018–2023

Therapeutic Area [a]	Number in Sample that Went into Shortage from 2018–2023	Total Number of Marketed Drugs in Sample from 2018–2023	Proportion of Sample that Went into Shortage from 2018–2023	Related Characteristics of Therapeutic Area				
				Mean Number of Sponsors per Molecule-Strength-Form [c]	Level of Concen-tration	Mean Annual HHI per Market [d]	Percent of Drugs in Therapeutic Area that are Generics	Average Annual Sales per Market (Billions) [e]
Ophthalmology	118	609	19.4%	2.4	High	1,977	72.9%	$12.2
Gastrointestinal	311	1,603	19.4%	3.1	Medium	1,130	84.6%	$15.9
Pain Medication	549	3,099	17.7%	3.5	Low	501	86.4%	$17.0
Central Nervous System	1,178	7,561	15.6%	4.9	Low	466	88.1%	$67.8
Immunomodulators	93	774	12.0%	2.2	Medium	1,703	59.4%	$103.0
Oncology	196	1,737	11.3%	2.2	Low	752	67.5%	$82.8
Anti-infective	329	3,048	10.8%	3.1	High	3,312	86.7%	$41.4
Cardiovascular	495	4,579	10.8%	4.5	Low	675	88.9%	$19.2
Endocrine	195	2,783	7.0%	2.5	Medium	1,324	70.7%	$118.0
Respiratory	31	772	4.0%	2.5	Medium	1,431	78.6%	$39.0
Hematology	27	1,954	1.4%	3.1	Medium	1,410	72.1%	$45.2
Genitourinary	6	705	0.9%	5.0	High	3,093	88.2%	$4.8
Dermatology	2	1,277	0.2%	3.4	Low	612	81.2%	$6.8
Other [b]	211	963	21.9%	2.1	Low	514	71.4%	$6.4
All Therapeutic Areas	***3,772***	***31,837***	***11.8%***	***3.3***	***Medium***	***1,374***	***81.6%***	***$39.7***

[a] Vaccines are not presented as a line item because data are missing at a higher rate than in other therapeutic areas, but they are included in the overall total ("All Therapeutic Areas").
[b] "Other" includes dietetics, vitamins and minerals, allergen tests, hospital solutions, and other miscellaneous categories classified by IQVIA as "other therapeutic class."
[c] Mean was taken after calculating, on an annual basis, the number of unique drug sponsors that own the same molecule, strength, and dosage form.
[d] HHI was computed for each market, in each calendar year from 2018–2023.
[e] Calculated on an annual basis using IQVIA NSP sales.

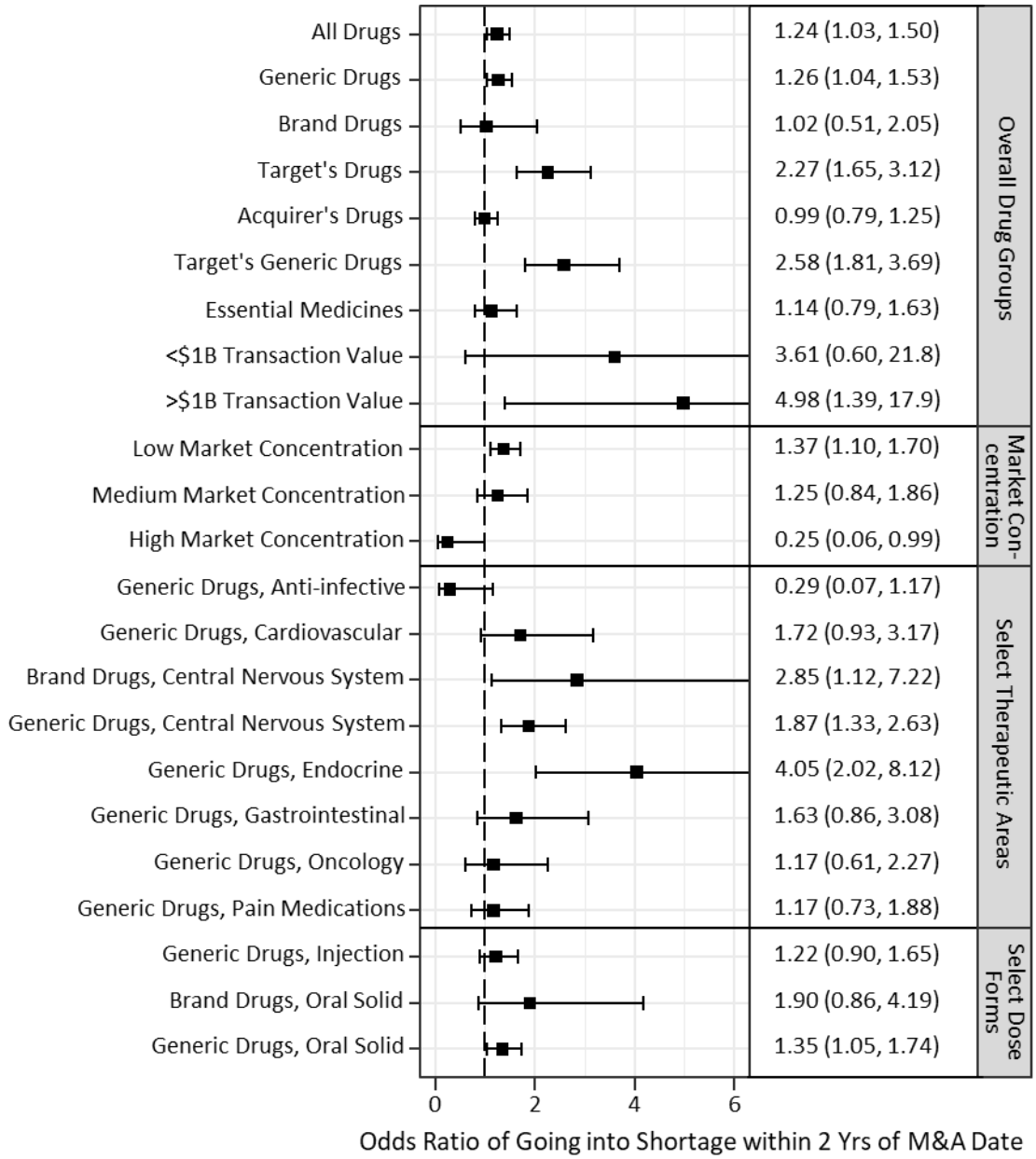
Using the matched drug dataset, we compared the proportion of drugs that went into shortage within two years of the M&A date, both for M&A drugs and comparable non-M&A drugs.[28] Overall, drugs involved in M&As had 24.3 percent higher odds of going into shortage within a two-year period than comparable drugs not involved in M&As ($p = 0.0249$) (see Figure 12). Generic drugs involved in M&As had 26.4 percent higher odds of going into shortage than comparable generic drugs that were not involved in an M&A ($p = 0.0202$). For the target company's drugs, the odds of going into shortage within two years of an M&A were 2.265 times the odds for comparable non-M&A drugs ($p < 0.0001$), which corresponds to a 126.5 percent increase in the odds of going into shortage, but the 95 percent confidence interval around this point estimate was wide (64.7 to 211.7 percent increase). There was no evidence of brand drugs ($p = 0.9453$) or the acquirer's drugs ($p = 0.9906$) going into shortage at a higher rate, as both odds ratios were very close to 1.0, with high p values.

In our sample, essential medicines had 13.6 percent higher odds of going into shortage in a two-year period if involved in an M&A, but the evidence for this finding was weaker, and a larger sample size would be needed to extrapolate beyond our sample ($p = 0.5528$). Interestingly, drugs sold in competitive markets had higher odds of shortage if involved in an M&A ($p = 0.0055$), whereas drugs sold in highly concentrated markets had lower odds of shortage if involved in an M&A ($p = 0.0465$). Drugs involved in transactions valued over $1 billion were substantially more likely to go into shortage within two years after the M&A than comparable non-M&A drugs; the confidence intervals for this finding were very wide, but the evidence for a nonzero difference compared to non-M&A drugs was nonetheless strong ($p = 0.0198$).

Figure 12 also presents odds ratios for various therapeutic areas and dosage forms. M&A drugs were associated with higher shortage risks than non-M&A drugs in the case of generic endocrine drugs (odds ratio = 4.05, $p < 0.0001$), generic central nervous system drugs (odds ratio = 1.87, $p = 0.0003$), and generic oral solids (odds ratio = 1.35, $p = 0.0229$). We also observed elevated shortage risks for generic gastrointestinal drugs (odds ratio = 1.63, $p = 0.1871$), generic cardiovascular drugs (odds ratio = 1.72, $p = 0.1269$), generic pain medications (odds ratio = 1.17, $p = 0.5971$), generic injectables (odds ratio = 1.22, $p = 0.2341$), and brand oral solid (odds ratio = 1.90, $p = 0.1764$)—though the evidence for these was weaker and larger sample sizes would be needed to generalize these results beyond our sample. As Figure 12 shows, some of the confidence intervals were wide in the subgroup analyses, particularly in cases where sample size was limited.

[28] As described previously, we compared the two drugs over the same calendar time. We matched M&A drugs to non-M&A drugs on the basis of calendar month and year, brand status (brand vs. generic), molecule type (biologic vs. small molecule), dosage form, and price quintile within drug groupings.

Figure 12. Odds Ratios of Shortage within 2 Years of M&A Date, 2018–2023 [a]



[a] Odds ratio of 1 indicates that M&A drugs and non-M&A drugs have equal odds of going into shortage within two years of M&A date. The common odds ratios are calculated by stratifying on the groups that we used to match M&A drugs to non-M&A drugs, i.e., calendar month and year, brand status (brand vs. generic), molecule type (biologic vs. small molecule), dosage form, and subgroup price quintile. Brand drugs include biologics and biosimilars that are marketed with brand names. Differences between therapeutic areas may be partly due to differences in the ratio of generics to brands. Odds ratios computed as odds of going into shortage given that drug was involved in M&A divided by odds of going into shortage given that drug was not involved in M&A. Error bars show 95 percent confidence intervals. For complete data values, see Table B - 7.

5.4.2 Essential Drugs and M&As

Using the full drug dataset of 31,837 drugs, we found that essential medicines listed on the ARMI EML had 11.6 percent higher odds of being involved in an M&A than non-essential medicines (p = 0.0307) (see Table 5). In our full drug sample, essential medicines on the ARMI EML made up 14.7 percent of the drugs involved in M&As during the study period, compared to 13.4 percent of drugs not involved in M&As during the study period. Essential medicines listed in the EO EML had 4.8 percent higher odds of being involved in an M&A, though the association was weaker (p = 0.3490).

