Copenhagen Economics

REGULATORY DATA PROTECTION FOR PHARMACEUTICALS

How adopting regulatory data protection will impact patients, industry, and Brazilian society

March 2023

Executive summary

Innovation in the biopharmaceutical industry requires significant investments. Intellectual property rights, such as regulatory data protection (RDP), are in place to incentivise innovation.

RDP is a key feature of the World Trade Organisation Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) and is included in many trade agreements. The importance of RDP in promoting innovation has been recognized by both developed and developing markets such as Chile, Mexico, and Colombia.

Policy makers lack important evidence

In 2002, Brazil enacted data package exclusivity that introduced RDP for veterinary and agricultural products, while explicitly excluding products for human use (biopharmaceutical products). Recently, a report from the University of Rio de Janeiro has reinvigorated the discussion.

Our ambition with this report is to close the knowledge gap by building on the University of Rio de Janeiro report. We provide comprehensive, data-based evidence to study the impact of RDP on the availability of both innovative and generic medicines, healthcare expenditures, and foreign direct investment.

Currently, the debate focuses on rising healthcare expenditure and a weaker generic and biosimilar industry as consequences of introducing RDP. We find that not to be true. In fact, we find evidence of the opposite, starting with the availability of innovative medicines.

RDP leads to more available medicines

Introducing RPD in Brazil will make it more attractive for innovative biopharmaceutical companies to offer their medicines in Brazil. We have examined the experiences from those markets providing RDP and predict that the number of innovative medicines in Brazil may increase by 34-39% (equal to 570 new innovative medicines) due to Brazil introducing RDP.

More available medicines create a positive ripple effect

With 570 more innovative medicines available, the generic and biosimilar industry has more 'raw material' to leverage. Across the 18 markets investigated, we find that 2.5 generic and biosimilar medicines are on average available for every innovative medicine. The number for Brazil is slightly higher at 3.2, possibly due to the market's strong generic and biosimilar industry. With more innovative medicines available to fuel the generic and biosimilar industry, we expect an additional 1,800 generic and biosimilar products to become available in Brazil over time.

The availability of additional innovative medicines leads to more foreign direct investment going into Brazil from the innovative industry. We find that the number of new clinical trials can be expected to increase to more than 1,000 per year, which is more than double the current yearly average. This is a major investment as on average 73% of the total cost of developing an innovative medicine and bringing it to the market is research and development. The reason for the increase is likely to be caused by the Brazilian market becoming more important to the innovative companies. That in turn incentives them to include more Brazilian patients in clinical trials as it will allow the companies to present ANVISA with clinical data for the market's own population. This improves the relevance of the data for ANVISA thereby improving chances of receiving a marketing authorisation (and later reimbursement).

With increasing clinical trial investments going into Brazil, we find that the market has an opportunity to build a high value Brazilian innovative industry alongside a growing generic and biosimilar industry. Learning from markets that have been able to grow innovative industries, we find they followed a three-step strategy. The first step is to put in place a robust system of protecting innovation including RDP.

Were Brazil to follow a similar three-step strategy, we believe that the Brazilian innovative and generic industries could grow from today's 6.6 bn USD to 10.2 bn USD in total. This growth will support a whole ecosystem of suppliers and partners. We find that this may add another 14.4 bn USD to the Brazilian economy effectively driving a total of 24.7 bn USD of Brazilian gross domestic product (GDP). This can sustain almost 800.000 local jobs.

Healthcare expenditure to stay unchanged

We find that in most markets that have introduced RDP, healthcare expenditure increased in the short run but reverted to its initial trajectory after 5-10 years. We believe there are three reasons for this pattern:

First, for most available medicines, RDP does not extend the period of protection from generic entry. This means that generic entry continues to exert a downward pressure on healthcare costs. Second, innovative medicines launched thanks to the presence of RDP allow for savings on other, more ineffective healthcare services over time. Third, markets prioritise spending on innovative medicines in line with the market's willingness to invest in improved healthcare. Availability of new medicines does not decide Brazil's future healthcare expenditure, Brazilian politicians do.

In conclusion

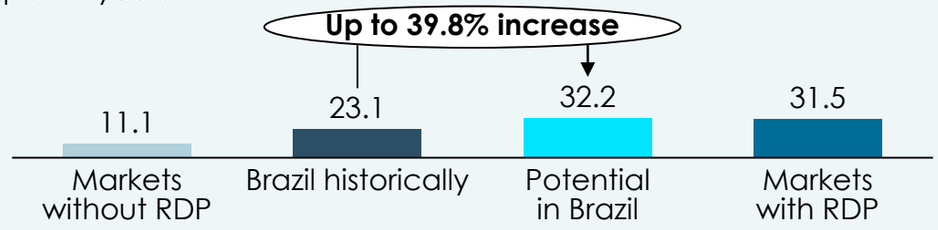
Based on rigorous analyses across 53 markets covering more than 10 years, we find strong evidence of multiple benefits of adopting RDP in Brazil. We find benefits for patients, the generic and innovative industries and the Brazilian economy.

Insights and conclusions (1/2)

We find that the introduction of **regulatory data protection (RDP) increases the availability of innovative treatments.** Our estimates show up to a 39.8% increase in the availability of all medicines launched globally in the past 5 years in Brazil, equivalent to 570 medicines, which would bring the availability of innovative medicines to par with the average in markets with RDP.

Availability of innovative medicines

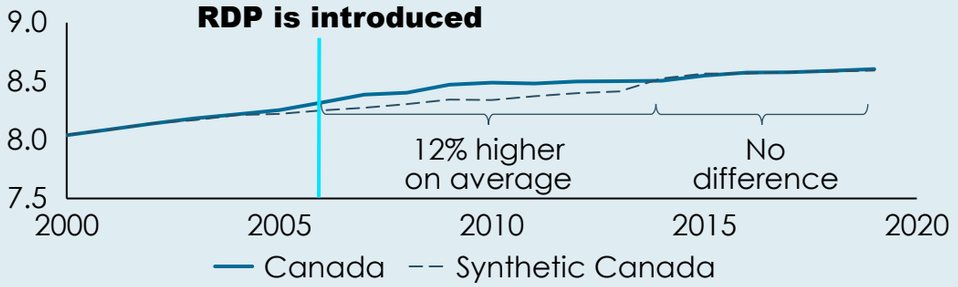
Share available of all innovative medicines launched globally in the past 5 years



Our results indicate a **short-term increase** in healthcare expenditures between 7% and 15% – but **no long-run effect on healthcare expenditures**.

Healthcare expenditures - example from Canada

Log of healthcare expenditures per capita



The bulk of innovative medicines that becomes available implies higher short-run expenditures…

…but **85% of medicines do *not* gain additional protection** from a 5-year RDP period

Innovative medicines are a prerequisite for generics and biosimilars.

If generic entry occurs, healthcare systems benefit from lower prices

After protection expires, generic entry is enabled

Medicine is sold exclusively

Innovative medicine is launched

More innovative pharmaceuticals are likely to **increase the number of generics and biosimilars** to the benefit of patients, the generic industry, and healthcare budgets.

3.17 generics/biosimilars

per innovative medicine available in Brazil

Note: Results and insights are based on analyses of data from IQVIA, the World Bank, WHO, WIPO patent database, and more on Brazil and up to 53 other markets in the period 2000-2019 carried out by Copenhagen Economics.

Insights and conclusions (2/2)

Our estimates suggest that the number of **clinical trials in Brazil could increase by 138%** (from 445 on average to 1,059) with the introduction of RDP

~2.9 more clinical trials

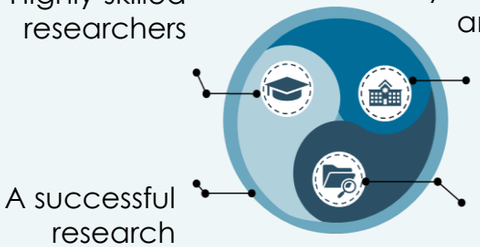
per million capita associated with the introduction of RDP

RDP is a **steppingstone towards a successful R&D-intensive pharmaceutical industry** in Brazil

1. Strong and predictable system to protect innovation

Necessary but not sufficient condition

2. A supportive research ecosystem

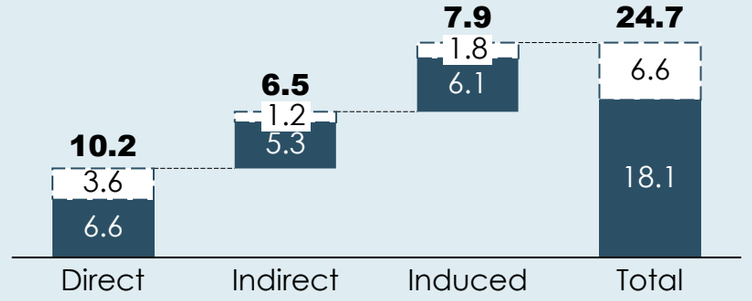


3. Attractive incentives and incubators, access to funding opportunities

If Brazil reaches its strategic potential, we estimate an **additional 6.6 bn USD supported** by the industry in Brazil totalling 24.7 bn USD, and an **additional 33,000 jobs.**

Economic footprint of the pharmaceutical industry

GDP supported, 2021 USD values



+33,000 additional jobs

directly supported by the pharmaceutical industry if Brazil achieves its strategic potential…

…on top of the current 76,600 jobs directly supported currently by the Brazilian pharmaceutical industry

Note: Results and insights are based on analyses of data from IQVIA, the World Bank, WHO, WIPO patent database, and more on Brazil and up to 53 other markets in the period 2000-2019 carried out by Copenhagen Economics.

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Appendices and references

1
BRAZIL IS CONSIDERING INTRODUCING RDP FOR PHARMACEUTICALS

Many markets support innovation by providing protection for the data submitted to regulatory authorities

- Regulatory data protection balances and advances the public's interest in incentivising the development and testing of new medicines and enabling the availability of lower-cost (generic) alternatives.
- Brazil does not provide RDP for biopharmaceutical products, but its introduction features in the public debate.
- In this report, using real world data, we evaluate the impact of RDP in markets that have enacted such protection and draw lessons for Brazil.

Bringing innovative medicine to the market involves lengthy, risky, and costly development processes. It takes, on average, 10 to 15 years and around 3 bn USD[1] to develop an innovative medicine and bring it to the market. Protecting and incentivising the data generated from clinical trials is therefore key to ensuring that innovators have the necessary certainty and predictability to continue investing in bringing innovative and more effective medicines to patients.

RDP provides incentives for investment in innovative medicines

Intellectual property rights, such as RDP, are in place around the world to incentivise innovation. RDP provides critical incentives for investment in innovative medicines and cures by providing protection against unfair commercial use of the comprehensive package of information that biopharmaceutical innovators must create and submit to regulatory authorities to demonstrate the safety and efficacy of a medicine for marketing approval. As such, RDP is a time-limited protection during which other parties are prevented from referencing directly or indirectly relying on the innovator's test or other data to obtain marketing authorisation for a generic or biosimilar medicine without the innovator's permission.

Around the world, RDP is considered a necessary building block for a robust innovative biopharmaceutical industry. Indeed, it is a key feature of the World Trade Organisation Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) and is included in many trade agreements. The importance of RDP in promoting innovation has been recognized by both developed and developing markets. Chile, Mexico, and Colombia enacted RDP for a fixed period of five years of exclusivity. In the European Union it is 10 years and in the United States it is 5 to 12 years.[2]

RDP complements patents

While a patent is concerned with the underlying invention that might someday become a medicine, i.e. the input, RDP is concerned with the data package associated with the safety and efficacy of a product, i.e. the results. As separate and independent protections (see Table 1 summarizing some key differences between the two protections), patents and RDP work together to provide innovators with the certainty that if they succeed in developing a safe and effective new medicine, they will have a sufficient period during which their invention and/or data will be protected such that they have the opportunity to recoup their significant investments and secure funds to engage in future innovation.

RDP is critical for biologic innovation

RDP can be particularly important in those situations where either a patent is not available or where the patent may not adequately protect the innovative medicine. For example, biologics, which are produced inside living structures such as animal cells or bacteria, are more complex and more difficult to characterise compared to small molecules and therefore can be more difficult to protect through a patent. In such instances – including for cutting-edge technologies such as cell and gene therapies – RDP is critical for innovation.[3] For these reasons, innovative biotechnology companies are more likely to prioritise making their medicines available in economies with RDP.

RDP creates a powerful incentive for innovators to invest in the development of safe and effective medicines, while also allowing generic and biosimilar companies to eventually rely on the originator's proprietary data by foregoing (in full or in part) independent clinical studies.

Table 1. Comparing RDP and patents

	RDP	Patent protection
Protection	Data from clinical trials	Compound previously unknown
Starting point	MA of the medicine	Date of filing patent application
Length	5 to 12 years	20 years

Note: MA is short for Market Authorization
Source: Based on Copenhagen Economics (2018).

Notes: 1) DiMasi et al. (2016). DiMasi et al. (2016) estimate a pre-approval cost estimate of 2.558 bn. (2013 USD). This corresponds to 2.975 2021 USD using the CPI reported by The World Bank. / 2) For further details see Interfarma (2021) / 3) Ellis (2017).

Brazil is considering introducing RDP for medicines for human use

Currently, Brazil does not have RDP for medicines for human use. In 2002, Brazil introduced RDP for veterinary and agricultural products, while explicitly excluding products intended for human use (biopharmaceutical products). The question of offering RDP for biopharmaceutical products has featured in the political debate in Brazil since the ratification of the TRIPS Agreement and has only further intensified since 2002.

Access to generic medicines is an important consideration in the debate

In general, the debate in Brazil on the introduction of RDP is framed as a trade-off between ensuring lower cost medicines through the swift entry of generics and biosimilars and facilitating access to innovative medicines.

RDP plays an important role in enabling lower-cost generic and biosimilar medicines to enter the market. Specifically, upon expiration of the RDP term, regulators permit generic and biosimilar companies to refer to, and rely on, the innovator's data. It is precisely because they do not have to undergo the same lengthy development process that generics and biosimilars can be sold at a lower price compared to innovative medicine. In this way, RDP systems balance and advance the public's interest in both incentivizing the development and testing of new medicines and enabling the availability of lower-cost alternatives.

Currently evidence is lacking

One study that has garnered interest during the RDP debate in Brazil is the report published by the University of Rio de Janeiro (hereafter, 'the University report'). The report studies the impact for Brazil of adopting RDP and was published in August 2021. The University report highlights the benefits of the absence of RDP in terms of supporting early entry of low-cost generic and biosimilar medicines.

The University report bases its conclusions on an ex-ante assessment of the effects of introducing RDP, looking at what might happen in Brazil 30 years after adopting RDP today. Critically, it relies on a number of assumptions. The main assumptions are, first, that the relative price of a protected product is 4.79 times higher. Further, the model assumes that the number of innovative products introduced each year is the same. Finally, the model assumes that all introduced products have a patent pendency of 16 years. This implies that the remaining patent protection for all introduced medicines is 4 years and that RDP will always provide protection beyond the patent term. This last assumption is not borne out by the facts, as noted in Chapter 3.

Further, as the University report itself recognises, additional evidence is required to complement their study. In particular, the report emphasises the need for an ex-post evaluation. This implies analysing the actual impact of RDP in economies that introduced RDP in the past and then isolating the impact on the output measures of concern, such as the availability of innovative medicines for patients and healthcare expenditure, using robust statistical methods. These insights can then be used to gauge the likely implications for Brazil of introducing RDP.

In particular and of great importance for policymakers in Brazil, ex-post methodologies allow studying the effect of RDP on various aspects of concern, including the availability of innovative medicines. The University report only allows the modelling of the direct effects that come with an extended period of protection.

This is in contrast to an ex-post model which takes into account the effects on access to new medicines not currently available in Brazil nor dynamic effects on healthcare expenditure, the generic and biosimilar industry or gross domestic product (GDP) in the market.

This report uses real world data to fill the gap

In this report, we provide that ex-post evidence, which gives critical insight as to how RDP would benefit Brazilian patients, government and industry, both generic and innovative.

We undertake a comprehensive assessment of the effects of introducing RDP. Our assessment is based on robust statistical analyses that utilise data from 53 markets over a 10-year period or longer to identify the effect of RDP. In particular, we study the effect of RDP on the availability of innovative medicines, healthcare expenditure, and the pharmaceutical industry. In addition, we describe the economic potential of RDP as a stepping stone towards a successful R&D-intensive pharmaceutical industry in Brazil. Further details on our methodology and results are described in the Appendix to this report.

