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The Effect of Patent Expiration on Medicine Prices. Evidence From the H2 Antagonists' Market in India.

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Abstract

Pharmaceuticals in developing countries encounter major challenges in gathering required knowledge and capabilities to compete with pharmaceuticals in the United States, Europe and Japan. Even though patents provide financial and legal incentives to innovate, they prohibit developing countries from accumulating knowledge. With patents being enforced globally, pharmaceuticals in developing countries are not permitted to apply the newest innovations to improve their products or processes. This comes at the expense of the societal welfare of the developing countries. On the other hand, patent expirations in pharmaceutical industries may serve as opportunities for these countries. In the long run patent expirations enhance the knowledge of pharmaceuticals in developing countries at relatively low costs. Therefore, this research on patents and medicine prices contributes to a greater understanding of the opportunities and obstacles of patents and patent expiry. The aim is to investigate pharmaceutical price changes in the Indian H2 antagonists' market after patent expiration. With over 20% of the Indian population living under the national poverty line, research on the effects of patent expiration on pharmaceutical prices is of great importance to Indian society. Consequently, this thesis serves as a foundation for policy recommendations, with the goal of increasing the societal welfare in India and other developing countries. This thesis adopts a fixed effects model together with several difference-in-difference analysis to estimate the results. The results suggest that products with certain characteristics experience a decrease in price after patent expiry. However, other product characteristics experience an increase in price after patent expiration. In addition, these effects are potentially subjected to biases and unrepresentative market conditions. Nevertheless, the results of this study provide a strong basis for future studies on medicine prices after patent expiration in developing countries.

Keywords: Pharmaceutical industry, Patent (Expiration), India, Difference-in-difference, Panel Data Analysis

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1. Introduction

The dynamic pharmaceutical industry constantly develops and improves medications to enhance the health of society. For instance, the COVID-19 crisis illustrates the tremendous innovative capabilities of the pharmaceutical industry, through the rapid development and production of vaccines within only several months. Despite the substantial progression and competence of this industry, the accumulated technological capabilities that have emerged over the last decades will bring even larger opportunities (Forbes, 2019; McKinsey, 2018). With an investment of 83 billion US dollars in pharmaceutical research & development (R&D) in 2019, the United States (US) is predominantly accountable for the current accumulation of knowledge and pharmaceutical product development. The US investments represent over half the world's annual expenditure in pharmaceutical R&D (Congressional Budget Office, 2021).

However, developing countries face major challenges in enhancing their pharmaceutical capabilities due to high entry barriers, generated by the sizeable capacities of western pharmaceuticals such as in the US (Chataway, Tait & Wield, 2007). These capacities in developed countries allow for faster and more advanced product development, way beyond the abilities of pharmaceuticals in developing countries. With the Indian pharmaceutical industry valued at 41 billion US dollars in 2020 (IBEF, 2021), there is a major valuation difference in comparison to the US industry, which is valued at 1.3 trillion US dollars in 2014 (SelectUSA, n.d.). Along with the scarcity of abilities faced by the developing countries, R&D costs are at an eminently high level in the pharmaceutical industry (DiMasi, Grabowski & Hansen, 2016). Subsequently, non-western pharmaceuticals are more financially constrained. The difficulty of accessing external finance is a limitation in India across all high technological dependent industries (Sasidharan, Lukose & Komera, 2015). Subsequently, this hampers the catch up of Indian pharmaceuticals, compared to the major pharmaceuticals based in developed countries.

Regardless of these major constraints, developing countries seek to benefit from innovations introduced in western industries as well. By removing the obstacles of high R&D costs, pharmaceuticals in developing countries can adopt the introduced innovations to their products and processes. This technique is known as firm upgrading, through which techniques or technologies of developed countries are adopted by developing countries (Verhoogen, 2020). This concept ensures pharmaceuticals in developing countries to advance their expertise and proficiency by acquiring new information at a more affordable price.

Nevertheless, copying and adopting technologies is not as straightforward, since patents play a major role in all knowledge intensive sectors such as the pharmaceutical industry (Grabowski, 2002). With patents generally lasting for 20 years (FDA, 2020), other businesses are not permitted to copy innovations that are patented. This provides the founders of the patent with a temporary monopoly, or a significant advantage in terms of costs or efficiency. Therefore, patents provide a great incentive for investments in innovation, such as in highly technologically dependent industries that are characterised by low imitation and high development costs (Grabowski, 2002).

Since the imitation costs in the pharmaceutical industry are relatively low (Grabowski, 2002), pharmaceuticals in developing countries may want to adopt the technique of firm upgrading, to boost their capabilities. Nevertheless, only after the patent expiration date, other businesses are free to adopt the techniques or knowledge of the patent (FDA, 2020). For instance, by producing a generic version of a previously patented medication. A decrease in price is the result of more pharmaceuticals entering the market and the lower production costs in the competitive industry. Subsequently, the drug becomes available to a wider audience and enhances societal welfare. The increase in societal welfare is especially relevant for developing countries, such as India.

With 273.1 million Indian citizens living below the national poverty line in 2011, pharmaceutical prices are a determining factor in human well-being (World Bank, 2020). A slight increase in medicine prices may significantly affect the accessibility of medication in India, as 21.9% of the Indian population is heavily budget constrained (Banerjee & Duflo, 2007; World Bank, 2020). Chaudhuri, Goldberg & Jia (2006) articulate that patent enforcement has a negative effect on welfare in the Indian economy. In addition, Duggan, Garthwaite & Goyal (2016) illustrate a significant negative effect of patent introduction on medicine prices in the Indian pharmaceutical sector. Subsequently, with medication being of great importance in terms of human well-being, Indian inhabitants are forced to reduce their already budget constraint expenditures on food and other costs of living, to afford their medicines.

Despite the impact of prices on societal welfare, Kanavos & Vandoros (2011) mention the lack of research on patents and patent expiry and its relation to pharmaceutical prices. A noticeable exception of Vondeling et al. (2018) examines the effect of patent expiry on drug prices, suggesting a decrease in prices after patent expiry. Nevertheless, these results are only representative for the studied cluster of developed countries. Therefore, Vondeling et al. (2018) mention the importance of gathering country specific data. No studies have examined the effect of patent expiry on prices in the Indian pharmaceutical industry. Enhancing technological capabilities, through the adaptation of knowledge after a patent expiration, may have a decreasing effect on the pharmaceutical prices in developing countries. So, a study that examines the effect of patent expiry on prices in India contributes to a greater understanding of patents in developing countries. The aforementioned theories and studies hence result in the following research question:

What is the effect of patent expiration of top selling medicine on pharmaceutical market prices in the Indian H2 antagonists' market?

The discussion on patents and pharmaceutical prices grew in 2021, as a consequence of the COVID-19 crisis. Developed countries have been able to buy large quantities of vaccines to prevent the number of hospitalised inhabitants in their country from increasing (United Nations, 2021). As a result, the more prosperous countries have been able to vaccinate most of their citizens (World Bank, 2021). However, developing countries have merely been able to acquire vaccines, which strengthens the discussion on whether the patent on the

COVID-19 vaccine should be enforced in developing countries (European Parliament, 2021; Reuters, 2021). Several organisations state that pharmaceuticals should take their social responsibility and open source the vaccine for developing countries (European Parliament, 2021; United Nations, 2021). Therefore, research on the effect of patent expiry on medicine prices contributes to the discussion on patent enforcement in developing countries.

This thesis studies the role of patent expiration on drug prices in the Indian H2 antagonists' market through the application of several econometric techniques. Moreover, research on medicine characteristics such as being solid, combined or multinational produced, gives a better understanding on price changes after patent expiry. In addition, this research gathers additional knowledge on patent expiry and its effect on prices, by studying a regulatory exception. The results suggest that there is a relation between the patent expiration of Aciphex and product characteristics on the retail and wholesale prices in the Indian H2 antagonists' market. The fixed effects models of several hypotheses find both increasing and decreasing significant effects on prices after patent expiration in interaction with product characteristics. However, the difference-in-difference analyses mostly find insignificant results. Therefore, there are signs of a relation between the interaction of patent expiration and product characteristics on pharmaceutical prices. However, it remains unknown what the sign and magnitude of this effect is. Moreover, the insignificant results of the difference-in-difference analysis and concerns regarding Granger causality, imply that a causal relation between patent expiration and product characteristics on pharmaceutical prices is not present. So, the findings contribute to a greater understanding of patent expiration effects on prices in the Indian H2 antagonists' market. Currently, literature on the effects of patent expiry on prices in developing countries is lacking. Nevertheless, literature has studied patent expiration in the context of developed countries. However, pharmaceutical prices in developed countries have less of a societal impact due to a well-established infrastructure in terms of insurance and healthcare, compared to developing countries. Thus, budget constrained citizens in developing countries are affected more by changes in pharmaceutical prices. This research establishes the foundation for future studies on the effect of patent expiry on pharmaceutical prices in developing countries. Therefore, this thesis contributes to the literature on patent expiry in developing countries, while increasing knowledge and awareness to enhance societal welfare in developing countries.

Next, the theoretical framework elaborates on theories and studies applied for the construction of the hypotheses. This part discusses the applied datasets and variables of interest thoroughly by debating their appliance and relevance. Furthermore, the methodology section discusses the selected econometric methods to answer the hypotheses. Moreover, an illustration of the assumptions that come with the selected methods are demonstrated, to sustain the robustness and validity of the results. The results section examines the findings of the hypotheses. Furthermore, additional robustness checks ensure the validity of the results. Then, the limitations section elaborates on the implications and limitations of this research. In addition, the recommendation section discusses topics for future studies. Once the results, limitations and recommendations are elaborated, a conclusion is drawn.

2. Theoretical Framework

This part of the research examines the theoretical framework, including an analysis on the H2 antagonists' market and an elaboration on the constructed hypotheses. Firstly, a section on related literature discusses patents and patent expiration in the context of firm upgrading in developing countries. The next part studies literature on the Indian pharmaceutical industry. In addition, a market analysis explores the Indian H2 antagonists' market. Subsequently, the last section focuses on the construction of the hypotheses, applying the aforementioned theories and literature.

2.1 Related Literature

Patents are the exclusive intellectual property rights of the creations by the human mind, which are especially relevant for knowledge intensive sectors, such as the pharmaceutical industry (Lehman, 2003). For a limited period, typically 20 years, third parties are excluded from applying the knowledge of active patents to their products or processes. In the pharmaceutical industry high R&D costs are involved with the development of medication. Due to the exclusivity granted by a patent, pharmaceuticals can financially benefit from their investments in R&D. Therefore, patents ensure innovation in the long term, as third parties are unable to apply the knowledge of your innovations for a limited period. This gives pharmaceutical businesses financial and legal incentives to innovate, where in the absence of patents, these incentives are lacking due to imitations (Lehman, 2003). The introduction of the Trade-Related Intellectual Property Rights (TRIPS) agreement means that patents are enforced globally. Subsequently, international regulation prevents Indian firms from copying patented US medicines. However, after patent expiration pharmaceutical businesses are unconstrained to produce and sell patented medicines, after approval from the national medical agency (EMA, n.d.).

In the past, the imitation of drugs through reverse engineering[1] reduced incentives to innovate (Chaudhuri et al., 2006) and even led to the postponement of innovations. Any suspension of innovations decreases societal welfare in both developed and developing countries. Nevertheless, international patent enforcement eliminates this problem. Hence, this illustrates the importance of patent regulation for innovations and societal welfare (Mukherjee & Pennings, 2004).

The urgency for patents is elaborated by Lehnman (2003), showing that for innovation to occur, the right financial and legislative incentives must be present. In addition, the ease of imitation in the pharmaceutical industry means that there is a strong case in favour of global patent enforcement. Nevertheless, Deardorff (1992) shows the drawbacks of patents, indicating that patents only enhance the overall welfare of the country in which the inventions are introduced. Having a patent granted in a specific country will increase the welfare through the sales of the patented product. However, the author states that the total global welfare loss is bigger, compared

[1] Reverse engineering is the process of transforming products into concepts and models, where the conventional approach of product development is to transform concepts into actual products (Varady, Martin & Cox, 1997). Any copying or reverse engineering of patent products is illegal, as it is a violation of intellectual property rights.

to the gains made by the country in which the innovation is originally introduced (Deardorff, 1992). This difference derives from the loss of market position of competing firms in other countries, resulting in higher pharmaceutical prices. Thus, the increase in price means that the affordability of the medication declines. This is predominantly relevant in developing countries such as India, due to its budget constraint inhabitants (World Bank, 2020).

Furthermore, for developing countries it remains challenging to be innovative due to their lack of capabilities. Deardorff (1992) illustrates that innovations enhance domestic economic growth and increase societal welfare. Nevertheless, the firm upgrading technique is a possible solution to pharmaceuticals in developing countries. Firm upgrading is the process of applying innovations of expired patents by other businesses. Verhoogen (2020) illustrates that the benefits of this firm upgrading approach are twofold. Firstly, at relatively low costs, developing countries can produce generic medicines, making medication more widely accessible for inhabitants of developing countries. Secondly, new techniques and technologies are mastered by these pharmaceutical firms in developing countries, increasing the capabilities of these businesses. In the long run this enables pharmaceuticals in developing countries to catch up with the pharmaceuticals in the developed world. So, after patent expiry pharmaceuticals in developing countries may want to adopt the approach of firm upgrading. Not only will this increase firm knowledge, but it also enhances societal welfare.

Despite patent expiration presenting opportunities to developing countries through firm upgrading, the literature has not studied the effects of patent expiry on pharmaceutical price changes in developing countries. Vondeling et al. (2018) mention the necessity of gathering country specific data to analyse the consequences of patent expiration on prices within specific countries. Therefore, this thesis focuses on investigating the effect of a patent expiration on price changes in the Indian H2 antagonists' market. The reasons for selecting the Indian market are twofold. Firstly, the Indian pharmaceutical market is affected by the TRIPS agreement, preventing firms from copying patented drugs. This is especially relevant since the Indian pharmaceutical market used to be characterised by imitation and reverse engineering. Therefore, drug prices were lower and more affordable to its inhabitants (Chaudhuri et al., 2006). Secondly, the Indian pharmaceutical industry experienced major obstacles after the introduction of the TRIPS agreement (Chaudhuri et al., 2006). Abrol, Prajapati & Singh (2017) state that policymakers must seek to improve the capacities to innovate, as currently this prevents developing countries from major developments in the pharmaceutical industry. A way to accumulate knowledge is by adopting the techniques of developed countries, for instance through the application of innovations after patent expiration.

However, patents and patent expiration effects in the Indian pharmaceutical industry are understudied. A noteworthy article by Chaudhuri et al. (2006) examines the effect of patent protection in the Indian pharmaceutical industry. Prior to the introduction of the TRIPS agreement, US patents were not recognized in several foreign markets. An example of this is the Indian Patent Act of 1970, which invoked that foreign patents on pharmaceutical products were not recognized by the Indian legislators. This changed with the introduction of

the TRIPS agreement in 1995, as from that moment patents were recognized and enforced globally. With pharmaceuticals investing significant amounts of money in the development of new innovations (Congressional Budget Office, 2021), the TRIPS agreement would provide international financial and legal protection. Hence, the owners of patents started to financially benefit from their innovations globally, where previously foreign industries would take away a large proportion of the financial gains (Lehnman, 2003). Chaudhuri et al. (2006) state that the lack of legislation had negative consequences on the rate of development, as the financial benefits of innovations were limited to the domestic market.

Moreover, the 1995 TRIPS agreement granted a transition period until 2005 for developing countries to adjust to the new agreement. Subsequently, Indian pharmaceuticals were no longer allowed to copy patented drugs, for instance through reverse engineering. As a result, those firms that applied these reverse engineering techniques, were affected most by the new agreement. This means that the development costs of new and existing drugs rose significantly (Ashwin, Krishnan & George, 2016). The TRIPS agreement faced a lot of resistance, particularly from developing countries. Those countries were afraid of a substantial increase in prices that would come at the expense of the welfare of its inhabitants. On the other hand, the western pharmaceutical businesses were in favour of these regulations. Previously, they were unable to financially benefit from their innovation in foreign markets, because of foreign patent infringements (Chaudhuri et al., 2006).