Table 5. Frequency and Odds of being in an M&A, Essential and Non-essential Drugs, 2018–2023 [a]

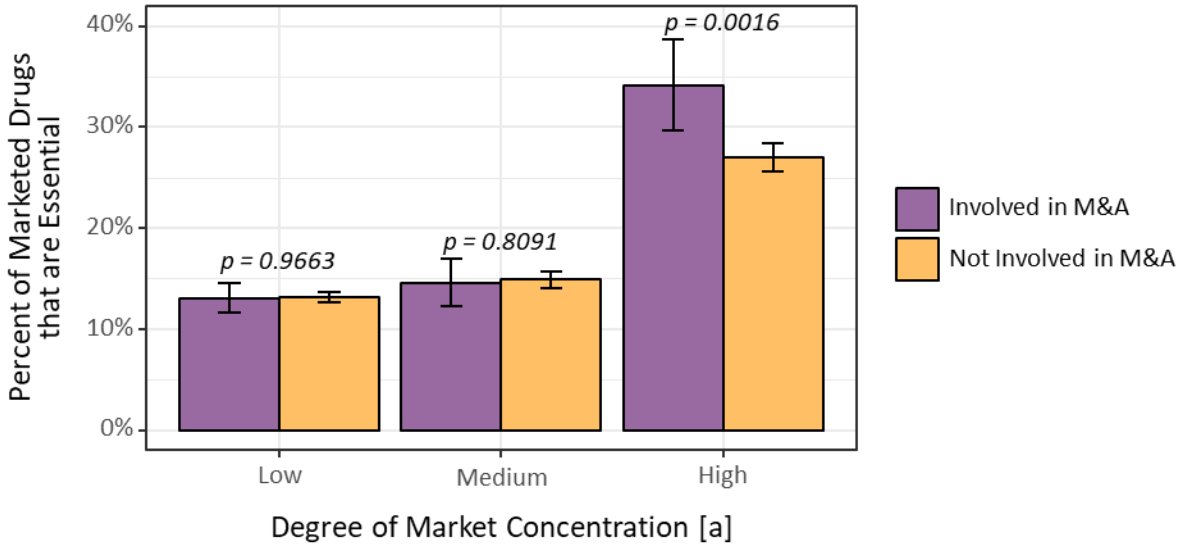
	EO EML [b]		ARMI EML [c]		Either EO or ARMI EML	
	M&A [d]	Non-M&A [e]	M&A	Non-M&A	M&A	Non-M&A
Number of "non-essential" drugs *not* on designated EML	3,018	23,883	3,067	24,468	3,017	23,868
Number of essential drugs on designated EML	577	4,359	528	3,774	578	4,374
Percent that are on the designated EML	16.1%	15.4%	14.7%	13.4%	16.1%	15.5%
Odds of being essential	0.1910	0.1830	0.1720	0.1540	0.1920	0.1830
Odds ratio [f]	1.0475 (p = 0.3490)		1.1161 (p = 0.0307)		1.0454 (p = 0.3710)	

[a] Counts of drugs refer to the number of 9-digit NDCs.
[b] The EO EML is the Executive Order Essential Medicines List published by FDA, which focuses on medicines treating both chronic and acute diseases.
[c] The ARMI EML is the list published by the Department of Health & Human Services' (HHS) Office of the Assistant Secretary for Preparedness and Response and the Next Foundry for American Biotechnology at the Advanced Regenerative Manufacturing Institute, which focuses on essential medicines treating acute diseases.
[d] Number of drugs involved in an M&A at some point in the study period (2018–2023).
[e] Number of drugs not involved in an M&A at any point in the study period (2018–2023).
[f] Odds ratio calculated as odds of being involved in M&A given that the drug is essential divided by odds of being involved in M&A given that the drug is not essential. p value is for the test of equal odds.

In highly concentrated markets, essential medicines (as defined by the combined EO EML and ARMI EML) were significantly more likely to be involved in M&As between 2018 and 2023 than non-essential medicines (p = 0.0016; see Figure 13).[29] In particular, essential medicines made up 34.1 percent of sample drugs involved in M&As, compared to 26.9 percent of sample drugs not involved in M&As. In low-concentration and medium-concentration markets, essential medicines were as likely to be involved in M&As as non-essential medicines.

[29] As in Section 5.2, markets are defined by broad therapeutic areas.

Figure 13. Percent of Drugs that are Essential, by Market Concentration and M&A Involvement, 2018–2023



[a] Low, medium, and high market concentrations are defined as an HHI of <1,000, 1,000–1,8000, and >1,800, respectively. p values are for the two-sample test of equal proportions.

6 DISCUSSION

6.1 Overall Findings

M&A activity in the pharmaceutical industry is common, and literature suggests M&As may affect prices, supply, and market competition. In our sample, 11.3 percent of drugs were involved in M&As, and the public health impact of even a single shortage after an M&A can be substantial. M&As occur for many reasons, e.g., to increase market power; to reduce risk through diversification; to take advantage of economies of scale and scope; and to reap tax advantages. In the pharmaceutical industry, consolidating the operations of two companies can yield gains in manufacturing and marketing efficiency, higher returns, and/or more effective bundling of therapeutic area portfolios, thereby improving a company's bargaining power with supply chain intermediaries, including prescribers. M&As can also represent a shift in strategic focus or a response to market competition. For example, acquisitions may prevent a competitor from buying key assets. Additionally, acquisition of companies with products in early-stage development can also allow companies to maintain their drug pipelines in the face of patent expirations, unanticipated failures in clinical trials, or increased competition.

During our study period, 2010–2023, we observe two trends for M&As in the pharmaceutical industry—a shift toward higher-value deals and an increase in early-stage product acquisitions. While median deal value increased slightly from 2010 through 2023, much of the growth in deal values was attributable to an increasing frequency of M&As valued over $1 billion. These high-value deals tend to be conducted by large pharmaceutical companies and may increase their market share—particularly because a high valuation also generally involves a large target company and thus represents a substantial consolidation of the market. The market share held by the four, eight, or 20 largest firms is an important metric of

market concentration (Feldman, et al., 2022), and the rise in the frequency of high-value M&As could signal an overall reduction in market competition in the pharmaceutical sector over this period. Even though our study did not account for confounding factors, such as new product launches, changes in patient population, and demand, we did observe an increase in HHI from 2018–2023, on average, and this increase coincided with a rise in high-value M&As. In 2010, there were only 11 pharmaceutical deals valued over $1 billion, but in 2023, there were 21. Deals over $1 billion made up a disproportionate share of total deal value (in dollars) during 2010–2023, even though they were far less common than those under $1 billion.[30]

Several of the largest pharmaceutical companies completed as many M&As valued over $1 billion in 2021–2023 as they did in the preceding 11 years from 2010–2020. For example, Pfizer—which became the first drug company to exceed $100 billion in annual sales partly due to the success of its COVID-19 vaccine (Carey, 2023)—completed 10 M&As exceeding $1 billion in 2010–2023. Half of these M&As occurred in 2021-2023. Sanofi completed 11 M&As each valued over $1 billion from 2010–2023, with five of them occurring in the last three years (2021–2023). Amgen and Eli Lilly both completed nine such M&As, and four were completed in 2021–2023.

The growing focus on acquiring companies with early-stage products was visible from 2010–2023 and was particularly pronounced in 2021–2023, when preclinical drug companies made up the largest share of M&A targets (13.8 to 19.6 percent depending on the year). This likely represents an effort by pharmaceutical companies to invest in innovator drugs to maintain a strong development pipeline. In fact, 2021 and 2022 were the first years in the study period when the proportion of M&As involving early-stage development companies was greater than that involving late-stage development or approved drug companies. Interest rates began rising in 2022, which likely created challenges with debt financing, and there may have been an uptick in early-stage companies seeking to be acquired (Bernauer, et al., 2024). This interest was apparently reciprocated by acquirers, which were willing to dedicate a larger proportion of their M&A investments to acquiring early-stage companies and products compared to previous years. The level of investment in acquiring early-stage products implies that R&D activity in the pharmaceutical market remains robust. M&As targeting companies with approved products were relatively constant during 2016–2020 but experienced a significant decrease during 2020–2021. M&As involving approved products returned to their pre-COVID levels from 2022 onward.

In addition to using M&As to maintain robust pipelines of innovator drugs, companies also frequently used M&As to acquire approved products, many of which are generics. Generic drugs have some of the highest baseline risks of going into shortage (Schweitzer, 2013; U.S. Food and Drug Administration, 2020; The White House, 2021; Gagnon & Volesky, 2017). We found that these risks were even higher for generic drugs involved in M&As. During 2018–2023, generic drugs involved in an M&A had 26.4 percent higher odds of going into shortage within two years of the M&A date compared to similar generics not involved in an M&A ($p = 0.0202$).

[30] Over the full 14-year study period, only 14.0 percent of all deals with known transaction value exceeded $1 billion.

The shortage risk was even more elevated for generic drugs owned by the target company (odds ratio = 2.58, $p < 0.0001$). This elevation in shortage risk may be indicative of post-M&A strategies intended to extract value from the deal. Following an acquisition, companies may take advantage of economies of scale and/or scope (Hammoudeh & Nain, 2024), for example by consolidating manufacturing lines, combining duplicate divisions (R&D, corporate, purchasing, etc.), using higher purchasing power to negotiate lower raw material costs, reducing excess inventory/carrying costs, or relocating manufacturing plants abroad. These measures often increase shortage risk by reducing manufacturers' supply resiliency. Unexpected production disruptions due to manufacturing quality issues, natural disasters, or other factors affecting a single company can have significant ramifications for patients when that company's product comprises a large portion of the market supply for that drug. The impact of M&As may be substantial; 11.3 percent of drugs in our overall drug dataset were involved in M&As at some point during the six-year period, when counting both the target's drugs and the acquirer's relevant drugs.

For generic drugs, M&As were associated with a large downward effect on quantity sold and a modest upward effect on prices. The downward effect on quantity sold grew in magnitude during the two years after an M&A. We find that quantity sold decreased by an average of 41.2 percent for generic drugs involved in M&As, compared to a 32.9 percent decrease for comparable non-M&A generics ($p = 0.0562$) by the end of the second year. A reduction in quantity sold is a common precursor to some (but not all) drug shortages (U.S. Food and Drug Administration, 2020), and the accelerated decline is consistent with our finding that generic drugs involved in M&As have a higher odds of going into shortage. The impact on prices was much smaller and more difficult to discern due to greater uncertainty and wide variation in price growth among the drugs in our sample. Two years after an M&A, we find that generic WACs declined by 11.9 percent, compared to 10.0 percent for similar drugs that were not involved in M&As ($p = 0.1139$). M&As were also associated with a slight upward effect on the NSP invoice price, but this effect was less than 3 percent and disappeared during the second year after an M&A. Differences in price of a few percentage points are very small in dollar terms given how inexpensive generic drugs are.