2
RDP INCREASES THE AVAILABILITY OF INNOVATIVE MEDICINES

Markets with RDP have access to three times more innovative medicines

- We find that availability of innovative medicines in Brazil could increase by 34% to 39%.
- In actual numbers that means 570 more innovative medicines over time if RDP is implemented.
- This is because RDP would provide new protection for innovative medicines, thereby improving the business case for a company to launch.

In this chapter, we evaluate the potential impact that introducing RDP in Brazil could have on the availability of innovative medicines in Brazil, i.e. the share of innovative medicines launched globally that are also launched in Brazil.

Economic theory suggests that more innovative medicines would be available in markets with RDP compared to markets without RDP. The reason is that RDP would provide new protection for medicines, thereby improving the business case for a company to launch.

In the remainder of this chapter, we present ex-post analyses to understand whether the data evidence supports the economic rationale of increased availability due to the introduction of RDP.

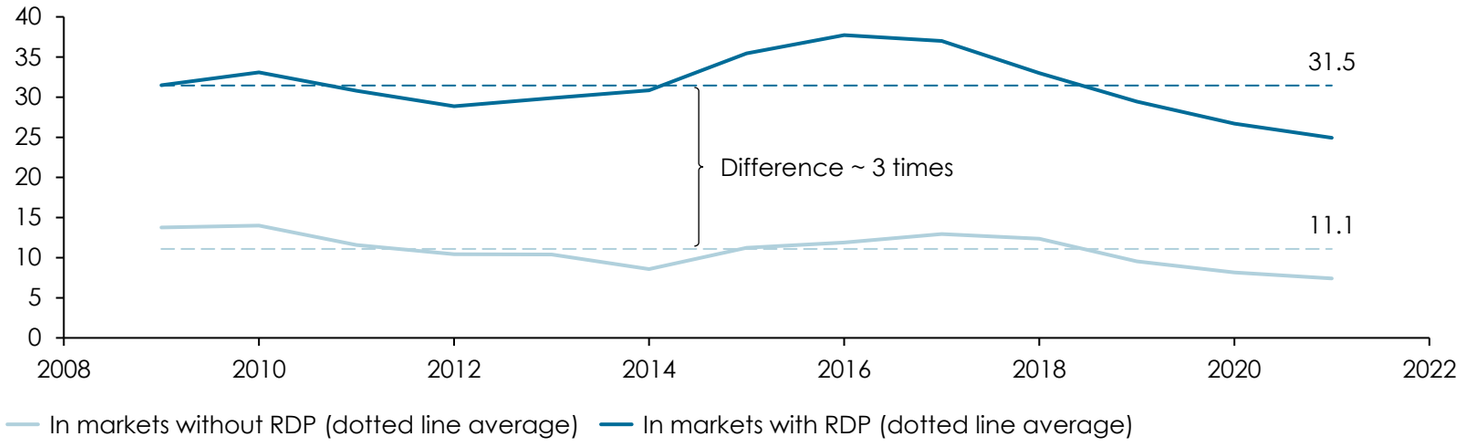
Markets with RDP have higher availability of innovative medicines

Statistical analyses across 53 markets, where some have introduced RDP and others have not, provide strong evidence that RDP increases the availability of innovative medicines. These results mean that if Brazil were to introduce RDP, patients could expect access to more innovative medicines that are currently not available in Brazil.

Comparing the share of innovative medicines approved out of all innovative medicines launched globally in the last 5 years, we find that markets with RDP have on average 31.5 per cent of innovative medicines available in at least one market in the world (dark blue line in Figure 1), while markets without RDP have on average 11.1 per cent of innovative medicines available (light blue line). The difference means that patients in markets with RDP have around three times as many innovative medicines available as patients in markets without RDP.

The reason for part of this difference is that RDP improves the business case for a company to launch its innovative medicine. The business case would be improved because the company would have better chances to generate revenue to recoup the investment that went into developing and launching the innovative medicine (and those medicines that failed) due to later generic entry. In contrast, without RDP, companies producing generic products could obtain regulatory approval for a generic version of the medicine by relying on the data of the marketing authorisation of the innovative medicine as soon as the information is made public. In this case, the innovative company may not have sufficient time to sell the innovative medicine prior to facing competition from generic versions, threatening its ability to recoup its investment.

Figure 1. Availability of innovative medicines
Percent of innovative medicines available[1]



Note: 1) Based on 53 markets, see Appendix A for an outline. Total averages are across markets and years.
Source: Copenhagen Economics based on data from IQVIA.

RDP could increase availability of innovative medicines by 34% to 39% in Brazil

Statistical analyses show the importance of RDP for launching innovative medicines

To understand the potential effects of adopting RDP in Brazil, we apply statistical models covering 53 markets over a period of 11 years containing data on RDP, size of the population, GDP per capita, healthcare spending, and more, see Appendix for a detailed description of our methodology and results. This allows us to identify how much of the three-fold difference in availability is associated with RDP.

In Table 2, we report the precise estimation results of the statistical modelling. The RDP estimate is in bold and shows a result of 0.092, i.e. RDP is associated with a 9.2 percentage points increase in availability. Based on the statistical modelling, we find RDP to be responsible for roughly 40% of the difference in availability found in Figure 1.

The average availability in Brazil between 2009 and 2018 was 23.06%, which means that the availability of innovative medicines in Brazil could increase by around 34.7-39.8% compared to the current level, see Box 1.[1] These results are statistically significant, which means that the estimated effect is attributable to the presence of RDP and not due to chance.

Table 2. The link between RDP and availability of innovative treatments

Percentage points increase in availability of innovative medicines associated with RDP

	Type of statistical model
	DPD model[3]
RDP[1]	**0.0918****
Controls[2]	Yes
Markets	53

Notes: Significant at the 10% (*), 5% (**) and 1% (***) level. / 1) Percentage of unique new and innovative molecules (new active substances that have been approved by major global regulatory bodies) launched in a market compared to all new and innovative molecules launched globally, within a 5-year lookback period (encompasses medicines launched locally (numerator) and globally (denominator) between the year of record and 5 years prior). / 2) For the DPD model, control variables include log of GDP per capita (purchasing power parity (PPP) adjusted) in constant 2020 values, log of healthcare expenditures per capita (PPP-adjusted) in constant 2020 values, share of population aged 65+, log of population in million, and year dummies. In addition, first and second lag of 5-year availability and first lag of all control variables (except year dummies) are included. / 3) Arellano-Bond tests, Sargan test, Hansen test, and difference-in-Hansen tests all hold, see Appendix C.

Source: Copenhagen Economics based on data from IQVIA, WHO and World Bank.

Box 1. Estimation of the effect on the availability of innovative medicines in Brazil

- The availability of innovative medicines in Brazil for the last 5 years is 23.06%
- The dynamic panel data (DPD) model estimated the increase to be 9.18%
- The SCM from Taiwan (see next page) estimates the increase to be 8%
- The increase in the availability of innovative medicine by 34.7% (0.08/0.2306) to 39.8% (0.0918/0.2306)

Notes: 1) Average 5-year availability in Brazil was 23.06% between 2009 and 2019. The range's lower bound stems from the SCM analysis on the next page divided by the average availability in Brazil, and the upper bound stems from the DPD analysis in Table 2. Based on synthetic control method and controlling for previous availability, and GDP per capita.

RDP increases availability of innovative medicines: case study in Taiwan

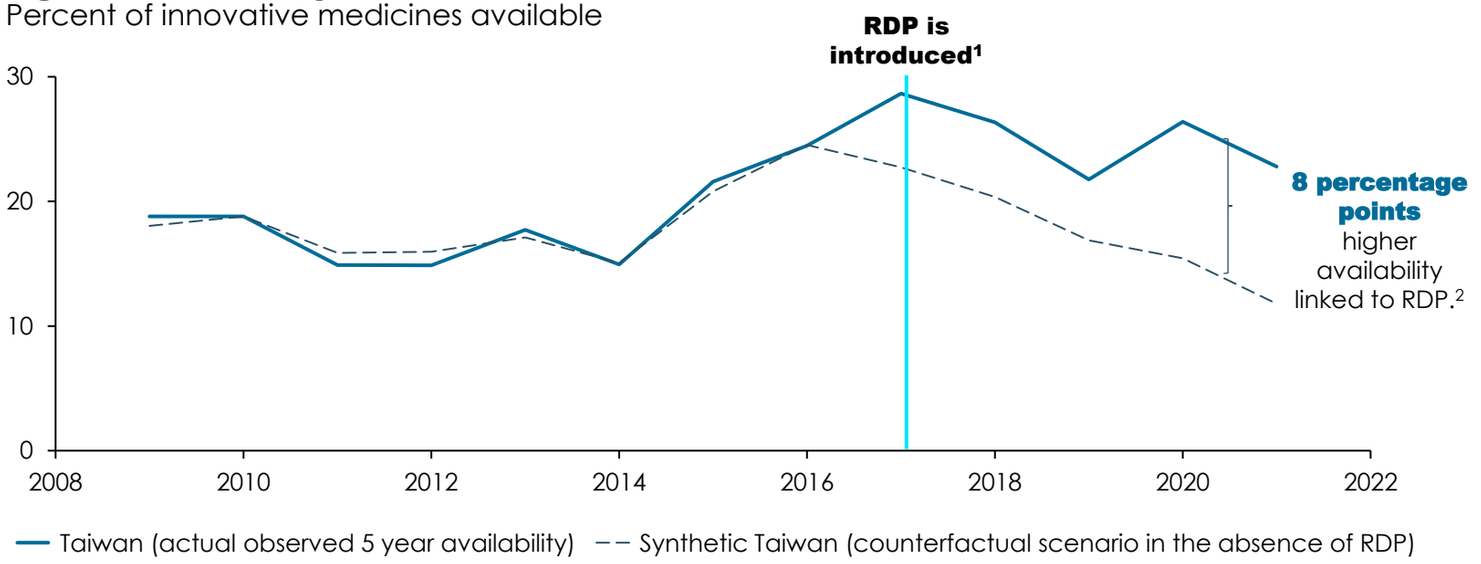
A case study finds similar results

To further investigate the robustness of our findings, we look at the implications in a concrete market that introduced RDP not so long ago. We take the case of Taiwan, where RDP was introduced in 2017. We first observe how the availability of innovative medicines developed over time before and after the introduction of RDP. Based on a statistical methodology called Synthetic Control Method or SCM (see Box 2), we estimate how the availability of innovative medicines *would have* developed in the absence of RDP. Hence, the SCM does not just compare the availability of innovative medicines in Taiwan before and after the introduction of RDP, it actually estimates the most likely alternative development had RDP not been introduced. Then it compares the actual development of innovative medicines with the estimated development in the absence of RDP.

We find that Taiwan experienced an increase in the availability of innovative medicines following the introduction of RDP by up to 8 percentage points, see Figure 2. See Appendix B and C for a detailed description of our methodology and results, respectively, including additional similar type case studies.

Figure 2. Case study in Taiwan

Percent of innovative medicines available



Notes in footer. Source: Copenhagen Economics based on data from IQVIA, World Bank, WHO, WGI, and National Statistics, R.O.C. (Taiwan).

Box 2. The Synthetic Control Method

The Synthetic Control Method (SCM) allows to estimate the effect of introducing RDP on the variable of interest, in this case availability of innovative medicines, in markets where RDP was introduced. In the selected market, Market X, the effect is estimated as the difference between availability in the observed Market X with introduction of RDP and availability in the estimated "synthetic" Market X without the introduction of RDP.

The SCM constructs the "synthetic" Market X without the introduction of RDP using the information from other markets where RDP was not introduced. Information from these markets is used in such a way as to best match the characteristic of Market X before the introduction of RDP.

See Appendix B for further details.

Notes for Figure 2: Based on synthetic control method and controlling for previous availability, and GDP per capita. / 1) Ministry of Health and Welfare, Taiwan (2017, 2018), see link and link, note 9. / 2) Based on average difference between Taiwan and synthetic Taiwan in the post intervention years 2018 through 2021. The chance of obtaining a post/pre ratio as high as this one would be 0.19, i.e., the approximate p-value is 19%.

Availability of innovative medicines brings value to patients: cancer case study

Innovative medicines improve survival rates among cancer patients

The progress of research brings continued value to patients, caregivers and society as a whole. For example, innovative medicines have brought tremendous value to patients suffering from cancer, a non-communicable disease that is a leading cause of chronic disease-related death in the world.

Survival rates among cancer patients have been steadily increasing for decades alongside increased screening efforts and pharmaceutical innovation efforts. A recent study by Lichtenberg[1] points to the causal impact of the availability of new treatments on the outcomes of cancer patients. He shows that new cancer medicines launched in 36 markets during 2006-2010 reduced the number of disability-adjusted life years lost to cancer in 2015 in those markets by about 8.7%. Research into *chronic myeloid leukaemia* (CML) has played a dramatic role in improving treatment and survival rates for CML patients. Due to the advent of a new class of medicines known as tyrosine kinase inhibitors (TKIs), the 5-year survival rate has improved from less than 20% to more than 90%.

Increased availability is a critical opportunity for Brazil

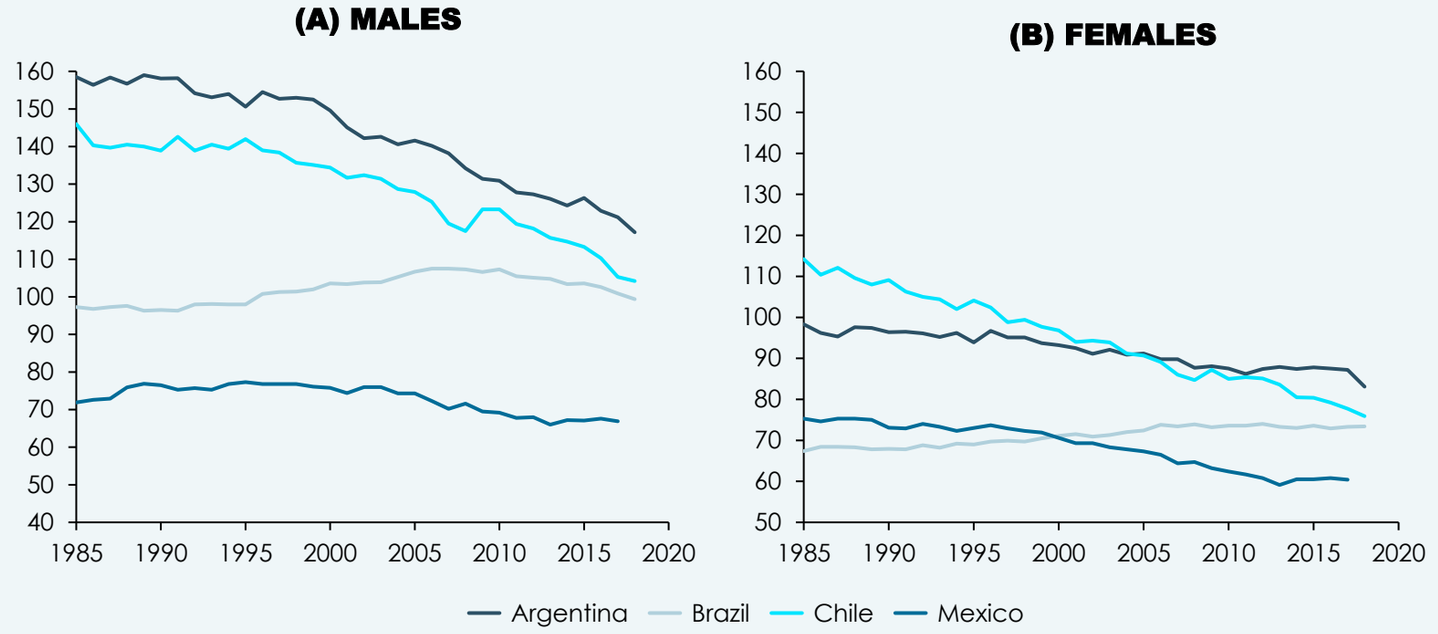
Increased availability of innovative medicines is especially important in Brazil, given the aging population and challenges with chronic diseases. Figure 3 shows age-standardised mortality rates for all cancer treatments in three Latin American countries: Brazil, Chile and Argentina as well as Mexico. While mortality rates in Argentina, Chile and Mexico have been decreasing over time, they have been increasing (and recently stabilized) in Brazil.

The study for Mexico allows us to establish a link between the availability of treatments and mortality rates. The estimates may suggest that new medicines launched during 1991–2001 reduced the age-standardised cancer mortality rate by 16%, i.e., at an average annual rate of about 1.6%.[2]

Brazil still struggles with increasing, although stabilising, mortality rates. Having access to the latest innovation means that patients in Brazil will not miss out on opportunities to live longer lives.