Chaudhuri et al. (2006) identify a significant increase in medicine prices in the Indian pharmaceutical industry, after the introduction of the TRIPS agreement. Moreover, the increase in medicine prices had a decreasing effect on the quantity demanded. Subsequently, the total welfare loss in India is estimated at 450 million US dollars. On the other hand, the financial gain for western pharmaceutical firms with a patent is estimated at 50 million US dollars[2]. However, the financial gains of the western pharmaceuticals are relatively small. Chaudhuri et al. (2006) state that the profits of the most selling patented drug, of a major German pharmaceutical called Bayer, is estimated at 640 million US dollars annually. With that in mind, a total annual gain of 50 million US dollars is relatively small for the entire western pharmaceutical industry.

Moreover, Chaudhuri et al. (2006) suggest that the TRIPS agreement and its consequences on patent enforcement, had a negative effect on the welfare of citizens in India. This decrease in consumer surplus is caused by increased retail prices. Dutta (2011) endorses these findings, by arguing that the welfare loss of the global society is estimated at 378.5 million. This comes down to an average annual welfare loss of 9 million per patented drug. However, the welfare gain of the pharmaceutical patent holders is estimated at 1.4 million per patented drug, after the global patent enforcement. Thus, the welfare gain of the patent enforcement is relatively small for western pharmaceuticals, compared to the welfare loss of developing countries. (Dutta, 2011).

[2] Claims are made that the 50 million US dollars estimate is made in the context of no price regulation, which enables pharmaceutical enterprises to freely adjust their prices. Chaudhuri et al. (2006) state that an annual gain of 19.6 million US dollars for these western businesses with a patent, is deemed more realistic.

Furthermore, Duggan et al. (2016) study the TRIPS agreement, by investigating the effect of the new patent system in India in terms of prices, quantities sold and market structure. Duggan et al. (2016) build on the study of Chaudhuri et al. (2006) by further elaborating on a small regulatory aspect that might have impacted their results. The TRIPS agreement mentions that any investments made by firms, before the introduction of the TRIPS agreement in 2005, remain protected. Therefore, if an investment by Indian pharmaceuticals in a patented drug was made prior to the introduction of the TRIPS agreement, the regulation permits these businesses to continue the production of patented medicines. This was accomplished to avoid Indian citizens from encountering massive increases in their medical expenditures. Any increase in medicine prices is far from ideal as the Indian inhabitants are highly budget constrained (World Bank, 2020). Nevertheless, those businesses that benefited from this exception were obligated to pay royalties to the owner of the patent. In addition, regulation ensures that in the case of patented drugs being too expensive for a large proportion of a country, generic versions of the drugs will enter the market. This is of great importance as 21.9% of the Indian population was living under the national poverty line in 2011. Therefore, any increase in price could have serious consequences for the accessibility of drugs for a large proportion of Indian citizens (World Bank, 2020).

All in all, the results of the article by Duggan et al. (2016) suggest a modest significant increase in price after the patent enforcement introduction of approximately three percent. Even though the increase remains relatively small, compared to the findings of (Chaudhuri et al., 2006), a three percent increase may still have a major impact on the affordability of the medicines in developing countries. Yet, the effects on quantities sold are insignificant, suggesting that the regulatory exceptions on patent enforcements made, did not have a diminishing effect on changes in demand. In addition, the generic version of drugs remains available in some cases with high medication prices. However, it is uncertain how this has affected Indian societal welfare. Nevertheless, Duggan et al. (2016) and Chaudhuri et al. (2006) illustrate the importance of patents and regulation in the pharmaceutical industry.

2.2 The H2 Antagonists' Market

Before moving to the construction of the hypotheses, this section examines the H2 antagonists' market. The framework used to conduct the market analysis is the Porter's five forces model (Porter, 2008), which analyses the market players, competition and price elasticity. Lastly, this section elaborates on some additional distinguishing characteristics of the Indian H2 antagonists' market. H2 antagonists are the collective of drugs that decrease the production of stomach acids. Subsequently, these medicines treat gastroesophageal reflux disease, gastrointestinal ulcers and other gastrointestinal hypersecretory conditions. Rabeprazole and famotidine are medicines labelled under the umbrella of H2 antagonists.

Rabeprazole is the generic version of a previously patented drug known by the brand name Aciphex. Originally, Aciphex was developed and patented by a Japanese pharmaceutical called Eisai (FiercePharma, 2012). Eventually, the medicine was brought to the market through a cooperation between the Japanese pharmaceutical Eisai and the US pharmaceutical Johnson & Johnson (FiercePharma, 2012). This patent was

granted in 1986 and expired by May 2013, after which it has been produced by numerous pharmaceuticals as a generic drug (Drugs.com, 2021a). Famotidine is a similar drug to rabeprazole, which was brought to the market under the brand name Pepcid. The drug was patented by the Japanese pharmaceutical Yamanouchi (Drugs.com, 2020; European Patent Office, n.d.). The patent of Pepcid expired several years prior to the patent expiration of Aciphex. Additional detailed information on these two generic medicines, including the selection criteria can be found in section 3.1 of the Data & Methodology section.

Next, the market of H2 antagonists is studied by applying Porter's five forces model, starting with the competition element (Porter, 2008). The international pharmaceutical sector is a highly competitive industry (Saha et al., 2006). The competition element of the pharmaceutical industry is most vividly illustrated through the generic medication market. Price competition between pharmaceuticals is the highest in these generic markets, as businesses are free to enter the market. Therefore, competition in this part of the industry has a decreasing effect on the price of generic medicines (Saha et al., 2006).

However, this has not always been the case as previously patents played a determining role. Caves et al. (1991) argue that there is a clear trade-off between competition and innovation, as illustrated by the H2 antagonists' market. During rabeprazole's active patent period prior to 2013, the pharmaceuticals Eisai and Johnson & Johnson were price setters and could act as duopolistic market players. However, this changed after the patent expirations of H2 antagonist's product as the generic versions of the drug became available. Currently, the H2 antagonists' market is characterised by high price competition, with a high number of producers.

In addition to the high levels of price competition in generic pharmaceutical markets, there is a high level of competition among gathering knowledge in the pharmaceutical industry. Pharmaceuticals that introduce inventions can strengthen their financial position. These inventions are only occurring if pharmaceuticals have sufficient human capabilities and know-how. Therefore, these researchers are considered the driving force behind innovations (Lui, 2014), especially in the case of the Indian pharmaceutical industry (Kamath, 2008). Recently, the H2 antagonists' market has not seen radical innovations introduced. Despite the lack of major innovations, researchers contribute to improving the current design, for instance through enhancing the profitability. Moreover, enhanced technological capabilities in the future means that pharmaceuticals are competing to attract the best researchers (Forbes, 2019; McKinsey, 2018). This allows them to have a competitive advantage in the future. Thus, there is a strong competition within the entire pharmaceutical industry to attract the best researchers, as these are considered of major importance for the introduction of innovations in the pharmaceutical industry.

Next, the type of market players in the H2 antagonists' market are discussed. New entrants rarely make their way into the pharmaceutical industry, predominantly because of the high entry barriers. These include financial constraints, such as a lack of economies of scope and a lack of accumulated knowledge, compared to the existing pharmaceuticals (Lizuka, 2009). Despite the lack of new big pharmaceutical businesses, smaller

groups of researchers develop ideas and concepts that eventually lead to innovations. With the H2 antagonists' market being a generic medicine market, the large manufacturers exploit their scale advantages to produce these products at low costs. This enables them to operate in the competitive market for generic medication. New entrants may pursue the production of generic medicines, while they are expected to have difficulties with the costs to obtain an approval by the national medicine agency (Saha et al., 2006).

The larger pharmaceuticals have a lot of power if they manage to obtain a patent. Prices are generally dictated, as these patents allow for monopolistic behaviour by these pharmaceuticals. The argument made by pharmaceutical businesses is that the high costs encountered during the R&D phase are compensated by the profit margins added to the wholesale prices (Caves et al., 1991). However, in generic medicine markets competition is generally a lot higher, which decreases the prices of generic medicines. Thus, the market power of producers in generic markets is lower, compared to the power of producers in patented drug markets (Magazzini, Pammolli & Riccaboni, 2004).

On the other hand, consumers have very little power when it comes to affecting the prices of pharmaceutical products. Since medicines are vital to sustaining people's health, consumers cannot reject entering these markets. People need drugs to remain healthy and suppress symptoms, meaning that they are required to take medicines to sustain their current standard of living. So, the demand for medicines remains relatively unchanged after a change in price. Therefore, the price elasticity of demand for both patented and generic drugs is inelastic (Yeung et al., 2018).

Moreover, the pharmaceutical industry is characterised by its high level of regulations. Price regulation or other types of regulatory constraints are imposed by governments to increase societal welfare. However, Puig-Junov, (2010) shows that regulation has a negative effect on pharmaceutical prices. In addition, Bardey, Bommier & Jullien, (2010) state that regulation has a negative effect on innovations in the pharmaceutical industry, which decreases societal welfare too. This limits the development of new medicines and the introduction of innovations. Danzon & Chao (2000) articulate that despite regulation having a declining effect on prices, it has a negative impact on the overall competition in generic markets. Hence, these authors argue that in the absence of any regulation, the market reaches the optimal price level.

Aside from the high level of regulation in the Indian pharmaceutical industry, there are some additional distinguishing factors of the H2 antagonists' market. In the H2 antagonists' market, drugs can be a combination of ingredients. In the case of a combined rabeprazole drug, the active ingredient rabeprazole is strengthened via other ingredients. Rabeprazole remains the active ingredient, but the composition of the medicine differs. However, there are also drugs that do not have this composition of different ingredients, which are known as non-combined medicines. Furthermore, multinationals and non-multinationals pharmaceuticals in India produce H2 antagonists. Another distinctive characteristic of the Indian H2 antagonists' market is that medicines come in solid and non-solid versions. The prescribed version predominantly depends on the characteristics of solid and

non-solid H2 antagonists, which is further discussed in section 3.2. As stated in the related literature section, certain businesses were able to benefit from a regulatory exception of the TRIPS agreement, which allowed businesses to produce rabeprazole, while the patent of rabeprazole was active. These are the most important characteristics of the H2 antagonists' market that are relevant for the construction of the hypotheses in section 2.3, with further detail provided on the relevant characteristics of H2 antagonists in section 3.2.

2.3 Hypotheses

In the next section the hypotheses study several medicine characteristics such as solid, combined or multinational produced. In addition, hypothesis five studies a regulatory exception. Different econometric techniques are used to study these hypotheses. The retail prices are the price paid by consumers to the retailer, where the wholesale prices are the price paid by the retailer to the manufacturer of the pharmaceutical products.

2.3.1 Hypothesis 1: The Effect of Patent Expiration on Prices

Saha et al. (2006) suggests that the generic medicines market in the US is one of the main reasons for major cost savings in US healthcare, through the substitution of branded drugs by generic medication. The 1984 introduced Hatch-Waxman Act (Hatch-Waxman Act, 2018) allowed for a significant reduction in costs through the production of generic medicines. Along with the research and development costs, the energy in terms of time and money required to obtain a FDA approved drug, are the predominant entry barriers for entrants in pharmaceutical markets. The Hatch-Waxman act of 1984 lowered these entry barriers, bringing more players to the generic pharmaceutical markets. As more generic medicine suppliers enter the market, prices decline and competition increases. The price competition is especially intense in the period just after the patent expiration, since new entrants seek to seize as much market share as possible (Saha et al., 2006).

On the other hand, Gupta, Shah & Ross (2019) observe an increase in generic drug prices and a shortage in generic drug availability in the US. Historically, generic drug prices tend to decline as competition increases, yet the authors argue that currently there is a lack of competition in these US generic drug markets. Gupta, Shah & Ross (2019) highlight the important role fulfilled by the FDA, who should address and promote price competition in these US generic medicine markets. Despite the concerns regarding the availability of generic medicines, the general assumption remains that prices decrease once a patent expires and a generic medicine becomes available (Gupta, Shah & Ross, 2019; Magazzini, Pammolli & Riccaboni, 2004; Saha et al., 2006). This research studies the branded drug Aciphex (rabeprazole), of which the patent expired in 2013. More detailed information on rabeprazole is provided in Chapter three. Subsequently, this thesis studies the price changes of rabeprazole after Aciphex' patent expiration in 2013, for the Indian H2 antagonists' market.

Furthermore, Ghazali, Yee & Muhammad (2008) study the relation of the consumer price index (CPI) and the producer price index (PPI) in Malaysia. Even though this thesis does not study the CPI and PPI, these indexes offer information on the relation between retail and wholesale prices in the Indian economy. Ghazali,

Yee & Muhammad (2008) find a long-term equilibrium relation, which means that both retail and wholesale prices react similarly to exogenous shocks. Nevertheless, the magnitude after the patent expiration differs for retail and wholesale prices. For instance, wholesale prices might decrease due to the patent expiration. However, retail prices may not decline as fast, as retailers may seek the opportunity to increase their profit margins (Ghazali et al., 2008). Therefore, the retail and wholesale prices are studied separately to identify possible deviations in prices after patent expiry. Despite some arguments that state prices do not necessarily decline after a patent expiration, the general assumption remains that prices decline after patent expiry (Gupta, Shah & Ross, 2019; Magazzini, Pammolli & Riccaboni, 2004; Saha et al., 2006).

Hypotheses A and B only study the rabeprazole dataset. Furthermore, hypothesis 1 does not study specific medicine characteristics. Therefore, hypothesis 1 studies the retail and wholesale prices after patent expiry, for non-combined and solid medicine. The reason for having this fixed set of characteristics is explained in section 3.2 and Appendix 1. All in all, the aforementioned theories hence result in the following hypotheses:

Hypothesis 1A: The retail price of rabeprazole declined after the patent expiration of Aciphex.

Hypothesis 1B: The wholesale price of rabeprazole declined after the patent expiration of Aciphex.

Contrary to hypotheses A and B, hypotheses C and D study both rabeprazole and famotidine datasets. In addition, characteristics such as inflation and regulatory changes are not considered for hypotheses A and B, even though they may have an impact on the price changes of rabeprazole during the period of interest. To identify the effect of patent expiration on prices, a counterfactual is introduced. This counterfactual is designed to illustrate what would have happened to the price of rabeprazole in case that the patent of Aciphex had not expired. Through the comparison with the counterfactual, the effect on the retail and wholesale price is studied after the patent expiration, while considering characteristics such as inflation and regulatory changes. Further details on the exact approach and the assumptions of the applied methods are presented in the ensuing methodology section. For this study, famotidine serves as the counterfactual for hypotheses 1 – 4. The aforementioned theories result in the following hypotheses:

Hypothesis 1C: The retail price of rabeprazole decreases more than the retail price of famotidine after Aciphex' patent expiration.

Hypothesis 1D: The wholesale price of rabeprazole decreases more than the wholesale price of famotidine after Aciphex' patent expiration.

2.3.2 Hypothesis 2: The Effect of Patent expiration on Combined and Non-Combined Medicine

The second set of hypotheses studies an additional characteristic through the introduction of combined and non-combined pharmaceutical products. A combined medicine of rabeprazole contains multiple active ingredients, where a non-combined medicine contains only one active ingredient. As an example, this means that for rabeprazole, the benefit of having multiple active ingredients is that it limits the production of stomach acids. Nevertheless, it also serves as a remedy against symptoms caused by excess stomach production. However, with one active ingredient, users have to take multiple non-combined medicines to treat the condition and the symptoms. So, combined medicines have multiple active ingredients that deal with multiple issues, while a non-combined medicine only has one active ingredient that only serves as a remedy to a single issue. Regardless of the number of active ingredients, the medicine keeps the name of the main active ingredient. Hence, this results in having both combined and non-combined rabeprazole and famotidine medicines.