For brand drugs, M&As were associated with an upward effect on WACs or list prices but virtually no effect on NSP invoice prices. This discrepancy may provide insight into how brand manufacturers extract value after an M&A. Larger increases in the WAC likely indicate more cost to the payer and healthcare plan, as WACs are often used as benchmarks for negotiating reimbursement rates. Yet, while manufacturers control the WAC and decide whether to increase the drug's list price, these higher payments may not be reaching the manufacturer. There are many intermediaries in the pharmaceutical supply chain that handle the drug or process the claim, including the healthcare provider (e.g., hospitals, clinics, pharmacies), the insurance company and/or pharmacy benefit manager (PBM), and the wholesaler. All of these entities have the potential to capture the increase in payments when the manufacturer raises their list price. This may, in fact, be what happens following an M&A. Compared to the WAC, the NSP invoice price is a better (but still limited) representation of what manufacturers actually earn from the sale of their drugs. Our finding that WACs rise more rapidly after an M&A, but

NSP invoice prices do not, suggests that manufacturers may be raising brand drug list prices without invoicing providers at higher rates. In effect, manufacturers may be allowing supply chain intermediaries to keep the increases in payment from the beneficiary and payer/healthcare plan.

While the manufacturer may not be receiving higher net payments for the brand drug, these pricing dynamics would make the manufacturer's product more profitable to the supply chain intermediaries, which could increase the drug's volume sales. The differential trends in the WAC and NSP invoice prices therefore could generate higher volume sales and more total revenue for the manufacturer. This dynamic is consistent with our finding that M&As were associated with an upward effect on quantity sold, which appeared to grow over time. Because of larger uncertainty, this effect was most discernible in the second year after an M&A, at which time brand drug quantity sold had dropped by 24.4 percent compared to 31.9 percent for their non-M&A counterparts ($p = 0.0822$). While this upward effect on quantity sold was most visible two years after the M&A, WACs only grew noticeably faster in the first six months ($p = 0.0032$). By the end of the second year after the M&A, brand drug WACs had increased as much as non-M&A brand drugs, on average.

This finding of a short-term upward effect on brand drug prices is consistent with the literature. For example, Feng et al. (2023) found that WAC prices increased for branded on-patent drugs involved in horizontal M&As with low transaction values (defined as having a transaction value below $200 million). Bonaime and Wang (2024) found that, when acquirers and targets had similar product offerings, average prices of the acquirer's drugs increased by 2.2 percent, but the effect only lasted for about one year after the M&A.

6.2 Strengths and Limitations

This study has several strengths. Assessing a 14-year study period from 2010–2023 provides insight into year-to-year variation and facilitates the identification of broader longitudinal trends. Additionally, we used historical data from the Orange Book, Purple Book, and CBER NDA/ANDA to reconstruct drug ownership at the time of the M&A, which allowed linkage with drug-level sales data using historical archives of the NDC Directory. We also assembled historical archives of the FDA drug shortage lists, which expanded the analysis beyond ongoing or recently resolved shortages. The cohort analysis of drug shortages provides greater evidence of a link to M&As because we removed imbalance in confounders and compared M&A drugs to non-M&A drugs over the same time period.

The study also has limitations. Our analysis of M&As was limited in its ability to assess the prevalence of vertical versus horizontal integrations, since most forms of vertical integration were excluded by our inclusion criteria and by our study's focus on pharmaceutical manufacturers specifically. The intended focus of the study was on U.S. markets, but the pharmaceutical industry is highly global, and we did not exclude M&As based on the companies' geographic locations. This may have led to some M&As being included in our study that were focused on non-U.S. markets.

In the drug-level analysis, we used the period from 2018 through 2023 to assess shortages, pricing changes, and drug quantity sold after an M&A. This period included the COVID-19 pandemic as well as two years of high inflation. Transitory effects of the pandemic may have affected our findings. Additionally, not all drug data could be used in the cohort analysis because some M&A drugs do not have any matching non-M&A drugs. This reduced the statistical power, particularly for subgroup analyses. In our drug analysis, we attempted to include all prescription drugs marketed in the United States from 2018–2023, but omissions occurred due to incomplete coverage in the underlying data sources.[31] These omissions may have upwardly biased the HHI calculations, since the omitted companies make their markets more competitive than we estimated using the available data. In addition, calculations of HHI are based on defining a market by the aggregate therapeutic class, a procedure that can be too broad in some circumstances and too narrow in others (Feldman, et al., 2022). When assessing mergers, DOJ and FTC use product substitutability to define markets of products that compete with each other (U.S. Department of Justice and the Federal Trade Commission, 2023). While we used therapeutic area as an approximate definition of a pharmaceutical market, many products sold in the same aggregate therapeutic area are not substitutable or in direct competition. Using smaller markets would likely lead to higher estimates of HHI than we present in our study.

Our analysis focused on the company most directly involved in the manufacture of a given drug, as indicated by the ownership of the drug application according to FDA sources. In some cases, after an M&A, the target company continued to exist as a subsidiary of the acquirer. Subsidiaries or inactive companies that may have continued to be listed as the drug sponsor in FDA data sources (e.g., the Orange and Purple Books) were not collapsed into their parent companies. Not accounting for parent companies and corporate structures could negatively bias our HHI calculations and cause underestimates of the true concentration of pharmaceutical markets. Additionally, the selection of FDA's drug shortage list allowed us to study drug shortages that had the most impact. However, FDA's drug shortage list only includes national shortages, and our analysis does not capture the extent to which M&As affect availability of drugs at a sub-national level. There are likely some supply shortfalls that occurred during the study period that were attributable to an M&A but were excluded from the FDA shortage list because other market participants were able to meet the demand. Finally, while our drug-level analysis aimed to reduce imbalances between the M&A cohort of drugs and the non-M&A cohort of drugs, additional evidence and analyses are needed before the associations we present can be interpreted as causal. M&As are one of a variety of factors that can influence drug prices, the quantity of drug sold, shortages, or market concentration, and our study accounts for some but not all possible confounders.

[31] Some 9-digit NDCs listed in IQVIA NSP were not retained in our final drug dataset because they did not have matching records in the drug ownership datasets, the NDC Directory, or both. This led to a 2.1 percent reduction in total sales due to exclusions of non-matching NDCs, but some of the non-matching drugs may have been appropriately excluded because they were out of scope (e.g., including OTCs).

6.3 Future Directions

One promising area of further research is a broader analysis of vertical integrations beyond pharmaceutical manufacturers. Drug prices, quantities sold, and shortages may be affected by M&As involving intermediaries of the pharmaceutical supply chain that do not conventionally manufacture drugs. Nevertheless, we excluded medical device companies, wholesalers, distributors, pharmacies, PBMs, and insurance companies from the study unless they had been classified in one of the pharmaceutical manufacturing NAICS. Increasingly, however, these other intermediaries are merging with or acquiring manufacturing companies, or they are engaging in M&As that may affect the number of drug suppliers in the market. In 2020, Blue Cross Blue Shield, one of the largest insurance companies, partnered with Civica Rx, a non-profit drug company, as part of an attempt to manufacture lower-priced generic drugs (Jaspen, 2020). In 2023, CVS Health Corp launched Cordavis, "a wholly owned subsidiary that will work directly with manufacturers to commercialize and/or co-produce biosimilar products" (CVS Health, 2023).

A similar company called NUVAILA was launched in 2024 by Optum Health Solutions, a subsidiary of OptumRx (Fein, 2024), the second largest PBM in the United States based on market share (Guardado, 2024). PBMs create formularies that influence drug use in the pharmaceutical market, particularly of retail drugs. Negotiations conducted by PBMs can lead to exclusive contracts with a single drug manufacturer in exchange for lower prices (U.S. Federal Trade Commission, 2024), which could reduce the number of drug suppliers, thereby increasing the risk of drug shortages. This is particularly relevant given the consolidation of PBMs and health insurers in the United States. Similar dynamics can exist with wholesalers, which are also highly concentrated in the United States and often act as price setters in generic drug markets. Evaluating the effects of M&As involving other supply chain intermediaries would be a useful area of further study.

Future research into how M&As affect the number of manufacturers in pharmaceutical markets and the geographical dispersion of manufacturers would also be useful. These changes could contribute to a less diversified pharmaceutical supply chain and could impact manufacturers' ability to respond nimbly to sudden changes in supply or demand. As generics are historically the most prone to shortage, further research related to the impact of M&As on geographical dispersion of the supply chain for generics would also be useful (The White House, 2021).

7 CONCLUSION

We evaluated the characteristics of 3,006 M&As between pharmaceutical manufacturers from January 2010 through December 2023. In our sample, transaction values increased over time, in part due to a growing number of high-value pharmaceutical M&As. M&A activity and annual transaction value peaked in 2015–2016. There were some more recent indications of increasing consolidation between companies working in different pharmaceutical industries. Moreover, mergers and acquisitions (rather than asset transfers or divestitures) have made up a growing share of pharmaceutical M&As in recent years. There has been a shift away from

acquiring private companies, with more targets being publicly traded pharmaceutical companies that are smaller than the acquirer. Approved drugs have declined as the focus of pharmaceutical M&As and have been replaced by companies working in early-stage drug development. Companies with oncology drugs made up the biggest therapeutic category among M&A target companies, mainly in the final years of the study period. After an M&A, both generic and brand drugs experienced decreases in quantity sold, and the decline was faster for generics involved in M&As compared to similar generics not involved in M&As. Overall, we found that M&As are associated with an increase in the risk of drug shortages. Generic drugs in particular were significantly more likely to go into shortage within the two years after an M&A than were similar non-M&A drugs. Elevations in the risks of generic drug shortages and, possibly, essential medicines could have large impacts on the U.S. drug market because generics and essential medicines already have high baseline levels of drug shortage risk.

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APPENDIX A: DETAILED METHODOLOGY

This Appendix provides a more detailed description of the data sources, how they were merged, and the analytic methodology.

A.1 Data Sources

A.1.1 IQVIA National Sales Perspective (2018–2023)

IQVIA NSP is a nationally representative database covering over 90 percent of U.S. drug supply volume in terms of dollar sales, sales of packages, and API unit sales. Data are reported for multiple distribution channels, including retail, mail, and non-retail, and metrics are reported on a monthly basis, covering all payers. We used IQVIA NSP data to estimate NSP prices and the quantities sold for drugs in our sample.

We collapsed the IQVIA NSP sales data across distribution channels and pack information (including the last two digits of the 11-digit NDC), such that each row corresponded to a unique 9-digit NDC and month-year. For each 9-digit NDC, we calculated total sales in IQVIA NSP sales dollars, total sales in WAC dollars, total packages sold, total extended units sold, and total quantity sold in kg or IU. After aggregating values for each 9-digit NDC, we computed the average NSP price per extended unit as total NSP dollar sales divided by total extended units sold, and we computed the average WAC per extended unit as total WAC dollar sales divided by total extended units sold. We also collapsed the Form (TLC3) variable by selecting the first letter of each 3-digit code. We further aggregated dosage forms A (systemic oral solid regular) and B (systemic oral solid long acting) to create a single designation for oral solids and likewise combined codes F (systemic injectable regular) and G (systemic injectable long lasting) into a single designation for injections. We inflated all sales values to 2023 dollars using the seasonally adjusted consumer price index for medical care (U.S. Bureau of Labor Statistics, 2024).

