Price Maintenance Premium and R&D Investment Behavior

A Thesis

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Abstract

This paper examines the efficacy of the Price Maintenance Premium (PMP), a policy first introduced in 2010 in Japan that creates price premium for innovative drugs in Japan, using a pooled dataset of 9 major firms over the period of 1995 to 2023. The findings reveal that the number of drugs eligible for PMP application has a significant positive effect on research intensity, measured by firm's R&D investment. Consistent with earlier studies, expected returns, represented by cash flows, are identified as important explanatory variable influencing R&D intensity. However, profit shows insignificance, which contrasts with the results observed in an earlier sample period.

Keywords: Pharmaceuticals; Price Maintenance Premium (PMP); R&D; Innovation; Cash Flow; Expected returns

JEL Classification Number: L65, O31, O33

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1. Introduction

On average, pharmaceutical companies invest hundreds of millions of dollars over many years into research and development (R&D) to bring a single new chemical entity (NCE) to market. Recent estimates suggest that it usually takes approximately 10 to 15 years and costs a huge amount of capital investment to achieve regulatory approval for a new drug (Chugai Pharmaceutical Co., Ltd.). These R&D activities include discovery research, preclinical testing, and successive, time-consuming clinical trials. Clinical trials are essential to demonstrate safety, efficacy, and quality before the Ministry of Health, Labour and Welfare (MHLW) in Japan will approve a new drug for marketing.

Due to the significant benefits promised by new drug innovations and the substantial costs associated with the innovation process, numerous researchers have investigated the determinants of pharmaceutical R&D, including changes in political regulations. However, relatively few studies have specifically analyzed how drug price premiums influence pharmaceutical R&D investment. This study contributes to the literature by providing a deeper understanding of the effects of drug price premiums, particularly in the Japanese pharmaceutical market. Building on prior research, this paper analyzes firm-level economic data from Japan, covering the period from 1995 to 2023, to examine the impact of the Price Maintenance Premium (PMP) introduced in 2010. The PMP allows pharmaceutical companies to be exempt from regular drug price revisions, which are conducted every one to two years, and ensures that newly developed drugs retain their initial high prices, primarily during the patent protection period. This exemption would provide additional incentives for pharmaceutical companies to invest in innovation. For this analysis, I employ an analytical model with the same basic structure as those used in earlier studies.

The remainder of the paper is organized as follows: Section 2 introduces the concept of drug price regulation and discusses the Price Maintenance Premium policy in detail. Section 3 reviews the literature and Section 4 develops the empirical framework to assess the effects of PMP on R&D investment. Section 5 reports the major findings and implications for policy and industry practice. Section 6 concludes.

2. Backgrounds

2.1 Drug Price Revisions in Japan

The prices of drugs covered under insurance-based medical care are determined by the Japanese government. Drug prices represent the amount that patients and insurers pay to medical institutions and pharmacies for medications. In principle, these prices are reviewed every two years through a process called drug price revision.

This system exists because a large proportion of the drug costs borne by patients is subsidized by public health insurance. The goal of drug price revisions is to adjust artificially set drug prices closer to the market prices determined by competitive forces. This helps prevent overpayment by public insurance and ensures that drug prices remain fair and sustainable within the healthcare system. During the revision process, the government conducts surveys to collect data on the actual market prices of drugs, known as market transaction prices, which reflect the prices at which pharmaceutical wholesalers sell drugs to medical institutions and pharmacies. Based on these data, the government adjusts the official drug prices, including a slight margin to provide profits for pharmaceutical companies. However, due to regular price revisions—almost always resulting in price reductions—pharmaceutical wholesalers are compelled to offer lower prices to ensure that hospitals and pharmacies can maintain their profit margins. This dynamic has led to a downward trend in drug prices across the board, creating challenges for pharmaceutical companies to sustain profitability while continuing to invest in innovation.

2.2 Institutional Designs to Maintain Drug Development Incentives

In countries with social health insurance systems, such as Japan, drug prices are regulated and set by public authorities. This system often results in lower drug prices, which can reduce pharmaceutical companies' incentives to invest in drug development due to diminished returns on innovation. To mitigate this issue, Japan introduced the Price Maintenance Premium (PMP) policy. The PMP exempts newly developed drugs from regular price reductions that are typically implemented every one to two years. This exemption allows these drugs to retain their initially set high prices until the next scheduled price revision, which typically occurs within one to two years after their market launch but is not strictly tied to the patent protection period.

There are a few countries which have similar systems that maintain the prices of new drugs for a fixed period. Examples include Germany and South Korea. Under Germany’s Pharmaceutical Market Reorganization Act (AMNOG), pharmaceutical companies can freely set prices for new drugs during the first year after their launch. After this initial period, drug prices are renegotiated based on evaluations by health technology assessment bodies. South Korea’s new drug pricing system is similar to Japan’s, where the prices of newly launched drugs are maintained for a designated period, providing stability for pharmaceutical companies to recover their R&D investments.

2.3 Price Maintenance Premium (PMP)

The Price Maintenance Premium (PMP) is a special measure in Japan's drug pricing system that partially exempts certain new drugs from price reductions during regular drug price revisions. Initially introduced on a trial basis during the 2010 drug price revisions, the PMP was formally institutionalized in 2018 as part of comprehensive reforms to the

drug pricing system. However, the 2018 reforms introduced stricter criteria for eligibility compared to the original trial framework.