With other active ingredients part of a combined medicine of rabeprazole, a shift in price of the non-rabeprazole ingredient(s) is possibly allocated to the effect of the patent expiration. Subsequently, the distinction is made between combined and non-combined rabeprazole, to estimate the effect of Aciphex' patent expiration on prices. This gives an estimate of patent expiration that is unaffected by the changes in price of the non-rabeprazole ingredients.

Suh et al. (2000) study the effects of multiple-source entry on price competition after patent expiration in the pharmaceutical industry. Multiple-source medications are defined as drugs marketed by any firm other than the original owners of the patent, which contain the same strength and dosage as the product of the original patent owner. Suh et al. (2000) suggest that the owners of the patent continue to increase their prices after patent expiration, where new entrants with multiple-sourced medicines experience a significant decrease in prices over time. These multiple-sourced medicines increase the price competition in the generic pharmaceutical markets, allowing consumers to benefit from lower prices. Moreover, the multiple-sourced medicines tend to focus more on price sensitive markets, with a high probability of successful entry. In these price sensitive markets, the owners of the patent must eventually comply with the price competition. Suh et al. (2000) find a decrease of roughly 12 percent in the first four years after patent expiration in markets with high price competition. Additionally, the quantity sold by the inventor of the patent decreases on average by 30 percent, while the new entrants in the market experience a growth of quantities sold, and an increase in market share.

All in all, Suh et al. (2000) suggest that new entrants in markets that were previously dominated by patents, produce at lower prices allowing them to be more competitive. As a result, price competition increases in these generic drug markets. Therefore, prices of rabeprazole declined significantly, caused by the increased availability and enhanced price competition of rabeprazole after the patent expiration. So, the increased price competition in the rabeprazole market only leads to a decrease in price of rabeprazole, while other medicine prices are expected to remain unaffected by Aciphex' patent expiration. The combined products only contain a certain percentage of the rabeprazole ingredient, which makes the medicine cheaper for that specific percentage

only, rather than the full 100%. Therefore, those products of rabeprazole that are combined are expected to have a higher price, compared to those products that are a non-combined product of rabeprazole.

Unlike the previous hypothesis, hypothesis 2 studies combined and non-combined drugs. Nevertheless, hypothesis 2 only studies solid medicine. The solid and non-solid characteristics of medicines are studied in hypothesis 4. The conducted literature leads to the following hypotheses:

Hypothesis 2A: The retail price of non-combined rabeprazole decreases more than the retail price of combined rabeprazole after Aciphex's patent expiration.

Hypothesis 2B: The wholesale price of non-combined rabeprazole decreases more than the wholesale price of combined rabeprazole after Aciphex's patent expiration.

Similar to hypotheses 1C and 1D, the famotidine dataset is used to construct a counterfactual to determine retail or wholesale price changes for combined and non-combined products. The non-combined rabeprazole prices after patent expiration are expected to be lower, compared to the combined rabeprazole prices. The counterfactual is introduced to study what would have happened to the price of non-combined medicine had the patent of Aciphex not expired. Subsequently, the non-combined rabeprazole prices after the patent expiration are compared to combined famotidine prices. This theory leads to the following hypotheses:

Hypothesis 2C: The retail price of non-combined rabeprazole decreases more than the retail price of combined famotidine after Aciphex' patent expiration.

Hypothesis 2D: The wholesale price of non-combined rabeprazole decreases more than the wholesale price of combined famotidine after Aciphex' patent expiration.

2.3.3 Hypothesis 3: The Effect of Patent Expiration on Multinationals and non-Multinationals Medicine

Next, the role of multinational and non-multinational pharmaceutical enterprises is studied in the context of retail and wholesale price changes, in the Indian H2 antagonists' market after Aciphex' patent expiration. Roa (2008) suggests that multinationals in India focus on the patent section of the pharmaceutical industry. With their technological and human capabilities, multinationals invest heavily in R&D to discover and explore new drugs to enhance their knowledge. This means that they are more likely to obtain a patent for their new inventions, compared to the smaller pharmaceuticals who have less financial and technical capabilities. Multinationals focus on R&D in the hope to acquire a new patent, which allows them to secure great financial benefits in case of a successful patent application. Moreover, the author claims that the medium to smaller pharmaceuticals in the Indian market are more engaged in the production of generic medicines (Roa, 2008). Nevertheless, Roa (2008) argues that multinationals are put under public pressure, in developing countries such as India, due to the increasing demand for affordable medication. Similar to the case of the US, the increased

demand for affordable drugs means that multinationals are expected to fulfil their social corporate responsibility, by being a supplier in the Indian generics market (Gupta, Shah & Ross, 2019).

Additionally, Greene (2007) states that the largest proportion of Indian pharmaceuticals is medium to small, where only a limited number of large multinationals have entered the Indian pharmaceutical market over the last few decades. Greene (2007) studies the role of Indian pharmaceutical businesses in the generic medicine markets. Indian pharmaceuticals have a cost advantage, compared to these multinationals, as they produce at half the cost price encountered by multinationals. In addition, Greene (2007) states that India needs large quantities of affordable drugs, which has resulted in Indian pharmaceuticals being responsible for roughly 20% of the world production in high-quality, low-cost generic pharmaceutical products. This cost advantage mainly derives from the relatively low wage costs encountered by small to medium sized pharmaceuticals. This suggests that non-multinational Indian pharmaceuticals tend to produce drugs at lower costs, relative to multinationals (Greene, 2007). A partial explanation of these findings lies within the lack of focus by multinationals on the generic drug markets, as multinationals are primarily interested in R&D and innovations to acquire patents (Roa, 2008).

Furthermore, the imitation of generic pharmaceutical products has increased the accumulated knowledge of Indian pharmaceuticals over the last decades (Kale & Little, 2007). Kale & Little (2007) state that the imitation of products in the Indian pharmaceutical industry provides a base for the development of capabilities and knowledge of smaller Indian pharmaceuticals. Moreover, product and process imitation have an enhancing effect on future innovations and R&D of these Indian pharmaceuticals, to catch up with the western businesses over time (Greene, 2007).

Patent expiration intensifies the price competition in developing pharmaceutical markets. Saha et al. (2006), Gupta, Shah & Ross (2019) and Magazzini, Pammolli & Riccaboni (2004) state that the pharmaceuticals which produce at lower costs can acquire a bigger market share in generic Indian pharmaceutical markets. Smaller sized Indian pharmaceuticals accumulate knowledge and capabilities through the process of imitation. In combination with the cost advantages of these Indian enterprises, the Indian market presents an excellent environment to study the effects of patent expiration, and the differences between multinationals and non-multinationals on medicine prices. With the distinction between multinationals and non-multinationals, the price of those businesses that are the least competitive, and least focused on the generic medicine market, are expected to have higher prices.

Hypothesis 3 studies multinationals and non-multinationals. In addition, hypothesis 3 only investigates solid and non-combined medicines. This gives a more profound image of the difference between multinationals and non-multinationals. Therefore, the aforementioned theories lead to the following hypotheses:

Hypothesis 3A: **The retail price of multinational produced rabeprazole is higher, compared to the retail price of non-multinational produced rabeprazole after Aciphex' patent expiration.**

Hypothesis 3B: **The wholesale price of multinational produced rabeprazole is higher, compared to the wholesale price of non-multinational produced rabeprazole after Aciphex' patent expiration.**

Hypotheses C and D study both rabeprazole and famotidine datasets. To identify the effect of multinationals and patent expiration on prices, a counterfactual is introduced. This counterfactual illustrates what would have happened to the multinational price of rabeprazole, had the patent of Aciphex not expired. This means the analysis considers characteristics such as inflation and regulatory changes. Similar to the last hypotheses, famotidine serves as the counterfactual. Hence, the aforementioned theories result in the following hypotheses:

Hypothesis 3C: **The retail price of multinational produced rabeprazole is higher, compared to the retail price of non-multinational produced famotidine after Aciphex' patent expiration.**

Hypothesis 3D: **The wholesale price of multinational produced rabeprazole is higher, compared to the wholesale price of non-multinational produced famotidine after Aciphex' patent expiration.**

2.3.4 Hypothesis 4: The Effect of Patent Expiration on Solid and non-Solid Medicine

Next, the differences between solid and non-solid medicines, in interaction with patent expiry, is studied. Drugs that have the same intended effect, can be supplied through different ways, such as capsules, pills, or injections. These differences in the construction of the medicines or the approach through which the medicine is provided, may affect the production costs and cause deviations in average prices of drugs. For instance, certain solid medicines must be taken orally, where others must be dissolved in water prior to the medicine intake. Even the pace through which the medicine reaches the blood may differ depending on the purpose and type of medication, as an injection may be a faster approach in reaching the blood compared to a slow releasing drug.

Drugs are roughly divided into solid and non-solid types of drugs. There are numerous advantages and disadvantages when discussing the differences between solid and non-solid drugs. For instance, solid medicines have the advantages of greater stability, being easier to transport, easier to store and less complicated in terms of dosage selection (Committee for Medicinal Products for Human Use, 2006; Nunn & Williams, 2005). Therefore, solid drugs are less expensive, relative to the non-solid counterparts (Lajoinie et al., 2014; Salunke et al., 2011). With non-solid medicines significantly more expensive compared to solid medicines in the Indian pharmaceutical market, solid drugs are a more accessible option for the budget constrained Indian inhabitants (Banerjee & Duflo, 2007).

Solid medicines are the more accessible alternative in terms of costs, therefore, competition in these markets is at a higher level as well. Aside from the numerous advantages of solid drugs, non-solid alternatives are more expensive, caused by the more sophisticated production techniques required to develop and produce non-solid medication (Lajoinie et al., 2014). Therefore, competition is lower, as these more sophisticated production techniques require certain skills and know-how, which are not possessed by all pharmaceutical enterprises. With Aciphex' patent expiration opening a new submarket in the Indian pharmaceutical sector, firms want to claim as much market share as possible in a highly competitive environment. Subsequently, pharmaceuticals produce at the lowest costs possible, to be competitive and gain market share. Therefore, pharmaceuticals seek to produce solid medication, as it is less expensive, compared to non-solid alternatives. Moreover, the investment required to gain the skills necessary to produce non-solid medication, makes most pharmaceuticals reluctant to enter this non-solid part of the new market. Hypothesis 4 studies solid and non-solid medicine, however, similar to hypotheses 1 and 3, only non-combined medicines are considered. This leads to the construction of the following hypotheses:

Hypothesis 4A: The retail price of solid rabeprazole is lower, relative to the retail price of non-solid rabeprazole after Aciphex' patent expiration.

Hypothesis 4B: The wholesale price of solid rabeprazole is lower, relative to the wholesale price of non-solid rabeprazole after Aciphex' patent expiration.

Hypotheses C and D study both rabeprazole and famotidine datasets. To identify the effect of solid products and patent expiration on prices, a counterfactual is introduced. This counterfactual illustrates what would have happened to the solid medicine price of rabeprazole, had the patent of Aciphex not expired. This means the analysis considers characteristics such as inflation and regulatory changes. Again, famotidine serves as the counterfactual to this hypothesis. Hence, the aforementioned theories hence result in the following hypotheses:

Hypothesis 4C: The retail price of solid rabeprazole is lower, relative to the retail price of non-solid famotidine after Aciphex' patent expiration.

Hypothesis 4C: The wholesale price of solid rabeprazole is lower, relative to the wholesale price of non-solid famotidine after Aciphex' patent expiration.

2.3.5 Hypothesis 5: The Effect of Patent Expiration and the TRIPS agreement on Medicine

The last set of hypotheses discusses the TRIPS agreement and the exception made for pharmaceuticals who had invested in the production of patented drugs, prior to the introduction of the TRIPS agreement in 2005. An important regulatory exception was made for pharmaceuticals in developing countries that had invested in either the production or the research of a patented medicine. These pharmaceuticals were permitted to continue the

production and disposal of these patented products. However, they were required to pay royalties to the patent' owners (Duggan et al., 2016).

With these businesses having relatively less competition compared to other pharmaceutical markets, prices are expected to be higher in the less competitive markets. Additionally, the compulsory payment of royalties to the owners of the patent means that pharmaceuticals are likely to charge higher prices. With that in mind, having gathered a significant amount of knowledge on the patented product, this hypothesis expects these pharmaceuticals to produce at a very competitive price once the patent expires. Therefore, with the accumulated knowledge and without the royalty payment requirements, this hypothesis expects that the pharmaceuticals who produced prior to the introduction of the TRIPS agreement were able to set lower prices.

Furthermore, a study on the effect of the TRIPS agreement introduction in the Indian market suggests that both welfare loss and the increase in prices were significant (Watal, 2000). This article illustrates the need for price regulation to dampen the negative effects of the TRIPS agreement on Indian society. Those firms that were able to benefit from the TRIPS exception encountered less competition at first. However, this changed into a fiercely competitive market after the patent expiration. With an increase in price competition, those pharmaceuticals that were able to benefit from the TRIPS exception had accumulated the knowledge and capabilities over the years of the active patent (Watal, 2000). This enabled these pharmaceuticals to produce at lower prices, compared to new entrants (Watal, 2000). Therefore, the following hypotheses are constructed:

Hypothesis 5A: The retail prices of rabeprazole brands that applied the TRIPS agreement exception decreased more, relative to retail prices of brands that did not apply the TRIPS agreement exception after Aciphex' patent expiration.

Hypothesis 5B: The wholesale prices of rabeprazole brands that applied the TRIPS agreement exception decreased more, relative to wholesale prices of brands that did not apply the TRIPS agreement exception after Aciphex' patent expiration.

Unlike the previous hypotheses, hypothesis 5 does not conduct an additional analysis by introducing a counterfactual. The patent of famotidine expired in 2003. Therefore, a comparison could lead to biased results as there is an overlap in the patent expiration of famotidine and the introduction of the TRIPS agreement. The next chapter explains and discusses the applied data. This includes the selection criteria of the datasets and an introduction of all variables used in the analyses. Moreover, this section gives additional information on the selected methods to perform the analysis, including its assumptions.

3. Data & Methodology

The ensuing section discusses the adopted datasets thoroughly, by elaborating why the selected drugs are compelling and appropriate for this thesis. Next, an in-depth description of the variables of interest and explanatory variables illustrates the application of these variables. Then this section provides information on the data preparation and data analysis. Furthermore, the applied control variables are explained in terms of their application and relevance to the research. Lastly, this part focuses on the quantitative methods that are selected to answer the hypotheses. This includes an illustration on the selection process and assumptions of the most appropriate econometric techniques.

3.1 Datasets

The datasets on rabeprazole and famotidine are retrieved from the All-Indian Organisation of Chemists and Druggists (AIOCD), which provides firm level data on Indian medication prices over the period 2011 – 2016 (AIOCD, n.d.). Firstly, this section discusses the dataset on rabeprazole. Lastly, this part examines the famotidine dataset.

The H2 antagonist rabeprazole is appropriate for the analysis, starting with the fact that it is a commonly prescribed medication (Drugs.com, 2021a). Rabeprazole is relatively accessible, compared to more expensive drugs, such as cancer medication (Bloomberg, 2020). With rabeprazole being produced by numerous pharmaceuticals (Drugs.com, 2021a), both multinationals and non-multinationals, issues regarding monopoly power or duopoly agreements are avoided. Thus, this thesis studies the effects of a patent expiration on pharmaceutical price changes in a competitive market, preventing biases from affecting the results through price and output agreements. Secondly, numerous pharmaceuticals produced rabeprazole as a generic product in India, while the patent of Aciphex was still active. This is legal under the exception made by the TRIPS Agreement (Duggan et al., 2016). Previous studies focus on the direct consequences of this agreement in terms of welfare loss. Subsequently, this research studies patent expiration effects on drug prices, in combination with the long-term effects of the TRIPS agreement. Additionally, a lawsuit between an Indian pharmaceutical and the Japanese patent owner, ruled that the patent was rightfully granted to Eisai (The Economic Times, 2007; Thepharmaletter.com, 2007). This illustrates that regardless of the exception of the TRIPS agreement, the rabeprazole patent was enforced globally. Therefore, the aforementioned reasoning confirms that rabeprazole is an excellent medication to study effects of patent expiration on price changes in the Indian pharmaceutical market.