Table A - 1 presents the variables included from IQVIA NSP along with those that we created for analysis purposes.

Table A - 1. IQVIA NSP Variables, January 2018 – December 2023

Variable	Description
Raw Metrics	
Date	Calendar month and year
Product	Trademark name (for brand drugs and branded generics) or main active ingredient (for generics)
Brand/generic	Identifies the drug as a brand, generic, or branded generic
Product launch date	Date the product entered the U.S. market
Form TLC3	Dosage form of the drug (tablets uncoated regular ordinary, vial regular intramuscular only, dermatological lotion, etc.)
Strength	Amount of active ingredient per pill, per unit volume, etc.
11-digit NDC	Unique three-segment number issued by FDA that identifies a drug's labeler, product, and package
Biologic	Indicator for whether the drug is a biologic or a small molecule

Variable	Description
Pack size	Number of containers in one package
Pack quantity	Number of individual units in one container
Molecule(s)	The molecule name of the active ingredient
Major class	Type of drug (antibacterial, antithrombotic, anti-Alzheimer, etc.)
Minor class	Sub-type of drug
Packages sold	Number of packages sold
Extended units sold	Number of pills/capsules/etc. or mL of total substance sold
API units sold [a]	Amount of API sold in grams or international units (IU)
Computed Metrics	
Simplified dosage form	Simplified dosage form variable that collapses the 216 levels of Form (TLC3) into 17 broader categories
Total sales in NSP invoice dollars	Sum of NSP invoice sales across all channels and packages of that 9-digit NDC and month; represents the invoice amount charged by wholesalers or drug manufacturers
Total sales in WAC dollars	Product of the WAC and the number of packages sold, summed across all channels and packages of that 9-digit NDC and month
Average NSP price per extended unit	Total sales in NSP dollars divided by total number of extended units sold
Average WAC per extended unit	Total sales in WAC dollars divided by total number of extended units sold

[a] For substances with multiple APIs, we summed the API units of each ingredient.

A.1.2 Drug Shortages List (2018–2023)

FDA requires drug manufacturers to provide notification to FDA about finished drug product and API manufacturing discontinuations and interruptions (U.S. Food & Drug Administration, 2024). If FDA determines that the drug is in shortage in the United States, then FDA adds the manufacturer's drug (potentially including multiple 11-digit NDCs) to its official drug shortage list. Both CBER and the Center for Drug Evaluation and Research (CDER) maintain and publish a separate list of ongoing and recently resolved drug shortages. Drugs are only listed on the shortage list database while the shortage is ongoing and for six months after the shortage is resolved.[32] Because many shortages that occurred between 2018–2023 could be missing from the current list, we used the Internet Archive (Internet Archive, 2024) to extract historical versions of both the CDER and CBER lists of drug shortage data.

To assemble the full historical drug shortages list from 2018–2023, we aggregated drug shortage information from three FDA data sources:

- We downloaded all 39 available snapshots of the csv downloadable file with ongoing or recently resolved CDER drug shortages, with snapshots covering the period December 29, 2019, through December 21, 2023 (U.S. Food & Drug Administration, 2024).

- We extracted 84 snapshots ranging from January 9, 2018, through December 1, 2022, of a shortage webpage that lists all CDER drugs in shortage (U.S. Food & Drug

[32] FDA states, "Resolved shortages remain on the list for 6 months and discontinued shortages remain on the list for 1 year." (U.S. Food & Drug Administration, 2024)

Administration, 2024). The extracted CDER drug shortage webpage contains a complete list of drugs in shortage but does not include the NDCs or shortage start date. For this information, a separate more detailed page was extracted for each drug on the list. We extracted 13,040 of these drug-specific pages that were linked from the 84 snapshots.

- We extracted all 43 available snapshots of a CBER webpage with details on all ongoing drug shortages (U.S. Food & Drug Administration, 2024). The snapshots ranged from May 3, 2019, through December 22, 2023.

Combining the three sources above, we created a historical FDA drug shortage list covering the period from January 2018 through the end of December 2023 that included all 11-digit NDCs that went into shortage and the month and year the shortage began (Table A - 2). In some cases, NDCs were expressed as a 10-digit code, which represents the format reported by the manufacturer to FDA. We converted these to 11-digit codes by adding a leading 0 in the appropriate location (Anderson, 2023). In 3.9 percent of cases (137 out of 3,538 total extracted 11-digit NDCs), the NDC was missing or incomplete, and we searched the NDC Directory and did Internet research to identify the correct 11-digit NDC code. After extracting all 11-digit NDCs, we collapsed to the level of 9-digit NDC and de-duplicated records by only retaining unique combinations of 9-digit NDC and drug shortage start date.

Table A - 2. FDA Drug Shortage Variables, January 2018 – December 2023

Variable	Description
Date	Calendar month and year
9-Digit NDC	Unique two-segment number issued by FDA that identifies a drug's labeler and product
Shortage indicator	Indicates a shortage began for the listed NDC in the listed month
Reason for shortage	When available, the cause of the drug shortage, as reported by the manufacturer
FDA center	The agency (either CDER or CBER) with jurisdiction over the drug and that reported the shortage

A.1.3 FDA Orange Book, FDA Purple Book, and CBER's NDA and ANDA List (2018–2023)

The Orange Book is an FDA publication of drug products that are approved on the basis of safety and effectiveness by FDA under the Federal Food, Drug, and Cosmetic Act. It lists the application number and application holder. Cumulative supplements are published monthly that show new drug approvals and changes in ownership. We used the Orange Book to establish drug ownership at the time of the M&A for most NDAs and ANDAs.

The Purple Book is an FDA dataset of FDA-licensed biological products regulated by CDER, including licensed biosimilar and interchangeable products, and FDA-licensed allergenic, cellular and gene therapy, hematologic, and vaccine products regulated by CBER. For the period from February 2020 through December 2023, we downloaded Excel files available from FDA (U.S. Food & Drug Administration, 2024). For earlier periods when these files were not published, we used all available Internet Archive extracts of lists of approved Biologics License Applications (BLAs) that were separately published by CDER (U.S. Food & Drug Administration,

2019) and CBER (U.S. Food & Drug Administration, 2019). As with the Orange Book, we used the Purple Book to establish drug ownership at the time of the M&A for BLAs.

While CBER primarily operates in the area of biological products, it also has jurisdiction over a small number of drugs approved as NDAs and ANDAs. We used the Internet Archive to extract historical snapshots of a PDF document that lists approved CBER NDA/ANDAs (U.S. Food & Drug Administration, 2024). We extracted all 14 snapshots of the PDF document that were available during the study period. In the four cases where an application changed ownership, we conducted research on the companies to determine the date of the transaction. We used these lists to supplement the drug ownership information from the Orange and Purple Books.

Using the annual publications and monthly cumulative supplements of the Orange Book (Hyman, Phelps & McNamara PC, 2024), we extracted the variables listed in Table A - 3 for all NDA and ANDA drugs listed in the Orange Book from 2018–2023. The same information was extracted for BLAs using the downloadable Excel files of the Purple Book (U.S. Food & Drug Administration, 2024), which cover the period from February 2020 through December 2023. We combined the Purple Book files with information extracted from the CDER BLA list (U.S. Food & Drug Administration, 2019) and CBER BLA list (U.S. Food & Drug Administration, 2019), which provided BLA ownership information for 2018–2019. For the few cases of NDAs and ANDAs under CBER's jurisdiction, we gathered the information in Table A - 3 from historical archives of CBER's NDA/ANDA listing (U.S. Food & Drug Administration, 2024).

Table A - 3. FDA Drug Ownership Variables, January 2018 – December 2023

Variable	Description
Date	Calendar month and year
Application number	Unique NDA or ANDA number issued by FDA and associated with the drug's application for approval
Applicant	Name of company that owns listed Application at the listed month
FDA center	Indicates whether the drug is under the jurisdiction of CDER or CBER

A.1.4 National Drug Code (NDC) Directory (2018–2023)

The NDC Directory is an FDA dataset with information on over-the-counter (OTC) and prescription drugs. It identifies drugs by their unique NDC code as well as their application number (i.e., NDA, ANDA, or BLA number). The information is collected from mandatory biannual submissions by registered drug companies. It is updated daily and represents a comprehensive listing of finished drug products that are marketed in the United States. We used the NDC Directory to associate a company's historical ownership of a given drug application (i.e., NDA, ANDA, or BLA number) with a specific set of 9-digit NDCs that were on the market during that time.

Because discontinued drugs are removed from the NDC Directory, we extracted all 13 available snapshots of the NDC Directory (at the level of 9-digit NDCs) using the Internet Archives, which had archival dates ranging from May 2, 2017, through February 5, 2024. For months in the study period that did not have an Internet Archive snapshot, we used data from the most recent preceding snapshot. In cases where a product was approved between two

snapshot dates (or was missing from all earlier snapshot(s) despite still being on the market during that period), we used data from the most recent future NDC Directory snapshot. If a single 9-digit NDC was associated with multiple application numbers at a single point in time, we retained only the earlier application number. In a very small number of cases (n=26 products, or 0.01 percent of all 9-digit NDCs), a drug was listed both as an OTC and as a prescription drug in different records; we classified these drugs as prescription drugs. For our NDC Directory dataset, we filtered out any months outside the study period (i.e., before 2018 or after 2023) (see Table A - 4).

Table A - 4. NDC Directory Variables, January 2018 – December 2023

Variable	Description
Date	Calendar month and year
Application number	Unique NDA, ANDA, or BLA number issued by FDA and associated with the drug's application for approval; the number starts with "ANDA," "NDA," or "BLA," followed by the six-digit code
9-digit NDC	Unique two-segment number issued by FDA that identifies a drug's labeler and product
Molecule	Molecules name of the API(s); referred to as "non-proprietary name" in the NDC Directory
Product	Trade name of the drug, if a brand; referred to as the "proprietary name" in the NDC Directory
Molecule type	Either biologic or small molecule
Dosage form	The physical form (e.g., pill, solution, ointment) in which the finished drug is marketed for use
Route of administration	The manner of administering the drug to the human body (e.g., oral, intravenous, subcutaneous injection)
OTC indicator	Indicates whether or not the drug is listed exclusively as an OTC drug

A.1.5 Essential Medicines Lists

We combined the EO EML published by FDA (U.S. Food & Drug Administration, 2020) with the ARMI EML (HHS ASPR and ARMI, 2022) and created a variable indicating which source designated each drug as essential. The EO EML includes drugs that are "most needed for patients in U.S. acute care medical facilities, which specialize in short-term treatment for severe injuries or illnesses, and urgent medical conditions" (U.S. Food & Drug Administration, 2020). Drugs in the ARMI EML "were identified as either critical for minimum patient care in acute settings or important for acute care, with no comparable alternative available" (HHS ASPR and ARMI, 2022). We used the EO EML and ARMI EML to identify essential medicines involved in M&As.

