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AN EXAMINATION OF PHARMACEUTICAL SUPPLY CHAIN INTERMEDIARY MARGINS IN THE U.S. RETAIL CHANNEL

FINAL

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EXECUTIVE SUMMARY

The U.S. supply chain for prescription drugs is highly complex, involving several intermediaries between drug manufacturers and patients. Negotiations among these supply chain intermediaries, which include pharmacy benefit managers (PBMs), pharmacies, and wholesalers, are private and the terms of their contracts are confidential. The complexity of the supply chain coupled with the lack of price transparency and opacity of interactions among supply chain intermediaries has resulted in misaligned market incentives that likely contribute to increasing prescription drug costs in the United States. Effective policies that broaden access to prescription drugs and reduce prescription drug prices while encouraging innovation must be predicated on identifying the actors and incentives that raise drug prices without increasing their value to the end user. Thus, it is important to understand where along the pharmaceutical supply chain substantial margins are generated.

In this report, we estimate the percentages of drug expenditures that are allocated to each stakeholder in the supply chain, including manufacturers. Then, we examine the gross margins (hereinafter referred to as "margins") of three primary intermediaries in the U.S. retail[1] prescription drug supply chain, namely wholesalers, retail pharmacies, and PBMs from Quarter 1 (Q1) 2020 to Quarter 4 (Q4) 2022.[2]

ES.1 METHODOLOGY

We estimate margins by modeling flows of payment through the pharmaceutical supply chain on a per-prescription basis. In our stylized model, money enters the system from two major sources—claim reimbursements paid by third-party payers (i.e., public and private insurers) and copays paid by insured beneficiaries.[3] These two financial streams make up the total drug expenditures, which flow from the PBM to the pharmacy to the wholesaler to the manufacturer. At each stage of the supply chain, a portion of these expenditures is retained to cover costs and profit, and the rest is passed along (Congressional Budget Office, 2022; Miller, et al., 2019).

We incorporate additional payment flows within the supply chain based on the strategies intermediaries use to compete for market share and maximize their profits. For example, drug manufacturers compete for formulary coverage by negotiating confidential rebates with PBMs, which results in manufacturers having a "net" price that is less than the invoice price at the time of sale (Centers for Medicare & Medicaid Services, 2017). We account

[1] For the purposes of this analysis, the retail prescription channel includes prescription drugs sold through independent pharmacies, chain stores, and food stores. Mail pharmacy sales are excluded.

[2] Margins represent the portion of revenue from pharmaceutical sales retained after accounting for acquisition costs. Manufacturers were excluded from the investigation of margins because this study did not quantify the costs associated with manufacturing or developing pharmaceuticals. The analysis of expenditures is intended to illustrate manufacturers' earnings in the context of the other intermediaries without making claims about manufacturing costs.

[3] The terms "beneficiary," "patient," and "consumer" all imply somewhat different roles, but in the context of retail prescription drug markets, all refer to the person obtaining a prescription medication from a retail outlet (i.e., independent pharmacy, chain store, or food store) for self-administration.

for off-invoice rebates and discounts and apply these to the computed sales and acquisition costs to capture the "net" transaction values. This includes not only rebates but also direct and indirect remuneration (DIR) that the PBMs recoup from pharmacies.[4]

Of the 24,395 unique retail drugs that we identified as being in scope for this study, we determined that 7,128 met the inclusion criteria.[5] Of those, we analyzed 3,270 for which we had complete data and price estimates at each stage of the supply chain.

For this sample of 3,270 prescription drugs sold primarily through retail outlets, this study estimates net acquisition costs and net sales prices using a variety of public data sources, including National Average Drug Acquisition Cost (NADAC), State Drug Utilization Data (SDUD), Federal Supply Service Schedule Pharmaceutical Pricing (FSS), and the Affordable Care Act Federal Upper Limit (FUL), as well as several proprietary datasets, including IQVIA National Sales Perspective (NSP), IQVIA PayerTrak, and SSR Health. In addition to the data sources above, we also relied on several published studies and reports including PBM Annual Reports published by the Iowa Insurance Division (Iowa Insurance Division, 2020-2023) and a 2019 Government Accountability Office (GAO) report on the use of PBMs and efforts to manage drug expenditures and utilization (United States Government Accountability Office, 2019).

ES.2 KEY FINDINGS

Our results suggest that PBMs' margins steadily increased from 23 percent in 2020 to 31 percent in 2022, while wholesalers' margins were roughly constant at 5 to 6 percent and pharmacies' margins decreased from 7 to 3 percent. Several factors may have contributed to the increase in PBMs' margins, including PBM market structure and rising DIR fees paid by pharmacies. In our model, margins are sensitive to pharmacy DIR, which we estimate increased by $9.5 billion or 46.8 percent from 2020 to 2022. During this time, we estimate that pharmacies' total margins on retail drugs decreased by $10.9 billion, or 47.2 percent.[6] We find that, during our study period, PBMs received higher margins than pharmacies or wholesalers on nearly all types of retail drugs—brands, generics, biologics, small molecules, drugs for the treatment of acute conditions, drugs for the treatment of chronic conditions, drugs with long market tenure, and drugs with short market tenure.

Compared to generic drugs, brand drugs yielded higher margins for PBMs and wholesalers but lower margins for pharmacies, in dollar terms. For all three intermediaries, generic drugs had higher margin percentages than brand drugs. In 2022, margin percentages on

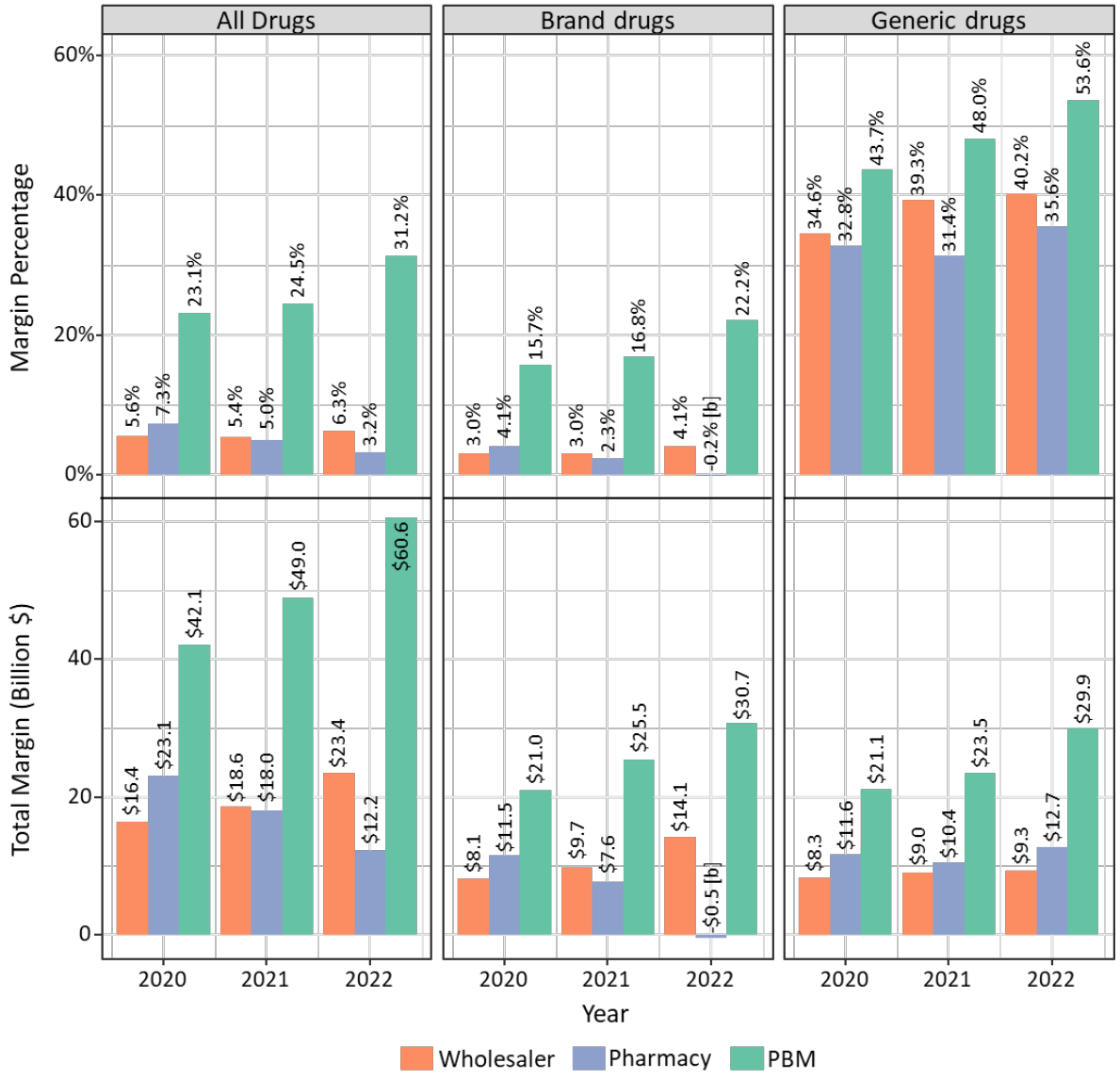
[4] DIR comprises payments made by a pharmacy to a PBM, including (a) retrospective price concessions to "true up" the PBM's actual reimbursements to the pharmacy with contract rates, (b) penalties assessed by the PBM based on the pharmacy's performance metrics (e.g., generic dispense rates), and (c) network participation fees that the PBM charges to the pharmacy.

[5] Specifically, drugs met the inclusion criteria if they were listed in the NADAC between 2020 and 2022 and had at least 80 percent of total sales in the retail channel according to IQVIA NSP.

[6] The estimated increase in DIR fees is partly due to the model's assumptions, as data on DIR was limited. Further research is needed on the magnitude of impact DIR has on the margins of PBMs and pharmacies. See Appendix B.5 for details on how DIR was estimated in this study and the assumptions that we used.

generic drugs were 40.2 percent for wholesalers, 35.6 percent for pharmacies, and 53.6 percent for PBMs (see Figure ES- 1). Generic drugs also had roughly four times the utilization of brand drugs. Nonetheless, despite generics having higher volume sales and yielding higher margin percentages, PBMs and wholesalers still earned more margin dollars from brand drugs than they did from generic drugs, because brand drugs are far more expensive.

Figure ES- 1. Margin Percentage and Total Dollars by Intermediary, 2020-2022 [a]



[a] Figure presents weighted population estimates. Margin percentage is calculated as weighted total margin across all drugs divided by weighted total net sales.
[b] Pharmacies are estimated to have margins of -0.2% (-$0.5 billion) on brand drugs in 2022, which corresponds to a loss. The 95% confidence interval for this value, however, extends into the positive range. See Section 4.3.1.

ES.3 LIMITATIONS

This study used multiple data sources to generate estimates at the level of individual drugs where possible. However, in some cases, drug-specific estimates were not available, and

so we applied a single parameter estimate to all drugs in a given group. This approach may not fully capture likely heterogeneities across different drugs.

We do not estimate several price concessions manufacturer may make, including through copay assistance programs, 340B-related discounts, the best price provision of the Medicaid rebate, administrative fees and service fees paid to the PBM, and others. Not accounting for these concessions may lead to overestimating the manufacturer rebates paid to the PBM. This would lead to underestimated pharmacy margins and overestimated PBM margins, since our calculation of pharmacy DIR is based on the estimated value of the rebate.

The NADAC survey, while providing a comprehensive source of pharmacy acquisition costs, may tend to overrepresent smaller community pharmacies. Large chain pharmacies may be able to use their market position to negotiate better prices with wholesalers, which would result in higher margins to pharmacies than we have estimated.

Our study used Medicaid reimbursements calculated from prices in the SDUD database published by the Centers for Medicare & Medicaid Services (CMS), which we have treated as representative of the pre-rebate reimbursements PBMs receive from Medicare Part D and commercial healthcare plans. However, given the recent attention and legislative efforts targeting Medicaid drug spending, the SDUD prices may be downwardly impacted by pressure within Medicaid to maintain lower third-party reimbursements. To the extent that Medicare Part D or commercial plans pay higher prices for drugs, PBM margins may be higher than we estimated.

In some cases (e.g., particularly when analyzing biologics), the sample size was relatively small. Similarly, we analyzed a three-year period that included the COVID-19 pandemic. To the extent that the pandemic had temporary impacts on retail drug prices, these effects impact our findings.

ES.4 CONCLUSIONS

The results of this study provide insight into the distribution of drug expenditures across the members of the retail pharmaceutical supply chain. Estimates of intermediaries' margin percentages and retained shares of net expenditures could help inform policy discussions on lowering overall prescription drug spending in the United States.

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ABBREVIATIONS

Abbreviation	Definition
AHIP	America's Health Insurance Plans
AMP	Average Manufacturer Price
API	Active Pharmaceutical Ingredient
ASPE	Office of the Assistant Secretary of Planning and Evaluation
ATC	Anatomical Therapeutic Chemical
CAGR	Compound Annual Growth Rate
CHIP	Children's Health Insurance Program
CMS	Centers for Medicare & Medicaid Services
DIR	Direct and Indirect Remuneration
FDA	Food and Drug Administration
FFS	Fee-for-Service
FSS	Federal Supply Schedule
FTC	Federal Trade Commission
FUL	Federal Upper Limit
GAO	Government Accountability Office
GPO	Group Purchasing Organization
HHS	U.S. Department of Health and Human Services
MAC	Maximum Allowable Cost
MCO	Managed Care Organization
MEPA	Modernizing and Ensuring PBM Accountability Act
NADAC	National Average Drug Acquisition Cost
NARP	National Average Retail Price
NCPA	National Community Pharmacists Association
NDC	National Drug Code
NSP	IQVIA National Sales Perspectives
PBM	Pharmacy Benefit Manager
PCMA	Pharmaceutical Care Management Association
SDP	Office of Science and Data Policy
SDUD	State Drug Utilization Data
SEC	Securities and Exchange Commission
VA	U.S. Department of Veterans Affairs
WAC	Wholesale Acquisition Cost

GLOSSARY

Average Manufacturer Price (AMP). The post-concession price that manufacturers charge wholesalers.

Big Four price. The maximum prices manufacturers may charge for direct federal purchases made by Department of Veterans Affairs, the Department of Defense, the Public Health Service, and the Coast Guard, as published in the VA's pricing data list.

Cash price. The price a patient pays for a drug without insurance.

Drug tenure. Length of time the drug has been on the market.

Formulary. A list of drugs covered by a health plan. These are often developed and maintained by PBMs.

Gross margins. Gross margins represent earnings after subtracting payments that flow out of the intermediary from those received by that intermediary.

Manufacturer administrative fees. The administration fee that a manufacturer pays to a PBM. This fee includes fees for collecting data and administering rebates, among other service fees.

Manufacturer DIR (direct and indirect reimbursements) is a general term describing payments from manufacturer to PBM. Includes rebates and administrative fees.

Manufacturer rebates. Direct payments from manufacturer to PBM, often as a result of negotiations for drug formulary placement.

Margin percentage. Gross margin divided by the net sales price.

NADAC. The average price that a retail pharmacy pays for a drug.

National Drug Code (NDC). 11-digit unique numeric identifier for a given drug.

Pass-through contracts. A PBM contract structure in which the PBM passes the pharmacy reimbursement fee to the health plan.

Pharmacy DIR. Describes retroactive fees that PBMs charge pharmacies. Pharmacy DIR is often based on pharmacy performance metrics or quality metrics determined by the PBM.

Pharmacy reimbursement fee. The fee that a pharmacy charges PBMs for purchasing and dispensing drugs.

Spread pricing. A PBM pricing model in which the PBM charges the third-party payer more than it reimburses the pharmacy and collects the difference.

State Drug Utilization Data (SDUD) price. The amount that state Medicaid agencies reimburse PBMs for a drug.

Third-party payer administration fees. Fees that PBMs charge third-party payers/health plans. These are often in the form of a fixed fee on a per-prescription basis.

Wholesale Acquisition Cost (WAC). The manufacturer's "list price" of a drug, i.e., the price that manufacturers charge before any price concessions.

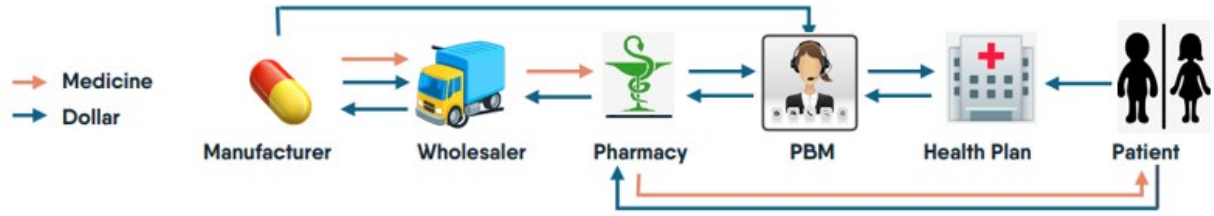
Wholesaler discount. Discount that wholesalers receive from the manufacturer on the WAC.

1 INTRODUCTION

Prescription drug spending in the United States totaled $603 billion in 2021, comprising 18 percent of total national healthcare spending (Parasrampuria & Murphy, 2022). From July 1, 2021, to June 30, 2022, the prices of 1,216 drugs increased at rates higher than inflation during that period (Bosworth, et al., 2022). Eight in 10 Americans say that the costs of prescription drugs are unreasonable, and 26 percent say they have trouble affording their drugs (Kirzinger, et al., 2023). Further, the increasing levels of pharmaceutical expenditures drove per capita annual spending on medications in the United States to $1,432 in 2021 (Organisation for Economic Cooperation and Development, 2023). This was 37 percent greater than Germany's 2021 expenditure ($1,042), 66 percent greater than Canada's ($865), and 78 percent more than Switzerland's ($803), the next three highest spending countries per capita in 2021 (Organisation for Economic Cooperation and Development, 2023).

Effective policies that broaden access to drugs and reduce drug costs while encouraging innovation must be predicated on identifying the actors and mechanisms that raise drug costs without increasing their value to the end user. However, assessing the margins of entities throughout the pharmaceutical supply chain is complicated by the lack of transparency surrounding the distribution of payments among these entities. The negotiations between pharmacy benefit managers (PBMs), pharmacies, health plans, wholesalers, and manufacturers (Figure 1) remain private, and the terms of their contracts are confidential. For example, health plans may know how much they reimburse for a drug, but they often do not know the actual net cost of that drug, which is dependent on the size of the rebates and discounts the PBM negotiates with the manufacturer, ostensibly on behalf of the payer (Feldman, 2020).

Figure 1. Schematic of Medicine and Dollar Flows Among Supply Chain Principals



Source: PBM Accountability Project (undated)
Note: This simplified graphic does not represent every relationship and intermediary in the supply chain or marketplace.

Thus, to develop effective and fair policies that reduce drug prices, it is important to understand at which points along the pharmaceutical supply chain are "excess profits" generated.[7] Gaining a better understanding of the magnitude of these intermediaries' margins is pertinent to broadening access and affordability to prescription drugs and lowering national

[7] The Oxford Dictionary of Economics defines "excess profits" as "Profits which are above the level necessary to retain an entrepreneur in the current line of business. Opinions that profits are excessive are usually based on comparisons, either with the rate of return on capital obtainable in other industries with a comparable degree of risk, or with the past profits of the same company" (Black, et al., 2009).

expenditures on prescription drugs, which have reached new heights over the past decade (Rome, et al., 2022).

Previous literature has examined the complexities of the pharmaceutical supply chain, evaluated policy options intended to lower drug expenditures, and developed empirical models to explain how payments flow through the system (Dusetzina, et al., 2017; Feng & Maini, 2023). In addition to limiting manufacturers' price increases to inflation and enabling the government to negotiate prices for some of the highest expenditure drugs, proposed policy interventions have included: 100 percent point-of-sale rebating (i.e., giving rebates to consumers); pricing and rebate transparency; giving PBMs fiduciary duties to health plans and/or beneficiaries; prohibiting PBMs from patient steering and clawing back reimbursements given to pharmacies; regulation of DIR; registration of PBMs with state pharmacy boards; oversight of formulary development; and requiring periodic audits of PBMs.[8] That said, Meador (2011) notes the following when discussing the National Community Pharmacists Association's Pharmacy Benefit Manager Licensure and Solvency Protection Act (NCPA Act):

> *The ideal reforms would combine the strict pricing and disclosure requirements of the NCPA Act with clear standards that explicitly and directly prohibit the anti-competitive business practices frequently complained of and stronger mechanisms to pass on savings to the consumer. It should be noted that there is a caveat to this arrangement: even with reform in the PBM industry, drug prices could remain high because of manufacturers. (Meador, 2011)*

1.1 Study Objectives

Using several public and proprietary data sources, this study estimates the margins of three intermediaries within the retail pharmaceutical drug supply chain[9]—wholesalers, pharmacies, and PBMs—for prescription drugs, defined at the 11-digit National Drug Code (NDC) level. By constructing a dataset that follows drugs from manufacturer to patient, we are able to analyze how certain drug characteristics impact the margins of these intermediaries. We consulted with two subject matter experts to confirm the validity of our approach, with the usual caveats regarding the possibility and potential impacts of data insufficiencies.

The analysis centers on prescription drugs sold through the retail channel (i.e., independent pharmacies, chain stores, and food stores, except mail-order pharmacies).[10] These retail drugs are covered under Medicare Part D plans, Medicaid, as well as by private insurers;

[8] Further discussion of these proposed policy interventions can be found in Appendix A: Compendium of State Statutes Addressing PBM Issues.

[9] The retail pharmaceutical drug supply chain refers to the supply chain of those prescription drugs obtained at independent pharmacies (excluding mail pharmacies), chain stores, and food stores by patients, who then self-administer the drug. This is distinct from drugs administered during hospitalizations or drugs administered by healthcare professionals in outpatient settings.

[10] Over-the-counter (OTC) medications were excluded because they are not handled by the same supply chain intermediaries since they generally are not covered by insurance.

hence, they represent the confluence of private and public interests in the prescription drug marketplace across all levels of the supply chain. Among federally sponsored prescription drug programs, drugs in the Medicare Part D market most closely resemble the much larger retail private prescription drug insurance market. In 2021, federal spending on Part D was $96 billion (Congressional Budget Office, 2021), or 21.4 percent of the $421 billion expended nationally for retail drugs (Parasrampuria & Murphy, 2022). Medicaid net spending for outpatient drugs in 2021 was $38.1 billion or 9.0 percent (Park, 2022). We separately assess brand and generic drugs because the cost and utilization of these types of drugs are different. Generics and biosimilars accounted for 91 percent of the prescriptions filled in the United States in 2021 but represented just 18.2 percent of prescription expenditures (Association for Accessible Medicines, 2022).

Our study aims to answer the following research questions:

1. How are total expenditures on retail drugs distributed throughout the supply chain across manufacturers, wholesalers, pharmacies, and PBMs?

2. What are the margins of wholesalers, pharmacies, and PBMs on retail drugs?

3. Do margins vary:
   a. Between generic and brand name drugs?
   b. Whether a drug treats acute or chronic conditions?
   c. Whether a drug is a biologic?
   d. How long a drug has been marketed (i.e., “drug tenure”)?

4. What has been the trend in intermediary margins between 2020-2022 for brand name drugs?

2 BACKGROUND

This study estimates the margins of retail drug supply chain intermediaries—wholesalers, pharmacies, and PBMs. The methodology we used for estimating supply chain margins requires data on acquisition costs of and revenues from goods sold. As described below in Section 3, margins of wholesalers, pharmacies, and PBMs are based primarily on price data available from several public and proprietary databases. We were able to estimate both acquisition costs and sales revenues on a per-drug basis by tracking data for individual drugs. This study does not provide analyses of margins of drug manufacturers or third-party payers/insurers. For manufacturers, we could not obtain manufacturing costs per drug. For third-party payers, revenues are based on premiums, which could not be disaggregated at the per-drug level, even when publicly traded companies made overall premium revenues available.

