Pharmaceutical Pricing

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Abstract

This chapter examines pharmaceutical pricing through a five-part framework: Cost, Customers, Channels, Competitors, and Compatibility. We synthesize how research and development (R&D) risk, patent and exclusivity rules, insurer design, healthcare providers, patients, and intermediaries including pharmacy benefit managers (PBMs), wholesalers, pharmacies, and group purchasing organizations (GPOs), jointly shape list and net prices. The chapter distinguishes small-molecule and biologic cost structures; explains how patents, generics, and biosimilars alter competitive conduct; and shows how formularies, cost-sharing, copay programs, and patient-assistance mechanisms reallocate spending. We also integrate recent policy interventions, including Medicare Part D reforms, transparency mandates, drug-importation rules, and the Inflation Reduction Act (IRA) negotiation authority, and discuss their implications for innovation incentives and patient access.

The chapter concludes with a forward-looking research agenda focused on developing innovative pricing models for high-cost therapies; examining global benchmarking and trade policies that influence R&D investment and affordability; assessing the effects of patient-assistance programs, copay coupons, and digital discount platforms; analyzing intermediary behavior and biosimilar competition within evolving market structures; and evaluating the impact of new U.S. pricing regulations through causal policy analysis.

1 Introduction

Pharmaceutical pricing emerges from the interaction of scientific uncertainty, economic incentives, and institutional design. High, risky research and development (R&D) investment and exclusivity protections unfold alongside multi-layered insurance, intermediation by pharmacy benefit managers (PBMs), wholesalers, pharmacies, and group purchasing organizations (GPOs), and expanding regulation. In this environment, the link between underlying costs and the prices faced by patients is indirect: strategic contracting, reimbursement rules, promotion, and policy choices generate a series of wedges—most prominently between list and net prices—that ultimately disconnect patient prices from production costs.

We organize the chapter around the five critical Cs of pricing (Albrecht et al., 2023). **Cost** examines R&D and manufacturing economics for small molecules and biologics, emphasizing the incomplete pass-through from production expenses to market prices and the global distribution of R&D investment under emerging benchmarking frameworks. **Customers** analyzes how insurance design, physician behavior, and

patient-assistance mechanisms—including copay coupons, accumulator bans, and cash-discount—shape affordability, adherence, and welfare outcomes. **Channels** investigates the roles of wholesalers, PBMs, retail pharmacies, and GPOs in transmitting and transforming prices through contracting, vertical integration, and information asymmetries along the supply chain. **Competitors** compares branded, generic, and biosimilar markets, highlighting how promotion, rebate structures, and physician adoption behavior generate distinct competition dynamics for biologics relative to small-molecule generics. **Compatibility** integrates perspectives on profitability, corporate responsibility, and regulation—including recent U.S. reforms such as the Inflation Reduction Act (IRA) negotiation authority, transparency mandates, state-level copay reforms, and renewed international benchmarking under the revived Most-Favored-Nation (MFN) framework.

Across these dimensions, three structural shifts motivate our synthesis. First, the rise of biologics, gene therapies, and precision medicine heightens the mismatch between fixed development outlays and per-dose pricing. Second, new channels—cash-discount platforms and vertically integrated PBM-insurer-pharmacy systems—reshape steering, pass-through, and transparency. Third, policy reforms in the United States and abroad, from negotiation and accumulator bans to MFN- style benchmarking, create natural experiments that will redefine competitive conduct and the allocation of surplus among payers, patients, and firms.

The following sections examine these dynamics in turn. Section 2 details R&D and manufacturing economics and the limits of cost-to-price pass-through. Section 3 studies consumers, physicians, and benefit design, including patient assistance, copay policy, and cash-discount cards. Section 4 analyzes intermediaries (wholesalers, PBMs, pharmacies, GPOs) as price-transmission mechanisms. Section 5 contrasts generic and biosimilar competition and the role of transparency. Section 6 integrates profitability, corporation social responsibity (CSR), and regulation, emphasizing marketing and cross-border spillovers from pricing rules. Section 7 sets a forward-looking research agenda on pass-through measurement, quasi-experimental policy evaluation (including IRA implementation and MFN targeting), market structure, biosimilar adoption, dynamic pricing, and AI-enabled price and access optimization.

2 Cost

Pharmaceutical pricing is a multifaceted issue, shaped by numerous factors throughout the entire journey of drug development and production. At the heart of this complexity are the costs tied to R&D and manufacturing. These costs play a critical role in determining whether new drugs can be economically viable and accessible to patients globally.

The R&D phase is fraught with challenges and demands significant resources, often stretching over years filled with scientific inquiry, clinical trials, and regulatory hurdles before a drug reaches consumers (DiMasi et al., 2016; Wouters et al., 2020). This stage is crucial for fostering innovation and discovering new therapies that address unmet medical needs. Nonetheless, the hefty financial outlay required for R&D significantly influences drug pricing, as companies strive to recover their investments and support ongoing research (Deloitte Centre for Health Solutions, 2023).

While research and development costs dominate overall pharmaceutical spending, manufacturing remains an essential, though unevenly important, component of drug pricing. For patented small-molecule drugs, production is relatively straightforward and accounts for only a small fraction of total costs, as R&D expenditures and marketing typically far exceed manufacturing outlays. In contrast, for generic small molecules, where R&D costs have already been absorbed by originators, manufacturing constitutes the primary cost component, though absolute production costs remain low due to process efficiencies and economies of scale.

By comparison, biologics, complex products derived from living organisms, require highly specialized and resource-intensive production processes that substantially elevate manufacturing expenses and, in turn, market prices (Farid et al., 2020; Shukla and Thömmes, 2010). Moreover, compliance with stringent good manufacturing practice and quality assurance standards further increases these costs (European Medicines Agency, 2022), shaping pricing strategies and influencing global supply dynamics.

This section investigates the intricate dynamics of R&D and manufacturing expenses, analyzing their impact on pharmaceutical pricing strategies. By scrutinizing the distinct challenges and cost structures associated with small molecule drugs and biologics, we aim to shed light on the economic forces driving the pharmaceutical industry.

2.1 Research and Development

Within this cost structure, R&D plays a central role in shaping pharmaceutical innovation and pricing incentives. Patent protection and the global distribution of R&D costs are equally vital. Patents grant a period of market exclusivity, encouraging the significant investments required for drug development (Grabowski, 2002). Patent exclusivity prevents generic entry during the patent period, shaping firms' pricing strategies and delaying affordability and access gains until generics enter after patent expiration. The international spread of R&D costs highlights the collaborative spirit of pharmaceutical innovation, with substantial contributions from the United States, Europe, and growing Asian markets (European Federation of Pharmaceutical Industries and Associations, 2024). Cross-border partnerships and cost-sharing agreements allow firms to pool scientific expertise, share clinical-trial risk across jurisdictions, and coordinate global launch strategies, with downstream implications for international price setting and market access (Munos, 2009).

2.1.1 Product Innovation

Product innovation in the pharmaceutical industry is a multifaceted endeavor, focused on discovering, designing, and developing new treatments to meet unmet medical needs and improve patient outcomes. This journey is laden with substantial scientific, regulatory, and financial risks, often demanding billions of dollars and many years of effort before a single product reaches the market (DiMasi et al., 2016; Wouters et al., 2020; European Federation of Pharmaceutical Industries and Associations, 2024). The high costs of innovation primarily arise from the intricate process of identifying promising molecular targets, conducting extensive clinical trials, and navigating complex global regulatory approvals.

Advancements in biomedical sciences, such as genomics, proteomics, and high-throughput screening techniques, play a crucial role in driving pharmaceutical innovation (Paul et al., 2010). Additionally, the increasing prevalence of chronic, complex, and rare diseases creates a demand for specialized treatments (Organisation for Economic Co-operation and Development, 2018). Health systems and payers also emphasize the need for evidence of cost-effectiveness and real-world value (Garrison Jr et al., 2007; IQVIA Institute for Human Data Science, 2023).

Pharmaceutical product innovation unfolds through a multi-phase R&D pipeline, each stage presenting its own challenges and costs:

- Discovery & Preclinical Testing: This initial phase focuses on pinpointing and validating therapeutic targets using both in vitro (lab-based) and in vivo (animal-based) experiments. These studies offer early safety profiles and efficacy signals, helping to narrow down potential candidate compounds (Scannell et al., 2012).

- Clinical Trials (Phases I–III): Candidates that show promise in preclinical testing move on to human trials. Phase I focuses on safety and dosage in a small group of healthy volunteers or patients. Phase II tests efficacy, fine-tuning dosage and assessing side effects in a targeted patient group. Phase III aims to confirm the therapeutic benefits over existing treatments or placebo in larger, more diverse populations (Wouters et al., 2020).
- Regulatory Review & Approval: Successful Phase III trials lead to the submission of a New Drug Application (NDA) or Biologics License Application (BLA) to regulatory bodies like the U.S. Food and Drug Administration (FDA) or the European Medicines Agency (EMA). Approval requires strong safety and efficacy data, high manufacturing quality, and clear labeling instructions (DiMasi et al., 2016).
- Post-Marketing Surveillance (Phase IV): Even post-approval, further studies often monitor long-term safety, broader patient outcomes, and potential off-label uses. This continuous monitoring adds to the overall costs of innovation.

Costs rise with each phase due to the complexities of clinical trials, the need for specialized manufacturing (particularly for biologics), and a high failure rate, with only a small percentage of candidates ultimately gaining approval (Deloitte Centre for Health Solutions, 2023; IQVIA Institute for Human Data Science, 2023). These factors create significant financial risk for companies, impacting how new products are priced.

Pharmaceutical innovation is inherently collaborative, relying on the combined strengths of academia, government, and industry to translate scientific discoveries into viable therapies. Academic institutions contribute foundational research and early-stage target identification, while private firms provide the capital, infrastructure, and commercialization expertise necessary to advance products through development and regulatory approval. Government agencies and public research institutes often play a catalytic role by funding high-risk basic research and fostering translational initiatives. Such public–private partnerships can accelerate the transition from laboratory findings to clinical applications by pooling expertise and resources (Munos, 2009; European Federation of Pharmaceutical Industries and Associations, 2024). However, they also raise important challenges concerning intellectual property rights, data governance, and revenue-sharing arrangements, underscoring the need for transparent frameworks that balance innovation incentives with public benefit.

The substantial and high-risk investment required for pharmaceutical product innovation exerts a direct and lasting influence on pricing strategies. Manufacturers typically set launch prices with the dual objective of recouping accumulated R&D expenditures and financing future research pipelines (DiMasi et al., 2016; Deloitte Centre for Health Solutions, 2023). This recovery pressure is intensified by the limited duration of effective patent exclusivity—often less than the nominal 20-year term once regulatory and development delays are accounted for—prompting firms to pursue substantial initial revenues before the entry of generics or biosimilars erodes market share (Grabowski, 2002; European Federation of Pharmaceutical Industries and Associations, 2024). Consequently, new drug launches have exhibited a steady upward trend in list and net prices over the past decade, reflecting both higher R&D risk and evolving market expectations (IQVIA Institute for Human Data Science, 2023). These dynamics have drawn heightened scrutiny from government agencies, insurers, and health technology assessment (HTA) bodies, which increasingly evaluate drugs not only on clinical benefit but also on cost-effectiveness and budget impact. Their collective challenge is to strike a sustainable balance between rewarding innovation and maintaining affordability and equitable access to essential therapies.

2.1.2 Patent Protection

Patent protection is a cornerstone of the pharmaceutical industry, providing innovators with exclusive rights to produce, use, and sell their patented inventions for a set period, usually 20 years from the filing date. This legal shield is essential for recouping the significant R&D investments needed to bring new drugs to market (DiMasi et al., 2016; Grabowski, 2002). Patents act as both an incentive and a reward for innovation, allowing companies to earn revenue during their market monopoly. Once this period ends, lower-priced generic alternatives can enter the market.

Pharmaceutical R&D involves exceptionally high costs, lengthy development timelines, and substantial risk, with only a small fraction of drug candidates ultimately reaching approval (Wouters et al., 2020). In the absence of patent protection, immediate price competition would erode potential revenues, making it difficult for firms to recover their investments and thereby weakening incentives for future innovation (Cockburn, 2009). Patent exclusivity provides a temporary period of market protection that allows innovators to earn a return on successful discoveries and reinvest in subsequent research. From a societal perspective, an effective patent system must balance dynamic efficiency, rewarding innovation and risk-taking, with static efficiency, which ensures that affordable access expands once generic or biosimilar competitors enter the market.

Pharmaceutical companies employ various strategies to extend or optimize their patent protection. One common method, known as “evergreening," involves acquiring secondary or follow-on patents for minor modifications of existing products, such as new formulations, dosing schedules, or routes of administration. These tactics can delay the entry of generic competition, allowing companies to maintain revenue beyond the original patent’s expiration. Additionally, regulatory mechanisms like “patent term restoration" (to compensate for time lost in development and regulatory review) and supplementary protection certificates (in the European Union) offer partial extensions of market exclusivity (National Academies of Sciences, Engineering, and Medicine. , 2020). Critics argue that these extensions may not always represent genuine scientific advancements and can hinder competition, keeping drug prices high. Recent policies such as the U.S. IRA’s negotiation provisions have renewed attention to the patent–price balance (HHS, 2023).

