

Pharmaceutical Pricing Regimes and Innovation: A Comparative Analysis of the United States, Europe, and Japan

Sandra Barbosu and Stephen Ezell*

Abstract

This chapter examines how pharmaceutical pricing regimes shape innovation incentives and patient access. Drawing on theoretical and empirical research, it develops a comparative framework linking pricing policies in the United States, Europe, and Japan to firm behavior: R&D investment, clinical development strategies, launch timing, and market participation. FDA approvals by applicant origin show a widening gap between the United States and both Europe and Japan, while clinical trial registrations show a similar divergence between the United States and Europe, most pronounced in early-stage development; the gap with Japan narrows. The literature reviewed here links these patterns to the effects of pricing regulation on firms' expected returns, though research capacity, public funding, and access to capital may also contribute, and the aggregate evidence cannot fully disentangle these influences. It concludes by considering pricing policy within the broader innovation ecosystem, the international distribution of innovation financing, and the potential to improve affordability through insurance design rather than lower manufacturer prices.

I. Introduction

Pharmaceutical policy confronts a fundamental tension between ensuring access to existing treatments and maintaining incentives to develop future therapies. The prospect of earning revenues from existing treatments provides firms with incentives to invest in future therapies, while the prices of those treatments contribute to current health expenditure. This tension between access and innovation – often described as the innovation-access trade-off – has shaped pharmaceutical policy for decades and has become increasingly prominent as biomedical innovation has advanced toward more complex and resource-intensive therapeutic modalities, including biologics, precision therapies, and gene therapies.¹ At the

* Barbosu: Information Technology and Innovation Foundation, Associate Director, Center for Life Sciences Innovation; Ezell: Information Technology and Innovation Foundation, Director, Center for Life Sciences Innovation, Executive Vice President, Global Innovation Policy

¹ Patricia M. Danzon and Adrian Towse, "Differential Pricing for Pharmaceuticals: Reconciling Access, R&D and Patents," *International Journal of Health Care Finance and Economics* 3, no. 3 (2003): 183–205.

same time, the extent to which pharmaceutical pricing influences innovation, and the mechanisms through which it does so, remain subjects of active scholarly debate.²

Countries differ substantially in how they seek to balance these competing objectives. The United States has traditionally relied more on market-based pricing mechanisms, whereas many European countries, along with Japan and other advanced economies, have adopted pharmaceutical price controls and centralized reimbursement systems. Such differences reflect both institutional variation and divergent policy judgments regarding the appropriate balance between containing healthcare expenditures in the present and encouraging the development of future therapies.

Differences in pharmaceutical pricing and reimbursement systems have increasingly coincided with shifts in the global geography of pharmaceutical innovation. Europe accounted for a substantial share of new medicines introduced globally throughout much of the postwar period and maintained a leading position in pharmaceutical research and development (R&D) through the 1980s. In the 1970s, European companies were introducing more than twice as many new drugs as their U.S. counterparts. Over subsequent decades, however, the center of pharmaceutical innovation shifted toward the United States, and by the early 2000s U.S.-based firms had become the dominant source of new drug development.³ Japan also experienced a decline over the same period – while Japanese-headquartered firms introduced 29 percent of the world’s new chemical entities in the 1980s, their share fell to 7 percent in the 2010s.⁴ These developments have prompted growing research interest in the extent to which differences in pharmaceutical pricing and reimbursement policies may have contributed to changing patterns of pharmaceutical innovation.

² Daron Acemoglu and Joshua Linn, “Market Size in Innovation: Theory and Evidence from the Pharmaceutical Industry,” *Quarterly Journal of Economics* 119, no. 3 (2004): 1049–1090.

³ Sandra Barbosu, Stephen Ezell, and Esther Serger, “Lessons from Europe’s Loss of Biopharma Leadership, and its Attempts to Recover,” (2026), Washington, DC: Information Technology and Innovation Foundation.

⁴ Stephen Ezell, “How Japan Squandered Its Biopharmaceutical Competitiveness: A Cautionary Tale,” (2022), Washington, DC: Information Technology and Innovation Foundation.

A large empirical literature suggests that policy choices, including those affecting pharmaceutical pricing and reimbursement, shape the expected returns to innovation and in turn influence firms' R&D investment decisions.⁵ These relationships are mediated by scientific capacity, market size, intellectual property regimes, and the broader legal and regulatory environment.

The public health and economic implications of these geographic shifts are substantial. Pharmaceutical innovation is associated with gains in life expectancy and reductions in disease burden, while the geographic concentration of R&D carries broader economic consequences for high-skill employment, capital investment, and tax revenues. The relationship between pricing policy and the geography of innovation is therefore not only a question of access to medicines but also one of economic competitiveness in a globally important, research-intensive industry.^{6,7}

This chapter examines how pharmaceutical pricing regimes influence firm behavior across three major markets: the United States, Europe, and Japan. Because pharmaceutical R&D and commercialization span national borders, firms make investment, development, launch, and market-entry decisions in response to expected returns across multiple jurisdictions. The evidence reviewed here suggests that policies constraining expected returns can weaken incentives for pharmaceutical innovation, with implications for the geographic distribution of R&D and patient access.⁸ The chapter also discusses how these effects interact with differences in research capacity, public funding, and the broader innovation ecosystem.

⁵ Margaret K. Kyle, "Pharmaceutical Price Controls and Entry Strategies," *Review of Economics and Statistics* 89, no. 1 (2007): 88–99; Acemoglu and Linn, "Market Size in Innovation: Theory and Evidence from the Pharmaceutical Industry."

⁶ Frank R. Lichtenberg, "Pharmaceutical Innovation and Longevity Growth in 30 Developing and High-Income Countries, 2000–2009," *Health Policy and Technology* 3, no. 1 (2014): 36–58.

⁷ Patricia M. Danzon and Eric L. Keuffel, "Regulation of the Pharmaceutical-Biotechnology Industry," in *Economic Regulation and Its Reform: What Have We Learned?* ed. Nancy L. Rose (Chicago: University of Chicago Press, 2014), 407–484.

⁸ Margaret K. Kyle, "Lessons for the United States from Pharmaceutical Regulation Abroad," *Journal of Economic Perspectives* 39, no. 2 (2025): 53–78.

The chapter characterizes the mechanisms through which pricing regimes operate and documents the patterns associated with them. The descriptive evidence presented in Section IV is consistent with the operation of pricing incentives, but these patterns may also reflect differences in research capacity, public funding, access to capital, and other factors. We do not attempt to disentangle the relative contributions of these factors, which would require more granular variation in pricing policies and firm responses than the aggregate data examined here provide.

The remainder of the chapter proceeds as follows. Section II draws on existing literature to develop a conceptual framework linking pricing regimes to pharmaceutical innovation. Section III compares pricing systems in the United States, Europe, and Japan. Section IV presents descriptive evidence on pharmaceutical innovation trends. Section V reviews evidence from existing studies on the relationship between pricing regulation and firm behavior and market outcomes, and Section VI discusses policy implications. Section VII concludes.

II. Conceptual Framework: How Pricing Regimes Shape Pharmaceutical Innovation

The economics of pharmaceutical innovation rest on a close linkage between expected returns and investment in R&D. Bringing a single new medicine to market typically requires 10 to 15 years of development, substantial upfront investment, and the assumption of considerable scientific and regulatory risk. Less than 12 percent of compounds entering human testing ultimately receive regulatory approval.⁹ Under these conditions, firms make R&D decisions based on expectations regarding future market opportunities and returns. The prospect of future revenues is therefore central to sustaining investment in pharmaceutical innovation.¹⁰

⁹ Joseph A. DiMasi, Henry G. Grabowski, and Ronald W. Hansen, “Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs,” *Journal of Health Economics* 47 (2016): 20–33.

¹⁰ Alfonso Gambardella, *Science and Innovation: The US Pharmaceutical Industry During the 1980s* (Cambridge: Cambridge University Press, 1995); Rebecca Henderson and Iain Cockburn, “Measuring Competence? Exploring Firm Effects in Pharmaceutical Research,” *Strategic Management Journal* 15, no.

Pharmaceutical pricing policy can involve a trade-off between affordability and innovation. Price controls and other forms of pricing and reimbursement regulation can reduce prices paid for medicines, potentially lowering costs for patients and payers. At the same time, by reducing expected revenues, such policies may weaken incentives to invest in risky and costly R&D. The central empirical question in the literature is how strongly pricing policies affect innovation incentives, and how these effects vary across therapeutic areas, patient populations, and time horizons.¹¹

A substantial body of research suggests that expected market returns influence pharmaceutical innovation. Studies examining variation in market size, revenues, and reimbursement policies generally find positive relationships between expected returns and innovative activity.¹² Acemoglu and Linn (2004), for example, estimate that increases in potential market size lead to substantial increases in new drug introductions, and Finkelstein (2004) finds similar effects following the expansion of Medicare vaccine coverage.¹³ Taken together, this literature provides support for the proposition that pricing and reimbursement policies can influence innovation through their effects on expected returns, although the magnitude of these effects remains an area of active debate.