To qualify for the PMP, pharmaceutical products must meet at least one of five requirements, such as demonstrating proven efficacy for rare or least-detected diseases, addressing significant unmet medical needs, or being recognized as essential by the Ministry of Health, Labour, and Welfare (MHLW). This policy is designed to incentivize pharmaceutical companies to invest in the development of innovative drugs that address unmet medical needs, particularly for conditions lacking effective treatments. Additionally, it aims to reduce the approval time lag (often referred to as "drug lag") between Japan and other countries, ensuring that Japanese patients have earlier access to breakthrough medications.

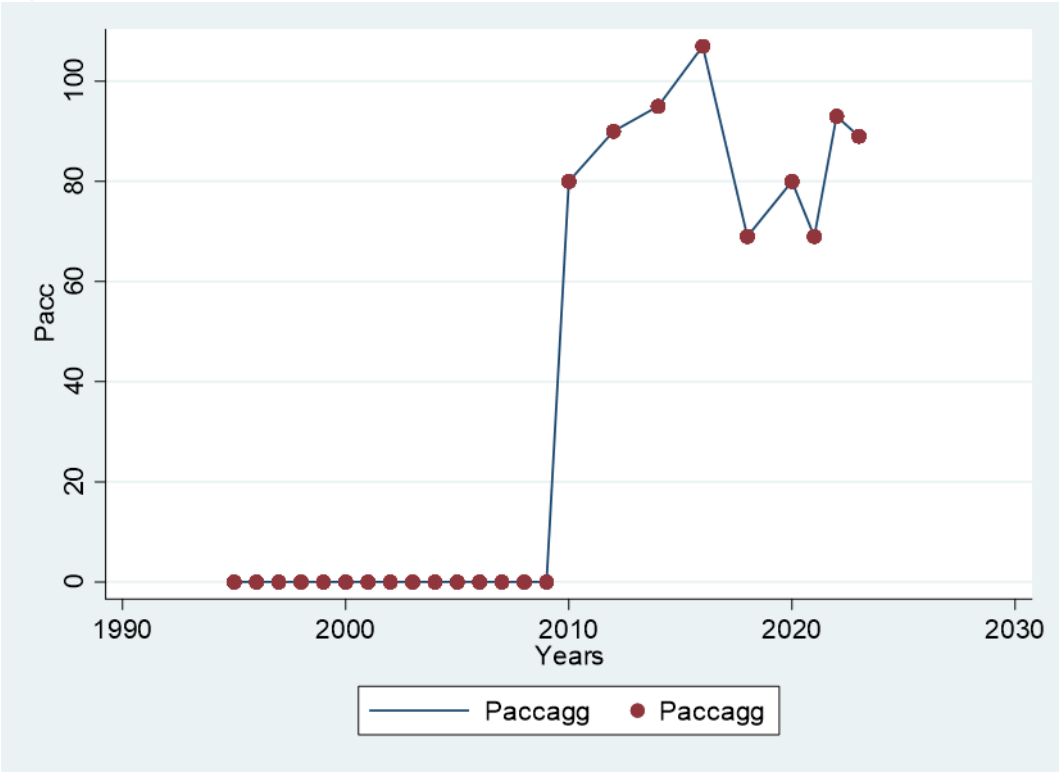
The annual aggregate number of acceptances for the Price Maintenance Premium (PMP) of nine major Japanese pharmaceutical companies[1] is depicted in Figure 1 and denoted as Pacc (Prime Acceptance). After the introduction of the PMP system in 2010, the number of acceptances showed a steady upward trend, peaking in 2016 with nearly 110 total acceptances. Notably, 2016 marked the final year before a major system amendment was implemented in 2018. Following the 2018 amendment, the number of acceptances declined sharply, dropping to less than two-thirds of the previous peak. Although there was an increase in 2020 and a subsequent decline in 2021, the trend reversed suddenly in 2022, with acceptances rising to over 90. This increase may be attributed to the COVID-19 pandemic, which began in late 2019. The pandemic likely spurred increased demand for vaccines and other pharmaceutical products, encouraging companies to develop innovations that qualified for the PMP.

The sharp decline after 2018 is likely attributable to the amendment of the system, which introduced stricter regulatory requirements for obtaining PMP rewards. These heightened requirements may have acted as a barrier, making it more challenging and costly for pharmaceutical companies to qualify for the premium. The 2018 amendment created a more rigorous framework for evaluating highly effective medicines, potentially incentivizing companies to focus on developing innovative drugs. Such drugs, being exempt from routine drug price revisions, offered a means to ensure sustainable profits.

Since the stricter requirements introduced in 2018 aimed to reduce government spending while promoting the growth of a globally competitive Japanese pharmaceutical market, it is essential to evaluate the effectiveness of the PMP system by examining its impact on firms' R&D investments and their ability to innovate in response to these regulatory changes.

[1] Nine companies include Astellas, Chugai, Eisai, Kaken, Nipro, Takeda, Rohto, Shionogi, and Torii.

Figure 1: PMP acceptances for 9 Japanese pharmaceuticals



3. Literature Review

Microeconomic theory suggests that pharmaceutical companies optimize their R&D spending by balancing marginal revenues (MR) and marginal costs (MC). According to Grabowski et al. (2000), a company invests significantly in R&D to develop new drugs, which, in turn, generates future income. This relationship can be expressed mathematically as follows:

$$MR(R, X) = MC(R, Z) \qquad (1)$$

where

- R represents spending on R&D;
- X includes other influential factors affecting the returns from new drug R&D, such as policy changes;
- Z represents a set of external factors associated with new drug R&D costs.