Patent exclusivity grants manufacturers temporary market power, often leading to higher launch prices due to limited competition (Grabowski, 2002). Firms justify these elevated prices as necessary to recoup substantial R&D expenditures and compensate for the high probability of failure across the development pipeline (DiMasi et al., 2016; Deloitte Centre for Health Solutions, 2023). However, payers and policymakers increasingly scrutinize such pricing practices to ensure that essential medicines remain affordable for both patients and health systems. HTA agencies, insurers, and government bodies now routinely evaluate new drugs through cost-effectiveness and budget impact analyses, using these findings to guide reimbursement negotiations and price caps (European Federation of Pharmaceutical Industries and Associations, 2024). In the United States, policy initiatives such as the IRA’s drug price negotiation provisions reflect growing efforts to realign exclusivity-driven pricing with societal value (HHS, 2023). Overall, patent protection and pricing dynamics remain deeply intertwined, shaping not only the financial sustainability of pharmaceutical innovation but also the affordability and accessibility of novel therapies.

2.1.3 International Share of R&D Cost

Pharmaceutical R&D is a global enterprise, with major contributions from the United States, the European Union, and an expanding group of Asian economies such as China and Japan (European Federation of Pharmaceutical Industries and Associations, 2024; Wouters et al., 2020). Historically, the United States

has accounted for the largest share of biopharmaceutical R&D spending, supported by a deep venture-capital market, extensive industry–academic collaboration, and a regulatory climate that rewards innovation (Cockburn, 2009). Europe remains a central R&D hub, sustained by public–private partnerships and world-class academic institutions, though its relative share has shifted over time as regulatory frameworks evolved and competition from emerging markets intensified (DiMasi et al., 2016).

Current estimates attribute roughly 40–50% of global pharmaceutical R&D spending to the United States and 25–30% to Europe, with the remainder spread across rapidly developing Asian markets (European Federation of Pharmaceutical Industries and Associations, 2024; Scannell et al., 2012). These regional differences mirror variations in pricing and reimbursement systems: in the U.S., higher average drug prices help offset the heavy costs of clinical trials and early-stage research (Grabowski, 2002), whereas price controls and stricter reimbursement in Europe and Asia constrain margins but broaden access to innovative therapies. Consistent with this mechanism, evidence from cross-country demand shocks indicates that pharmaceutical innovation responds strongly to expected market size and revenue rather than to development costs per se. Using quasi-exogenous variation in market size across countries and therapeutic classes, Dubois et al. (2015) show that larger effective demand generates substantially more pharmaceutical innovation.

The tension between innovation incentives and affordability keeps U.S. pricing policy tightly linked to international benchmarks. In 2018–2020, federal initiatives such as the American Patients First blueprint and the proposed MFN model sought to prevent Americans from paying more than patients in other high-income countries for certain Medicare-covered drugs (U.S. Department of Health and Human Services, 2018; Centers for Medicare & Medicaid Services, 2020). In 2025, the administration revived this international-comparison approach: an executive order directed the United States Department of Health and Human Services (HHS)/the Centers for Medicare & Medicaid Services (CMS) to set MFN pricing targets, and the White House announced company-specific MFN- style agreements (e.g., with Pfizer in September 2025 and AstraZeneca in October 2025) that extend MFN pricing to state Medicaid programs and enable direct-to-consumer discounts (U.S. Department of Health and Human Services, 2025; The White House, 2025a,b).

Legal analyses highlight unresolved questions regarding the statutory authority and durability of broad MFN mandates. Nonetheless, the renewed emphasis on international price comparison, now pursued through executive actions and voluntary MFN-style agreements, directly affects how global R&D costs are recovered and distributed (Congressional Research Service, 2025). These executive actions and MFN-style agreements complement broader U.S. pricing reforms that are discussed in detail in Section 6, where we examine how recent legislation and administrative actions jointly shape domestic and international pricing alignment.

Despite trailing the U.S. in total investment, Europe remains an attractive environment for advanced research. Large consortia funded by the European Commission and national governments facilitate resource and expertise exchange among companies, universities, and research institutes. Meanwhile, China, South Korea, and Singapore have dramatically expanded government-supported research, built state-of-the-art facilities, and promoted domestic entrepreneurship, gradually reshaping the geography of pharmaceutical R&D (Wouters et al., 2020).

Pharmaceutical innovation increasingly relies on international collaboration to leverage specialized expertise, recruit diverse patient populations, and spread financial risk (Munos, 2009). Global clinical trials allow firms to generate more representative safety and efficacy data and to accelerate multi-region regulatory submissions. Such cross-border efforts, while reducing per-country development costs, also require regulatory harmonization, data-governance alignment, and risk-sharing agreements—issues often negotiated through international bodies and trade associations (Cockburn, 2009).

The worldwide distribution of R&D costs thus shapes launch sequencing and pricing strategy. Firms typically introduce new products first in high-revenue markets like the United States to recoup development expenditures, followed by tiered-pricing or differential-access strategies in other regions (Verniers et al., 2011). Policymakers everywhere continue to balance the goals of sustaining innovation and ensuring affordability. Recent U.S. actions to benchmark domestic drug prices against those in peer countries, the revival of the MFN framework through 2025 executive orders and company-specific MFN agreements, reflect a broader global movement toward cross-national price coordination. As emerging economies expand their R&D roles, such international comparisons may accelerate the harmonization of policies aimed at controlling costs, promoting transparent pricing, and supporting equitable technology transfer. These developments underscore the interdependence of international R&D investment, pricing policy, and patient access.

2.2 Manufacturing Cost

While research and development often dominate discussions of pharmaceutical expenditures, manufacturing costs are a critical, yet frequently underestimated, determinant of a drug's final price. Converting a candidate compound into a safe, stable, and consistently high-quality product is capital-intensive and must comply with stringent GMP standards in specialized facilities (European Federation of Pharmaceutical Industries and Associations, 2024). The nature of the product strongly affects the costs: small-molecule drugs are generally less expensive to scale up than complex biologics, which depend on living systems and tightly controlled environments (DiMasi et al., 2016).

The spread of advanced manufacturing technologies, such as continuous processing, single-use bioreactors, and automated analytics, has the potential to reshape production economics. These innovations influence not only production costs but also global supply-chain resilience, competitive dynamics, and ultimately patient access to medicines (Wouters et al., 2020). The following subsections examine how manufacturing costs differ for small molecules and biologics and how these differences translate into distinct pricing strategies worldwide.

2.2.1 Small Molecule Drugs

Small-molecule drugs, defined by low molecular weight (typically under 1,000 daltons), form the backbone of modern pharmacotherapy. Their chemical synthesis methods make production comparatively predictable, allowing generics—from aspirin to statins—to dominate global volume. Manufacturing costs remain central to pricing, shaping both affordability and profitability. Understanding these costs clarifies how firms compete on efficiency and market access, particularly in lower-income regions.

Raw-material sourcing represents a major expense, especially for complex molecules, highlighting the importance of procurement strategy and supply-chain management. Efficient sourcing directly lowers cost of goods and expands access in price-sensitive markets.

Several factors contribute to the variability in manufacturing costs for small molecule drugs, each impacting production economics and pricing strategies:

- Complexity of the Molecule: Drugs requiring intricate synthesis or advanced purification techniques tend to incur higher costs. For instance, molnupiravir's patented synthesis route involves expensive reagents and multiple steps, in contrast to more streamlined alternatives (Peterson et al., 2022).
- Scale of Production: Larger production volumes can leverage economies of scale, reducing per-unit

costs. This is particularly important for generics, where scaling up from early-phase to commercial production optimizes resource utilization.

- Manufacturing Location: Geographic differences in labor, energy, and infrastructure costs significantly affect manufacturing expenses. Countries like India and China, which are key suppliers of active pharmaceutical ingredients (APIs), can offer costs as low as $1 per kilogram for generics, while complex APIs might exceed $10,000 per kilogram, driving outsourcing trends (Hill et al., 2018).

- Process Efficiency: Process efficiency, measured by metrics like Process Mass Intensity (PMI), which can range from 70 to 433 kg of materials per kg of API, is crucial. Efficient processes reduce material and waste costs, enhancing overall cost-effectiveness (McKinsey & Company, 2024).

Together these factors define the cost structure of small-molecule production, with scale and geography serving as key levers for cost reduction.

In pricing terms, manufacturing costs for small molecules often take a back seat to R&D and marketing expenditures, yet they remain fundamental. Low costs make intense price competition possible in generic markets, improving affordability and penetration in developing economies. By contrast, branded new chemical entities (NCEs) command higher prices under patent protection to recoup R&D outlays; after patent expiry, cost optimization determines post-exclusivity profitability. Strategic outsourcing to low-cost regions such as India illustrates how firms balance efficiency with quality in global pricing decisions.

2.2.2 Biologics

Biologics are pharmaceutical products derived from living organisms. They include a wide array of therapies such as monoclonal antibodies (e.g., adalimumab), vaccines, and gene therapies. Unlike small molecule drugs, biologics are manufactured through intricate biotechnological processes, leading to significantly higher production costs. These elevated costs have a substantial impact on pricing strategies, shaping the economics of pharmaceutical markets and influencing affordability, access, and competition.

In this section, we will explore the factors contributing to these high manufacturing costs, offering insights based on current industry data and academic research. Understanding these factors is crucial for comprehending the complex dynamics at play in the production and pricing of biologics.

Several factors influence the manufacturing costs of biologics, each of which has significant economic and strategic implications.

- Complexity of the Manufacturing Process: The use of living cells and processes such as aseptic filling drive up costs. Purification steps, like protein A chromatography, are particularly costly due to their specificity and resource demands (Shukla and Thömmes, 2010).

- Scale of Production: Larger production scales can reduce unit costs by spreading fixed expenses, such as facility costs, over a greater output. For instance, scaling up from pre-clinical volumes (hundreds of liters) to Phase III volumes (thousands of liters) can lead to significant cost reductions (Farid et al., 2020).

- Regulatory Requirements: Compliance with stringent GMP standards and validation, including process performance qualification (PPQ) batches, adds to expenses, reflecting the high safety standards required for biologics (Farid et al., 2020).

- Type of Biologics: Costs vary depending on the product type. Monoclonal antibodies (mAbs) produced using mammalian cells are generally more expensive than vaccines produced using microbial systems. Gene therapies involve additional complexities, such as personalized production (Makurvet, 2021).
- Manufacturing Location: Unlike small molecule drugs, which benefit from low-cost production in regions like India, biologics require sophisticated facilities often situated in high-cost areas like the US or Europe, limiting geographic cost advantages (Hill et al., 2018).

Scale and process complexity are decisive: larger runs reduce unit cost but demand heavy capital investment. For biologics, manufacturing expenses form a substantial share of overall cost even though R&D (roughly $1.8 billion per approved therapy) dominates total spending. These high production costs justify premium pricing for patented biologics consistent with their clinical value. Cost-reduction efforts, through continuous manufacturing, modular facilities, and biosimilar development, aim to expand affordability and access, though initial investments remain high. Outsourcing to specialized contract manufacturing organizations (CMOs) can enhance efficiency while maintaining quality.

Manufacturing costs are a cornerstone of pharmaceutical pricing, influencing both affordability and profitability. For small-molecule drugs, relatively low production costs underpin intense price competition among generics, expanding market access. Branded small-molecule products, in contrast, carry higher prices that reflect R&D recovery and patent protection. Biologics, with their complex production processes and strict regulatory oversight, command premium prices but remain the focus of efficiency initiatives. Technological advances and strategic approaches, such as biosimilar development and outsourcing to specialized CMOs, continue to reshape the cost structure of manufacturing, enhancing access while maintaining product quality. Understanding these interactions is essential for policymakers, manufacturers, and payers seeking to balance cost, value, and accessibility in an industry where innovation and public health must advance together.

2.2.3 Cost-to-Price Pass-Through and Empirical Evidence

While firms frequently justify high launch prices by citing large R&D outlays, empirical evidence shows a weak direct link between development cost and observed market price. Wouters et al. (2022) find no statistical relationship between firm-reported R&D investments and launch list prices across 60 U.S. drugs, suggesting that market power and payer incentives dominate cost-based explanations. Nevertheless, R&D costs remain substantial and heterogeneous across therapeutic areas, supporting price dispersion even when cost pass-through is incomplete (DiMasi et al., 2016; Wouters et al., 2020).

Manufacturing costs exhibit similarly uneven translation into prices. Cost-based benchmarking studies estimate that feasible production prices for many WHO essential small-molecule medicines could be a fraction of current market prices (Hill et al., 2018; Gotham et al., 2019). For biologics, process-development and quality-assurance expenses represent a materially larger share of total cost, explaining the slower post-entry price declines observed for biosimilars (Farid et al., 2020; Yang et al., 2020). Finally, shocks to API supply chains and trade frictions can raise marginal production costs with partial pass-through to retail prices, depending on contracting structure and market concentration. Overall, these studies highlight that while cost fundamentals set a floor for pricing, observed prices primarily reflect strategic and institutional layers added atop production economics.

3 Customer

In pharmaceutical markets, decision-making authority is distributed across consumers, payers, and decision makers, creating a complex and interdependent ecosystem. Patients, insurers, and physicians, respectively, exert distinct yet overlapping influences on drug access and pricing.

This section examines how these actors interact and how their incentives shape pharmaceutical pricing outcomes. The decision-making process for prescription drugs is especially intricate: physicians prescribe medications based on clinical judgment, yet patients ultimately bear much of the financial burden, with affordability largely determined by insurance coverage. Adding to this complexity, patient assistance programs (PAPs) and copay accumulator programs can both alleviate and exacerbate financial pressures, offering cost relief for some patients while introducing new barriers for others.