Figure 3. Cancer mortality rates in Brazil

Age-standardised rate (World) per 100 000, mortality, males and females



Notes: Results are shown on semi-log scale.
Age-standardised measure takes into account the differences in the age structure of the populations being compared.
Lines are smooth by the LOESS regression algorithm.
Source: Age-standardised cancer mortality rate data were obtained from Global Cancer Observatory (2023).

Notes: 1) Lichtenberg (2018). / 2) Lichtenberg (2017).

3
NO EVIDENCE OF LONG-TERM INCREASES IN HEALTHCARE EXPENDITURES

RDP does not lead to higher healthcare expenditure in the long term

- We find that healthcare expenditures do not increase over the long term (e.g., 5-10 years) in markets that introduced RDP.
- However, temporary short term increases are present, disappearing after 5-10 years. We believe there are three reasons behind this:

1. For most medicines, RDP does not extend the period of protection from generic entry.
2. Innovative medicines that are now launched thanks to the presence of RDP allow for savings on other healthcare services over times.
3. Markets are able to prioritise spending on innovative medicines in line with the market's willingness to invest, thus controlling healthcare budgets.

In this chapter, we evaluate the potential impact that introducing RDP in Brazil would have on healthcare expenditure in Brazil.

The current debate in Brazil incorrectly suggests that healthcare expenditure will increase with the introduction of RDP. That argument is predominantly based on the incorrect assumption that the entry of lower-cost generic and biosimilar medicines will be postponed by extending overall exclusivity periods of innovative medicines.

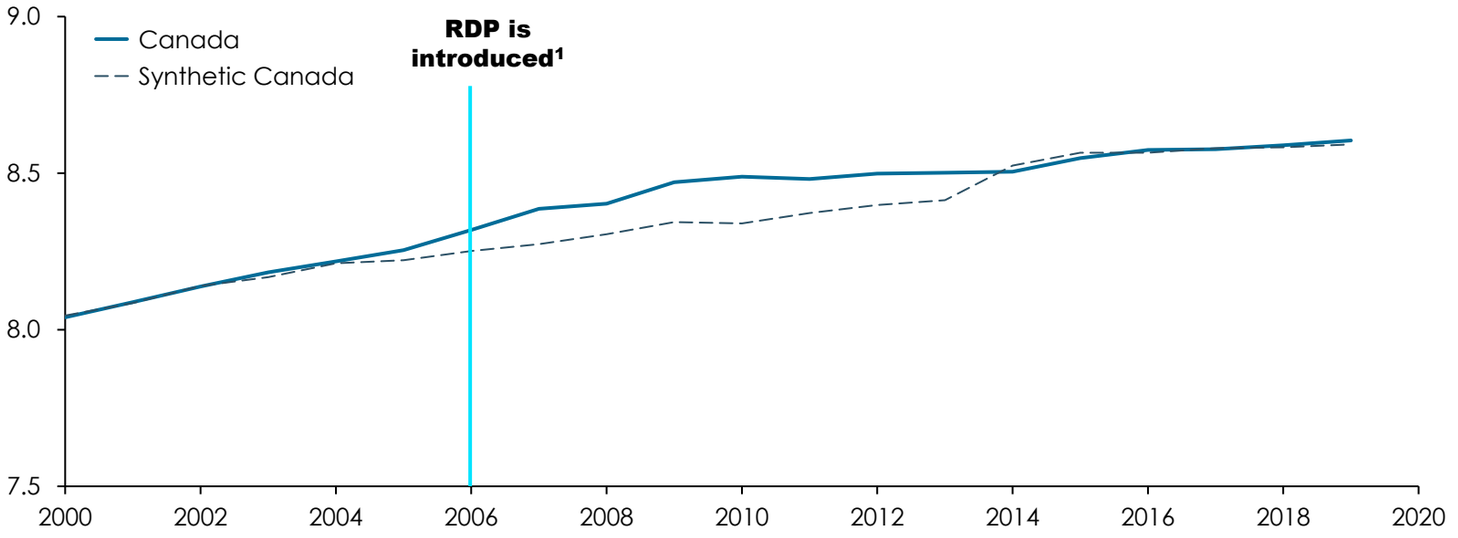
In the remainder of this chapter, we present detailed ex-post analyses to understand whether the evidence supports this view.

We do not find that RDP drives up healthcare expenditure in the long term

Based on multiple robust statistical analyses, we find no support for the argument that RDP systematically leads to higher healthcare expenditure in the long term. More specifically, we find that in most markets that introduced RDP, the healthcare expenditure rose in the short term only to revert back to its initial level after 5–10 years. This finding is consistent across many markets that introduced RDP and is demonstrated for Canada in Figure 4 and shown in Appendix C for the remaining markets.

Figure 4. Healthcare expenditures in Canada

Log healthcare expenditure per capita, PPP-adjusted, constant 2020 values



Notes: Based on synthetic control method and controlling for previous levels of healthcare expenditures, share of population aged +65, and GDP per capita. The chance of obtaining a post/pre ratio as high as this one would be 0.80. / 1) 8 years of RDP introduced. Source: Copenhagen Economics based on data from IQVIA, World Bank, WHO, and WGI.

Real world data highlights that short-term increases in healthcare expenditure is temporary

The findings from using the SCM case study method are consistent with an analysis of data for all 53 markets with and without RDP over 20 years. We find indications of a short-run increase in healthcare spending of 14.14%, which is consistent with the SCM results, see DPD model results in Table 3. However, the long-run estimate in the FE model is economically small (~1% increase) and statistically insignificant, which indicates no long-run effect.

These results suggest that the availability of new innovative treatments offering better treatment of patients increases medicine expenditure in the short term because they are used to improve the treatment of patients, but that savings occur elsewhere, and healthcare expenditure is overall managed in the long run.

The consistent finding of increases in the short term that cancels out in the long term warrants a deeper analysis. See next page.

Table 3. The link between RDP and healthcare expenditures
Percentage increase in healthcare expenditures associated with RDP

	Type of statistical model	
	DPD model[3]	**FE linear model[4]**
RDP[1]	**0.1414*** (p = 0.089)	**0.009987** (p = 0.3942)
Controls[2]	Yes	Yes
Markets	53	53

Notes: Significant at the 10% (*), 5% (**) and 1% (***) level. / 1) Log of healthcare expenditures in PPP-adjusted constant 2020 values. / 2) For DPD model, control variables include log of GDP per capita (PPP-adjusted) in constant 2020 values, share of population aged 65 +, log of population in million, and year dummies. In addition, first and second lag of log of healthcare expenditures and first lag of all control variables (except year dummies) are included. For FE model, control variables include log of GDP per capita (purchasing power parity (PPP) adjusted) in constant 2020 values, share of population aged 65+, log of population in million, and year dummies. / 3) Arellano-Bond tests, Sargan test, Hansen test, and difference-in-Hansen tests all hold, see Appendix C. / 4) There is modest autocorrelation, see Appendix C.
Source: Copenhagen Economics based on data from IQVIA, WHO and World Bank.

Studying the impact of RDP on different groups of medicines suggests a more nuanced effect on healthcare expenditure

Three reasons Brazil will be able to manage healthcare expenditure

We have identified three reasons why markets that introduce RDP, including potentially Brazil, can manage their healthcare expenditure in the long run while reaping the benefits for patients of access to new, innovative medicines.

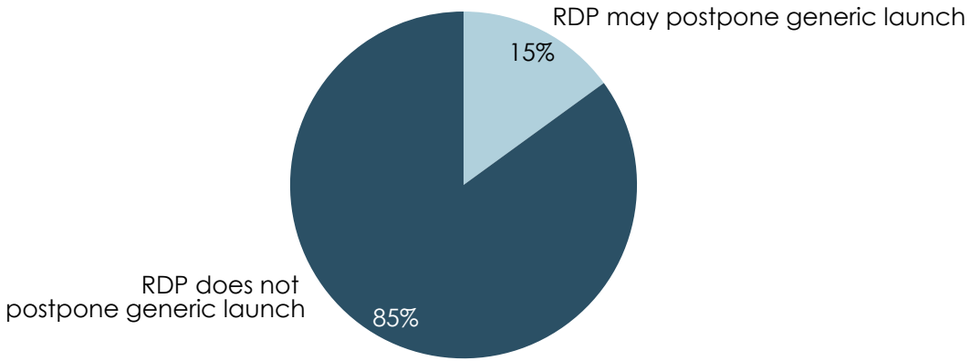
RDP does not extend the period of protection for the majority of medicines

First, we find that most innovative medicines introduced in Brazil have more than 5 years left of patent protection, in which case adding a 5-year RDP term would not extend protection beyond the patent period for those medicines.

We have assessed how RDP would interact with patent protection for the innovative medicines approved in Brazil in the past 10 years. Based on a sample of 139 innovative medicines,[1] we find that in 118 (85%) cases, the remaining patent protection at the time of regulatory approval was equal to or longer than 5 years, see Figure 5. This means that a 5-year RDP term would not have postponed generic entry for up to 85% of these innovative medicines. In fact, that figure is likely an underestimate due to longstanding patent examination inefficiencies in Brazil. This suggests that the effect of expenditure on innovative medicines currently launched in Brazil would be limited. Our conclusions are based on a subsample of innovative medicines available in Brazil with accessible information on remaining patent protection, see Appendix B for further details.

Figure 5. RDP would not affect follow-on launch for the majority of available medicines

Percent of innovative medicines



Notes: We identified 1,401 innovative medicines currently marketed in Brazil. Out of these, for 361 information on the date of approval was available and approval occurred in the past 10 years. Based on the information on the constraining patent in the US for the same medicine, we identified the patent in Brazil belonging to the same patent family. Information on the filing date of the constraining patent in Brazil was available for 182 medicines. Of these, 139 had an active patent in January 2023. These are the ones ultimately included in the analysis. Patent expiry date was estimated assuming full term of the patent, 20 years.

Source: Copenhagen Economics based on Globaldata database, WIPO

Innovative medicines may reduce spending on less efficient services

Second, consider all the new innovative medicines that would be made available to Brazilian patients due to RDP. These are medicines that are not launched today in Brazil but that we found in Chapter 2 would be launched as a consequence of introducing RDP. Notwithstanding that expenditures on additional innovative medicines is a new added item on the healthcare budget, they allow for savings on a number of other healthcare services.

As new and more effective treatments are used to treat patients, use of older and less effective treatments decrease. Innovative medicines can allow patients to avoid repeated visits to healthcare practitioners and exams, to avoid expensive surgeries, or to cure diseases whose previous standard of care included life-long treatments and frequent healthcare interventions. This means that innovative treatments can be a tool to increase efficiency of healthcare spending, i.e. obtain higher value for every dollar spent,[1] in addition to improving or transforming the life of patients. Furthermore, well treated patients can often re-enter the labour market, contributing to wealth creation for themselves and their families while adding to Brazil's GDP and taxes.

Notes: 1) See Appendix B.

Studying the impact of RDP on different groups of medicines suggests a more nuanced effect on healthcare expenditure

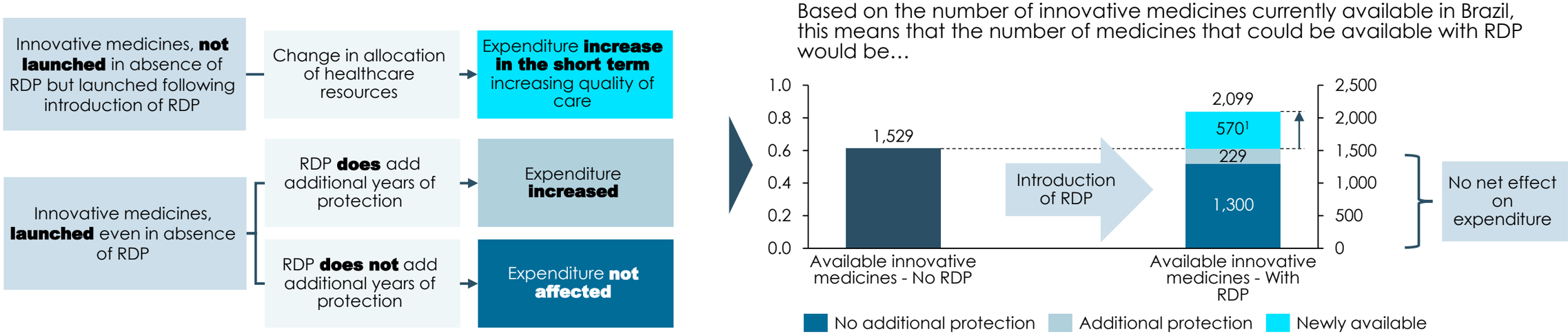
Markets set priorities for healthcare spending

Third, markets tend to incur healthcare expenditures in line with the priorities and prevent healthcare expenditures from increasing exponentially. An example of such markets are European markets. Despite an increasing number of innovative medicines and an overall increase in healthcare expenditures, medicine spending as share of healthcare expenditures have remained relatively stable over the last 20 years.[1]

In Figure 6, we show the relationship between increased availability and healthcare expenditures. On the one hand, some medicines will not be launched in the absence of RDP.[2] If these are launched after the introduction of RDP, it will imply a short-run increase in healthcare expenditures due to better quality of care, see the left-hand side of Figure 6. On the other hand, some medicines have been launched in the absence of RDP. A part of these medicines, we find the majority of them, will actually *not* gain additional protection, which implies no effect on healthcare expenditures. A minor share will gain additional protection and be associated with an increase in expenditures.

Our estimates suggest that around 570 new innovative medicines will become available to patients in Brazil if RDP is introduced, see the right-most part of Figure 6. Brazil currently has 1,529 innovative medicines available. If RDP was introduced, our estimates suggest that 1,300 medicines (85%) will *not* gain additional protection and will thus have no net effect on healthcare expenditures. The remaining 15% (229 medicines) of the currently available medicines may be subject to additional protection.

Figure 6. How does RDP affect expenditure?



Notes: See Appendix B for further description of the patent analysis. / 1) New available medicines estimated based on statistical model using the average of the DPD estimate and SCM estimate, i.e., 37.25% ((34.7+39.8)/2), see Box 1.
Source: Copenhagen Economics based on Globaldata database and WIPO.

Notes: 1) IQVIA (2022). See link / 2) This stems from the analysis in Chapter 2 showing increased availability of innovative medicines associated with RDP.

4
RDP IS AN OPPORTUNITY FOR THE GENERIC AND INNOVATIVE PHARMACEUTICAL INDUSTRY

RDP represents an opportunity for generics and biosimilars

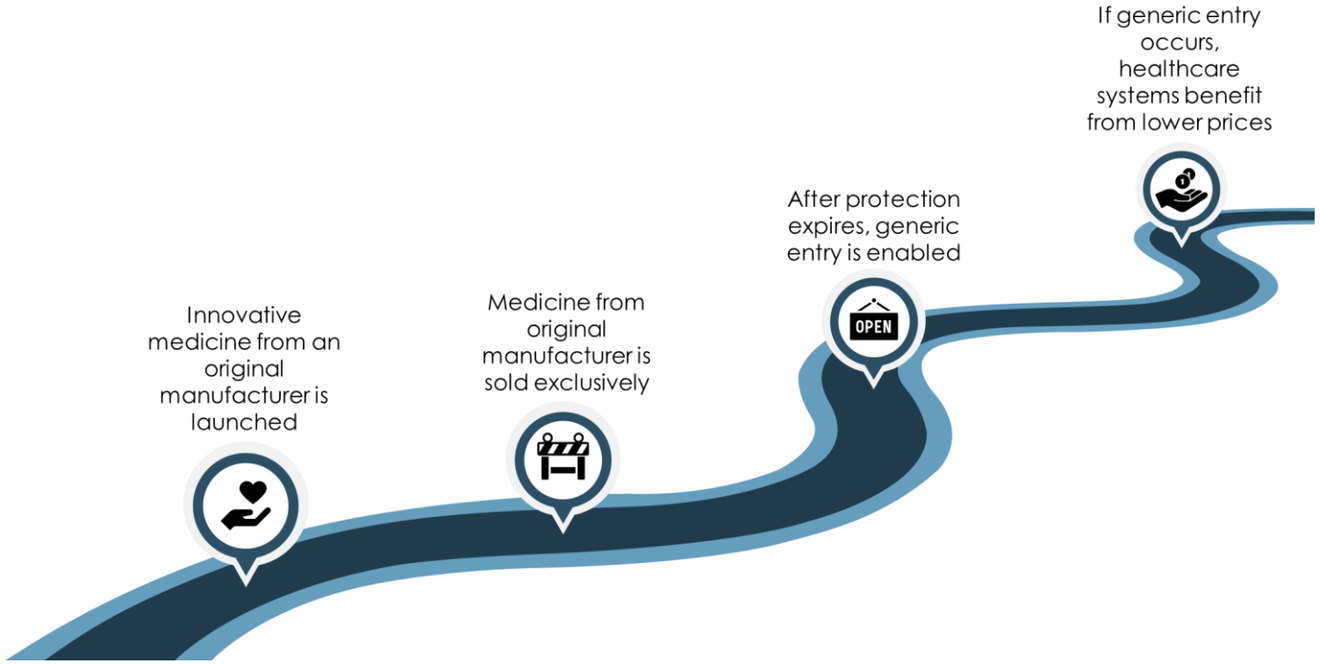
- Innovative medicines fuel the generic and biosimilar industry. For each innovative medicine available in Brazil, 3.17 generic or biosimilars become available.
- By increasing the availability of innovative medicines, RDP represents an opportunity for growth for the generic and biosimilar industry.
- RDP is expected to increase the attractiveness of Brazil, attracting FDI and increasing the number of clinical trials.
- We estimate that RDP may increase the number of clinical trials in Brazil from 454 today to 1,060. Brazil would jump from the 79th place to the 60th place in the global ranking of clinical trials per one million inhabitants.