The second dataset on famotidine facilitates the application of a difference-in-difference analysis. This approach ensures a robustness analysis, by controlling for unobservable characteristics that may have had an impact on rabeprazole prices. The selection criteria to ensure a robust analysis are threefold. Firstly, the medicine facilitates the application of the additional econometric analysis and is required to fulfil the same medical objective. In the case of this study, the medicine decreases stomach acid production and belongs to the umbrella

of H2 antagonists. The reasoning behind this is that the medicines should be in the same overall market, thus being exposed to roughly the same exogenous shocks. Subsequently, this facilitates an impartial comparison through a reliable counterfactual. Had a medication of another market been selected for the comparison with rabeprazole, additional research would be required to ensure that this other medication is not affected by external shocks specific to that submarket. Secondly, the patent of the compared medicine, in this case famotidine, must have expired long before the period of interest started. Had the selected medicine experienced a recent patent expiration, this would decrease the possibility of constructing a valid and unbiased counterfactual. With the patent of famotidine expired over a decade prior to the period of interest, biases caused by the counterfactual are less likely. Lastly, no issues regarding the effectiveness or other factors such as lawsuits or production issues should be a factor in the price of the counterfactual. Famotidine complies with all these criteria. Section 3.4.2 discusses the formal assumptions of the selected econometric approach.

3.2 Variables

The following chapter describes all relevant variables, starting with the variables of interest. Both variables of interest give information on the retail and wholesale prices of rabeprazole and famotidine over the period 2011 to 2016. Retail prices are the amount of money paid by consumers for the medicines. Likewise, wholesale prices are the amount of money paid by retailers to the manufactures of these pharmaceutical products. Ghazali, Yee & Muhammad (2008) state that both retail and wholesale prices have a long-term equilibrium, suggesting that they react similarly to exogenous shocks such as a patent expiration.

The construction of the variables of interest is as follows. Since the quantity of each package of medication differs, the variable 'Units per Pack' is used to calculate the price per unit of the rabeprazole and famotidine. The illustrated formulas (1,2) calculate the retail and wholesale price for a single unit or dosage. Therefore, the price of an entire package of medicine is divided by the number of units that the package contains. There is no necessity in calculating the price per milligram (mg), as only the 20 milligram prices of rabeprazole and famotidine are studied. Hypothesis 2 is the only exception, as combined and non-combined medicines are studied. The current approach of studying the price per unit, facilitates a robust analysis on price changes, after a patent expiry in the Indian H2 antagonists' market.

Retail price = *Price paid by consumer to the retailers / Number of units per package* *(1)*

Wholesale price = *Price paid by the retailer to the manufacturer / Number of units per package* *(2)*

The variable 'price_ptr' provides the price paid by the retailer to the manufacturer. In addition, the price paid by the consumer to the retailer is given by the variable 'price_mrp'. To construct the wholesale price per unit, the variable 'price_ptr' is divided by the variable 'Units per Pack'. The variable 'Units per Pack' gives the number of units or dosages present in the package. This process is repeated for the retail price, but this time, the variable 'price_mrp' is divided by the variable 'Units per Pack'. Both the retail (1) and wholesale (2) price of rabeprazole and famotidine per unit are calculated in Indian Rupees.

Furthermore, an additional reason for not calculating the price per milligram is a limitation regarding the construction of the dataset. This prevents the computation of the price per milligram, as the strength of all active ingredients are mentioned in the dataset. Subsequently, calculating the price per milligram may give biased results. Moreover, the most prescribed dosage strength of rabeprazole and famotidine is 20 milligrams per unit. This is the strength that is most frequently produced and sold, which makes it the most interesting dosage strength. As competition is likely the highest in the 20 milligram H2 antagonists' market, the effects of niche dosage markets on H2 antagonist prices are removed. Only for hypothesis 2, all dosage strengths are included since this hypothesis specifically studies the price changes of combined and non-combined rabeprazole after the patent expiration of Aciphex.

Before further studying these differences between retail and wholesale price, this paragraph discusses the different number of observations between the hypotheses. These differences derive from what the hypotheses are studying. For instance, hypothesis 2 studies the effects of combined and non-combined medicine. This partially explains the different number of observations for each hypothesis. The origin of these differences between the hypotheses is further elaborated when discussing the specific explanatory variable of each hypothesis. Moreover, Appendix 1 discusses and shows an overview of the differences between hypotheses. This appendix illustrates that hypothesis 1 is the main model, which is similar to hypotheses 3 and 5. Only hypotheses 2 and 4 differ in terms of their observations due to their specific research goals.

Table 1 illustrates that the mean retail price of rabeprazole is higher, compared to the mean wholesale price. This is the case for all hypotheses. Moreover, the difference between the retail and wholesale price is roughly between one and two Indian Rupees. In addition, the average units per package for rabeprazole is roughly 10 units for all data on rabeprazole. Similar to rabeprazole, retail prices of famotidine are generally one to two Indian Rupee(s) higher, compared to the wholesale prices. The applied datasets of hypothesis 4 have higher retail and wholesale prices compared to the other hypotheses, which is also the case for the rabeprazole data. The average units of famotidine per package is roughly 13, with the units per package ranging between 1 and 15. On average, the units per package are higher compared to rabeprazole.

The variable 'Month' is a numeric variable ranging from 1 – 67, where month number (1) indicates that an observation was made for the month January in 2011. Furthermore, the number (67) shows that an observation was made for the month July in 2016. Consequently, the variable 'Month' is of great importance for this panel dataset, as it facilitates the differentiation of the period before and after Aciphex' patent expiration. To make a clear distinction between both periods, a binary variable is introduced, which is called 'Patent Expiration'. Since the patent of rabeprazole officially expired by May 2013, the variable 'Patent Expiration' is given the value (0) for all months from 1 up and until 28. For all months after Aciphex' patent expiry, the variable 'Patent Expiration' is given the value (1).

Table 1: Descriptive Statistics Rabeprazole and Famotidine Data

		Rabeprazole			Famotidine		
		Hypothesis 1, 3 & 5	**Hypothesis 2**	**Hypothesis 4**	**Hypothesis 1 & 3**	**Hypothesis 2**	**Hypothesis 4**
Retail Price							
	Mean (SD)	5.10 (3.24)	7.11 (5.87)	7.49 (11.54)	2.50 (9.95)	2.49 (9.81)	2.78 (10.38)
	[Min, Max]	*[0.78, 65]*	*[0.78, 149.49]*	*[0.57, 85.62]*	*[0.15, 66.25]*	*[0.15, 66.25]*	*[0.15, 66.25]*
Wholesale Price							
	Mean (SD)	3.83 (2.15)	5.40 (4.53)	5.64 (8.69)	1.29 (5.83)	1.30 (5.75)	1.52 (6.34)
	[Min, Max]	*[0.64, 30.53]*	*[0.1, 114]*	*[0.45, 68.50]*	*[0.12, 52]*	*[0.12, 52]*	*[0.12, 52]*
Units per Pack							
	Mean (SD)	10.26 (1.40)	10.13 (1.27)	9.82 (3.74)	13.49 (1.61)	13.52 (1.60)	13.38 (1.95)
	[Min, Max]	*[1, 20]*	*[1, 30]*	*[1, 100]*	*[1, 14]*	*[1, 15]*	*[1, 14]*
Month							
	Mean (SD)	34.41 (19.49)	35.72 (19.45]	34.38 (19.45)	32.83 (19.81)	32.17 (19.96)	32.96 (19.85)
	[Min, Max]	*[1, 67]*	*[1, 67]*	*[1, 67]*	*[1, 67]*	*[1, 67]*	*[1, 67]*
Combination							
	Mean (SD)	-	0.63 (0.48)	-	-	0.03 (0.16)	-
	[Min, Max]	-	*[0, 1]*	-	-	*[0, 1]*	-
Multinationals							
	Mean (SD)	0.09 (0.29)	0.06 (0.24)	0.08 (0.28)	0.09 (0.29)	0.09 (0.28)	0.09 (0.29)
	[Min, Max]	*[0, 1]*	*[0, 1]*	*[0, 1]*	*[0, 1]*	*[0, 1]*	*[0, 1]*
Solid							
	Mean (SD)	-	-	0.91 (0.29)	-	-	0.99 (0.10)
	[Min, Max]	-	-	*[0, 1]*	-	-	*[0, 1]*
TRIPS exception							
	Mean (SD)	0.31 (0.46)	-	-	-	-	-
	[Min, Max]	*[0, 1]*	-	-	-	-	-
Patent Expiration							
	Mean (SD)	0.58 (0.49)	0.60 (0.49)	0.58 (0.49)	0.53 (0.50)	0.52 (0.50)	0.53 (0.50)
	[Min, Max]	*[0, 1]*	*[0, 1]*	*[0, 1]*	*[0, 1]*	*[0, 1]*	*[0, 1]*
Number of Observations		10,014	34,144	11,011	741	762	748

Source: *All-Indian Organization of Chemists and Druggists (AIOCD) for the period 2011 until 2016 (AIOCD, n.d.).*

Table 1 shows an evenly distributed dataset when it comes to the number of observations per month. This indicates no issues regarding heteroskedasticity for both datasets. Nevertheless, to confirm this suggestion, additional robustness checks are conducted in section 4.2. The dummy on patent expiration gives a similar image, as the mean is around 0.52 to 0.60. Subsequently, roughly half of the observations derive from the period before Aciphex' patent expiration, and the other half of the observations derive from the period after the patent expiration of Aciphex.

The variable on combined and non-combined medicine is the main explanatory variable for hypothesis 2. The datasets contain a binary variable, which is called 'Combination'. Table 1 shows that for the rabeprazole data, roughly 63 percent is a combined medicine. This only concerns hypothesis 2, as for the other hypotheses combined drugs have been excluded from the dataset. However, for famotidine only 3 percent of the medicines are combined. Next, the explanatory variable 'Multinational' yields information on whether the product is produced by a MNE (1) or a non-MNE (0). This binary variable is applied for the analysis of hypothesis 3. The descriptive data illustrated in Table 1 suggests that for rabeprazole and famotidine, between 6 and 9 percent of the businesses are multinational.

Furthermore, hypothesis 4 studies the effect of patent expiration on price changes for different types of medicines. The type of drugs through which the medicine is provided can vary between capsules, tablets, injections, infusions, sachets and gels, all of which may experience different price changes as a result of a patent expiration. Both solid and non-solid medicine are compared, to identify the effect of the patent expiration on medicine prices. Therefore, hypothesis 4 introduces the binary variable on whether a medicine is solid (1) or non-solid (0). Subsequently, there are no restrictions on the types of medicine, to ensure a valid comparison. Therefore, there is a relatively high number of observations when studying hypothesis 4, compared to the base model. Table 1 illustrates that 91 and 99 percent of rabeprazole and famotidine are solid products, respectively.

The analysis of hypothesis 5 uses an explanatory variable regarding the launch date of the pharmaceutical product. As formerly mentioned, the exceptions made by the TRIPS agreement meant that those businesses that had invested in patented drug production, were permitted to keep producing the patented drug. The variable 'Brand Launch Date' is used to provide information on when the medicine was launched into the market. To apply this information, the variable is converted to a binary variable. Those with a launch date later than January 2005 are given the value (0) for the generated variable 'TRIPS exception'. In addition, the brands with a launch date prior to January 2005 are given the value (1). As illustrated by Table 1, 31 percent of the brands started prior to the introduction of the TRIPS agreement. Nevertheless, this shows that a significant group had the opportunity to benefit from the exception of the TRIPS agreement. This hypothesis only uses rabeprazole data, due to potential biased results, caused by the patent expiration of famotidine in the same period.

In a normal situation, pharmaceuticals are not permitted to produce and sell patent drugs when the patent of a medicine is still active. Similar to the exception of firm investments in patented medicine prior to the

introduction of the TRIPS agreement, an additional regulatory exception is introduced regarding scarcity. In the case of shortages and high market prices, the regulations state that some pharmaceuticals are allowed to produce and sell patented drugs. The aim of this exception is to prevent the societal welfare in countries from decreasing due to exorbitant prices. Therefore, some pharmaceuticals have a starting date between the introduction of the TRIPS agreement and the patent expiration. However, these did not exploit the TRIPS exception regarding previous investments. Therefore, they belong to the post-TRIPS exception group.

In addition to the elaborated variables of interest and explanatory variables, some control variables are implemented into the model. To account for differences between periods of time, month fixed effects are added to the model. Month fixed effects are able to capture the changes within the variable 'Month' across time. These month specific effects are otherwise allocated to the coefficients of other explanatory variables. Furthermore, product fixed effects are implemented too, which seek to capture the within product changes across time.

3.3 Descriptive Statistics

This section discusses additional descriptive statistics, to identify any potential issues in the data. This is accomplished through a correlation matrix, which tests for high correlations between variables. Additionally, a Variance Inflation Factor (VIF) test is performed to test for potential multicollinearity.

3.3.1 Correlation Matrix

Through a correlation matrix, correlations between different variables are illustrated in a clear overview. These correlations allow for the identification of potential concerns, for instance when a correlation between two variables is too high. A correlation is considered too high if it is higher than 0.8, as it potentially causes multicollinearity issues (Green, 1991). The correlation matrix of the variables used for this thesis are illustrated in Table A, which can be found in Appendix 2.

As indicated by the correlation matrix, there are two correlations higher than 0.8. According to the rule of thumb by Green (1991), these correlations are cause for concern regarding multicollinearity. The first high correlation is observed between the retail and wholesale price, which has a correlation of 0.972. Even though this would normally be a concern, the retail and wholesale price are both studied in separate models for the entire duration of this thesis. Therefore, neither variable is applied to give explanatory power to the other variable. Another high correlation of 0.862 is observed between the variables 'Month' and 'Patent Expiration'. The binary variable 'Patent Expiration' is constructed through the variable 'Month'. The variable 'Month' is added to both econometric models, which gives reason for multicollinearity concerns. Therefore, a Variance Inflation Test is performed as well.

3.3.2 VIF Test

A Variance Inflation Factor (VIF) test is performed to study the robustness of the data by ensuring that there are no multicollinearity issues. Subsequently, a VIF score higher than 10, indicates a high likelihood of multicollinearity issues (Shrestha, 2020). Any VIF score lower than 5, indicates a moderate correlation, with no real indication of any multicollinearity issues (Shrestha, 2020). Table B in Appendix 2 illustrates that there are no VIF scores greater than 5, suggesting that there are predominantly moderate correlations between variables (Shrestha, 2020). All in all, the Variance Inflation Factor (VIF) test indicates no issues with multicollinearity for these datasets.

3.4 Quantitative methods

The ensuing section examines the selection of the econometric approaches, which facilitate the analyses of the hypotheses. This research adopts two different quantitative methods, which are explained in terms of their selection criteria and assumptions. The generated hypotheses of section 2.3 provide two sets of hypotheses. The hypotheses marked with the letter 'A' and 'B' study the rabeprazole dataset, whereas those hypotheses labelled with the letter 'C' or 'D' study both the rabeprazole and famotidine datasets. Therefore, the latter hypotheses call for a different econometric approach to answer the hypotheses.

3.4.1 Hypotheses 1-5A & 1-5B

Hypotheses 'A' and 'B' study the effect of the Aciphex's patent expiration on rabeprazole price changes in the H2 antagonists' market, while considering product characteristics. The theoretical framework section discusses these characteristics that have a relation to the price changes of rabeprazole after a patent expiry. Subsequently, this thesis studies the effect of patent expiry on rabeprazole prices, in interaction with a characteristic of the H2 antagonists. Therefore, the primary objective is to establish an estimated effect of said interaction term. To study what econometric technique is most appropriate for the analysis of the hypotheses, the Hausman test is conducted.