The optimal level of R&D spending (R*) can therefore be expressed as a function of these variables:

$$R^* = f(X, Z) \qquad (2)$$

Grabowski et al. (2000) found that the availability of internal funds, or cash flow, which is a component of X, positively affects optimal R&D investment. Similarly, an increase

in expected returns—another element of X—also has a positive effect on R&D investment levels.

Mahlich et al. (2006) adapted Grabowski's (2000) model, originally developed for the U.S. pharmaceutical market, to analyze the Japanese pharmaceutical industry. By applying this model to data from 15 Japanese pharmaceutical companies from 1987 to 1998, Mahlich and Roediger-Schluga investigated the relationship between expected returns, cash flows, and R&D expenditures. The study found that expected returns and cash flows were statistically significant determinants of R&D investment in the Japanese market, suggesting that pharmaceutical companies in Japan, like their U.S. counterparts, rely heavily on these financial indicators when making decisions about R&D spending. Furthermore, the study suggested that the Japanese regulatory environment for drug pricing might reduce the rewards of innovation success compared to markets where drug prices are freely set, such as the U.S.

Giaccotto et al. (2005), building on Grabowski's model, adopted some political regulatory into explanatory variables such as Kefauver-Harris amendment to the Food, Drug, and Cosmetic Act of 1938. The act greatly increased the regulatory requirements associated with bringing a pharmaceutical product to market. They found the amendment may have had a negative effect on firm's R&D intensity.

The impact of pharmaceutical regulations has been examined directly in several studies. Incorporating Vernon's (2005) model, Shalkh et al. (2020) found that pharmaceutical regulations in European countries may negatively affect R&D intensity, which is consistent with the observations of Eger et al. (2014). Shalkh et al. (2020) highlighted that stringent price controls and reimbursement policies in Europe could discourage investment in innovative drug development.

Despite the growing body of literature on pharmaceutical regulation globally, there is limited research evaluating the impact of Japan's Price Maintenance Premium (PMP) on pharmaceutical companies' R&D expenditures. To the best of the author's knowledge, no studies to date have used an empirical model, as represented by Grabowski (2000), specifically designed to assess the causal relationship between PMP incentives and R&D intensity. Nakamura et al. (2015), however, conducted a simulation analysis to evaluate the potential increase in individual pharmaceutical companies' sales resulting from the PMP. Their findings revealed that, with the PMP in place, pharmaceutical sales were 7.2% higher compared to a hypothetical scenario without the incentive. After accounting for the effects of general sales growth trends, the PMP was estimated to have contributed a 2.3% increase in sales.

Kakihara et al. (2016) found that reducing price premium on newly invented drugs had a significantly larger negative impact on future R&D incentives compared to price reductions on generics. Specifically, the reduction in incentives for R&D was

approximately twice as large when the price premium on new drugs was lowered, compared to the effect of reducing prices for generics. These findings suggest that the PMP may play a modest but measurable role in enhancing pharmaceutical revenues, which could indirectly support R&D investments.