In this chapter, we investigate the effect of RDP on Brazil's pharmaceutical industry. We assess the effect on both the generics and biosimilars industry and the innovative industry. This is an important aspect of the debate as Brazil has a sizeable generics industry. In addition, Brazil is increasing its efforts to develop its biosimilar industry. Our overall conclusion is that RDP represents an opportunity for growth over time for both the generics and biosimilars industry and the innovative pharmaceutical industry.

Innovative medicines are the building block of the pharmaceutical ecosystem

The pharmaceutical ecosystem is driven by the efforts of innovative medicine developers that bring medicines to the market through a long, costly and risky development process. These medicines are then sold on the market under exclusivity for a limited period to allow the developer to recoup the costs and risks of its investment. Once the exclusivity period expires, generic or biosimilar manufacturers may seek marketing authorisation for their versions of the medicine based in full or in part on the data created and submitted by the innovator showing that the medicine is safe and effective. Given that generic/biosimilar manufacturers incur significantly less cost and risk to launch their products, they are able to sell their products at a lower price, thereby reducing healthcare spending for that particular medicine. This role of innovative medicines in the pharmaceutical ecosystem is illustrated in Figure 7.

Figure 7. The role of innovative medicines in the pharmaceutical ecosystem



Source: Copenhagen Economics.

For each innovative medicine available in Brazil 3.17 generic or biosimilars become available

The importance of innovative medicine in the pharmaceutical ecosystem and for developing generic/biosimilar medicine becomes apparent when examining the relationship between the two. We estimate that, generally, for each innovative medicine available on the market, approximately 2.5 generic or biosimilars become available over time, see Figure 8. In Brazil, for every innovative medicine, 3.17 generics become available on the market.

This means that without innovative medicines there would be no generics or biosimilars. The presence of innovative medicines is an opportunity for manufacturers of generics and biosimilars to bring more products to the market over time. This positive effect allows us to put into perspective the possible later entry to the market of a generic or biosimilar that the introduction of RDP would bring to a share of innovative medicines.

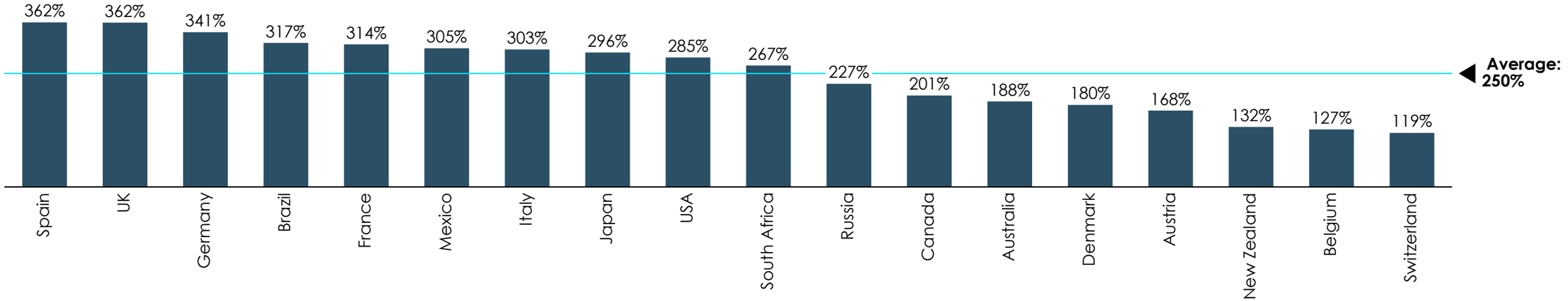
Growth in the generic and biosimilar industry

Our estimates suggest that RDP would increase the availability of innovative medicines by 34-39% compared to the current level, see Chapter 2. Over time, after the expiry of protection periods, the current estimate implies that 3.17 generic or biosimilar medicines could become available in Brazil for each available innovative medicine. This suggests that RDP is an opportunity for growth over time, not a threat, for generic and biosimilar manufacturers in Brazil.

Concerning innovative medicines that have been launched even in the absence of RDP, RDP would not necessarily lengthen the period of protection. Our calculation based on a sample of innovative medicines marketed in Brazil and launched in the past 10 years suggests that a 5-year RDP would not lengthen the protection period for up to 85% of medicines, see page 17. The effect of RDP on timing of generic or biosimilar entry could therefore concern a rather limited share of innovative medicines that have been launched even in the absence of RDP.

Figure 8. Implication of presence of original products for availability of generics

Ratio between generic medicines (and biosimilars) available and innovator medicines



Note: Generics are defined as generic and biosimilar medicines. Innovators include both NME medicines and non-NME. All markets with available data are included. Outliers (defined as markets with a ratio larger than 700% or smaller than 100%) are removed. These include India (3,857%), China (1,238%), South Korea (1,147%), Indonesia (709%) and Israel (83%).
Source: GlobalData (2023): medicines by approval.

RDP contributes to increasing the number of clinical trials (1/2)

As more innovative medicines are made available in Brazil, innovative companies increase their presence to properly manage the increased market authorisation and pricing and reimbursement activities that follow. This in itself constitutes an increase in foreign direct investments (FDI) into Brazil. An increased presence and, thereby, interest in Brazil as a market, will make it more attractive for innovative companies to increase their investments in development and clinical trials in Brazil. That enables data to be produced in Brazil, which would be better integrated with Brazilian patient communities, physicians, research facilities, academia, and government agencies.

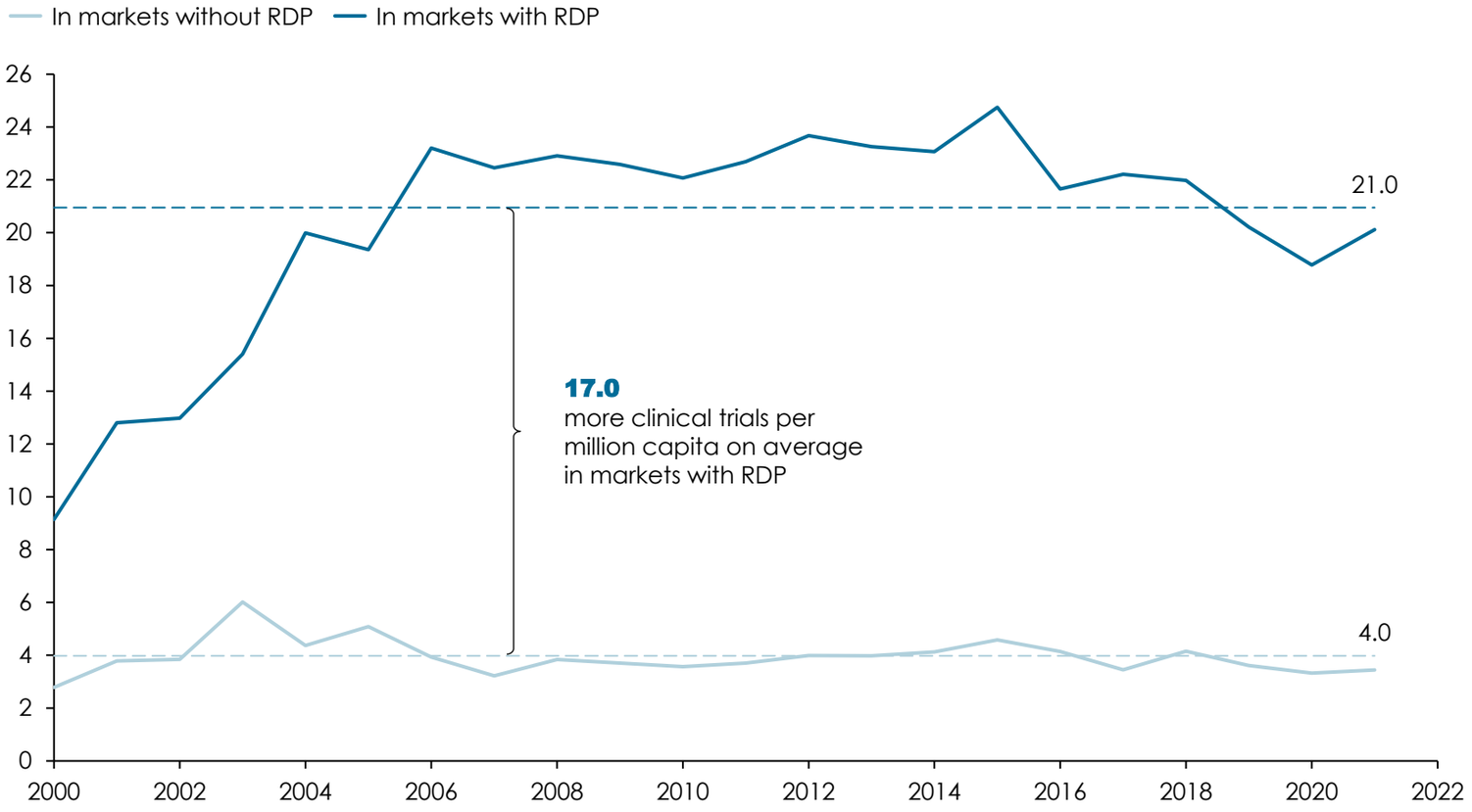
In addition to adding FDI and providing for more high productive research and development jobs in Brazil, clinical trials help strengthen the healthcare system by improving the standard of care, improving infrastructure and ensuring continuous training of professionals. Clinical trials represent investments, both internally and from abroad, sustaining the national and local economy. Research has quantified the internal rate of return on investment in clinical research to lie between 39% and 64%.[1]

More clinical trials are conducted in markets with RDP

When we compare the average number of clinical trials conducted in markets with and without RDP, we find that markets with RDP have on average 21 clinical trials per million capita, while markets without RDP have on average 4. This means a difference of 17 clinical trials per million capita, see Figure 9. However, a simple comparison does not allow us to draw conclusions on the causality of the relationship between RDP and the number of clinical trials. This is because the difference could be due to other characteristics of these markets.

Figure 9. Average number of clinical trials

Number of clinical trials per million capita[1]



Note: 1) Based on 54 markets, see Appendix A for an outline. Total averages are across markets and years.
Source: Copenhagen Economics based on data from IQVIA.

Notes: 1) Smith et al. (2019), Craig et al. (2020), Health Economics Research Group et al. (2008).

RDP contributes to increasing the number of clinical trials (2/2)

Statistical analyses find evidence of a positive effect

We use robust statistical methodologies to identify how much of this difference is due to the presence of RDP. We developed a statistical model covering 54 markets and 19 years of data on the presence of RDP, accounting for GDP, etc. Once controlling for these characteristics, we find evidence that RDP increases the number of clinical trials conducted in a market.

In Table 4 below, we report the estimation results of the statistical modelling. The RDP estimate is in bold and indicates 2.9 more clinical trials per million. The estimate is significant (p=5.8%).

Case studies find similar results

To further investigate our findings, we look at the implications in a specific market that introduced RDP. For instance, we take the case of Taiwan, where RDP was introduced in 2017. We first observe how clinical trials developed over time before and after the introduction of RDP. Based on an SCM (see Box 2 on page 12), we estimate how the clinical trials would have developed in the absence of RDP. Hence, the SCM does not just compare the number of clinical trials in Taiwan before and after the introduction of RDP, it estimates the most likely alternative development had RDP not been introduced, and then it compares the actual development in innovative medicines with the estimated development in the absence of RDP.

We estimate that Taiwan experienced 3.2 more clinical trials per million capita following the introduction of RDP, see Figure 10.

Table 4. The link between RDP and clinical trials

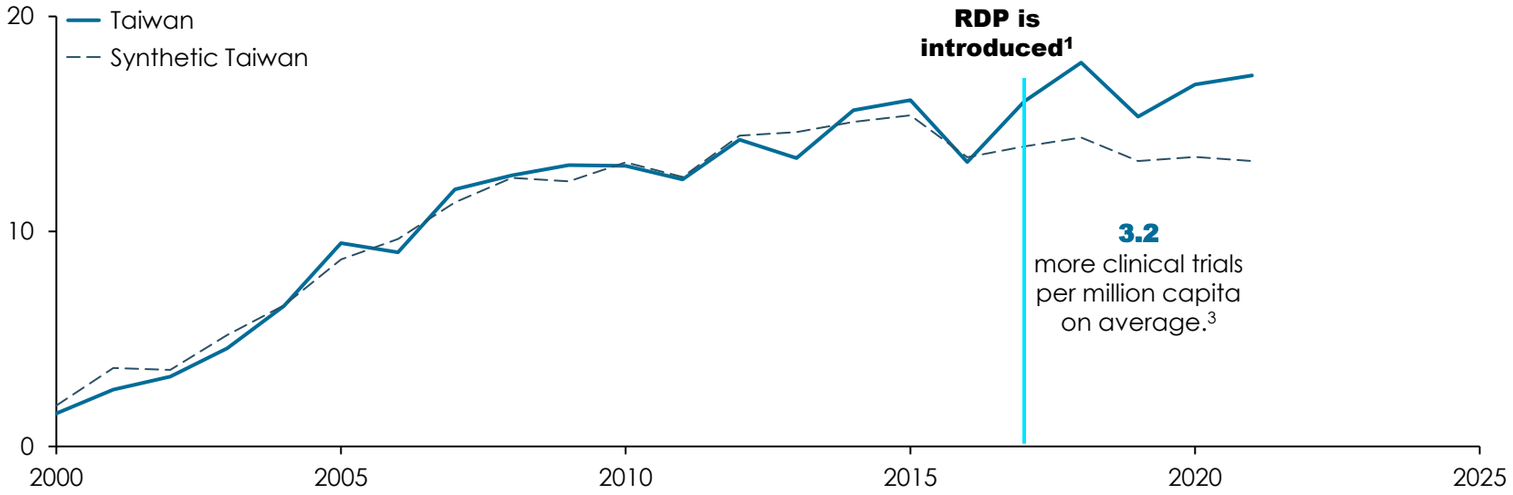
Increase in clinical trials per million capita associated with RDP

	Type of statistical model
	DPD model[3]
RDP[1]	**2.8656*** (p = 0.0581)
Controls[2]	Yes
Markets	54

Note: See page footnotes.
Source: Copenhagen Economics based on data from IQVIA, WHO and World Bank.

Figure 10. Clinical trials in Taiwan

Number of clinical trials per million capita



Note: Based on synthetic control method and controlling for previous levels of clinical trials, and GDP per capita. / 1) Ministry of Health and Welfare, Taiwan (2017, 2018), see link and link, note 9. / 3) Based on average difference between Taiwan and synthetic Taiwan in the post intervention years 2018 through 2021. The chance of obtaining a post/pre ratio as high as this one would be 0.33, i.e., the approximate p-value is 33%.
Source: Copenhagen Economics based on data from IQVIA, World Bank, WHO, WGI, and National Statistics, R.O.C. (Taiwan).

Notes for table 4: Significant at the 10% (*), 5% (**) and 1% (***) level. Standard errors in parentheses and p-values in brackets. / 1) Number of clinical trials per million capita. / 2) In the DPD model, control variables include log of GDP per capita (purchasing power parity (PPP) adjusted) in constant 2020 values, log of healthcare expenditures per capita (PPP-adjusted) in constant 2020 values, log of physicians per 1,000 inhabitants, and year dummies. In addition, first and second lag of clinical trials per capita and first lag of all control variables (except year dummies) are included. / 3) Arellano-Bond tests, Sargan test, Hansen test, and difference-in-Hansen tests all hold, see Appendix C.