Ho and Pakes (2025) further argue that pharmaceutical innovation generates global benefits while being financed disproportionately by U.S. consumers. Modeling a counterfactual in which prices converge internationally, they find that U.S. prices could fall substantially

S1 (1994): 63–84; Henry G. Grabowski and John M. Vernon, “A New Look at the Returns and Risks to Pharmaceutical R&D,” *Management Science* 36, no. 7 (1990): 804–821.

¹¹ Darius Lakdawalla, “Economics of the Pharmaceutical Industry,” *Journal of Economic Literature* 56, no. 2 (2018): 397–449.

¹² John A. Vernon, “Examining the Link Between Price Regulation and Pharmaceutical R&D Investment,” *Health Economics* 14, no. 1 (2005): 1–16; Carmelo Giaccotto, Rexford E. Santerre, and John A. Vernon, “Drug Prices and Research and Development Investment Behavior in the Pharmaceutical Industry,” *Journal of Law and Economics* 48, no. 1 (2005): 195–214; Frank R. Lichtenberg, “Pharmaceutical Innovation and the Burden of Disease in Developing and Developed Countries,” *Journal of Medicine and Philosophy* 30, no. 6 (2005): 663–690.

¹³ Acemoglu and Linn, “Market Size in Innovation: Theory and Evidence from the Pharmaceutical Industry”; Amy Finkelstein, “Static and Dynamic Effects of Health Policy: Evidence from the Vaccine Industry,” *Quarterly Journal of Economics* 119, no. 2 (2004): 527–564.

only if pharmaceutical prices in other high-income countries increased markedly, with prices rising to approximately 148 percent of current levels in Germany, 197 percent in France, 263 percent in Italy, and 287 percent in Spain. Their analysis highlights the extent to which current global pharmaceutical innovation depends on cross-country differences in pricing and suggests that the U.S. pricing premium functions as an important source of financing for worldwide pharmaceutical R&D.¹⁴

The relationship between pricing regulation and innovation is mediated by a range of factors, including market size, scientific capabilities, intellectual property protections, regulatory efficiency, access to capital, and the broader structure of the innovation ecosystem. Pricing regimes therefore influence innovation through a series of intermediate firm decisions regarding R&D investment, clinical development, launch timing, market participation, and investment location. The remainder of this section develops these mechanisms and their implications for comparative analysis.

A. Mechanisms of Price Regulation

Pricing regimes vary considerably in their institutional design. At one end of the spectrum are relatively market-oriented systems that allow manufacturers substantial discretion in setting launch prices, subject to competition, payer negotiations, and regulatory constraints. Historically, the United States has been among the most market-oriented pharmaceutical pricing systems in the world, relying primarily on negotiations among manufacturers, insurers, pharmacy benefit managers, and other market participants rather than direct government price controls. The recent introduction of Medicare drug price negotiation under the Inflation Reduction Act and proposals for Most-Favored-Nation pricing represent an important shift toward greater government involvement in pharmaceutical price determination.

At the other end of the spectrum are systems that rely on government intervention to regulate pharmaceutical prices. Although countries often combine multiple instruments,

¹⁴ Kate Ho and Ariel Pakes, “Policy Options for the Drug Pricing Conundrum,” *Proceedings of the National Academy of Sciences* 122, no. 9 (2025): e2418540122.

common forms of pharmaceutical price regulation include direct price-setting, international reference pricing, health technology assessment (HTA)-based reimbursement, and expenditure-control mechanisms. While these approaches differ in their institutional design and implementation, they operate through a common economic mechanism: they influence the revenues firms expect to earn from successful innovation and therefore affect incentives for pharmaceutical R&D.

Though operating through different channels, these mechanisms influence expected revenues by limiting pricing flexibility, conditioning reimbursement on demonstrated value, or constraining firms' ability to sustain higher prices across markets. Differences in pricing policy can therefore shape not only medicine affordability but also the volume, direction, and geographic distribution of innovative activity.

Direct price-setting. Direct price-setting involves government authorities establishing maximum allowable prices for medicines, either at launch or through periodic revision. Japan's National Health Insurance drug pricing system, which sets prices through a comparator-based formula revised biennially, and annually since 2021, is one example.¹⁵ Direct price-setting compresses launch prices and expected revenue trajectories throughout a drug's lifecycle, making firms' strategic decisions at launch and during subsequent price revisions more consequential, thereby affecting the timing and availability of new medicines. Kyle (2007) finds that pharmaceutical price controls are associated with delayed launches and reduced availability of new medicines, particularly in more heavily regulated markets.¹⁶

International reference pricing. International reference pricing links the price of a drug in one country to its price in a basket of reference countries, creating price interdependencies across markets. When a firm accepts a low price in one country, reference-pricing mechanisms reduce the maximum allowable price in other countries that reference it. This

¹⁵ "Japan's FY2026 Drug Pricing Reform," Windrose Consulting Group, <https://www.windrosecg.com/posts/japan-fy2026-reforms>.

¹⁶ Margaret K. Kyle, "Pharmaceutical Price Controls and Entry Strategies," 88–99.

creates incentives for the strategic sequencing of product launches across markets, encouraging firms to enter higher-price markets first while delaying, or even forgoing, entry into lower-price markets that may anchor price comparisons. As a result, international reference pricing can affect both prices and the timing and availability of new medicines.¹⁷

Health technology assessment-based reimbursement. Health technology assessment (HTA) involves independent bodies evaluating the clinical and cost-effectiveness of new medicines relative to existing alternatives, with reimbursement decisions contingent on the results. The United Kingdom’s National Institute for Health and Care Excellence (NICE), Germany’s Federal Joint Committee (G-BA), and France’s Haute Autorité de Santé each conduct health technology assessments to inform reimbursement decisions.¹⁸ NICE is notable for explicitly incorporating cost-effectiveness thresholds into reimbursement recommendations, while Germany and France place greater emphasis on assessments of comparative clinical benefit.¹⁹ By linking reimbursement to demonstrated incremental value, HTA-based reimbursement creates incentives for firms to generate specific types of clinical evidence and to target indications in which superiority over existing treatments can be demonstrated. Thus, HTA functions not only as a pricing and reimbursement instrument, but also as a determinant of the composition of the development pipeline.

The combined effect of these mechanisms depends on which instruments are deployed, how they interact, and the institutional capacity that supports their implementation. Comparing pricing systems therefore requires attention not only to formal policy instruments but also to the procedural details that shape their operation, including the speed of HTA review, the stringency of cost-effectiveness thresholds, the composition of reference baskets, and the frequency of price revisions. In practice, most pharmaceutical

¹⁷ Kyle, “Pharmaceutical Price Controls and Entry Strategies”; Patricia Danzon, Y. Richard Wang, and Liang Wang, “The impact of price regulation on the launch delay of new drugs – evidence from twenty-five major markets in the 1990s,” *Health Economics* 14, no. 3 (2005): 269–292.

¹⁸ N. Allen, L. Liberti, S. R. Walker, and S. Salek, “A Comparison of Reimbursement Recommendations by European HTA Agencies: Is There Opportunity for Further Alignment?” *Frontiers in Pharmacology* 8 (2017): 384.

¹⁹ Christopher McCabe, Karl Claxton, and Anthony J. Culyer, “The NICE Cost-Effectiveness Threshold: What It Is and What That Means,” *Pharmacoeconomics* 26, no. 9 (2008): 733–744.

pricing systems combine several of these mechanisms simultaneously, making the effects of any individual pricing instrument contingent on the broader institutional framework in which it operates.

III. Institutional Context: Global Pricing Systems

Having established the conceptual framework linking pharmaceutical pricing regimes to firms' innovation incentives, this section examines the institutional contexts through which prices are determined in three of the world's largest pharmaceutical markets: the United States, Europe, and Japan. As these regions employ different pricing systems, they provide the context for the comparative evidence presented in Section IV.

A. United States

The United States is characterized by the most market-oriented pharmaceutical pricing system among high-income countries. Unlike most peer nations, the U.S. government has not historically regulated drug prices at launch. Instead, prices have generally been determined through negotiations between manufacturers and private payers, including pharmacy benefit managers acting on behalf of insurers and employer plans, and other market participants. This system has produced comparatively high drug prices for prescription medicines, with average U.S. prices approximately 278 percent of prices in 33 OECD comparison countries combined.²⁰ The resulting revenue premium has supported a substantial share of global pharmaceutical R&D.²¹

The relative absence of direct government price regulation in the United States has been a structural feature. The passage of the 1984 Hatch-Waxman Act led to market-based solutions of increasing competition by establishing finite periods of market exclusivity while simultaneously providing access to lower cost generics following patent expiration.²²

²⁰ Andrew W. Mulcahy, Daniel Schwam, and Susan L. Lovejoy, "International Prescription Drug Price Comparisons: Estimates Using 2022 Data," *RAND Health Quarterly* 11, no. 3 (2024): 5.