4. Regression Model

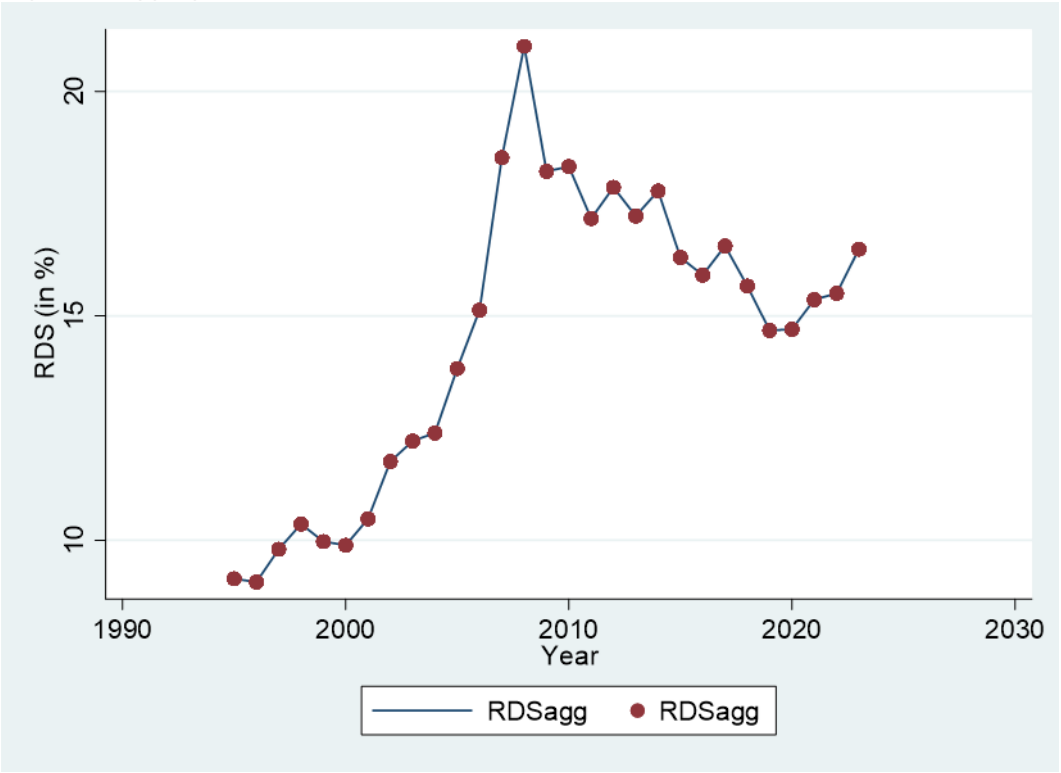
4.1 Data

This study utilizes data on firm financial variables obtained from Moody's Orbis. The data are taken from consolidated income and balance sheet statements which include the firm's total sales and expenditures for all products and services on a global basis. Major consideration in selecting the sample of firms was the availability of R&D expenditures for the complete 1995 – 2023 period. This led to a sample of nine firms, which includes Astellas, Chugai, Eisai, Kaken, Nipro, Takeda, Rohto, Shionogi, and Torii. Also, data on number of acceptances for Price Maintenance Premium (PMP) was taken from the Ministry of Health, Labor and Welfare who issued the list of accepted companies for the application of the PMP and listed the number of accepted drugs to maintain their original prices.

Seven companies—Astellas, Chugai, Eisai, Kaken, Takeda, Shionogi, and Torii—are members of the Japan Pharmaceutical Manufacturers Association (JPMA), an organization that includes companies considered to be innovative-intensive. Nipro is the only company in the dataset that is a member of the Japan Generic Medicines Association (JGMA), which represents generic-intensive companies. Rohto, on the other hand, is not a member of either JPMA or JGMA. This is due to its focus on over-the-counter (OTC) health products, cosmetics, and pharmaceutical products, rather than ethical drugs, which are the primary focus of both JPMA and JGMA members.

In focusing on R&D trends, while Mahlich et al. (2006) observed an upward trend in R&D intensity from 1987 to 1998, my analysis concentrates on more recent years, from 1995 to 2023. I identified a mountain-like trend in the aggregated data of 9 companies (Figure 2). The graph depicts the aggregate R&D-to-sales (RDS) ratio of nine Japanese pharmaceutical companies, showing a peak of approximately 20% in 2008, followed by a decline to around 15% in 2020. This decline may be attributed to the global financial crisis that began in 2007, which led to a freezing of credit markets, making it more difficult for pharmaceutical companies to secure financing for R&D investments.

Figure 2: Aggregate R&D to sales ratio (%)



4.2 Theoretical Model

Based on the review in Section 3, I propose the following hypothesis.

Hypothesis: The acceptance of the Price Maintenance Premium (PMP) ensures that pharmaceutical companies experience an increase in expected returns, enabling them to allocate more resources toward R&D investment.

To investigate the hypothesis, following Grabowski's (2000) and Mahlich's (2006), I specify the regression model shown below:

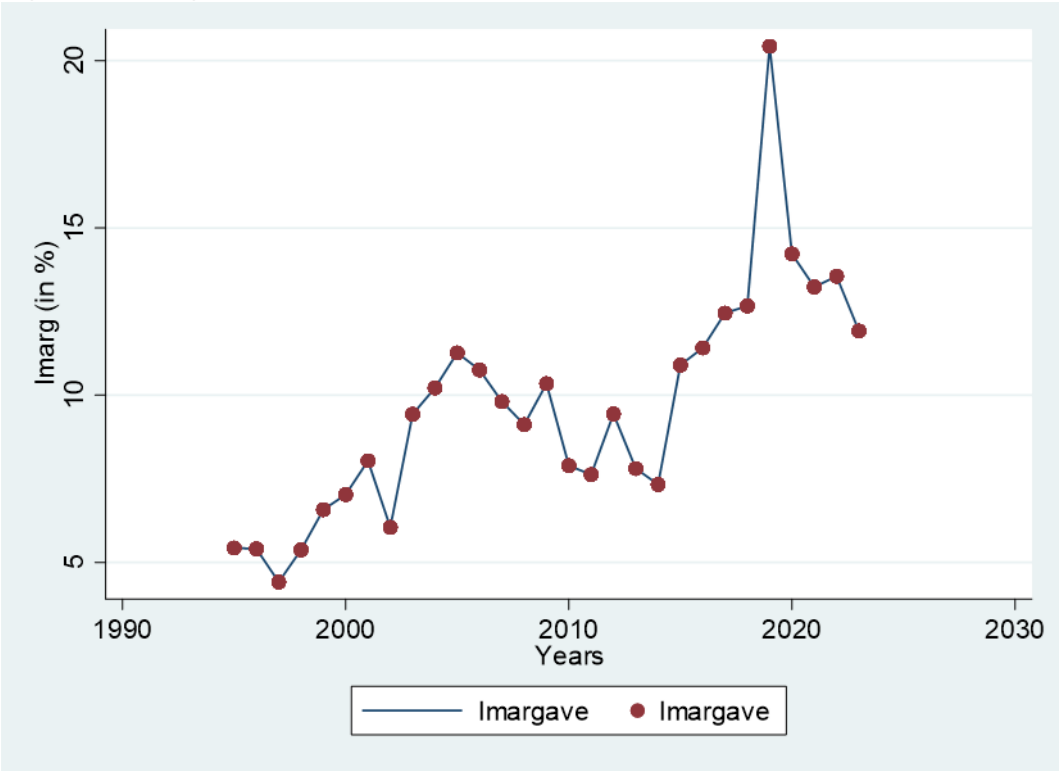
$$RDS_{it} = \mathrm{f}\,(\mathrm{E}\pi_t, \mathrm{CFS}_{it-1}, \mathrm{D}_i) \qquad (3)$$