Our statistical analyses find indicative evidence that RDP contributes to increasing the number of clinical trials intensity

We repeat the same analysis for all markets where RDP was introduced and data availability allowed us to perform the estimation. These are Japan, Canada, Croatia, Chile, see Appendix.

We find that in some markets (Taiwan, Japan and Croatia) the number of clinical trials per million inhabitants increased after the introduction of RDP, while in others (Canada and Chile) it decreased. The decrease in certain markets could be due to other factors working in the opposite direction. For instance, in Canada, RDP was introduced at the same time as the extension of RDP in Europe. We therefore consider the evidence from the SCM analyses to be only indicative of a positive effect of RDP on the number of clinical trials.

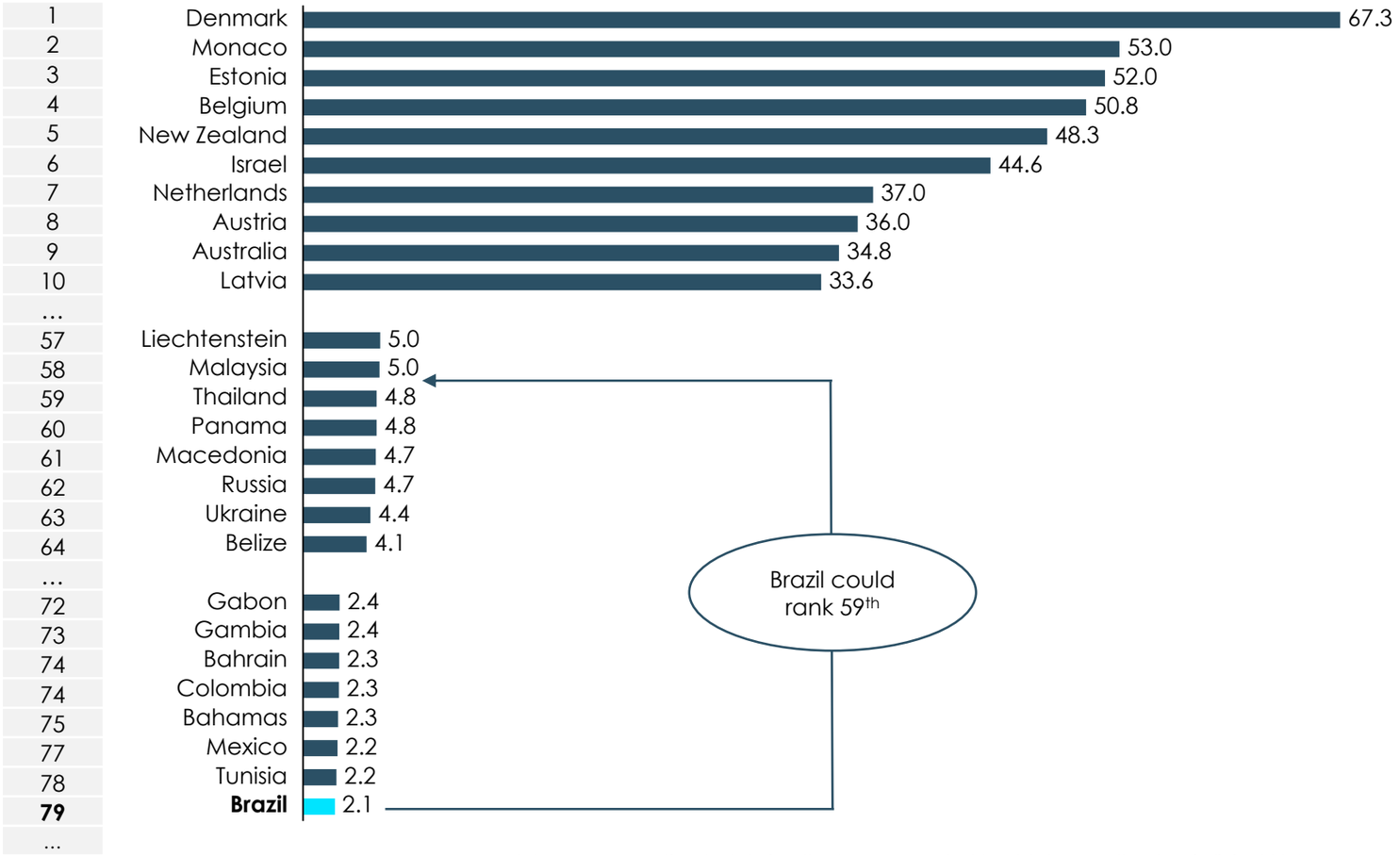
RDP would increase the number of clinical trials in Brazil

When looking at Brazil, we observe that it has few clinical trials given the size of the population. It currently ranks 79, see Figure 11. Using the estimate of ~2.9 more clinical trials per one million inhabitants coming from the statistical analysis, Brazil could jump from 79th place to 59th place with almost 4.9 clinical trials per year. This means that the average number of clinical trials in Brazil could increase by 138% from 445 to 1,059[1] with the introduction of RDP.

Hence, Brazil has the potential to further strengthen its clinical trial activities given its economic and demographic size. This would be both through investments of international companies that would now find Brazil more attractive and through the scaleup and transition of the national pharmaceutical industry towards a more R&D-intensive industry. Introducing RDP would be a step in supporting these activities.

Figure 11. Clinical trials 2011-2021

Average number of clinical trials per million inhabitants per year



Note: Average estimated during the ten-year period to obtain an estimate of clinical trials per year.
Source: Copenhagen Economics based on GlobalData, and World Development Indicators.

Notes: 1) Based on DPD estimate in Table 4 of 2.8656 more clinical trials per million capita and an estimated 214.3 million inhabitants in Brazil (see the World Bank, link). This yields an increase of 614 more clinical trials, which added to the existing 454 yields 1,060 (difference due to rounding).

5
RDP HAS A BROADER POTENTIAL FOR THE BRAZILIAN ECONOMY

RDP is the first step towards a successful R&D-intensive pharmaceutical industry in Brazil

- An R&D-intensive pharmaceutical industry directly and indirectly contributes to a market's economy through high value-added activities.
- The introduction of RDP, within a strong system of protection of innovation, is the first step towards fostering a market's pharmaceutical industry.
- Brazil could decide to follow a three-step strategy deployed by markets with large innovative industries where RDP adoption is the first step; this could lead to a large and wealth creating innovative industry in Brazil

A strong system of protection of innovation is a key element present in all markets with a thriving R&D-intensive pharmaceutical industry. Therefore, introducing RDP to its system of protection of innovation would be a necessary (but not sufficient) step for Brazil towards growing an innovative, R&D-intensive pharmaceutical industry.

The upside of an innovative pharmaceutical industry

An R&D-intensive pharmaceutical industry, directly and indirectly, contributes to a market's economy through the creation of a large number of highly-skilled, high-paying jobs. This industry's productivity is superior to the average of a market's economy. For instance, in the US and Switzerland, markets with a successful R&D-intensive pharmaceutical industry, the productivity measured in total value added per full-time employee (FTE) is over 2.5 times, and 4 times higher than the total economy, respectively.[1]

Three steps in fostering an innovative pharmaceutical industry

While a system of protection of innovation is a key first step, other building blocks are required for a successful R&D-intensive pharmaceutical industry. Through the experience of successful markets, we have identified two additional elements, see Figure 12. These are a supportive research ecosystem and attractive incentives and incubators with access to funding opportunities. We describe these in turn in the following pages.

Finally, we illustrate the economic potential for Brazil of introducing and executing the three-step strategy, thus succeeding in developing a successful innovative pharmaceutical industry, see pages 30 and 31.

Figure 12. Key elements for an R&D-intensive pharmaceutical industry – starting with protecting innovation

Necessary but not sufficient condition

1 Strong and predictable system to protect innovation

System of tools to protect innovation. RDP has an important role within this system.

2 A supportive research ecosystem

a. Highly-skilled researchers and research excellence.
b. A strong healthcare system infrastructure and an adequate regulatory framework to support research and clinical trials.
c. Data infrastructure to facilitate clinical research.
d. A culture of collaboration as an enabler of a successful research ecosystem.

3 Attractive incentives and incubators, access to funding opportunities

Attractive incentives and incubators that enable start-ups and researchers to establish new and successful life-science companies. Access to funding opportunities.

Source: Copenhagen Economics.

Notes: 1) Copenhagen Economics based on PitchBook Venture Investment database (2020), BAK Economics AG (2021) and Ministry of Foreign Affairs of Denmark (2021).

Step 2 is about fostering a supportive research ecosystem

We find that a second key element for a thriving R&D-intensive pharmaceutical industry is the research ecosystem. While each market has its specificities, the following key elements appear to be crucial building blocks of such an ecosystem, see Figure 13.

Highly-skilled researchers and research excellence

A key element of a successful research ecosystem is a top-quality national education system, which allows the relevant skills to be built during schooling years, and top universities offering key courses and connections to international networks of high-quality university-level research and teaching programs.

In addition, being an attractive market for talented researchers from abroad is also important. Key factors influencing the attractiveness of a market for international talents are not only the quality of the national education and research system but also incentives such as income tax benefits and competitive academic salaries.

Brazil already has researchers with a high level of competence in clinical research, many being considered opinion leaders.[1] Studies have also shown that Brazilian researchers are contributing to prominent research topics worldwide in all areas, with the number of papers published abroad by Brazilian authors increasing at the same rate as the total number of papers published.[2] While formal training to prepare doctors for careers as investigators is in its infancy in Brazil, the learning environment seems to be rapidly transforming into a collaborative and flexible environment.[3] These findings suggest that Brazil has indeed a potential to further strengthen its education and research system to meet the growing demand for qualified professionals and researchers.

A supportive infrastructure and an adequate regulatory framework

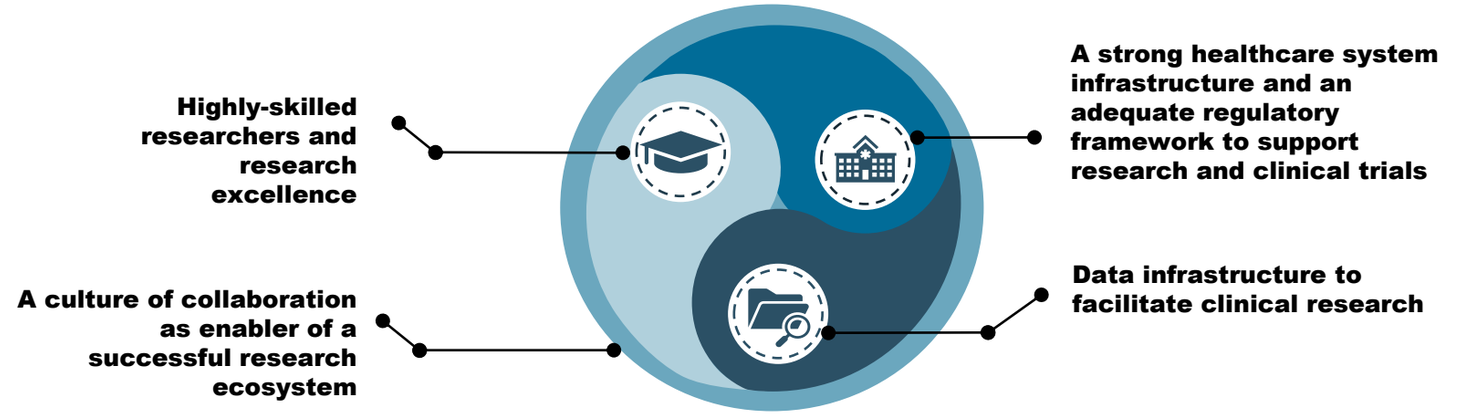
Clinical research requires a well functioning and accommodating healthcare system. This includes innovative and up-to-date knowledge and infrastructure, such as specialised high-quality care centres with sufficient capacity and healthcare professionals.

In the past 30 years, Brazil has progressed in improving the well-being of its citizens: introducing a universal coverage system has allowed Brazil to virtually reach health care coverage for all its citizens. At the same time, it still faces significant challenges around inequality of access to and quality of care, as well as a new and changing epidemiologic profile of its population. Continuously strengthening its healthcare system will not only deliver towards the primary goal of keeping Brazilians healthy and delivering high-quality, sustainable health care but also sustain the growth in clinical research.

Clinical research also requires an adequate regulatory framework. This includes an effective regulatory authority with sufficient resources and clear and predictable processes governing clinical trial research.

The Brazilian ethical and regulatory environment is modern and up to date with ethical standards and technologies in clinical research.[1] Clinical research in the market is supervised by ANVISA, which since 2010 is the regional reference authority and has the highest degree of the WHO certification on the basis of competence and efficiency.[4] Some opportunities for development have been discussed, such as increasing competitiveness of the approval times for clinical trials, and ensuring sufficient resources for the regulator.[5] Brazil is therefore well positioned to further strengthen its regulatory system.

Figure 13. Building blocks of a supportive research ecosystem



Notes: 1) Gouy et al. (2018), page 351. / 2) McManus et al. (2020). / 3) Arai et al. (2018). / 4) PAHO (2018). / 5) Interfarma (2021).

Step 2 is about fostering a supportive research ecosystem

Data infrastructure to facilitate clinical research

Data has become an increasingly important input in many sectors, and the healthcare sector is no exception. Electronic health records, disease registries, and real world data plays a role all along the value chain, from development to patient delivery and post-authorisation monitoring. Therefore, data infrastructure is a key element for a successful pharmaceutical research ecosystem today.

In practice, this requires common standards for the collection, storing and use of the data, ensuring that stakeholders can easily obtain an overview of databases and their content to make use of available resources, the possibility of integration of different data sources, accessibility and ability to share data, ensuring conformity with anonymisation and data protection regulation obligations.

Brazil has already recognised the potential of health data and has launched an ambitious digital health strategy. According to the OECD, it already generates a large amount of digital health data within key national health datasets.[1] The next steps to strengthen and fully utilise its health data include: strengthening data governance and accountability, improving data collection and data comparability and supporting evidence-based policy design with inclusive health data.[2]

A culture of collaboration as an enabler of a successful research ecosystem

Pharmaceutical R&D is expensive and risky, and it requires a significant amount of resources. A culture and environment of collaboration fosters efficient use of resources and increases the ability of a market to commercialise discoveries.

The markets with the most successful pharmaceutical R&D industry encourage collaboration between the public and private sectors, academia and companies, as well as interdisciplinary collaboration. Physical closeness is also often observed (whole value chain in one place), with research hubs, start-up clusters and incubators. We observe this in practice in many successful markets where R&D is concentrated in a few cities or regions.

Notes: 1) OECD (2021), Chapter 2. / 2) OECD (2021), Chapter 4.

Step 3 is about financial incentives including funding opportunities

A third key element is funding. Access to adequate funding opportunities is particularly relevant for research institutes, start-ups and SMEs that often work to turn scientific discoveries into viable treatments. These are mostly early-stage companies that operate without an ongoing revenue but require substantial resources for their research projects. Accessing funding opportunities is vital for their survival and ultimate success.

Incentives such as R&D tax deductions for start-ups and SMEs

When looking at markets with a successful R&D pharmaceutical industry we observe that tax deductions on research funding and similar incentives for start-ups are common. For instance, in Switzerland start-ups are partially exempt from corporate and capital taxes at a cantonal level for up to ten years, and Denmark offers over-tax deductions for investments in research.

Funding programmes for promising research institutes, start-ups and SMEs

Many markets have funding programmes for start-ups and SMEs, either fully public or provided through public-private partnerships. Establishing these programmes and ensuring their visibility and easy access for candidates provides a substantial support to the R&D intensive ecosystem of a market.

Incubators and accelerators facilitate transition from research to entrepreneurship

Incubators and accelerators enable start-ups and researchers to establish new and successful life-science companies, facilitating the creation of innovation districts/hubs where closeness of start-ups, life-sciences companies, researchers and funding institutions accelerate opportunities for knowledge sharing and growth.

Assistance to navigate regulatory environment and funding opportunities

Start-ups and SMEs often struggle to navigate a market's regulatory environment and be aware of available funding opportunities. Free or low-cost assistance indirectly frees up crucial resources in start-ups and SMEs, contributing to making the difference between success and failure.