²¹ Kyle, "Lessons for the United States from Pharmaceutical Regulation Abroad."

²² Stephen Ezell and Leah Kann, "A Bipartisan Success: Celebrating 40 Years of the Hatch-Waxman Act," *Hatch Foundation Policy Review* (2025): 5.

The result has been a system in which branded drug prices are typically high during the patent-protected period and decline rapidly upon entry of generic competition, with generic medicines generally priced substantially below their international comparators. In fact, 90 percent of U.S. prescriptions are for generic drugs, and the average co-pay for generic drugs in the United States is \$6.16, with 92 percent of all generics having a co-pay of less than \$20.²³ This structure of high prices during patent exclusivity and low prices thereafter is a distinctive feature of the U.S. system.

U.S. strength in pharmaceutical innovation has been reinforced by complementary institutional factors. The Bayh-Dole Act of 1980 enabled universities and other institutions to patent inventions arising from federally funded research, supporting the development of university technology-transfer systems.²⁴ The Orphan Drug Act of 1983 introduced incentives, including market exclusivity and tax credits, to encourage the development of treatments for rare diseases.²⁵ The Prescription Drug User Fee Act of 1992 strengthened the FDA's capacity to review drug applications and helped reduce review times. Sustained federal investment through the National Institutes of Health (NIH), whose budget reached approximately \$48 billion in 2025 (substantially higher than those of comparable agencies in other countries, with China's Natural Science Foundation second at \$5.8 billion) has supported the basic biomedical research foundation underpinning pharmaceutical innovation.²⁶ The United States has also substantially outpaced the European Union in

²³ IQVIA, The Use of Medicines in the U.S. 2023 (April 2023), <https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/the-use-of-medicines-in-the-us-2023/the-use-of-medicines-in-the-us-2023.pdf>; Association for Accessible Medicines, "The U.S. Generic & Biosimilar Medicines Savings Report," September 2023, <https://accessiblemeds.org/wp-content/uploads/2024/11/AAM-2023-Generic-Biosimilar-Medicines-Savings-Report-web.pdf>.

²⁴ David C. Mowery, Richard R. Nelson, Bhaven N. Sampat, and Arvids A. Ziedonis, "Ivory Tower and Industrial Innovation: University-Industry Technology Transfer Before and After the Bayh-Dole Act," (Stanford, CA: Stanford University Press, 2004).

²⁵ "The Orphan Drug Act: Legal Overview and Policy Considerations," Congress.gov, <https://www.congress.gov/crs-product/IF12605>.

²⁶ National Institutes of Health, Budget (Bethesda, MD: U.S. Department of Health and Human Services, 2025). Sandra Barbosu and Sarina Fereydooni, "How NIH-Funded Science Supports U.S. Biopharmaceutical Innovation," (2026), Washington, DC: Information Technology and Innovation Foundation.

biotechnology venture capital funding over the past decade, with the gap reaching as much as tenfold in 2021, when U.S. funding was up to ten times greater (\$102 billion PPP).²⁷

The Inflation Reduction Act of 2022 introduced the most significant change to U.S. pharmaceutical pricing policy in decades, with the government seeking a more active role in drug price regulation. The Medicare Drug Price Negotiation Program authorizes the Department of Health and Human Services to negotiate prices for a defined set of high-expenditure drugs, with negotiated prices first taking effect in 2026. The Act introduced differential treatment of small molecules and biologics, with the former eligible for negotiation nine years after approval and the latter eligible after thirteen years.²⁸

B. Europe

Europe's pharmaceutical pricing landscape is the result of several decades of policy evolution. Between 1960 and 1965, European firms produced approximately 65 percent of all new global medicines, and as late as 1990, European pharmaceutical R&D investment exceeded that of the United States.²⁹

Beginning in the 1980s, many European nations implemented a wide array of pharmaceutical price control tools, including international (and regional) reference pricing systems, cost-focused health technology assessments, global prescribing budgets that held provider organizations accountable for exceeding spending budgets, profit controls that capped what insurers could pay for groups of similar drugs, and rules limiting the use of higher-priced medicines to hospitals.³⁰

²⁷ Cesar Barraza-Botet, Daniel Nadal, and David Winickoff, “Biotech start-ups in Europe: Why does the EU lag behind competitors and what can policymakers do about it?” *OECD*, April 2026.

²⁸ Juliette Cubanski, Tricia Neuman, and Meredith Freed, “FAQs about the Inflation Reduction Act's Medicare Drug Price Negotiation Program,” Kaiser Family Foundation (2023), <https://www.kff.org/medicare/issue-brief/faqs-about-the-inflation-reduction-acts-medicare-drug-price-negotiation-program/>.

²⁹ Ezell, “Lessons from Europe’s Loss of Biopharma Leadership, and its Attempts to Recover.”

³⁰ Lakdawalla et al., “U.S. Pharmaceutical Policy In A Global Marketplace” (2008), https://www.rand.org/content/dam/rand/pubs/reprints/2009/RAND_RP1380.pdf; David J. Gross, “International Pharmaceutical Spending Controls: France, Germany, Sweden, and the United

In Germany, the Health Reform Act of 1989 introduced a national reference price system for reimbursable drugs, grouping them into three classes and setting each class's reimbursement ceiling at the average price of the drug and therapeutically similar products.³¹ A U.S. Government Accountability Office report notes that in 1993 Germany added across-the-board price cuts on drugs outside the reference system and reduced nonprescription prices.³² A study of average prices per defined daily dose across eight therapeutic classes found that each class's average price fell immediately after reference prices were introduced.³³

In the Netherlands, the 1996 Medicine Prices Act set maximum prices for prescription medicines from the average price of similar drugs across a four-country basket: Belgium, France, Germany, and the United Kingdom.³⁴ In October 2020 Norway replaced Germany in the basket, reflecting its lower price levels and further reducing Dutch prices.³⁵

In France, the GAO report characterizes post-1980 regulation as relying on product-by-product price controls, with prices set through a three-step process: safety and efficacy review, assessment of therapeutic advance over existing drugs, and review of expected benefits to the national economy. Blanket directives limited price changes, including one in 1991 mandating a 2.5 percent decrease on all drugs.³⁶ Since 2013 pricing decisions have

Kingdom,” *Health Care Financing Review* 15, no. 3 (1994): 127–140, <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4193451/>.

³¹ Giovanni Giuliani, Gisbert Selke, and Livio Garattini, “The German experience in reference pricing,” *Health Policy*, 44, no. 1 (1998): 73-85, <https://www.sciencedirect.com/science/article/abs/pii/S0168851098000128>.

³² U.S. Government Accountability Office (GAO), “Prescription Drugs: Spending Controls in Four European Countries,” (GAO, May 1994), 56, <https://www.gao.gov/assets/hehs-94-30.pdf>.

³³ Giuliani, Selke, and Garattini, “The German experience in reference pricing.”

³⁴ Livio Garattini, Dante Cornago, and Paola De Compadri, “Pricing and reimbursement of in-patent drugs in seven European countries: a comparative analysis,” *Health Policy* 82, no. 3 (2007): 330–339, <https://pubmed.ncbi.nlm.nih.gov/17125881/>.

³⁵ “Keeping medicines affordable,” Government of the Netherlands, <https://www.government.nl/topics/medicines/keeping-medicines-affordable>.

³⁶ GAO, “Prescription Drugs: Spending Controls in Four European Countries.”

incorporated cost-effectiveness evaluation by the Economic and Public Health Committee, alongside comparator prices, and are reviewed at least every five years.³⁷

For Sweden, GAO reported that in 1993 the government established reimbursement by reference pricing, setting the reimbursable amount for brand-name drugs with generic equivalents, or directly for drugs outside the system, at the price of the lowest generic equivalent plus 10 percent. Variants of these mechanisms remain embedded in today's systems, including fixed reimbursement prices in France and profit limits in the United Kingdom.³⁸

C. Japan

Japan's position in global pharmaceutical innovation has undergone a marked reversal over recent decades. In the 1980s, Japan accounted for 29 percent of all new chemical entities introduced globally, a share that decreased to 7 percent in the 2010s. From 1995 to 2018, its share of global value added in the pharmaceutical industry declined from 18.5 to 5.5 percent, and its share of global pharmaceutical R&D had fallen by approximately half from 14.1 percent in 1987 to 7.3 percent in 2018. This decline reflects a combination of pricing policy and ecosystem-level factors, including faltering government investments in basic scientific research, weak industry-university relations, a more-slowly evolving regulatory system, and challenges with internationalization.³⁹

Japan's pharmaceutical pricing system operates through the National Health Insurance drug price list, which sets the official reimbursement price using a comparator methodology supplemented by innovation premiums. A distinctive feature is the downward revision of prices through periodic price revisions.⁴⁰

³⁷ Veronique C. Raimond et al., "Why France spends less than the United States on drugs: a comparative study of drug pricing and pricing regulation," *The Milbank Quarterly*, 99, no. 1 (2021): 240–272, <https://pmc.ncbi.nlm.nih.gov/articles/PMC7984670/>.