The results of the Hausman test, illustrated by Appendix 3, suggest no rejection of the null hypothesis in any of the analysed hypotheses. Consequently, the decision on what econometric technique is most appropriate remains unanswered. The random effects model captures the effect of time variant and invariant characteristics. However, this research studies the interaction terms, meaning that estimating the effect of time invariant characteristics is not relevant. Only the coefficients of the relevant interaction term are essential to answer the hypotheses. In addition, a Wooldridge serial correlation test studies whether there is serial correlation present in the data (Wooldridge, 2010). Table C of Appendix 5 illustrates that serial correlation is indeed an issue in this panel dataset. Serial correlation is more of an issue to the random effects model, as it uses both within and between variation to estimate the coefficients. Therefore, the chosen model includes brand clustered standard errors, which accounts for serial correlation and heteroskedasticity in the datasets.

However, including clustered standard errors does not solve correlation across observation. Therefore, a fixed effects model is more appropriate for the analysis of the hypotheses. Through fixed effects, only the within variation is estimated, which prevents biases caused by correlations of time invariant characteristics across observation from affecting the results. The fixed effects model de-means these time invariant characteristics, solving the issue of correlation across observations. Through a fixed effects model with product and month fixed effects, this thesis aims to study the effects of medicine characteristics in interaction with patent expiration on prices in the Indian H2 antagonists' market. As previously stated, clustered standard errors are included to account for serial correlation and heteroskedasticity issues. Moreover, the fixed effects model comes with the strict exogeneity assumption. This assumption implies that the estimated effect is unbiased if the idiosyncratic error of the error term is uncorrelated with the variable of interest at any time. However, to satisfy this proposition one must identify the correlation of the relevant variables and all other variables, also those variables that are not included in the data. Therefore, it is not possible to check the strict exogeneity assumption.

Hypotheses 1-5A & 1-5B yield the following formula:

$$\boldsymbol{Y_{it}} = \beta_0 + \beta_1 * patexp_t + \beta_2 * X_i + \beta_3 * patexp_t * X_i + u_i + d_t + \varepsilon_{it}$$

The above formula illustrates the equation used for the analysis, where Y is the retail price for hypotheses A and the wholesale price for all hypotheses B. In the subscript of this formula, t represents time, while i refers to an observation. Subsequently, Y_{it} refers to either the retail or wholesale price of an observation for a certain period. Furthermore, $patexp_t$ is a binary variable that takes value 1 after May 2013, but value 0 prior to May 2013. In addition, the variable of interest is illustrated through X_i, which changes per hypotheses: H1) X_i= 0, H2) X_i = combination_i, H3) X_i = multinational_i, H4) X_i= solid_i, H5) X_i = TRIPSexcpt_i. At all times X_i is a dummy variable. These variables on product characteristics are also studied in interaction with $patexp_t$, as illustrated by $patexp_t * X_i$. This interaction term is of great importance for answering the hypotheses. Furthermore, u_i is the product fixed effects and $d_t$is the introduced month fixed effects. The introduction of these product and month fixed effects means that the estimates on the $patexp_t$ and X_i will likely be omitted, as these fixed effects capture the effect of time and product characteristics. These fixed effects capture the within changes of time and product characteristics, making the $patexp_t$ and X_i estimates collinear with fixed effects. The justification for adding these time and product fixed effects is that this study is primarily interested in the interaction of the patent expiration and the product characteristic. Furthermore, adding these fixed effects increases the validity by controlling for unobserved factors and solving the issue of correlation across observations. Hypotheses 1A and 1B do not include time fixed effects, as these hypotheses do study the interaction of product characteristics and patent expiration. Subsequently, had time fixed effects been included, they would capture the estimated effect of the relevant variable, causing collinearity issues. In addition, the idiosyncratic error is illustrated through ε_{it}, which cannot be correlated to the variable of interest at any time according to the strict exogeneity assumption. There is no unobserved heterogeneity in the formula, as the fixed effects model accounts for between variation by de-meaning the data.

3.4.2 Hypotheses 1-4C & 1-4D

Hypotheses one to four, marked with the letter 'C' or 'D', differ from the first set of hypotheses as they study both the rabeprazole and famotidine dataset. The aim of this additional approach is to identify the effect, by controlling for unobservable characteristics that would otherwise have been allocated to other variables of interest. By applying the famotidine data, factors such as inflation are considered when studying the effect of patent expiration on rabeprazole price changes. Subsequently, the results are more robust and have a higher external validity. The econometric approach applied for the hypotheses 1-4C and 1-4D is the difference-in-difference approach. This difference-in-difference approach is particularly useful when it comes to estimating the effects of government interventions or exogenous shocks (Angrist & Krueger, 1999). Moreover, this approach provides unbiased estimates in the case of studying exogenous shocks or policy changes (Olden & Møen, 2020).

The main assumption of the difference-in-difference approach is the parallel trend assumption, which seeks to identify whether the treatment and control group have the same trend in the absence of the treatment. This is necessary as the control group facilitates the construction of the counterfactual. By establishing a visual confirmation that the price trends prior to the event of interest follow a similar trend, the main assumption of the difference-in-difference technique is satisfied. This means that the time-varying factors of treatment and control groups are similar in the periods before the treatment. Moreover, time-invariant factors that differ between the treatment and the control group are less important for the parallel trend assumption, as these do not change due to exogenous shocks. Consequently, when studying the parallel trend assumption, absolute price of both drugs may differ, as long as their price trends prior to the patent expiration are similar. The control group facilitates the construction of the counterfactual, which estimates what would have happened to the treatment group, had this group not experienced the treatment.

For this thesis, the treatment group is the rabeprazole dataset, as this medicine experienced a patent expiration during the period of interest. The famotidine dataset facilitates the construction of the control group, when performing the difference-in-difference analyses. The results of the parallel trend assumption estimates are illustrated by Appendix 4. The trends are assumed to be parallel in case that the 95% confidence intervals of the treatment and control group have a large overlap (Callaway & Sant'Anna, 2021). Concerns regarding the satisfaction of the parallel trend assumption can be raised if the retail and wholesale price trends of rabeprazole and famotidine do not illustrate a parallel trend. Even though the assumption of the difference-in-difference technique may not be satisfied, this research continues to contribute to the research of price change after patent expiration. However, this means that the results may not be interpreted as causal effects. Nevertheless, the research still contributes through the establishment and recognition of correlations between relevant factors. However, Appendix 4 illustrates that the 95% confidence interval of rabeprazole and famotidine prices overlap prior to Aciphex' patent expiration in 2013. Therefore, the parallel trend assumption is satisfied (Callaway & Sant'Anna, 2021).

Hypothesis 1-4C & 1-4D yield the following formula:

$$\boldsymbol{Y_{it}} = \beta_0 + \beta_1 * patexp_t + \beta_2 * rabe_i + * \beta_3 * X_i + \beta_4 * patentexp_t * X_i + \beta_5 * patentexp_t * rabe_i + \beta_6 * rabe_i * X_i + \beta_7 * patentexp_t * rabe_i * X_i + u_i + d_t + e_{it}$$

The aforementioned formula illustrates the equation used for the difference-in-difference analysis, where Y is the retail price for hypotheses C and the wholesale price for all hypotheses D. In the subscript of this formula, t represents time, while i refers to an observation. Subsequently, Y_{it} refers to either the retail or wholesale price of an observation for a certain period. Similar to the fixed effects equation, $patexp_t$ is a binary variable that takes value 1 after May 2013, but value 0 prior to May 2013. In addition, the variable of interest is illustrated through Xi, which changes per hypotheses: H1) X_i= 0, H2) X_i = combination_i, H3) X_i = multinational_i, H4) X_i= solid_i. This is a dummy variable. The difference-in-difference model studies these variables in interaction with $patexp_t$, as shown by $patexp_t * X_i$. In addition, the model studies the X_i binary variable in interaction with the binary variable $rabe_i$. Furthermore, $rabe_i$ and $patexp_t$ are also included in the model. The most relevant interaction term is the interaction of $patentexp_t * rabe_i * X_i$, which is used to answer the hypotheses. Once again, u_i is the product fixed effects and d_t is the introduced month fixed effects. The variables on product and time characteristics will be omitted after the introduction of these fixed effects. This is caused by collinearity, as the fixed effects absorb the effect of the product and time variables. These fixed effects consider the unobserved time invariant heterogeneity. The idiosyncratic error is illustrated through ε_{it}, which cannot be correlated to the variable of interest at any time. There is no unobserved heterogeneity in the formula, as the fixed effects model accounts for between variation by de-meaning the data. Again, clustered standard errors are included, to account for within cluster standard correlation and the potential of heteroskedasticity. These clustered standard errors are introduced at the brand level.

4. Results

The ensuing section focuses on the results that came to light when studying the aforementioned hypotheses. All hypotheses are studied in chronological order, as explained in section 2.3. For illustration purposes, the results of hypotheses A and C are shown in the left column of each table, concerning the retail price. Moreover, the columns on the right side display the results of hypotheses B and D on the wholesale prices. At the end of this section, general concluding remarks are made about the findings of these hypotheses. Lastly, Chapter 4.2 examines some additional robustness checks.

4.1 Results

4.1.1 Hypothesis 1: The Effect of Patent Expiration on Prices

This first section studies the effect of rabeprazole retail and wholesale price changes after the patent expiration of Aciphex in 2013. The hypotheses predict a decline in retail and wholesale price of rabeprazole after Aciphex' patent expiration. The results of hypothesis 1A, illustrated by the first column of Table 3.1, suggests that the retail price of rabeprazole is estimated to increase by 0.47 Indian Rupees after Aciphex' patent expiration. This effect is significant at the 5% significance level. Therefore, hypothesis 1A is rejected, which argues that the retail price of rabeprazole declines after the patent expiration of Aciphex.

Furthermore, the third column of Table 3.1 illustrates the results of hypothesis 1B. The result of the analysis suggests that the wholesale price of rabeprazole is estimated to increase by 0.43 Indian Rupees after the patent expiration of Aciphex. This effect is significant at the 1% significance level. Therefore, hypothesis 1B is rejected, which states that the wholesale price of rabeprazole declines after the patent expiration of Aciphex.

Moreover, the second column of Table 3.1 displays the results of hypothesis 1C. The interaction term of rabeprazole and the patent expiration, suggests that for rabeprazole the retail price increases after the patent expiration by 3.97 Indian Rupees, relative to the retail price of famotidine prior to Aciphex' patent expiration. However, this effect is insignificant. Thus, hypothesis 1C is rejected, which suggests that the retail price of rabeprazole decreases more than the retail price of famotidine after Aciphex' patent expiration.

Lastly, the fourth and last column of Table 3.1 discloses the results of hypothesis 1D. According to these suggested results, rabeprazole experienced an increased wholesale price of 1.85 Indian Rupees after Aciphex' patent expiration, relative to the wholesale price of famotidine prior to the patent expiration. However, this effect is insignificant. Therefore, hypothesis 1D is rejected, which states that the wholesale price of rabeprazole decreases more than the wholesale price of famotidine after Aciphex' patent expiration. The collinearity of product and time fixed effects with the variables on 'Patent Expiration' and 'Rabeprazole' causes the omitted results of these variables. This phenomenon is relevant for all hypotheses, meaning that all omitted results are caused by the introduction of product and time fixed effects. However, this causes no obstacles for the interpretation of the results, as this research primarily studies the interaction terms in answering the hypotheses.

Table 3.1: The Fixed Effects & Difference-in-Difference Model Results of Hypothesis 1 on Retail and Wholesale Prices of Rabeprazole After Aciphex' Patent Expiration.

	Retail Price		Wholesale Price	
Variables	**Hypothesis 1A**	**Hypothesis 1C**	**Hypothesis 1B**	**Hypothesis 1D**
Patent Expiration	0.47**	Omitted	0.43***	Omitted
	[0.20]	-	*[0.08]*	-
Rabeprazole		Omitted		Omitted
		-		-
Patent Expiration # Rabeprazole		3.97		1.85
		[3.44]		*[1.23]*
Constant	4.84***	2.79	3.58***	2.66***
	[0.12]	*[1.85]*	*[0.04]*	*[0.66]*
Number of Observations	10,006	10,747	10,006	10,747
Month Fixed Effects	No	Yes	No	Yes
Product Fixed Effects	Yes	Yes	Yes	Yes

Note: Brand Clustered Standard Errors are included for all hypotheses.
Robust Standard Errors in Brackets: *** p<0.01, ** p<0.05, * p<0.1

4.1.2 Hypothesis 2: The Effect of Patent expiration on Combined and Non-Combined Medicine

The second set of hypotheses study the additional distinction between combined and non-combined variants of rabeprazole. The distinctive characteristic between combined and non-combined products derives from the possibility of including changes in prices of other ingredients, which cause biased estimated effects. The results of hypothesis 2A are shown in the first column of Table 3.2. These results suggest that having combined rabeprazole after the patent expiration, compared to non-combined rabeprazole prior to Aciphex' patent expiration, increases the retail price of rabeprazole by 0.37 Indian Rupees. This effect is significant at the 5% significance level. So, hypothesis 2A is accepted, which argues that the retail price of non-combined rabeprazole decreases more than the retail price of combined rabeprazole after Aciphex' patent expiration.

Furthermore, combined rabeprazole after Aciphex' patent expiration is suggested to have a wholesale price which is 0.16 Indian Rupees higher, relative to the wholesale price of non-combined rabeprazole prior to Aciphex' patent expiration. This is significant at the 5% significance level. Thus, hypothesis 2B is accepted, which states that the wholesale price of non-combined rabeprazole decreases more than the wholesale price of combined rabeprazole after Aciphex's patent expiration.

Table 3.2: The Fixed Effects & Difference-in-Difference Model Results of Hypothesis 2 on Combined & non-Combined Rabeprazole Retail & Wholesale Prices After Aciphex' Patent Expiration.

	Retail Price		Wholesale Price	
Variables	**Hypothesis 2A**	**Hypothesis 2C**	**Hypothesis 2B**	**Hypothesis 2D**
Patent Expiration	Omitted -	Omitted -	Omitted *[0.09]*	Omitted -
Rabeprazole		Omitted -		Omitted -
Patent Expiration # Rabeprazole		2.09 *[1.65]*		1.06* *[0.60]*
Combination	Omitted -	Omitted -	Omitted -	Omitted -
Patent Expiration # Combination	0.37** *[0.17]*	2.07 *[1.65]*	0.16** *[0.08]*	0.96 *[0.59]*
Rabeprazole # Combination		Omitted -		Omitted -
Patent Expiration # Rabeprazole # Combination		-1.70 *[1.66]*		-0.80 *[0.60]*
Constant	6.97*** *[0.07]*	5.46*** *[0.95]*	5.34*** *[0.03]*	4.49*** *[0.34]*
Number of Observations	34,116	36,291	34,116	36,291
Month Fixed Effects	Yes	Yes	Yes	Yes
Product Fixed Effects	Yes	Yes	Yes	Yes

Note: Brand Clustered Standard Errors are included for all hypotheses.
Robust Standard Errors in Brackets: *** p<0.01, ** p<0.05, * p<0.1

Next, hypotheses 2C and 2D apply the difference-in-difference technique by controlling for unobservable characteristics that may have affected the price of rabeprazole. Subsequently, the interaction term of patent expiration, rabeprazole and a combined drug is used to answer hypothesis 2C, which is illustrated through the second column of Table 3.2. Having combined rabeprazole after the patent expiration, compared to having non-combined famotidine before the patent expiration, decreases the retail price by 1.70 Indian Rupees. Nevertheless, this effect is insignificant. Therefore, hypothesis 2C is rejected, which states that the retail price of non-combined rabeprazole decreases more than the retail price of combined famotidine after Aciphex' patent expiration. Again, time and product fixed effects are collinear with variables such as 'Patent Expiration' and 'Combination', generating omitted results for these variables.

The fourth column of Table 3.2 displays the results of hypothesis 2D, which is used to study the effect of wholesale price changes after the patent expiration of combined and non-combined rabeprazole. According to these results, having combined rabeprazole after the patent expiration is expected to have a decreasing effect on the wholesale price by 0.80 Indian Rupees, compared to non-combined famotidine prior to the patent expiration. This effect is found to be insignificant. Subsequently, hypothesis 2D is rejected, which states that the wholesale price of non-combined rabeprazole decreases more than the wholesale price of combined famotidine after Aciphex' patent expiration.