The combined EML is the only dataset (Table A - 5) that does not depend on calendar time. Since their initial publications, the lists of essential medicines have not changed. Drugs designated as essential were therefore assigned that status for their entire study period (2018–2023). Some products, like source plasma, were excluded from our study because they do not have sales information in IQVIA NSP and are not assigned an NDC number. We also excluded OTCs from the study, which include essential medicines like alcohol-based hand sanitizers. In one case, the EO EML identified "sodium bicarbonate 5% injection" as essential, while the ARMI

EML did not specify a strength. We therefore designated sodium bicarbonate as essential according to both lists if the strength was 5 percent and essential according to ARMI EML if the strength was not 5 percent.

Table A - 5. Essential Medicines List Variables

Variable	Description
Date	Calendar month and year
Molecule	Molecule name of the API(s)
Dosage form	The physical form in which the finished drug is marketed for use; in some cases, this variable includes a route of administration
Strength	Quantity of the active ingredient per pill, unit volume, etc.; in most cases, this is not specified and all strengths were considered essential
EML source	Indicates whether drug is designated as essential on the EO list, ARMI list, or both

A.1.6 FactSet (2010–2023)

FactSet is a comprehensive database on mergers and acquisitions involving public and private companies worldwide. It combines more than 200 databases from industry-leading suppliers and analytical tools into a single information system. It has data on transactions beginning in 1980 and covers over 86,000 companies. Information is sourced from "8-Ks, Business Wire, PRNewswire, Stock Exchanges, company websites, and other news sources" (FactSet, 2024). We used FactSet as the primary dataset for identifying in-scope M&A deals completed between January 1, 2010, and December 31, 2023. We indexed all transaction values to 2023 dollars using the seasonally adjusted consumer price index for medical care (U.S. Bureau of Labor Statistics, 2024).

If a transaction had a clearly erroneous value (e.g., $0 or trillions of dollars), we replaced the value using published information about the transaction. If the transaction value was not published elsewhere, we deleted the value so that it was missing but retained the transaction in our dataset. In cases where an M&A had multiple parent entities listed, we assigned the single most appropriate parent entity (e.g., based on ownership) or selected the parent company with complete financial information. We used the deal information to assign a single deal type to each M&A. Deals tagged by FactSet as a divestment, asset purchase, or forced regulatory divestiture were classified as asset transfers/divestitures. We classified deals as acquisitions if they were tagged by FactSet as being an exit, tender offer, venture backed acquirer, auction, reverse takeover, leveraged buyout, financial buyer, insolvency, going private, management buyout, privatization, secondary buyout, competing bid, unsolicited bid, investor buyout, collar, club deal private equity group, bidder controlling shareholder, and employee buyout. Deals tagged by FactSet as a merger of equals were designated as mergers. Table A - 6 presents the FactSet variables used in this analysis.

Table A - 6. FactSet Variables, January 2010 – December 2023

Variable	Description
Raw Metrics	
Date	Calendar month and year when the transaction was completed
Company	Name of company involved in transaction

Variable	Description
Role	Either acquirer or target
CUSIP number	9-digit unique company identifier issued by American Banking Association
Primary NAICS	Classifies businesses by type of economic activity and industry; the primary NAICS indicates the main economic activity and industry of the company
Secondary NAICS	Classifies businesses based on secondary economic activities or industries they engage in
Target shares owned at transaction announcement	The percentage of the target company's stock owned by the acquirer at the time the transaction was publicly announced
Target shares owned at completion	The percentage of the target company's stock owned by the acquirer at the completion of the transaction
Transaction value	Calculated as base equity value plus the value of the target's outstanding net debt (where applicable), with outstanding net debt defined as total short- and long-term interest-bearing debt less any cash and cash equivalents. The target's outstanding net debt is only included in the Transaction Value calculation if (a) the acquirer is seeking to own 100% of the target, (b) the target is a non-financial company, and (c) the target's outstanding net debt is publicly disclosed (or the acquirer publicly states it is assuming a specific amount of liabilities). Otherwise, transaction value is equal to amount paid for the portion of the target acquired (base equity value).
Computed Metrics	
Type of transaction	Identifies the transaction as a merger, an acquisition, or a divestiture/asset transfer

Note: Definitions adapted from FactSet data dictionary (FactSet, 2024).

A.1.7 Compustat (2010–2023)

Compustat is a database with financial and market information on public and private companies worldwide. Compustat North America has information about North American companies dating back to 1950. Compustat Global Vintage covers international companies, with data dating back to 1993. The North American dataset gathers information from annual and quarterly balance sheets, income statements, cash flow statements, and supplementary data (Standard & Poor's, 2003). We used both Compustat North America and Compustat Global Vantage to access annual and quarterly financial information for companies involved in transactions. Compustat financial variables are reported in local currencies, which we converted into U.S. dollars (USD) using exchange rates for the month when the data were reported (International Monteary Fund, 2024). The resulting values in USD were then adjusted for inflation to 2023 USD using the seasonally adjusted consumer price index for medical care (U.S. Bureau of Labor Statistics, 2024). Table A - 7 presents the Compustat variables we used in the analysis.

Table A - 7. Compustat Variables, January 2010 – December 2023

Variable	Description
Raw Metrics	
Date	Calendar month and year; for variables updated quarterly or annually, we applied the reported amounts to each corresponding month
Company	Name of company [a]
Book Value of Equity	Represents the historical value of a company's common equity. Equal to Stockholders Equity Parent, if populated. Otherwise calculated as Common

Variable	Description
	Ordinary Equity plus Total Preferred/Preference Stock (Capital). Otherwise calculated as Total Assets minus Total Liabilities minus Minority Interest (balance sheet). Otherwise calculated as Total Assets minus Long-Term Liabilities.
Market Value of Equity	Represents the market value of a company's common equity. It calculated as Price Close times Common Shares Outstanding.
Revenue	Value of the money generated from normal business operations
Computed Metrics	
Book to Market Ratio	Calculated as the Book Value of Equity divided by the Market Value of Equity
Earnings before interest, taxes, depreciation and amortization (EBITDA)	Earnings before interest, taxes, depreciation, and amortization

[a] While subsidiary companies may be listed in Compustat, the reported financials are typically consolidated with the parent company's financial statements (1) when the parent company owns at least 50 percent of the subsidiary, and possibly also (2) when the parent company owns 20 to 49 percent (U.S. Securities and Exchange Commission, 2020).
[b] Descriptions adapted from Compustat data dictionary and published definitions (Standard & Poor's, 2003) (Standard & Poor's, 2002) (Center for Research in Security Prices, 2023).

A.1.8 DealForma (2010–2023)

DealForma is a database covering a range of pharmaceutical deals and includes information on over 35,000 companies and 4,000 M&As (DealForma, 2024). We used the DealForma data to supplement the information in FactSet. For example, DealForma identifies the type of assets involved in the M&A, the type of M&A deal, the therapeutic area and primary technology of the target company's leading asset, the type of pharmaceutical companies involved in the M&A, the stage of development of the target products, and the type of target products (biologics, small molecules, formulations, etc.). We only used DealForma records that successfully matched to an in-scope FactSet M&A; the DealForma dataset was not used to expand the sample of M&A deals. We did, however, use DealForma to implement some exclusion criteria, specifically the exclusion of cell/gene therapy companies, and the exclusion of deals involving devices or diagnostics.

We also used DealForma to assist in classifying deals. Deals marked as acquisitions or acquisition options in DealForma were designated as acquisitions in our dataset. Deals categorized as reverse mergers in DealForma were designated as mergers. Deals marked as a business unit purchase or platform/product purchase in DealForma were designated as asset transfers/divestitures in our dataset. To harmonize deal types between FactSet and DealForma, we deferred to the DealForma classification type if available, and used the FactSet classification otherwise.

Table A - 8. DealForma Variables, 2010 – 2023

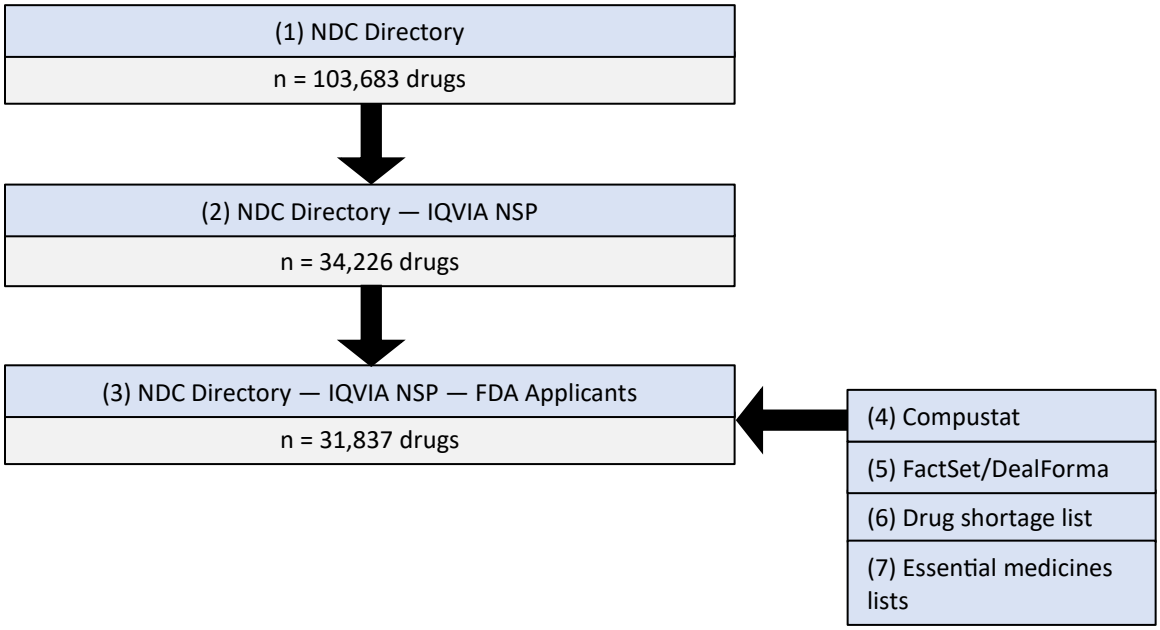
Variable	Description
Target	Target company in transaction
Acquirer	Acquirer company in transaction
Stage signed	Stage of acquired company's most advanced asset in deal
Deal type	Type of deal (acquisition, company formation, platform/product purchase, etc.)