³⁸ GAO, "Prescription Drugs: Spending Controls in Four European Countries."

³⁹ Ezell, "How Japan Squandered Its Biopharmaceutical Competitiveness: A Cautionary Tale."

⁴⁰ Trinity Life Sciences, *Japan Pricing Policy Reform 2024: Accelerating Access and Innovation* (Waltham, MA: Trinity, 2024).

The 2012 price maintenance premium was introduced to mitigate revenue erosion for ground-breaking drugs by deferring the price cuts to the end of the patent protection period, but its eligibility requirements were criticized for a lack of transparency and for implicitly leaving out emerging smaller biotechnology companies. Japan's 2024 pricing policy reforms aimed to support innovation while also addressing drug lags and drug losses by simplifying the price maintenance premium system and creating premiums for incentivizing the early introduction of new therapies in Japan.⁴¹

IV. Descriptive Trends in Pharmaceutical Innovation

Sections II and III described the mechanisms and institutional differences that shape pharmaceutical innovation across major markets. In this section, we explore how two dimensions of pharmaceutical innovation – novel drug approvals and the geographic distribution of clinical trials – relate to the framework developed above, focusing on the United States, Europe, and Japan, which have different pricing regimes.

A. Data

We draw on two complementary datasets. FDA drug approval data help identify the locations of firms bringing innovative medicines to market, while global clinical trial data from ClinicalTrials.gov capture where clinical development takes place. Together, these datasets allow us to examine patterns in pharmaceutical innovation across markets, distinguishing between where such firms are based and where they conduct clinical development.

FDA approvals by applicant origin. The first dataset covers 1,362 novel FDA drug approvals (new molecular entity (NME) and new biologics) from 1985 to 2024. We manually identified the country of headquarters of each applicant firm.⁴² Firms were then grouped into four regions: the United States (975 approvals), Europe (312), Japan (39), and

⁴¹ Trinity Life Sciences, Japan Pricing Policy Reform 2024.

⁴² “Compilation of CDER New Molecular Entity (NME) Drug and New Biologic Approvals,” FDA, <https://www.fda.gov/drugs/drug-approvals-and-databases/compilation-cder-new-molecular-entity-nme-drug-and-new-biologic-approvals>.

the rest of the world (36). This measure captures the headquarters location of the firm commercializing each medicine, not necessarily where it was developed. Because large pharmaceutical firms operate global R&D networks and frequently in-license compounds developed elsewhere, applicant origin is best interpreted as an indicator of where firms bringing novel medicines to market are based, rather than where the underlying innovation was generated.

Clinical trial activity by region. The second dataset, from ClinicalTrials.gov, comprises interventional drug and biological trials from around the world.⁴³ Coverage of trials initiated before 2009 is incomplete and uneven across regions. Registration was voluntary for most trials until the International Committee of Medical Journal Editors made it a condition of publication in July 2005, and the FDA Amendments Act imposed a statutory requirement only in September 2007; the requirement took effect several months later, and compliance accumulated with a lag.⁴⁴ We therefore restrict the analysis to trials initiated between 2009 and 2024. Trials without phase information, Phase 4 trials, and combined-phase trials were excluded to facilitate consistent comparisons across development stages, leaving an analytic sample of 98,408 Phase 1, Phase 2, and Phase 3 trials. Trials are further classified as industry- or non-industry-sponsored for each trial's lead sponsor. Industry sponsors account for 50,218 trials (51.0 percent), with the remainder sponsored by academic medical centers, government agencies, and other non-commercial organizations.

We note that the dataset has two limitations. First, ClinicalTrials.gov is one of several national and regional registries, so it may understate non-U.S. activity, particularly for development programs not directed at the U.S. market. Second, multinational trials are assigned to each region in which they have sites, meaning that the series captures participation in clinical development rather than mutually exclusive regional shares.

⁴³ “ClinicalTrials.gov,” NIH National Library of Medicine, <https://clinicaltrials.gov/search?viewType=Card>.

⁴⁴ “Update on Trials Registration: Is this clinical trial fully registered?” May 2005, https://www.icmje.org/news-and-editorials/update_2005.html; “FDA Amendments Act of 2007,” <https://www.fda.gov/regulatory-information/selected-amendments-fdc-act/food-and-drug-administration-amendments-act-fdaaa-2007>.

B. Empirical Approach

This section presents both measures over time: long-run trends in FDA novel drug approvals by applicant origin, and clinical trial activity by region, funder type, and development phase.

Trends in FDA Novel Drug Approvals by Applicant Origin

Figure 1 plots the annual number of FDA drug approvals by applicant origin, distinguishing the United States, Europe, Japan, and the rest of the world. It shows that the United States has an upward trend and the most FDA-approved drugs in each year of the sample, with European, Japanese, and Rest of World contributions flat or only marginally rising, and a widening gap between the United States and Europe over time.

In particular, drugs originating in the United States average 17 per year in the 1980s, 23 in the 1990s, 20 in the 2000s, 27 in the 2010s, and 39 in the 2020s, with a peak of 46 in 2020 – a pronounced rise over approximately four decades. Drugs originating in Europe show no comparable increase: they average 7 per year in the 1980s, 10 in the 1990s, 6 in the 2000s, 8 in the 2010s, and 8 in the 2020s, with a peak of 21 in 1996. Further, the widening of the U.S.–Europe gap is concentrated in the post-2014 period.

Contributions from Japan and the rest of the world remain small throughout. Drugs originating in Japan average fewer than 1 per year before 2010, rise to slightly over 2 per year across the 2010s, and fall back to 0.6 per year in the 2020s, below their 2000s level. Overall, Japan and the rest of the world together account for only 5.5 percent of FDA approvals in the sample period.

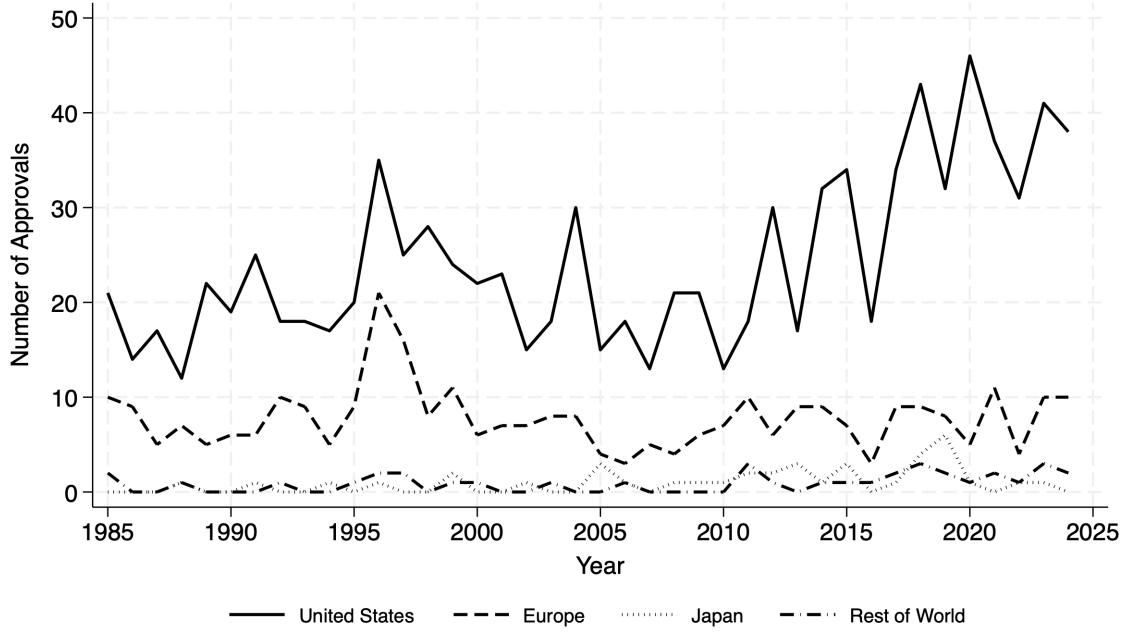


Figure 1. FDA new drug approvals by applicant origin, 1985-2024

To quantify the magnitude visible in Figure 1, we estimate a pooled regression of the form:

$$Approvals_{it} = \alpha + \beta_1 Trend_t + \beta_2 Europe_i + \beta_3 Japan_i + \beta_4 (Europe_i \times Trend_t) + \beta_5 (Japan_i \times Trend_t) + \varepsilon_{it}$$

where $Approvals_{it}$ is the annual number of FDA novel drug approvals for region i in period t , $Trend_t$ is a linear time index running from 1 in 1985 to 40 in 2024, and $Europe_i$ and $Japan_i$ are regional indicators with the United States as the omitted reference category. The specification is descriptive and does not identify a causal relationship between pricing regimes and approval counts.

Table 1 reports the regression results. The coefficient on $Trend$ ($\beta_1 = 0.473$) captures the annual trend for the United States, implying that U.S.-originated FDA approvals rose by approximately half an approval per year between 1985 and 2024.