3.1 Consumers and Insurance

Consumers respond to drug prices through intertwined economic, informational, and behavioral channels. Although overall demand for prescription medicines is relatively price-inelastic, out-of-pocket costs can meaningfully affect adherence, treatment discontinuation, and therapeutic substitution. Faced with higher copayments or coinsurance, many patients reduce medication use or switch to lower-cost alternatives, while others forgo treatment altogether, especially for chronic or asymptomatic conditions (Danzon et al., 2015a).

Evidence from the RAND Health Insurance Experiment demonstrates that consumers react strongly to the prices they face at the point of care. The estimated elasticity of medical spending with respect to out-of-pocket price is approximately –0.2, with larger responses for discretionary and outpatient services (Newhouse and the Insurance Experiment Group, 1993). Subsequent studies in Medicare and employer-sponsored plans show that higher cost sharing reduces both office visits and prescription utilization, though some of these savings are offset by higher downstream spending among patients (Baicker and Goldman, 2011; Brot-Goldberg et al., 2017; Goldman et al., 2007). Nonlinear benefit designs also produce sharp behavioral responses: under Medicare Part D, beneficiaries reduce utilization and bunch near coverage thresholds when marginal prices rise, consistent with significant price sensitivity in prescription demand (Einav et al., 2015). Field evidence also shows that when out-of-pocket prices fall to zero, consumer responses can be discrete rather than marginal. Using Swedish prescription data and a regression discontinuity design, Ching et al. (2022) document a significant zero-price effect, whereby the share of patients choosing the lowest-priced drug increases when its copayment drops to zero.

Beyond direct price exposure, information and perception also shape consumer behavior and effective prices. Direct-to-consumer advertising (DTCA) enhances patient awareness of diseases and available treatments (Liu and Gupta, 2013), which can prompt more patients to seek medical consultation (Liu and Gupta, 2011; Liu et al., 2020). In addition, even when visits would have occurred regardless, DTCA increases the likelihood that patients request specific therapies during physician encounters (Liu and Gupta, 2011). These mechanisms can raise prescriptions for branded drugs relative to generic alternatives. The awareness generated by DTCA can also produce spillover effects within drug classes: rather than increasing sales only for the advertised brand, advertising may expand total category demand and benefit competing products as well (Liu and Gupta, 2011; Liu et al., 2015; Shapiro, 2018).

Beyond direct price exposure, information and perception shape consumer behavior and effective prices. Direct-to-consumer advertising (DTCA) increases brand awareness and stimulates patient requests for specific therapies (Pareek et al., 2019), often raising prescriptions for branded over generic products (Liu and

Gupta, 2011). While DTCA can enhance disease awareness and promote earlier diagnosis, it also generates spillovers within drug classes. Instead of only increasing sales of the advertised brand, it often expands total category demand.(Shapiro, 2018).

Insurance companies, in turn, play a crucial role as payers, influencing access through formulary restrictions and cost-sharing mechanisms. The U.S. health insurance system differs from those of most other countries in several key respects. Unlike nations with universal public coverage (e.g., the United Kingdom, Canada, Sweden), the United States relies heavily on employer-sponsored and privately purchased insurance. This structure mitigates adverse selection but limits equity and can create "job lock," tying coverage to employment. The U.S. also provides means-tested programs such as Medicaid to promote equity but at the cost of higher taxes and potential moral hazard. To control moral hazard, the system relies on cost-sharing (e.g., copayments and deductibles), which curbs overconsumption but can compromise equity relative to countries with zero-cost-sharing models.

In terms of health-system regulation, the United States depends largely on private hospitals governed by antitrust laws, limiting direct government intervention but sometimes fostering an expensive "medical arms race." Additionally, "last-resort" laws ensure emergency care regardless of ability to pay, improving equity but increasing fiscal burden (Bhattacharya et al., 2014).

The differences in insurance systems between the United States and other countries highlight the trade-off in health policy among the three competing goals of "health," "wealth," and "equity," which is called the health policy trilemma. This trilemma is closely related to the adverse effects of health insurance coverage. The health insurance market is characterized by severe information asymmetry, which exacerbates market failure and market distortions, leading to selection problems and pricing inefficiencies(Boone, 2024). Information asymmetry typically reduces consumers' price sensitivity(Danzon et al., 2015a), resulting in moral hazard effects. Simultaneously, information asymmetry also contributes to adverse selection, where individuals with poor health are more likely to purchase insurance, while healthier individuals may opt out of the market. As a result, achieving an "optimal" health policy remains unattainable. Insurers can only mitigate the adverse effects of health insurance through strategies such as co-payment mechanisms, contractual provisions (e.g., deductibles), differential pricing, and cost-sharing mechanisms(Herr and Suppliet, 2017).

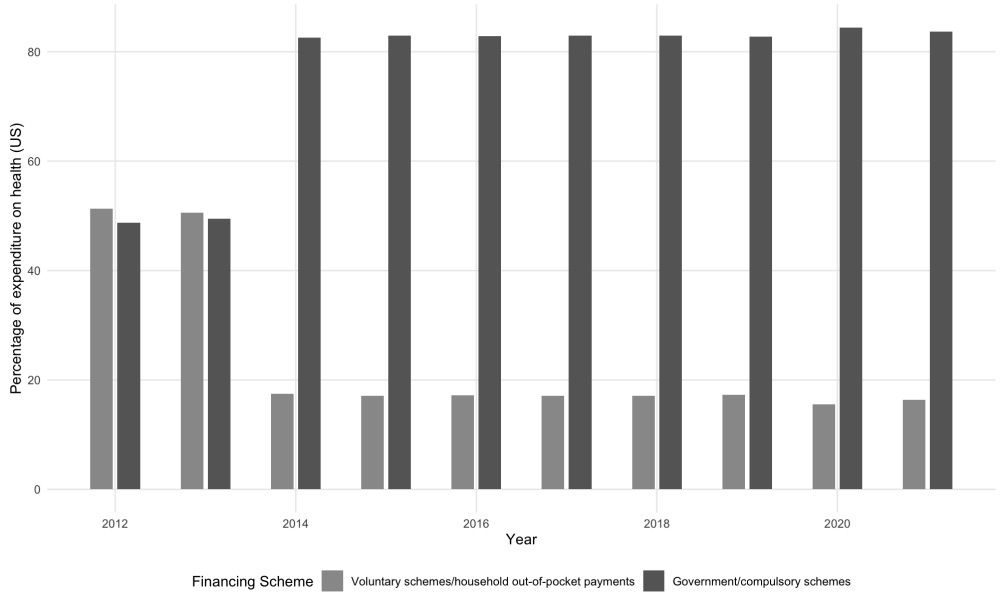

Figure 1: Out of pocket and compulsory government health spending, United States

Source: Data from OECD, Health spending. `https://www.oecd.org/en/data/indicators/health-spending`. Accessed on Feb 10, 2026.

At the same time, the government can also design better insurance policies to mitigate the adverse effects of insurance and enhance social welfare. As illustrated in Figure 1, government/compulsory healthcare expenditure in the United States has demonstrated a consistent upward trajectory over the observed period, while the proportion of out-of-pocket expenditure has gradually declined. This trend is particularly pronounced during the 2013–2014 period, reflecting a significant shift in the financial burden from individuals to public funding sources. The significant shift can largely be attributed to the implementation of the Affordable Care Act (ACA)[1], which has primary goal to make affordable health insurance available to more people, thereby reducing out-of-pocket costs for patients.

Prescription drug coverage provides a clear illustration of how public insurance design can influence prices and utilization without administratively setting prices. Under Medicare Part D, the federal government relies on private plan competition and formulary contracting rather than direct price controls. Using the introduction of Part D, Duggan and Scott Morton (2010) show that enrollees paid lower prices and increased utilization relative to being uninsured, with larger price reductions concentrated in therapeutic classes facing greater competition. Subsequent work demonstrates that these pricing outcomes are mediated by consumer choice frictions and insurer incentives: beneficiaries often select dominated plans and respond imperfectly to price signals (Abaluck and Gruber, 2011, 2016), but gradually learn and switch toward lower-cost options over time (Ketcham et al., 2012), while subsidy design and plan competition shape insurers' contracting and bidding behavior (Decarolis et al., 2020). Together, this evidence underscores how insurance design, rather than direct price regulation, shapes the effective prices faced by patients.

There have indeed been several policies designed to correct distortions and improve efficiency in the health insurance market. The Medicare Part D Reforms (2019) required insurers to provide more flexible drug plans

[1]The Patient Protection and Affordable Care Act, referred to as the Affordable Care Act or "ACA" for short, is the comprehensive health care reform law enacted in March 2010. `https://www.hhs.gov/healthcare/about-the-aca`.

within the Part D program. The Transparency in Coverage Rule (2020) mandated private health insurance plans and employer-sponsored health plans to disclose pricing information. The IRA granted Medicare Part D the authority to negotiate drug prices. These policies aim to reduce patients' out-of-pocket expenditures, enhance transparency in the health insurance market, and encourage insurers to improve the efficiency of pharmaceutical benefit management.

3.2 Physicians

Physicians' prescribing behavior reflects a complex interplay of professional judgment, economic incentives, institutional constraints, behavioral tendencies, and informational frictions. These forces determine not only whether a physician opts for a brand-name drug or its generic equivalent but also how such choices aggregate to influence overall market efficiency. Physicians do not respond to full market prices in a standard consumer sense. Instead, physicians respond to drug prices primarily through institutional and behavioral channels rather than direct price sensitivity. Formularies and utilization management tools implemented by PBMs shape prescribing by promoting on-formulary or lower-cost substitutes through education, prior authorization, and incentive alignment (Shrank et al., 2009).

Empirical evidence confirms that physicians' price responsiveness is limited. Since prescribers often lack direct knowledge of drug prices, their decisions reflect weak sensitivity to price signals. Using drug-switching data, Shin et al. (2026) estimate that only about 28.5% of physicians in the statin category are primarily cost-saving oriented, while most base decisions on perceived clinical benefit, habit, or concern of side effects. This heterogeneity underscores the modest role of price in everyday clinical decision-making.

Physician-directed marketing exerts substantial influence on prescribing behavior. Pharmaceutical firms deploy personal selling through sales representatives (detailing) (Gönül et al., 2001; Ching and Ishihara, 2010, 2012; Liu et al., 2016), the distribution of free drug samples, sponsorship of professional meetings and educational events (Liu et al., 2015; Narayanan et al., 2004), and advertising in medical journals (Liu and Gupta, 2012) to maintain brand familiarity and reinforce prescribing inertia. Beyond informational outreach, financial incentives such as consulting fees, honoraria for speaking engagements, and research sponsorships further strengthen brand loyalty among prescribers (Bergman et al., 2021). A large structural modeling literature examines how physician learning, detailing, and heterogeneous treatment preferences shape prescribing decisions in pharmaceutical markets (Ching et al., 2019).

Overall, prescribing behavior is relatively inelastic to marginal price changes but highly responsive to institutional incentives and marketing structures that shape the effective price landscape and influence patient welfare. From the firm's perspective, pricing and promotional efforts are therefore jointly determined strategic choices rather than independent instruments. For example, Chintagunta and Desiraju (2005) analyze Prozac, Zoloft, and Paxil across the United States and major European markets and show that pricing and detailing responses reflect both within-market demand sensitivity and across-market strategic interactions.

The preference for branded medications stems not only from promotional influence but also from behavioral inertia and habit formation. Frank and Zeckhauser (2007) find that physicians tend to stick with established prescribing patterns rather than switching to alternatives, even when those alternatives are clinically similar and less expensive. Likewise, Nair et al. (2010) show that physicians frequently conform to peers' prescribing norms rather than respond purely to price signals or economic incentives. Such habitual behaviors sustain market distortions by extending the dominance of branded drugs well beyond their patent exclusivity periods.

Although promotional activities reinforce brand loyalty, physicians also operate within institutional and

economic settings that promote generic adoption. Hospital formularies and insurance reimbursement policies often restrict access to costly brand-name drugs, while pay-for-performance (P4P) models and centralized drug procurement systems align prescribing incentives with cost-effectiveness (Yip et al., 2014). Similarly, tiered formularies and prior authorization requirements, coupled with higher copayments for branded drugs, create financial disincentives that encourage the use of generics and improve adherence (Goldman et al., 2004).

In line with these institutional incentives, policymakers often intend to restrict branded promotion to encourage generic uptake. Evidence, however, suggests that such restrictions do not uniformly increase generic utilization in specific settings. In combination therapies, promotional spillovers from branded to generic components can occur when physicians perceive them as part of an integrated regimen. Liu et al. (2017) show that curbing brand promotion in these contexts can inadvertently reduce prescriptions of generic drugs that are part of the same therapeutic regimen as the targeted branded product. Similarly, Liu et al. (2026) find that limiting comparative detailing, where branded drugs are contrasted with alternatives, may remove indirect exposure that benefits generics, thereby dampening their adoption. Taken together, these findings indicate that while targeted promotional limits are designed to advance cost-effectiveness objectives, their broader behavioral and informational repercussions may yield unintended consequences for generic uptake in certain settings.

Understanding physicians' prescribing decision processes is crucial for policymakers and healthcare stakeholders seeking to design more effective drug pricing strategies, control healthcare expenditures, and ensure that market forces facilitate a more efficient shift from brand-name to generic drug utilization.