Variable	Description
Primary therapeutic area	Primary therapy area of the deal based on most advanced asset of target company
Primary technology	Target company's primary modality/technology of its leading asset
Asset type	Category of target company's leading asset in deal (drug, device, company/business/facility, etc.)
Deal status	Indicates if the M&A or asset purchase is still active, was terminated, or was completed

A.2 Merging All Datasets

We used the historical NDC Directory as the basis for combining all datasets because the NDC Directory contains the most comprehensive accounting of finished human prescription drugs (U.S. Food & Drug Administration, 2022), with records for each month from January 2018 through December 2023. The final dataset thus contained a single observation for each unique 9-digit NDC, month, and year. Figure A - 1 shows each step of merging and the number of matching drugs (i.e., 9-digit NDCs) at each stage with non-missing data from all merged datasets.

Figure A - 1. Number of Drugs (9-digit NDCs) by Merging Step



To construct the analytic dataset, we began with the historical NDC Directory (see step 1 of Figure A - 1). Using month and 9-digit NDC, we merged the processed IQVIA NSP dataset into the historical NDC Directory (step 2), which led to a match for 34,226 drugs (i.e., 9-digit NDCs). Next, using month and application number, we merged the historical FDA applicant information (consisting of the Orange Book records, Purple Book records, and CBER NDA/ANDA records) into the analytic dataset (step 3), which resulted in only a slight reduction in the number of records. We next merged in the Compustat data by matching the Compustat company name to the FDA Applicant name (step 4). This step involved harmonizing the Applicant names as they

appear across all historical records of the Orange Book, Purple Book, and CBER NDA/ANDA list, and then matching the harmonized names to the company names in Compustat. We did this using a manual review, which was aided by a fuzzy match to generate an initial list of similar names that were candidates for grouping into a single harmonized name. The expectation was that many records would not match to the Compustat data, since Compustat primarily contains data on public companies required to disclose their financial information.

Next, we merged FactSet/DealForma data into the analytic dataset using CUSIP number (step 5), which is also present in Compustat. Before this merging, we combined the FactSet and DealForma datasets by matching the names of the acquiring companies and the target companies, as well as an approximate match of the date the deal was announced. As with other matching procedures, we used fuzzy matching to generate an initial list of candidate matches and then performed manual review to select the valid matches. To harmonize the classification of deal type, we relied on the DealForma designation if it was available, and we used the FactSet designation otherwise.

We also merged in the drug shortages records using month and 9-digit NDC (step 6), and the EML information using the molecule, dosage form, and strength, all of which also appear in the NDC Directory (step 7). In step 6, we successfully matched 89.2 percent of the extracted 9-digit NDCs in the drug shortage lists to our analytic dataset. The remaining 10.8 percent likely include drugs that are out of scope (e.g., OTCs, products that do not have NDCs, products that do not have sales data in IQVIA NSP). In step 7, to merge the EML data, we performed broad word searches of the drugs described in the EML, and then manually reviewed matches with the NDC Directory to identify drugs that meet the EML description of active ingredients, route of administration, strength in some cases. Where the EML specifies active ingredient(s), we designated drugs in the NDC Directory as essential only if all of the drug's active ingredients were listed in the EML. Drugs with additional active ingredients not specified by the EML were not designated as essential since both the FDA EO EML and the ASPR EML include additional line items to indicate additional active ingredients as essential where relevant (e.g., the FDA EO EML and the ASPR EML both include ceftazidime separately from ceftazidime-avibactam). In cases where the EML specifies a type of product rather than the active ingredients (e.g., "continuous renal replacement solution," "thrombin products," "tetanus vaccine"), we included all products meeting this description, even if, e.g., the tetanus vaccine contains other antigens besides tetanus toxoids, such as diphtheria toxoids or pertussis antigens. The EML and NDC Directory did not always describe the route of administration to the same degree of specificity (e.g., the EML lists "intramuscular" and NDC Directory lists "injection"). We therefore created a crosswalk of exact matches and possible matches between the two data sources and then performed manual review to identify valid matches. In cases where the EML specified a particular strength, we only designated NDCs as essential if they had the specified strengths.

A.3 Detailed Analytic Framework

A.3.1 Descriptive Analysis of M&As

We analyzed the characteristics of pharmaceutical M&As using the full sample of M&As meeting the inclusion criteria from January 2010 through December 2023. Within this M&A sample, the rate of missingness varied widely by variable. Rather than considering only full and complete records, we analyzed each M&A variable separately, using the available non-missing records of that variable. We performed Augmented Dickey-Fuller trend tests to assess the stationarity of the observed time series and identify changes, e.g., due to trends or seasonality. To calculate the average annual percent growth in the median M&A transaction value, we fit a linear model of the form:

$$\text{median MA value} = \alpha \exp(\lambda t) \quad \text{or} \quad \ln(\text{median M\&A value}) = \alpha + \lambda t \qquad (1)$$

where the initial value α and growth rate λ are parameters to be estimated. We calculated the average annual growth from the estimated growth rate parameter, as $\exp(\lambda) - 1$.

A.3.2 Descriptive Analysis of Drugs

Using the full drug dataset of 31,837 drugs, we evaluated the characteristics of drugs involved in M&As. This drug-level dataset included data from January 2018 through December 2023, which is the period of time for which IQVIA NSP data were available and monthly historical snapshots of FDA datasets were extracted. We used this dataset to evaluate the frequency and rate at which M&As target various types of drugs in the sample (e.g., brands versus generics, therapeutic area, type of molecule), and to calculate the odds ratio of a drug being involved in an M&A if it is essential versus non-essential.

When analyzing the drugs involved in M&As, we included (a) all drugs owned by the target company and transferred to the acquiring company, (b) any brand drugs owned by the acquiring company with the same therapeutic area as the target drugs, and (c) any generic drugs owned by the acquiring company with the same dosage form as the target drugs.[33] In cases where the target company only sold certain drugs from its portfolio (and did not transfer all of its marketed drugs), we identified the specific drugs involved in the M&A and flagged only those drugs that we could identify as having transferred ownership. For drug-level analyses, we considered each unique 9-digit NDC to be a different drug. We linked the M&A data to the IQVIA NSP data and designated a main drug portfolio type (original biologics, biosimilars, small molecule brands, or small molecule generics) to each company based on its largest line of business by sales dollars.

[33] We used the IQVIA NSP variable "major class" to identify matching therapeutic areas. To identify matching dosage forms, we used the IQVIA variable "Form (TCL1)." We combined oral solids into a single group and combined injections into a single group.

A.3.3 Matched Analysis of Drug Shortages

This analysis required identifying a cohort of "control" drugs that were not involved in an M&A but had similar characteristics as the cohort of "treated" drugs that were involved in M&As. We performed exact matching to remove imbalance in possible confounders. For each drug involved in an M&A in a given month, we identified all "control" drugs that were marketed in that same month and had the same brand status (brand versus generic), molecule type (small molecule versus biologic), dosage form, and price group. The price groups were formed by calculating quintiles of the NSP price per extended unit over the full dataset within groupings of brand status, molecule type, and dosage form. We matched on price because lower-cost drugs may be more likely to go into shortage. We repeated this matching process separately for each month in the dataset when an M&A occurred. Matching on the month and year allowed us to compare the M&A drugs to the non-M&A drugs (a) over equal periods of time, which is important since the probability of drug shortage generally increases as more time passes, and (b) over the same calendar time, which reduces the impact of any temporal confounders. In a given month, non-M&A drugs were selected from the set of drugs in our sample that were not involved in an M&A at any point during the study period. A single non-M&A drug was permitted to serve as a control in more than one month if the drug's matching group(s) were involved in multiple M&As over the study period.[34] In this report, we use the term "matching group" to refer to the distinct groupings of month, form, brand status, molecule type, and price. To maximize sample size, we retained all data for any matching groups with at least one M&A drug and at least one non-M&A drug.

Using this matched dataset, we calculated the common (i.e., adjusted) odds ratio of going into shortage within a two-year period of the M&A date. We calculated the odds ratio for all drugs in the matched drug dataset and also for various subgroups (e.g., therapeutic classes, dosage forms). Odds ratios were calculated as the odds of going into shortage given involvement in an M&A divided by the odds of going into shortage given no involvement in an M&A. We stratified the calculation of common odds ratios using the matching groups to control for between-group differences in the baseline odds of going into shortage. We performed the Cochran-Mantel-Haenszel (CMH) test to assess whether the common odds ratio differed significantly from the null value of 1. The common odds ratio was calculated using Equation 2, summing over all matching groups. In Equation 2, n_g represents the number of drugs in a given matching group g (e.g., $n_g^{(\text{M\&A, short})}$ is the number of drugs in group g that were involved in an M&A and went into shortage within two years of the M&A date), and N_g is the total number of drugs in group g.

$$\text{OR}_{\text{common}} = \frac{\sum_g \left(n_g^{(\text{M\&A, short})} n_g^{(\text{non-M\&A, not short})} / N_g \right)}{\sum_g \left(n_g^{(\text{non-M\&A, short})} n_g^{(\text{M\&A, not short})} / N_g \right)} \quad (2)$$

[34] Each drug's price group was reassigned in each month because drugs change prices over time, and to identify drugs that were similar at the time of the M&A.

A.3.4 Matched Analysis of Price Changes and Quantity Sold

We also used the matched dataset to compare the cohort of M&A drugs to the cohort of non-M&A drugs and assess whether they experienced different changes in price or quantity sold after the M&A date. Following the method of Bonaime & Wang (2024), we estimated the change in price and quantity sold in the following way, considering post-M&A periods of X = 1–6 months, 1–12 months, and 13–24 months, excluding the month of the M&A[35] from both the pre-M&A and post-M&A periods.

$$\Delta\text{price} = \ln\left(\frac{\text{price in months } X \text{ after M\&A}}{\text{price in months 1-12 before M\&A}}\right) \quad (3)$$

$$\Delta\text{quantity} = \ln\left(\frac{\text{quantity sold in months } X \text{ after M\&A}}{\text{quantity sold in months 1-12 before M\&A}}\right) \quad (4)$$

Because we aggregated to the level of 9-digit NDC (which collapses across packages with different sizes, etc.), we estimated prices using the per-extended-unit price:

$$\text{price in months } X = \frac{\text{total sales in months } X}{\text{total extended units sold in months } X} \quad (5)$$

We used a linear model with robust standard errors to test the statistical significance of the difference between the natural log of the price ratio, Δprice, for M&A drugs versus non-M&A drugs. We performed the same procedure for the natural log of the quantity ratio, Δquantity. Letting $x_{\text{involved in M\&A}}$ be an indicator for whether the drug was involved in an M&A and x_g represent the matching group[36], the model was specified as follows:

$$\Delta\text{price or } \Delta\text{quantity} = \beta_0 + \beta_1 x_{\text{involved in M\&A}} + \beta_2 x_g \quad (6)$$

Separate regression models were fitted for brand drugs and generic drugs. p values for the coefficients β_1 were used to assess the strength of the association. The average effect of M&As on the pre-to-post percent change is $\exp(\beta_1) - 1$, which corresponds to the percent change for M&A drugs compared to non-M&A drugs. We also calculated the average expected pre-to-post percent change in price across all n observations in the sample, which we then transformed out of the logarithmic scale:

[35] We filtered the matched drug dataset based on the required pre-M&A and post-M&A periods. For example, we excluded M&As that occurred in 2018 because there was not sufficient data to measure the average price in the 12 months prior to the M&A.