Nevertheless, because both manufacturers and third-party payers have drawn much attention due to ongoing concern regarding societal expenditures on prescription drugs and

patient access, we briefly discuss recent findings regarding the revenues and roles of these intermediaries in the retail drug supply chain.

2.1 Third-Party Payers/Healthcare Plans

In 2021, the top 10 health insurance plan companies—commonly called third-party payers—wrote $561 billion in direct premiums, or 61.7 percent of the industry total of $910.5 billion (Federal Insurance Office, 2022). The top five companies accounted for 48 percent of the total direct premiums written.[11] Third-party payers provide prescription drug insurance to anyone with a prescription drug plan. This includes most Medicare beneficiaries—commonly referred to as Part D insurance—and Medicaid beneficiaries, as well as individuals with private insurance obtained through an employer, the individual marketplace, or another pooled risk group. Prescription drug insurers have a formulary of drugs that are covered for their beneficiaries. Insurers and PBMs can negotiate rebates from drug manufacturers, which are shared with the payer or plan sponsor, in exchange for better formulary placement and benefit management. Estimating the margins of third-party payers is problematic because most insurers provide prescription coverage as part of an overall health insurance package (which includes inpatient and outpatient health care services), and it is difficult to separate the costs and revenues associated with prescription drug insurance from those of overall health insurance. Sood et al. (2017), estimated gross and net margins for insurers at 22 percent and 3 percent, respectively. However, their study, as mentioned above, relied heavily on the financial filings of publicly-traded companies, and for insurance companies, Sood et al. (2017) were unable to separate margins associated with medical claims from margins associated with pharmacy claims, since the two are combined in health insurers' financial results.

2.2 Pharmacy Benefit Managers

PBMs negotiate with manufacturers on behalf of insurers to secure better deals on covered drugs, usually in the form of rebates from manufacturers. They also negotiate with pharmacies to set the amount that an insurance company will reimburse a pharmacy for drugs (Commonwealth Fund, 2019). In addition to rebate and reimbursement negotiations, PBMs' revenues result from providing such services as account management, claims processing, eligibility management, formulary management, mail-order pharmacy, member services, plan implementation and changes, and utilization management (Burns, 2022). The three largest PBMs, CVS Health/ Caremark, Cigna/ Evernorth/ Express Scripts, and UnitedHealth/ OptumRx, account for 79 percent of the market for PBM services; the six largest occupy 96 percent of the market (Table 1). The remaining 4 percent of the PBM market is served by 60 smaller firms.

Table 1. Market Shares of the Six Largest PBMs in the United States

PBM	Market Share
CVS Health / Caremark	33%

[11] The top five health insurance companies by direct premiums written in 2021 were UnitedHealth Group, Elevance Health (Anthem), Centene Corp., Humana, and Health Care Services Corp. (HCSC). CVS Health was sixth (Federal Insurance Office, 2022).

PBM	Market Share
Cigna / Evernorth / Express Scripts	24%
UnitedHealth / OptumRx	22%
Humana Pharmacy Solutions	8%
Prime Therapeutics / Magellan Rx	5%
MedImpact Healthcare Systems	4%

Source: Fein (2023)

PBMs have been criticized for keeping a percentage of manufacturer rebates and for "spread pricing," in which PBMs charge insurance companies more than they reimburse pharmacies for a drug and keep the difference. Rebates are used almost exclusively with brand drugs[12] with marketed competitors and thus partly counteract high list prices while serving as an important PBM revenue source. With generic drugs, rebates are typically not offered by manufacturers because generics' list prices are substantially lower, so PBMs earn revenue through spread pricing. The difference between the payment the PBM receives from the insurer and the payment it makes to the pharmacy is referred to as the "spread." The dollar amounts of rebates are confidential, as are PBMs' price spreads. As the middleman, PBMs have a large influence on drug prices, but their pricing is particularly opaque (Stomberg, 2021).

Overall, PBM margins at the company level have been estimated at between 3 and 6 percent by various researchers in aggregate; however, there is significant variation at the drug level. According to an analysis by Metcalf and Weinberg (2017), PBMs can minimize their perceived margin percentages by counting as revenue the full value of all the drugs that they contract for on behalf of their clients, rather than the final price after accounting for rebates and discounts. Though this is an acceptable accounting practice, it artificially inflates the denominator of the fraction representing PBMs' operating margins (Metcalf & Weinberg, 2017).[13] Without these artificially inflated revenue figures, the operating margins of Express Scripts and CVS more than double to 15 and 10 percent, respectively (Metcalf & Weinberg, 2017).

Manufacturer rebates have been one method PBMs have used to increase their margins, though there is evidence that this practice is diminishing (United States Government Accountability Office, 2019). PBMs say that the rebates they negotiate from manufacturers benefit plan sponsors and customers, and that higher drug costs are due to manufacturer price

[12] Data in SSR Health suggest that biosimilars provide rebates to PBMs. Biosimilars are biologic products that, like generic drugs, are approved based on comparison with a reference listed drug (aka originator biologic). Unlike traditional small molecule generic drugs, biosimilars are given brand names and may undergo large-scale clinical trials.

[13] The authors gave an explanatory example of the distinction between *agents* facilitating a transaction and *principals* participating in a transaction: "When Expedia books a $100 hotel room, it typically counts as revenue only the sum that it pockets through commissions and other fees and calculates its profit margins from that. Walgreens and other retailers, by contrast, account for the full value of many of the goods they sell in their top-line figures because, among other factors, they take control of the goods before selling them. For the most part, the big PBMs treat themselves as principals when they tally their sales – which means they book the entire value of drug transactions as revenue" similar to Walgreens and other retailers (Metcalf & Weinberg, 2017).

increases (Eyles, 2022). Nevertheless, these rebates are at times paid by manufacturers to the PBM as a *quid pro quo* for an advantage, such as inclusion on a formulary tier that advantages the manufacturer over competitors (Shepherd, 2019; Cole, et al., 2019; Seeley & Kesselheim, 2019). Manufacturers are incentivized to provide these rebates because higher formulary placement can lower beneficiaries' copays, which in turn, can drive up their drug's utilization. In commercial plans, for example, out-of-pocket costs are lower because they are often based on the formulary tier rather than the plan's negotiated drug price.[14] In Medicare Part D out-of-pocket costs are a percent of the list price of a drug. A portion of the manufacturer rebate is retained by the PBM, and the remainder is passed along to the plan.

PBMs margins are also derived from administrative fees, which have traditionally been payments the insurance plan makes to the PBM (though some PBMs are also charging fees to manufacturers, possibly to make up for diminishing rebates). PBMs often charge a fixed administrative fee per prescription associated with a pass-through contract. Pass-through contracts were designed as an alternative to traditional PBM contracts and were intended, in part, to reduce spread pricing. In pass-through contracts, the third-party payer pays the PBM the same price for drugs as the PBM reimburses the pharmacy, thereby eliminating any spread between the PBM's sale and acquisition costs. In some cases, however, pass-through contracts can lead to higher prices for the third-party payer. For example, the PBM may voluntarily pay pharmacies higher prices on pass-through claims (leading to higher prices for the third-party payer), thereby allowing the PBM to pay lower prices to the pharmacy on its traditional contracts. This practice may allow the PBM to increase its price spread on traditional contracts while still collecting administrative fees on pass-through contracts (RxBenefits, 2020). In general, PBMs' market dominance can provide a level of flexibility that allows them to generate margins despite attempts to reduce spending, like pass-through contracts.

The research mentioned throughout this section highlight the fact that complexities within the pharmaceutical supply chain have led to anomalous outcomes, such as manufacturers losing revenue despite raising list prices, and PBMs gaining revenue by incentivizing consumers to choose a more expensive brand drug over a generic. A detailed catalogue of the many contractual mechanisms that some PBMs have been using—or been accused by critics of using—is beyond the scope of this study. That said, PBMs have been retaining some of the rebates that they negotiate from manufacturers (rebates that could be passed on entirely to insurers or customers), protecting the opacity of their contract terms, engaging in spread pricing, patient steering, and other similar practices, and have been successfully sued by states and pharmacy networks for a variety of overcharges and anti-competitive actions (Meador, 2011; Feldman, 2020; Kakani, et al., 2020; Trish, et al., 2022; Myshko, 2023). Their influence over drug prices and their position of influence with regard to pharmacies, health plans, and manufacturers, have made PBMs a target of federal and state

[14] For this reason, a more expensive brand drug with high formulary placement may receive more utilization than a drug that costs the plan less but has lower formulary placement.

legislators seeking to ameliorate the financial burden on society of high prescription drug expenditures.

Some state governments have taken the lead on regulating the PBMs, especially after the 2020 Supreme Court ruling in Rutledge v. Pharmaceutical Care Management Association (PCMA) confirmed that states have the right to regulate PBMs (Fuse-Brown & McCuskey, 2020). So far in 2023, 15 states have enacted 18 laws, and in 2022 alone, 12 states enacted 19 pieces of legislation targeted at PBMs (National Academy for State Health Policy, 2023; Myshko, 2023). These laws are focused on eliminating gag clauses, requiring price reporting, and requiring PBMs to register with the state, among other reforms (see Appendix A for a compendium of state-level PBM regulations).

It is possible that the increasing attention that PBMs have experienced in recent years may have influenced some to modify their revenue enhancement strategies away from spread pricing and rebate retention by becoming vertically integrated with health insurers and/or pharmacies. The three largest PBMs have merged with or been acquired by health insurers—Express Scripts by Cigna in 2018 and CVS Caremark with Aetna in 2017; Optum Health evolved from United Health's 2005 acquisition of the regional insurer PacifiCare, which had an in-house PBM. Guardado (2023) analyzed the status of vertical integration of PBMs and commercial drug insurers at the national, state, and metropolitan statistical area (MSA) levels. Guardado (2023) found that, "Nationally, 70 percent of drug lives were covered by a vertically integrated insurer in 2021." At the state level, integrated PBM/insurer companies covered a total of 63 percent of covered lives, although the figures ranged from six percent in South Dakota to 97 percent in Utah. Similarly, across 383 MSAs, 63 percent of covered lives were served by an integrated PBM/insurance entity. This vertical integration provides the insurance division of the merged entity with more direct oversight of PBM functions that affect insurance revenues (e.g., rebate pass throughs; "utilization management strategies" such as prior approvals and step therapies). Integrated PBM/insurance entities that provide PBM services to outside insurers—four of the top 10 vertically integrated PBMs service other insurers in addition to their own—may have potential competitive advantages over the 30 percent of non-integrated PBMs (Guardado, 2023).[15] Vertical integration also enables insurers to avoid potentially contentious negotiations and disputes with PBMs, such as the years-long dispute between ExpressScripts and Anthem. Although Anthem had originally sued ExpressScripts for overbilling, ultimately, ExpressScripts won a $15 billion judgment from Anthem, *Anthem, Inc. v. Express Scripts, Inc.*, 16-cv-2048 (ER) (S.D.N.Y. Mar. 8, 2023).

Recently, Congress has proposed several bipartisan bills aimed at regulating how PBMs function within the retail drug supply chain. These include Senate bill 127, the Pharmacy Benefit Manager Transparency Act of 2023, which aimed to ban certain PBM tactics, such as spread pricing and clawback fees, and the Modernizing and Ensuring PBM Accountability Act (MEPA),

[15] Guardado (2023) states: "An important question is whether non-vertically integrated insurers face higher PBM prices, which could then translate to higher premiums."

which sought to delink PBM income from prescription drug prices, required enhanced reporting and PBM audits among other measures, though these proposals were not enacted.

Another source of PBM revenue is DIR fees, which the PBM assesses to the pharmacy. These fees may arise, for example, if PBM reimbursements exceed negotiated contract rates. DIR also can include penalties based on pharmacy metrics like generic dispense rates, as well as network participation fees that that PBM charges the pharmacy.

2.3 Pharmacies

There are a total of 61,715 pharmacies in the United States of which 37,954 (61.5 percent) are chain stores, 23,521 (38.1 percent) are regional franchises or independently owned pharmacies, and 240 (0.4 percent) are government pharmacies based on a Geographic Information System (GIS) analysis of consumer access to pharmacies by Berenbrok, et al. (2022). Pharmacies typically purchase medications from wholesalers and derive their margins from reimbursements from PBMs. The reimbursements PBMs provide pharmacies often are based on an ingredient cost plus a fixed dispensing fee that the pharmacy charges for each filled prescription (for example, see, (Centers for Medicare & Medicaid Services, 2022)). Overall, U.S. pharmacy prescription sales were reported to provide a gross margin of 21.0 percent, net of rebates, in 2018 (Fein, 2019). Generic drugs return a higher margin percentage to pharmacies than brands, but because generics are so much cheaper than brands, the value of these margins are still lower than for brands on a per drug basis. In 2018, the generic dispensing rate for all pharmacies was 85.6 percent. The comparative margins for brand versus generics in 2012 were estimated by Drug Channels as 9.6 percent and 51.0 percent, respectively (Fein, 2017).

2.4 Wholesalers

Wholesalers acquire drugs from manufacturers at the wholesale acquisition cost (WAC, also known as the list price) from which is subtracted a variety of fees and discounts, such as handling fees or ancillary “prompt payment” discounts for submitting early payment (Stomberg, 2021). The three largest pharmaceutical wholesalers are McKesson, AmeriSourceBergen, and Cardinal Health. Combined, these companies account for approximately 90 percent of all wholesale drug activity in the U.S. (Seeley, 2022). A recent examination of wholesalers’ role in the supply chain by Seeley (2022) stated, “[t]he difference between what wholesalers pay for brand-name drugs and what they charge pharmacies can represent a major source of revenue for wholesalers, although it remains a very small fraction of overall brand-name drug prices and spending.” However, “[i]n most branded-drug markets, wholesalers act as price-takers, often selling at the same discounted WAC that they buy at, such as WAC minus 5 percent” (Seeley, 2022). Despite being price takers and having low average margin percentages, the high price of brand drugs still can generate substantial revenues for wholesalers.

Wholesalers earn additional revenues from handling generic drugs. Even though the prices of most generic drugs are significantly lower than brands, generic drugs comprise 90 percent of all retail prescriptions filled in the United States. Seeley (2022) estimated the range of wholesaler markups of generic drugs between 10 percent and 15 percent, which would generally equate to roughly $5-10 for a typical package (assuming a per-package cost to the wholesaler of roughly $60).

Larger wholesalers also derive revenue through horizontal and vertical expansion, which allows them to provide other services, such as: negotiating improved rebate sharing from PBMs on behalf of independent pharmacies or pharmacy chains; offering proprietary drug distribution data to other supply chain intermediaries; drug repackaging; supplying medical devices, other medical products, and information technology (IT) platforms; and, increasingly, distributing specialty drugs.

2.5 Manufacturers

Generally, drug manufacturers conduct the research and development necessary to gain regulatory approval and bring new drugs to market. They also incur costs to acquire raw materials and to manufacture the drug. Manufacturers establish list prices for their products and have attracted public and regulatory attention due to rising drug prices and consumer expenditures.[16] Although manufacturers receive a plurality of drug expenditures, their operating expenses and risk levels are likely to far exceed those of other intermediaries of the pharmaceutical supply chain. Sood et al. (2021) calculated the adjusted "excess returns" at the firm level from 2013 through 2018 for 21 of the largest drug and biotech companies, as well as some of the largest wholesalers, and PBMs/insurers/pharmacies. They defined "excess returns" as follows: "A firm makes 'excess returns' if it generates more profits than expected given the risk associated with their investments…. Excess returns were therefore calculated as the difference between return on invested capital (ROIC) and the expected returns given risk, which is known as the weighted average cost of capital (WACC)." They considered the average excess returns of S&P 500 companies as a benchmark. Their results showed manufacturers having the lowest aggregate rate of adjusted excess returns (1.7 percent), which was less than half the rate of adjusted excess returns realized by S&P 500 companies (Table 2). This contrasted with

[16] Two major pieces of legislation—Hatch-Waxman and the 2009 Biologics Price Competition and Innovation Act (BPCIA)—were enacted mainly to foster competition in brand drug markets in response to the high prices set by manufacturers.

insurers/PBMs/retailers (i.e., retail pharmacies), who collectively had average excess returns of 5.9 percent, and wholesalers, who were at 8.1 percent (Sood, et al., 2021).[17, 18]

Table 2. Excess Returns in the Drug Supply Chain, 2013 – 2018

Supply Chain Segment	Average Unadjusted Excess Returns 2013 - 2018 [a]	Average Adjusted Excess Returns 2013 - 2018 [b]
Pharmaceutical Manufacturers	4.7%	1.7%
Biotech Manufacturers	13.1%	9.6%
Wholesalers	9.3%	8.1%
PBMs/Insurers/Retailers	5.9%	5.9%
S&P 500	4.2%	3.6%

Source: Sood, et al. (2021)
[a] R&D spending included as an expense.
[b] R&D spending treated as part of investment capital.

In an earlier study, Sood et al. (2017), also examined 2015 U.S. Securities and Exchange Commission (SEC) filings by the largest firms at various levels of the supply chain, as well as data from the National Average Drug Acquisition Cost (NADAC) database and the National Average Retail Price (NARP) dataset from the Centers for Medicare and Medicaid (CMS) for 2013. Table 3 presents the gross and net margins they calculated for five supply chain sectors. The authors then used these results to calculate the distribution of a hypothetical $100 expenditure at a retail pharmacy for prescription drugs in the United States (Table 4). They stated, "…roughly $17 goes to drug production costs, [an additional] $41 accrues to the manufacturers (a third of which is net profit), and $19 accrues to insurers ($3 of which is net profit). PBMs keep about $5 ($2 net profit), pharmacies keep $15 ($3 net profit), and wholesalers keep about $2 (30 cents net profit). Total net profit on a $100 expenditure is $23, of which $15 is captured by manufacturers and the remaining $8 by intermediaries." (Sood, et al., 2017) The authors noted that their study had several limitations, not the least of which is reliance on publicly filed financial statements that can be affected by numerous factors unrelated to financial activity within the supply chain.[19]

Our current study was designed in part to avoid many of the limitations noted by Sood et al. (2017), by relying on sales data at the drug level, which, while they may have occasional

[17] The authors attributed the high rate of adjusted excess returns among biotech companies (9.6 percent) to the approval and marketing of several blockbuster biologics.
[18] Sood et al. (2021) noted several limitations to this study, including: (1) reliance on data from financial statements, "which can be misreported or manipulated through standard accounting methods"; (2) inability to disaggregate excess returns of PBMs from insurers and pharmacies/retailers due to vertical integration of many of the larger PBMs with retail drug chains and insurers; (3) the excess returns of pharmaceutical firms include returns on all investments, not just pharma revenues; and (4) reporting of rebates "may lag sales and therefore cause revenues to be overstated for manufacturers or understated for insurers/PBMs/retailers."
[19] "Key data are not always publicly available, and even the data presented in financial statements may be reported in inconsistent and opaque ways. Some of the largest players in certain sectors are privately held and make no financial data public. Thus, all our estimates are to some extent incomplete and inexact" (Sood, et al., 2017).

reporting errors or omissions, do not suffer from the same disadvantages as firm-level financial data.

Table 3. Average Gross and Net Margins for Each Sector, Individual Firm Margins Weighted by U.S. Sales (Sood et al., 2017)

Sector	All Drugs		Brand Only		Generic Only	
	Gross Margin	Net Margin	Gross Margin	Net Margin	Gross Margin	Net Margin
Manufacturer	71.1%	26.3%	76.3%	28.1%	49.8%	18.2%
Wholesaler	3.7%	0.5%	1.0%	NA	18.5%	NA
Insurer	22.2%	3.0%	22.2%	NA	22.2%	NA
PBM	6.3%	2.3%	2.0%	NA	8.0%	NA
Pharmacy	2.1%	4.0%	3.5%	NA	42.7%	NA

Source: Sood, et al. (2017)
NA = Not available

Table 4. Distribution of $100 Expenditure Entering the Supply Chain

Sector	Cost of Production	Retained Earnings	Net Profit
Manufacturer	$17	$41	$15
Wholesaler	N/A	$2	$0.30
Insurer	N/A	$19	$3
PBM	N/A	$5	$2
Pharmacy	N/A	$15	$3
Total	$17	$82	$23.30

Source: Sood, et al. (2017). N/A indicates not applicable.

In a similar vein, Van Nuys et al. (2021) focused on the distribution of net expenditures for a single class of products, insulin, the cost of and access to which had become a national and global public health concern (Beran, et al., 2018) (Office of the Assistant Secretary for Planning and Evaluation, U.S. Department of Health & Human Services, 2022). Van Nuys et al. (2021) found that "[b]etween 2014 and 2018, mean list prices of 32 insulin products increased by 40.1 percent (from $19.6 to $27.5), while mean net prices received by manufacturers decreased by 30.8 percent (from $10.5 to $7.3). … [T]he share of a hypothetical $100 insulin expenditure accruing to manufacturers decreased by 33.0 percent (from $69.7 to $46.7) and the share accruing to health plans decreased by 24.7 percent (from $13.8 to $10.4). The share of insulin expenditures retained by [PBMs] increased by 154.6 percent (from $5.6 to $14.4), the share retained by pharmacies increased by 228.8 percent (from $6.2 to $20.4), and the share retained by wholesalers increased by 74.7 percent (from $4.6 to $8.1)" (Van Nuys, et al., 2021). These results of Van Nuys et al. (2021) are summarized in Table 5.

Table 5. Distribution of $100 Expended on 32 Insulin Products, 2014 and 2018

Sector	2014	2018	Δ	Percent Δ
Manufacturer	$69.71	$46.73	-$22.98	-33.0%
Wholesaler	$4.63	$8.09	+$3.46	+74.7%
Insurer	$13.82	$10.40	-$3.42	-24.7%
PBM	$5.64	$14.36	+$8.72	+154.6%
Pharmacy	$6.21	$20.42	+$14.21	+228.8%

Sector	2014	2018	Δ	Percent Δ
Mean List Price	**$19.60**	**$27.45**	**+$7.85**	**+40.1%**
Mean Net Price to Manufacturers	**$10.53**	**$7.29**	**-$3.24**	**-30.8%**

Source: Van Nuys, et al. (2021)

The authors noted one limitation to their study was a "lack [of] complete time-series data on transaction prices at each step of the distribution system…" and that "therefore the split of excess earnings among intermediaries may be imprecise." They stated that "our results are best interpreted as suggesting trends in insulin markets generally rather than as providing a precise picture of a particular insulin market." (Van Nuys, et al., 2021)

These studies by Sood et al. (2017; 2021), and Van Nuys et al. (2021) demonstrate important trends and anomalies in the drug supply chain. They represent three distinct assessments: (1) an attempt to use financial data from a sample of individual firms in each sector, coupled with sales data, to calculate aggregated gross and net margins in each supply chain sector (Sood, et al., 2017); (2) an attempt to derive average risk-adjusted "excess returns" within each supply chain sector (Sood, et al., 2021); and (3) focusing on one high profile drug market (insulin) to reveal price increases over five years and how distribution of expenditures for insulin products shifted across supply chain sectors during that time (Van Nuys, et al., 2021).

This study did not examine margins for manufacturers because data on manufacturers' acquisition costs for ingredients were not available at the drug level, and there may be debate about the extent to which manufacturers' margins should account for the cost of drug development. However, this study contributes new information by estimating the proportion of expenditures manufacturers retain, the net prices at which manufacturers sell drugs to wholesalers, and the magnitude of rebates or other DIR paid by manufacturers and pharmacies to PBMs.

3 METHODOLOGY

This section provides an overview of our methodology and presents the data sources. For an expanded discussion of these topics, see Appendix B: Detailed Methodology.

3.1 Data and Definitions

Table 6 shows payments made among the intermediaries of the retail drug supply chain.