3.3 Patient Assistance Programs (PAPs)

PAPs are manufacturer-sponsored initiatives designed to reduce financial barriers to prescription drug access. These programs typically offer free or subsidized medications to patients meeting defined eligibility criteria, often targeting individuals with limited or no insurance coverage.

PAPs operate through several models, each with distinct implications for market behavior. Some provide direct free-drug access to low-income patients, especially for specialty products with high list prices. Others function as copayment-assistance programs, offsetting patients' out-of-pocket costs while leaving insurer reimbursement unchanged. A third model channels manufacturer funding through independent charitable foundations that distribute financial support. Across these structures, PAPs aim to improve affordability by mitigating immediate cost burdens.

Yet, growing evidence shows that these programs can distort market incentives rather than reduce systemic costs. By shielding patients from true prices, PAPs weaken price sensitivity and enable manufacturers to sustain or increase list prices (Zullig et al., 2017). Their administrative complexity, such as income verification and physician documentation, further limits access for those most in need (Choudhry et al., 2009). Critically, most PAPs focus exclusively on brand-name products, excluding generics and biosimilars that could enhance competition (Collier et al., 2022). This selective support sustains monopolistic pricing and shifts, rather than alleviates, financial burdens as insurers and public programs adjust reimbursement structures to offset continued high expenditures (Lee et al., 2023).

The oncology market exemplifies these dynamics. Although PAPs can temporarily ease financial strain for patients, they rarely exert downward pressure on overall prices. Studies find that median assistance per prescription covers only a fraction of total treatment costs, leaving high price benchmarks intact (Zullig et al., 2017). By selectively alleviating affordability concerns, PAPs also reduce manufacturers' fear of market

resistance, thereby facilitating higher launch prices for new therapies (Kesselheim and Daval, 2024).

A key reinforcing mechanism lies in how PAPs interact with insurance reimbursement. In many cases, PAPs absorb patients' cost-sharing obligations without affecting the total payment from insurers, allowing list prices to remain inflated (Kyle and Ridley, 2007). Regulatory scrutiny has intensified as some PAPs resemble indirect inducements that promote brand loyalty. The Pfizer v. HHS ruling underscored these concerns, arguing that such programs may distort competition by privileging brand exclusivity over cost efficiency (Kesselheim and Daval, 2024). In response, insurers and PBMs have implemented copay accumulator programs, preventing manufacturer assistance from counting toward deductibles, thereby curbing PAPs' benefit for insured patients and further complicating affordability dynamics.

To realign PAPs with their intended purpose, policy reforms should target transparency and competitive neutrality. Public disclosure of PAP funding and expenditures would clarify their pricing impact, while expanding eligibility to include generics and biosimilars could introduce downward pressure on prices (Mascardo et al., 2012). Regulators might also condition manufacturer participation on verifiable price-moderation commitments, ensuring that patient assistance complements, rather than substitutes for, genuine affordability. Collectively, these reforms could restore PAPs' role as instruments of access rather than mechanisms that inadvertently sustain high prices.

3.4 Cash-Discount Cards

Beyond manufacturer copay coupons used within insurance benefits, patients increasingly rely on pharmacy cash-discount cards such as *GoodRx*, which process transactions outside insurance networks. These programs lower point-of- sale prices, especially for generics, by accessing PBM discount networks while treating purchases as cash claims, yielding sizable savings relative to undiscounted cash prices for generics but smaller gains for branded drugs (Hong and Shcherbakova, 2021).

Because discount-card fills bypass deductibles and accumulator tracking, they neither count toward out-of-pocket limits nor directly affect insurer spending, yet they can erode formulary steering and negotiated rebate leverage. PBMs have begun integrating these discount prices into benefit designs to retain bargaining power. Early evidence suggests modest adherence improvements among price-sensitive populations but raises policy questions about transparency and data governance (Curran et al., 2024). As these platforms grow, they constitute a parallel pricing channel whose interactions with copay accumulators and maximizer programs warrant systematic study.

3.5 Copay Accumulator Programs and Policy

The copay accumulator programs, implemented by insurance companies, limits the benefits patients may receive from manufacturer-sponsored assistance programs. These policies prevent patient copay assistance from counting toward their deductibles and out-of-pocket maximums, leading to higher overall costs for patients despite the availability of coupons and assistance programs.

State policies regarding these programs vary, with some states enacting legislation to regulate or prohibit the practice, aiming to enhance patient affordability and access to necessary medications. By understanding the complexities of these roles and policies, stakeholders can better navigate the pharmaceutical landscape and advocate for policies that improve patient affordability and market efficiency.

The introduction of copay assistance programs, particularly copay coupons, has significantly altered the landscape of pharmaceutical pricing and market competition. Copay coupons, initially introduced to

alleviate financial burdens for patients, have become a strategic tool for pharmaceutical manufacturers to sustain high drug prices while maintaining patient demand for branded medications. By offsetting high copayments imposed by insurers, these coupons weaken the incentives embedded in tiered formulary designs that encourage cost-conscious choices. Research has shown that after Massachusetts lifted its ban on copay coupons, brand-name drugs that introduced such programs saw a 16% increase in prescription volume, despite the availability of lower-cost generic alternatives. Rather than increasing competition and driving prices downward, copay coupons function as a form of price discrimination, allowing brand-name drug manufacturers to selectively subsidize specific patient groups. This distortion ultimately leads to a decline in the market share of generic drugs (Dafny et al., 2017).

The pharmaceutical market operates within a multi-tiered pricing structure where insurers and PBMs negotiate drug prices through rebates and formulary placement. The fundamental goal of this structure is to balance access and cost-effectiveness by promoting the use of lower-cost alternatives while managing expenditures on high-cost therapies. However, copay coupons disrupt this mechanism by insulating patients from the cost-sharing differentials that insurers put in place to encourage cost-effective prescribing behavior. The design of tiered formularies relies on the assumption that patient cost-sharing influences purchasing decisions, but when manufacturers intervene with direct-to-patient subsidies, the market dynamics shift in favor of higher-priced brand-name medications. As a result, insurers face mounting financial pressures, which they often address by increasing premiums, raising deductibles, or imposing stricter utilization controls (King et al., 2019; Dafny et al., 2024; Moon et al., 2024).

In response to these coupon promotion behaviors, insurers and PBMs introduced copay accumulator adjustment programs (CAAPs) as a countermeasure to manufacturer-sponsored discounts. These programs ensure that copay assistance from drug manufacturers no longer applies toward a patient's deductible or out-of-pocket maximum. With the introduction of CAAPs, once a patient exhausts their copay assistance, they must still meet the full deductible before insurance coverage takes effect. CAAPs aim to reduce the artificial demand created by copay coupons, but it also introduces new financial risks for patients who rely on assistance to afford high-cost prescriptions. (Sherman et al., 2019) analyzed specialty drug adherence and found that CAAPs lead to increased medication abandonment, particularly among patients with chronic conditions requiring biologic treatments. After the implementation of copay accumulator programs, therapy discontinuation rates among high-deductible health plan (HDHP) enrollees rose sharply, as patients encountered unexpected out-of-pocket expenses once their copay assistance funds were depleted. For insurers, CAAPs serve as a necessary tool to counteract the market distortions caused by manufacturer-sponsored coupons, but for patients, they introduce significant financial instability that can negatively impact medication adherence (Nabhan et al., 2018).

The policy response to copay accumulator programs has varied across states. Several states, including Arizona[2], Illinois[3], and West Virginia[4], have passed legislation banning CAAPs in state-regulated insurance plans, effectively reinstating the prior system in which manufacturer assistance counted toward deductibles and out-of-pocket limits. These bans have been justified on the grounds that they improve medication adherence and reduce financial strain on patients, particularly those requiring high-cost specialty treatments. Patel et al. (2024) studied the impact of these state-level bans and found that in the months following implementation, patients experienced a 41% to 63% reduction in out-of-pocket medication costs, along with

[2]State Policy, Arizona, 2019 https://legiscan.com/AZ/text/HB2166/2019.

[3]State Policy, Illinois, 2025 https://legiscan.com/IL/text/SB1682/id/3101617.

[4]State Policy, West Virginia, 2019 https://trackbill.com/bill/west-virginia-house-bill-2770-fairness-in-cost-sharing-calculation-a
1660686/.

a measurable increase in treatment adherence and persistence. However, these bans also create new financial challenges for insurers, who must now absorb higher costs for branded medications without the ability to use accumulators to regulate spending.

Recent regulatory changes surrounding copay accumulator programs have implications that extend well beyond short-term affordability gains. When insurers are restricted from offsetting manufacturer-sponsored assistance, their leverage to negotiate lower net drug prices diminishes. Although bans on copay accumulators can reduce patients' immediate out-of-pocket costs, they simultaneously reinforce pricing strategies that sustain high list prices rather than encourage genuine price reductions. The broader outcome is a market characterized by diminished pricing transparency, as manufacturers continue to depend on complex discount and assistance mechanisms instead of lowering list prices directly. The growing prevalence of alternative funding arrangements—such as copay maximizer programs—illustrates this adaptive equilibrium, in which payers, manufacturers, and regulators continually recalibrate strategies to navigate an evolving policy landscape (Choi et al., 2024).

The ongoing debate over Copay Accumulator Programs underscores the complexities of balancing affordability, market efficiency, and cost containment within the pharmaceutical industry. While manufacturer assistance programs provide critical financial relief for patients, they also contribute to systemic inefficiencies by distorting price competition and sustaining high list prices. Insurers, in turn, implement cost-sharing mechanisms that attempt to realign pricing incentives, yet these strategies often introduce unintended burdens on patients. State-level policy interventions, particularly accumulator bans, shift the balance in favor of short-term patient relief but may contribute to longer-term cost growth by reinforcing manufacturers' reliance on copay assistance programs rather than price reductions. As stakeholders continue to grapple with these challenges, the need for a more sustainable framework, one that aligns incentives across manufacturers, insurers, and patients, becomes increasingly apparent. Regulatory approaches that enhance pricing transparency, encourage competition, and promote value-based pricing models may offer a path forward, ensuring that affordability measures do not simply redistribute costs but instead create lasting improvements in pharmaceutical market efficiency (Cavalier et al., 2023).

4 Channel of Distribution

The pharmaceutical distribution system represents a complex network of stakeholders that collectively influence how medications move from manufacturers to patients and how prices are determined at each stage. Unlike more straightforward consumer markets, pharmaceutical pricing involves multiple intermediaries who shape economic outcomes through a variety of mechanisms including contracting practices, bargaining power dynamics, information asymmetries, and regulatory constraints. This section examines four critical channel stakeholders, wholesalers, pharmaceutical benefit managers (PBMs), retail pharmacies, and group purchasing organizations (GPOs), analyzing their respective roles in the pharmaceutical ecosystem and their impacts on pricing.

Pharmaceutical wholesalers serve as the logistical backbone of the distribution system, purchasing products from manufacturers and distributing them to downstream entities (RxRise, 2024). Their business models have evolved from traditional buy-and-hold approaches with investment buying to fee-for-service arrangements and, in some cases, direct-to-pharmacy models (Iacocca et al., 2013). Though operating on slim margins (approximately 6.3% in 2022), wholesalers influence pricing through their negotiation of manufacturer discounts, strategic inventory management, and contractual arrangements with partners throughout

the supply chain (Eastern Research Group, 2025).

Pharmaceutical benefit managers (PBMs) occupy a pivotal position as third-party administrators of prescription drug programs for various payers (Mattingly et al., 2023). PBMs exert substantial influence on pharmaceutical pricing through formulary development, rebate negotiations with manufacturers, pharmacy network establishment, and claims processing. The market concentration among three dominant PBMs, controlling 79% prescriptions in the United States in 2023, raises important questions about their pricing power, potential conflicts of interest, and the distribution of benefits from the rebates they negotiate (Qato et al., 2024).

Retail pharmacies represent the primary patient-facing component of the pharmaceutical channel. While seven major pharmacy chains accounted for two-thirds of U.S. prescription dispensing revenues, the market maintains a complex competitive structure where independent pharmacies continue to operate alongside these dominant players (Drug Channels, 2024). Pharmacies influence pricing through their retail markup structures, negotiations with PBMs for preferred network status, and formulary power for generic medications. Price dispersion across pharmacies remains substantial even for identical products, reflecting both market fragmentation and information frictions.

Group purchasing organizations (GPOs) function as procurement intermediaries that aggregate the purchasing volume of healthcare providers to secure preferential pricing from manufacturers. Protected by regulatory "safe harbor" provisions, GPOs generate revenue primarily through contract administration fees paid by manufacturers. Their pricing impact manifests through collective bargaining power, transaction cost reductions, and specialized contracting strategies such as sole-source arrangements and tiered discounts.

The following sections examine each of these stakeholders in detail, analyzing their market contexts, pricing mechanisms, and relevant academic literature. By understanding how these channel members interact with one another, with manufacturers, and with patients, we can develop more comprehensive models of pharmaceutical pricing dynamics, identify inefficiencies in the current system, and propose evidence-based strategies for policy interventions that balance innovation incentives with affordability and access objectives.

4.1 Wholesalers

Pharmaceutical wholesalers are essential intermediaries in the pharmaceutical supply chain, operating between manufacturers and downstream entities including retail pharmacies, hospitals, and healthcare facilities. They perform critical functions such as inventory management, order fulfillment, temperature-controlled storage and transportation, regulatory compliance, pharmaceutical repackaging, and reimbursement support (Zhao, 2023). Although wholesalers rarely set list prices directly, they materially influence how manufacturer price changes are transmitted through the channel and how margins are allocated across supply chain participants.