4.1.3 Hypothesis 3: The Effect of Patent Expiration on Multinationals and non-Multinationals Medicine

The third set of hypotheses study the distinction between multinationals and non-multinational produced goods in terms of the retail and wholesale prices after Aciphex' patent expiry. The first column of Table 3.3 provides the results of hypothesis 3A. The results demonstrate the interaction effect of patent expiration and multinational on retail price changes in the Indian H2 antagonists' market. The retail price of multinational produced rabeprazole is expected to increase by 0.02 Indian Rupees, compared to non-multinationals produced rabeprazole prior to the patent expiration. However, this result is insignificant. So, hypothesis 3A is rejected, which states that the retail price of multinational produced rabeprazole is higher, compared to the retail price of non-multinational produced rabeprazole after Aciphex' patent expiration.

Additionally, hypothesis 3B is displayed by the third column of Table 3.3. The results imply that the wholesale price of multinational produced rabeprazole is expected to decrease by 0.04 Indian Rupees after Aciphex' patent expiration, compared to non-multinational produced rabeprazole before the patent expiration. Nevertheless, this effect is insignificant as well. Accordingly, hypothesis 3B is rejected, which states that the wholesale price of multinational produced rabeprazole is higher, relative to the wholesale price of non-multinational produced rabeprazole after Aciphex' patent expiration.

Furthermore, the results of hypothesis 3C, shown in the second column of Table 3.3, suggest that the interaction between patent expiration and multinationals has a negative effect on the retail price of rabeprazole. The retail price of multinational produced rabeprazole after the patent expiration decreases by 3.98 Indian Rupees, compared to the retail price of non-multinational produced famotidine prior to Aciphex' patent expiration. This effect is insignificant. Thus, hypothesis 3C is rejected, which states that the retail price of multinational produced rabeprazole is higher, compared to the retail price of non-multinational produced famotidine after Aciphex' patent expiration.

Table 3.3: The Fixed Effects & Difference-in-Difference Model Results of Hypothesis 3 on Multinational & non-Multinational produced Rabeprazole Retail & Wholesale Prices After Aciphex' Patent Expiration.

	Retail Price		Wholesale Price	
Variables	**Hypothesis 3A**	**Hypothesis 3C**	**Hypothesis 3B**	**Hypothesis 3D**
Patent Expiration	Omitted -	Omitted -	Omitted -	Omitted -
Rabeprazole		*Omitted* -		*Omitted* -
Patent Expiration # Rabeprazole		4.38 *[3.81]*		2.02 *[1.36]*
Multinational	Omitted -	Omitted -	Omitted -	Omitted -
Patent Expiration # Multinational	0.02 *[0.28]*	4.00 *[3.81]*	-0.04 *[0.19]*	1.66 *[1.37]*
Rabeprazole # Multinational		Omitted -		Omitted -
Patent Expiration # Rabeprazole # Multinational		-3.98 *[3.82]*		-1.71 *[1.38]*
Constant	5.10*** *[0.01]*	2.56 *[2.06]*	3.83*** *[0.01]*	2.56*** *[0.74]*
Number of Observations	10,006	10,747	10,006	10,747
Month Fixed Effects	Yes	Yes	Yes	Yes
Product Fixed Effects	Yes	Yes	Yes	Yes

Note: Brand Clustered Standard Errors are included for all hypotheses.
Robust Standard Errors in Brackets: *** p<0.01, ** p<0.05, * p<0.1

In the fourth column of Table 3.3, the results of the analysis on hypothesis 3D are illustrated, which suggest a decreasing effect of the patent expiration on the wholesale price. The wholesale price of multinational produced rabeprazole after the patent expiration decreases by 1.71 Indian Rupees, compared to the wholesale price of non-multinational produced famotidine prior to Aciphex' patent expiration. However, this effect is insignificant. Therefore, hypothesis 3D is rejected, which states that the wholesale price of multinational produced rabeprazole is higher, compared to the wholesale price of non-multinational produced famotidine after Aciphex' patent expiration. Again, the variables 'Multinational', 'Rabeprazole' and 'Patent Expiration' are collinear with the time and product fixed effects, thus resulting in omitted results.

4.1.4 Hypothesis 4: The Effect of Patent Expiration on Solid and non-Solid Medicine

The following set of hypotheses study the distinctive characteristics of solid and non-solid medicine, and the effect on rabeprazole prices after Aciphex' patent expiration in the Indian H2 antagonists' market. The first column of Table 3.4 illustrates the results of hypothesis 4A. These results imply that having solid rabeprazole after the patent expiration, compared to non-solid rabeprazole prior to Aciphex' patent expiration, decreases the rabeprazole retail price by 2.48 Indian Rupees. This effect is significant at the 1% significance level. Therefore, hypothesis 4A is accepted, which states that the retail price of solid rabeprazole is lower, relative to the retail price of non-solid rabeprazole after Aciphex' patent expiration.

Table 3.4: The Fixed Effects & Difference-in-Difference Model Results of Hypothesis 4 on Solid & non-Solid Rabeprazole Retail & Wholesale Prices After Aciphex' Patent Expiration.

	Retail Price		**Wholesale Price**	
Variables	**Hypothesis 4A**	**Hypothesis 4C**	**Hypothesis 4B**	**Hypothesis 4D**
Patent Expiration	Omitted -	Omitted -	2.10*** *[0.68]*	Omitted -
Rabeprazole		Omitted -		Omitted -
Patent Expiration # Rabeprazole		-31.55*** *[0.96]*		-25.65*** *[0.77]*
Solid	Omitted -	Omitted -	Omitted -	Omitted -
Patent Expiration # Solid	-2.48*** *[0.90]*	-38.01*** *[3.57]*	-1.74** *[0.72]*	-29.25*** *[1.43]*
Rabeprazole # Solid		Omitted -		Omitted -
Patent Expiration # Rabeprazole # Solid		35.54*** *[3.70]*		27.51*** *[1.61]*
Constant	8.79*** *[0.47]*	26.71*** *[0.23]*	6.55*** *[0.38]*	21.06*** *[0.18]*
Number of Observations	11,002	11,750	11,002	11,750
Month Fixed Effects	Yes	Yes	Yes	Yes
Product Fixed Effects	Yes	Yes	Yes	Yes

Note: Brand Clustered Standard Errors are included for all hypotheses.
Robust Standard Errors in Brackets: *** p<0.01, ** p<0.05, * p<0.1

Moreover, hypothesis 4B studies the wholesale price of solid, compared to non-solid rabeprazole after the patent expiration of Aciphex, for the Indian H2 antagonists' market. This analysis is illustrated in the third column of Table 3.4. The wholesale price of solid rabeprazole after Aciphex' patent expiration is expected to be 1.74 Indian Rupees lower after the patent expiration, relative to the wholesale price of non-solid rabeprazole sold prior to Aciphex' patent expiration. This effect is significant at the 5% significance level. Thus, hypothesis 4B is accepted, which states that the wholesale price of solid rabeprazole is lower, relative to the wholesale price of non-solid rabeprazole after Aciphex' patent expiration.

Furthermore, hypothesis 4C studies the effect of retail prices of solid rabeprazole, compared to non-solid famotidine during the period of the patent expiration of Aciphex. As illustrated by Table 3.4, the retail price of solid rabeprazole after Aciphex' patent expiration, is suggested to be 35.54 Indian Rupees more expensive, relative to the retail price of non-solid famotidine sold prior to Aciphex' patent expiration. This effect is significant at the 1% significance level. So, hypothesis 4C is rejected, which states that the retail price of solid rabeprazole is lower, relative to the retail price of non-solid famotidine after Aciphex' patent expiration.

Lastly, the results of hypothesis 4D are studied, which investigate the effect of patent expiration on wholesale prices of solid rabeprazole. The fourth and last column of Table 3.4 displays the results of hypothesis 4D. The wholesale price of solid rabeprazole after Aciphex' patent expiry, is suggested to be 27.51 Indian Rupees more expensive, relative to the wholesale price of non-solid famotidine sold prior to Aciphex' patent expiration. This effect is significant at the 1% significance level. Therefore, hypothesis 4D is rejected, which states that the wholesale price of solid rabeprazole is lower, relative to the wholesale price of non-solid famotidine after Aciphex' patent expiration.

4.1.5 Hypothesis 5: The Effect of Patent Expiration and the TRIPS agreement on Medicine

The last set of hypotheses study the TRIPS exception as introduced by the TRIPS agreement of 1995. The results of hypothesis 5A, presented in Table 3.5, suggest an increasing effect of the Aciphex' patent expiration on the retail price of rabeprazole. Having a brand that was launched before 2005 and rabeprazole that is sold after the patent expiration, increases the retail price of rabeprazole by 0.28 Indian Rupees, relative to a brand launched after 2005 and sold before the patent expiration. However, this effect is insignificant. Therefore, hypothesis 5A is rejected, which states that the retail prices of rabeprazole brands that applied the TRIPS agreement exception decreased more, relative to retail prices of brands that did not apply the TRIPS agreement exception after Aciphex' patent expiration.

Lastly, the results of hypothesis 5B are studied, by analysing the same TRIPS agreement and its interaction with the patent expiration. The interaction term of the patent expiration and the TRIPS exception is suggested to be positive. However, this effect was found to be insignificant. Subsequently, hypothesis 5B is rejected, which states that the wholesale prices of rabeprazole brands that applied the TRIPS agreement

exception decreased more, relative to wholesale prices of brands that did not apply the TRIPS agreement exception after Aciphex' patent expiration.

Table 3.5: The Fixed Effects Model Results of Hypothesis 5 on the TRIPS Exception on Retail & Wholesale Price of Rabeprazole after Aciphex' Patent Expiration.

	Retail price	Wholesale Price
Variables	**Hypothesis 5A**	**Hypothesis 5B**
Patent Expiration	Omitted -	Omitted -
TRIPS Exception	Omitted -	Omitted -
Patent Expiration # TRIPS Exception	0.28 *[0.34]*	0.02 *[0.14]*
Constant	5.05*** *[0.06]*	3.82*** *[0.02]*
Number of Observations	10,006	10,006
Month Fixed Effects	Yes	Yes
Product Fixed Effects	Yes	Yes

Note: Brand Clustered Standard Errors are included for all hypotheses.
Standard Errors in Brackets: *** p<0.01, ** p<0.05, * p<0.1

4.1.6 Concluding remarks

All in all, after performing the analyses on the interaction between patent expiration and pharmaceutical product characteristics, the results imply that there is a relation of Aciphex' patent expiration and product characteristics on the retail and wholesale price of rabeprazole in the Indian H2 antagonists' market. However, this relation is not similar to the expected relation in most cases. For instance, the results of hypothesis 1 imply an increasing effect on rabeprazole prices after patent expiration. On the other hand, the suggested results of hypothesis 4 imply a decreasing effect on drug prices. Furthermore, when applying the difference-in-difference methods, the results on patent expiration and product characteristics are largely insignificant. According to previous literature the prices of products with certain characteristics were expected to decrease after patent expiration (Saha et al., 2006; Gupta, Shah & Ross, 2019; Magazzini, Pammolli & Riccaboni, 2004). Despite some contradictory findings, the results do imply that there is a relation between the interaction of the patent expiration and product characteristics on the retail and wholesale prices of rabeprazole in the Indian H2 antagonists' market. Nevertheless, the results of the difference-in-difference analysis find insignificant results. Therefore, questions regarding the effect of patent expiration on pharmaceutical prices in India remain unanswered. A more in-depth description of the results is displayed in Chapter 6 (Conclusion).

4.2 Robustness checks

The following section elaborates on robustness checks that are performed to analyse the validity of the results. These robustness checks identify potential concerns, regarding the applied data or suggested results. This is achieved through a series of statistical tests.

First, section 3.4 mentions the potential issues of heteroskedasticity and serial correlation in the dataset. Appendix 2 illustrates that serial correlation is an issue, which should be considered for the analysis. This is achieved through the application of clustered standard errors and the introduction of time and product fixed effects. Through the analysis of a scatter plot, potential concerns regarding heteroskedasticity are observed. Nevertheless, this scatterplot is not able to statistically prove heteroskedasticity (Appendix 2, Figure A & B). Figure A and B illustrate that heteroskedasticity is a potential limitation as the variance of the residual concerning the retail and wholesale price is unevenly distributed. As the retail or wholesale price increases, the variance in the residual increases too. The application of clustered standard errors in panel datasets are useful, since they are robust to heteroskedasticity (Arellano, 1987; Vogelsang, 2012). Therefore, even though heteroskedasticity is a concern, through the adaptation of clustered standard errors, issues regarding heteroskedasticity and serial correlation are resolved. Section 3.4 elaborates on the Woolridge serial correlation test, as displayed by Table B of Appendix 5. The results of this analysis suggest that serial correlation is an issue to this dataset. However, through clustered standard errors and fixed effects, causality issues because of heteroskedasticity should be avoided.

Furthermore, a test on Granger causality is performed, which studies reverse causality. A Vector autoregressive model (VAR) is introduced, which studies the relation between two variables that change over time. In the case of Granger causality, the dependent variable influences the independent variable. However, the independent variable also influences the dependent variable. The application of a Granger causality Wald test yields the results, displayed by Table A in Appendix 5. These results suggest a rejection of all null hypotheses. For instance, this means that the null hypothesis that the lags of 'Retail Price' does not Granger cause the variable "Patent Expiration', is rejected. Thus, the causality of the suggested results must be interpreted with a high level of caution as this Vector autoregression (VAR) test gives signs of potential reverse causality issues. Subsequently, one is reluctant to speak of a causal effect when interpreting the results.

Lastly, this robustness section studies the problem of attrition in panel datasets. Attrition is the phenomenon when one is unable to follow an observation or item/person, for the entire period of interest. The arising issue is the endogenous incompleteness, where one may ask whether being unable to follow an observation, item or person over the entire period of interest is at random, or whether this primarily happens to a selected part of the dataset. This gives a sign of potential biases, as having an observation for a certain period, may be associated with a certain outcome. To test this, three different scenarios are studied, which are an observation being in the next wave, for a number of waves and being in all waves. A wave represents a period, which is a monthly observation for the data on rabeprazole and famotidine. Subsequently, the results show

whether the dropout of observations is at random, or whether there is a pattern. Such a pattern is reason for concern. A potential issue could be the dropout of observations caused by bankruptcy, changes in the market structure or pharmaceuticals not willing to produce a certain medicine. As a result, these changes cause biased results, decreasing the validity and representativeness of this study.

The results are shown in Table B of Appendix 5, which illustrates that there are no concerns regarding attrition when testing on an observation for being in all waves, for several waves and in the next wave. Therefore, there is no indication that having an observation in period 1 up and until 67 has any effect on the price of rabeprazole. Furthermore, having a series of observations for several waves also does not indicate any effect on the price of rabeprazole either. Also, having an observation in the next wave has no effect on the price of rabeprazole. Therefore, attrition is not a concern to this study.

5. Limitations & Recommendations

The ensuing section debates the limitations with regards to the applied data, selected methodology and assumptions. Moreover, possible approaches on how these limitations are overcome, are debated in this segment as well. Firstly, the concerns and limitations on the theoretical framework section are elaborated. Then, this section discusses the limitations of the data and methodology section, as well as possible approaches to overcoming these limitations. Lastly, the recommendations section presents a view on future studies, which contribute to the literature on patent expiration, price effects and the Indian pharmaceutical industry.

5.1 Limitations

Rabeprazole is selected for the analysis on the effect of patent expiration on price changes in the Indian H2 antagonists' market. As stated in section 3.1, rabeprazole is commonly prescribed to tackle issues regarding excess stomach acid production. One of the selection criteria hinges on the competitiveness and availability of the drug. The argument suggests that having a medicine that is commonly used and prescribed is exposed to a competitive market, which yields a more representative image of the effect of patent expiration on pharmaceutical price changes. The rabeprazole market is highly competitive, where producers have little influence on the price. So, the selection of rabeprazole is well-considered, and found to be appropriate for the analysis on patent expiration effects on pharmaceutical prices. However, the fact that rabeprazole is commonly prescribed may bring an unforeseen effect too. Exogenous shocks could be underestimated or might not affect the price at all, as the intense competition does not allow for producers to add the additional expense of the exogenous shocks to their prices.