Table 6. Types of Payments in the Retail Drug Supply Chain

Payment Type	Description
Wholesale acquisition cost	Manufacturer's list price to wholesalers or other bulk purchasers.
Wholesaler net acquisition cost	Actual price paid, net of fees and discounts, by wholesaler to manufacturer (is typically less than the listed WAC).
National average drug acquisition cost	National estimate of the net price paid by pharmacies for a drug.
State Drug Utilization Data price	The average price paid by state Medicaid agencies for a drug, averaged across all states and all plan types (including Managed Care Organizations

Payment Type	Description
	and Fee-for-Service). Used to estimate pre-rebate reimbursement rates to PBMs by all payers.
Copay	An out-of-pocket payment made by the beneficiary to the pharmacy for a prescription drug, which represents the beneficiary's shared portion of the cost.
Pharmacy direct and indirect remuneration	Payments made by the pharmacy to the PBM, including retrospective price concessions to "true up" the PBM's actual reimbursements to the pharmacy with contract rates, penalties assessed by the PBM based on the pharmacy's performance metrics (e.g., generic dispense rates), and network participation fees that the PBM charges to the pharmacy.
Manufacturer rebate	A payment made by the manufacturer to the PBM based on a drug's utilization. Some of this rebate is retained by the PBM, and the rest is passed on to the manufacturer.
Manufacturer administrative fees	Fees paid by the manufacturer to the PBM (other than the rebate).
Third party payer administrative fees	Fees paid by third-party payers to the PBM per prescription on pass-through contracts.
Manufacturer DIR	A broad term that captures all payments from the manufacturer to the PBM, including both rebates and administrative fees.

We used the following datasets for this analysis. For all datasets, we used a period spanning the beginning of 2020 to the end of 2022; these represented the most recent data available at the time of our analysis.

- **National Average Drug Acquisition Cost** is a price database published by CMS based on the Retail Drug Survey, a national survey of all retail community pharmacies. The NADAC is the average price at which sampled pharmacies purchase a drug from manufacturers or wholesalers, including some discounts. We used the NADAC to estimate wholesalers' net sales price, which we assume is equal to pharmacies net acquisition cost. We also used the database of NADACs to define the universe of retail drugs. This may not capture some drugs only sold through specialty pharmacies or pharmacies that dispense prescriptions primarily through the mail, for which pharmacies' net acquisition costs are not available.

- **IQVIA National Sales Perspective (NSP)** is a nationally representative database of U.S. drug supply volume reported monthly. IQVIA NSP covers nearly the full universe of drug utilization across all channels (retail, non-retail, and mail), although we focus exclusively on the retail channel. For this analysis, we filtered IQVIA NSP to include only drugs that appear in the NADAC dataset. Then, because third-party payers may reimburse these retail drugs at different rates when dispensed in non-retail channels, we further subset the retail drugs to those with at least 80 percent sales in retail channels (excluding mail), according to IQVIA NSP. We used NSP's reported value of the WAC, which is the manufacturer's list price. In cases where a single NDC had multiple WACs in retail channels, we used the WAC for the original manufacturer package sold. From the WAC, we calculated wholesalers' net acquisition cost (which is generally less than the WAC) as

well as rebates PBMs collect from manufacturers.[20] IQVIA NSP also reports total mass (in kg) or activity (in IU) sold of the active pharmaceutical ingredient (API), as well as the number of extended units sold (i.e., smallest amount of the drug). We used these extended units to compute weights and to estimate total utilization of the sampled retail drugs across all markets (Medicaid, Medicare Part D, and commercial plans). Thus, the analysis is based on a nationally representative sample of all retail sales for prescription drugs in the United States.

- **IQVIA PayerTrak** is a database of prescription drug utilization in the United States by payer type and provides monthly national projections of the number of prescriptions filled and average copay by payer. We used these data to calculate average copays across all states and payer types for each drug in our sample, weighted by projected total prescriptions (TRx).[21] We matched PayerTrak copays to drugs in our sample using the molecule (combined molecule), product name, formulation (form TLC3), strength, brand/generic status, USC3 designation, corporation, manufacturer, and product launch date.

- **SSR Health** is a database of brand drugs' gross (i.e., WAC) and net prices from the perspective of the drug manufacturer. SSR Health's database contains quarterly data on rebates and other price concessions since 2007, averaged across all payers. We used the gross-to-net discount rates, which show manufacturers' total price concessions as a fraction of the WAC by market (Medicaid, non-Medicaid, and overall). From these gross-to-net discount rates and from the estimated wholesaler discounts, we computed the estimated size of manufacturer rebates as a fraction of the WAC.

- **State Drug Utilization Data (SDUD)** is published by CMS and reports the number of units reimbursed and dollars spent on drugs by state Medicaid agencies, before adjusting for rebates paid into the Medicaid Drug Rebate Program. We used the SDUD prices (which do not account for rebates) to estimate pre-rebate reimbursements that third-party payers make to PBMs in all plans, including Medicaid, Part D Medicare, and commercial plans. In SDUD, drug sales include both the retail and non-retail channels, which cannot be disaggregated.

- **Federal Supply Service (FSS) Schedule Pharmaceutical Pricing File** is published by the U.S. Department of Veterans Affairs (VA) and provides data on maximum prices that pharmaceutical manufacturers may charge for direct federal purchases made by the Big Four federal agencies (i.e., the Department of Veterans Affairs, the Department of Defense, the Public Health Service, and the Coast Guard) (U.S. Department of Veterans

[20] As discussed in greater detail below, wholesalers' discount off the WAC was assumed to be nine percent for brand drugs. For generic drugs, wholesalers' discount off the WAC was estimated based on Federal Supply Service Schedule pricing data. See details below.

[21] When calculating the weighted average copay in IQVIA PayerTrak, we excluded cash payments, since copays only apply to payments made with insurance.

Affairs, Office of Procurement, Acquisition and Logistics, 2023).[22] A recent study used Big Four prices to estimate net prices of brand drugs (3 Axis Advisors, 2023). Since generic drugs have no PBM rebates, we used the Big Four prices to estimate wholesalers' net acquisition costs.[23]

- **The Affordable Care Act Federal Upper Limit (FUL)** is a pricing database published monthly by CMS to establish the maximum allowable Medicaid reimbursement for multiple source drugs. The FUL is calculated as either 175 percent of reported utilization-weighted average manufacturer prices (net of rebates) of pharmaceutically equivalent products available for purchase by retail pharmacies, or the NADAC price, whichever is greater. We used FUL to estimate the reimbursement from PBMs to pharmacies for generic drugs.

- **National Drug Code Directory** is a database maintained by the U.S. Food & Drug Administration (FDA) of drugs sold in the United States, which expresses NDCs in 10-digit formats. We converted these 10-digit NDCs into 11-digit NDCs by adding a leading 0 at the appropriate location (Maryland Department of Health Center for Immunization, n.d.) and merged the NDC Directory into the CMS and IQVIA NSP datasets to assist in converting package quantity into API quantity.

As stated above, we define a drug as being a unique 11-digit NDC, and our analytic dataset tracks all pricing and sales volume information at the drug level from Q1 2020 through Q4 2022. The datasets above were used to apply the inclusion criteria. We used the IQVIA NSP dataset to identify and exclude (a) non-prescription drugs and (b) drugs with no API utilization data, since the API unit was used as a stratifying variable when calculating weights (see Section 3.4).[24] We used the NADAC survey to identify retail drugs, which allowed us to exclude non-retail drugs from our study. Similarly, in IQVIA NSP, we excluded non-retail channels in order to quantify just the retail drug sales.[25] Drugs only sold through specialty pharmacies and mail-order drugs are also excluded from the universe and omitted from the study because their price information is less readily available, as they do not have a NADAC and are not included in CMS's pharmacy survey of retail drugs.

[22] The VA negotiates this price with manufacturers on behalf of all direct federal purchasers. The price is determined in part through negotiation but also through statute. For example, "[d]uring a multiyear contract period, an FSS may not increase faster than the net price charged to the most-favored commercial customer" (Congressional Budget Office, 2021).

[23] Without estimating these discounts, wholesalers would have negative margins on nearly every drug since the WAC is generally higher than the NADAC (which approximates wholesalers' net sale price). In our sample, the NADAC is 0.52 times the WAC for generic drugs and 0.96 times the WAC for brand drugs, based on median ratios of the NADAC per API unit to the WAC per API unit.

[24] Drugs with no API data were not represented in the sample, and thus their margins could not be estimated. They were also excluded from our estimate of the universe of prescription retail drug sales. This exclusion likely has a small effect, as these NDCs make up less than 1 percent of drugs in IQVIA NSP.

[25] The retail channel includes sales to independent pharmacies, chain stores, and food stores; mail pharmacy sales are classified separately in IQVIA NSP and were not included in retail sales for purposes of this study.

3.2 Theoretical Framework

In this section, we provide mathematical definitions of the monetary quantities that we estimated. In the Section 3.3, we describe how we estimated those quantities from the available data.

In general, we define the margin $Y_{x,i}^{(t)}$ for a given intermediary x on a drug i for time t as the difference between the total incoming payments for the drug during that time and the total outgoing payments. For wholesalers and pharmacies, the drug-level margin $Y_{x,i}^{(t)}$ is equal to the difference between the sales price (net of discounts and rebates) $S_{x,i}^{(t)}$ and the acquisition cost (net of discounts and rebates) $A_{x,i}^{(t)}$.

$$Y_{x,i}^{(t)} = S_{x,i}^{(t)} - A_{x,i}^{(t)} \tag{1}$$

For wholesalers, the margin is the difference between the net sales price (which we label $\text{NADAC}_i^{(t)}$) and the net acquisition cost. We estimated wholesalers' net acquisition cost as the WAC minus all wholesaler discounts $d_{\text{whole},i}^{(t)}$:[26]

$$Y_{\text{whole},i}^{(t)} = \text{NADAC}_i^{(t)} - \left(\text{WAC}_i^{(t)}\right)\left(1 - d_{\text{whole},i}^{(t)}\right) \tag{2}$$

For pharmacies, the net sales price is the beneficiary copay $C_i^{(t)}$ plus the net payment from the PBM $A_{\text{PBM},i}^{(t)}$. The net payment $A_{\text{PBM},i}^{(t)}$ is equal to the total payment from the PBM less the pharmacy's DIR $D_{\text{pharm},i}^{(t)}$.

$$Y_{\text{pharm},i}^{(t)} = \left(C_i^{(t)} + A_{\text{PBM},i}^{(t)}\right) - \text{NADAC}_i^{(t)} \tag{3}$$

$$\text{where } A_{\text{PBM},i}^{(t)} = \text{PBM reimbursement} - D_{\text{pharm},i}^{(t)}$$

For PBMs, the margin calculation is more complicated. The payment flows into the PBM include the SDUD payment from the third-party payer, the pharmacy DIR, $D_{\text{pharm},i}^{(t)}$, and the manufacturer DIR, $D_{\text{manf},i}^{(t)}$. The PBM retains a fraction, k_{pharm}, of the pharmacy DIR (which we assume to be 100 percent) and a fraction, k_{manf}, of the manufacturer DIR. These fractions are not indexed by drug i or time t because we assumed they were the same for all drugs and time periods as we did not have time-specific or drug-specific estimates. The payments made by the

[26] As discussed in greater detail below, for brand drugs, we assumed the wholesaler discount is 9 percent at all times t and for all NDCs i. For generic drugs, the wholesaler discount varies by year and NDC i and was estimated from VA FSS data.

PBM include the pharmacy reimbursement, the non-retained pharmacy DIR, and the non-retained manufacturer DIR. The margin is:

$$Y_{\text{PBM},i}^{(t)} = \text{SDUD}_i^{(t)} + k_{\text{manf}} D_{\text{manf},i}^{(t)} + k_{\text{pharm}} D_{\text{pharm},i}^{(t)} - (\text{PBM reimbursement})_i^{(t)} \quad (4)$$

In summary, we calculate wholesalers' and pharmacies' margins in dollars as the difference between the net sales price and the net acquisition cost. For PBMs, we calculated the dollar margin as this difference plus any retained manufacturer DIR, such as manufacturer rebates. We used net prices to account for the effects of discounts and rebates to better reflect intermediaries' actual financial experience. For PBMs, rebates from the manufacturer constitute an additional flow that is distinct from the sale to the payer and the acquisition from the pharmacy. The effect of this additional flow is to lower the PBM's net sales price (because a portion of the rebate is passed on to the third-party payer) and to increase the margin (because the remaining proportion is retained by the PBM). For all three parties, we define the margin percentage as the margin divided by the net sales price.

In addition to calculating margins, we also computed the total expenditures, which we define to be the total net payments made by the third-party payer and the beneficiary. We estimate the total expenditures $E^{(t)}$ at time t, for all drugs i, as the SDUD payment and beneficiary copay less the portion of the manufacturer rebate that the PBM passes on to the payer:

$$E^{(t)} = \sum_i \text{SDUD}_i^{(t)} + C_i^{(t)} - k_{\text{manf}} D_{\text{manf},i}^{(t)} \quad (5)$$

In addition to estimating each intermediary's margin percentage, we also estimated the fraction of total expenditures $E^{(t)}$ that each intermediary retains. This fraction is calculated using the intermediary's margin or the amount of payer/beneficiary spending that the supply chain entity retained:

$$\begin{matrix}\text{fraction of total expenditures} \\ \text{retained by intermediary } x \text{ at time } t\end{matrix} = \frac{\sum_i Y_{x,i}^{(t)}}{E^{(t)}} \quad (6)$$

While we are unable to calculate the margin percentages for manufacturers, we can estimate the portion of expenditures that manufacturers receive as the total expenditures minus the margins of all other intermediaries (see equation 7). However, this may not be directly comparable to the portion of expenditures that other intermediaries retain since we have not accounted for manufacturers' acquisition costs (which, unlike the acquisition costs of the other intermediaries, is not a price for the finished product and thus could include sourcing, production, or R&D costs, depending on definitions).

$$\begin{matrix}\text{amount of total expenditures} \\ \text{retained by manufacturer at time } t\end{matrix} = E^{(t)} - \sum_{x \neq \text{mfr}} \sum_{i} Y_{x,i}^{(t)} \quad (7)$$

In Section 3.3, we describe how these quantities were estimated. In Section 3.4, we describe how the drug-level margins $Y_{x,i}^{(t)}$ are scaled up using utilization and weights to estimate aggregate margins M_x, margin percentages $\%M_x$, and aggregate margin per package m_x for each intermediary when aggregating across all drugs in a given time period.

3.3 Modeled Payment Flows for Drugs Sold Through Retail Pharmacies

For each sampled prescription retail drug, we modeled the flows of payment through the pharmaceutical supply chain on a per-prescription basis (Figure 2). Table 7 shows the data sources and calculation methods for each payment flow. Broadly, the stylized model begins with the main financial input into the system, the reimbursement from the payer. This initial payment is passed along through the supply chain, and at each stage, the intermediary keeps a portion and uses the rest to reimburse the next stakeholder. We assume the sum of the dollar amounts retained by the intermediaries and manufacturers equals the total inputs into the system, thus forming a closed system among the entities shown in Figure 2. In addition to the payer's reimbursement, a secondary input is the beneficiary's copay, and together, these make up the total financial inputs. There are also upward payment flows in the diagram, which represent rebates that manufacturers pay to PBMs and pharmacy DIR. The total expenditures refer to the net spending, i.e., the total payments by the beneficiary and the payer minus the portion of the manufacturer rebate that is passed on to the payer.

3.3.1 Brand Drugs

The left part of Figure 2 presents our stylized model for the payment flows of a brand drug prescription. Below, we describe each of these flows through the supply chain, though not necessarily in the chronological order in which they are usually incurred or paid.

When a drug is dispensed, the third-party payer provides payment to the PBM (flow 1). The PBM may retain an administrative fee on a per-prescription basis (flow 2), and it passes the remainder to the pharmacy (flow 3) to cover ingredient costs and dispensing fees. The pharmacy also receives a copay from the beneficiary (flow 4). Pharmacies may pay one or more types of direct and indirect remuneration (DIR) fees to PBMs (flow 5), which can be assessed after the point of sale. The PBM may retain a portion of this DIR fee (flow 6) and pass the rest on to the third-party payer (flow 7), though our calculations assume that all of the pharmacy DIR is retained by the PBM. The pharmacy purchases the drug from the wholesaler at a net price that accounts for rebates and discounts (flow 8). The wholesaler purchases the drug from the manufacturer at a discounted rate off the WAC (flow 9). The manufacturer often passes some of the payment on to the PBM as a rebate and/or administrative fees (flow 10). A portion of this rebate is retained by the PBM (flow 11), and the rest is passed on to the third-party payer (flow 12).

We modeled the third-party payer reimbursement (flow 1) using the SDUD price calculated from published CMS data. When calculating the price based on the SDUD CMS data, we used both the Managed Care Organization (MCO) and Fee-for-Service (FFS) reimbursement amounts. We assumed the administrative fee (flow 2) is $2.00 per prescription when averaged across pass-through contracts (which may apply a typical fee of approximately $4.00 (RxBenefits, 2020) and traditional contracts (which would not have such a fee). In addition, our estimate of $2.00 is consistent with an average spread of 0.8 percent on brand drugs, as reported in a 2018 Ohio Auditor of State report (Yost, 2018). Based on our analysis, applying exactly 0.8 percent would have yielded an average per-prescription administrative fee of $2.45 for brand drugs in our sample.

Figure 2. Payment Flows per Prescription for a Drug Sold Through the Retail Channel

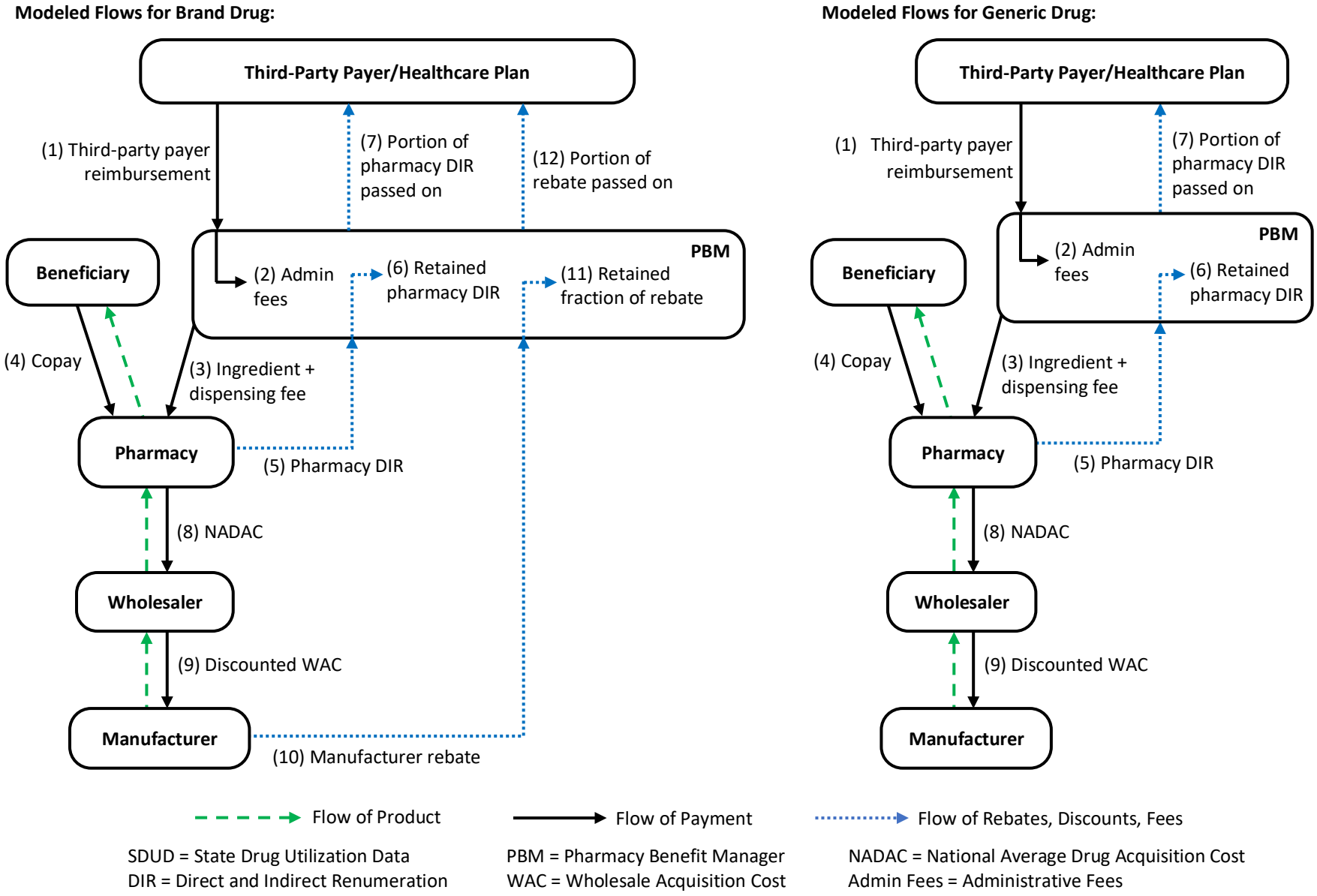


Table 7. Data Sources for Modeling Payment Flows

Payment Flow	Data Source(s) and Calculation Method	
	Brand Drugs	**Generic Drugs**
(1) Third-party payer reimbursement	Estimated from CMS State Drug Utilization Data (2020-2022)	Estimated from CMS State Drug Utilization Data (2020-2022)
(2) Administrative fees	Assumed to be $2 per package sold, based on market research and a 0.8% total price spread on brands reported by the Ohio Auditor of State (Yost, 2018)	Not estimated separately because this is incorporated into the calculation of (3) for generics
(3) Ingredient + dispensing fee	(1) – (2)	Estimated as the CMS FUL price
(4) Copay	Calculated from IQVIA PayerTrak (2020-2022), or average copay of $56 if data not available (Association for Accessible Medicines, 2022)	Calculated from IQVIA PayerTrak (2020-2022), or average copay of $6 if data not available (Association for Accessible Medicines, 2022)
(5) Pharmacy DIR	Estimated as 13.7% of (10) [a]	Assumed to equal 8% of the difference between the pharmacy's sales price and purchase price
(6) Retained pharmacy DIR	Assumed to be 100% of collected pharmacy DIR	Assumed to be 100% of collected pharmacy DIR
(7) Portion of pharmacy DIR passed on	(5) – (6)	(5) – (6)
(8) NADAC	Calculated from CMS NADAC survey (2020-2022)	Calculated from CMS NADAC survey (2020-2022)
(9) Discounted WAC	Assumed to be 9% of WAC listed in IQVIA NSP (United States Government Accountability Office, 2019)	Calculated from the WAC in IQVIA NSP (2020-2022), with a discount based on Big Four prices (2020-2022)
(10) Manufacturer rebate	Calculated from SSR Health (2020-2022) and WAC in IQVIA NSP (2020-2022) [b]	Assumed to be $0 for generic drugs
(11) Retained fraction of rebate	Assumed to be 0.4% based on report by U.S. Government Accountability Office (2019)	Assumed to be $0 for generic drugs
(12) Portion of rebate passed on to third-party payer	(10) – (11)	(10) – (11)

[a] We assumed the PBM retains 12.4% of the total collected DIR based on Iowa PBM Annual Reports (2021-2022). We modeled the total collected DIR as (manufacturer rebate) + (pharmacy DIR), and we modeled the retained amount as (0.4%)(manufacturer rebate) + (100%)(pharmacy DIR). Therefore: (12.4%)(manufacturer rebate + pharmacy DIR) = (0.4%)(manufacturer rebate) + (100%)(pharmacy DIR), which simplifies to (pharmacy DIR) = (13.7%)(manufacturer rebate). See Section 3.3.1 for more details.

[b] We have not modeled all price concessions made by the manufacturer, including, for example, 340B discounted prices and manufacturer payments made through copay assistance programs. This likely leads to an overestimate of the rebate and, consequently, pharmacy DIR.