The interaction coefficients are of primary interest. The $Europe \times Trend$ coefficient ($\beta_4 = -0.498$) implies a European trend of $0.473 - 0.498 = -0.025$ approvals per year, and the $Japan \times Trend$ coefficient ($\beta_5 = -0.425$) implies a Japanese trend of $0.473 - 0.425 = 0.048$

approvals per year. The European trend is not statistically distinguishable from zero ($p = 0.54$). The Japanese trend is distinguishable from zero ($p = 0.01$) but negligible beside the U.S. trend of 0.473, so the U.S.-Japan gap widens alongside the U.S.-Europe gap.

Table 1. FDA new drug approvals by applicant origin, 1985-2024

Variable	Coefficient
Trend	0.473*** (0.089)
Europe	-6.365*** (2.065)
Japan	-14.685*** (1.746)
Europe $\times$ Trend	-0.498*** (0.098)
Japan $\times$ Trend	-0.425*** (0.091)
N	120
R ²	0.838

Notes: Robust standard errors in parentheses. Cluster-robust standard errors are not reported because the number of regional clusters (three) is too small for reliable inference. *** $p < 0.01$, ** $p < 0.05$, * $p < 0.10$.

Figure 2 visualizes the fitted regression from Table 1. Points show the average number of FDA novel drug approvals within two-year bins by applicant region, and the overlaid lines show the fitted regression trends. The steep U.S. trajectory, set against the European and Japanese ones, shows the same widening regional gaps visible in Figure 1.

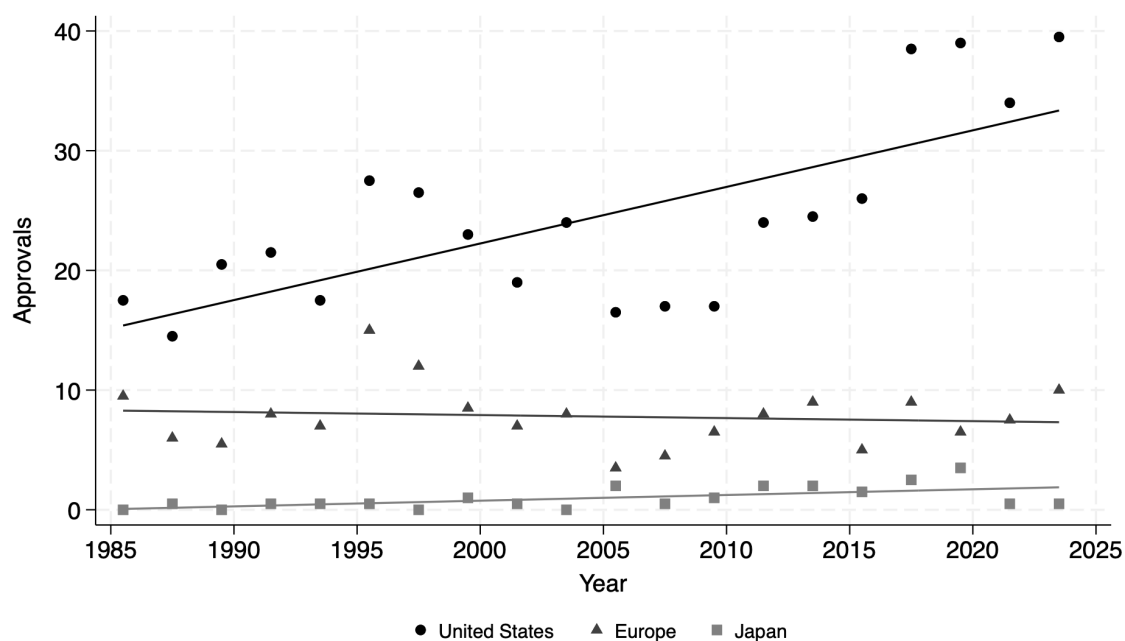


Figure 2. Binned scatter plot of FDA new drug approvals by applicant origin, 1985–2024

Trends in Clinical Development by Region

Figures 3, 4, and 5 report clinical trials with at least one site in each region, by development phase and sponsor type, while Table 2 provides an illustration of the underlying counts at four benchmark years.

Table 2. Clinical trials by region, development phase and sponsor type, selected years

Panel A. Industry-sponsored

Year	Phase	U.S.	Europe	Japan	Total
2009	Phase 1	521	371	51	1,215
2009	Phase 2	575	429	52	1,016
2009	Phase 3	422	381	117	847
2014	Phase 1	640	405	65	1,359
2014	Phase 2	525	287	58	849
2014	Phase 3	480	398	147	875
2019	Phase 1	627	413	73	1,475

2019	Phase 2	522	353	84	882
2019	Phase 3	476	380	185	797
2024	Phase 1	654	319	69	1,705
2024	Phase 2	449	271	89	844
2024	Phase 3	387	332	192	826

Panel B. Non-industry-sponsored

Year	Phase	U.S.	Europe	Japan	Total
2009	Phase 1	429	75	3	594
2009	Phase 2	602	281	6	1,153
2009	Phase 3	113	179	3	454
2014	Phase 1	530	115	6	808
2014	Phase 2	531	299	8	1,194
2014	Phase 3	104	173	4	531
2019	Phase 1	603	90	4	998
2019	Phase 2	684	355	9	1,712
2019	Phase 3	143	197	9	633
2024	Phase 1	472	66	3	1,111
2024	Phase 2	594	246	10	2,067
2024	Phase 3	115	149	5	667

Note: Japanese non-industry counts are small, and the corresponding ratios are unstable.

Figure 3 presents cumulative counts for 2009-2024, combining industry- and non-industry-sponsored trials. The United States leads in every phase, but its advantage over Europe narrows as development advances: 17,652 Phase 1 trials versus 7,459 in Europe (a ratio of 2.4); 18,258 versus 10,306 in Phase 2 (a ratio of 1.8); and 9,320 versus 9,072 in Phase 3 (just over 1). Japan shows a different pattern, with its lowest relative presence in early development, with 1,121 Phase 1 trials, roughly one-fifteenth of the U.S. total, and its strongest presence in Phase 3 clinical development, with 2,775 trials.

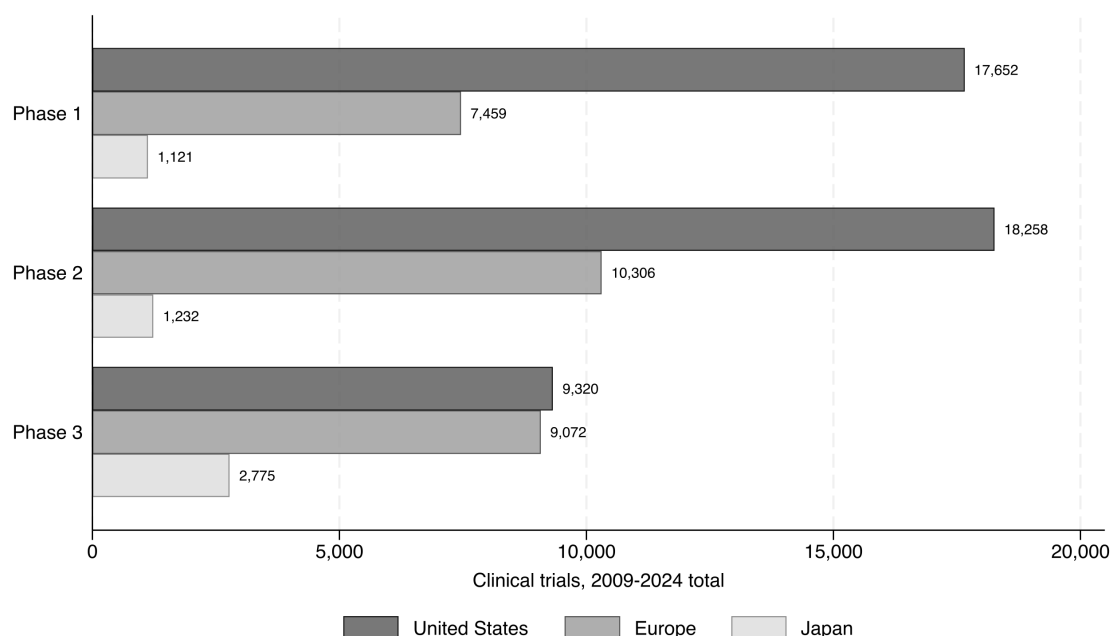


Figure 3. Clinical trials by region and development phase, cumulative 2009-2024

Note: Counts are trials with at least one site in the region; a trial sited in more than one region is counted in each. Totals combine industry and non-industry sponsors.

Figures 4 and 5 distinguish between industry and non-industry-sponsored trials. Figure 4 shows that the United States has more industry-sponsored trials than Europe at every phase and in every year, with the widest gap in early-stage development. The ratio of U.S. to European Phase 1 trials rises from 1.40 in 2009 to 2.05 in 2024. In Phase 2, the ratio increases more modestly, from 1.34 to 1.66, while in Phase 3 it remains essentially unchanged, moving from 1.11 to 1.17. The U.S. advantage over Europe is therefore largest in early-stage and smallest in late-stage industry-sponsored clinical development.