Attracting and supporting matching to venture capital opportunities

Venture capital has become a key source of funding for pharmaceutical and biotech start-ups and companies. Venture capital provides the necessary resources for these companies to embark on long and risky development projects that they are not able to finance through incoming revenues. For instance, in the US 4,423 start-up companies received backing from venture capital between 2000 and 2019.[1]

Start-up ecosystem in Brazil: promising outlook

In Brazil, several ministries and government agencies are involved in the innovative start-up ecosystem, with many programmes for start-ups that operate through matching funds. Brazil also has a large number of incubators, technology parks and accelerators, and The National Programme of Incubators and Technology Parks (PNI) has achieved good outcomes. However, the start-up ecosystem still faces challenges in Brazil. For instance, R&D tax credits are not easily available to start-ups due to the tax regime they operate in, some redundancies and lack of coordination exist among certain programmes, and some of them are still of a very small scale.[2]

Box 4. Successes of the PIPE funding program

The Technological Innovation in Small Businesses programme (PIPE) is a pioneering platform that has been supporting technology-based companies in Brazil for over 20 years. The programme has supported many successful R&D projects:

Recepta Biopharma developed the **monoclonal antibody** RebmAb 200 in collaboration with the Butantan Institute, building on a project funded by the Partnership for Technological Innovation programme (PITE). The US company Mersana created a medicine for cancer treatment based on these antibodies, which has proceeded to clinical trials in humans. Successful licensing and testing progress have helped to secure Recepta's first revenue of R$8 million. This success was largely supported by the value and knowledge provided by the earlier PITE-supported project. If approved, Recepta would own marketing rights to the medicine in Brazil and intends to supply it to the national health care system.

Three PIPE-supported firms have developed **new medical devices** for application areas such as cardiology, pneumology, neurology, and emergency care. In particular: lung ventilators to assist patient breathing in intensive care units (ICUs) and a portable model for use in ambulances, a wireless electrocardiography device to monitor heart rate and arrhythmias outside a hospital or in an emergency setting, and a portable device for noninvasively monitoring intracranial pressure in trauma, hydrocephalus and stroke patients.

Source: Pesquisa (2017).

Notes: 1) PitchBook Venture Investment database (2020). / 2) OECD (2020), Chapter 7.

The R&D-intensive pharmaceutical industry contributes to the Brazilian economy but has further potential

- We find that the Brazilian pharmaceutical industry currently directly supports GDP by 6.6 bn USD. When including indirect and induced effects, the supported GDP contribution is 18.1 bn.
- If Brazil achieves its strategic potential, the directly supported GDP can increase to 10.2 bn USD, and 24.7 bn when including indirect and induced effects.
- The increase in supported GDP also implies an increase in employment. We estimate that the direct number of jobs supported in the pharmaceutical industry can increase from 76,600 to 109,600. When including indirect and induced effects, the number of supported jobs increases from 653,000 to 776,000.

An R&D-intensive pharmaceutical industry contributes to a market's economy through generated and supported gross domestic product (GDP) contribution. The contribution can be estimated through a direct, indirect and induced supported effect.[1] The direct effect arises directly in the pharmaceutical industry, whereas the indirect effect arises along the pharmaceutical industry's value chain, and the induced effect arises through the spending of the employees suppliers' and sub-suppliers' employees.

We estimate that the current innovative and generic and biosimilar industry supports a GDP contribution of 6.6 bn USD. This number increases with 5.3 bn and 6.1 bn to 18.1 bn when taking indirect and induced effects into account respectively, see Figure 14.

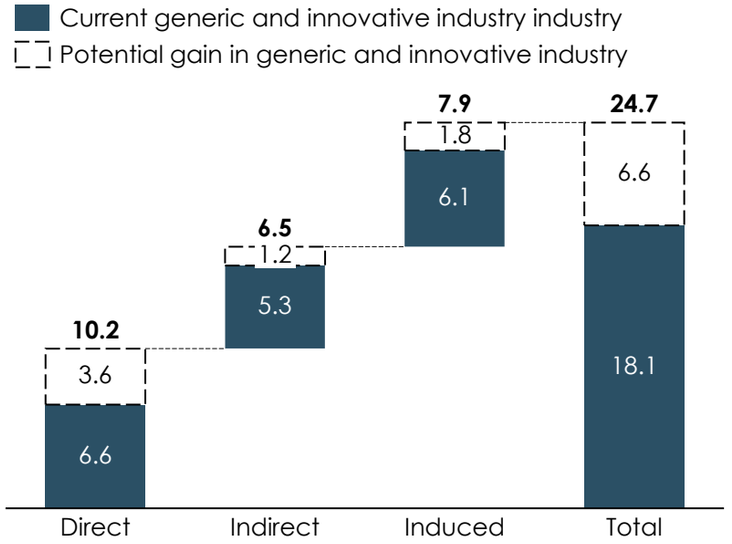
The industry can directly support an additional 3.6 bn USD if Brazil achieve its strategic potential

If Brazil can achieve its potential at levels equivalent to those in the United Kingdom and Germany (used as a measure of ambition for Brazil), we find that the directly supported GDP contribution could increase by 54% corresponding to 3.6 bn, totalling a total direct effect of 10.2 bn. We benchmark Brazil against Germany and the United Kingdom, as these markets are large, have a well-developed pharmaceutical sector and a well-functioning pharmaceutical ecosystem. We estimate that the potential indirect effect is 1.2 bn, and the potential induced effect is 1.8 bn. In total, this implies an increase in supported GDP of 6.6 bn to 24.7 bn.

To analyse the implications of Brazil reaching its strategic potential, we model a situation where direct pharmaceutical industry in Brazil has a similar size of that in the UK and Germany. We account for an unchanged trade pattern in Brazil, i.e., that increase in the industry will not transition into the same trade pattern as we observe in the UK and Germany. The reason for doing so is that Brazil has the potential to produce more nationally and thus import less input materials and other factors. This will enable Brazil to benefit more from a larger industry. We account for economies of scale associated with a larger industry by modelling a lower increase in employment than the increase in percent of GDP, see next page. By doing so and having one-to-one changes in the induced effect, we model a situation where productivity in the industry and wages paid are higher than currently, which is what is observed in other markets with a thriving R&D-intensive pharmaceutical industry.

Figure 14. The footprint of the pharmaceutical industry and potential gain
Supported GDP, billion USD, 2021 values

Direct effect arises directly in the pharmaceutical industry. Indirect effect arises along the pharmaceutical industry's value chain. Induced effect arises through spending of the employees, suppliers' employees and sub-suppliers' employees, see Appendix B for a more detailed description.



Note: Differences in totals are due to rounding. / 1) Potential effect is modelled based on achieving Brazil's strategic potential estimated as a direct effect of the combined pharmaceutical industry constituting approximately 0.7% of GDP as in Germany and the UK holding any derived effects on other part of the economy constant.
Source: Copenhagen Economics based on WIOD, Interfarma (2022), and ANVISA (2021).

Notes: 1) See Appendix B for an explanation of the direct, indirect and induced effects and our approach.

Even more jobs can be supported by the R&D-intensive pharmaceutical industry in Brazil if it achieves its strategic potential

An R&D-intensive pharmaceutical industry does not only contribute to GDP but also to a market's employment through generated and supported employment. The contribution can be estimated through a direct, indirect and induced supported effect just as for the GDP contribution.[1]

Currently, the pharmaceutical industry[2] directly supports 76,600 jobs in Brazil. In addition to the direct effect, the pharmaceutical industry also has large effects on employment along its value chain, and through spending in other industries implying larger activity and need for labour. We estimate that approximately 243,000 jobs are indirectly supported by the pharmaceutical industry, and additionally, 333,000 jobs are supported through induced effects. When taking all effects into account, the industry currently supports a total of 653,000 jobs in Brazil, see Figure 15.

The industry can directly support an additional 33,000 jobs if Brazil achieves its strategic potential

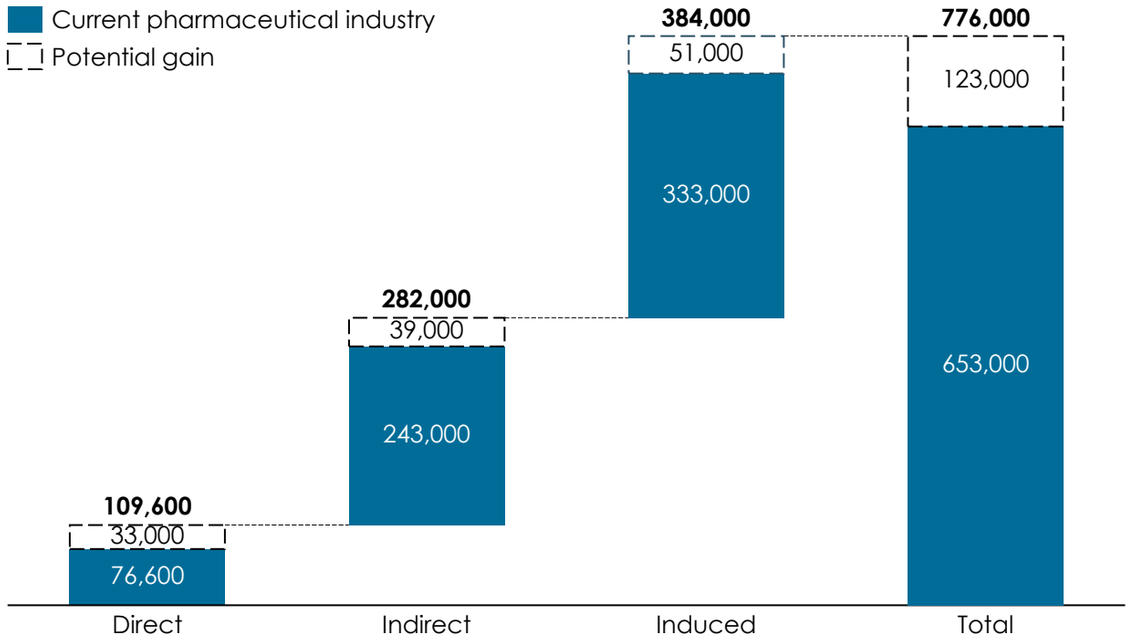
We estimate that the direct effect in the strategic potential scenario is an increase of 33,000 jobs directly supported by the industry, 39,000 jobs supported indirectly and 51,000 induced jobs, see Figure 18.

The direct effect is created by the increase in GDP of 54%. However, due to increased productivity and economies of scale, we do not assume that the direct number of jobs supported will increase by 54%. Instead, we assume that an increase in GDP of 1% leads to an increase in employment of 0.8%.[3] We impose this productivity assumption to reflect that the gains are created in the innovative industry in which the employees are relatively more productive and high-paid.

In addition to the directly supported jobs, an increase in the industry will also imply an increase in the indirect and induced supported jobs. The indirectly supported jobs will increase by 39,000 jobs to 282,000. This effect is created along the value chain of the pharmaceutical industry. When the pharmaceutical industry increases in size, it will also demand more inputs along its value chain. This supports an increase in indirect effects. Additionally, when more jobs are supported both directly and indirectly, the additional number of employees will spend their higher wages elsewhere in the economy, thereby also increasing demand and eventually also demand for labour. We estimate an induced effect of 51,000 supported jobs to 384,000. In total, we estimate a potential increase in the number of jobs supported by the pharmaceutical industry of 123,000 to 776,000 if Brazil achieves its strategic potential.

Figure 15. Current and potential employment gain in the innovative and generic and biosimilar industry
Number of jobs supported

Direct effect arises directly in the pharmaceutical industry. Indirect effect arises along the pharmaceutical industry's value chain. Induced effect arises through spending of the employees, suppliers' employees and sub-suppliers' employees implying a larger demand in other industries and a larger need for employees.



Note: Potential effect is modelled based on achieving Brazil's strategic potential estimated as a direct effect of the combined pharmaceutical industry constituting approximately 0.7% of GDP as in Germany and the UK holding any derived effects on other part of the economy constant.
Source: Copenhagen Economics based on WIOD, Interfarma (2022), and ANVISA (2021).

Notes: 1) See Appendix B for an explanation of the direct, indirect and induced effects and our approach. / 2) The pharmaceutical industry is limited to original and generics + similar production of medicines for human use. / 3) Based on PwC (2009).

Roadmap towards a successful innovative pharmaceutical industry

③ Attractive incentives and incubators, facilitating access to funding opportunities

- R&D tax deductions for start-ups and SMEs
- Funding programmes/grants for promising start-ups
- Facilitate network/showcase start-ups for private funding purposes
- Facilitate creation of LS innovation districts/hubs, closeness of start-ups, LS companies, researchers and funding institutions
- Create a network of support providers for start-ups to guide research and matching to available funding opportunities
- Support start-ups and SMEs to navigate the regulatory landscape through regulatory compliance support
- Attract and support matching to venture capital opportunities

② Supportive research ecosystem

Data infrastructure to facilitate clinical research

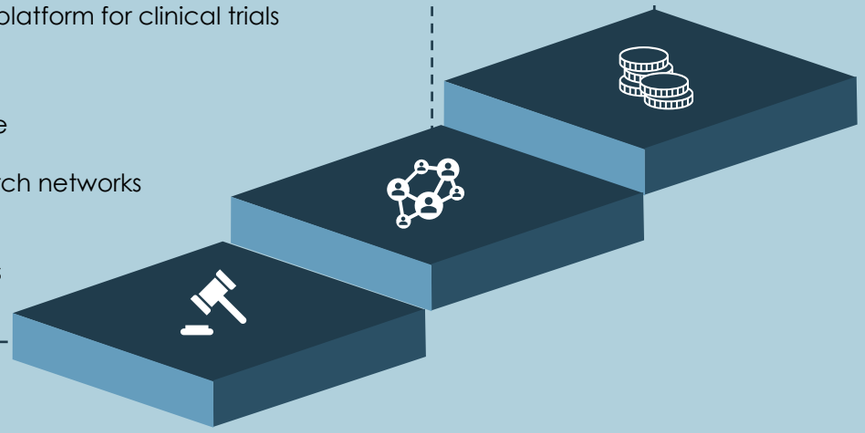
- A single point of entry for data overview, guidance and application for access to health data
- Establishment of a secure national analysis platform for health data
- Build guidance/common standards for the collection, storing and use of health records data.
- Transparent use and the highest standards in data protection maintained to build public trust

A strong healthcare system infrastructure and an adequate regulatory framework to support research and clinical trials

- Strong healthcare system
  - Up-to date innovative facilities
  - Excellence in standard of care
  - Ensure and incentivise doctors' capacity to contribute to clinical trials
- Regulatory framework for clinical trials:
  - Ensure sufficient resources for regulatory authority
  - Efficient approval of clinical trials
  - Predictable and clear regulation of clinical trials
  - Establishment of a national digital platform for clinical trials

Highly-skilled researchers and research excellence

- Ensure national educational pathways for continuous development of relevant skills set:
  - Identify relevant skills set
  - Assess education programmes against relevant skills set and map gaps
- Support national research centres of excellence
  - Ensure adequate infrastructure
  - Facilitate participation in international research networks
- Attraction of highly educated researchers:
  - Consider income tax benefits
  - Ensure competitiveness of academic salaries



① Strong and predictable system to protect innovation

- Predictable and timely patent protection system
- Efficient private enforcement system
- RDP

APPENDICES AND REFERENCES

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APPENDIX A
DATA

We have constructed a unique panel dataset

Construction of the dataset used in the analyses

To carry out the macroeconomic analyses on the implications of regulatory data protection (RDP), we have assembled a unique dataset. The dataset, constructed as a panel dataset, shows that we obtained data on a range of variables for many markets in the years 2000 to 2021.

In Table A.1., we present information on eight key variables used in the analyses. The first variable is a dummy indicating whether a market had RDP in a specific year and if yes, the length of RDP. The next three variables (availability of medicines, healthcare expenditures, and clinical trials) are the main outcome variables in our analyses. Availability statistics constructed from IQVIA MIDAS data, market regulatory data, and other data sources and cover 59 markets.

The remaining variables are collected from The World Bank, WHO, and Worldwide Governance Indicators, which are all publicly available databases. Macroeconomic data on Taiwan is not available from these databases. Instead, we collect information on Taiwan from the National Statistics, R.O.C. (Taiwan).

We have retrieved all monetary variables from the databases in current local currencies, except data received from IQVIA MIDAS, which is reported in current USD. To avoid misinterpretation of changes caused by exchange rate fluctuations and inflation, we have transformed all monetary values into constant (2020) purchasing power parity (PPP) adjusted values. By using constant PPP-adjusted values, we obtain estimates of changes that are not influenced by general price changes. This ensures that the effects we are estimating are indeed associated with RDP and not other macroeconomic conditions such as inflation, currency fluctuations, and purchasing power.