We modeled the pharmacy reimbursement (flow 3) as the difference between the third-party payer reimbursement and the PBM's retained fee: (flow 3) = (flow 2) – (flow 1). The copay (flow 4) is estimated from IQVIA's PayerTrak dataset as a weighted average across all states and payers. In cases where copay information was not available in IQVIA PayerTrak or could not be

matched to a specific drug, we used an average copay of $56 for brand drugs and $6 for generic drugs, based on a 2022 report (Association for Accessible Medicines, 2022).[27]

We used NADAC to model the net price between the pharmacy and wholesaler (flow 8). CMS's Retail Price Survey only covers retail pharmacies and accounts for most rebates and discounts that the wholesaler provides to the pharmacy. We modeled the wholesaler's net acquisition cost (flow 9) by taking 91 percent of the WAC published in IQVIA NSP, which is equivalent to one minus the 9 percent discount rate estimated by researchers at the Urban Institute (Epstein, et al., 2023) based on a Government Accountability Office (GAO) study (2019) that compared average manufacturer prices (AMPs) to WACs for top-selling drugs.

We estimated manufacturer rebates (flow 10) from SSR Health data on mean gross-to-net discounts. We accounted for statutory rebates paid to the Medicaid Drug Rebate program, which generate no revenue for the PBM and are separate from the rebates manufacturers collect. We did not estimate the administrative fees that manufacturers pay PBMs. We assumed the PBM retains 0.4 percent of the manufacturer rebates (flow 11) based on a GAO study (2019), and that the remaining 99.6% of the manufacturer rebate is passed on to the third-party payer (flow 12). Calculations of manufacturer rebates are discussed in detail in Appendix B.4.

Our estimates of total pharmacy DIR that the PBM collects (flow 5) and retains (flow 6) are based on a number of inputs and assumptions. We modeled the total DIR retained, $\mathrm{DIR}_{\mathrm{ret}}$, as being made up of a retained portion $p_{\text{ret, pharm DIR}}$ of the collected pharmacy DIR $\mathrm{DIR}_{\mathrm{ph}}$ and a retained portion $p_{\text{ret, mfr reb}}$ of the manufacturer rebate $\mathrm{reb}_{\mathrm{mfr}}$:

$$\mathrm{DIR}_{\mathrm{ret}} = \left(p_{\text{ret, pharm DIR}}\right)\left(\mathrm{DIR}_{\mathrm{ph}}\right) + \left(p_{\text{ret, mfr reb}}\right)\left(\mathrm{reb}_{\mathrm{mnf}}\right) \tag{8}$$

The proportion of total DIR retained, $p_{\text{ret, tot DIR}}$, can be expressed as the ratio of total retained DIR to total collected DIR. We modeled the total collected DIR as the sum of manufacturer rebates and collected pharmacy DIR:

$$p_{\text{ret, tot DIR}} = \frac{\text{total DIR retained in \$}}{\text{total DIR collected in \$}} = \frac{\mathrm{DIR}_{\mathrm{ret}}}{\mathrm{reb}_{\mathrm{mfr}} + \mathrm{DIR}_{\mathrm{ph}}} \tag{9}$$

Combining equations 8 and 9 yields the expression below:

[27] Because PayerTrak does not contain 11-digit NDC, we used other characteristics (e.g., manufacturer, product name, molecule, formulation, launch date) to match PayerTrak records to NSP records. Among our sample, 82.1 percent of generic drugs (n=2,762) and 83.7 percent of brand drugs (n=297) successfully matched to PayerTrak. The average copays were only used for roughly 18 percent of the sample.

$$p_{\text{ret, tot DIR}} = \frac{(p_{\text{ret, pharm DIR}})(\text{DIR}_{\text{ph}}) + (p_{\text{ret, mfr reb}})(\text{reb}_{\text{mnf}})}{\text{reb}_{\text{mfr}} + \text{DIR}_{\text{ph}}} \quad (10)$$

$$\text{DIR}_{\text{ph}} = \frac{p_{\text{ret, tot DIR}} - p_{\text{ret, mfr reb}}}{p_{\text{ret, pharm DIR}} - p_{\text{ret, tot DIR}}} \text{reb}_{\text{mnf}} \quad (11)$$

We used equation 11 to estimate the collected pharmacy DIR (flow 5), DIR_{ph}. We assumed the retained pharmacy DIR (flow 6) equals the collected pharmacy DIR (flow 5), and that the portion of pharmacy DIR passed on to the third-party payer (flow 7) is zero. We estimated the quantities in equation 11 in the following way:

- $p_{\text{ret, tot DIR}}$: We estimated the proportion of total DIR retained to be 12.4 percent based on 2021 and 2022 PBM Annual Reports submitted to the state of Iowa, the two most recent years available at the time of the study (Iowa Insurance Division, 2020-2023).[28]
- $p_{\text{ret, pharm DIR}}$: We assumed the proportion of pharmacy DIR retained by the PBM is 100 percent.
- $p_{\text{ret, mfr reb}}$: We assumed the proportion of manufacturer rebate retained by the PBM is 0.4 percent for all plans, based on the GAO analysis of manufacturer rebates in Part D plans.
- reb_{mnf}: We calculated the manufacturer rebate for each brand drug using the drug's WAC, the SSR Health gross-to-net discount data, and the other modeled discounts the manufacturer gives to the supply chain (namely, the wholesaler discount).

Applying the above estimates to equation 11 yields the following. Both the pharmacy DIR and rebate are indexed by time t and drug i:

$$\text{DIR}_{\text{ph},i}^{(t)} = (0.137)\left(\text{reb}_{\text{mnf},i}^{(t)}\right) \quad (12)$$

This methodology is discussed in greater detail in Appendix B.5. Based on our scan of the literature, estimating the DIR associated with specific brand drugs is a novel aspect of our methodology. A limitation in our approach to estimating DIR is that it does not capture any pharmacy DIR that the PBM passes along to the payer. This does not impact our calculation of pharmacy margins, but this omission may lead to overestimates of PBM margins, though in general, we expect that the DIR passed along to the payer is small relative to the total DIR that

[28] We used 2022 and 2023 Annual Reports, which provide data from 2021 and 2022, respectively. While data were available for 2020, we did not use these reports because "several PBMs did not submit annual reports in that year because they either unintentionally applied to be certified as a PBM or requested to voluntarily surrender their Iowa PBM certificate" (Iowa Insurance Division, 2020-2023).

PBMs collect across all of their market segments (i.e., Medicare, Medicaid, and commercial markets).

3.3.2 Generic Drugs

For generic drugs, which are shown on the right side of Table 7, we computed margins largely using the same methodology as in Section 3.3.1. However, flows (10), (11), and (12) are omitted because drug manufacturers do not provide rebates to PBMs for generic drug products and SSR Health data, which we used to estimate net prices (including Medicaid rebates), was not available for generic drugs. Additionally, we used the FUL data to estimate PBMs' reimbursement rates to pharmacies (flow 3). As with brand drugs, we estimated the flows over the period from 2020 through 2022.

Because manufacturers do not provide rebates to the PBM for generics, pharmacy DIR was estimated differently. Fein (2019) reported that the net value of pharmacy DIR paid to Part D plans was approximately eight percent of pharmacies' gross profits in 2017. We used this as an estimate of the average pharmacy DIR assessed when a generic drug is dispensed. Thus, we reduced both the pharmacy sales price and the PBM acquisition cost by eight percent of (pharmacy sales price) – (pharmacy acquisition cost) to account for pharmacy DIR. As with brand drugs, we assumed that all of the DIR is retained by the PBM. Estimating DIR for generic drugs is a novel approach.

To estimate wholesalers' net acquisition costs (flow 9), we compared WACs in IQVIA NSP to historical and current "Big Four" prices in the VA FSS price file (U.S. Department of Veterans Affairs, Office of Procurement, Acquisition and Logistics, 2023). Using the generic retail drugs that were listed in the FSS files, we formed groupings based on WAC quintiles, and then for each group, we calculated an average discount from WAC to the Big Four price. We applied these discounts to drugs in our sample based on their WAC quintile group; the resulting discounted WAC was the estimated net acquisition cost to wholesalers. For more details, see Appendix B.3.

3.4 Designing Weights for the Sample

We computed weights for our sample of 3,720 drugs so that the margins in the sample could be scaled up to the full target population in order to characterize the margins of all retail sales (excluding mail-order sales). Although Table 8 suggests that the sample largely reflects the characteristics of the target population, the sample was based on data availability rather than random selection, and thus unintended imbalance could exist between the sample and the target population of drugs. For example, products with more packaging options may be overrepresented since the sample was based on the availability of data at the 11-digit NDC level, and drugs with multiple packages (e.g., 30-pill bottles, 60-pill bottles) or marketed by multiple labelers (e.g., all made by the same manufacturer) will tend to have more 11-digit NDCs. As an attempt to correct for this, the weights were calculated using each drug's sales of extended units, as reported in IQVIA NSP, since extended units would tend to be lower for a

drug whose real utilization is distributed across multiple packages.[29] Specifically, we broke the sample into strata s based on whether the drug is a brand or generic, whether the drug treats an acute or a chronic condition, and whether the API is measured in kg or IU. The API unit was used to define strata because, within the sample, API unit was found to have a statistically significant impact on the margin per package. For each sampled drug i in a given stratum s, we calculated the drug's weight $w_i^{(t)}$ at time t using:

$$w_i^{(t)} = \frac{\text{total extended units sold in stratum } s \text{ at time } t \text{ in population}}{\text{total extended units sold in stratum } s \text{ at time } t \text{ in sample}} \quad (13)$$

Based on the sample, the weighted sum of all expenditures in 2022 is equal to $234.8. This is highly similar to the total invoice sales in IQVIA NSP, which equals $249.6 billion for all retail drugs and retail channels (excluding mail pharmacies).

To calculate an intermediary x's total margin M_x in dollars, we then summed the individual margins across all sampled drugs i and all time points t of interest (e.g., a given calendar year):

$$M_x = \sum_t \sum_i \left(P_i^{(t)} w_i^{(t)} Y_{i,x}^{(t)} \right) \quad (14)$$

where $P_i^{(t)}$ is the number of packages sold of the i^{th} drug at the time point t, and $Y_{i,x}$ is the margin per package for the i^{th} drug at the time point t for the intermediary x. To calculate the total or aggregate margin percentage, we divided the intermediary's total margin M_x by its total net sales:

$$\%M_x = \frac{M_x}{\sum_t \sum_i \left(P_i^{(t)} w_i^{(t)} S_{i,x}^{(t)} \right)} \quad (15)$$

where $S_i^{(t)}$ is the net sales price per package for the i^{th} drug and for the intermediary x at the time point t. The margin per package m_x for a given intermediary x was computed by dividing the intermediary's total margin M_x by the weighted total packages sold:

$$m_x = \frac{M_x}{\sum_t \sum_i \left(P_i^{(t)} w_i^{(t)} \right)} \quad (16)$$

[29] The precise interpretation of extended units varies by drug, but it typically refers to the number of pills, mL of liquid, or grams of powder sold.

3.5 Descriptive Analysis of Margins

We used descriptive statistics to characterize the margins of pharmaceutical supply chain entities. We applied the computed weights (see Section 3.4) to extrapolate from our sample of 3,720 drugs and to generate estimates for the full population of drugs sold through retail pharmacies. We compared intermediaries based on their weighted total margins in dollars across all drug sales, weighted aggregate margin percentage across all drug sales, weighted mean margins per package, and retained shares of total expenditures. We performed subgroup analysis based on drug characteristic (e.g., brand versus generic, acute versus chronic, biologic versus small molecule, short market tenure versus long market tenure, etc.). We also examined trends in these quantities for brand drug, generic drug, and all drugs, by intermediary, during the Q1 2020-Q4 2022 period.

3.6 Sensitivity Analysis

We performed two sensitivity analyses to assess the degree of uncertainty in the main findings. These analyses were conducted using the full sample of generic and brand drugs.

First, to assess the sampling error, we conducted a Monte Carlo analysis consisting of 1,000 bootstrap samples constructed by sampling the original dataset with replacement. We recalculated the main results for each bootstrap sample and then constructed empirical 95 percent confidence intervals by selecting the 2.5^{th} and 97.5^{th} quantiles from each main result's empirical distribution.

Second, to assess the model uncertainty, we selected five key parameters and adjusted each in turn by increasing and then decreasing the parameter by 20 percent of its original assumed value. The adjusted parameters include: (a) the percentage of manufacturer rebate the PBM retains, (b) wholesalers' discount off the WAC on generic drugs, (c) wholesalers' discount off the WAC on brand drugs, (d) the mean administrative fee PBMs charge the third-party payers on a per-prescription basis, and (e) the proportion of gross profit that pharmacies pay PBMs as generic drug DIR.

4 RESULTS

This section presents the final sample that was selected for analysis, as well as our key findings on drugs sold through retail pharmacies. Unless noted otherwise, the following analysis presents weighted population-level estimates for calendar year 2022. For the trend analyses on brand and generic drugs, we present estimates for the full time series from 2020 to 2022.

4.1 Sample of Drugs Sold Through Retail Pharmacies

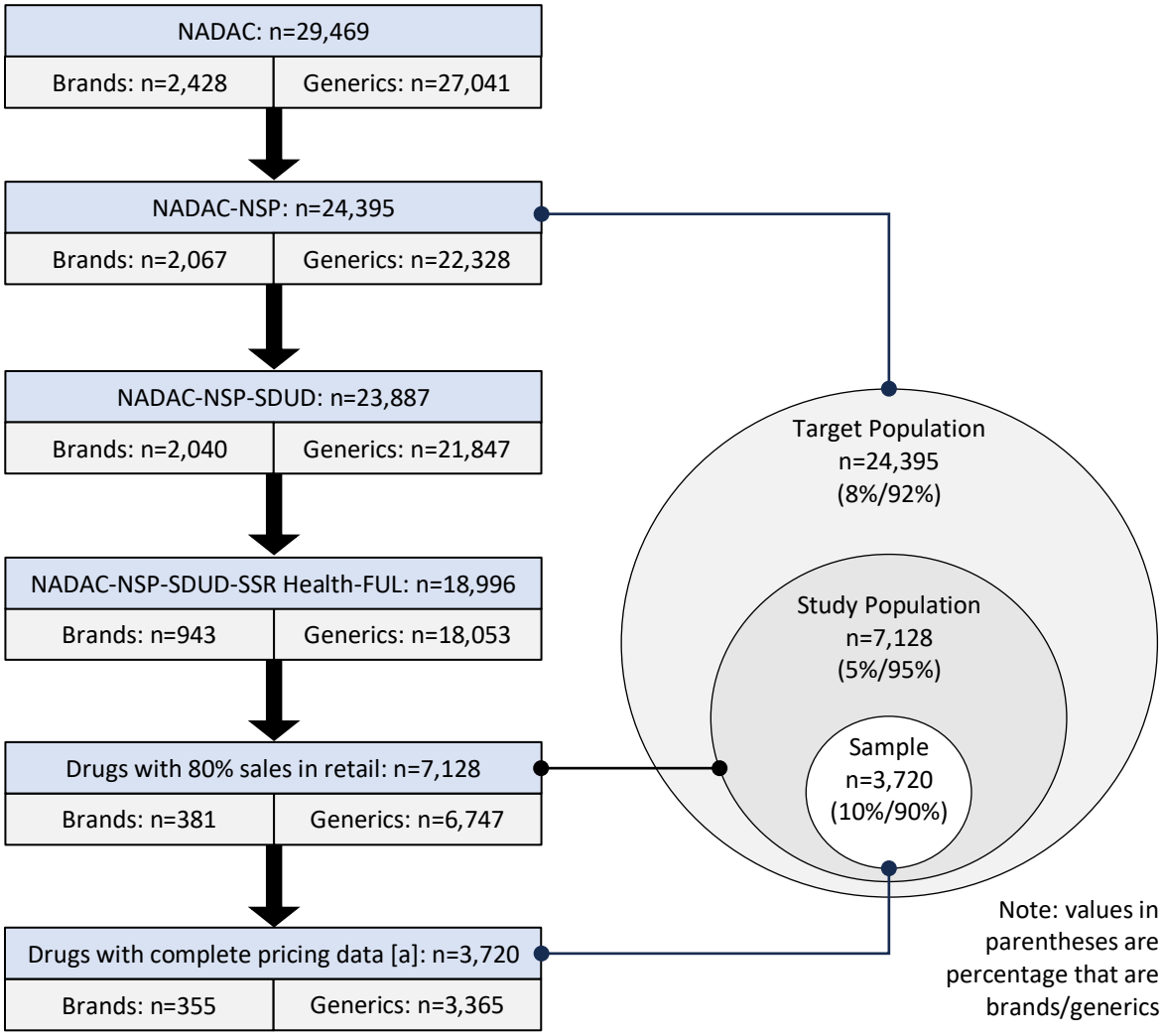
4.1.1 Drugs Selected for Sample

The right half of Figure 3 presents the number of distinct retail drugs (i.e., the count of 11-digit NDCs) in the target population, the study population, and the final sample. The target

population was identified as 24,395 retail drugs listed in NADAC with verified retail sales in IQVIA NSP (excluding mail-order pharmacy sales). The study population is the subset of the target population meeting the inclusion criterion of having at least 80 percent sales in retail channels, of which there are 7,128. While this study does aim to characterize the margins of drugs with fewer than 80 percent sales in retail channels, such drugs were not considered for the sample because their reimbursements in SDUD may not be representative of retail prices, since SDUD may also include drug payments to hospital, outpatient clinics, or physician offices if billed separately from the provided healthcare services. Of the 7,128 retail drugs with at least 80 percent sales in retail channels, the final sample included 3,720 drugs for which pricing and reimbursement data were available at every level of the supply chain (including, for brand drugs, information on gross-to-net discounts).

The left half of Figure 3 shows the number of drugs that were retained at each step of merging the datasets. The final two steps do not represent dataset merging but rather the reduction in drug count when (a) applying the inclusion criterion and (b) identifying the sample with valid pricing and reimbursement information at every stage of the supply chain.

Figure 3. Selection of Sample of Retail Drugs (11-digit NDCs), 2020-2022



[a] Only includes those for which (a) pricing and reimbursement data were available at every level of the supply chain for both brand and generic drugs, and (b) gross-to-net discount data were available for brand drugs.

Prior to merging, sources that reported data more frequently than the quarter were aggregated to the level of quarter. (See Appendix B.1.) Additionally, because SDUD data is not always reported per unit, we performed a manual review of outlying values to assess whether the reimbursements were expressed on a per-package or per-unit basis. We checked for related inconsistencies, such as a WAC expressed per unit rather than per package or a NADAC expressed per package despite having a listed unit of "eaches." In almost all such cases, external verification was possible by comparing the reported price and pack information to wholesalers' websites, and a correction was made to convert the prices to the same units throughout all datasets. In a very small number of cases (n=8), manual exclusions were made

because a product's unit appeared to be inconsistent across datasets, and the prices could not be clearly identified as per-package or per-unit.[30]

4.1.2 Comparing Sample to Target Population

In general, the target population of drugs is well represented by the final sample. Table 8 compares the distribution of the sample and the target population on a variety of drug characteristics. Both the sample and the full population have approximately the same proportion of brands to generics, small molecules to biologics, and drugs treating chronic conditions to drugs treating acute conditions. The distribution of anatomical therapeutic chemicals (as identified in IQVIA NSP) is also similar between the target population and the sample. This suggests that there are not large imbalances between the sample and population in the types of drugs.

Table 8. Comparison of Study Sample to Target Population by Drug Characteristic

	Target Population	Sample
Type of Drug		
Generic	92% (n=22,328)	90% (n=3,365)
Brand	8% (n=2,067)	10% (n=355)
Type of Compound		
Small Molecule	99% (n=24,246)	99% (n=3,689)
Biologic	1% (n=149)	1% (n=31)
Treats Acute vs. Chronic Condition		
Chronic	69% (n=16,809)	72% (n=2,672)
Acute	31% (n=7,586)	28% (n=1,048)
Anatomical Therapeutic Chemical		
Nervous System	33% (n=8,056)	38% (n=1,406)
Cardiovascular System	20% (n=4,916)	21% (n=764)
Alimentary Tract and Metabolism	10% (n=2,423)	9% (n=340)
Anti-infectives for Systemic Use	7% (n=1,657)	5% (n=191)
Dermatologicals	7% (n=1,611)	7% (n=245)
Genito Urinary System and Sex Hormones	6% (n=1,519)	3% (n=123)
Musculo-skeletal System	5% (n=1,116)	7% (n=270)
Systemic Hormonal Preparations	3% (n=743)	3% (n=114)
Respiratory System	3% (n=730)	3% (n=97)
Sensory Organs	2% (n=496)	1% (n=49)
Antineoplastic and Immunomodulating Agents	2% (n=468)	1% (n=45)
Blood and Blood Forming Organs	2% (n=453)	1% (n=55)
Various	<1% (n=111)	<1% (n=11)
Antiparasitic Products, Insecticides and Repellents	<1% (n=84)	<1% (n=10)
Hospital Solutions	<1% (n=11)	0% (n=0)
Diagnostics	<1% (n=1)	0% (n=0)

[30] See Appendix B.1 for more detail.

4.1.3 Detailed Sample Characteristics

Table 9 shows the number of observations and distinct drugs for each year in the study period, by drug characteristic.[31] Figure 3 shows the total number of drugs selected for the sample. Across all years, our final sample contained 3,720 distinct drugs with pricing data for all supply chain intermediaries. Of this sample, 355 were brand drugs and 3,365 were generic drugs. A drug was considered to have a "long" tenure if it had been on the market for more than 9 years if a small molecule, and more than 13 years if a biologic. Both long-tenure and short-tenure drugs are well represented in the sample (1,451 and 2,566 drugs, respectively). Drugs treating chronic conditions (n=2,672) outnumber drugs treating acute conditions (n=1,048) in the sample. There are 31 biologics in the sample, though none are 351(k) biosimilars, and roughly half (n=13) are insulin products.

Table 9. Sample Characteristics

Drug Characteristic	Total Number of Quarterly Observations of Drugs (Total Number of Unique Drugs) [a]			
	2020	2021	2022	2020-2022
Generic	7,897 (2,390)	9,390 (2,754)	10,773 (3,103)	28,060 (3,365)
Brand	1,054 (313)	951 (271)	925 (251)	2,930 (355)
Long Tenure [b] [c]	3,495 (1,060)	4,026 (1,179)	4,627 (1,311)	12,148 (1,451)
Short Tenure	5,456 (1,732)	6,315 (1,930)	7,071 (2,115)	18,842 (2,566)
Biologic	103 (27)	104 (28)	107 (27)	314 (31)
Small Molecule	8,848 (2,676)	10,237 (2,997)	11,591 (3,327)	30,676 (3,689)
Acute Condition	2,579 (754)	2,811 (850)	3,171 (940)	8,561 (1,048)
Chronic Condition	6,372 (1,949)	7,530 (2,175)	8,527 (2,414)	22,429 (2,672)
Total	8,951 (2,703)	10,341 (3,025)	11,698 (3,354)	30,990 (3,720)

[a] The listed value is the number of unique quarterly observations of drugs. The value in parentheses is the number of unique drugs. For example, on average in 2020, there were 7,897/2,390 = 3.3 observations per drug, indicating that most generic drugs had a complete time series and were observed in all four quarters of 2020.
[b] "Long" tenure refers to having more than 13 years or more than 9 years on the market for biologics and small molecules, respectively.
[c] The sum of long-tenure drugs and short-tenure drugs is greater than the number of drugs in the sample because some drugs' status changed during the study period.