The increase in the Phase 1 ratio is concentrated in the final years of the sample, warranting caution in interpreting the trend. European counts fluctuate between 338 and 430 from 2009 through 2021 before falling to 364, 305, and 319, with comparable declines in Phases 2 and 3. Regulation (EU) No 536/2014 (Clinical Trials Regulation) began applying in January 2022, replacing national submission procedures with a centralized system through the Clinical Trials Information System (CTIS), which became mandatory for new

applications in January 2023.⁴⁵ Part of the measured divergence in the final years may therefore also reflect this administrative transition rather than a shift in where clinical development takes place. Restricting the analysis to 2021 and earlier, the Phase 1 ratio still rises from 1.40 in 2009 to 1.74 in 2021 – an increase, but a smaller one.

Japanese participation follows a different pattern from Europe's, with changes concentrated in later development phases. Among industry-sponsored trials, the ratio of U.S. to Japanese trials falls from 11.06 to 5.04 in Phase 2 and from 3.61 to 2.02 in Phase 3 between 2009 and 2024, while in Phase 1 it ends close to its initial level. The U.S. advantage over Japan therefore narrows in later-stage development but remains broadly unchanged in early-stage development.

Japan illustrates the distinction between participation in clinical development and the origination of new medicines. Industry-sponsored Phase 3 trial counts rose from 117 in 2009 to 192 in 2024, despite a pricing regime in which prices are set administratively and revised downward on a fixed schedule. Japan's rising Phase 3 presence partly reflects the inclusion of Japanese sites in multiregional trials. Since Japan's 2007 "Basic Principles on Global Clinical Trials" allowed data from such trials to support Japanese approval, sponsors have routinely included Japanese sites in global Phase 3 studies.⁴⁶ Phase 3 accounts for 54 percent of Japanese trials, compared with 21 percent in the United States and 35 percent in Europe. Yet Japan's share of new chemical entities introduced globally fell from 29 percent in the 1980s to 7 percent in the 2010s, while Japanese-headquartered firms account for just 39 of the 1,362 FDA approvals examined here.⁴⁷ This contrast underscores that participation in late-stage clinical development does not necessarily translate into a strong position in originating new medicines.

⁴⁵ "Clinical trials – Regulation EU No 536/2014," European Commission, https://health.ec.europa.eu/medicinal-products/clinical-trials/clinical-trials-regulation-eu-no-5362014_en.

⁴⁶ "Basic Principles on Global Clinical Trials," <https://www.pmda.go.jp/files/000153265.pdf>.

⁴⁷ Ezell, "How Japan Squandered Its Biopharmaceutical Competitiveness: A Cautionary Tale."

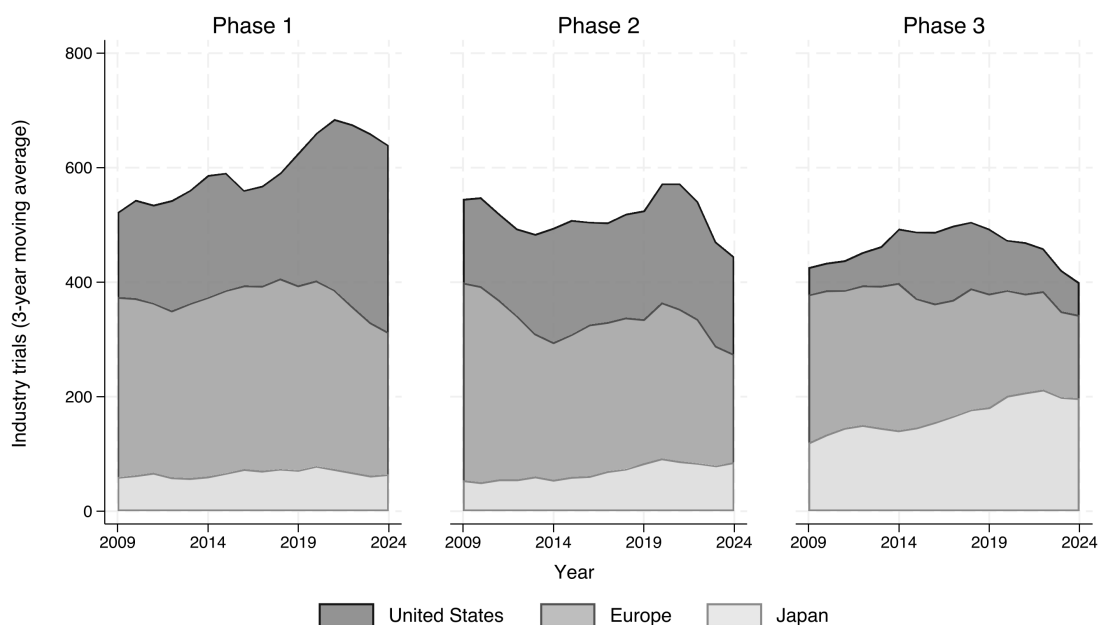


Figure 4. Industry-sponsored clinical trials by region and phase, 2009-2024

Note: Three-year centered moving average. Each series is plotted from 0, so a region's count is read at the upper boundary of its shaded area, not from the thickness of the band. Areas overlap and are not additive.

Figure 5 shows that these patterns extend to non-industry-sponsored trials, with some important differences. The United States leads Europe in Phases 1 and 2 by a wider margin than among industry-sponsored trials, while in Phase 3 the pattern reverses, with European counts exceeding U.S. counts throughout the period. Non-industry-sponsored activity is particularly limited in Japan, where academic and public sponsors account for roughly 5 percent of recorded trials, compared with 44 percent in the United States and 35 percent in Europe, although domestic registries capture some Japanese activity not reflected in these data. We return to these contrasts in Section IV.C.

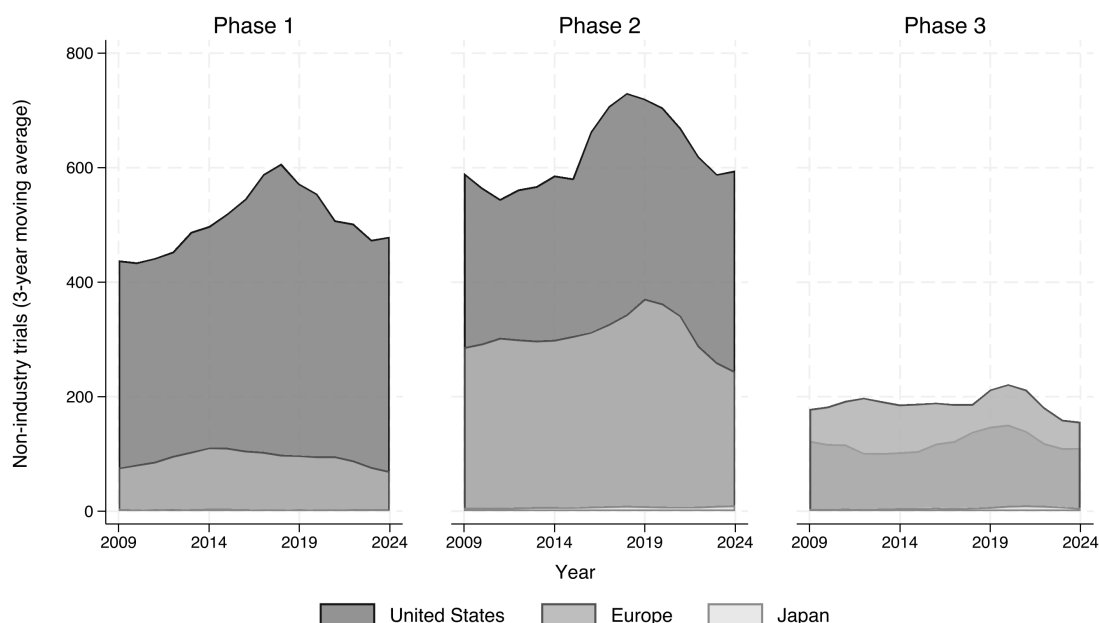


Figure 5. Non-industry-sponsored clinical trials by region and phase, 2009-2024

Note: Constructed as in Figure 4 and plotted on the same vertical scale. In Phase 3, European counts exceed U.S. counts, so the European area extends above the U.S. area in that panel.

C. Discussion

Interpreting the geographic distribution of clinical trials requires distinguishing the factors that shape trial location at different stages of development. While pricing regimes influence the expected returns to pharmaceutical innovation, trial location also reflects recruitment costs, regulatory requirements, and the geographic distribution of research capabilities.

Late-stage trial location depends substantially on enrollment economics. Phase 3 trials require large patient populations, making recruitment speed and cost important considerations in where they are conducted. Research has documented how differences in per-patient costs have contributed to the relocation of industry-sponsored trials to emerging regions, including Eastern Europe and Latin America.⁴⁸

⁴⁸ Fabio A. Thiers, Anthony J. Sinskey, and Ernst R. Berndt, “Trends in the Globalization of Clinical Trials,” *Nature Reviews Drug Discovery* 7, no. 1 (2008): 13-14.