Where

- RDS_{it} = R&D spending divided by sales for firm i in year t
- $E\pi_t$ = index of expected returns to R&D in pharmaceuticals in year t
- CFS_{it-1} = cash flow divided by sales for each firm in year t-1
- D_i = dummy variable for firm i

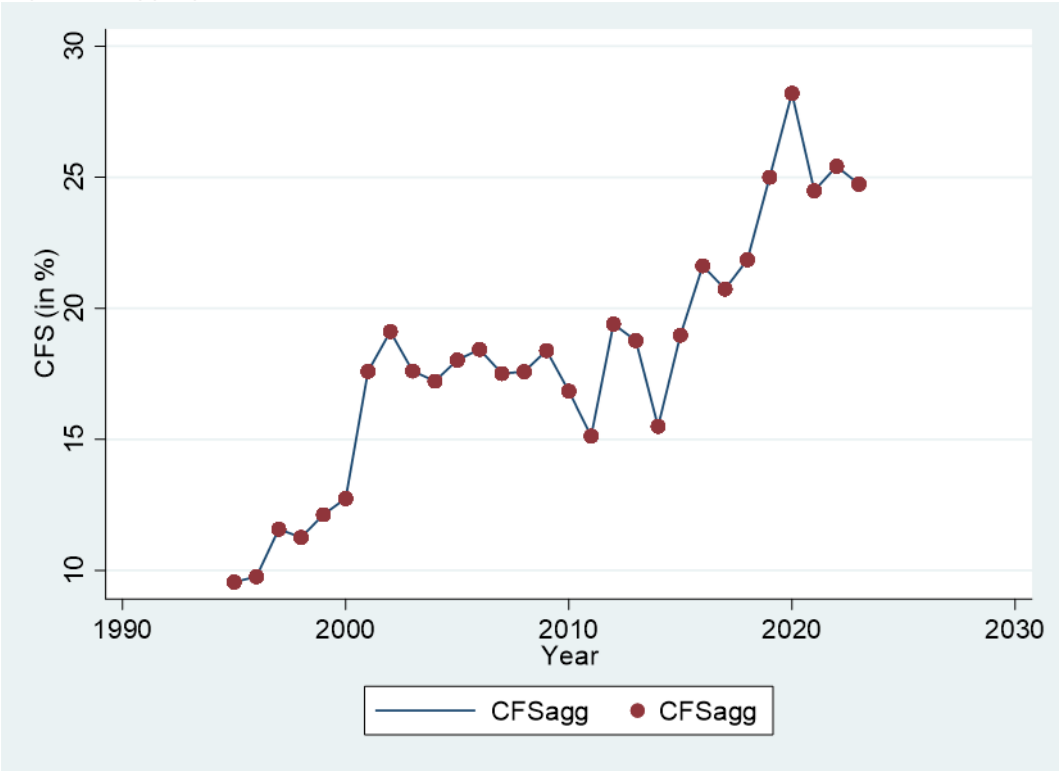
For $E\pi_t$, previous studies use two variables: new product sales and profit. In this study, however, only the effect of profit is considered due to data limitations. The variable represents the industry margin, which is defined as profits divided by sales. Figure 3 plots the average profit, as the percentage of total sales, over all firms and shows that it increased during the 1990s to the early 2000s, and then declined until the mid-2010s, but rose again afterward.

Figure 3: Average profit sales ratio (%)



The CFS_{it-1} variable is designed to measure a firm's internally generated funds before investments in R&D, other capital assets, and before the payment of dividends. In this study, net income before depreciation and amortization (D&A) is used as the representation. The aggregate CFS variable across all firms is plotted in Figure 4. Note that it has been increasing sharply up to the early 2000s, and then flatten unchanging till the rate 2010s, lastly going up again. As noted by Grabowski et al. (2000), I found that the one-year lag performs statistically better than the two-year lag.

Figure 4: Aggregate cash flow share in total sales (%)



Firm dummy variables were introduced for eight of nine firms to capture all firm differences between firms and over time. In the regression results, I do not report the coefficients of individual dummy variables.

Table 1 presents the summary statistics for the variables used in the panel data analysis. Note that the values for Imarg and CFS are expressed as percentages. The statistics indicate that the average profit-to-sales ratio, represented by Imarg, is approximately 10%. Additionally, the CFS values reflect data from one year prior.

Table 1: Descriptive statistics of the panel data

Variables	(1) No. of obs.	(2) Mean	(3) S.D.	(4) Min.	(5) Max.
RDS	261	11.44	6.97	0	30.7
Pacc	261	2.96	7.01	0	35
Imarg	261	9.66	8.43	-8.48	63.65
CFS	224	15.95	9.53	2.39	65.94
D	261	5	2.59	1	9

Since there may be a correlation between variables, especially between Pacc and Imarg (as Pacc could potentially boost a firm's profit), I conducted a correlation check. The inception coefficient between Pacc and Imarg is 0.18, so I am confident that no interaction variable is needed for them. Furthermore, as the cash flow data is from the previous year, there may not be a relationship where Pacc affects CFS, thereby increasing the number. The figure is shown in Table 2.