4.2 Descriptive Analysis

4.2.1 Share of Expenditures by Intermediary and Drug Type

Figure 4 presents the share of total expenditures retained by each intermediary in 2022. The corresponding dollar amounts are shown in Appendix C.2. Manufacturers retained the majority of expenditures (73.6 percent) on brand drugs in 2022, whereas supply chain intermediaries retained the majority of expenditures (78.9 percent) on generic drugs. This is consistent with supply chain dynamics. Brand drug manufacturers have more market power and serve as price setters rather than price takers given their position as exclusive suppliers of

[31] Appendix C.1 provides sample counts when a drug is defined as a unique manufacturer-molecule (active ingredient)-formulation combination.

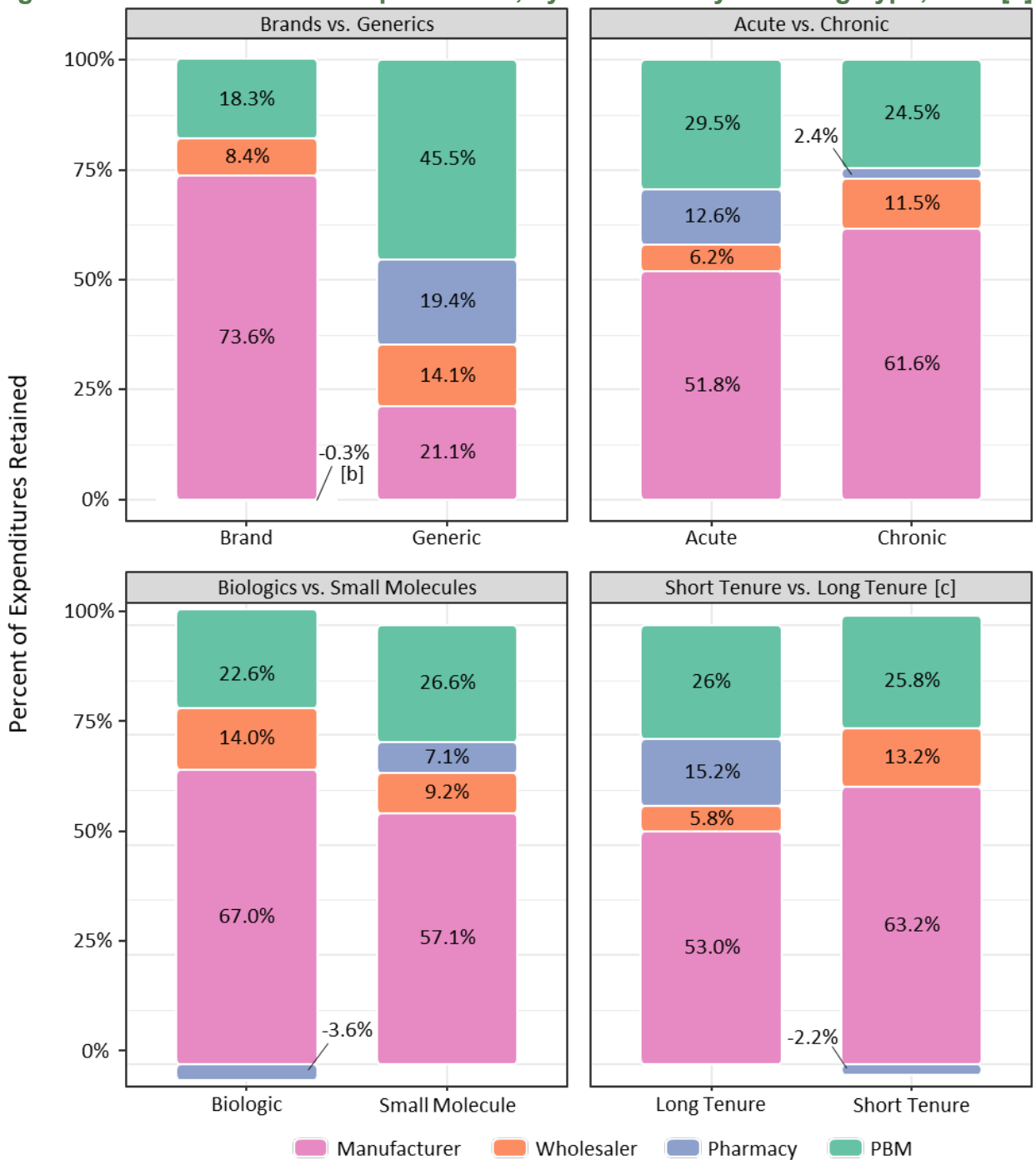
their drugs. In contrast, intermediaries have more power to negotiate lower prices for generic drugs because often there is more than one supplier for a given generic drug. While the degree of consolidation is high for all three intermediaries, PBMs appeared to be most successful at leveraging their market power for greater margins. We estimate that PBMs retained 18.3 percent of total expenditures on brands in 2022, compared to 8.1 percent retained by wholesalers and pharmacies combined. In 2022, PBMs retained an estimated 45.5 percent of expenditures on generics, compared to 33.5 percent retained by wholesalers and pharmacies combined.

The share of expenditures that manufacturers retained on brand drugs varies by several characteristics. In 2022, manufacturers received 53.0 percent of total expenditures on all drugs with a long tenure, compared to 63.2 percent of total expenditures on all drugs with a short tenure. This is likely a consequence of shorter-tenure drugs tending to be in periods of market exclusivity, whereas longer-tenure drugs tend to have more competition, which reduces manufacturers' market power. Manufacturers received a greater share of expenditures on biologic drugs (67.0 percent) than on small molecule drugs (57.1 percent) in 2022. However, because biologics are far more likely to be dispensed in healthcare settings than by retail pharmacies, this finding may not be representative of biologics in general.

Pharmacies saw substantial discrepancies in retained expenditures across drug characteristics in 2022 according to our estimates. Pharmacies retained -0.3 percent of expenditures on brand drugs. While this represents a loss, the 95 percent confidence interval extends into the position range (see Section 4.3.1.). By comparison, pharmacies retained 19.4 percent of expenditures on generic drugs. Similarly, pharmacies retained far more of the expenditures on acute drugs (12.6 percent) than they did of chronic drug expenditures (2.4 percent). Pharmacies are also estimated to have losses on short-tenure drugs, of which they retained -2.2 percent of expenditures, but gains on long-tenure drugs, of which they retained 5.8 percent of expenditures.

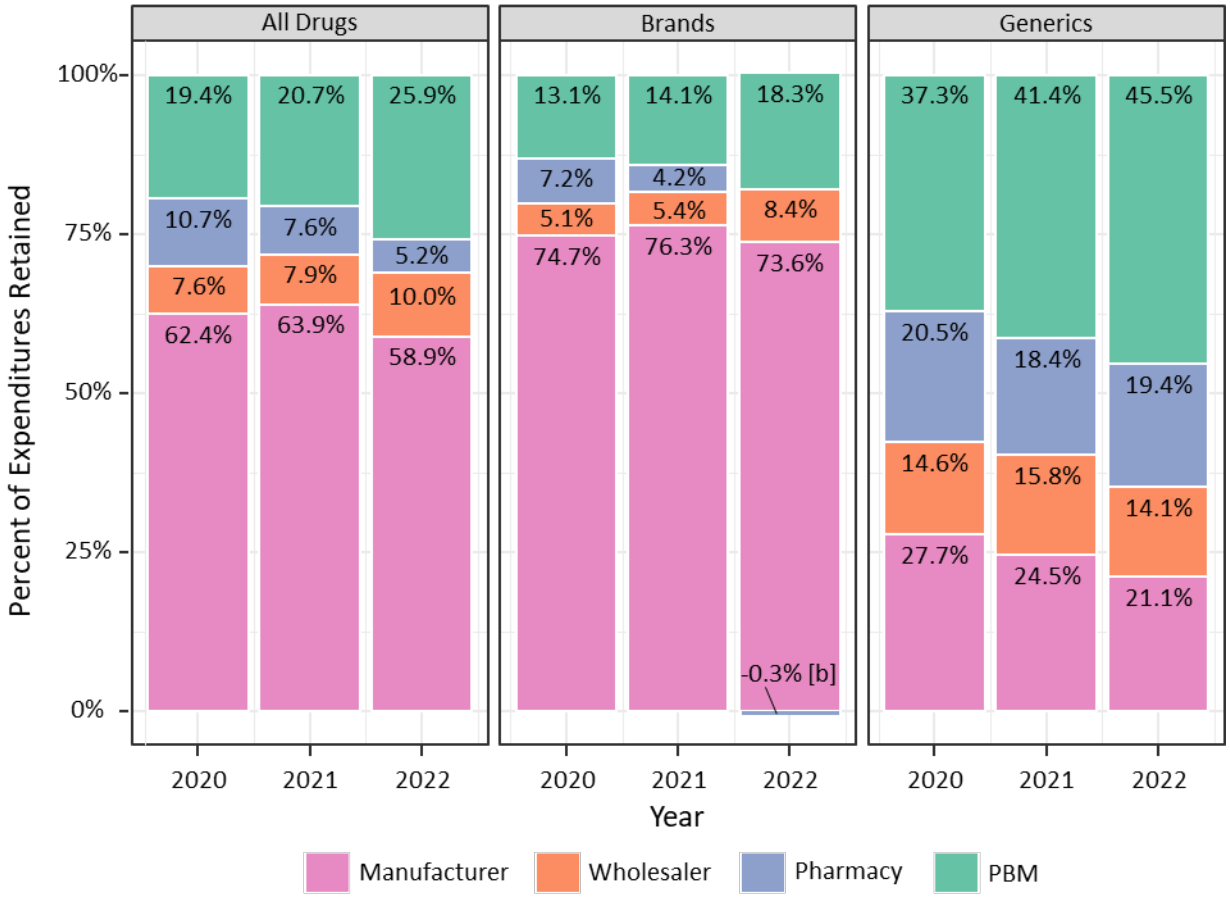
Figure 5 presents trends in retained expenditures from 2020 through 2022. Based on our model, PBMs have captured an increasing share of total expenditures, both on generic drugs and brand drugs. Manufacturers' share of expenditures has been roughly constant for brands but decreasing for generics. Pharmacies, on the other hand, have retained a roughly constant share of generic drug expenditures, but a decreasing share of brand drug expenditures. Wholesalers saw an increase in their share of brand drug expenditures in 2022 but otherwise were roughly constant over the study period, both on brands and generics.

Figure 4. Retained Share of Expenditures, by Intermediary and Drug Type, 2022 [a]



[a] Figure presents weighted population estimates. Values may not sum to 100% due to rounding.
[b] Bar is too small to show; pharmacies are estimated to have retained -0.3% of total brand drug expenditures in 2022. While this is a loss, the 95% confidence interval extends into the positive range. See Section 4.3.1.
[c] "Long" tenure refers to having more than 13 years or more than 9 years on the market for biologics and small molecules, respectively.

Figure 5. Retained Share of Expenditures, by Intermediary, 2020-2022 [a]



[a] Figure presents weighted population estimates. Values may not sum to 100% due to rounding.
[b] Pharmacies are estimated to have retained -0.3% of total brand drug expenditures in 2022, which corresponds to a loss. The 95% confidence interval for this value, however, extends into the positive range. See Section 4.3.1.

4.2.2 Margins by Intermediary

In this section, we present estimated margins on drugs sold through retail pharmacies for wholesalers, pharmacies, and PBMs. Margins are calculated in several forms, including dollars per package, total dollars across all drug sales, and aggregate percentage terms across all drug sales.

Table 10 displays margins in 2022 for wholesalers, pharmacies, and PBMs. Table 11 shows margin percentages from 2020 through 2022, including both the sample statistics and the population estimates.

Table 10. Aggregate Margins for Brand and Generic Drugs Sold Through the Retail Channel by Intermediary, 2022

Type of Drug	Intermediary	Sample Size (n) [a]	Median Net Sales Price per Package in Sample	Margin per Package [b]	Total Margin (Billions) [b]	Margin Percentage [b] [c]
Brand	Wholesaler	251	$655.1	$24.3 ($14.6, $32.2)	$14.1 ($8.5, $19.5)	4.1% (2.5%, 5.3%)
	Pharmacy		$641.7	-$0.9 (-$15.1, $12.0)	-$0.5 (-$9.0, $7.1)	-0.2% (-2.5%, 2.1%)
	PBM		$322.1	$52.6 ($50.1, $55.2)	$30.7 ($26.1, $35.4)	22.2% (20.6%, 23.9%)
Generic	Wholesaler	3,103	$18.3	$5.3 ($5.0, $5.6)	$9.3 ($8.8, $9.7)	40.2% (38.6%, 41.5%)
	Pharmacy		$25.1	$7.3 ($7.1, $7.5)	$12.7 ($12.0, $13.5)	35.6% (34.5%, 36.6%)
	PBM		$41.1	$17.1 ($16.4, $17.9)	$29.9 ($28.6, $31.4)	53.6% (52.7%, 54.6%)
All drugs	Wholesaler	3,354	$20.8	$10.0 ($7.6, $12.3)	$23.4 ($17.7, $28.7)	6.3% (4.8%, 7.5%)
	Pharmacy		$28.4	$5.2 ($1.6, $8.5)	$12.2 ($3.6, $20.0)	3.2% (0.9%, 5.3%)
	PBM		$45.7	$26.0 ($24.6, $27.4)	$60.6 ($55.6, $65.5)	31.2% (29.8%, 32.8%)

[a] Number of unique drugs (i.e., 11-digit NDCs) in the sample.
[b] Weighted population estimates are shown. Values in parentheses are 95% confidence intervals (see Table 13).
[c] Margin percentage is calculated as weighted total margin across all drugs divided by weighted total net sales.

Table 11. Aggregate Margin Percentage in Sample and Population, by Intermediary, Year, and Type of Drug [a]

Type of Drug	Intermediary	Margin Percentage in Sample [b]			Margin Percentage, Population Estimate [b]		
		2020	2021	2022	2020	2021	2022
Brand	Wholesaler	4.5%	4.2%	4.7%	3.0%	3.0%	4.1%
	Pharmacy	3.2%	1.3%	-0.8%	4.1%	2.3%	-0.2%
	PBM	15.3%	16.6%	21.9%	15.7%	16.8%	22.2%
	Sample Size [c]	313	271	251	N/A	N/A	N/A
Generic	Wholesaler	34.2%	38.8%	39.4%	34.6%	39.3%	40.2%
	Pharmacy	33.5%	32.3%	36.6%	32.8%	31.4%	35.6%
	PBM	44.8%	48.7%	54.2%	43.7%	48.0%	53.6%
	Sample Size	2,390	2,754	3,103	N/A	N/A	N/A
Total	Wholesaler	7.0%	6.9%	6.8%	5.6%	5.4%	6.3%
	Pharmacy	6.7%	4.6%	2.8%	7.3%	5.0%	3.2%
	PBM	23.5%	25.5%	31.3%	23.1%	24.5%	31.2%
	Sample Size	2,703	3,025	3,354	N/A	N/A	N/A

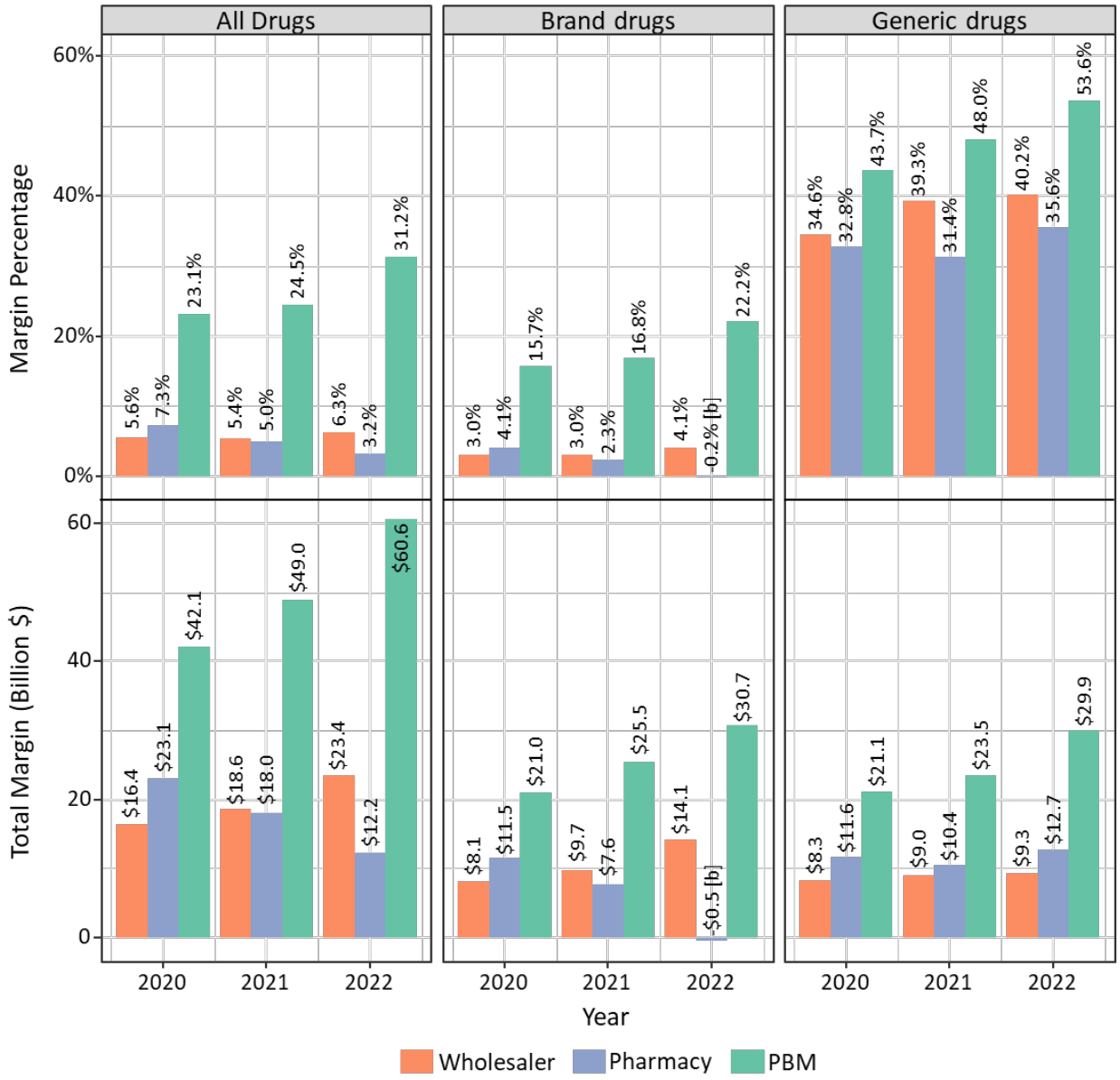
[a] Table presents weighted population estimates.
[b] Margin percentage is calculated as total weighted margin across all drugs divided by total weighted net sales.
[c] Number of unique drugs (i.e., 11-digit NDC) in the sample. Sample size is not applicable for the full population.

PBMs had the greatest total margins in total dollars and the highest margin percentages among the intermediaries in 2022. PBM margins were $60.6 billion (31.2 percent), wholesaler margins were $23.4 billion (6.3 percent), and pharmacy margins were $12.2 billion (3.2 percent). As with total expenditures, PBMs were more effective than the other intermediaries at using their market power to secure higher margins, both in dollar and percentage terms. This advantage of PBMs over the other intermediaries was estimated both for brand and generic drugs.

Across each of the three intermediaries, generic drugs generated greater margins as a percentage of the net sales price but lower margins by dollar value—with the sole exception of pharmacies, which generated more margin dollars on generics than brands. Dollar margins from generics are generally lower because they are far less expensive than brand drugs. Table 10 shows that, in 2022, compared to generics in the sample, brands had a median net sales price that was 7.8 times higher for PBM sales, 25.6 times higher for pharmacy sales, and 35.8 times higher for wholesaler sales.

Figure 6 presents margins on an annual basis for brand drugs, generic drugs, and all drugs, by intermediary. The top panel shows percent margins, and the bottom panel shows total dollar margins.

Figure 6. Margins by Intermediary, 2020-2022 [a]



[a] Figure presents weighted population estimates. Margin percentage is calculated as weighted total margin across all drugs divided by weighted total net sales.
[b] Pharmacies are estimated to have margins of -0.2% (-$0.5 billion) on brand drugs in 2022, which corresponds to a loss. The 95% confidence interval for this value, however, extends into the positive range. See Section 4.3.1.

Some trends and patterns are noticeable in Figure 6. PBM margins steadily rose year over year, as did wholesaler margins on generic drugs. Wholesaler margins on brand drugs rose, while their margins on generics were approximately constant. In contrast, pharmacy margins on generic drugs remained roughly the same from one year to the next, while their margins on brand drugs declined over the study period.

4.2.3 Margins by Intermediary and Drug Characteristic, 2022

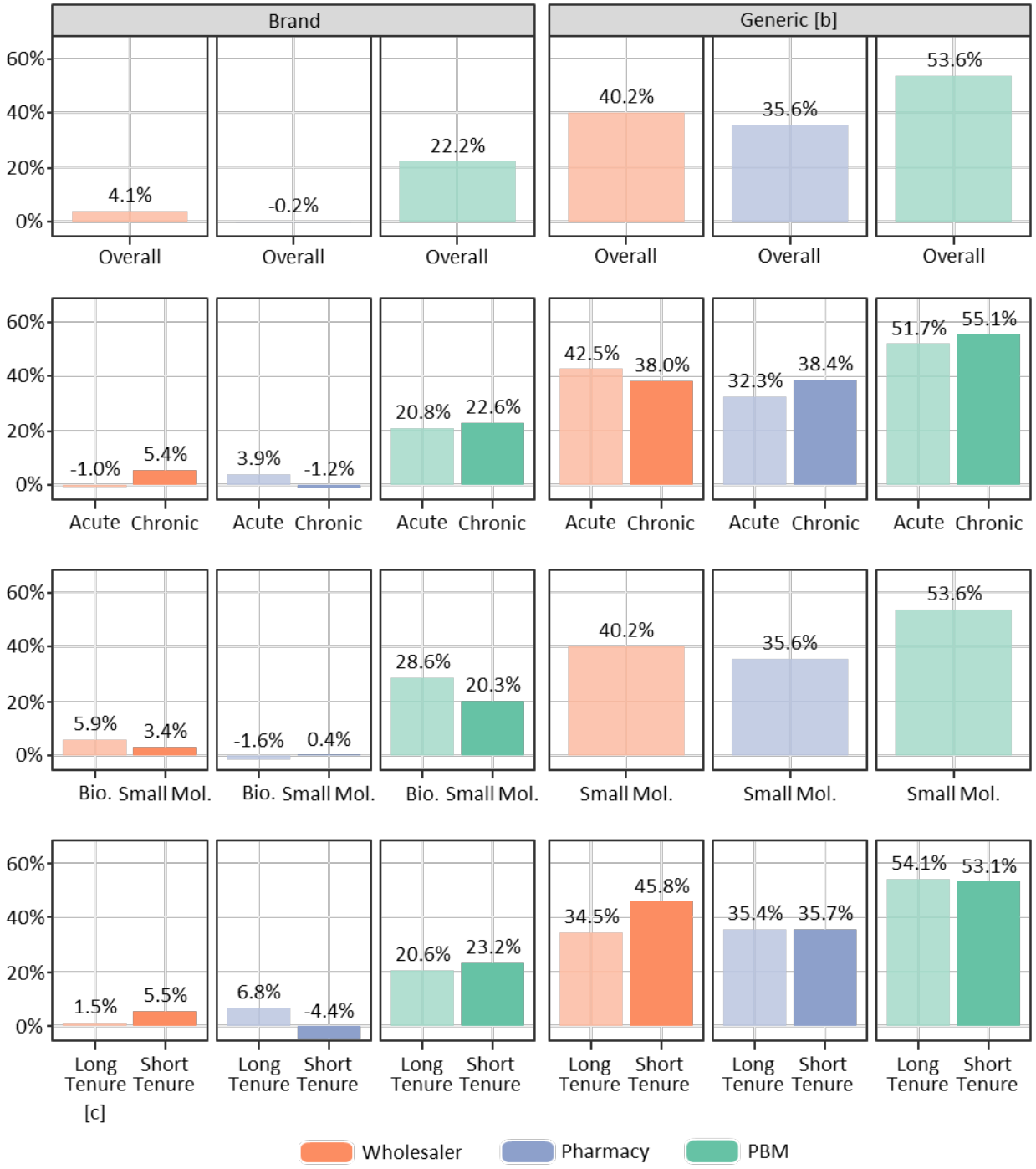
This section compares intermediaries' margins in 2022 by various drug characteristics, including drugs with a long versus short tenure in the market, biologics versus small molecules, and drugs treating chronic versus acute conditions. Figure 7 presents margin percentages across all drug sales by intermediary and drug characteristic for this year.