Table A.1. Overview of key variables in the macroeconomic analyses

Variable	Unit used in the analyses	Data source	Years
RDP and RDP years	A dummy for whether or not a market has RDP, and if yes, the length	IFPMA, see link	2000-2021
Availability of medicines	Percentage of unique new and innovative molecules launched in a market compared to all new and innovative molecules launched globally within a 5-year lookback period	IQVIA MIDAS	2009-2021
Healthcare expenditures	Log of current healthcare expenditure in constant (2020) PPP adjusted value per capita	WHO, see link	2000-2020
Clinical trials	Number of clinical trials per million capita (based on population size)	IQVIA MIDAS , and per capita adjustment made by CE based on The World Bank, see link	2000-2021
Population	Population, total	The World Bank, see link and National Statistics, R.O.C. (Taiwan), see link	2000-2021
GDP	Log of GDP in constant (2020) PPP adjusted value per capita	Calculated by CE based on The World Bank, see link, and link; and National Statistics, R.O.C. (Taiwan), see link	2000-2021
Share of population aged 65+	Population aged 65 and above as share of total population	The World Bank, see link, and National Statistics, R.O.C. (Taiwan), see link	2000-2021
Physicians per 1,000 inhabitants	Log of number of physicians per 1,000 inhabitants	The World Bank, see link, and Directorate-General of Budget, Accounting and Statistics, R.O.C. (Taiwan), see link	2000-2018

Note: PPP = purchase power parity. GDP = gross domestic product.
Source: Copenhagen Economics.

We include up to 54 markets in our analyses

Synthetic control method

In the estimations using the synthetic control method (SCM), the markets included are determined by the data availability. It is, for example, only possible to estimate an effect on the availability of medicines in Taiwan. This is because data on the availability of medicine starts in 2009, so to estimate an effect of RDP we need to look at a market that has implemented RDP after 2009. Amongst the markets included in the dataset, this is only true for Taiwan.

Also, the markets included in the donor pool are limited to markets with full data coverage and markets in which no similar change happened. This means that markets in the European Union cannot be included in the donor pool, as the European Union extended the length of RDP in 2004 and coverage in 2005.[1] The markets included in the donor pool are the remaining available markets, see a full list in Table A.2.

DPD with system GMM and FE with AR(1)

We utilise data covering 53 markets over 11 years (2009-2019) for availability of medicines and over 20 years (2000-2019) for healthcare expenditures, respectively, see Table A.2. We utilise data covering 54 markets over 19 years (2000-2018) for clinical trials. We cap all analyses in 2019 to avoid the results being skewed by the covid-19 pandemic. Key control variables in the clinical trials specification are not available in 2019 (see *Physicians per 1,000* in Table A.1), which makes the last year of analysis 2018. We omit the US and China throughout our analyses since these are significant outliers, e.g., healthcare expenditures in the US are much larger than in other markets. Other differences between the markets included are solely driven by data availability.

The panel is strongly balanced in the two former analyses but unbalanced in the latter due to occurrences of missing information on physicians per 1,000. Both DPD with system GMM and FE with AR(1) which is used for healthcare expenditures in the long-run are equally suited to analyse balanced and unbalanced panel data.[2]

Table A.2. Markets included in each of the analyses

Variable	Synthetic control method	DPD with system GMM
Availability of medicines	**Donor pool:** Belarus, Brazil, Egypt, Hong Kong, Indonesia, India, Korea, Lebanon, Mexico, Philippines, Singapore, Serbia, Thailand, Vietnam, and South Africa **Intervention market:** Taiwan	Algeria, Australia, Austria, Belarus, Belgium, Brazil, Bulgaria, Canada, Chile, Colombia, Croatia, Czechia, Denmark, Egypt, Estonia, Finland, France, Germany, Greece, Hungary, India, Indonesia, Ireland, Israel, Italy, Japan, Kuwait, Latvia, Lithuania, Luxembourg, Malaysia, Mexico, Netherlands, New Zealand, Norway, Philippines, Poland, Portugal, Romania, Russian Federation, Serbia, Singapore, Slovak Republic, Slovenia, South Africa, Spain, Sweden, Switzerland, Taiwan, Thailand, Turkey, United Kingdom, Vietnam (balanced)
Healthcare expenditures[1]	**Donor pool:** Armenia, Australia, Bangladesh, Bahrain, Belarus, Bolivia, Brazil, Brunei, Costa Rica, Djibouti, Dominican Republic, Algeria, Ecuador, Egypt, Georgia, Honduras, Haiti, Indonesia, India, Iran, Jamaica, Jordan, Cambodia, Laos, Sri Lanka, Morocco, Moldova, Madagascar, Mexico, North Macedonia, Mauritius, Nepal, New Zealand, Oman, Pakistan, Peru, Philippines, Papua New Guinea, Singapore, El Salvador, Serbia, Seychelles, Thailand, Tunisia, Ukraine, Uruguay, Vietnam, and South Africa **Intervention markets:** Taiwan, Canada, Japan, Croatia, Chile	Algeria, Australia, Austria, Belarus, Belgium, Brazil, Bulgaria, Canada, Chile, Colombia, Croatia, Czechia, Denmark, Egypt, Estonia, Finland, France, Germany, Greece, Hungary, India, Indonesia, Ireland, Israel, Italy, Japan, Kuwait, Latvia, Lithuania, Luxembourg, Malaysia, Mexico, Netherlands, New Zealand, Norway, Philippines, Poland, Portugal, Romania, Russian Federation, Serbia, Singapore, Slovak Republic, Slovenia, South Africa, Spain, Sweden, Switzerland, Taiwan, Thailand, Turkey, United Kingdom, Vietnam (balanced)
Number of clinical trials	**Donor pool:** Australia, Belarus, Brazil, Egypt, Hong Kong, Indonesia, India, Korea, Mexico, New Zealand, Philippines, Singapore, Serbia, Thailand, Vietnam, and South Africa **Intervention markets:** Taiwan, Canada, Japan, Croatia, Chile	Australia, Austria, , Belgium, Brazil, Belarus, Bulgaria, Canada, Chile, Colombia, Croatia, Czechia, Denmark, Egypt, Estonia, Finland, France, Germany, Greece, Hungary, Indonesia, Indonesia, Ireland, Italy, Japan, Kuwait, Latvia, Lebanon, Lithuania, Lithuania, Malaysia, Mexico, Netherlands, New Zealand, Norway, Philippines, Poland, Portugal, Romania, Russian Federation, Saudi Arabia, Serbia, Singapore, Slovak Republic, Slovenia, South Africa, Spain, Sweden, Switzerland, Taiwan, Thailand, Turkey, United Arab Emirates, United Kingdom, Vietnam (unbalanced due to missing information on physicians per 1,000 inhabitants)

Notes: For healthcare expenditures we also perform a fixed effects model with AR(1) to capture the long-run effect.
Source: Copenhagen Economics.

Note: 1) European Commission (2004). / 2) Roodman (2009).

APPENDIX B
METHODOLOGY

We apply three different macroeconomic models to estimate the effect of introducing RDP

We estimate the effect of introducing RDP by applying three different macroeconomic techniques, see Figure A.1:

1. Synthetic control method (SCM)
2. Dynamic panel data (DPD) model with system generalised method of moments (system GMM)
3. Fixed effects (FE) model with an autoregressive error term (AR(1) disturbance)

Common for all models is that they estimate a post-intervention effect, i.e. we are estimating the effect of introducing RDP in markets that have actually introduced RDP, as opposed to modelling hypothetical scenarios based on strong assumptions.

SCM is a highly internally valid method to evaluate the implications of policy interventions[1] such as the implications of RDP. In short, the SCM approach constructs a synthetic comparison market (counterfactual scenario) to evaluate what would have happened in the market that implemented RDP if it had not done so. The SCM analyses show valid estimates of the effect of introducing RDP in specific markets and can thus be seen as **case studies** on what has happened that have high internal validity. However, since the method is limited to analysing the few markets that have implemented RDP over the past 22 years, the generalisability of the results (external validity) is modest. In other words, we cannot be certain that the effect we find from introducing RDP in, say, Taiwan will happen in other markets if they are to introduce RDP as well.

To obtain **more generalisable results** with high external validity that are valid across markets, we use **DPD modelling with system GMM and an FE model with AR(1) disturbance**. The DPD model allows us to model situations where the outcome of interest depends on its own past realisations. This is particularly relevant in the current context since, e.g., healthcare expenditures in a given year largely depend on healthcare expenditures in the previous year(s).

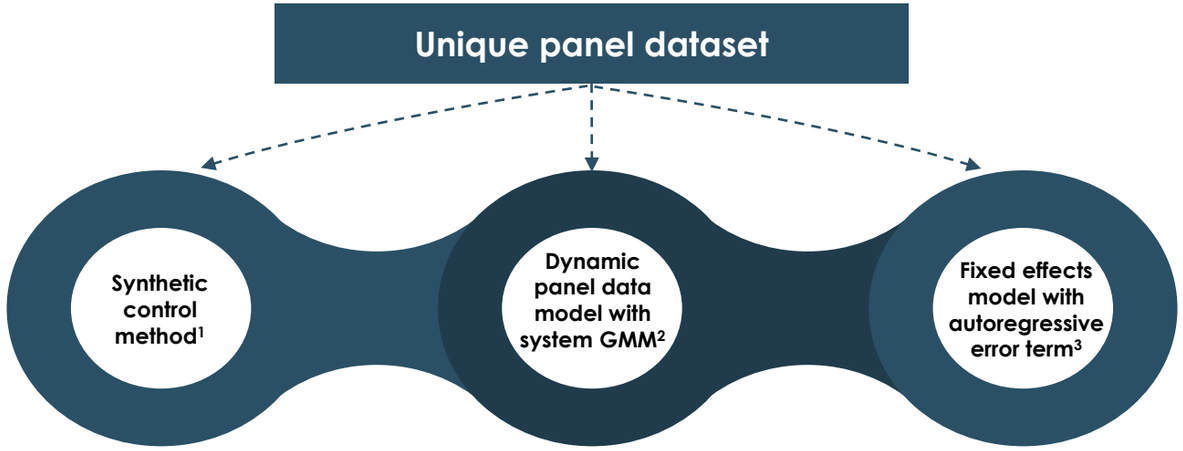
The DPD modelling with system GMM is the most efficient estimator for DPD. These models rely on all available data in up to 53 markets, which makes the results more generalisable (externally valid) than the SCM approach. The results are, however, sensitive to the exact specification and thus have lower internal validity than the SCM approach.

We primarily interpret the outcomes of the DPD model as an estimate of the causal effect of RDP, as the DPD model allows the outcome of interest to depend in its own past relation. However, for healthcare expenditures, we also use an FE model with AR(1) disturbance.

We do so because the FE models with AR(1) disturbance can be interpreted as the **long-run implications** of RDP. This is a simple model where we model a potential first-order autoregressive error term.

In the following pages, we will describe each of the models in detail and show how they are applied in this report.

Figure A.1. Methodologies



Note: 1) Abadie, Diamond and Hainmueller (2010). / 2) Arellano and Bond (1991), Arellano and Bover (1995), and Blundell and Bond (1998). / 3) Baltagi (2008).
Source: Illustration by Copenhagen Economics.

Note: 1) Abadie et al. (2010).

Synthetic control method (1/2)

When estimating the effect of an event or intervention at an aggregate, e.g. market, level, researchers often use comparative case studies. In this report, we wish to estimate the effect of introducing RDP on the availability of medicines, healthcare expenditures, and the number of clinical trials in markets that have done so. Specifically, we estimate the effects associated with the introduction of RDP in Japan in 2003, Chile in 2005, Canada in 2006, Croatia in 2006, and Taiwan in 2017.

Our aim is to compare the actual outcomes with a counterfactual scenario, i.e., what would the outcomes have been if RDP had not been introduced. The effect caused by the introduction of RDP is the difference between the actual and the counterfactual scenario in an adequately controlled setup. However, the counterfactual scenario does not exist and cannot be observed, i.e., what would have happened in market X if RDP had not been introduced. As a consequence, we need to estimate the counterfactual scenario.

The key to estimating the counterfactual scenario is that the actual and counterfactual scenarios follow the same trend before intervention. However, often that will not happen, see Figure A.2, which depicts a scenario in which an intervention happened in 1989 in the market marked with blue. At face value, other markets (so-called non-treated units) marked with grey do not follow the same trend and development as the treated unit in blue. By inspecting the figure, it becomes clear that none of the markets followed the same trend before the intervention, and hence no market can be used to estimate the counterfactual scenario.

To estimate the counterfactual scenario, we use the synthetic control method (SCM) by which we construct a synthetic market based on the characteristics of the markets included in the so-called donor pool, i.e., the grey lines in the Figure A.2. The synthetic market is constructed as the best weighted average of the markets included in the analysis that matches the market exposed to the intervention, i.e. the introduction of RDP, given some key assumptions, see Box A.1.[1] This is done by the following:[2]

Suppose the sample consists of J units in the donor pool and 1 treated unit, i.e. the total sample size is $J + 1$ units. The pre-intervention characteristics of the treated unit can be more accurately predicted by a combination of untreated units than by any single unit. The synthetic control is therefore constructed as a $(J \times 1)$ vector of weights $W = (w_2+, \dots, +w_{J+1})'$, where all units receive a non-negative weight and the weights sum to 1, i.e., $0 \leq w_j \leq 1$ for $j = 2, \dots, J + 1$ and $w_2 + \cdots + w_{J+1} = 1$.

The vector of weights, W, is selected such that the synthetic control matches the treated united as much as possible in the pre-intervention period. In other words, if X_1 is a $k \times 1$ vector containing the values of the pre-intervention characteristics of the treated unit, and X_0 is a $k \times J$ matrix collecting the values of donor pool, the weights in W are selected to minimise the difference between the treated unit and the synthetic control represented by $X_1 - X_0 W$.

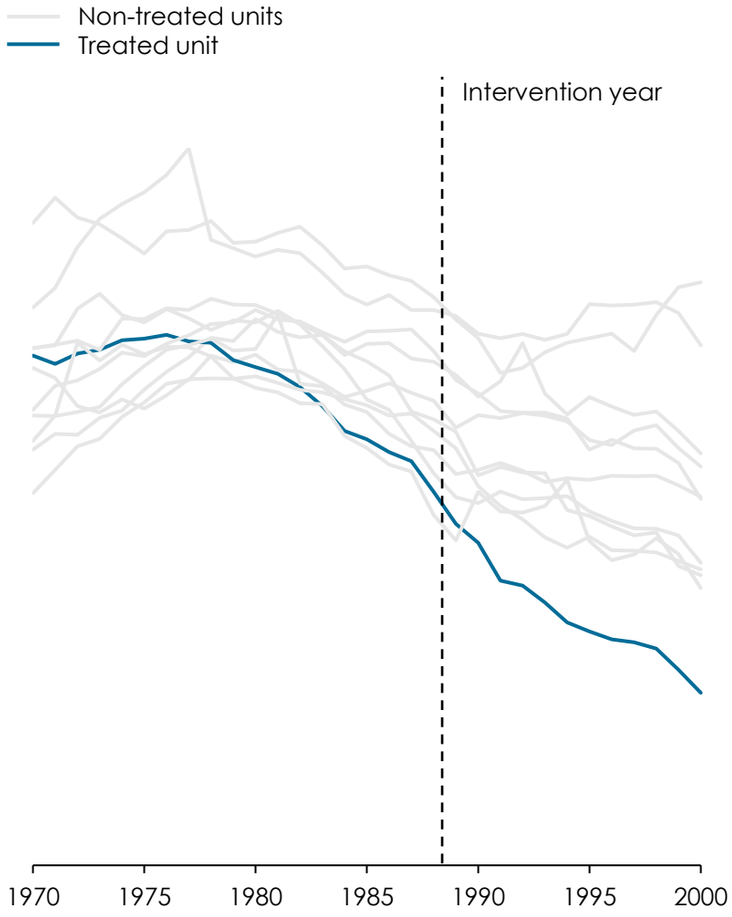
< *continued on the next page* >

Box A.1. Key assumptions of SCM

Assumption	Assessment
Treated units and potential control units in the donor pool are similar.	Similar levels in variables known to influence outcome variable.
There is no spill-over of effects of intervention into potential control units.	Based on background knowledge of researchers.
No external shocks in potential control units.	Based on background knowledge of researchers and desk research.