Table 2: Correlation check

	Pacc	Imarg	CFS
Pacc	1.00		
Imarg	0.18	1.00	
CFS	0.23	0.48	1.00

4.2 Regression Model

To account for unobserved heterogeneity in the sample, I estimate a fixed-effects specification of my baseline model as conducted by Mahlich et al. (2006). The regression model, called Model 1, can be expressed as follows.

$$RDS_{it} = \beta_1 Imarg_{it} + \beta_2 CFS_{it-1} + D_i + \varepsilon_{it} \qquad (4)$$

As the first extension of Model 1, I add my focal variable, Pacc, which represents prime acceptance in the first place. Pacc refers to the number of accepted drugs for the adaptation of the Price Maintenance Premium (PMP). Model 2 thus becomes:

$$RDS_{it} = \beta_1 Pacc_{it} + \beta_2 Imarg_{it} + \beta_3 CFS_{it-1} + D_i + \varepsilon_{it} \qquad (5)$$

The fixed-effects model isolates time-varying effects by focusing on within-entity variation rather than between-entity variation. Specifically, it examines how a particular company changes over time, rather than making comparisons across different entities. This approach allows for the isolation of the impact of variables that exhibit variation within an entity over time, controlling for unobserved, time-invariant heterogeneity across entities.

5. Results

The regression equations are presented in Table 3. The first column reports the estimation results for Model 1, which uses profit and cash flow as the baseline variables. The second column shows the results for Model 2, which focuses on the number of prime acceptances held by each company. On the right-hand side, the estimation results from previous studies are provided for comparison. Overall, the equations in Models 1 and 2 are quite similar. However, it is noteworthy that while Imarg (profit-to-sales ratio) demonstrated significant positive effects in previous studies, it is statistically insignificant in both models in this analysis.

In Models 1 and 2 of Table 3, CFS is highly significant and exhibits the expected signs. The coefficients for the cash flow-to-sales ratio (CFS) range from 0.14 to 0.16, suggesting that a 1% increase (or decrease) in the CFS ratio is estimated to increase (or decrease) R&D intensity by approximately 0.15%. These results are higher compared to the coefficients of 0.12 and 0.06 reported in previous studies.

The insignificance of profit, as indicated by the coefficient on Imarg, and the strong effect of cash flow, represented by CFS, on R&D intensity, could be attributed to a lack of confidence in future earnings due to regular drug price revisions. Pharmaceutical companies have faced frequent price revisions, during which drug prices are often set lower than before. This trend may have led them to rely more on internal cash flows, rather than expected future profits, for R&D investment.

The inclusion of Pacc in Model 2 seems to support the hypothesis that the Prime Maintenance Premium (PMP) has a positive effect on R&D investment. The coefficient of the number of acceptances for the PMP variable, Pacc, is 0.15, while the coefficient of CFS has a slightly lower t-statistic. This suggests that one additional acceptance for PMP would increase R&D intensity by 0.15%, while one fewer acceptance would decrease R&D intensity by the same amount.

To summarize the findings, there is strong evidence to show that PMP is an important determinant factor for pharmaceutical R&D.

Table 3: Regression output

	Model 1	Model 2	G&V (2000)	M&R (2006)
	1995 - 2023	1995 - 2023	1980 - 1994	1987 - 1998
	Coef. (t-value)	Coef. (t-value)	Coef. (t-value)	Coef. (t-value)
Pacc	-	0.15 (3.11) ***	-	-
Imarg	-0.03 (-0.77)	-0.02 (-0.52)	0.77 (9.47) ***	0.322 (4.09) ***
CFS	0.16 (4.54) ***	0.14 (3.83) ***	0.12 (4.14) ***	0.058 (1.90) *
Constant	8.35 (14.78) ***	8.33 (15.04) ***	-0.18 (10.32) ***	6.296 (4.09) ***
R^2 / F	0.21 / 61.11	0.28 / 57.37	0.92 / 141.0	0.444 / 42.85
N	224	224	164	179

Note :
G&V (2000) : Grabowski et al. (2000) ; M&R (2006) : Mahlich et al. (2006).
Statistically significant at the* 10% level; statistically significant at the ** 5% level; statistically significant at the *** 1% level.

6. Conclusion

This paper focuses on the effect of price regulation on pharmaceutical research and development and suggests that the Price Maintenance Premium (PMP) has a significant impact on pharmaceutical firms' R&D. The results also highlight that expected returns,

represented by cash flow, have a positive effect on R&D investment, while no such effect is found for profit, which was observed in previous studies using data from earlier sample periods.

The analysis has several important implications. In particular, it confirms the efficacy of the Price Maintenance Premium (PMP), providing evidence to support its continued use in the future. While drug price revisions and reductions can lead to a more competitive market with lower drug prices, the PMP would incentivize pharmaceutical companies to develop innovative medicines, ensuring their long-term sustainability. Lower drug prices would benefit not only patients but also the national economy, particularly in Japan, where universal health insurance is in place and medical expenses for patients are partially covered by the government. Furthermore, a more stringent implementation of the PMP could lead to a more efficient use of financial resources, particularly in the allocation of Japan's increasing social welfare budgets. This, in turn, could boost Japan's global competitiveness in drug innovation, positioning the country as a leader in the pharmaceutical sector.

In this paper, I have provided a deeper understanding of the determinants of R&D outlays. Further research is needed to examine the recent amendment to the Price Maintenance Premium (PMP). In 2024, the PMP was revised to enhance price maintenance for innovative drugs by expanding eligibility criteria. The reforms also introduced new price premiums to encourage the early introduction of new drugs to Japan and eased the requirements for granting these premiums.