The U.S. pharmaceutical wholesale market has experienced substantial consolidation, with the top three distributors controlling approximately 90% of the market (Zhao et al., 2012). Despite this concentration, wholesale distribution operates under slim margins, averaging about 1.2% during 1995–2008, and relies on high-volume operations and sophisticated inventory management systems (Berndt and Newhouse, 2010). Consequently, profitability depends heavily on contractual arrangements and inventory practices rather than large resale markups.

Traditionally, wholesalers operated under a Buy-and-Hold (BNH) model, purchasing drugs at Wholesale Acquisition Cost and reselling them to pharmacies with a markup. A defining feature of this model was "investment buying," whereby wholesalers accumulated excess inventory in anticipation of predictable man-

ufacturer price increases, a practice that could generate up to 40% of gross margins (Iacocca et al., 2013). Foundational work by Berndt and Newhouse (2010) explains how predictable annual price increases created systematic arbitrage opportunities and shaped pricing dynamics within the distribution channel. Over time, however, consolidation and improvements in information technologies reduced markup levels and narrowed these arbitrage margins.

Beginning in the early 2000s, the industry shifted toward Fee-for-Service (FFS) agreements, under which wholesalers receive explicit compensation from manufacturers for distribution services while reducing speculative inventory accumulation (Zhao et al., 2012). Analytical models developed by Zhao et al. (2012) demonstrate that FFS contracts can improve total supply chain profits by mitigating inventory inefficiencies and identify Pareto-improving fee structures that benefit both manufacturers and wholesalers.

More recently, some manufacturers have experimented with Direct-to-Pharmacy (DTP) models, where drugs remain manufacturer-owned until reaching retailers and wholesalers function primarily as logistics providers (Iacocca et al., 2013). Using multi-period production–inventory models, Iacocca et al. (2013) compare BNH, FFS, and DTP systems and find that DTP arrangements can outperform alternative models in terms of overall supply chain efficiency, highlighting how ownership structure and contract design shape pricing transmission and inventory incentives.

Empirical research documents a long-run compression of wholesaler markups alongside evolving discount structures. Berndt and Newhouse (2010) report that wholesaler-to-pharmacy markups declined from approximately 15.3% to 11.9% between 1966 and 1977, while Zhao (2023) provide more recent evidence of continued margin pressure as revenue models increasingly rely on service-based compensation. Several studies also examine regulatory influences on wholesale pricing dynamics. Berndt and Newhouse (2010) analyze how the Prescription Drug Marketing Act of 1987 constrained arbitrage opportunities while preserving manufacturers' ability to maintain price discrimination across market segments.

Overall, wholesalers operate with limited direct price-setting authority but exert meaningful influence through bargaining, contract design, inventory management, and the transmission of manufacturer pricing decisions across the pharmaceutical supply chain.

4.2 Pharmaceutical Benefit Managers

PBMs are third-party administrators of prescription drug programs for commercial health plans, self-insured employer plans, Medicare Part D plans, the Federal Employees Health Benefits Program, and state government employee plans. Originally created in the 1960s to process pharmaceutical claims, PBMs have evolved into powerful intermediaries that significantly influence pharmaceutical pricing and distribution.

PBMs occupy a central position in the pharmaceutical supply chain, serving as the interface between drug manufacturers, insurers, and pharmacies. Their core functions include developing and managing formularies, negotiating rebates with manufacturers, establishing pharmacy networks, processing pharmacy claims, and operating mail-order and specialty pharmacy services. Through formulary placement, tier design, and network contracting, PBMs exert substantial influence over prescribing incentives, patient cost-sharing, and manufacturer access to demand.

The pharmaceutical market has experienced significant consolidation, with three major PBMs, CVS Caremark, Express Scripts, and OptumRx, accounting for 79% U.S. prescriptions in 2023 (Qato et al., 2024). Vertical integration further complicates this structure, as many PBMs own retail and mail-order pharmacies, raising concerns about conflicts of interest and self-preferencing behavior.

PBMs influence pricing primarily through rebate negotiations and formulary design. Manufacturers offer

rebates in exchange for preferred placement, while PBMs determine copayment tiers and reimbursement rates for pharmacies. The resulting system produces a divergence between list and net prices: list prices may rise even as net prices after rebates decline, with intermediaries capturing part of the spread. Using detailed claims and contract data, Feng and Maini (2024) show that although PBMs can negotiate lower net prices, limited patient switching dampens utilization responses, muting the pass-through of rebates to realized spending and patient-facing prices. This dynamic underscores how PBMs affect both pricing levels and the distribution of surplus within the channel.

Theoretical research has examined PBMs through formal economic modeling. Kouvelis et al. (2015) develop a model of competition among PBMs for client organizations, analyzing how formulary and pricing decisions shape market equilibrium. They identify the existence of a pure Nash equilibrium in aggregate formulary and price decisions, showing that each PBM's optimal formulary reflects welfare-adjusted cost minimization for its plan sponsor. Extending this framework, Kouvelis et al. (2018) analyze price competition among branded manufacturers distributing through a common PBM, highlighting co-opetition dynamics in which manufacturers compete for share while jointly influencing the PBM's overall market size. They introduce a "market expansion index" capturing the PBM's ability to expand demand relative to aggregate drug attractiveness, demonstrating how this index affects pricing strategies and profitability.

Contract design between employers and PBMs further shapes rebate dynamics. Gür Ali and Mantrala (2010) employ a mathematical simulation model to examine how employer–PBM contract elements and pharmaceutical rebates influence outcomes. They show that brands offer rebates in exchange for the PBM's ability to shift prescription share, but reduce these rebates when PBMs actively promote generic substitution. This work emphasizes the strategic interaction between rebate structures and utilization management tools.

Empirical research has also sought to quantify financial flows within the pharmaceutical distribution system. Schulman and Dabora (2018) analyze financial data from major pharmaceutical manufacturers and document a substantial increase in rebates and other payments to intermediaries. Between 2011 and 2016, manufacturer net revenues grew by an average of 2.7% annually, while rebates and related payments increased by 15% annually. By 2016, such payments accounted for 52% of net revenue, up from 29.2% in 2011. Complementing this evidence, Geng and Pelton (2022) use a theoretical framework to demonstrate how PBMs' negotiating leverage affects pricing outcomes and how growing rebate demands can constrain manufacturers' net revenue growth despite rising gross sales.

Taken together, PBMs operate as powerful bargaining intermediaries whose influence extends beyond administrative processing to formulary control, rebate extraction, and surplus allocation. Their strategic position within the pharmaceutical channel contributes to the widening gap between list and net prices and plays a central role in shaping both manufacturer incentives and patient-facing costs.

4.3 Retail Pharmacies

Retail pharmacies represent a critical link in the pharmaceutical supply chain, serving as the primary interface between manufacturers, insurers, and patients. Positioned downstream of manufacturers and wholesalers, pharmacies purchase prescription drugs from wholesalers and dispense them to consumers, earning revenue through dispensing fees, retail markups, and sales of non-pharmaceutical products. The sector has experienced substantial consolidation, with five large chains accounting for roughly 60% of prescription revenues in the United States, while independent pharmacies continue to coexist alongside these dominant players (Starc and Swanson, 2021).

Despite this concentration, retail pharmacy markets exhibit substantial price dispersion, even for narrowly

defined prescription drugs. Using posted prices, Sorensen (2000) shows that within a geographic market the highest price for a prescription is often more than 50% higher than the lowest available price, with dispersion declining for drugs purchased repeatedly as consumers learn and search. More recent evidence using Medicare Part D claims confirms that this dispersion persists in modern, highly intermediated insurance settings (Starc and Swanson (2021)). These patterns indicate that retail pharmacy markets remain far from perfectly competitive, creating scope for insurer steering and selective contracting.

Retail pharmacies influence pharmaceutical pricing through several channels. Pharmacies negotiate reimbursement rates with PBMs and insurers for inclusion in preferred pharmacy networks, affecting both prices and prescription volume. In addition, pharmacies exercise "formulary power" in generic markets by choosing among manufacturers supplying therapeutically equivalent products, contributing further to price variation (Starc and Swanson, 2021). These institutional features interact closely with insurance design and consumer cost sharing.

Building on this environment of persistent price dispersion, Starc and Swanson (2021) analyze preferred pharmacy networks as a form of selective contracting in Medicare Part D. They find that plans with more restrictive preferred networks pay lower retail drug prices. These effects reflect both enrollee steering toward lower-cost pharmacies and enhanced bargaining leverage arising from the threat of exclusion. Consistent with the importance of steering incentives, plans with a higher share of low-income subsidy (LIS) enrollees, who face attenuated copay differentials across pharmacies, pay substantially higher prices.

Structural demand estimates further clarify the consumer-side foundations of these effects. Starc and Swanson (2021) show that preferred pharmacy status significantly increases pharmacy demand among non-LIS enrollees, raising preferred pharmacies' market share by roughly 8 percentage points, while LIS and very high-spending enrollees are much less responsive. Counterfactual analysis indicates that preferred networks generate modest cost savings, approximately 1% of annual drug spending, but that these savings are offset by consumer surplus losses from restricted access, highlighting a central trade-off between cost containment and access in pharmacy network design.

These findings place retail pharmacy networks within a broader literature on selective contracting in healthcare markets. For example, Gruber and McKnight (2016) show that limited hospital networks can generate substantial savings in medical care, illustrating how intermediaries can exert competitive pressure even when end users are relatively price-insensitive.

4.4 Group Purchasing Organizations

GPO aggregate the purchasing power of healthcare providers to negotiate contracts with pharmaceutical manufacturers and other suppliers. In pharmaceutical markets, GPOs primarily serve hospitals and health systems, aiming to secure lower prices and reduce procurement costs through collective bargaining and standardized contracting (Wetrich, 1987). The prevailing business model relies on multiple revenue streams, including membership fees paid by providers, contract administration fees (CAFs) paid by manufacturers, and administrative fees from authorized distributors (Oakley, 2022). Importantly, CAF arrangements are protected by "safe harbor" provisions introduced in a 1987 amendment to the Social Security Act, exempting GPOs from anti-kickback rules that would otherwise prohibit such payments.

Economic theory highlights several channels through which GPOs can affect pharmaceutical prices. By consolidating demand, GPOs may intensify competition among manufacturers and extract lower prices, particularly in markets with multiple suppliers. In a Hotelling-style model with duopoly manufacturers, Hu and Schwarz (2011) show that GPOs can increase price competition and reduce procurement prices,

countering claims that GPOs are inherently anticompetitive. However, their analysis also suggests that intensified price competition may dampen incentives for innovation. Extending this framework, Hu et al. (2012) develop a game-theoretic model with heterogeneous providers and show that the welfare effects of GPOs are context dependent rather than uniformly positive.

Other theoretical work emphasizes the informational role of GPOs. Zhou et al. (2017) model GPOs as intermediaries that facilitate information sharing among providers and suppliers. Under certain conditions, this informational advantage allows GPOs to coordinate procurement and achieve Pareto improvements, suggesting that price effects may arise not only from bargaining power but also from improved coordination in fragmented markets.

Empirical evidence on GPO pricing effects is mixed and closely tied to market structure. Using quasi-experimental variation in French hospital procurement, Toulemon (2018) finds that group purchasing reduces medicine prices by about 2% on average, with substantially larger reductions—around 9%—in oligopolistic markets and negligible effects in monopoly settings. Consistent with this heterogeneity, Blair and Durrance (2014) conclude that GPOs tend to promote competition among manufacturers, but that their impact depends critically on the degree of supplier concentration.

More critical perspectives highlight potential downsides of GPO contracting. Bruhn et al. (2018) argue that vendor fee arrangements may disproportionately favor large manufacturers, creating barriers to entry for smaller suppliers and increasing reliance on a narrow set of supply chains. Such dynamics raise concerns about long-run market concentration, supply resilience, and the distribution of surplus along the supply chain.

Taken together, the literature suggests that GPOs can lower procurement costs under certain market conditions, particularly where supplier competition is viable and information frictions are salient. At the same time, their effects are sensitive to institutional design, fee structures, and market concentration, and existing models largely abstract from long-run dynamics such as entry, exit, and innovation. These limitations point to an important research agenda on how GPOs shape pharmaceutical pricing, competition, and supply stability over time.

5 Competition

5.1 Branded competition

Brand-name prescription drugs in the United States have experienced dramatic price increases over the past decade. This trend is driven largely by patent protections and regulatory exclusivity that grant manufacturers temporary monopolies. Nearly all top-selling brand-name drugs have seen substantial price hikes over relatively short periods. For instance, Wineinger et al. (2019) reported a median price increase of 76% for 49 leading drugs between 2012 and 2017, with most drugs raising their list prices multiple times annually. This environment of limited price competition is rooted in the fact that, under market exclusivity, companies face little pressure to reduce prices—even when several cheaper drugs are available for the same therapeutic indication.

A key distinction in understanding drug pricing lies between the published list price and the net price that manufacturers actually receive after rebates and discounts. Hernandez et al. (2020) noted an approximate 159% increase for 602 branded drugs over a decade, while net prices have risen more moderately by around 60% over a similar period. This difference is primarily due to the substantial rebates negotiated with insurers

and PBMs, which on average have offset about 62% of the increases in list prices. However, this dynamic creates a two-tiered pricing system: although the actual revenue for manufacturers is moderated, many insured patients end up paying cost-sharing amounts (via deductibles or coinsurance) based on the higher list price, thereby bearing the burden of these increases directly (Rome et al., 2021).