[36] The matching group x_g is a categorical variable with more than two levels and was coded as a series of dummy variables in the regression, i.e., $\beta_2 x_g = \sum_{g=1}^{G-1} \beta_2^{(g)} x_g$, where x_g is the binary indicator variable for the g^{th} group out of G total groups and $\beta_2^{(g)}$ is the corresponding coefficient.

$$\left(\frac{\text{price in months } X \text{ after M\&A}}{\text{price in 12 months before M\&A}}\right)_{\text{non-MA, mean}} = \exp\left(\frac{1}{n}\sum\left(\beta_0 + \beta_2 x_g\right)\right) \quad (7)$$

$$\left(\frac{\text{price in months } X \text{ after M\&A}}{\text{price in 12 months before M\&A}}\right)_{\text{MA, mean}} = \exp\left(\frac{1}{n}\sum\left(\beta_0 + \beta_1 + \beta_2 x_g\right)\right) \quad (8)$$

We considered three price metrics. The WAC is the "list price" offered by the drug manufacturer. It is rarely actually paid but often serves as a basis for price negotiations with payers or plan sponsors. We also analyzed the IQVIA NSP invoice price paid to the manufacturer or wholesaler by healthcare providers (pharmacies, outpatient facilities, hospitals, etc.). While a helpful benchmark, the NSP invoice price does not account for off-invoice discounts or rebates.

A.3.5 Market Concentration and HHI

We defined drug markets by therapeutic area and calculated the HHI within each market over a one-year period before and after each M&A in that therapeutic area. For these calculations, we harmonized company names across and within the various FDA drug ownership data sources to account for variations in spelling, abbreviations, etc. We used these harmonized FDA company identifiers to calculate each company's market share. Our harmonized company identifiers, however, did not collapse subsidiaries into their parent companies. When calculating HHI before or after the M&A, both the pre-M&A and post-M&A periods excluded the month when the M&A occurred. We mapped the IQVIA NSP "Major Class" variable onto 14 main therapeutic areas: Genitourinary, Gastrointestinal, Endocrine, Hematology, Cardiovascular, Anti-infective, Pain Medication, Immunomodulators, Central Nervous System, Respiratory, Dermatology, Oncology, Ophthalmology, Vaccines, and Other (which includes dietetics, vitamins and minerals, allergen tests, hospital solutions, and other miscellaneous categories classified by IQVIA as "Other Therapeutic Class"). For this analysis, we used data from 2018–2023 but only included M&As conducted during 2019-2022 in order to guarantee that one full year of sales data was available for the pre-M&A and post-M&A HHI calculations. We computed HHI as:

$$\text{HHI}_m = \sum_i \left(\frac{\text{company } i\text{'s one-year IQVIA NSP sales in drug market } m}{\text{sum of all IQVIA NSP sales in drug market } m} \times 100\right)^2 \quad (9)$$

For each market, we calculated the average change in HHI per M&A in that therapeutic area. We also computed the average change in HHI per M&A across all markets (still defining markets by therapeutic area). We used one-sample Wilcoxon signed rank test to assess the statistical significance of changes in HHI.

APPENDIX B: SUPPLEMENTAL TABLES

Table B - 1. M&As by Year and Transaction Type, 2010–2023

Year	Type of Transaction				
	Acquisition	Divestiture/ Asset Purchase [a]	Merger	Unknown	Total
2010	77	60	3	56	196
2011	78	68	2	57	205
2012	59	70	0	45	174
2013	70	77	1	62	210
2014	90	68	4	69	231
2015	99	100	1	66	266
2016	93	98	4	72	267
2017	76	83	8	47	214
2018	76	66	5	67	214
2019	66	66	10	53	195
2020	85	54	8	57	204
2021	110	54	7	67	238
2022	76	65	2	67	210
2023	80	52	8	42	182
Total	1,135	981	63	827	3,006
Percent of Total with Known Type	52.1%	45.0%	2.9%	N/A	100.0%
p value [b]	0.3188	0.6753	N/A	N/A	N/A

N/A = not applicable.
[a] "Divestiture/asset purchase" includes business unit purchases and platform/product purchases.
[b] p value calculated from Augmented Dickey-Fuller test for stationarity.

Table B - 2. Average Annual M&A Transaction Values, 2010–2023

Year	Transaction Value (Million 2023 $)				
	Average	SD	Median	IQR	Sample Size
2010	594.55	1,667.16	66.79	380.71	126
2011	524.79	1,919.65	55.03	359.15	131
2012	578.59	1,683.74	58.87	386.58	103
2013	500.39	1,662.96	61.93	299.96	124
2014	932.59	3,048.56	124.06	571.53	144
2015	1,938.97	7,335.41	162.48	896.49	162
2016	1,096.83	5,054.10	73.18	438.46	164
2017	746.50	3,224.58	81.15	447.31	120
2018	464.34	1,379.77	37.98	204.50	124
2019	2,557.12	12,753.61	86.19	505.83	120
2020	1,617.24	8,384.77	79.39	512.63	126
2021	980.51	3,943.49	97.35	502.61	127
2022	627.74	1,696.66	108.77	394.04	115
2023	1,327.72	4,963.52	86.04	436.34	108
p value [a]	0.0387	N/A	0.2338	N/A	N/A

[a] p value calculated from Augmented Dickey-Fuller test for stationarity. p values not computed for standard deviation (SD), interquartile range (IQR), or sample size.

Table B - 3. M&As by Type, 2010–2023

	Number of M&As															
	2010	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**	**Total**	**% of Total**
Transaction Value (Million 2023 USD)																
<$5M	17	18	19	22	15	14	22	10	31	18	16	14	10	14	240	13%
$5–25M	17	32	20	28	31	26	33	21	21	21	27	23	19	17	336	19%
$25–100M	35	28	17	18	23	30	40	33	26	24	23	27	24	24	372	21%
$100–500M	32	28	23	34	35	41	31	28	21	26	28	29	40	27	423	24%
>$500M	25	25	24	22	40	51	38	28	25	31	32	34	22	26	423	24%
Target Company Primary Therapeutic Area (When Applicable) [a]																
Oncology	11	13	7	12	13	15	18	12	15	15	19	23	17	17	207	25%
Central Nervous System	8	8	6	7	13	14	9	6	3	8	15	10	8	12	127	15%
Anti-infective	9	12	8	6	14	16	11	11	9	3	5	5	9	5	123	15%
Immunomodulators	7	3	7	2	5	3	4	4	5	2	5	8	3	9	67	8%
Endocrine	6	5	5	3	1	5	4	5	4	3	8	6	0	8	63	8%
Dermatology	2	5	4	4	4	3	8	1	1	5	5	4	5	3	54	6%
Ophthalmology	0	1	1	2	6	1	2	2	3	2	3	1	4	4	32	4%
Other	2	4	4	1	1	4	1	2	2	4	1	2	2	1	31	4%
Cardiovascular	1	1	1	3	2	2	2	5	2	2	2	2	4	1	30	4%
Gastrointestinal	2	3	3	3	3	3	1	1	1	3	1	0	1	2	27	3%
Genitourinary	3	1	0	1	3	3	1	1	4	2	1	1	1	5	27	3%
Hematology	3	2	2	1	2	1	2	0	1	3	4	2	3	1	27	3%
Respiratory	0	1	0	1	2	2	1	1	0	2	4	2	2	2	20	2%
Target Company Primary Technology (When Applicable) [a]																
Small Molecule	30	42	30	23	45	44	29	25	22	27	40	31	34	38	460	53%
Biologic	15	8	10	12	19	18	21	12	14	16	28	30	16	26	245	28%
Formulation	5	9	6	8	2	4	4	2	5	6	5	5	2	0	63	7%
Other	5	3	4	4	4	9	10	7	8	9	6	12	7	5	93	11%
Type of Deal																
Acquisition	77	78	59	70	90	99	93	76	76	66	85	110	76	80	1,135	52%
Asset Transfer/Divestiture	60	68	70	77	68	100	98	83	66	66	54	54	65	52	981	45%
Merger	3	2	0	1	4	1	4	8	5	10	8	7	2	8	63	3%
Phase of Development of Highest-Value Asset of Target Company																
Platform / Discovery	4	5	1	2	1	5	8	6	4	2	12	8	8	3	69	3%

	Number of M&As															
	2010	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**	**Total**	**% of Total**
Preclinical / IND	5	4	4	5	10	4	9	7	5	9	4	9	11	11	97	4%
Phase I	5	3	2	5	8	7	6	3	9	2	11	11	3	6	81	4%
Phase II	12	12	13	8	13	12	11	8	13	14	19	13	6	16	170	8%
Phase III	8	6	4	6	3	7	12	8	9	10	12	11	7	9	112	5%
Approved	22	27	19	21	38	35	21	17	17	20	18	13	21	20	309	14%
Not Disclosed	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0%
Not Applicable	7	11	10	8	11	10	10	14	8	11	8	26	8	7	149	7%
Highest-Value Asset of Target Company																
Biosimilar	0	0	0	0	0	0	1	1	0	0	0	0	0	0	2	0%
Brand	30	30	29	24	41	55	45	12	9	27	33	29	29	7	400	18%
Generic	5	6	6	4	5	8	4	1	1	1	1	2	1	0	45	2%
OTC	3	6	5	2	2	1	0	0	0	1	1	1	0	0	22	1%

[a] The target company's primary therapeutic area and primary technology were identified using DealForma, which was only available for M&As that successfully matched to DealForma.