Moreover, with this thesis solely focusing on the Indian pharmaceutical market, the results are less applicable to other countries. With over 20% of the Indian citizens living under the national poverty line (World Bank, 2020), the role of the government, multinationals, and other NGOs, such as the United Nations, is an important factor in establishing a growth in societal welfare. Undoubtedly, an increased intensity of corporate social responsibility of both businesses and governments of the more developed countries, provides a strong foundation to enhance the societal welfare in developing countries. With this increased understanding, policy makers can design legislation that removes barriers, which currently prevent inhabitants of developing countries from experiencing an increase in their welfare. This is in line with the increased discussion on patent enforcement in developing countries during a health crisis (European Parliament, 2021; United Nations, 2021). Thus, along with the scientific interest of understanding the effect of patent expiration on prices, the societal impact is significant too. Subsequently, the current research on the Indian market is not representative to other countries.

Furthermore, over the last decade the availability of generic medicines has decreased across all pharmaceutical markets (Gupta, Shah & Ross, 2019). Thus, the combination of an increasing demand and a limited number of suppliers, means that the generic markets are subjected to scarcity. This heavily impacts the representativeness of this study. How much this scarcity affects the rabeprazole and famotidine markets needs

to be further examined to make any claims. However, it is highly feasible that scarcity affects the results in some way.

Next, Table 1 illustrates the data on the variables 'Solid', 'Combination' and 'Multinational'. This table displays a low percentage of non-solid relative to solid, combined relative to non-combined and multinational compared to non-multinational. Even though this gives an accurate representation on the ratio of the variables 'Solid' 'Combined' and 'Multinational' in India, it gives reasons for concern. The low percentage of these variables means that the number of observations for the non-solid, combined and multinational products, might be too little to ensure a valid comparison. Nevertheless, it is important to have an accurate representation on the ratios of these variables with regards to the external validity. Even though the impact of having these ratios is unknown, having a skewed number of observations is not optimal for the validity of the analysis.

Furthermore, the construction of the dataset does not allow for the calculation of the price per milligram. Even though the current approach of calculating the price per unit is sufficient to perform the analysis, ideally one calculates the price per milligram. Currently, it is not possible to implement all observations, as there is the potential of biased results. Depending on the differences between the implemented and non-implemented observations, the results could be over- or underestimated. Therefore, one wonders whether the results are representative, as certain unit sizes are excluded for several hypotheses. So, the construction of some variables prohibits calculating the price per milligram, which hampers comparison possibilities and decreases the validity of the results. In addition, section 4.2 discusses the issues of heteroskedasticity and Granger causality. Consequently, one must be reluctant to speak of a causal effect of patent expiration on pharmaceutical prices. Even though clustered standard errors solve the issue of heteroskedasticity, Granger causality remains a concern to the validity of the results.

For the methodology section, a limitation arises concerning the fixed effects model. The fixed effects model comes with the strict exogeneity assumption. Section 3.4.2 mentions the difficulty of complying with the assumption. Concerns regarding the satisfaction are brought to light, especially since the level of introduced control variables is low. Factors that might be correlated to the dependent and independent variable are inflation, export and import. Adding these factors to the model ensures the satisfaction of the strict exogeneity assumption. However, the current concerns of having a low number of control variables are sufficient to be reluctant to speak of a causal relation. So, not being able to satisfy the strict exogeneity assumption is a clear limitation of this study. Currently, the lack of control variables prohibits the satisfaction of the strict exogeneity assumption. However, the absence of these variables potentially causes biased results too. With factors such as import and export not taken into account, this study cannot identify whether there is scarcity in the market and how this may have affected the results.

A common issue in scientific literature is the assumption of the difference-in-difference technique, which requires the parallel trend assumption to hold. The satisfaction of this assumption is a requirement for the results

to be valid, robust and representative. However, complying with the assumption is often rather difficult, as trends may not be perfectly parallel, which then has implications on the suggested finding of a research. Nevertheless, research often remains valuable to the literature on that specific topic. Testing for the 95% confidence interval trends of both the retail price and wholesale price, shows an overlap for the majority of the months prior to the patent expiration, as illustrated by Figure C & D of Appendix 4. This is a common approach to testing the parallel trend assumption (Callaway & Sant'Anna, 2021). Nevertheless, with no statistical tests being available to analyse whether the parallel trend assumption is satisfied, the results should be interpreted with a level of caution. So, even though the approach of studying the 95% confidence interval is a common approach to studying the parallel trend assumption, factors such as the spread in observed prices may affect the reliability of this test. Therefore, satisfying the parallel trend assumption is difficult if no statistical test is presented in the future.

The results tables in section 4.1 suggest that certain variables are omitted due to collinearity with the time and product fixed effects. Therefore, it is not possible to study the effect of having a product of rabeprazole, compared to having a product of famotidine on either the retail or wholesale prices, for the fixed effects and difference-in-difference models in section 4.1. Even though these variables are not essential to answer the hypotheses or research question, these coefficients could yield scientific relevant information. Therefore, the omitted variables are a limitation, as they may yield scientific relevant information.

5.2 Recommendations

This section elaborates on the recommendations for future studies in the field of patent expiration, price effects and the Indian pharmaceutical industry. The previous section discusses the limitations of this thesis, which are used to construct suggestions on future studies.

To gain further understanding of the effects of patent expiration on pharmaceutical prices, this study must be replicated using a series of alternative medicines. A subsequent study must be conducted using several medicines over the same period, to allow for a comparison of the different pharmaceuticals markets and medicines in different international markets. This contributes to a profound understanding of patent expiry on pharmaceutical prices. In addition, markets such as duopolies or monopolies are less exposed to the element of competition. However, studying such markets yields a greater understanding of the effect of patent expiration in different market types. So, replicating this study in different international and national markets, for a variety of medicine and multiple time periods gives a thorough understanding on the effects of patent expiration on pharmaceutical prices.

Furthermore, future studies can build upon this study by extending it to different countries and markets that have the same characteristics as the pharmaceutical market. Subsequently, replicating this study in other technological dependent industries provides a more profound view on the role of patents in all types of countries

and markets, while considering the ideas of the previous paragraph. In addition, one can extend these studies further by looking at the relation with market shocks. For instance, one can study the effect of patent expiration on prices in times of scarcity. This gives a more accurate understanding on patent expiration effects in different economic climates. In addition, research can compare the different effects of patent expiration on prices in different economic climates. Moreover, one may want to consider investigating the influence of unofficial medicine markets (black markets) too, as this can heavily influence the results.

Moreover, the current distribution of variables, as discussed in section 5.1, displays that a more evenly distribution of observations for all variables is desirable. Nevertheless, one should consider and maintain the representativeness of these variables at any time. In addition, future studies should gather data that allows for the calculation of the price per milligram. This yields a more representative image, as the price per milligram of one medicine is easier compared to the price per milligram of another medicine. This yields more valuable information, since comparing the price per milligram is more straightforward.

In addition, future studies should apply a balanced dataset to their analysis, to prevent issues regarding attrition. Such a balanced dataset only allows for observations that are present throughout the entire period of interest. Then, problems regarding attrition are prevented. However, this is likely to limit the number of observations used for the analysis. So, in line with seeking to gather a balanced dataset, one should aim to retrieve as many observations as possible. Despite attrition not being an issue to this research, a balanced dataset prevents issues regarding attrition from the beginning. Furthermore, the current number of control variables is low. Other researchers must seek to gather sufficient relevant control variables, as this gives valid and representative results. In case future studies adopt the fixed effects model, this aids them with the satisfaction of the strict exogeneity assumption. Additionally, this thesis has several omitted variables, which are not relevant to answer the hypotheses. However, they may yield relevant information. Therefore, future studies should seek to apply an econometric approach that provides the effects of these variables.

Along with research of patent expiration on price changes, the medical world might be interested in the effects of patent expiration on human wellbeing. Such research is especially relevant in countries with budget constrained inhabitants. Factors that may be relevant are stress, health score, happiness and (corporate) performance. Alternatively, future research may want to study the effect of patent introduction in certain markets. Studying the long-term effect of patent entry and patent expiration in the same market may bring new insights to the literature. In addition, future studies should consider gathering the data on any of the suggested future studies themselves. Since this is sensitive corporate information, governments can play a crucial role in gathering this data. Through legal enforcement, legislative bodies can increase their understanding on patents and patent expiration on pharmaceutical prices. Even though gathering such data is highly sophisticated, it yields a greater understanding of the pharmaceutical market. Consequently, this may increase societal welfare of developed and developing countries.

6. Conclusion

All in all, this thesis studies the effect of patent expiration on pharmaceutical prices in the Indian H2 antagonists' market. A range of different product characteristics in interaction with the effect of patent expiry on medicine prices in the Indian market are analysed. Additionally, by studying scientific literature on patent expiration, price effects and the Indian pharmaceutical industry, a theoretical framework is constructed, which provides the foundation for the empirical analysis. These analyses study firm level data through the application of econometric techniques such as the fixed effects and difference-in-difference models.

The first set of hypotheses expects the retail and wholesale price of rabeprazole to decline after the patent expiration of Aciphex. However, the analysis of the fixed effects model suggests an increasing effect on the price after the patent expiration. The difference-in-difference analysis yields insignificant results. For hypotheses 1A and 1B, this can be explained through potential biases caused by unobserved characteristics. The suggested results of hypotheses 1C and 1D have taken the unobserved characteristics into account. Nevertheless, as stated by Gupta, Shah & Ross (2019), medicine prices have experienced a significant increase in the US due to scarcity. Even though the authors do not imply that medicine prices of other countries have increased, it is possible that those prices have increased too. Especially, since the US is the most dominant market player in the pharmaceutical industry. Nevertheless, the results of the fixed effects suggest that the prices of rabeprazole increased after the patent expiration, while the results of the difference-in-difference analysis are insignificant. Therefore, the first set of hypotheses is rejected.

Moreover, when studying the combined and non-combined medicine prices, for hypotheses 2A and 2B, a significant effect was found. These findings suggested that the patent expiration had a significant increasing effect on the prices of combined rabeprazole. This is in line with the expectations according to the conducted literature. Nevertheless, when conducting the difference-in-difference analyses of hypotheses 2C and 2D, insignificant effects were found. This means that based on the comparison of combined and non-combined medicines, it is not possible to statistically prove that the patent expiration has a decreasing effect on the price of non-combined rabeprazole. This is caused by the insignificant results of the difference-in-difference analysis. Moreover, hypotheses 2A and 2B do not prove that non-combined rabeprazole decreased in price, as it only suggests that combined rabeprazole after the patent expiration was more expensive compared to non-combined rabeprazole prior to the patent expiration.

Furthermore, the third hypothesis studies the role of multinationals and the price of rabeprazole after the patent expiration. However, the fixed effects and difference-in-difference models did not yield any significant results. Therefore, the hypotheses are rejected.

In addition, the fourth set of hypotheses study the difference between solid and non-solid rabeprazole, after the patent expiration. The hypotheses 4A and 4B, which use the fixed effects model for the analysis, suggest a decreasing effect on the price of solid products after the patent expiration. However, hypotheses 4C and 4D suggest an increasing effect. According to the results, the retail price of solid rabeprazole after Aciphex' patent expiration, is suggested to be higher, relative to the retail price of non-solid famotidine sold prior to Aciphex' patent expiration. Due to mixed results, it remains difficult to assess whether the patent expiration had a significant effect in the case of solid and non-solid products of rabeprazole. Potentially, the globally increased medicine prices have affected these results (Gupta, Shah & Ross, 2019). Nevertheless, no conclusions can be drawn, based on the comparison of solid and non-solid rabeprazole prices after Aciphex' patent expiration, apart from that there is a possible relation between the interaction of patent expiration and the product characteristic on the price of rabeprazole.

The last set of hypotheses on the TRIPS exception do not yield any significant results. Therefore, there are no indications that the exception made by the TRIPS exception had an effect in combination with patent expiration on either the retail or wholesale price during the period of interest.

All in all, the results imply that in some cases there is a relation between the patent expiration and the price change of drugs. However, the analyses are not in line with the predicted results, according to previous studies. Moreover, the analysis of two hypotheses did not yield any significant results. Nevertheless, this study provides a new insight in the determining factors of price changes in the Indian H2 antagonists' market. The mixed results give an incentive for future studies to analyse specific market conditions, and the role of patent expiration in developing countries. As illustrated by the introduction, the discussion on patent enforcement in developing countries has increased. Therefore, policy makers should investigate the importance of patents in developing countries and how they could contribute to a greater societal welfare.

The research question studies what the effect of patent expiration of top selling medicine is on pharmaceutical market prices in the Indian H2 antagonists' market. All in all, the results suggest that there is a moderate relation between patent expiration and the price changes of pharmaceutical products in the Indian H2 antagonists' market. However, due to a combination of mixed and insignificant results, no conclusions regarding the sign or the magnitude can be drawn. The mixed results are potentially caused by an increase in demand for generic drugs (Gupta, Shah & Ross, 2019). In addition, concerns regarding reverse causality mean that one is reluctant to speak of a causal effect. Therefore, this thesis only speaks of a sheer correlation between patent expiration and pharmaceutical prices. These correlations should be further studied, to get a valid outcome on the magnitude of these correlations. Further research on patents and the role of prices in developing countries should replicate this study in different countries with different medicines. Alternatively, studies should investigate the effect of patent expiration in different market types. Moreover, by studying a balanced panel dataset with more control variables, future research should be able to further estimate the relation between patent expiration and pharmaceutical prices in developing countries.

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Appendix 1

Section 2.3 describes that a total of 5 sets of hypotheses are tested to study the effect of Aciphex' patent expiration on the price changes of rabeprazole. Each of these hypotheses study different parameters through a variety of variables. Due to assumptions made in section 3.2, certain hypotheses apply a slightly adjusted dataset, to facilitate their analysis. This appendix is designed to increase understanding of the assumptions and restrictions made for all hypotheses of the fixed effects models and the difference-in-difference analyses. The same set of assumptions holds for the analyses of all hypotheses. However, no difference-in-difference analysis is conducted concerning hypothesis 5.

Hypotheses 1, 3 & 5

Hypotheses 1, 3 and 5 all use the same dataset. As described by section 3.2 assumptions concerning combined and solid products as well as dosage strength are made to ensure the robustness of the results. This leads to the following set of assumptions, leading to the same data set used by hypotheses 1, 3 and 5.

- Dosage strength of rabeprazole is restricted to 20 milligrams only.
- Combined products of rabeprazole are not considered for the analysis.
- Non-solid products of rabeprazole are not considered for the analysis.

Hypothesis 2

Hypothesis 2 studies the relation of combined and non-combined products on the price change of rabeprazole after the patent expiration of Aciphex. With this hypothesis focusing on the variable 'Combination', the restriction on the combination variable as illustrated by the previous model, is removed. This leads to the following assumption of hypothesis 2.

- Non-solid products of rabeprazole are not considered for the analysis.

Hypothesis 4

Lastly, hypothesis 4 studies the solid and non-solid rabeprazole products in terms of price changes after the patent expiration. The main variable of interest is 'Solid', which indicates whether a product of rabeprazole is solid (1) or not (0). Similar to hypothesis 2, now the assumption on solid and non-solid products of rabeprazole is removed, leading to the following assumptions used by hypothesis 4.

- Dosage strength of rabeprazole is restricted to 20 milligrams only.
- Combined products of rabeprazole are not considered for the analysis.

Appendix 2

On the left correlation matrix Table A is presented, while on the right-side Table B with the results of the Variance Inflation Factor (VIF) test can be found.