Rather than engaging in direct price competition, pharmaceutical companies have opted for non-price competitive strategies, notably heavy investment in advertising and marketing. The industry spends significantly on direct-to-consumer advertising and "detailing" to healthcare providers. Rizzo (1999) demonstrated that such promotional activities lower the price elasticity of demand; as physicians and patients become more familiar with and loyal to a specific brand, they are less responsive to price differences. This focus on building brand loyalty through aggressive marketing not only reinforces the elevated prices but also creates barriers for new competitors trying to enter the market. In markets where multiple brand-name drugs are available for the same condition, these companies often increase prices in tandem rather than engaging in competitive undercutting.

Adding to the complexity, pricing strategies in the pharmaceutical market can sometimes be counterintuitive. Conventional economic theory might suggest that incumbents would lower prices in anticipation of new competition, a tactic known as limit pricing. Yet, evidence from the U.S. market indicates that companies may actually raise their prices when potential competitors, such as biosimilars or new branded entrants—are on the horizon(Ellyson and Basu, 2021). This phenomenon, sometimes referred to as the "prescription drug paradox," occurs because once a generic or biosimilar enters the market, the most price-sensitive patients tend to switch, leaving a core group of brand-loyal, less price-sensitive consumers. With this captive market, incumbents can justify higher prices, thereby maximizing revenue before facing the full brunt of competition (Frank and Salkever, 1997).

Looking toward the future of Pharmaceutical pricing, the era of unchecked branded drug price inflation is likely to wane as competitive forces strengthen. Branded drug prices in the U.S. are expected to stabilize or even decline in real terms over the coming years under the influence of generics, biosimilars, policy measures, and payer pressure. Pharmaceutical companies, in turn, will evolve by balancing price with value – embracing more competitive pricing, pursuing continuous innovation, and delivering services that reinforce the worth of their products.

5.2 Generic Competition

The entry of generic drugs following patent expiration fundamentally reshapes pharmaceutical market dynamics. Generic manufacturers introduce bioequivalent alternatives at substantially lower prices, intensifying price competition and disrupting incumbent dominance. Although standard economic theory predicts uniform price declines under increased competition, empirical evidence reveals a more segmented outcome. Generic entry produces steep price reductions within the generic segment, while branded drug prices often remain stable or even increase (Regan, 2008). Demand-side dynamics reinforce this segmentation. Using structural models of post-patent pharmaceutical competition, Ching (2010a) show that consumer learning about generics is gradual and heterogeneous, slowing diffusion and allowing branded products to retain substantial demand even as lower-priced substitutes become available. Extending this framework, Ching (2010b) develop a dynamic oligopoly model in which firms and consumers jointly learn about generic drug quality and entry occurs endogenously, demonstrating how learning and strategic interaction shape pricing, entry timing, and market evolution after patent expiration.

Regulatory frameworks shape the extent and intensity of generic competition. In the United States,

the Hatch–Waxman Act facilitates entry through Abbreviated New Drug Applications, allowing firms to demonstrate bioequivalence rather than replicate costly clinical trials. However, competitive intensity varies across drug categories. Pre-expiration brand revenue strongly predicts the number of generic entrants, with higher-revenue drugs attracting more competitors and experiencing larger post-entry price declines (Morton, 2000). Drug characteristics also matter: treatments for chronic conditions and oral solid formulations typically experience deeper generic penetration due to predictable demand and ease of replication (Morton, 2000).

While regulatory design promotes entry, incumbent firms deploy a portfolio of strategic responses to limit competitive erosion. One widely studied tactic is the introduction of authorized generics (AGs)—generic versions produced by the originator firm and marketed under separate labels. By launching an AG at patent expiration, the incumbent captures part of the generic segment while reducing expected profits for independent entrants, thereby discouraging entry (Kong and Seldon, 2004).

Product reformulation provides another mechanism for managing post-patent competition. Firms frequently introduce extended-release versions, combination therapies, or modified formulations prior to patent expiration, securing new intellectual property protection. This strategy—often referred to as "product hopping"—shifts demand from the soon-to-expire molecule to a reformulated version, forcing generic manufacturers to conduct additional bioequivalence testing and delaying competitive pressure (Wilkie et al., 2012).

Pricing responses further reflect strategic segmentation. Rather than competing directly on price, originator firms may exploit the "Generic Competition Paradox" by focusing on relatively price-insensitive consumers, particularly those insulated by insurance coverage (Regan, 2008). Empirical evidence confirms that generic prices fall sharply—declining by approximately 83% as the number of sellers rises to between 6 and 15, and by an additional 52% when the market expands beyond 40 sellers (Wiggins and Maness, 2004). In contrast, branded prices frequently remain unchanged or increase (Regan, 2008). Some firms complement this approach with tiered pricing, rebates, or loyalty programs that preserve margins among insured patients while ceding the most price-sensitive segment to generics (Kong, 2009).

Beyond reformulation and pricing strategies, legal mechanisms also shape post-entry competition. Pay-for-delay agreements, where brand-name firms compensate generic manufacturers to postpone entry, represent one of the most controversial practices (Yao and Liu, 2025). Although privately profitable, such settlements have attracted antitrust scrutiny for delaying consumer access to lower-cost alternatives. Regulatory authorities in both the United States and Europe increasingly challenge these agreements to preserve the competitive balance envisioned under patent law.

Substitution policies further influence the distribution of post-entry gains. In systems with automatic substitution, pharmacists dispense generics unless otherwise specified, accelerating diffusion and amplifying cost savings. In physician-driven prescribing systems, however, branded firms retain greater leverage through established prescribing relationships and familiarity, allowing them to sustain market share despite generic availability (Janssen, 2023).

The broader consequences of generic competition extend to innovation incentives and long-run industry structure. Although generic entry substantially reduces drug expenditures and enhances access, it compresses post-patent rents and may weaken expected returns to R&D investment (Regan, 2008). Concerns are particularly salient in high-risk therapeutic areas such as biologics and rare diseases. At the same time, competitive pressure may reallocate innovation toward genuinely differentiated therapies rather than incremental modifications. Balancing cost containment with incentives for pharmaceutical innovation remains a

central policy challenge.

5.3 Biosimilar Competition

5.3.1 Biosimilar Characteristics

Biosimilars have emerged as an important category within the pharmaceutical industry, offering a cost-effective alternative to expensive biologic therapies. However, they differ fundamentally from small-molecule generics in terms of molecular structure, regulatory approval, and pricing strategies. These differences significantly impact their adoption, market penetration, and competition landscape.

Unlike small-molecule generic drugs, which are chemically synthesized and identical to their reference drugs, biosimilars are produced from living organisms, making them structurally complex and inherently variable. This means that biosimilars are "highly similar" rather than identical to their reference products (Sekhon and Saluja, 2011). Due to this complexity, the development process for biosimilars requires extensive analytical characterization, functional assays, and clinical trials to ensure biosimilarity without clinically meaningful differences (Declerck and Simoens, 2012). Furthermore, the production process for biosimilars must maintain strict control to minimize variations, as even minor changes in the manufacturing environment can lead to differences in efficacy and immunogenicity (Krishnan et al., 2015).

The market penetration of biosimilars has been slower than that of generics due to multiple barriers, including physician hesitancy, regulatory uncertainty, and competition from reference biologic manufacturers (Stern et al., 2021). Many physicians remain hesitant to prescribe biosimilars due to concerns about immunogenicity and long-term efficacy, despite regulatory assurances of safety and effectiveness (van de Vooren et al., 2015).

A key distinction between biosimilars and generics is the concept of interchangeability. In the United States, a biosimilar must receive an FDA designation of interchangeability before it may be substituted at the pharmacy level without prescriber authorization, subject to applicable state substitution laws (U.S. Food and Drug Administration, 2023). This differs from generics, which are automatically substitutable. Therefore, the regulatory approval process for biosimilars is significantly more complex than for generic drugs. While generics can rely on bioequivalence studies, biosimilars must undergo a stepwise comparability exercise. Biosimilars are approved under the Biologics Price Competition and Innovation Act (BPCIA) of 2009, which provides an abbreviated pathway for biosimilar approval but requires significantly more data than the approval process for generics (Stern et al., 2021). In contrast, the EMA has established a more streamlined regulatory framework, allowing biosimilar manufacturers to extrapolate clinical efficacy and safety data across multiple indications, provided they can demonstrate similar mechanisms of action (Declerck and Simoens, 2012).

The competitive dynamics of biosimilars differ significantly from generics due to pricing strategies, manufacturing complexity, and market exclusivity. While generics enter the market with steep price cuts due to multiple competitors, biosimilars face high entry costs and complex manufacturing constraints, leading to less aggressive price reductions (Declerck and Simoens, 2012; Stern et al., 2021). In the U.S., the reference biologic (Remicade) retained 81% market share in Medicare Part B in 2018, despite biosimilars being priced at a 17-23% discount (Dickson and Kent, 2021). Furthermore, originator companies employ defensive lifecycle management (LCM) strategies, such as new formulations and aggressive pricing tactics, to slow down conversion to biosimilars and maintain their market share (Emerton, 2013).

5.3.2 Biosimilars Pricing Competitions

Biosimilars face unique challenges in market entry, pricing competition with originator biologics, and intra-biosimilar competition, which collectively shape their ability to drive down healthcare costs. The three key issues in biosimilar competition are how biosimilar market entry affects drug pricing, how competition unfolds among biosimilars and against brand-name biologics, and the strategies that brand-name manufacturers employ in response to biosimilar competition.

How Biosimilar Market Entry Affects Drug Pricing

The competitive influence of biosimilars begins with the expiration of reference biologic patents. A major barrier to biosimilar-driven price reductions is the extensive patent litigation pursued by originator manufacturers—a practice often described as the patent thicket strategy. The history of patent litigation and active efforts by reference product licensees to create legal obstacles effectively delay biosimilar entry and protect originators' investments in the US market (Megerlin et al., 2013).

Unlike small-molecule generics, which typically enter the market immediately after exclusivity ends and reduce prices by 70–90% within the first year, biosimilars face protracted delays due to patent disputes, regulatory hurdles, and complex payer contracting. Even after launch, biosimilar competition produces more modest price decreases, generally ranging from 15–35% (Mulcahy et al., 2022).

Empirical evidence confirms these incremental effects. Frank et al. (2022) find that each additional biosimilar entrant reduces market prices by approximately 5.4–7.0%, reflecting both price cuts by reference biologic manufacturers and demand shifts toward lower-cost biosimilar alternatives. However, the magnitude of these effects varies considerably across therapeutic classes, depending on competitive intensity, interchangeability designations, and payer adoption practices (Stern et al., 2021).

Competition Between Biosimilars and Brand-Name Biologics

Another important issue to explore is competition between biosimilars and brand-name biologics. Brand-name biologic manufacturers respond aggressively to biosimilar competition to preserve market share and limit price erosion. Some originator biologic manufacturers adopt price reduction and rebate strategies, often preemptively lowering prices in response to anticipated biosimilar entry, while offering significant rebates and discounts to PBMs and insurers, making it financially unattractive for them to cover biosimilars over the reference biologic (Falit et al., 2015).

Furthermore, originator biologic manufacturers may leverage their broader product portfolios to penalize hospitals that select biosimilars, for instance, by denying discounts on other patented products, thereby creating significant barriers to biosimilar uptake and maintaining market dominance (Megerlin et al., 2013). To counteract biosimilar erosion, manufacturers may introduce biobetters, which are improved versions of the original biologic with enhanced efficacy, longer dosing intervals, or new delivery mechanisms.

Biosimilar-to-Biosimilar Competition

Unlike generic drug markets, where price competition among manufacturers leads to steep discounts, biosimilar markets exhibit a more gradual competitive landscape due to high development costs and regulatory constraints. The intensity of biosimilar-to-biosimilar competition depends on the number of biosimilars available for a given reference biologic and the pricing strategies adopted by competing manufacturers.

The first biosimilar entrant has a first-mover advantage, often capturing the largest market share and setting the initial price benchmark. Subsequent biosimilars must compete on price and market access strategies (Frank et al., 2022). In the European Union, biosimilar-to-biosimilar competition has resulted in price reductions of 9.3% to 27.3%, depending on the molecule and the number of competitors (Car et al., 2023). In contrast, in the United States, biosimilar competition remains limited due to fewer entrants and more

restrictive rebate contracts (Mulcahy et al., 2022).

Biosimilar market entry significantly alters the pricing dynamics of biologics, but its impact is moderated by regulatory barriers, payer policies, and competitive strategies from brand-name manufacturers. While biosimilars introduce price competition, the magnitude of cost savings is often constrained by patent litigation, rebate-driven market structures, and physician prescribing behavior.

While biosimilar entry promotes pricing competition, its overall impact on drug costs is highly dependent on market structure, payer incentives, and regulatory policies. Additionally, biosimilar-to-biosimilar competition is slower and less aggressive than small-molecule generic competition, leading to more modest price reductions. As biosimilar markets mature, further price reductions may occur, but brand-name biologic manufacturers will continue to employ strategic measures to mitigate competitive threats. Future policy interventions, such as reforming rebate structures, increasing biosimilar uptake incentives, and accelerating patent litigation resolutions, will be essential in maximizing the cost-saving potential of biosimilars.