As seen in Figure 7, PBMs' margins were 22.2 percent on brand drugs overall and 53.6 percent on generic drugs overall in 2022. Neither of these values varies substantially based on drug characteristic. Wholesalers had very small margin percentages on brand drugs, including slightly negative margins for drugs treating acute conditions, but high margin percentages on generic drugs. Wholesalers earned slightly higher margin percentages on generic drugs treating acute conditions than on those treating chronic conditions (42.5 percent versus 38.0 percent in 2022) and on generic drugs with a short tenure than on those with a long tenure (45.8 percent versus 34.5 percent).

We found pharmacy margin percentages on brand drugs were slightly negative overall in 2022 (-0.2 percent), although the 95 percent confidence interval extends into the positive range (-2.5 percent, +2.1 percent).[32] We similarly found that pharmacies earned relatively small margins across all drug characteristics. We estimate that they earned negative margins on brand drugs treating chronic conditions (-1.2 percent in 2022), which are partially offset by small positive margins on drugs treating acute conditions (3.9 percent). On generic drugs, in contrast, pharmacies had higher margin percentages on drugs treating chronic conditions (38.4 percent in 2022) than on drugs treating acute conditions (32.3 percent). Similarly, pharmacies' larger negative margins on brand drugs with a short tenure (-4.4 percent in 2022) were mostly offset by positive margins on drugs with a long tenure (6.8 percent).

[32] See Table 13 for 95 percent confidence intervals. As discussed in Section 6, our methodology may overestimate the DIR that PBMs assess pharmacies because the calculation of pharmacy DIR is based on the estimate of manufacturer rebates, and we did not model all discounts manufacturers give to supply chain entities. Similarly, as shown in Section 4.3.1, the point estimate for pharmacy margins on brands increases to 1.7 percent when we assume PBMs retain 9.92 percent of DIR (i.e., 20 percent lower than the original estimate of 12.4 percent).

Figure 7. Margin Percentage, by Intermediary and Drug Type, 2022 [a]

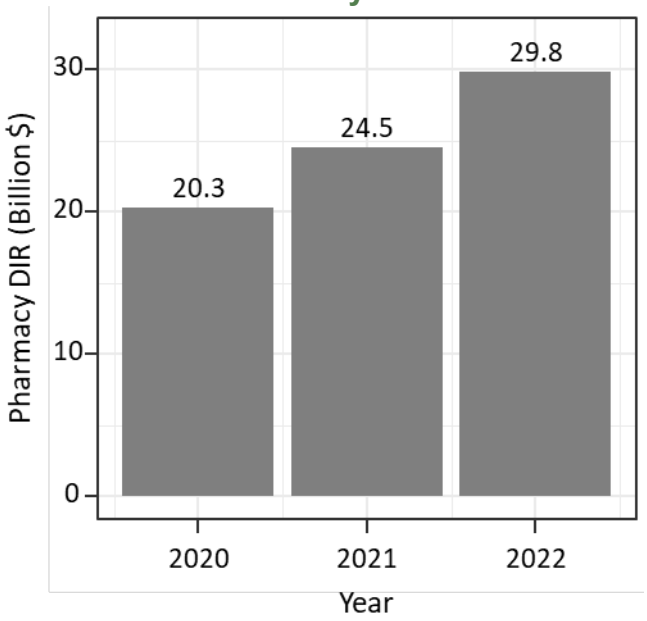


[a] Figure presents weighted population estimates. Margin percentage is calculated as weighted total margin across all drugs divided by weighted total net sales. "Bio." = biologic, and "Small Mol." = small molecule.
[b] Margins not shown for biologic generic drugs because the sample contained no biosimilar drugs.
[c] "Long" tenure refers to having more than 13 years and more than 9 years on the market for biologics and small molecules, respectively.

4.2.4 Increase in DIR over Time

Based on our analysis, increasing PBM margins are, in part, a result of rising pharmacy DIR. In our model, we assume PBMs do not pass any pharmacy DIR through to the payer, and we calculate pharmacy DIR from the total DIR that PBMs collect.[33] Figure 8 shows the increase from 2020 to 2022 in the collected pharmacy DIR, all of which we assume PBMs retain.

Figure 8. Estimated Pharmacy DIR on All Retail Drugs



The issue of increasing DIR was the subject of a recent CMS rulemaking, which went into effect on January 1, 2024, and requires all DIR to be estimated at the point of sale so that Medicare Part D beneficiary copays are calculated from the true cost of the drug rather than an artificially inflated price (Centers for Medicare & Medicaid Services, 2022). The CMS rule estimated that total pharmacy price concessions in Medicare Part D rose by 107,400 percent from 2010 to 2020. By our estimate, retail pharmacy DIR across Medicare, Medicaid, and commercial claims rose by another 46.8 percent during the study period, from $20.3 billion in 2020 to $29.8 billion in 2022 (see Figure 8).

To validate our methods, we re-estimated pharmacy DIR across all health insurance markets using the values published in Table 2 of CMS's final rule (Centers for Medicare & Medicaid Services, 2022), reproduced below as Table 12. Then, we compared our original DIR estimates to the re-estimates for the year 2020, and we compared the compound annual growth rate in pharmacy DIR according to our model to the compound annual growth rate according to the CMS data.

[33] Based on our analysis of PBM Annual Reports published in Iowa (Iowa Insurance Division, 2020-2023), PBMs retain 12.4 percent of the total DIR they collect, which we estimate as the sum of manufacturer rebates and pharmacy DIR.

To calculate the DIR re-estimates, we (a) divided the Part D estimates published by CMS by 0.30 since Medicare Part D makes up approximately 30 percent of retail drug spending (Cubanski, et al., 2019), and then (b) multiplied by (1 - 0.39) = 0.61 because we excluded mail-order sales, which are approximately 39 percent of total retail drug sales (Parasrampuria & Murphy, 2022). These new DIR estimates are shown in Figure 9, alongside our model's pharmacy DIR estimates from Figure 8. The two estimates are highly similar for 2020—$19.4 billion according to the re-estimates compared to our model's estimate of $20.3 billion. Moreover, using the three most recent years of CMS data (2018-2020), the compound annual growth rate in pharmacy DIR is 22.6 percent. This is highly similar to our model's estimated compound annual growth rate in pharmacy DIR of 21.2 percent over the three-year period from 2020-2022.[34]

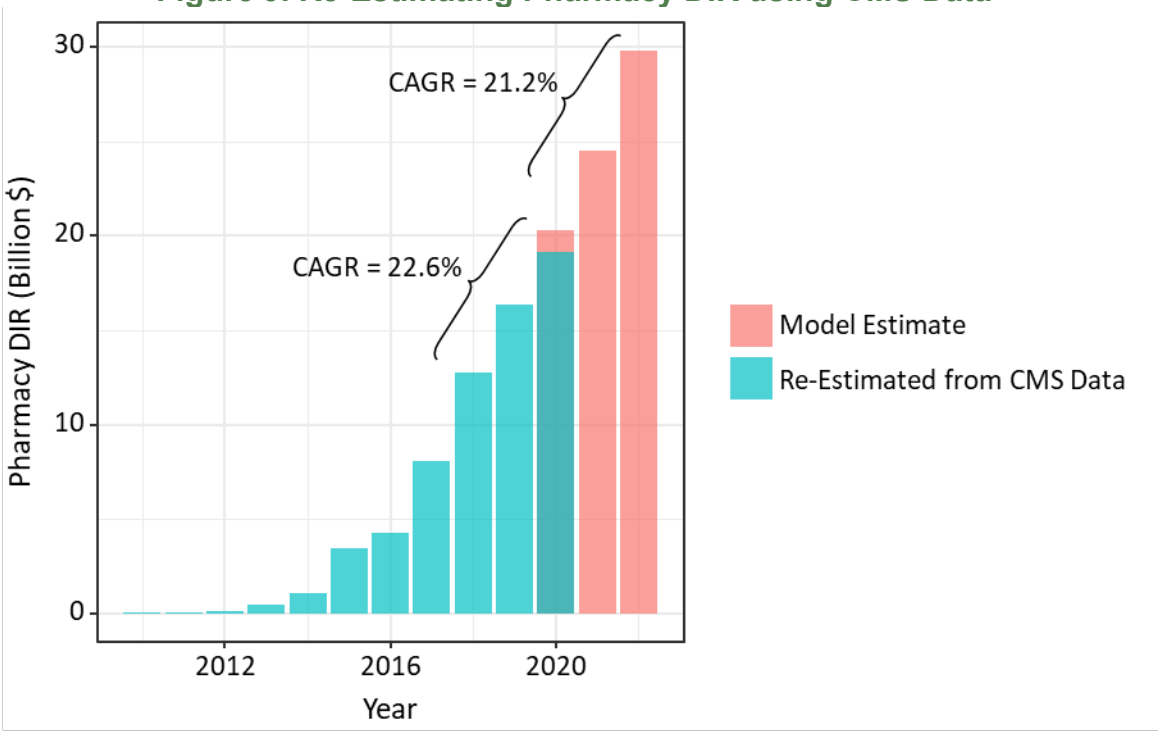
Table 12. Reproduction of Table 2 from CMS Final Rule (2022)

Contract Year	Total Pharmacy Price Concessions	% Change
2010	$8,869,347	--
2011	$8,582,354	-3.2%
2012	$68,086,163	693.3%
2013	$228,573,206	235.7%
2014	$538,421,239	135.6%
2015	$1,719,179,214	219.3%
2016	$2,125,460,000	23.6%
2017	$4,001,741,355	88.3%
2018	$6,339,517,817	58.4%
2019	$8,130,024,785	28.2%
2020	$9,535,197,775	17.3%
CAGR 2010 – 2020 [a]	101.0%	
CAGR 2018 – 2020 [a]	22.6%	

[a] "CAGR" = Compound annual growth rate, computed as $\left[\left(\frac{\text{final value}}{\text{initial value}}\right)^{1/\text{number of years that passed}} - 1\right] \times 100\%$.

[34] Using the CMS-based DIR estimates, the compound annual growth rate in pharmacy DIR is ($19.4B/$12.9B)$^{0.5}$ = 22.6%. Using our estimates, the compound annual growth rate in pharmacy DIR is ($29.8B/$20.3B)$^{0.5}$ = 21.2%.

Figure 9. Re-Estimating Pharmacy DIR using CMS Data



Note: "CAGR" = compound annual growth rate. Re-estimates are based on CMS 2022 final rule (Centers for Medicare & Medicaid Services, 2022), assuming Part D makes up 30 percent of retail drug spending and mail-order sales make up 39 percent of retail drug spending.

Based on this comparison, we may have slightly overestimated the pharmacy DIR (discussed in detail in Section 6). However, the discrepancy may also be a consequence of PBMs collecting higher DIR in non-Medicare markets where DIR reporting is not required. These limitations notwithstanding, the growth in DIR according to our study is in line with historical growth.

4.3 Sensitivity Analysis

4.3.1 Assessing Sampling Error with 95 Percent Confidence Intervals

To evaluate the sampling error, we performed a Monte Carlo simulation consisting of 1,000 bootstrapped samples. Each bootstrap sample was equal in size to the original dataset and was generated by sampling the original dataset with replacement. We computed the margins for each bootstrapped dataset and calculated a bootstrapped 95 percent confidence interval by determining the 2.5th percentile and the 97.5th percentile of the set of 1,000 margin values. We also calculated the mean value across the set of 1,000 margin values.

Table 13. Empirical 95% Confidence Intervals for Margin Percentage, 2022 [a]

Type of Drug	Intermediary	Margin Per Package in $ (95% Conf. Interval)	Total Margin in Billion $ (95% Conf. Interval)	Margin Percentage [b] (95% Conf. Interval)
Brand	Wholesaler	$24.3 ($14.6, $32.2)	$14.2 ($8.5, $19.5)	4.1% (2.5%, 5.3%)
	Pharmacy	-$1.0 (-$15.1, $12.0)	-$0.6 (-$9.0, $7.1)	-0.2% (-2.5%, 2.1%)
	PBM	$52.7 ($50.1, $55.2)	$30.8 ($26.1, $35.4)	22.2% (20.6%, 23.9%)
Generic	Wholesaler	$5.3 ($5.0, $5.6)	$9.3 ($8.8, $9.7)	40.2% (38.6%, 41.5%)
	Pharmacy	$7.3 ($7.1, $7.5)	$12.7 ($12.0, $13.5)	35.5% (34.5%, 36.6%)
	PBM	$17.1 ($16.4, $17.9)	$29.9 ($28.6, $31.4)	53.6% (52.7%, 54.6%)
All Drugs	Wholesaler	$10.1 ($7.6, $12.3)	$23.4 ($17.7, $28.7)	6.3% (4.8%, 7.5%)
	Pharmacy	$5.2 ($1.6, $8.5)	$12.1 ($3.6, $20.0)	3.2% (0.9%, 5.3%)
	PBM	$26.0 ($24.6, $27.4)	$60.7 ($55.6, $65.5)	31.3% (29.8%, 32.8%)

[a] Table presents weighted population estimates. The point estimate is the mean across all 1,000 simulations.
[b] Margin percentage is calculated as weighted total margin across all drugs divided by weighted total net sales.

As Table 13 shows, the 95 percent confidence intervals are very narrow, with the margin percentages having confidence interval widths of roughly 5 percentage points at most. It is worth noting that, for pharmacies' margins on brand drugs, the 95 percent confidence interval extends into the positive range, from -2.5% to 2.1%. The low sampling error indicates that the large sample yielded high degrees of precision. The mean values in Table 13 are highly similar to the main estimates of Table 10, suggesting that there is very little, if any, bootstrap bias.

We also calculated 95 percent confidence intervals for the share of total expenditures that each intermediary retains (see Table 14). As above, the confidence intervals are narrow, indicating that sampling error is low.

Table 14. Empirical 95% Confidence Intervals for Total Expenditures, 2022 [a]

Type of Drug	Intermediary	Total Expenditure in Billion $ (95% Confidence Interval)	Perc. Retained of Total Expenditures (95% Confidence Interval)
Brand	Wholesaler	$14.2 ($8.5, $19.5)	8.4% (5.0%, 11.1%)
	Pharmacy	-$0.6 (-$9.0, $7.1)	-0.4% (-5.3%, 4.2%)
	PBM	$30.8 ($26.1, $35.4)	18.2% (17.0%, 19.3%)
	Manufacturer	$124.7 ($109.1, $140.9)	73.8% (71.1%, 76.9%)
Generic	Wholesaler	$9.3 ($8.8, $9.7)	14.1% (13.4%, 14.7%)
	Pharmacy	$12.7 ($12.0, $13.5)	19.3% (18.7%, 20.0%)
	PBM	$29.9 ($28.6, $31.4)	45.5% (44.6%, 46.3%)
	Manufacturer	$13.9 ($13.3, $14.5)	21.1% (20.5%, 21.8%)
All Drugs	Wholesaler	$23.4 ($17.7, $28.7)	10.0% (7.5%, 11.9%)
	Pharmacy	$12.1 ($3.6, $20.0)	5.2% (1.6%, 8.5%)
	PBM	$60.7 ($55.6, $65.5)	25.8% (24.8%, 26.9%)
	Manufacturer	$138.6 ($123.1, $154.6)	59.0% (56.7%, 61.5%)

[a] Table presents weighted population estimates. The point estimate is the mean across all 1,000 simulations.

4.3.2 Sensitivity of Results to Individual Parameters

To assess uncertainty associated with the model assumptions, we selected five parameters (listed below) and recalculated margins when decreasing or increasing only one parameter at a time. Each parameter was decreased and increased by 20 percent its original value, yielding low and high re-estimates. We adjusted the following model assumptions:

- For brand drugs, PBMs retain 12.4 percent of the total DIR they collect, which includes manufacturer rebates and pharmacy DIR.
- For generic drugs, wholesalers pay 100 percent of the Big Four price. In our main analysis, this leads to wholesalers receiving a 65.1 percent discount off the WAC, on average, among the full target population.[35]
- For brand drugs, wholesalers receive a uniform discount of 9 percent off the WAC.
- PBMs charge an average administrative fee of $2 per brand prescription.
- For generic drugs, PBMs assess pharmacies a total DIR fee equal to eight percent of gross profit.

We found that, in most cases, 20 percent variation in the parameter produces relatively small changes in the margin percentages (Table 15). With only a few exceptions, the aggregate margin percentages varied by less than four percentage points.

Table 15. Results of Sensitivity Analysis [a]

Parameter [b]	Type of Drug	Intermediary	Aggregate Margin		
			Total (Billions)	Per Package	Percentage [c]
PBMs' retained 12.4% of collected DIR on brands	Brand	Pharmacy	(-$7.5, $6.0)	(-$12.8, $10.3)	(-2.2%, 1.7%)
	Brand	PBM	($24.1, $37.6)	($41.4, $64.6)	(17.5%, 27.2%)
Wholesalers pay 100% of Big Four price for generics	Generic	Wholesaler	($0.9, $17.6)	($0.5, $10.1)	(3.9%, 76.4%)
Wholesalers receive 9% discount off WAC for brands	Brand	Wholesaler	($7.5, $20.7)	($12.9, $35.6)	(2.2%, 6.0%)
	Brand	Pharmacy	(-$1.4, $0.4)	(-$2.5, $0.6)	(-0.4%, 0.1%)
	Brand	PBM	($29.8, $31.6)	($51.1, $54.2)	(20.6%, 24.0%)
PBMs charge an admin fee of $2 per brand claim	Brand	Pharmacy	(-$0.8, -$0.3)	(-$1.3, -$0.5)	(-0.2%, -0.1%)
	Brand	PBM	($30.5, $30.9)	($52.2, $53.0)	(22.0%, 22.4%)
PBM DIR is 8% of pharmacy profit for generics	Generic	Pharmacy	($12.5, $13.0)	($7.2, $7.4)	(35.2%, 36.0%)
	Generic	PBM	($29.7, $30.1)	($17.0, $17.2)	(53.3%, 53.9%)

[a] Weighted population estimates are presented. Intermediaries whose margins did not change in a given scenario are not shown.
[b] Each parameter was decreased and increased by 20 percent of its original assumed value.
[c] Margin percentage is calculated as total weighted margin across all drugs divided by total weighted net sales.

[35] Within the sample, the average wholesaler acquisition discount is 66.2 percent off WAC for generic drugs.

Among the parameters we evaluated, margins are most sensitive to changes in the assumption that wholesalers pay 100 percent of the Big Four price to acquire generics. Adjusting this to 80 percent and 120 percent caused wholesalers' generic margins to vary from 3.9 percent to 76.4 percent, which is a very wide range in response to only 20 percent variation in the assumption. PBMs' margins on brand drugs are sensitive to the assumption that total retained DIR is 12.4 percent of the total DIR they collect (including rebates and pharmacy DIR). A 20 percent change in this parameter (from 9.9 to 14.9 percent) caused pharmacy margins on brands to vary from -2.2 to +1.7 percent, and these parameter adjustments also caused pharmacy margins on brands to vary from 17.5 to 27.2 percent, which is a relatively large spread.

Overall, the results are not highly sensitive to the original assumptions, with the main exception of wholesalers' margins on generic drugs. In addition, PBMs' margins on brand drugs also have moderate model uncertainty. The other margins were largely unchanged when we adjusted the selected parameters.

5 DISCUSSION

Our study builds on the stylized model of Van Nuys et al. (2021) by accounting for certain payments (e.g., including pharmacy DIR) that occur after the point of sale and by expanding the sample of drugs, thereby providing further insight into the flow and distribution of money through the retail pharmaceutical supply chain in the United States. Using data at the drug level, we estimate the magnitude of off-invoice rebates and discounts as well as the DIR payments that PBMs recoup from pharmacies, thereby capturing net sales and acquisition costs among the retail supply chain intermediaries. Our overarching findings, discussed in depth below, are broadly in line with those of Sood, et al. (2017) and Van Nuys, et al. (2021).

Our results suggest that PBMs' margins have steadily increased from 2020 through 2022, outpacing wholesalers and pharmacies, across all types of drugs. We find that, during the study period, PBMs received higher margins than pharmacies or wholesalers on nearly all types of retail drugs—brands, generics, biologics, small molecules, drugs for the treatment of acute conditions, drugs for the treatment of chronic conditions, drugs with long market tenure, and drugs with short market tenure. Moreover, PBMs have increased their margins on retail drug sales by $18.5 billion from 2020 to 2022. This increase has been in spite of recent legislative efforts by states requiring PBMs to pass through 100 percent of manufacturer rebates to the payer (see Appendix A: Compendium of State Statutes Addressing PBM Issues). Several factors may have contributed to this increase, including PBM market structure and rising DIR fees paid by pharmacies. First, the market in which PBMs operate is highly concentrated, with three companies controlling 79 percent of the U.S. healthcare market in 2022 (Fein, 2023). This oligopolistic market structure coupled with the critical role PBMs play in formulary management may have allowed PBMs to extract higher margins by negotiating larger rebates from drug manufacturers and increasing the DIR fees levied on pharmacies. Moreover, the vertical integration among PBMs, insurers, specialty pharmacies, and providers also strengthens PBMs' ability to extract favorable contract arrangements from other supply chain

intermediaries.[36] Second, the high degree of consolidation of PBMs across the entire U.S. health insurance market increases their ability to create flexible reimbursement structures with pharmacies, which may allow them to comply with efforts to curb spread pricing while recouping profits in other markets. For example, PBMs' contracts with pharmacies may specify overall average reimbursement rates across all contracts and all health insurance markets (Medicare, Medicaid, and commercial), which may allow PBMs to more than offset the lower profits they make under Part D plans with higher gains realized from commercial plans. Third, according to our analysis of public disclosures by PBMs in Iowa (Iowa Insurance Division, 2020-2023), PBMs retain 12.4 percent of total DIR. Based on our model assumptions, DIR rose over the study period, which contributed to our estimates of increasing PBM margins.[37]

As PBM margins have risen, pharmacies' margins have decreased. In 2020, we estimate that pharmacies' total margin on retail drugs was $23.1 billion. By 2022, this had dropped to $12.2 billion—a decrease of $10.9 billion, or 47.2 percent. In our model, this is driven largely by DIR that PBMs assess to pharmacies, which increased since we calculated pharmacy DIR in part from manufacturer rebates, which also rose during the study period. In particular, we estimate that pharmacy DIR rose from $20.3 billion in 2020 to $29.8 billion in 2022—an increase of $9.5 billion or 46.8 percent. The rising DIR therefore makes up a vast majority of the $10.9 billion loss of margins that pharmacies experienced from 2020 to 2022. This estimated increase in DIR is relatively consistent with previous DIR growth reported by CMS (see Figure 9).

Brand drugs yield higher margins for PBMs and wholesalers but lower margins for pharmacies in dollar terms compared to generic drugs. For all three intermediaries, generic drugs had higher margin percentages: 40.2 percent for wholesalers, 35.6 percent for pharmacies, and 53.6 percent for PBMs in 2022. Generic drugs also had roughly four times the utilization of brand drugs in 2022. Nonetheless, PBMs and wholesalers each earned more margin dollars from brand drugs than they did from generic drugs, because brand drugs are far more expensive. Manufacturers, in particular, benefited from the sale of brand drugs, capturing nearly three-quarters of drug spending on brands by payers and beneficiary copays in 2022. Given that brand drugs account for roughly 80 percent of all drug spending, this is a major driver of overall spending and costs to patients.