Table B - 4. Counts of All Drugs in 2018–2023 Drug Dataset, by Therapeutic Areas and Brand Status

Therapeutic Area	Number of Marketed Prescription Brand Drugs in Sample, 2018–2023	Number of Marketed Prescription Generic Drugs in Sample, 2018–2023
Anti-infective	406	2,642
Cardiovascular	509	4,070
Central nervous system	903	6,657
Dermatology	240	1,037
Endocrine	816	1,967
Gastrointestinal	247	1,356
Genitourinary	83	622
Hematology	545	1,409
Immunomodulator	314	460
Oncology	565	1,172
Ophthalmology	165	444
Other	275	688
Pain	420	2,679
Respiratory	165	607
Vaccine	212	164

Table B - 5. Changes in Price and Quantity Sold for M&A Drugs versus Non-M&A Drugs

Metric	Brand Status	Post-M&A Period [a]	Mean Percent Change [b]		Mean Effect of M&A on Pre-to-Post Change [c]	Robust p value [d]
			M&A Drugs	Non-M&A Drugs		
Quantity Sold	Brand	1–6 months	-15.7%	-13.6%	-0.024 (-0.113, 0.065)	0.5988
		1–12 months	-10.9%	-15.6%	0.056 (-0.037, 0.146)	0.2445
		13–24 months	-24.4%	-31.9%	0.110 (-0.013, 0.222)	0.0822
	Generic	1–6 months	-24.3%	-19.0%	-0.066 (-0.131, -0.006)	0.0320
		1–12 months	-25.4%	-18.7%	-0.082 (-0.148, -0.024)	0.0069
		13–24 months	-41.2%	-32.9%	-0.124 (-0.269, 0.004)	0.0562
NSP Price per Extended Unit	Brand	1–6 months	2.2%	1.7%	0.005 (-0.013, 0.023)	0.5762
		1–12 months	1.0%	1.9%	-0.009 (-0.028, 0.009)	0.3254
		13–24 months	3.6%	3.6%	0.000 (-0.027, 0.027)	0.9929
	Generic	1–6 months	-3.1%	-5.2%	0.021 (0.005, 0.037)	0.0097
		1–12 months	-4.4%	-6.6%	0.024 (0.006, 0.040)	0.0069
		13–24 months	-12.2%	-12.0%	-0.002 (-0.042, 0.037)	0.9043
WAC per Extended Unit	Brand	1–6 months	3.7%	2.1%	0.015 (0.005, 0.025)	0.0032
		1–12 months	3.4%	2.7%	0.007 (-0.004, 0.018)	0.1949
		13–24 months	4.9%	5.1%	-0.002 (-0.028, 0.024)	0.8810
	Generic	1–6 months	-4.0%	-4.6%	0.006 (-0.006, 0.019)	0.3318
		1–12 months	-4.6%	-5.6%	0.011 (-0.003, 0.025)	0.1157
		13–24 months	-10.0%	-11.9%	0.022 (-0.005, 0.048)	0.1139

[a] Both the post-M&A period and the pre-M&A period excluded the month of the M&A. The pre-M&A period included the 12 months prior to the M&A.

[b] The mean percent change was estimated as Δprice = ln(average value in post-M&A period / average value in pre-M&A period). The mean value of Δprice was estimated from a linear model regressing Δprice on M&A status and matching group. Final estimates of percent change were transformed out of the logarithmic scale: mean percent change = 100% × [exp(mean value of Δprice) – 1].

Metric	Brand Status	Post-M&A Period [a]	Mean Percent Change [b]		Mean Effect of M&A on Pre-to-Post Change [c]	Robust p value [d]
			M&A Drugs	Non-M&A Drugs		

[c] The effect is the average percent change in Δprice for M&A drugs compared to non-M&A drugs. For example, in the first row, the average effect is approximately (-0.157 + 1)/(-0.136 + 1) – 1 = -2.4%.
[d] Robust standard errors and p values were used.

Table B - 6. Change in HHI per M&A Deal, by Therapeutic Area, 2018–202

Therapeutic Area [a]	Pre-M&A HHI		Post-M&A HHI		Difference		Percent Difference [b]		Sample Size
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	Mean (SD	Median (IQR)	Mean (SD)	Median (IQR)	
Genitourinary	2,964 (1,089)	3,344 (1,998)	3,513 (701)	3,906 (852)	549 (505)	562 (627)	27.6% (30.7%)	16.8% (42.2%)	8
Gastrointestinal	1,004 (158)	1,069 (275)	1,171 (269)	1,173 (298)	167 (153)	94 (65)	15.9% (12.3%)	11.5% (6.4%)	14
Hematology	1,334 (278)	1,345 (538)	1,502 (253)	1,533 (431)	167 (59)	171 (41)	13.5% (6.2%)	13.5% (4.6%)	18
Endocrine	1,224 (149)	1,261 (259)	1,378 (216)	1,382 (344)	154 (74)	120 (87)	12.2% (4.4%)	10.4% (4.9%)	17
Cardiovascular	619 (77)	621 (105)	694 (159)	675 (240)	75 (107)	86 (111)	11.4% (16.6%)	15.1% (18.5%)	18
Anti-infective	3,345 (232)	3,460 (265)	3,466 (102)	3,510 (122)	121 (187)	65 (253)	4.0% (6.2%)	1.8% (8.3%)	15
Pain Medications	439 (54)	435 (58)	449 (73)	429 (133)	9 (86)	17 (124)	3.2% (18.2%)	3.7% (29.3%)	19
Immuno-modulators	1,671 (39)	1,664 (35)	1,707 (79)	1,710 (129)	36 (64)	45 (81)	2.1% (3.8%)	2.7% (4.6%)	12
Other [c]	517 (47)	527 (33)	522 (37)	540 (53)	5 (62)	27 (59)	1.9% (12.3%)	5.2% (11.1%)	8
Central Nervous System	471 (19)	479 (13)	475 (8)	474 (11)	4 (21)	-3 (30)	1.0% (4.7%)	-0.6% (6.3%)	19
Respiratory	1,402 (53)	1,387 (16)	1,411 (50)	1,419 (73)	10 (80)	39 (58)	0.8% (5.5%)	2.9% (4.2%)	7
Dermatology	628 (50)	631 (73)	630 (35)	626 (28)	2 (52)	29 (82)	0.7% (8.1%)	4.4% (13.6%)	7
Oncology	761 (117)	731 (246)	719 (79)	687 (127)	-43 (64)	-50 (110)	-4.7% (8.1%)	-5.5% (13.8%)	19
Ophthalmology	2,108 (101)	2,131 (188)	1,951 (125)	1,958 (82)	-157 (149)	-218 (206)	-7.3% (7.1%)	-10.0% (9.1%)	8
All Therapeutic Areas	1,225 (900)	928 (1,035)	1,298 (951)	1,041 (1,123)	73 (189)	48 (138)	5.9% (14.1%)	5.9% (13.6%)	190

SD = standard deviation; IQR = interquartile range.

[a] Vaccines are excluded because sales data are missing at a higher rate than other therapeutic areas. M&As between 2019–2022 were analyzed to ensure one full year of data when calculating HHI before and after the M&A.

[b] Mean and median percent difference are calculated as the mean and median, respectively, of the percent difference in HHI from the year before the M&A to the year after the M&A, across all observed M&As in the therapeutic area.

[c] "Other" includes dietetics, vitamins and minerals, allergen tests, hospital solutions, and other miscellaneous categories classified by IQVIA as "other therapeutic class."

Table B - 7. Odds Ratio of Shortage within 2 Years of M&A Date, 2018–2023

Group	Number of Drugs in Shortage within Two Years of M&A Date		Number of Drugs Not in Shortage within Two Years of M&A Date		Common Odds Ratio [a]			
	Involved in M&A	Not Involved in M&A	Involved in M&A	Not Involved in M&A	Point Estimate	95% Lower Confidence Limit	95% Upper Confidence Limit	p value [b]
All Drugs	112	1,768	2,017	25,207	1.2435	1.0316	1.4988	0.0249
Generic Drugs	103	1,556	1,594	21,379	1.2639	1.0410	1.5345	0.0202
Brand Drugs	9	212	423	3,828	1.0247	0.5116	2.0523	0.9453
Target's Drugs	45	1,415	780	22,644	2.2654	1.6467	3.1167	<0.0001
Acquirer's Drugs	67	1,580	1,239	23,529	0.9918	0.7885	1.2475	0.9906
Essential Medicines	25	375	318	3,362	1.1361	0.7916	1.6304	0.5528
Low Market Concentration	83	1,260	1,282	15,338	1.3682	1.1010	1.7002	0.0055
Medium Market Concentration	27	307	498	6,013	1.2510	0.8409	1.8611	0.3067
High Market Concentration	2	120	231	2,899	0.2479	0.0621	0.9893	0.0465
M&As over $1 Billion in Value	11	3	257	398	4.9769	1.3878	17.8486	0.0198
M&As under $1 Billion in Value	20	7	321	477	3.6092	0.5976	21.7984	0.3919
Generic Drugs, Anti-infective	2	113	141	2,060	0.2904	0.0723	1.1666	0.0922
Generic Drugs, Cardiovascular	12	201	225	3,418	1.7170	0.9306	3.1680	0.1269
Brand Drugs, Central Nervous System	6	28	104	551	2.8488	1.1246	7.2168	0.0527
Generic Drugs, Central Nervous System	42	633	313	5,356	1.8723	1.3338	2.6282	0.0003
Generic Drugs, Endocrine	13	28	109	1,534	4.0471	2.0184	8.1151	<0.0001
Generic Drugs, Gastrointestinal	13	116	96	935	1.6253	0.8571	3.0821	0.1871
Generic Drugs, Oncology	8	71	90	738	1.1729	0.6064	2.2686	0.7587
Generic Drugs, Pain Medications	13	145	228	1,896	1.1719	0.7323	1.8753	0.5971
Generic Drugs, Injection	34	365	413	3,090	1.2182	0.8983	1.6521	0.2341
Brand Drugs, Oral Solid	7	102	280	2,334	1.9022	0.8642	4.1870	0.1764
Generic Drugs, Oral Solid	69	1,140	992	16,734	1.3499	1.0493	1.7366	0.0229

[a] Common odds ratios are calculated by stratifying on groups used to match M&A drugs to non-M&A drugs, i.e., calendar month and year, brand status (brand vs. generic), molecule type (biologic vs. small molecule), dosage form, and subgroup price quintile; computed as odds of going into shortage given that drug was involved in M&A divided by odds of going into shortage given that drug was not involved in M&A.

[b] p value is for the stratified Cochran-Mantel-Haenszel test of equal odds of a drug going into shortage given that it was involved in an M&A vs. not involved in an M&A.

Table B - 8. Counts of M&As by Target and Acquirer NAICS, 2010–2023 [a]

Target Company NAICS	Acquiring Company NAICS [b]				
	325411 Medicinal and Botanical Manufacturing	**325412 Pharmaceutical Manufacturing**	**325414 Biological Product Manufacturing [c]**	**541714 Research and Development in Biotechnology [d]**	**Total**
325411: Medicinal and Botanical Manufacturing	48	235	51	22	255
325412: Pharmaceutical Manufacturing	186	2,176	325	121	2,289
325414: Biological Product Manufacturing [c]	18	243	136	24	318
541714: Research and Development in Biotechnology [d]	29	414	160	97	504
Total	240	2,747	572	237	3,006

[a] Counts are based on primary or secondary NAICS. The sum of the counts is more than the total number of M&As (3,006) because some companies have multiple in-scope NAICS codes.
[b] Acquirers were selected for the sample if they had either NAICS 325412 or 325414. Nonetheless, the selected acquirers also work in NAICS 325411 and 541714.
[c] Excludes diagnostic manufacturer.
[d] Excludes nanobiotechnology.