5.4 Price Transparency

Price transparency in the pharmaceutical industry refers to the openness and accessibility of information regarding drug prices, including the net prices paid by different buyers after considering rebates, discounts, and other pricing mechanisms. It encompasses various dimensions, including transparency in pricing structures, procurement processes, and cost components such as R&D, production, and marketing expenses. Price transparency has been increasingly emphasized as a mechanism to enhance market efficiency, improve patient access to medicines, and foster fair competition among pharmaceutical firms. However, the implications of greater transparency remain potential trade-offs between price reductions, differential pricing strategies, and pharmaceutical innovation.

The significance of price transparency lies in its potential to correct information asymmetries in the pharmaceutical market. The opacity of drug pricing, particularly the use of confidential pricing agreements, often results in inefficiencies where different purchasers pay widely varying prices for the same drug, leading to inequities in access. Greater transparency can empower governments, insurers, and patients with better information, thereby enabling more informed decision-making and improving bargaining power in price negotiations. Hinsch et al. (2014) found that price transparency mechanisms can facilitate more favorable contract negotiations and lead to policy adjustments that reduce procurement inefficiencies. Moreover, transparency initiatives can enhance public trust in the healthcare system by making pricing mechanisms more accountable and understandable to stakeholders.

Despite these benefits, excessive transparency may discourage firms from offering lower prices in certain markets due to fears of reference pricing. In the pharmaceutical sector, where differential pricing plays a crucial role in ensuring affordability across different income groups, excessive transparency may inadvertently lead to price convergence rather than price reductions. Ridley (2005) argued that international reference pricing and transparency efforts could lead to price compression, thereby undermining price differentiation strategies that make medicines more accessible in low-income countries. This could ultimately reduce access to essential medicines for disadvantaged populations and incentivize manufacturers to set uniform prices, potentially making drugs unaffordable in lower-income settings.

Another challenge is the potential impact on pharmaceutical innovation. As Simoens (2011) noted, the high R&D costs of orphan drugs must be recouped from a small patient base, often resulting in monopolistic pricing. He argues that a transparent and evidence-based approach is essential to expose these cost structures and inform reimbursement decisions, rather than allowing firms to maximize prices within the constraints of

limited negotiating power from payers. Researchers have also proposed machine learning–based approaches to identify physicians who are more likely to treat rare disease patients, thereby reducing marketing costs for orphan drugs (Cai et al., 2025). Similarly, Shaw and Mestre-Ferrandiz (2020) cautioned that increased transparency, combined with international reference pricing, could undermine the incentives for innovation by reducing expected returns on new drug development. The trade-off between transparency and innovation highlights the complexity of designing policies that balance affordability with continued investment in pharmaceutical R&D.

Given these complexities, improving price transparency in the pharmaceutical industry requires targeted strategies that enhance visibility while preserving market incentives for differential pricing and innovation. One approach is the development of structured medicine price information mechanisms that provide reliable and comparable pricing data while maintaining flexibility for pricing differentiation. Hinsch et al. (2014) reviewed multiple international pricing databases, including WHO's Global Price Reporting Mechanism, which help policymakers and procurement agencies make informed purchasing decisions. By standardizing price reporting frameworks and ensuring that price data are contextualized with procurement conditions, such mechanisms can enhance transparency without eliminating pricing flexibility.

A second strategy is value-based pricing, which ties drug prices to clinical effectiveness and patient outcomes rather than external reference prices. Carapinha (2024) proposed value-based tiered pricing (VBTP) as a method of improving transparency while allowing for differentiated pricing based on national income levels. Under this system, countries with higher purchasing power pay more for innovative treatments, while lower-income countries benefit from reduced prices. This approach aligns incentives for pharmaceutical companies to maintain affordable pricing in developing countries without fearing price reference effects in wealthier markets.

Additionally, regulatory interventions also play a critical role in promoting transparency. The 2019 World Health Assembly (WHA) resolution called for greater disclosure of net prices paid for medicines in national healthcare systems, signaling a global commitment to improving transparency (Shaw and Mestre-Ferrandiz, 2020). However, policymakers must carefully design transparency policies to ensure that they do not inadvertently undermine equitable pricing structures.

In healthcare markets, transparency efforts must also account for the role of insurance systems and reimbursement mechanisms. Sinaiko and Rosenthal (2011) emphasized that in healthcare, unlike consumer goods markets, price transparency alone may not drive cost reductions because patients often rely on insurance coverage rather than direct price comparisons. Consequently, transparency initiatives should be integrated with broader healthcare financing reforms that enhance cost-effectiveness and patient access.

Overall, price transparency in the pharmaceutical industry presents both opportunities and challenges. While it has the potential to enhance efficiency, reduce procurement costs, and promote accountability, excessive transparency could disrupt market mechanisms that enable differential pricing and sustain pharmaceutical innovation. A balanced approach that combines structured price information mechanisms, value-based pricing, and negotiated agreements can enhance transparency while mitigating adverse effects. Future research should explore the long-term impact of transparency policies on global drug pricing dynamics and investigate how digital health technologies, such as blockchain-based pricing registries, can enhance transparency without exposing sensitive commercial data. By aligning transparency initiatives with economic and market realities, policymakers can foster a pharmaceutical ecosystem that supports affordability, access, and innovation.

6 Compatibility

Pharmaceutical pricing operates within a multifaceted landscape where strategies must align with corporate profitability, societal expectations, and regulatory frameworks—a concept termed compatibility. This alignment ensures sustainable success amid substantial R&D costs, ethical imperatives for access, and diverse legal constraints. This section synthesizes academic literature and industry practices, organizing research thematically into economic modeling approaches, empirical studies, and policy analyses. This comprehensive analysis serves as a resource for researchers and industry professionals seeking to understand compatibility in pharmaceutical pricing.

6.1 Corporate Profitability

The pharmaceutical industry presents a distinctive economic environment in which corporate profitability and pricing strategies are tightly linked to innovation incentives. Firms face extraordinary R&D costs, estimated at approximately $125 million per approved product in the 1980s (Scherer, 1993) and rising to roughly $800 million in later decades (Filson and Masia, 2007), combined with high failure rates, patent-driven market exclusivity, and substantial regulatory oversight. These structural features create a pricing environment in which firms seek to recoup large fixed investments within limited exclusivity windows, often generating high margins on successful products while absorbing losses on failed projects.

Formal economic models clarify how these incentives shape pricing behavior. Early theoretical work by Scherer (1993) characterizes pharmaceutical markets as bifurcated, with price-sensitive and price-insensitive segments. This framework helps explain the "generic competition paradox," in which branded manufacturers may maintain or even increase prices following patent expiration while ceding volume to generics. Subsequent models refine this insight. Longo (2010) shows that under certain demand elasticities, strategic price reductions in selected markets can increase global profits. Miraldo (2009) demonstrates that reference pricing across countries creates cross-market price externalities, potentially inducing firms to delay entry in lower-income markets to preserve higher prices in reference-linked markets.

Empirical evidence confirms that pharmaceutical profitability has historically exceeded all-industry averages. Scherer (1993) documents returns on equity substantially above industrial benchmarks during the late twentieth century, even after accounting adjustments for R&D intensity. However, profit measurement is complicated by accounting conventions that expense R&D and marketing costs rather than capitalizing them, potentially biasing reported returns. Moreover, revenue distributions are highly skewed: Grabowski et al. (2002) find that while most new drugs fail to recover R&D costs, a small fraction generate quasi-rents several times larger than development expenditures, consistent with a high-risk, high-reward innovation model.

Policy interventions interact directly with these profit dynamics. In international markets, direct price controls and external reference pricing systems constrain manufacturer pricing, leading to persistent cross-country price disparities (Scherer, 1993; Maini and Pammolli, 2023). Recent work by Maini and Pammolli (2023) shows that external reference pricing can incentivize firms to delay product launches in lower-income countries to protect prices in higher-income markets, with estimated profit gains of approximately €18 million per drug from such strategic delay. Computational models by Filson and Masia (2007) further suggest that even moderate profit reductions can meaningfully affect innovation, firm survival, and market structure over time, with disproportionate impacts on smaller or newer firms.

Taken together, the literature highlights a central tradeoff: policies that compress pharmaceutical profits

may reduce static prices but risk dampening dynamic innovation incentives. Conversely, high margins on successful products may be necessary to sustain investment in risky R&D pipelines. Understanding how profitability, pricing, and regulation interact remains critical for designing policies that balance affordability with long-run innovation.

6.2 Corporate Social Responsibility

Corporate social responsibility (CSR) in pharmaceuticals centers on pricing, access, intellectual property practices, and research prioritization decisions that shape the distribution of life-saving treatments. Because medicines directly affect survival and quality of life, pharmaceutical firms face heightened expectations regarding fairness, transparency, and global access.

Pharmaceuticals are often treated as "special goods," for which purely market-based pricing raises ethical concerns (Parker-Lue et al., 2015). Ethical scrutiny is especially pronounced in the orphan drug context. Hemphill (2010) documents cases of extraordinary price escalation following orphan designation and questions whether legal exclusivity provisions justify pricing that materially restricts access. While orphan drug legislation was designed to correct market failure, legal compliance alone does not resolve debates about distributive justice.

Strategic CSR frameworks distinguish between symbolic gestures and embedded responsibility. Bruyaka et al. (2013) show that firms engaged in orphan drug development frequently combine economic opportunity, regulatory incentives, and ethical narratives. However, many firms fail to integrate these dimensions into sustained, visible commitments that meet criteria of centrality, specificity, and stakeholder engagement. Orphan drug development constitutes strategic CSR only when pricing, access programs, and communication practices are aligned with long-term patient welfare rather than short-term reputational signaling.

Benchmarking initiatives increase accountability in this domain. Lee and Kohler (2010) demonstrate that access-to-medicine indices and NGO evaluations expose discrepancies between corporate rhetoric and actual access outcomes, shaping investor behavior and reputational capital. Transparency mechanisms thus transform CSR from voluntary philanthropy into a competitive legitimacy market. Firms that demonstrate measurable commitments to affordability, voluntary licensing, and equitable distribution derive reputational advantages, while opacity increases regulatory and political risk.

Common CSR instruments include differential pricing across income levels, patient assistance programs, public–private partnerships, and voluntary licensing agreements. Yet empirical evidence suggests that differential pricing often fails to align with income gradients in middle- and low-income countries, limiting affordability despite formal CSR commitments (Danzon et al., 2015b). CSR effectiveness therefore depends not only on firm intent but also on procurement systems, insurance coverage, and national regulatory capacity.

Ethical CSR in pharmaceuticals cannot be confined to philanthropic donations or public relations campaigns. Nussbaum (2009) argues that the industry's legitimacy depends on embedding responsibility within core commercialization decisions. This includes transparent pricing rationales, responsible use of exclusivity rights, and collaborative engagement with governments and civil society. Where CSR remains peripheral, tensions between profitability and access reemerge cyclically; where CSR is integrated into governance structures, firms are more likely to achieve durable compatibility between innovation incentives and societal trust.

CSR in the pharmaceutical industry therefore functions as a governance mechanism that mediates expectations about fairness, innovation, and global health equity. Its credibility rests less on isolated philanthropic initiatives than on sustained alignment between pricing strategy, regulatory engagement, and access

outcomes.

6.3 Regulation

6.3.1 Regulation and Pharmaceutical Pricing

Pharmaceutical pricing is shaped by extensive regulatory intervention aimed at containing healthcare expenditures while preserving patient access to innovative therapies. Unlike conventional consumer markets, pharmaceutical markets exhibit information asymmetries, insurance-induced price insensitivity, and patent-based market power, which motivate direct price oversight.

Two principal regulatory instruments dominate international practice: price cap regulation and external reference pricing (ERP). Price caps establish maximum allowable prices at either the manufacturer or retail level, directly limiting the exercise of market power. External reference pricing links domestic prices to those observed in a basket of reference countries, typically through average or minimum price formulas. ERP creates interdependent pricing structures in which price reductions in one country propagate across multiple markets.

Parallel trade represents a third and institutionally distinct regulatory constraint, particularly within the European Economic Area. Under the principle of free movement of goods, intermediaries may purchase pharmaceuticals in low-price countries and resell them in higher-price markets. This arbitrage mechanism imposes indirect price discipline on manufacturers and limits the sustainability of international price discrimination. Parallel trade thus functions as a market-mediated regulatory force that interacts strategically with both ERP and national price caps.

These mechanisms operate jointly with patent protection, generic entry, reimbursement negotiations, and global launch sequencing. While regulation improves static efficiency by lowering prices, concerns persist regarding its impact on dynamic efficiency through altered innovation incentives.

Game-theoretic analyses formalize these trade-offs. Chen et al. (2019) model price cap regulation using a Stackelberg framework and distinguish between one-sided regulation and linkage price caps covering the entire supply chain. They show that one-sided regulation frequently harms the regulated entity while benefiting unregulated partners, whereas linkage caps can improve both economic and social outcomes. Bardey et al. (2010) develop a dynamic model of reference pricing that demonstrates how ERP affects not only pricing decisions but also R&D intensity and the type of innovation pursued, disproportionately discouraging incremental innovation.

Empirical studies identify nuanced behavioral responses. Brekke et al. (2015) exploit exogenous variation in Norwegian price caps and show that stricter regulation reduces parallel import competition and produces heterogeneous profit effects depending on exposure to arbitrage. Jaikumar et al. (2024) document how firms reallocate promotional effort away from regulated molecules following price controls, attenuating intended policy effects. Li and Wu (2022) show that firms treat regulatory ceilings as focal points, strategically bunching prices at caps rather than proportionally reducing them.