References

Chugai Pharmaceutical Co., Ltd. (n.d.). くすりを創る [Kusuri wo tsukuru: Drug development]. Retrieved January 2, 2025, from https://www.chugai-pharm.co.jp/ptn/medicine/create/create001.html

Eger, S. & Mahlich, C. J. (2014). Pharmaceutical regulation in Europe and its impact on corporate R&D. *Health Economics Review,* 4(23)

Glaccotto, C., Santerre, R. E., & Vernon, J. A. (2005). Drug price and research and development investment behavior in the pharmaceutical industry. *Journal of law and Economics*, 48(1), 195-214

Grabowski, H. G. & Vernon, J. M., (2000). The determinants of pharmaceutical research and development expenditures. *Journal of Evolutionary Economics*, 10, 201–215.

IN-Information Systems, Ltd. eol. Retrieved July 5, 2024, from https://ssl-eoldb-jp.glim-ezp.idm.oclc.org/EolDb/CompanyInfoBasic.php?SID=10515

Japan Generic Medicines Association. (n.d.). GE 薬協について [GE yakkyo ni tsuite: About GE Medicines Association]. Japan Generic Medicines Association. Retrieved July 5, 2024, from https://www.jga.gr.jp/information/member.html

Japan Pharmaceutical Manufacturers Association. (n.d.). 会員会社 *[kain gaisha: Member Companies]*. Japan Pharmaceutical Manufacturers Association. Retrieved July 5, 2024, from https://www.jpma.or.jp/about/member/index.html

Kakihara, K., Nakamura, H., & Wakutsu, N. (2016). 医療保険財政負担軽減と研究開発インセンティブ低下抑制の両立に向けた政策検討における割引率の活用－新薬創出等加算のシミュレーションによる経済分析－ (Iryo hoken zaisei futan keigen to kenkyu kaihatsu insentibu teika yokusei no ryoritsu ni muketa seisaku kentou ni okeru waribikiritsu no katsuyou: Shinyaku soushutsu tou kasan no shimyureeshon ni yoru keizai bunseki). [Use of discount rates in policy considerations for reducing the burden on healthcare insurance finances while preventing decreased incentives for R&D: An economic analysis through simulations of the new drug creation support addition]. *Iryokezai kenkyu*, 28(2), 88–102. https://www.ihep.jp/wp-content/uploads/current/research/3/124/Vol.28_No.2_2016_3.pdf.

Mahlich, C. J. & Roediger-Schluga, T. (2006). The determinants of pharmaceutical R&D expenditures: Evidence from Japan. *Review of industrial Organization*, 28(2), 145-164

Ministry of Health, Labour and Welfare. (2010). *新薬創出・適応外薬解消等促進加算の対象品目を有する会社* [Shinyaku sōshutsu tekiōgaiyaku kaishōtō sokushin kasan no taishōhinmoku wo yusuru kaisha: The number of price maintenance premiums for each pharmaceutical]. Retrieved January 23, 2025, from https://www.mhlw.go.jp/bunya/iryouhoken/iryouhoken12/dl/index-072.pdf

Ministry of Health, Labour and Welfare. (2010). *薬価基準改定の概要* [Yakka kijun kaitei no gaiyō: Overview of drug price standard revision]. Retrieved July 5, 2024, from https://www.mhlw.go.jp/bunya/iryouhoken/iryouhoken12/dl/index-070.pdf

Ministry of Health, Labour and Welfare. (2012). *新薬創出・適応外薬解消等促進加算の対象品目を有する会社* [Shinyaku sōshutsu tekiōgaiyaku kaishōtō sokushin kasan no taishōhinmoku wo yusuru kaisha: The number of price maintenance premiums for each pharmaceutical]. Retrieved January 23, 2025, from https://www.mhlw.go.jp/bunya/iryouhoken/iryouhoken15/dl/gaiyou_yakka_2.pdf

Ministry of Health, Labour and Welfare. (2012). *薬価基準改定の概要* [Yakka kijun kaitei no gaiyō: Overview of drug price standard revision]. Retrieved July 5, 2024, from https://www.mhlw.go.jp/bunya/iryouhoken/iryouhoken15/dl/gaiyou_yakka.pdf

Ministry of Health, Labour and Welfare. (2014). *新薬創出・適応外薬解消等促進加算の対象品目を有する会社* [Shinyaku sōshutsu tekiōgaiyaku kaishōtō sokushin kasan no taishōhinmoku wo yusuru kaisha: The number of price maintenance premiums for each pharmaceutical]. Retrieved January 23, 2025, from https://www.mhlw.go.jp/file/06-Seisakujouhou-12400000-Hokenkyoku/0000038949.pdf

Ministry of Health, Labour and Welfare. (2014). *薬価基準改定の概要* [Yakka kijun kaitei no gaiyō: Overview of drug price standard revision]. Retrieved July 5, 2024, from https://www.mhlw.go.jp/file/06-Seisakujouhou-12400000-Hokenkyoku/0000038947.pdf

Ministry of Health, Labour and Welfare. (2016). *新薬創出・適応外薬解消等促進加算の対象品目を有する会社* [Shinyaku sōshutsu tekiōgaiyaku kaishōtō sokushin kasan no taishōhinmoku wo yusuru kaisha: The number of price maintenance premiums for each pharmaceutical]. Retrieved January 23, 2025, from https://www.mhlw.go.jp/file/06-Seisakujouhou-12400000-Hokenkyoku/0000114722.pdf

Ministry of Health, Labour and Welfare. (2016). *薬価基準改定の概要* [Yakka kijun kaitei no gaiyō: Overview of drug price standard revision]. Retrieved July 5, 2024, from https://www.mhlw.go.jp/file/06-Seisakujouhou-12400000-Hokenkyoku/0000114718.pdf