Determining the margin percentages earned by intermediaries in the retail pharmaceutical supply chain and evaluating how these margins change by entity and by drug type provides valuable information on which factors might contribute to high prices of drugs

[36] For example, during 2022, there were several mergers between health insurance providers and PBMs that operate specialty pharmacies. These included the purchase of Aetna by CVS Health, the acquisition of Express Scripts by Cigna, the establishment of IngenioRx by Anthem, and the complex alliances formed between Express Scripts and Prime Therapeutics (Fein, 2022).

[37] The estimated increase in DIR fees is partly due to the model's assumptions, as data on DIR was limited. Further research is needed on the magnitude of impact DIR has on the margins of PBMs and pharmacies. See Appendix B.5 for details on how DIR was estimated in this study and the assumptions that we used.

sold through retail pharmacies. These estimates could help inform policy discussions on lowering overall prescription drug spending in the United States.

6 STUDY LIMITATIONS

This study used multiple data sources to generate estimates at the level of drug, where possible. However, in some cases, drug-specific estimates were not available, and so we applied a single parameter estimate to all drugs in a given group. For example, based on the work of Epstein et al. (2023) and the GAO study (2019), we assumed that wholesalers receive a nine percent discount off WAC for all brand drugs, which does not capture likely heterogeneities in wholesaler discounts across different brand drugs. Less expensive brand drugs with generic competition, in particular, may be more likely to have larger discounts than nine percent, which would lead to our study underestimating wholesaler margins on brands. Similarly, while the Big Four prices capture some differences in discounts, the Big Four data suggests that the wholesaler discount likely varies widely by drug. Furthermore, to the extent that Big Four prices approximate net prices, they may overestimate wholesaler discounts, which would only make up a portion of manufacturers' total price concessions. For example, like brand drugs, generic drugs are also generally subject to statutory Medicaid rebates and discounted 340B pricing that our methodology does not account for.

The NADAC survey, while providing a very comprehensive source of pharmacy acquisition costs, has some drawbacks. The NADAC tends to overrepresent smaller community pharmacies according to one expert we interviewed for this study. Large chain pharmacies may be able to use their market position to negotiate better prices with wholesalers, which would result in higher margins to pharmacies than we have estimated—potentially on all drugs. Further, NADACs primarily capture point-of-sale discounts the wholesalers provide pharmacies; these prices do not capture all retrospective concessions such as rebates for meeting sales targets. Accounting for these price concessions may slightly reduce wholesalers' margins and increase pharmacies' margins.

As described in Appendix B.4 Separating Manufacturer Rebates from Other Price Concessions, we disaggregated manufacturers' total gross-to-net discounts into only three components: rebates paid to the PBM, discounts provided to the wholesaler, and statutory rebates paid to Medicaid. A limitation is that we do not estimate other price concessions manufacturer may make, including copay assistance programs, 340B-related discounts, the best price provision of the Medicaid rebate, administrative fees and service fees paid to the PBM[38], and others. Not accounting for these other concessions leads to higher estimates of manufacturer rebates. Our methodology thus may overestimate the portion of gross-to-net discounts that are paid to the PBM as rebate. This would lead to underestimated pharmacy margins, since our calculation of pharmacy DIR is based on the value of the rebate. Additionally,

[38] Properly incorporating administrative fees paid by the manufacturer is especially important because these fees have increased recently, likely in response to the increased scrutiny of PBMs' handling of manufacturer rebates. For example, some PBMs have established group purchasing organizations (GPOs) that charge manufacturers service fees, administrative fees, data fees, etc. (Fein, 2022).

while the GAO study shows that PBMs retain rebates at 0.4 percent in Part D plans (2019), this proportion may be higher for commercial plans, which would lead to higher PBM margins than we estimated.

Our study used Medicaid reimbursements calculated from the CMS SDUD database. We have treated these SDUD prices as representative in general of the pre-rebate reimbursements PBMs receive, including from Medicare Part D and commercial healthcare plans. However, given the recent attention and legislative efforts targeting Medicaid drug spending, the SDUD prices may be influenced by greater pressure within Medicaid to maintain lower third-party reimbursements. Third-party reimbursement prices are likely higher in lines of business other than Medicaid MCOs. This may be particularly true for pharmacies, whose margins tend to be lowest in Medicaid MCOs and highest in Medicare, according to one expert interviewed for this study. Thus, the use of SDUD data may underestimate margins in general, but especially for pharmacies, and possibly also PBMs.

The CMS FUL data may tend to overestimate what the PBM pays the pharmacy. The FUL represents one of several pricing benchmarks that Medicaid agencies use to calculate drug reimbursements. In some cases, the reimbursement is based on state-published Maximum Allowable Costs (MACs), which can be lower that the FUL (Dolan & Tian, 2020). On the other hand, the FUL only provides a benchmark for ingredient reimbursement, which would be supplemented by a dispensing fee paid to the pharmacy.

Another limitation of our study is that we did not estimate manufacturers' margins. While the analysis of each intermediary's share of expenditures provides some insight into manufacturer earnings, the comparison of manufacturers to other intermediaries is incomplete because we have not accounted for manufacturers' costs—in part because of a lack of data, but also because of difficulties in defining an acquisition cost that is comparable to that of the other intermediaries. Unlike the other intermediaries in our analysis, manufacturers do not purchase a finished drug product, and thus a determination must be made about the specific costs to include (e.g., ingredient costs, labor costs, development costs).

In some cases (e.g., particularly when analyzing biologics), the sample size was relatively small. Moreover, the sampled drugs may overrepresent less expensive generic drugs and more expensive brand drugs, which may partly be a consequence of excluding drugs with higher medical benefit utilization. We compared the 30,990 observations in the sample with 32,806 observations of drugs over time that were not included in the sample because pricing data was not available for every supply chain intermediary. We found that:

- The mean SDUD price was 64 percent lower for sampled generic drugs than unsampled generic drugs, and 33 percent higher for sampled brand drugs than unsampled brand drugs.

- The mean WAC was 44 percent lower for sampled generic drugs than unsampled generic drugs, and 39 percent higher for sampled brand drugs than unsampled brand drugs.

- The mean NADAC was 76 percent lower for sampled generic drugs than unsampled generic drugs, and 32 percent higher for sampled brand drugs than unsampled brand drugs.

Finally, there may be additional unquantified uncertainty due to data limitations; to the extent that there is a lack of pricing transparency, the data we have relied on for this study may contain other unquantified biases. Further, margins may be driven by factors that the analysis did not account for, including drug shortage status, Herfindahl-Hirschman index (a measure of market concentration), and the manufacturer's size and location.

Nonetheless, the sample still leads to national estimates of drug utilization and spending on brands versus generics that are similar to those found in previous research. For example, using the extended unit-based weights to scale up from the sample to the population, we estimate that brand drugs made up 25.0 percent of retail drug utilization and 72.0 percent of retail drug expenditures in the United States in 2022. These are similar to the estimates for 2021 (of 20 percent and 80 percent, respectively) published by Parasrampuria & Murphy (2022).

7 CONCLUSION

This study combines drug prices at the drug level from multiple sources to calculate the margins received by wholesalers, PBMs, and pharmacies in the pharmaceutical supply chain. By comparing each intermediary's margins to their actual net sales price, we estimate that total margins for all retail drugs were 6.3 percent for wholesalers, 3.2 percent for pharmacies, and 31.2 percent for PBMs in 2022. PBM margins have been increasing at a faster pace than other intermediaries, potentially at the expense of pharmacy margins, which steadily decreased from 2020 to 2022.

Following the price of specific drugs through the supply chain, we evaluate how various drug characteristics impact the margins received by intermediaries. Supply chain intermediaries generally have higher margin percentages on generic drugs than on brand drugs but earn more margin dollars from brand drugs because of their higher prices. We observed differences in margins based on whether a drug treated acute or chronic illnesses, whether it was a biologic or small molecule drug, how long it has been in the market, and how much competition it faces in the market.

Future work can include (1) further refining our methodology for estimating pharmacy DIR payments and non-rebate forms of manufacturer DIR payments (e.g., administrative fees), both of which heavily impact PBMs' margins; (2) examining the impact of margins on drug shortages or supply chain resilience; (3) considering the margins of unmodeled intermediaries, such as secondary wholesalers, which purchase drugs at discounted rates from primary wholesalers and then sell the product to other wholesalers or to pharmacies; and (4) modeling additional manufacturer price concessions (e.g., in the 340B program) so that manufacturer rebates can be more accurately estimated.

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APPENDIX A: COMPENDIUM OF STATE STATUTES ADDRESSING PBM ISSUES

Definitions of Types of Legislation and state tables adapted from:
National Conference of State Legislatures (2022) State Policy Options and Pharmacy Benefit Managers (PBMs). https://www.ncsl.org/health/state-policy-options-and-pharmacy-benefit-managers.

Statutes enacted after March 23, 2022, are from: National Conference of State Legislatures, (n.d.) Prescription Drug State Bill Tracking Database, 2015-Present. Updated 09/11/2023. https://www.ncsl.org/health/prescription-drug-state-bill-tracking-database-2015-present

Types of Legislation

Cost disclosure/Anti-gag clause

The terms of PBM contracts with pharmacies and manufacturers are often proprietary and unknown to consumers and some purchasers, like employers. The terms can include a "gag clause," which restricts pharmacists from informing consumers of lower cost options, such as if a consumer purchases a prescription out of pocket rather than using the drug benefit through their insurance plan. Some states have banned the use of these gag clauses.

Giving PBMs Fiduciary Status

While some states impose fiduciary responsibilities[39] on PBMs, others require PBMs to exercise good faith and fair dealing while performing their contractual duties.

Controlling Maximum Allowable Cost (MAC) Lists

PBMs will establish an upper limit or maximum amount they will reimburse a pharmacy for generic and multi-source drugs. These maximum allowable costs (MAC) lists may consist of thousands of products. Some states regulate how often MAC lists are updated, and/or establish a way pharmacies can appeal when they dispute reimbursements.

Assuring Network Adequacy

Pharmacy network adequacy is often defined by the distance between a patient's residence and an accessible pharmacy. State laws generally set adequacy and eligibility standards for network participation. For example, Oklahoma's statute, 36 OK Stat § 36-6961 (2021), states that, in urban service areas, at least 90 percent of a PBM's covered

[39] "U.S. law and standards of professional conduct oblige fiduciaries to exercise a high standard of care, loyalty, and honesty in providing services to their clients and intermediaries. The fiduciary is required to prioritize the interests of the beneficiary over their own. Fiduciary duty is a serious obligation. If a fiduciary does not fulfill their duties, called a breach of fiduciary duty, the beneficiary could be entitled to damages" (Tretina, 2023). Fiduciary duties may vary depending on the nature and roles of the entities involved. However, the duties of honesty, loyalty, good faith, and the duty to disclose all information that could impact the beneficiary are apparently germane to the PBM/insurer/ patient relationship.

individuals must live within two miles of a pharmacy in the PBM's retail network. In suburban areas, 90 percent of covered individuals must live within 5 miles of a network pharmacy, and in rural service areas, 70 percent must live within 15 miles of a pharmacy in the PBM's network. Oklahoma also prohibits PBMs from denying participation in their network to any pharmacy "willing to accept the terms and conditions that the PBM has established for other pharmacies" already in their network. Other state legislation under this heading assures patients the right to use a pharmacy of their choice without penalty.

Anti-Patient Steering

Some PBMs require contracted health plan enrollees to visit their affiliated pharmacies, or pharmacies in which they have an ownership interest including retail, mail-order or specialty. Some states have made this unallowable.

Pharmacy Auditing Standards/Appeals Process

PBMs audit pharmacies to detect fraud, waste, and abuse. Some state laws are intended to assure the fairness of these audits and provide pharmacies a process for appeal. State laws are intended to provide guidelines on when and how pharmacy audits are conducted by PBMs. Some states have made PBMs subject to audit by a state agency.

Pharmacy Reimbursement/Clawbacks

Clawbacks occur when a health plan enrollee's copayment exceeds the total cost of the drug to their insurer, and the PBM "claws back" some, or all, of the overpayment from the pharmacy. Some states have chosen to prohibit these types of retroactive payments and at least 22 states have enacted some form of anti-clawback legislation.

Registration/Licensure

States may require PBMs to register or be licensed to conduct business, often through the state department of insurance or board of pharmacy.

Regulatory Agency/Enforcement

Many states that require PBM registration or licensure also authorize a specific agency to promulgate and enforce rules and regulations via fines, civil penalties, or license revocation.

Reporting/Transparency Requirements

Some states have implemented laws that require PBMs to disclose certain pricing and cost information such as data on rebates, payments and fees collected from drug manufacturers, insurers, and pharmacies. Frequently, these disclosures are limited to a specific state agency, which treats them as confidential business information.

Anti-Spread Pricing

In a spread pricing model, the PBM keeps a portion of the amount, or spread, between what the health plan pays the PBM and the amount that the PBM reimburses the

pharmacy for a beneficiary's prescription. With a pass-through contract, the PBM passes through the amount charged by the pharmacy to the health insurer. Since no spread is collected, PBMs typically charge an administrative fee. Some states have banned spread pricing.

Utilization Management Tools (e.g., Prior Authorization, Step-Therapy, Non-Medical Switching)

Utilization management tools are used by PBMs (on behalf of payers) to manage the costs of pharmaceutical and other treatments, often for non-medical reasons. "Prior authorization" requires providers to request approval from the PBM/insurer for a specific therapy before they can prescribe it. Step therapy requires a patient and their doctor to try specific treatments before switching to a more expensive or non-generic alternative. Non-medical switching occurs when a patient who is stable on one medicine is switched to another one for non-clinical reasons. Some states have legislated limits on the use of utilization management tools.

Other

Some states have pursued other activities related to PBM reform not highlighted in the above categories. For instance, in a reverse auction PBMs compete for a state's business and the lowest offer is awarded the contract. Other actions prohibit discriminatory practices against a pharmacy that participates in the federal 340B program.

Table A - 1. States with Statutes Addressing PBM-related Issues

Legislative Target	Number of States w/ Statute
Cost Disclosure/Anti-Gag Clause	44
Fiduciary Status for PBM	14
Maximum Allowable Cost Lists	35
Network Adequacy	28
Anti-Patient Steering	14
Pharmacy Reimbursement/Anti-Claw Backs	34
Pharmacy Auditing Standards/Appeals Process	43
Registration Licensure	43
Regulatory Agency/Enforcement	43
Reporting/Transparency Requirements	34
Anti-Spread Pricing	16
Limits to Utilization Management Tools	22
Other	21

Source: National Conference of State Legislatures (2022, March 23)

APPENDIX B: DETAILED METHODOLOGY

In this section, we describe elements of the methodology in greater detail.

B.1 Merging Data Sources and Exclusions from Sample

For this analysis, we combined drug-level information from the following datasets:

- CMS State Drug Utilization Data (SDUD) reports utilization and spending by state Medicaid agencies.
- CMS NADAC contains national estimates of pharmacies' acquisition costs.
- IQVIA NSP provides WACs, sales to providers, and utilization by API mass.
- IQVIA PayerTrak reports national projections for prescriptions filled as well as copays.
- SSR Health tracks manufacturers' total price concessions (rebates, discounts, etc.).
- VA FSS price lists contains Big Four prices, which we used to estimate wholesaler discounts on generic drugs.
- CMS FUL contains maximum allowable Medicaid reimbursements for multi-source drugs, which we used to estimate PBMs' payments to pharmacies for generic drugs.
- FDA National Drug Code (NDC) Directory contains drug information including the strength of the API.

We used 11-digit NDC codes to merge CMS SDUD, CMS NADAC, IQVIA NSP, VA FSS, CMS FUL, and FDA's NDC Directory. While IQVIA PayerTrak does not contain 11-digit NDC numbers, we were able to find exact matches to specific NDCs using the available fields (molecule, product name, formulation, strength, brand/generic status, USC3 designation, corporation, manufacturer, and product launch date). We used SSR Health data on gross-to-net discount rates in all markets, Medicaid markets, and non-Medicaid markets. SSR Health identifies these discounts at the level of brand name. Accordingly, we matched products' brand names in SSR Health to their proprietary name in the NDC Directory and applied the gross-to-net discount rates to all 11-digit NDCs associated with the given brand name.

In all cases, we matched datasets not only by drug, but also by time period. When datasets reported metrics by month, we aggregated monthly statistics into quarterly statistics. For IQVIA NSP, this involved taking a weighted average WAC, which we weighted by number of packages sold. For IQVIA PayerTrak, we used the projected number of national prescriptions (TRx) to weight the average copays for insured beneficiaries over time and across states and payer types. For NADAC, which is published every two weeks, we took an unweighted average of the available prices published within a quarter. Because the NADAC survey operates on a lag,

we adjusted the effective price date based on the survey publication date using the procedure modeled by 46Brooklyn (46Brooklyn, n.d.).[40]

When selecting the final sample, the following exclusions were made:

- In SDUD, we excluded a drug's observation at a given quarter only if both the FFS total reimbursement and MCO total reimbursement were missing. Otherwise, we used the non-missing value—or if both values were non-missing, we summed the non-missing reimbursements.
- We excluded drugs for which IQVIA data on total API sold (in kg or IU) was not available.
- For tractability when converting between price per package, price per unit, and price per API, we excluded drugs with multiple APIs.
- To facilitate conversion between package price, unit price, and API price, we excluded drugs that had inconsistent API strengths in different datasets or that presented a strength as a range rather than a definite value.
- We excluded observations of the WAC that were associated with a repackaged version of the drug (which constituted less than two percent of the identified retail drugs in IQVIA NSP) but retained WACs associated with the original package.
- We excluded drugs if, within a single month, the WAC or package information was not consistent across the retail observations.

In addition, we excluded specific drug products (collectively making up eight 11-digit NDCs) based on a manual review of outliers:

- We excluded VTAMA, which only had data for Q4 2022, because its SDUD reimbursement price was almost exactly double its WAC. The WAC was independently verified, suggesting that the SDUD price was likely reported in a different unit amount that could not be discerned.
- Similarly, we excluded Mounjaro and Asmanex Twisthaler due to inconsistencies across datasets, suggesting that prices were being reported with different units that could not be discerned. For example, for Asmanex Twisthaler, the SDUD reimbursement price per unit was three times the WAC per package.

B.2 Converting Between Packages, Units, and API

The datasets expressed prices in different terms. WACs in IQVIA were typically in dollars per package, while NADAC, FUL, and SDUD were expressed in prices per unit (i.e., $ per mL of package contents, $ per gram of package contents, or $ per each/pill). To convert from WACs

[40] In this procedure, each possible survey publication date is mapped to the month whose data would likely be captured by a survey published on that date. In general, the first possible publication date mapped to a given month is the second to last Wednesday of the following month, with the last date being the Tuesday before the second to last Wednesday of the month following that. In the case when a month has 31 days and ends on a Wednesday, the third to last Wednesday is used instead of the second to last Wednesday as the first publication date corresponding to data from the previous month.

per package to WACs per unit of package contents, we divided the listed WAC by the quantity in one package and by the size of one package (if relevant). To convert from WAC per unit to WAC per amount of API,[41] we identified the correct relationship between pack size, pack quantity, and API strength (and/or concentration) for each combination of formulation and pricing unit (either gram, mL, or each/pill according to NADAC), and we developed a unit-to-API price conversion for each drug group. We applied the same package-to-unit conversion for all price metrics given as prices per package, and the same unit-to-API conversion to all price metrics.

B.3 Estimating Wholesalers' Discounts Off WAC for Generic Drugs

To estimate the net price at which wholesalers acquire generic drugs, we used Big Four prices published by the VA in their FSS price list. We downloaded 23 historic FSS price lists published between January 1, 2020, and August 15, 2023. Each price list had a different "as of" date indicating when prices were updated. We selected the Big Four prices with contract periods that were active during the "as of" date and merged the resulting Big Four list with the IQVIA NSP retail drug dataset based on the 11-digit NDC, month, and year. We filtered the merged dataset to only contain generic retail drugs and calculated each drug's WAC-to-Big Four discount rate.[42] Instead of computing a single mean discount rate for all generics, we binned generic drugs into five groups based on their WAC price per unit. We found that quintiles of the WAC price per unit were the best predictors of the WAC-to-Big Four discount rate that a wholesaler would receive for a generic drug. We calculated these discounts in each year for each of the five generic drug groups, yielding five average wholesaler discount rates off WAC per year (Table B - 1).

Table B - 1. Mean WAC-to-Big Four Discount, based on Quintiles of WAC per Unit

WAC Quintile	Range of WAC per Unit	WAC-to-Big Four Discount			
		2020	2021	2022	2023
1	≤$0.17	66.1%	64.9%	69.0%	64.0%
2	>$0.17 to ≤$0.44	71.1%	72.3%	74.8%	59.5%
3	>$0.44 to ≤$1.18	73.2%	76.2%	75.3%	65.4%
4	>$1.18 to ≤$4.69	75.2%	78.3%	80.8%	84.4%
5	>$4.69	71.5%	72.3%	70.9%	61.8%

While the mean discount generally increases with WAC per unit, there is substantial noise in the data. Figure B - 1 shows the boxplot for each generic drug group when aggregated across the full time series. Each shaded point represents a different contract for a specific drug at a given time period from 2020 through August 2023.

[41] We expressed API amounts using mg of mass for nearly all drugs, and mega-units of activity for insulin.
[42] We removed matches for which (a) the difference in Big Four and WAC prices was more than 100 percent, (b) the Big Four price was greater than the WAC, or (c) the drug (11-digit NDC) had multiple Big Four prices from the same vendor in the same month.

Relatedly, four of the five generic groups experienced a substantial decline in the second half of 2022 compared to previous time periods, as Figure B - 2 shows.