Cross-border spillovers are particularly salient. Maini and Pammolli (2023) develop a moment inequality framework to separate strategic launch delays from administrative delays and show that ERP increases entry delays in lower-income European countries by up to one year per drug. Parallel trade further redistributes surplus across countries, linking domestic regulation to broader regional market dynamics.

Across theoretical and empirical approaches, the literature converges on a fundamental policy tension: price regulation reduces short-run expenditures but alters firm behavior in ways that affect innovation

incentives, launch timing, promotion strategies, and cross-border access. Pharmaceutical pricing regulation therefore operates not as a static constraint but as a strategic environment that firms actively optimize against.

6.3.2 Recent U.S. Policy Developments (2016–2025)

The United States pharmaceutical pricing landscape has undergone significant regulatory evolution from 2016 through 2025, marked by diverse approaches across three presidential administrations. These policy interventions reflect ongoing tensions between controlling healthcare expenditures, maintaining innovation incentives, and ensuring patient access. Unlike the traditional regulatory approaches of price caps and external reference pricing prevalent in other OECD countries, U.S. policy has pursued a more heterogeneous set of mechanisms, ranging from transparency requirements to negotiation frameworks.

Trump Administration I (2017–2020)

The first Trump administration introduced multiple initiatives aimed at pharmaceutical pricing reform. The American Patients First blueprint, released in 2018, established a four-pillar framework: lowering list prices, improving negotiation capabilities, reducing out-of-pocket costs, and increasing competition (U.S. Department of Health and Human Services, 2018). This blueprint represented a comprehensive attempt to address pricing through market-based mechanisms rather than direct price controls.

The most favored nation (MFN) model, introduced as an interim final rule in 2020, represented a significant departure from traditional U.S. pricing policy. The model would have pegged Medicare Part B drug payments to the lowest prices paid by peer countries, effectively importing international reference pricing into the U.S. system. However, the MFN Model faced immediate legal challenges and was enjoined before implementation, ultimately being rescinded (Centers for Medicare & Medicaid Services, 2021).

The HHS published the anti-rebate final rule in 2020, restructuring the safe harbor provisions under the Anti-Kickback Statute and removing protections for certain Part D rebates while creating new safe harbors for point-of-sale discounts and fixed-fee service arrangements. Implementation of this rule faced statutory delays, reflecting the complex interplay between regulatory reform and existing contractual arrangements in the pharmaceutical supply chain (U.S. Department of Health and Human Service, 2020).

Biden Administration (2021–2024)

The Biden administration's signature pharmaceutical pricing achievement was the passage of the IRA in 2022. The IRA fundamentally restructured Medicare's relationship with pharmaceutical pricing through several mechanisms: granting Medicare direct negotiation authority for high-expenditure drugs, implementing inflation rebates when price increases exceed the Consumer Price Index, capping insulin copayments at $35 for Medicare beneficiaries, and redesigning Part D with a $2,000 annual out-of-pocket cap beginning in 2025 (Commonwealth Fund, 2025; Kaiser Family Foundation, 2022)

The CMS operationalized the IRA's negotiation provisions by publishing Maximum Fair Prices (MFPs) for the first cohort of negotiated drugs, with implementation scheduled for 2026. CMS simultaneously advanced the second negotiation cycle, demonstrating the administration's commitment to rapid implementation of the IRA's pricing provisions (Centers for Medicare & Medicaid Services, 2024).

Trump Administration II (2025–Present)

The second Trump administration has pursued a hybrid approach, combining elements of the earlier MFN framework with continued implementation of certain IRA provisions. An April 2025 Executive Order directed HHS to expand price transparency requirements and revisit specific IRA elements, particularly the so-called "pill penalty" that creates differential treatment between small-molecule drugs and biologics in the

negotiation timeline (Executive Office of the President, 2025).

The White House released MFN fact sheets in September and October 2025, announcing company-specific agreements styled after the earlier MFN concept. These bilateral arrangements represent a departure from the comprehensive regulatory approach of the original MFN Model, instead pursuing negotiated agreements with individual manufacturers (The White House, 2025b).

CMS has continued implementing the IRA framework, publishing MFPs and managing the second negotiation cycle logistics, demonstrating institutional continuity despite changes in executive leadership (Centers for Medicare & Medicaid Services, 2024). Ongoing policy discussions focus on how these various interventions interact with projected IRA savings and their collective impact on pharmaceutical innovation incentives (Centers for Medicare & Medicaid Services, 2024).

These policy developments from 2016 through 2025 illustrate the evolving nature of U.S. pharmaceutical pricing regulation. Rather than adopting the comprehensive price control mechanisms common in other developed nations, the U.S. has pursued a patchwork of transparency requirements, negotiation frameworks, and market-based reforms. The effectiveness of these diverse approaches in balancing affordability, access, and innovation incentives remains an active area of policy debate and empirical research.

7 Future Research and Conclusion

As pharmaceutical pricing continues to evolve in response to economic pressures, policy changes, and technological advancements, several key areas warrant further research:

Innovative Pricing Models for High-Cost Therapies: With the rise of biologics, gene therapies, and personalized medicine, traditional per-dose or per-cycle pricing models struggle to align costs, value, and access. For these treatments, development and manufacturing involve massive fixed costs but minimal marginal production costs, making conventional cost pass-through mechanisms unsustainable. Future research should explore how pricing frameworks can better match the timing and uncertainty of these expenditures while preserving incentives for innovation.

Alternative models, such as value-based contracts, subscription arrangements ("Netflix models"), annuity payments, and outcome-based risk-sharing agreements—aim to link payment to demonstrated clinical benefit rather than sales volume. Evaluating their effectiveness requires understanding how cost components translate into negotiated prices and how payers measure realized value over time. Empirical studies could use contract-level or claims data to assess whether these models lower total spending, improve adherence, or simply reallocate financial risk among manufacturers, payers, and patients.

Cross-national comparisons are also needed to determine how institutional contexts affect the adoption and success of these novel pricing schemes. Countries differ in their capacity to implement performance tracking, manage long-term contracts, and absorb up-front investment risk. Modeling work could integrate dynamic cost pass-through and innovation incentives to simulate how value-based or subscription pricing influences global R&D investment and launch sequencing.

Ultimately, advancing research on innovative pricing models requires bridging cost accounting, health economics, and industrial organization to design mechanisms that balance affordability, dynamic efficiency, and equitable access to breakthrough therapies.

Globalization and Its Impact on Pharmaceutical R&D and Pricing: As pharmaceutical R&D becomes increasingly global, cross-border cost-sharing, international clinical trials, and harmonized regulatory standards distribute development risks and shape how firms recover expenses across markets. Yet, recent

initiatives to benchmark domestic prices to those abroad, such as the United States' "American Patients First" and MFN frameworks, introduce new feedback pressures into global pricing systems. When high-income countries tie their reimbursement levels to prices in lower-cost markets, manufacturers may respond by raising launch prices overseas or delaying entry to preserve revenue parity. Such dynamics can unintentionally elevate benchmark-country prices or dampen long-term incentives for R&D investment. Future research should examine how these U.S. benchmarking policies influence innovation incentives, affordability, and cross-national price alignment, and assess their spillover effects on global R&D investment and access. It should also explore how emerging markets, international trade agreements, and global supply chains affect drug affordability and access, particularly in developing regions.

Assessing the Effectiveness of PAPs, Copay Coupons, and Emerging Discount Platforms: While PAPs, copay coupons, and other manufacturer-sponsored assistance programs aim to alleviate patients' out-of-pocket costs, they also raise concerns about sustaining high list prices, distorting formulary incentives, and shifting costs to payers. Despite their growing prevalence, rigorous causal evidence on their long-term effects remains limited. Future research should quantify how these programs influence pricing strategies, medication adherence, and overall healthcare expenditures—especially in markets dominated by high-cost specialty drugs.

Emerging digital discount platforms, such as GoodRx and similar cash-discount cards, create a parallel channel for price competition outside traditional insurance benefits. These tools introduce new data opportunities but also new policy questions: do they expand access or weaken insurers' negotiating leverage and further obscure the effective net prices generated by rebate contracts? Research could exploit transaction-level or claims-linked data to measure substitution between insured and cash-discount purchases, identify distributional effects across income groups, and evaluate whether such platforms improve adherence or merely reallocate financial burden. Comparative studies of copay assistance, accumulator bans, and cash-discount adoption across states could further reveal how these mechanisms interact to shape affordability, competition, and net spending. Collectively, this agenda would help clarify whether patient assistance tools function as short-term safety nets or as structural contributors to persistent price inflation.

Intermediaries and Supply-Chain Dynamics in Pharmaceutical Pricing: Across the pharmaceutical value chain, intermediaries, including wholesalers, PBMs, retail pharmacies, and GPOs—play critical roles in determining how manufacturer prices translate into the amounts ultimately paid by payers and patients. Yet empirical evidence on how these entities influence price formation, market power, and pass-through remains limited. Future research should analyze how recent structural changes—ranging from vertical integration to new contracting models—affect price transmission, competition, and welfare.

The transition from traditional buy-and-hold to fee-for-service wholesale models has reshaped inventory management and pricing, but its measurable effects on margins and efficiency remain under-studied. Quasi-experimental designs exploiting phased contract adoption could quantify how these changes alter bargaining power and shortage risk. With specialty-drug distribution exceeding $160 billion annually, additional research should examine how information asymmetries between manufacturers, wholesalers, and pharmacies shape cost pass-through and whether dynamic contract structures can mitigate shortages while maintaining incentives.

PBMs exert substantial influence through formulary design, rebate negotiation, and pharmacy-network management, yet their overall impact on net prices and patient costs remains contested. Future work should disentangle how rebate structures, accumulator programs, and tiered formularies shape list-to-net price differentials and out-of-pocket spending. Structural models of PBM–manufacturer bargaining could measure

how consolidation and insurer integration affect pass-through and rebate transparency, while linked claims and financial data could reveal whether PBM activities improve affordability or merely reallocate surplus across supply-chain actors.

Persistent price dispersion across retail pharmacies—even for identical generic drugs—suggests the presence of search frictions, heterogeneous cost structures, and network steering. Research should develop structural models of pharmacy–insurer bargaining and link transaction-level prices to plan formularies and geography to identify the drivers of dispersion. Studies could also evaluate how discount-card platforms and online pharmacies reshape competition and how pricing disparities affect vulnerable populations in underserved areas. Such work would inform policies that balance efficiency, transparency, and equity in retail drug markets.

GPOs aggregate purchasing power to negotiate discounts, yet their long-term welfare and innovation effects remain poorly quantified. Firm- and contract-level analyses could test whether stronger GPO presence lowers procurement costs or suppresses entry by smaller manufacturers. Incorporating information-sharing and fee-structure data into empirical models would clarify how GPOs mediate information asymmetries between providers and manufacturers. Comparative studies of alternative revenue models, fixed-fee versus volume-based compensation, could reveal which mechanisms best align incentives for cost reduction while sustaining innovation and supply-chain resilience.

Understanding Competition in the Era of Biosimilars: Although the economics of small-molecule generics are well studied, competition in biosimilar markets remains comparatively underexplored. Biosimilars differ fundamentally from generics in production complexity, regulatory pathways, and physician adoption behavior, leading to slower diffusion and more modest price reductions. Future research should investigate how these structural differences shape competitive dynamics, marketing strategies, and welfare outcomes.

First, empirical work is needed to measure how biosimilar manufacturers allocate resources to physician-directed promotion and how such efforts interact with physician beliefs about interchangeability, clinical equivalence, and risk. Physician-level adoption data could reveal whether biosimilar uptake responds more to detailing, peer influence, or formulary positioning relative to price signals. Behavioral models linking physician learning, habit formation, and perceived immunogenicity risks would enrich understanding of biosimilar diffusion.

Second, market-structure studies could examine how contracting practices, such as rebate walls, exclusive agreements, and portfolio bundling by originator biologic firms, affect biosimilar entry, pricing, and long-run competition. Dynamic game or structural models could capture how both incumbents and entrants optimize prices and promotion under uncertain regulatory or interchangeability environments.

Third, comparative analyses across therapeutic classes and countries could clarify why biosimilar price reductions vary widely, from 15 % in the United States to over 40 % in parts of Europe, and how payer policies, physician education, and patient trust mediate these outcomes. Integrating promotion data, physician prescribing records, and formulary design into unified empirical frameworks would help bridge industrial organization and health-behavior perspectives.

Collectively, these lines of inquiry would expand the evidence base on biosimilar competition, informing policies that balance innovation incentives with meaningful price competition in biologic markets.

Evaluating the Impact of New Pricing Regulations: Recent U.S. policy reforms, such as the IRA, Medicare Part D price negotiations, state-level accumulator bans, and transparency mandates, are transforming the institutional landscape of pharmaceutical pricing. These interventions provide valuable natural

experiments for assessing how regulation affects drug prices, market competition, and innovation. Future research should use quasi-experimental methods, such as difference-in-differences and synthetic-control designs, to estimate causal effects on list and net prices, launch timing, patient outcomes, and firm R&D behavior, providing rigorous evidence on the effectiveness and unintended consequences of these reforms within the U.S. context.

By addressing these research gaps, scholars and policymakers can gain a more comprehensive understanding of pharmaceutical pricing mechanisms and develop strategies to improve market efficiency, accessibility, and innovation.

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