Ministry of Health, Labour and Welfare. (2018). *新薬創出・適応外薬解消等促進加算の対象品目を有する会社* [Shinyaku sōshutsu tekiōgaiyaku kaishōtō sokushin kasan no taishōhinmoku wo yusuru kaisha: The number of price maintenance premiums for each pharmaceutical]. Retrieved January 23, 2025, from https://www.mhlw.go.jp/file/06-Seisakujouhou-12400000-Hokenkyoku/0000197377.pdf

Ministry of Health, Labour and Welfare. (2018). *薬価基準改定の概要* [Yakka kijun kaitei no gaiyō: Overview of drug price standard revision]. Retrieved July 5, 2024, from https://www.mhlw.go.jp/file/06-Seisakujouhou-12400000-Hokenkyoku/0000197375.pdf

Ministry of Health, Labour and Welfare. (2019). *新薬創出・適応外薬解消等促進加算の対象品目を有する会社* [Shinyaku sōshutsu tekiōgaiyaku kaishōtō sokushin kasan no taishōhinmoku wo yusuru kaisha: The number of price maintenance premiums for each pharmaceutical]. Retrieved January 23, 2025, from https://www.mhlw.go.jp/content/12400000/000538499.pdf

Ministry of Health, Labour and Welfare. (2019). *薬価基準改定の概要* [Yakka kijun kaitei no gaiyō: Overview of drug price standard revision]. Retrieved July 5, 2024, from https://www.mhlw.go.jp/content/12400000/000538496.pdf

Ministry of Health, Labour and Welfare. (2020). *新薬創出・適応外薬解消等促進加算の対象品目を有する会社* [Shinyaku sōshutsu tekiōgaiyaku kaishōtō sokushin kasan no taishōhinmoku wo yusuru kaisha: The number of price maintenance premiums for each pharmaceutical]. Retrieved January 23, 2025, from https://www.mhlw.go.jp/content/12404000/000604022.pdf

Ministry of Health, Labour and Welfare. (2020). *薬価基準改定の概要* [Yakka kijun kaitei no gaiyō: Overview of drug price standard revision]. Retrieved July 5, 2024, from https://www.mhlw.go.jp/content/12404000/000613996.pdf

Ministry of Health, Labour and Welfare. (2021). *新薬創出・適応外薬解消等促進加算の対象品目を有する会社* [Shinyaku sōshutsu tekiōgaiyaku kaishōtō sokushin kasan no taishōhinmoku wo yusuru kaisha: The number of price maintenance premiums for each pharmaceutical]. Retrieved January 23, 2025, from https://www.mhlw.go.jp/content/12404000/000749286.pdf

Ministry of Health, Labour and Welfare. (2021). *薬価基準改定の概要* [Yakka kijun kaitei no gaiyō: Overview of drug price standard revision]. Retrieved July 5, 2024, from https://www.mhlw.go.jp/content/12404000/000749283.pdf

Ministry of Health, Labour and Welfare. (2022). *新薬創出・適応外薬解消等促進加算の対象品目を有する会社* [Shinyaku sōshutsu tekiōgaiyaku kaishōtō sokushin kasan no taishōhinmoku wo yusuru kaisha: The number of price maintenance premiums for each pharmaceutical]. Retrieved January 23, 2025, from https://www.mhlw.go.jp/content/12404000/000906780.pdf

Ministry of Health, Labour and Welfare. (2022). *薬価基準改定の概要* [Yakka kijun kaitei no gaiyō: Overview of drug price standard revision]. Retrieved July 5, 2024, from https://www.mhlw.go.jp/content/12404000/000942947.pdf

Ministry of Health, Labour and Welfare. (2023). *新薬創出・適応外薬解消等促進加算の対象品目を有する会社* [Shinyaku sōshutsu tekiōgaiyaku kaishōtō sokushin kasan no taishōhinmoku wo yusuru kaisha: The number of price maintenance premiums for each pharmaceutical]. Retrieved January 23, 2025, from https://www.mhlw.go.jp/content/12404000/001065657.pdf

Ministry of Health, Labour and Welfare. (2023). *薬価基準改定の概要* [Yakka kijun kaitei no gaiyō: Overview of drug price standard revision]. Retrieved July 5, 2024, from https://www.mhlw.go.jp/content/12404000/001069997.pdf

Ministry of Health, Labour and Welfare. (2024). *薬価基準改定の概要* [Yakka kijun kaitei no gaiyō: Overview of drug price standard revision]. Retrieved July 5, 2024, from https://www.mhlw.go.jp/content/12404000/001218693.pdf

MOODY'S. Orbis. Retrieved Oct 22, 2024, from https://orbis-r1-bvdinfo-com.glim-ezp.idm.oclc.org/version-20241204-2-0/Orbis/1/Companies/Search

Nakamura, H., & Wakutsu, N. (2015). 新薬創出等加算のメリットの要因分析とシミュレーション分析に基づく考察 [Shinyaku soushutsu tou kasan no meritto no

youin bunseki to shimyureeshon bunseki ni motozuku kousatsu: Factor analysis of the benefits of the Prime Maintenance Premium and discussion based on simulation analysis]. *Iryo to Shakai*, 25(2), 205−220.

Shaikh, M., Giudice, D. P. & Kourouklis, D. (2021). Revising the relationship between price regulation and pharmaceutical R&D investment. *Applied Health Economics and Health Policy,* 19*,* 217-229

Vernon, A. J. (2005). Examining the link between price regulation and pharmaceutical R&D investment. *Health Economics,*14, 1-16