Figure B - 1. WAC-to-Big Four Discount for Generic Drug Groups Defined by WAC per Unit

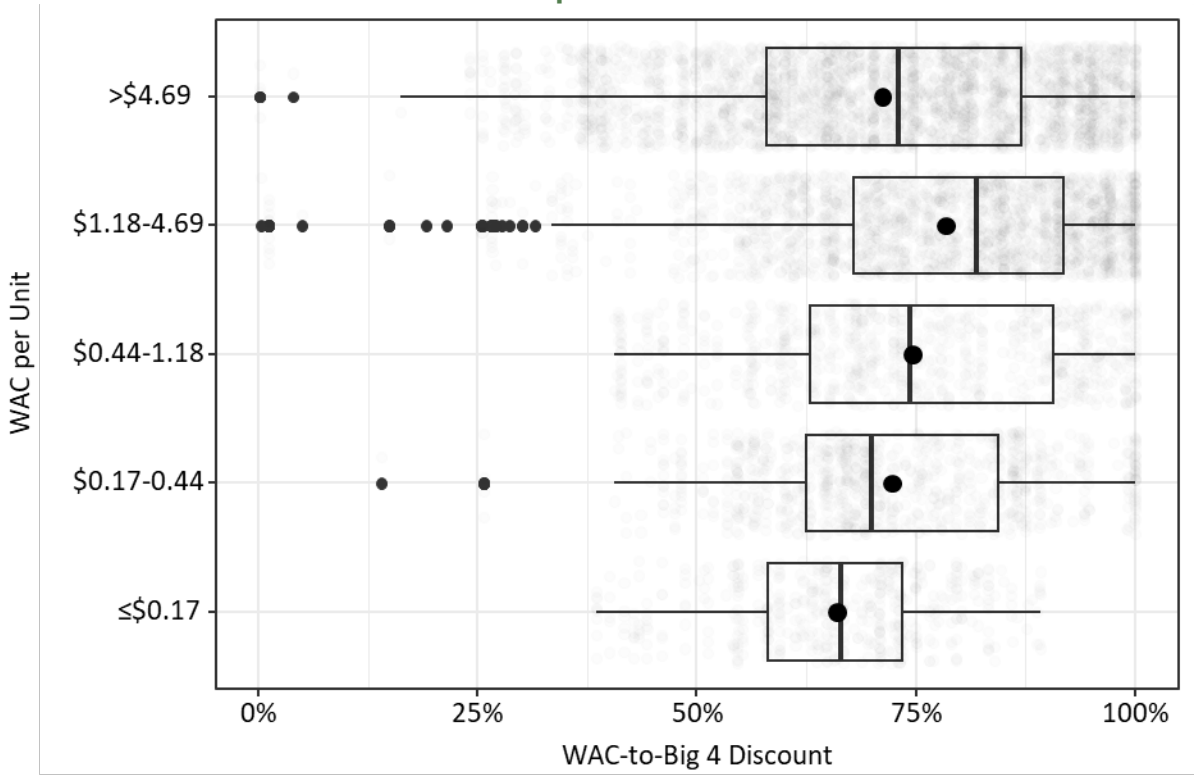
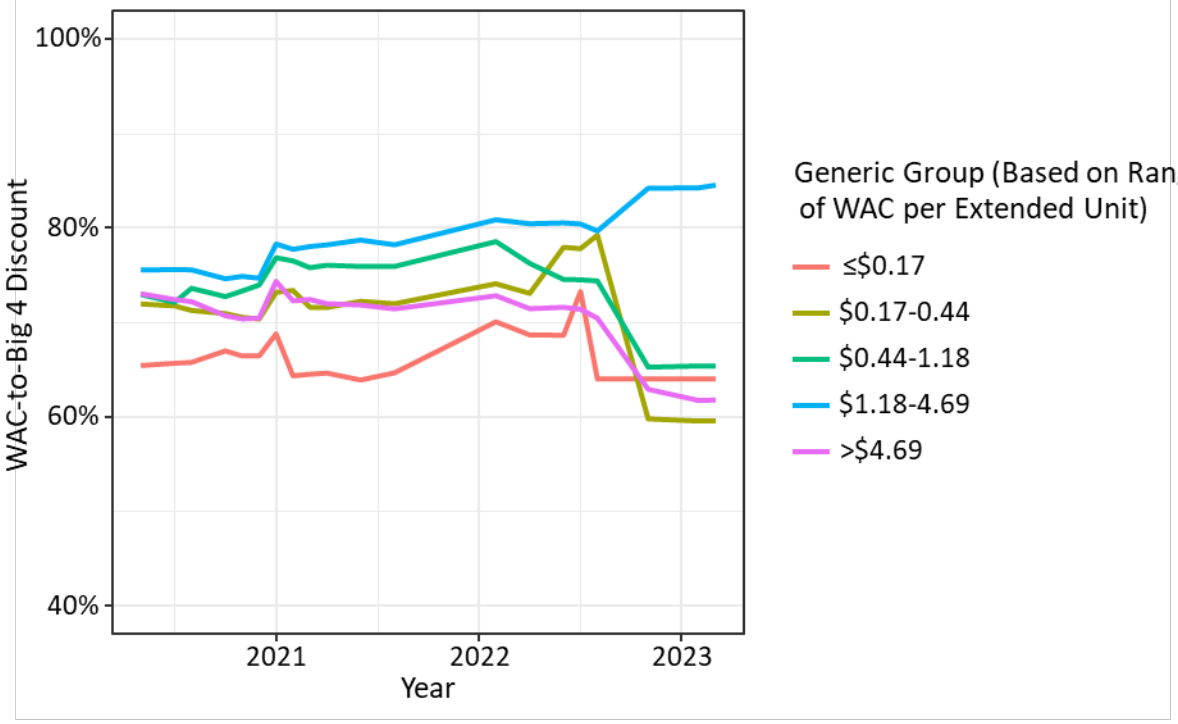


Figure B - 2. Trends in WAC-to-Big Four Discounts over Time, by Generic Group



B.4 Separating Manufacturer Rebates from Other Price Concessions

For brand drugs, a central estimate in our methodology is the total rebate a manufacturer pays to the PBM for a given drug. Ultimately, we use this estimate to calculate multiple sources of PBMs' margins from brand drugs.

To estimate rebates that manufacturers pay PBMs, we used data from SSR Health on gross-to-net discounts. These gross-to-net discounts capture all manufacturer price concessions, including rebates and administrative fees paid to the PBM, rebates paid to the Medicaid Drug Rebate Program, and discounts provided to the wholesaler, among other sources. In this section, we derive a formula for separating the manufacturer rebate (including administrative fees) from the other price concessions. We used this equation to estimate the rebates as a fraction of the WAC.

SSR Health provides three gross-to-net discount rates: the average discount on all units sold g_t, the average discount on Medicaid units g_M, and the average discount on non-Medicaid units g_n. The Medicaid discount g_M accounts for (a) the statutory rebate equal to 23.1 percent of AMP for brand drugs and 13 percent of AMP for generic drugs and (b) the inflation-based rebate when a drug's AMP increases faster than the rate of inflation. However, the Medicaid discount g_M does not account for discounts the manufacturer gives the wholesaler, and it does not account for the best price provision.

The gross profit from all units R_t can be divided up into the gross profits on non-Medicaid units R_n and the gross profits on Medicaid units R_M:

$$R_t = R_n + R_M \qquad (\mathrm{B}-1)$$

Based on the SSR Health gross-to-net definition, we estimate each of the gross profits R_t, R_n, and R_M as the difference between expenditures at the WAC price and expenditures at the net price. For example, the total gross profit is:

$$R_t = (u_{\mathrm{tot}})(\mathrm{WAC}) - (u_{\mathrm{tot}})(\mathrm{WAC})g_t \qquad (\mathrm{B}-2)$$

where the total number of units u_{tot} is equal to the number of non-Medicaid units sold u_n plus the number of Medicaid units sold u_M. Simplifying Eq. B-2 yields:

$$R_t = (1-g_t)(u_n + u_M)(\mathrm{WAC}) \qquad (\mathrm{B}-3)$$

Applying this to each term in Eq. B-1 gives the following:

$$(1-g_t)(u_n + u_M)(\mathrm{WAC}) = (1-g_n)(u_n)(\mathrm{WAC}) + (1-g_m)(u_M)(\mathrm{WAC}) \qquad (\mathrm{B}-4)$$

Eq. B-4 can be rearranged to give the ratio of Medicaid to non-Medicaid units in terms of the three gross-to-net discounts:

$$\frac{u_M}{u_n} = \frac{g_t - g_n}{g_M - g_t} \qquad (\mathrm{B}-5)$$

Eq. B-5 is derived from SSR Health's definitions of gross-to-net discounts which, in the case of the Medicaid units, does not account for prices concessions beyond the statutory Medicaid rebates. Thus, we can modify Eq. B-1 to re-allocate total gross profits R_t in a way that accounts for other concessions that may apply to Medicaid units. Doing so maintains the same total gross profits R_t but attributes a larger portion to Medicaid units and a smaller portion to non-Medicaid units. We use R_n^* and R_M^* for the updated estimates of gross profits in the non-Medicaid and Medicaid markets, respectively, where reallocating some price concessions to Medicaid units leads to a larger estimate of gross profits in Medicaid markets $R_M^* > R_M$ and a smaller estimate of gross profits in non-Medicaid markets $R_n^* < R_n$. However, this only constitutes a re-allocation of the total gross profits R_t, which remain the same:

$$R_t = R_n^* + R_M^* \qquad (\mathrm{B}-6)$$

The updated Medicaid gross profits R_M^* now account for the statutory Medicaid rebate (i.e., SSR Health's Medicaid gross-to-net discount g_M) as well as rebates that the PBM may receive on Medicaid units $d_M^{(\text{reb})}$ and discounts the wholesaler may receive $d_M^{(\text{oth})}$:

$$R_t = R_n^* + (\text{WAC})(u_M)\left(1 - g_M - d_M^{(\text{reb})} - d_M^{(\text{oth})}\right) \qquad (\text{B}-7)$$

Similarly, non-Medicaid gross profits R_n can also be broken into its constituent parts. In our model, we account for two main components, manufacturer rebates $d_n^{(\text{reb})}$ and wholesaler discounts $d_n^{(\text{oth})}$.

$$R_t = (\text{WAC})(u_n)\left(1 - d_n^{(\text{reb})} - d_n^{(\text{oth})}\right) + (\text{WAC})(u_M)\left(1 - g_M - d_M^{(\text{reb})} - d_M^{(\text{oth})}\right) \qquad (\text{B}-8)$$

We make the simplifying assumption that PBM rebates on brand drugs are the same for Medicaid and non-Medicaid units ($d_n^{(\text{reb})} = d_M^{(\text{reb})} \equiv d^{(\text{reb})}$), and likewise that wholesaler discounts are the same for Medicaid and non-Medicaid units ($d_n^{(\text{oth})} = d_M^{(\text{oth})} \equiv d^{(\text{oth})}$). Then, Eq. B-8 rearranges to:

$$\frac{R_t}{\text{WAC}} = u_n\left(1 - d^{(\text{oth})}\right) + u_M\left(1 - g_M - d^{(\text{oth})}\right) - (u_n + u_M)d^{(\text{reb})} \qquad (\text{B}-9)$$

$$d^{(\text{reb})} = \frac{u_n}{u_n + u_M}\left(1 - d^{(\text{oth})}\right) + \frac{u_M}{u_n + u_M}\left(1 - g_M - d^{(\text{oth})}\right) - \frac{R_t}{(\text{WAC})(u_n + u_M)} \qquad (\text{B}-10)$$

However, the expression $\frac{R_t}{(\text{WAC})(u_n+u_M)}$ is equal to SSR Health's definition of 1 – (total gross-to-net discount rate). Thus:

$$d^{(\text{reb})} = \frac{u_n}{u_n + u_M}\left(1 - d^{(\text{oth})}\right) + \frac{u_M}{u_n + u_M}\left(1 - g_M - d^{(\text{oth})}\right) - (1 - g_t) \qquad (\text{B}-11)$$

From Eq. B-5, it can be shown that:

$$\frac{u_M}{u_n + u_M} = \frac{g_t - g_n}{g_M - g_n} \quad \text{and} \quad \frac{u_n}{u_M + u_n} = \frac{g_M - g_t}{g_M - g_n} \qquad (\text{B}-12)$$

Combining Eq. B-11 and Eq. B-12 gives:

$$d^{(\text{reb})} = \frac{g_M - g_t}{g_M - g_n}\left(1 - d^{(\text{oth})}\right) + \frac{g_t - g_n}{g_M - g_n}\left(1 - g_M - d^{(\text{oth})}\right) - (1 - g_t) \qquad (\text{B} - 13)$$

We used Eq. B-13 to calculate $d^{(\text{reb})}$, the fraction of the WAC equal to the manufacturer rebate. We performed this calculation for each drug with SSR Health data, effectively separating out the rebate from wholesaler discounts and statutory Medicaid rebates. As stated in Section 3.3.1, we assume wholesalers receive a discount off WAC $d^{(\text{oth})}$ of 9 percent. In a small number of cases, we set the rebate to 0 percent because Eq. B-13 yielded a negative rebate. (For example, this could arise if the total gross-to-net discount was less than the assumed wholesaler discount of 9 percent.)

As described previously, we estimated that the PBM retains 0.4 percent of the manufacturer rebate. While the total rebate itself is quite large, the amount of the PBM retains is relatively small compared to other sources of PBM margins, and this is due to PBMs passing along a large portion of the manufacturer rebate to the third-party payer.

One limitation of Eq. B-13 is that it does not account for the best-price provision of the Medicaid rebate. However, this effect is likely relatively small. A recent study estimated that taking the best-price provision into account only led to an overall 2-3 percent reduction of AMP across 18 top-selling brand drugs between 2015 and 2019 (Clemans-Cope et al. 2023).

B.5 Estimating Pharmacy DIR

This section describes how we used the Iowa PBM Annual Reports(Iowa Insurance Division, 2020-2023) to estimate total DIR retained by PBMs, a portion of which we allocate to pharmacy DIR. In the Iowa PBM Annual Reports, each PBM discloses the total DIR they collect. According to the Iowa Code (Iowa Code 2023, Section 510B.1 (22, 3) , 2023):

> *[PBMs must report] all discounts and other negotiated price concessions paid directly or indirectly by a pharmaceutical manufacturer or other entity, other than a covered person, in the prescription drug supply chain to a pharmacy benefits manager, and which may be based on any of the following:*
> *a. A pharmaceutical manufacturer's list price for a prescription drug.*
> *b. Utilization.*
> *c. To maintain a net price for a prescription drug for a specified period of time for the pharmacy benefits manager in the event the pharmaceutical manufacturer's list price increases.*
> *d. Reasonable estimates of the volume of a prescribed drug that will be dispensed by a pharmacy to covered persons.*

The Iowa code further stipulates that this DIR (which the code refers to as "rebate," using a broad definition) does not include administrative fees that the manufacturer pays to the PBM; such administrative fees are reported separately in the Annual Reports.

In addition to the total DIR PBMs collect (excluding manufacturer administrative fees), the Iowa Annual Reports also show the amount of total DIR that the PBM retains. We aggregated these amounts for the years 2021 and 2022, which are presented in the reports from 2022 and 2023, respectively. We found that, on average PBMs retain 12.4 percent of the total DIR they collect from pharmacies and manufacturers:

$$\left(\text{manf. rebate} + \text{DIR}_{\text{ph}}\right)(0.124) = \text{total DIR retained} \qquad (\text{B} - 14)$$

where DIR_{ph} is the pharmacy DIR that the PBM collects. However, based on the 2019 GAO report, we assume only 0.4 percent of manufacturer rebate is retained.[43] We further assume that all of the collected pharmacy DIR is retained by the PBM.[44] Thus:

$$\text{DIR}_{\text{ph}} + (0.004)(\text{manf. rebate}) = \text{total DIR retained} \qquad (\text{B} - 15)$$

Setting Eq. B-14 equal to Eq. B-15 yields:

$$\left(\text{rebate} + \text{DIR}_{\text{ph}}\right)(0.124) = \text{DIR}_{\text{ph}} + (0.004)(\text{rebate}) \qquad (\text{B} - 16)$$

Rearranging Eq. B-16 gives an expression for the pharmacy DIR that the PBM collects.

$$\text{DIR}_{\text{ph}} = \left(\frac{0.124 - 0.004}{1 - 0.124}\right)\text{rebate} = (0.137)(\text{rebate}) \qquad (\text{B} - 17)$$

Accordingly, we assume that 13.7 percent of the computed rebate is pharmacy DIR that the PBM collects and retains in its entirety. While some DIR may be passed through to the payer (e.g., as in the case of Medicare Part D), much less is known about performance-based DIR, retrospective "true-up" fees (which often occur at the level of pharmacy networks), network participation fees, etc. However, one expert we spoke with speculated that PBMs may retain all or nearly all of these "non-traditional" forms of DIR, which likely contribute substantially to PBMs margins. Any pharmacy DIR that is passed through to the payer is not accounted in our model and would constitute an additional flow from PBM to payer. This would tend to decrease pharmacies' margins while leaving PBMs' margins unchanged.

[43] Iowa statute prohibits at least some forms of pharmacy DIR that we quantify in this report. Combining the Iowa PBM Annual Reports with the GAO report therefore carries an assumption that the fraction of total DIR that PBMs retain is the same in Iowa as in the United States overall, though there may be variation by state in the fraction of total DIR derived from pharmacy DIR versus other sources (e.g., manufacturer rebates).

[44] Here, we define pharmacy DIR broadly to capture all sources of DIR that a PBM collects from the pharmacy. This may include retrospective concessions to "true up" the PBMs' actual reimbursements with contract rates, penalties assessed by the PBM based on performance metrics, "pay-to-play" network participation fees, etc.

The methodology above is applicable for brand drugs whose rebates we calculated. For generic drugs, we assumed pharmacy DIR was 8 percent of the difference between pharmacies' sales price and acquisition cost, based on a 2019 analysis by Drug Channels Institute (Fein, 2019), as discussed in more detail previously.

APPENDIX C: ADDITIONAL ANALYSES

C.1 Study Sample Characteristics

Table C - 1 shows the number of unique molecule-formulation-manufacturer combinations in our sample. Table C - 2 presents the number of drugs and observations in the sample, by time period.

Table C - 1. Unique Molecule-Formulation-Manufacturer Combinations, 2022

Drug Characteristic	Number of Molecule-Form-Manufacturer Combinations			
	2020	2021	2022	2020-2022
Brand	122	107	97	136
Generic	1,113	1,267	1,433	1,540
Long Tenure [a]	477	538	608	666
Short Tenure	804	885	975	1,163
Biologic	14	13	13	14
Small Molecule	1,220	1,361	1,517	1,661
Acute Condition	436	491	542	598
Chronic Condition	808	896	1,001	1,090

[a] "Long" tenure refers to having more than 13 years or more than 9 years on the market for biologics and small molecules, respectively.

Table C - 2. Number of Drugs and Observations in Sample, by Time Period

Time Period	Number of Drugs (Number of Observations of Drugs) [a]						
	Type of Drug	Acute	Chronic	Biologic	Small Molecule	Long Tenure [b]	Short Tenure
2020-2022	Brand	83 (679)	272 (2,251)	31 (314)	324 (2,616)	203 (1,532)	194 (1,398)
	Generic	965 (7,882)	2,400 (20,178)	0 [c] (0)	3,365 (28,060)	2,363 (17,310)	1,257 (10,750)
	All Drugs	1,048 (8,561)	2,672 (22,429)	31 (314)	3,689 (30,676)	2,566 (18,842)	1,451 (12,148)
2020	Brand	64 (222)	249 (832)	27 (103)	286 (951)	167 (562)	166 (492)
	Generic	690 (2,357)	1,700 (5,540)	0 [c] (0)	2,390 (7,897)	1,565 (4,894)	894 (3,003)
	All Drugs	754 (2,579)	1,949 (6,372)	27 (103)	2,676 (8,848)	1,732 (5,456)	1,060 (3,495)
2021	Brand	68 (235)	203 (716)	28 (104)	243 (847)	136 (493)	136 (458)
	Generic	782 (2,576)	1,972 (6,814)	0 [c] (0)	2,754 (9,390)	1,794 (5,822)	1,043 (3,568)
	All Drugs	850 (2,811)	2,175 (7,530)	28 (104)	2,997 (10,237)	1,930 (6,315)	1,179 (4,026)
2022	Brand	67 (222)	184 (703)	27 (107)	224 (818)	140 (477)	123 (448)
	Generic	873 (2,949)	2,230 (7,824)	0 [c] (0)	3,103 (10,773)	1,975 (6,594)	1,188 (4,179)

Time Period	Number of Drugs (Number of Observations of Drugs) [a]						
	Type of Drug	Acute	Chronic	Biologic	Small Molecule	Long Tenure [b]	Short Tenure
	All Drugs	940 (3,171)	2,414 (8,527)	27 (107)	3,327 (11,591)	2,115 (7,071)	1,311 (4,627)

[a] Table presents number of unique drugs (i.e., 11-digit NDCs) in the sample for the given time period and with the given characteristic. Value in parentheses is number of unique observations of drugs (i.e., month and 11-digit NDC) in the sample.
[b] "Long" tenure refers to having more than 13 years or more than 9 years on the market for biologics and small molecules, respectively.
[c] The sample did not contain any biosimilar drugs.

C.2 Share of Expenditures, Detailed Tables

Table C - 3 presents the dollar values associated with the percentages of expenditures retained for each drug characteristic shown in Figure 4. For wholesalers, pharmacies, and PBMs these retained expenditures equal the total aggregate margins discussed in Section 4.2.2 and Section 4.2.3.

Table C - 3. Retained Expenditures of Retail Drugs, by Intermediary and Drug Characteristic, 2022 (Billions) [a]

Type of Drug	Intermediary	Overall	Acute	Chronic	Biologic	Small Molecule	Long Tenure [b]	Short Tenure [b]
Brand	Manufacturer	$124.6	$27.6	$97.1	$27.5	$97.1	$45.5	$79.1
	Wholesaler	$14.1	-$0.7	$14.9	$5.7	$8.5	$1.77	$12.4
	Pharmacy	-$0.5	$2.9	-$3.4	-$1.5	$0.9	$8.89	-$9.42
	PBM	$30.7	$6.4	$24.3	$9.2	$21.5	$11.1	$19.6
	Sample Size [c]	925	222	703	107	818	477	448
Generic	Manufacturer	$13.9	$6.4	$7.5	[d]	$13.9	$7.58	$6.32
	Wholesaler	$9.3	$4.7	$4.5	[d]	$9.3	$3.96	$5.30
	Pharmacy	$12.7	$5.3	$7.4	[d]	$12.7	$6.31	$6.43
	PBM	$29.9	$12.8	$17.1	[d]	$29.9	$14.9	$15.1
	Sample Size [c]	10,773	2,949	7,824	0	10,773	6,594	4,179
All Drugs	Manufacturer	$138.5	$34.0	$104.5	$27.5	$111.0	$53.1	$85.4
	Wholesaler	$23.4	$4.0	$19.4	$5.7	$17.7	$5.73	$17.7
	Pharmacy	$12.2	$8.2	$4.0	-$1.5	$13.7	$15.2	-$2.99
	PBM	$60.6	$19.2	$41.4	$9.2	$51.4	$26.0	$34.7
	Sample Size [c]	11,698	3,171	8,527	107	11,591	7,071	4,627

[a] Table presents weighted population estimates. Due to rounding, the totals for a given set of characteristics may not sum to the overall total for all drugs.
[b] "Long" tenure refers to having more than 13 years or more than 9 years on the market for biologics and small molecules, respectively.
[c] Sample size is the number of unique observations of drugs (i.e., month and 11-digit NDC) in the sample.
[d] Cannot be estimated because the sample did not contain any biosimilar drugs.

Table C - 4 shows the share of expenditures that each intermediary retains, by various drug characteristics.

Table C - 4. Retained Share of Total Expenditures on Retail Drugs, by Intermediary and Drug Type, 2022 [a]

Type of Drug	Intermediary	Acute	Chronic	Biologic	Small Molecule	Long Tenure [b]	Short Tenure [b]
Total Expenditures (Billion $)		$65.4	$169.3	$40.9	$193.9	$100.0	$134.8
Brand	Manufacturer	76.2%	73.1%	67.2%	75.9%	67.7%	77.8%
	Wholesaler	-2.0%	11.2%	13.9%	6.6%	2.6%	12.2%
	Pharmacy	8.0%	-2.6%	-3.6%	0.7%	13.2%	-9.3%
	PBM	17.8%	18.3%	22.5%	16.8%	16.5%	19.3%
	Total	100%	100%	100%	100%	100%	100%
	Sample Size [c]	222	703	107	818	477	448
Generic	Manufacturer	22.0%	20.4%	[d]	21.1%	23.2%	19.1%
	Wholesaler	16.2%	12.4%	[d]	14.1%	12.1%	16.0%
	Pharmacy	18.2%	20.3%	[d]	19.4%	19.3%	19.4%
	PBM	43.7%	46.9%	[d]	45.5%	45.4%	45.5%
	Total	100%	100%	[d]	100%	100%	100%
	Sample Size [c]	2,949	7,824	0	10,773	6,594	4,179
All drugs	Manufacturer	59.0%					
	Wholesaler	10.0%					
	Pharmacy	5.2%					
	PBM	25.8%					
	Total	100%					
	Sample Size [c]	11,698					

[a] Table presents weighted population estimates. Values may not add to 100% due to rounding.
[b] "Long" tenure refers to having more than 13 years or more than 9 years on the market for biologics and small molecules, respectively.
[c] Sample size refers to the number of unique observations of drugs (i.e., month and 11-digit NDC).
[d] Cannot be estimated because the sample did not contain any biosimilar drugs.