Regulatory and clinical considerations reinforce this pattern. Regulators may require local data from the populations in which a medicine will be marketed, while firms use late-stage trials to establish relationships with clinical investigators in target markets. Japan illustrates both mechanisms: its increased participation in clinical development is concentrated in Phase 3, where local data requirements and clinical relationships are particularly relevant. Its presence in late-stage trials, however, should not be interpreted as evidence of a similarly strong position in originating new medicines.

The geographic distribution of early-stage trials may reflect several complementary mechanisms. One possibility is that firms have greater discretion over whether and where to advance a compound in Phase 1, making trial location more sensitive to expected commercial returns. A complementary explanation is that early-phase trials tend to be conducted near the laboratories and specialist units where discovery research takes place. On this account, the United States lead reflects the strength of its research ecosystem, including sustained public funding, leading research institutions, robust venture capital, and university-industry linkages.

Note that the U.S.-Europe gap also appears among non-industry-sponsored trials: the ratio of U.S. to European Phase 1 trials rises from 5.72 in 2009 to 7.15 in 2024. This pattern suggests that differences in research capacity and the institutional environment also shape the geography of early-stage development. Academic and government-funded research can also respond to commercial incentives, as the prospect of downstream commercialization can influence which research projects attract funding and advance toward clinical development. Universities contributed patents underpinning half of novel FDA approvals between 2020 and 2024.⁴⁹ Further, NIH-funded research contributed to 354 of the 356 drugs approved by the FDA from 2010 to 2019.⁵⁰ Academic discoveries frequently reach patients through licensing agreements and spinout companies, connecting university research to the commercial development process. The incentives facing pharmaceutical

⁴⁹ Kevin Gardner and Michael Kinch, “We set out to quantify U.S. academic contributions to medicines. The results stunned even us,” *STAT*, June 6, 2025.

⁵⁰ Ekaterina G. Cleary, Matthew J. Jackson, Edward W. Zhou, and Fred D. Ledley, “Comparison of Research Spending on New Drug Approvals by the National Institutes of Health vs. the Pharmaceutical Industry, 2010-2019,” *JAMA Health Forum* 4, no. 4 (2023): e230511.

firms can therefore influence academic research indirectly, through the expected value of discoveries, opportunities for licensing, and the availability of capital to develop promising compounds.

The larger U.S. lead among non-industry sponsors may thus reflect the interaction of public research funding, technology transfer institutions, and commercial incentives. In the United States, the Bayh–Dole Act and the technology transfer infrastructure built around it facilitate the commercialization of publicly funded research, while robust NIH funding supports the underlying research base. These institutions connect public investment in discovery to commercial development, providing channels through which expected returns can influence the translation of research into new medicines.

Taken together, these data document a substantial U.S. lead both in novel medicines brought to market by U.S.-based firms and in clinical development, widest in early-stage trials. Over time, Europe has fallen further behind in industry-sponsored Phase 1 and Phase 2 activity while remaining close to parity in Phase 3, whereas Japan has narrowed the gap in later-stage trials with little change in early-stage work. These patterns are consistent with the hypothesis that differences in expected returns contribute to the geography of pharmaceutical innovation. However, the descriptive comparisons do not establish that pricing regimes caused the observed divergence. Research capacity, public funding, access to capital, and other institutional differences may also contribute. The concentration of early-stage activity in the United States may reflect both commercial incentives and the strength of its research ecosystem, while the location of late-stage trials is also influenced by recruitment costs and regulatory requirements.

V. Firm Behavior and Market Outcomes

Section IV documented differences in the geographic distribution of pharmaceutical approvals and clinical development. This section examines the firm-level responses through which pricing and reimbursement policies may affect innovation and patient access, drawing on empirical studies of R&D investment, market entry, launch timing, and medicine availability.

A. R&D Investment

Pricing regimes influence both firms' aggregate R&D investment and the allocation of those investments across therapeutic areas and technologies. Where expected revenues are reduced by price regulation, firms scale back projects at the margin.⁵¹ Acemoglu and Linn's estimates indicate that pharmaceutical innovation is highly responsive to expected market size, suggesting that even modest reductions in expected market size can translate into substantial reductions in new drug development.⁵²

Estimates of the magnitude of these effects suggest that they are economically meaningful. Golec and Vernon (2010) estimate that European pharmaceutical price controls reduced industry R&D investment by approximately 20 percent between 1986 and 2004, corresponding to roughly 46 fewer new medicines.⁵³ Similarly, Civan and Maloney (2009) estimate that absent OECD price controls, pharmaceutical revenues would have supported an additional \$17 to 22 billion in annual R&D investment and 10 to 13 additional new medicines each year.⁵⁴ Together, these estimates suggest that pharmaceutical pricing policies can materially affect R&D investment and, in turn, the pace of therapeutic innovation, although the magnitude of these effects depends on the setting and assumptions examined. The relative location of pharmaceutical R&D has shifted over time as countries' policy environments have diverged, with the United States increasingly attracting global pharmaceutical investment while Europe has experienced a relative decline.⁵⁵

⁵¹ DiMasi, Grabowski, and Hansen, "Innovation in the Pharmaceutical Industry."

⁵² Acemoglu and Linn, "Market Size in Innovation: Theory and Evidence from the Pharmaceutical Industry."

⁵³ Joseph Golec and John A. Vernon, "Financial Effects of Pharmaceutical Price Regulation on R&D Spending by EU versus US Firms," *Pharmacoeconomics* 28, no. 8 (2010): 615–628.

⁵⁴ Abdulkadir Civan and Michael T. Maloney, "The Effect of Price on Pharmaceutical R&D," *The B.E. Journal of Economic Analysis & Policy* 9, no. 1 (2009).

⁵⁵ Tim Wilsdon, Hannan Armstrong, Antun Sablek, and Peter Cheng, "Factors Affecting the Location of Biopharmaceutical Investments and Implications for European Policy Priorities" (CRA/EFPIA, October 2022).

Pricing policies also shape the composition of pharmaceutical innovation. Emerging evidence on the U.S. Inflation Reduction Act (IRA) illustrates the dynamic. The Act made small-molecule drugs eligible for Medicare price negotiation after nine years, compared with thirteen years for biologics (measured from FDA approval), thereby exposing small molecules to price regulation four years earlier. By reducing the expected commercial life of small-molecule products relative to biologics, the IRA has altered the expected returns to different drug types.

Early evidence points to a potential shift away from small-molecule development: industry analyses report substantial declines in early-stage investment, while surveys indicate that many pharmaceutical firms expect to reduce investment in small-molecule programs.⁵⁶ Recent research further finds that the IRA disproportionately discourages post-approval clinical research for small-molecule drugs relative to biologics.⁵⁷ This shift matters because small-molecule drugs can offer therapeutic advantages, including oral administration and lower manufacturing costs, that may improve patient experience and broaden patient access.

B. Market Entry, Launch Timing, and Sequencing

A well-established finding in the literature is that price regulation affects not only the prices firms charge but also firms' decisions about whether and when to enter a market. Analysis of pharmaceutical launch decisions across a large sample of drugs and countries indicates that pricing policies have significant effects on both the likelihood and timing of market entry. Firms headquartered in countries with pharmaceutical price controls reach fewer markets than those in countries without price controls, and companies are less likely to introduce medicines in additional markets after entering a price-controlled country.⁵⁸

⁵⁶ Vital Transformation, "The Impact of the Inflation Reduction Act on Small-Molecule Drug Investment" (industry analysis report, 2024).

⁵⁷ Hanke Zheng, Julie A. Patterson and Jonathan D. Campbell, "Early Impact of the Inflation Reduction Act on Small Molecule vs Biologic Post-Approval Oncology Trials," *Health Affairs Scholar* 3, no. 8 (2025): qxaf152.

⁵⁸ Kyle, "Pharmaceutical Price Controls and Entry Strategies," 88–99.

Evidence from 642 new drugs launched across 76 countries between 1983 and 2002 finds that price regulation delays the commercial availability of new medicines, whereas stronger and more extensive patent protection accelerates diffusion. Delayed market entry also postpones access to the health benefits associated with pharmaceutical innovation.⁵⁹

Pricing policies also generate strategic interactions across countries. Pricing regulation in one country can affect entry decisions in other countries, establishing a cross-border spillover mechanism that makes pharmaceutical pricing an international policy matter rather than a purely domestic one.⁶⁰ Research on parallel trade in the European Union shows that the legalization of parallel imports – products first sold at lower prices in other countries and subsequently resold across borders – delays launches into lower-price markets by reducing manufacturers’ ability to sustain price differences across countries.⁶¹ As the possibility of arbitrage links markets together, firms postpone entry into lower-price countries to preserve pricing flexibility in higher-price markets.⁶²

C. Patient Access

The effects of pharmaceutical pricing policies ultimately extend beyond firms to patients. Because commercial launch determines whether and when new therapies become available, pricing regimes that discourage market entry or delay product launches can postpone or deny patient access to innovative medicines.