Table A: Correlation Matrix of all Relevant Variables in the Rabeprazole & Famotidine Datasets

	Retail Price	Wholesale Price	Month	Units per Pack	Combination	Multinational	Solid	Patent Expiration	TRIPS Exception
Retail Price	1								
Wholesale Price	0.972***	1							
Month	0.079***	0.071***	1						
Units per Pack	-0.426***	-0.427***	-0.003	1					
Combination	0.091***	0.095***	0.056***	-0.028***	1				
Multinational	-0.045***	-0.041***	-0.049***	0.000	-0.046***	1			
Solid	-0.385***	-0.386***	0.010**	0.275***	0.201***	0.052***	1		
Patent Expiration	0.063***	0.058***	0.862***	-0.002	0.050***	-0.040***	0.007	1	
TRIPS Exception	0.011**	0.022***	-0.043***	0.001	-0.406***	0.020***	-0.230***	-0.039***	1

*** p<0.01, ** p<0.05, * p<0.1

Table B: Variance Inflation Factor (VIF) Test

Variable	VIF	1/VIF
Month	3.89	0.256995
Patent Expiration	3.88	0.257943
Wholesale Price	1.42	0.703676
Solid	1.35	0.738391
Combination	1.26	0.794311
Units per Pack	1.25	0.802942
TRIPS Exception	1.24	0.809471
Multinational	1.01	0.990443
Mean VIF	1.91	

Figure A

Figure A illustrates the relation of the fitted value and the residual retail price of rabeprazole. The figure is not an official test, meaning that it only serves illustration purposes to further understand whether this dataset is subjected to either heteroskedasticity or homoskedasticity. With 10,014 observations, a selection of observations is removed from the dataset to give a better overview on heteroskedasticity and homoskedasticity in the dataset. Therefore, 213 observations of which the fitted value was over 10, were deleted. The removal of these observations did not alter the outcome of the figure, it only serves illustration purposes.

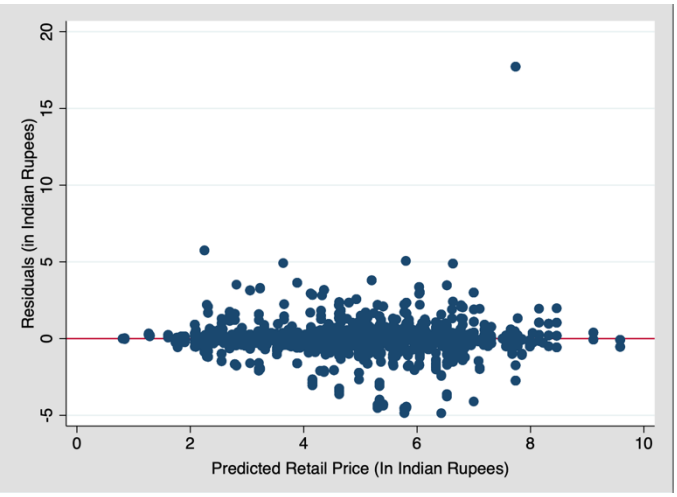

Figure A: Scatter plot on predicted retail price and the residuals to illustrate heteroskedasticity concerns.

Figure B

Figure B illustrates the same relation of the fitted value and the residual wholesale price of rabeprazole. The figure is not an official test, meaning that it only serves illustration purposes to further understand whether this dataset is subjected to either heteroskedasticity or homoskedasticity. With 10,014 observations, a selection of observations is removed from the dataset to give a better overview on heteroskedasticity and homoskedasticity in the dataset. Therefore, 213 observations of which the fitted value was over 10, were deleted. The removal of these observations did not alter the outcome of the figure, it only serves illustration purposes.

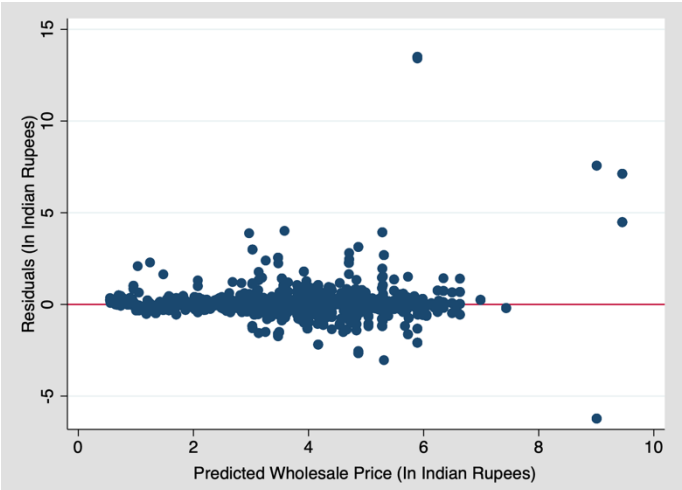

Figure B: Scatter plot on predicted wholesale price and the residuals to illustrate heteroskedasticity concerns.

Appendix 3

Appendix 3 illustrates the Hausman test for all hypotheses studied by this thesis.

Appendix 3: Hausman Test

Hypothesis 1: Hausman Test

Variable	Fixed	Random	Difference	Prob > Chi2
Patent Expiration	0.4655269	0.4668213	-0.0012945	0.6877

Hypothesis 2: Hausman Test

Variable	Fixed	Random	Difference	Prob > Chi2
Patent Expiration	0.4724685	0.473672	-0.0012035	0.3629
Patent ExpirationXCombination	0.3590386	0.3578932	0.0011455	0.3629

Hypothesis 3: Hausman Test

Variable	Fixed	Random	Difference	Prob > Chi2
Patent Expiration	0.4653184	0.4672323	-0.0019139	0.5775
Patent ExpirationXMultinational	0.0019969	-0.0048653	0.0068622	0.5775

Hypothesis 5: Hausman Test

Variable	Fixed	Random	Difference	Prob > Chi2
Patent Expiration	0.34341	0.3459969	-0.0025869	0.7132
Patent ExpirationXTRIPSexception	0.3103419	0.3086625	0.0016793	0.7132

Appendix 4

Appendix 4 illustrates the parallel trend assumption as discussed in section 3.4.2 (Hypotheses 1-4C & 1-4D), section 4.2 (Robustness Checks) and section 5.1 (Limitations). Figure C & D Illustrate the parallel trend assumption of rabeprazole and famotidine prior to the patent expiration of Aciphex through the estimated parallel trend and the 95% confidence interval, which is a common technique among researchers to validate the parallel trend assumption (Callaway & Sant'Anna, 2021). Figure C is an illustration of the retail price, while Figure D is an illustration of the wholesale prices of rabeprazole and famotidine.

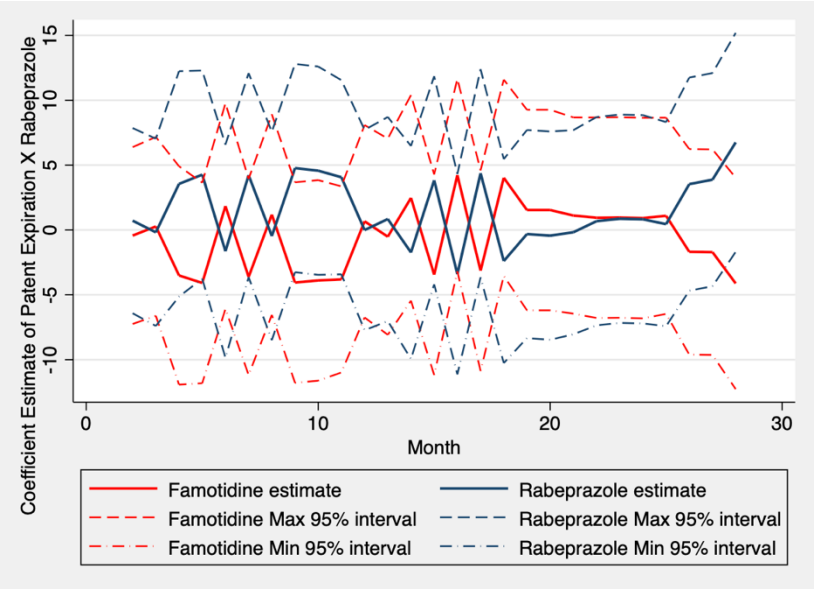

Figure C: Parallel Trend Assumption on Retail Prices in India.

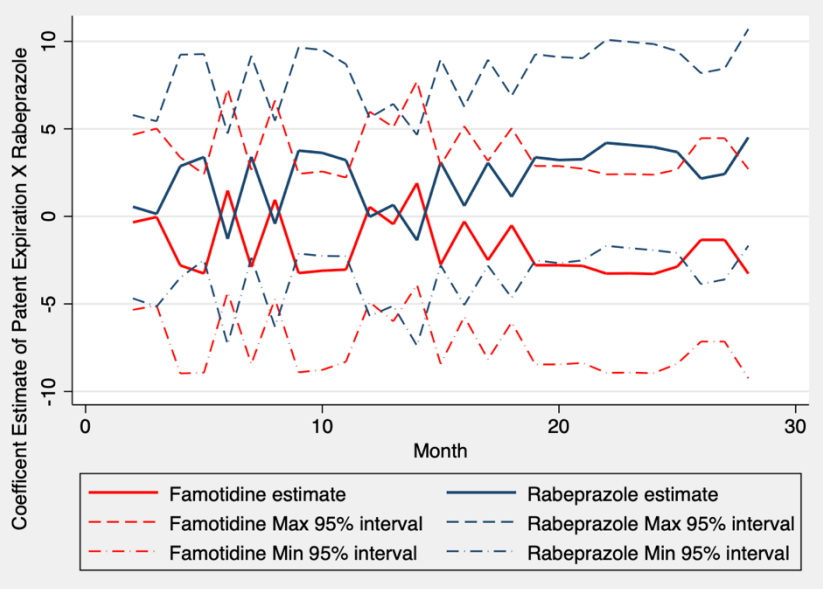

Figure D: Parallel Trend Assumption on Wholesale Prices in India.

With Figure C & D providing numerous lines regarding the estimates and 95% confidence intervals, additional figures are added to illustrate the overlap between the 95% confidence intervals of famotidine and rabeprazole. Figure E illustrates the overlap of the retail price in India, equal to Figure C. Furthermore, Figure F demonstrates the overlap of the wholesale price in India, similarly to Figure D. Both Figure E & F show a significant overlap between both medicines.

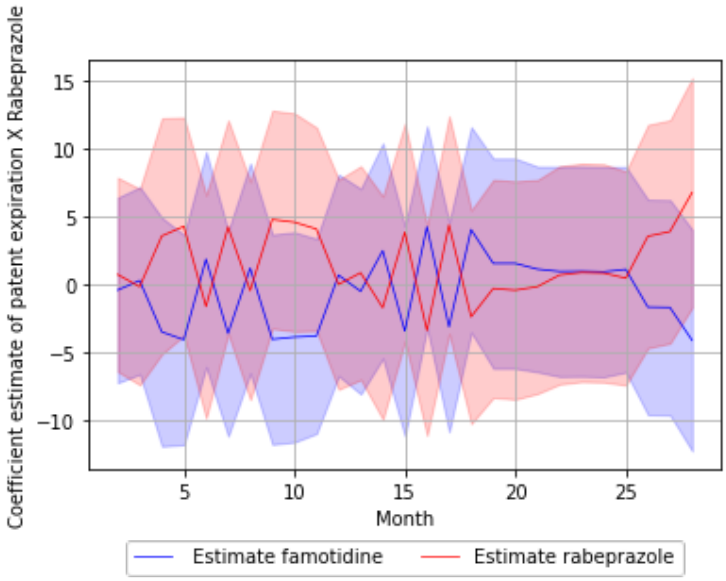

Figure E: Parallel Trend Assumption Overlap on Retail Price in India.

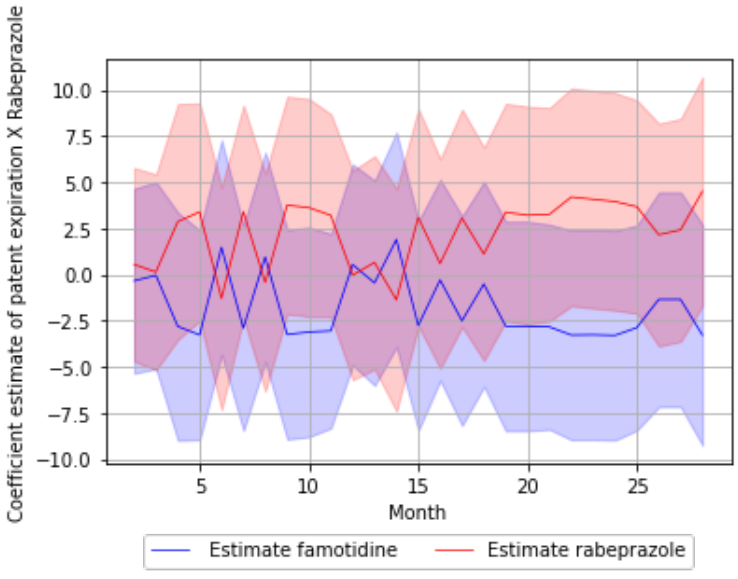

Figure F: Parallel Trend Assumption Overlap on Wholesale Price in India.

Appendix 5

Table A

Table A displays the results of the Vector autoregressive model on Granger causality.

Table A: Vector Autoregressive Results on Granger Causality.

Equation	Excluded	Chi2	*df*	Prob > Chi2
Hypothesis 1, 3 & 5				
Retail Price	Patent Expiration	2.815	*2*	0.245
Patent Expiration	Retail Price	2.750	*2*	0.253
Wholesale Price	Patent Expiration	1.327	*2*	0.515
Patent Expiration	Wholesale Price	0.890	*2*	0.641
Hypothesis 2				
Retail Price	Patent Expiration	1.740	*2*	0.419
Patent Expiration	Retail Price	2.469	*2*	0.291
Wholesale Price	Patent Expiration	1.842	*2*	0.398
Patent Expiration	Wholesale Price	0.556	*2*	0.757
Hypothesis 4				
Retail Price	Patent Expiration	1.819	*2*	0.403
Patent Expiration	Retail Price	3.051	*2*	0.218
Wholesale Price	Patent Expiration	0.541	*2*	0.763
Patent Expiration	Wholesale Price	0.348	*2*	0.840

*** p<0.01, ** p<0.05, * p<0.1

Table B

Table B displays the results on the attrition analysis of hypothesis 3A. The reason for selecting hypothesis 3 for the attrition analysis, is based on reasons mentioned Appendix 1. Hypothesis 3 applies the dataset of model 1, which are used for most hypotheses.

Table B: Attrition analysis on hypothesis 3A.

Variables	Number of Waves	All Waves	Next Wave
Patent Expiration	Omitted -	Omitted -	Omitted -
Multinational	-0.31 *[0.46]*	-0.09 *[0.36]*	-0.08 *[0.36]*
Patent Expiration # Multinational	-0.21 *[0.38]*	-0.21 *[0.28]*	-0.23 *[0.27]*
Next Wave			-0.00 *[0.17]*
All Waves		-0.11 *[0.25]*	
Number of Waves	-0.01 *[0.01]*		
Constant	5.61*** *[0.56]*	3.89*** *[0.19]*	3.85*** *[0.21]*
Number of Observations	10,014	10,014	10,014
Time Fixed Effect	Yes	Yes	Yes
Product Fixed Effects	No	No	No

Standard Errors in Brackets.
*** p<0.01, ** p<0.05, * p<0.1

Table C

Table A displays the results of the Wooldridge serial correlation test (Wooldridge, 2010). Performing this test identifies whether the dataset is exposed to serial correlation. The article by Drukker (2003) illustrates the approach of testing for serial correlation in panel data models as described by Wooldridge (2010).

Table C: Wooldridge Serial Correlation Test

	Model 1	Model 2	Model 3
F (1,254)	7233.75		
F(1,872)		49.29	
F (1,278)			2434.85
Prob > F	0.000***	0.000***	0.000***
	H0: No first order serial correlation		

Model 1 : Data applied when testing hypothesis 1, 3 & 5
Model 2 : Data applied when testing hypothesis 2
Model 3 : Data applied when testing hypothesis 4

*** p<0.01, ** p<0.05, * p<0.1
Source: Wooldridge, J. M. (2010). Econometric analysis of cross section and panel data. MIT press.