In the United States, which has historically relied more heavily on market-based pharmaceutical pricing than most OECD countries, innovative medicines have generally become available earlier than in countries with more extensive price regulation. For

⁵⁹ Iain M. Cockburn, Jean O. Lanjouw, and Mark Schankerman, “Patents and the Global Diffusion of New Drugs,” *American Economic Review* 106, no. 1 (2016): 136–164.

⁶⁰ Kyle, “Pharmaceutical Price Controls and Entry Strategies.”

⁶¹ Margaret K. Kyle, “Strategic Responses to Parallel Trade,” *The B.E. Journal of Economic Analysis & Policy* 11, no. 2 (2011): Article 2.

⁶² Kyle, “Strategic Responses to Parallel Trade.”

example, a Fraser Institute report finds that medicines are approved an average of 636 days (roughly 20 months) earlier in the United States than in Canada.⁶³

Among 290 new medicines introduced between 2011 and 2018, 89 percent were available in the United States, compared with 62 percent in Germany, 57 percent in Denmark, 56 percent in the Netherlands, 50 percent in Japan, 48 percent in France, and 48 percent in Switzerland. Comparable differences are observed for oncology therapies: of 82 new cancer medicines introduced during the same period, 96 percent were available in the United States, compared with 73 percent in Germany, 66 percent in Denmark, France, and the Netherlands, 62 percent in Switzerland, and 54 percent in Japan.⁶⁴

Taken together, these findings illustrate a central tradeoff in pharmaceutical pricing policy. Lower reimbursed prices can reduce current public expenditure, but they may also weaken commercial incentives for pharmaceutical innovation and discourage or delay market entry, limiting the range of therapies available to patients.

VI. Policy Implications

The preceding analysis has implications for the design of pharmaceutical pricing and reimbursement policy. Three issues are particularly important: how pricing policy interacts with the broader innovation ecosystem, how the costs of financing innovation are distributed internationally, and how affordability can be improved without relying exclusively on reductions in manufacturer prices.

A. Pricing Policy as Part of the Broader Innovation Ecosystem

Pharmaceutical pricing policy interacts with other institutions that shape the development and commercialization of new medicines. Regulatory efficiency, intellectual property (IP) protection, public investment in biomedical research, technology transfer

⁶³ Kristina Acri and Lauren Assad, “Timely Access to New Pharmaceuticals in Canada, the United States, and the European Union, 2026,” Fraser Institute, 2026.

⁶⁴ Doug Badger, “Examination of International Drug Pricing Policies in Selected Countries Shows Prevalent Government Control over Pricing and Restrictions on Access,” Galen Institute, 2019.

institutions, and access to entrepreneurial capital all influence firms' innovation decisions. Within this environment, firms respond not only to current prices but also to expectations about future returns, which influence R&D investment, market entry, launch timing, and investment location. These factors can reinforce one another. In Japan, sustained pricing pressure may compound existing weaknesses in the innovation ecosystem, while in Europe, shifts toward more stringent price controls may have contributed to the relative decline in pharmaceutical innovation. These cases illustrate why pricing reforms should be evaluated in the context of the institutions and capabilities that support research and commercialization.

The design of pricing instruments also matters. The IRA's differential treatment of small molecules and biologics illustrates how policy can alter expected returns across therapeutic modalities. By making small-molecule drugs eligible for Medicare price negotiation four years earlier than biologics, the Act changes the relative commercial incentives associated with the two categories. Early evidence of a shift away from small-molecule development suggests that differences in policy treatment can influence the composition of the pharmaceutical pipeline.⁶⁵ Policymakers should therefore assess whether distinctions between product categories create incentives that are disproportionate to differences in therapeutic value.

Pricing policy can also affect research beyond the pharmaceutical industry itself. As discussed in Section IV, universities supply a substantial share of the patents underlying new drug approvals, and academic discoveries reach the market through licensing and spinout formation. The expected commercial value of therapeutic research can therefore influence academic research priorities as well as private investment. Pricing reforms therefore operate not on the pharmaceutical industry in isolation but on a translational system that includes university research, technology transfer institutions, and the venture financing that connects them. This connection matters for policies governing public

⁶⁵ Tomas J. Philipson, Qi Zhao, Deyu Zhang, Kira Fujibayashi, and Heather Johnson, "Follow-On Cancer Drugs Target Earlier Stages Than Initial Drugs: Implications of the IRA: Article examines follow-on cancer drugs," *Health Affairs* 44, no. 12 (2025): 1448-1456.

research funding, technology transfer, and venture financing, which help translate scientific discoveries into new therapies.

B. International Dimensions of Pharmaceutical Pricing Policy

Pharmaceutical innovation is financed and commercialized across national borders, so pricing policies in one country affect incentives and access in others. Because the benefits of new medicines extend well beyond the markets that fund them, the distribution of revenues supporting pharmaceutical R&D raises questions about how the costs of sustaining innovation are shared internationally. These interdependencies suggest that pharmaceutical innovation exhibits characteristics of a global public good: it is non-rivalrous, even where patents render it temporarily excludable. Ho and Pakes' (2025) finding that the U.S. pricing premium finances worldwide R&D therefore means reforms to U.S. pricing carry consequences for innovation well beyond the United States.

This has prompted debate over how the costs of sustaining pharmaceutical innovation might be distributed more equitably across high-income countries. Two broad approaches are often considered: downward pressure on U.S. prices or reforms in peer economies that increase reimbursement for new therapies. The evidence reviewed in this chapter, particularly the European and Japanese experiences, raises concerns that further downward pressure on U.S. prices could weaken innovation incentives, while higher reimbursement in peer economies could reduce cross-country asymmetries in the contribution to global R&D. Trade agreements linking market access to reimbursement reform offer one possible channel, although coordinating pricing reforms across sovereign national health systems presents substantial practical and political challenges.

C. Instrument Choice and the Affordability Objective

Pharmaceutical pricing policy is often expected to achieve two objectives simultaneously: ensuring that patients can afford treatment and sustaining the revenues that support pharmaceutical innovation. These objectives are related but not identical. Patient affordability depends partly on insurance design, including coverage, deductibles, and

cost-sharing, while the revenues available to finance drug development depend on the prices paid to manufacturers.

This distinction creates scope for policy instruments to address patient costs without relying exclusively on lower manufacturer prices. For example, expanding insurance coverage or reducing patients' out-of-pocket expenses can improve affordability without requiring an equivalent reduction in manufacturer revenues, although these measures may increase public expenditure and overall utilization. Their effectiveness depends on the design of the insurance system and how additional costs are financed.

The policy implication is that affordability and innovation should be evaluated as related but distinct objectives. Policymakers should assess both how much patients pay to obtain medicines and how reimbursement policies affect the expected returns that support pharmaceutical R&D. This approach makes the trade-offs more explicit and broadens the range of policy options beyond a choice between lower drug prices and continued innovation.

VII. Conclusion

This chapter has examined how pharmaceutical pricing regimes shape innovation incentives and firm behavior in the United States, Europe, and Japan. The empirical literature reviewed here indicates that expected market returns influence firms' decisions concerning R&D investment, development, market entry, launch timing, and investment location.

The comparative evidence documents a growing U.S. lead in FDA approvals by applicant origin relative to both Europe and Japan, and a U.S. advantage over both regions in the level of clinical development activity, widest in early-stage trials, though only the gap with Europe has widened over time. The empirical literature also suggests that tighter price regulation can reduce R&D investment and delay or discourage market entry. Golec and Vernon (2010) estimate that European price controls reduced industry R&D investment by

roughly 20 percent between 1986 and 2004, equivalent to about 46 fewer new medicines.⁶⁶ Taken together, these findings support the view that pricing policies that constrain expected returns can weaken innovation incentives, although the magnitude of their effects varies across settings and policy instruments.

These differences cannot be explained by pricing policy alone. Research capacity, public funding, intellectual property protection, access to capital, and regulatory institutions also shape innovation outcomes, and these factors interact with pricing incentives over time. The international nature of pharmaceutical R&D and commercialization further complicates the relationship between national pricing decisions and innovation outcomes: revenues generated in individual markets contribute to a globally distributed innovation pipeline, while pricing policies can influence firms' investment and commercialization decisions across markets.

The evidence nevertheless has several limitations. The comparative analysis in Section IV is descriptive rather than causal and cannot isolate the contribution of pricing policy to the observed regional trajectories. The estimates reported in the empirical literature depend on the policies, periods, and markets studied. Further empirical work is needed to assess the effects of recent reforms, including America's IRA, and to establish how pricing regimes and broader innovation institutions jointly shape investment, the composition of pharmaceutical innovation, and the availability of new medicines.

⁶⁶ Golec and Vernon, "Financial Effects of Pharmaceutical Price Regulation on R&D Spending by EU versus US Firms."