Source: Copenhagen Economics based on Bouttell et al. (2018).

Figure A.2. Illustration of a sample and treated unit



Source: Illustration by Copenhagen Economics based on Abadie et al. (2010).

Notes: 1) Abadie, Diamond and Hainmueller (2010). / 2) Based on Abadie, Diamond and Hainmueller (2014).

Synthetic control method (2/2)

Once the synthetic control that matches the pre-intervention characteristics of the treated unit the best and therefore minimises the difference between the two is selected, we can estimate a treatment effect of the intervention, i.e., RDP. Figure A.3 shows an example of just this; the synthetic control market is represented as the dashed line, and in the pre-intervention period, the dashed line matches the treated market almost perfectly. However, after the intervention, the two lines diverge. The only difference between the two lines is the intervention, hence the "distance" between the two is interpreted as the treatment effect. Formally, this can be represented by the following Equation (1):[1]

Y_{jt} is the outcome of unit j (a unit in the donor pool) at time t, and Y_{1t} is the outcome of the treated unit at time t. In the post-intervention period t, the synthetic control estimator of the treatment effect is given by the comparison between the treated unit and the synthetic control at that period

(1) $treatment\ effect = Y_{1t} - \sum_{j=2}^{J+1} w_j^* Y_{jt}$.

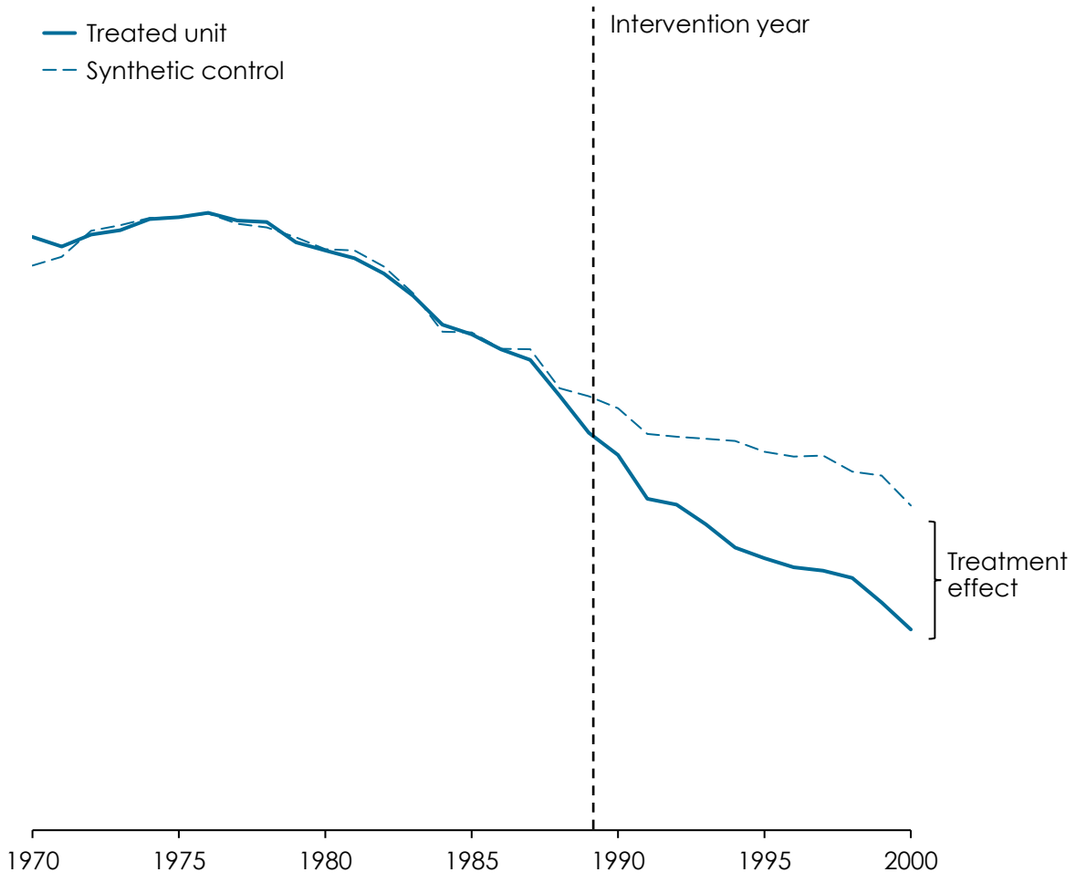
By constructing the synthetic control, ensuring pre-intervention fit between the two, and measuring the effect as the distance between the two lines, we are able to estimate the effect of RDP on selected outcome variables.[2] The use of statistical significance in comparative case studies like SCM is difficult because of the small sample nature of the data, and the absence of randomisation. However, through a series of falsification tests, one can draw conclusions on the inference.[3] One of these falsification tests is the "in-space placebo" in which the intervention is assigned to members of the donor pool. This creates a distribution of placebo effects, and these can be used to construct a p-value for each unit by calculating the fraction of such effects greater than or equal to the effect estimated for the treated unit. The smaller the sample size, the larger the fraction and hence the more difficult it is to obtain a small and significant p-value. The p-value is restricted to the question of whether or not the estimated effect of the actual intervention is large relative to the distribution of placebo effects.

All analyses are performed using the *synth* package in Stata/IC 15.1.

Validity of the synthetic control method

SCM is an internally valid method to evaluate the implications of policy interventions.[4] The SCM analyses show valid estimates of the effect of introducing RDP in specific markets, i.e. in markets that have actually introduced RDP. The SCM results can thus be seen as *case studies* of what has happened that have high internal validity. However, since the method is limited to analysing the few markets that have implemented RDP over the past 22 years, the generalisability of the results to other markets (external validity) is modest. In other words, we cannot be certain that the effect we find from introducing RDP in, say, Taiwan will happen in other markets if they are to introduce RDP as well.

Figure A.3. Illustration of a treated unit, synthetic control, and sample average



Source: Illustration by Copenhagen Economics based on Abadie et al. (2010), see link.

Notes: 1) Based on Abadie, Diamond and Hainmueller (2014). / 2) See for example Abadie, Diamond and Hainmueller (2014). / 3) Abadie et al. (2010), and Abadie et al. (2014). / 4) See for example examples listed in Bouttell et al. (2018).

Dynamic panel data model with system generalised method of moments (system GMM)

The dynamic panel data (DPD) model with system generalised method of moments (system GMM) is a robust way to apply in a situation with "small T, large N" panels, i.e., a panel dataset spanning "few" years but with "many" observations (markets), an outcome variable that is dynamic, i.e., depending on its own past realisations, and independent variables that are not strictly exogenous.[1] The modelling is based on seminal work by Arellano and Bond[2] and Arellano and Bover[3], and further refined by Blundell and Bond.[4]

We consider the following outcomes y, see Table A.1 for further explanation: availability of medicines, healthcare expenditures, and clinical trials per million capita. Our modelling consists of three sequential steps. If the test statistics outlined in Box A.2 are satisfactory[5], we apply the model in the first step. If not, we continue to Step 2. Again, if the test statistics are not satisfactory, we apply this model. If not, we continue to Step 3. Our baseline model in **Step 1** is the following:

$$(2)\ y_{it} = \alpha + rdp_{it}\delta + y_{i,t-1}\omega_1 + \boldsymbol{X}_{it}\boldsymbol{\beta} + \eta_i + \nu_t + \varepsilon_{it},$$

where y_{it} is the outcome in market $i = 1, \dots, N$ at time $t = 0, \dots, T$, rdp is a dummy variable equal to 1 if market i has RDP in year t, $\boldsymbol{X}$ are control variables, η are market time-invariant fixed effects, ν are year dummies, and ε is the error term. We interpret δ as the short-run effect of RDP on the outcome of interest. Models based on the specification in Equation (2) consistently fail the key test statistics outlined in Box A.1. In **Step 2**, we rely on the following specification:

$$(3)\ y_{it} = \alpha + rdp_{it}\delta + y_{i,t-1}\omega_1 + y_{i,t-2}\omega_2 + \boldsymbol{X}_{it}\boldsymbol{\beta} + \eta_i + \nu_t + \varepsilon_{it}.$$

Our analysis of healthcare expenditures has satisfactory test statistics with this specification. The model outlined for clinical trials is thus based on this specification. In **Step 3**, we rely on the following specification:

$$(4)\ y_{it} = \alpha + rdp_{it}\delta + y_{i,t-1}\omega_1 + y_{i,t-2}\omega_2 + \boldsymbol{X}_{it}\boldsymbol{\beta} + \boldsymbol{X}_{i,t-1}\boldsymbol{\kappa} + \eta_i + \nu_t + \varepsilon_{it}.$$

Our analyses of availability and clinical trials have satisfactory test statistics with this specification. The models outlined for these two outcomes are thus based on this specification.

Across all models, we use the *xtabond2* package in Stata/IC 15.1 to estimate DPD with system GMM.[1] We apply a two-step estimation procedure, apply robust Windmeijer corrected standard errors, apply small sample correction, and collapse the instrument set, see Box A.3. We instrument the first lag of the outcome variable with the second and earlier lags in Equation (2) and with third and earlier lags in Equations (3) and (4).[6] $\boldsymbol{X}$ consists of the control variables outlined in Table A.3 below for the three outcome variables. We model population, share of population aged 65+, and physicians per 1,000 inhabitants as predetermined but not strictly exogenous variables; that is, independent of current disturbances, these control variables can be influenced by past ones, which is similar to the outcome variable.

Box A.2. Test statistics

- **Sargan/Hansen** is a test of the overidentifying restrictions, asymptotically distributed as χ^2 under the null of instrument validity[1]
- **Arellano-Bond** is a test of autocorrelation aside from the fixed effects[2]

Notes: 1) Sargan (1958), and Hansen (1982)/ 2) Arellano and Bond (1991)
Source: Copenhagen Economics based on the references above.

Box A.3. Corrections

- We rely on a **two-step estimation procedure**
- We use **robust Windmeijer corrected standard errors**[1]
- We make a **small sample correction** to the covariance matrix estimate, resulting in t-test instead of z-test statistics for the coefficients and an *F* test instead of a Wald χ^2 test for overall fit
- We **collapse the instrument set** into one column to avoid the issue of too many instruments

Notes: 1) Windmeijer (2005), see link.
Source: Copenhagen Economics based on Roodman (2009), see link.

Table A.3. Control variables

Control variables (*X*) \ Outcome variables (*y*)	Availability of medicine	Healthcare expenditures[1]	Clinical trials[2]
Log of healthcare expenditures in PPP-adjusted constant 2020 values	X		X
Log of GDP per capita in PPP-adjusted constant 2020 values	X	X	X
Log of population in million	X	X	
Share of population aged 65+	X	X	
Log of physicians per 1,000 inhabitants			X

Notes: PPP = purchasing power parity. GDP = Gross Domestic Product. See Appendix A for further description of variables. / 1) Log of healthcare expenditures. / 2) Clinical trials per capita.
Source: Copenhagen Economics.

Notes: 1) Roodman (2009) / 2) Arellano and Bond (1991) / 3) Arellano and Bover (1995) / 4) Blundell and Bond (1998) / 5) Satisfactory test statistics include no autocorrelation beyond the included lags of the outcome variable, statistically significant Sargan test, statistically *in*significant Hansen test, and statistically insignificant difference-in-Hansen tests. / 6) For the outcome variable 5-year availability, we instrument the first lag of the outcome variable with the fifth and earlier lags since the running average over 5 years theoretically makes the second through fourth lags invalid instruments.

Fixed effects linear model with AR(1) disturbance

To analyse the long-run effect of RDP on healthcare expenditures, we apply the fixed effects linear model with AR(1) disturbance, which models a situation where the error term is first-order autoregressive[1], i.e.

$$(5)\ y_{it} = \alpha + rdp_{it}\delta + \boldsymbol{X}_{it}\boldsymbol{\beta} + \eta_i + \nu_t + \varepsilon_{it},$$

where

$$\varepsilon_{it} = \rho\varepsilon_{i,t-1} + \gamma_{it},$$

and where $\boldsymbol{X}$ are control variables (log of GDP per capita in PPP-adjusted constant 2020 values, log of population in million, and Share of population aged 65+) and all remaining variables are defined as on the previous page, and $|\rho| < 1$ and γ_{it} is independent and identically distributed (i.i.d.) with mean zero and variance σ_v^2.

Equation (5) is similar to Equation (2) applied with DPD with system GMM, with the exception that we model a first-order autoregressive error term and the lagged dependent variable is not included. The purpose of this model is to obtain an estimate of the association between RDP and healthcare expenditures in the long-run while enabling a test of serial correlation since the lagged outcome variable is not included as it was in the DPD model. We use the *xtregar* package in Stata/IC 15.1 to estimate FE with AR(1).

We find relatively high autocorrelation, which makes hypothesis testing invalid

We find that there is relatively high autocorrelation of 0.9011 for healthcare expenditures in the simple specification above in Equation (5), see Table A.6 in Appendix C. This implies that – although the point estimates are still unbiased – the standard errors are biased, which makes hypothesis testing invalid, and that the estimates are inefficient.[1]

One way of addressing this is to re-specify the model. However, for consistency with the DPD model, we have not chosen to do so since the inclusion of other variables may cause any differences we then observe between the two models. Since we still obtain unbiased estimates, we determine the association between RDP and healthcare expenditures in the long run by looking less at the statistical significance of $\hat{\delta}$, and more on the relative size and economic magnitude of the estimate.

In addition, we have estimated a simple fixed effects model (full model results not included) with clustered standard errors, which allows for valid inference even with autocorrelation.[1] This yields a p-value for $\hat{\delta}$ of 0.426, which supports a statistically insignificant long-run effect of RDP on healthcare expenditures.

We determine the autocorrelation coefficient using the generalised Durbin–Watson type statistics to test the OLS residuals from the fixed effects model for serial independence by Bhargava, Franzini, and Narendranathan.[2]

Notes: 1) Born and Breitung (2015). / 2) Bhargava et al. (1982).

Analysis of interaction between RDP and patent protection for innovative medicines in Brazil

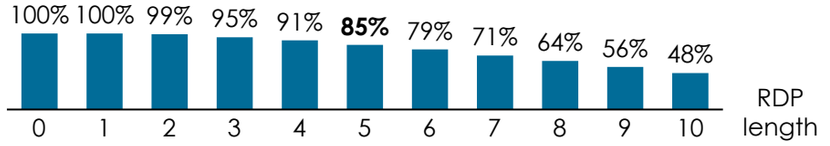
On this page, we describe the methodology used to identify the share of innovative medicines approved in Brazil that would benefit from a longer protection period in the presence of RDP.

From the "*medicines database*" from GlobalData[1], we collected the list of all 1,401 innovative medicines currently approved and marketed in Brazil. For 803 of these, information on the date of regulatory approval was available. We then restricted the sample to innovative medicines approved in the past 10 years, i.e., after 1 January 2013. This gave us a sample of 361 innovative medicines.

The next step consisted in identifying the information on patent protection for these innovative medicines in Brazil. To do so, we used information on the US patent for the same medicine.[2] We collected from the same database GlobalData information on the patent for the same medicine in the US. We then collected from the WIPO patent database[3] information on the filing date of the patent in Brazil belonging to the same patent family as the US patent. Information on the patent in Brazil was available for 182 (of the 361) innovative medicines. Of the 182 innovative medicines, 139 had a valid patent on 1st of January 2023. The rational of only selecting innovative medicines with a valid patent at 1st of January 2023 is to better reflect the future situation of approving patents and medicines in Brazil. This is the final sample of medicines included in our analysis. Innovative medicines that do not have a patent in Brazil or have not yet been granted a patent are not included. This also includes medicines currently awaiting patent granting. We then estimated the date of patent expiry assuming full term: the patent is assumed to expire 20 years after filing. Based on this information, we calculated the share of innovative medicines for which RDP would add years of protection under different assumptions on the length of RDP, see Figure A.4. We summarise some characteristics of the medicines included in the sample, see Figure A.5-A.7.

Figure A.4. Innovative medicines that would *not* obtain additional protection for different RDP length assumptions

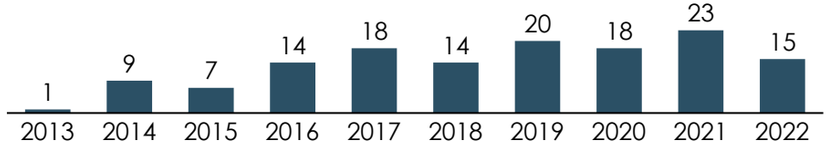
Share of medicines



Note: N = 182 medicines included in total in the analysis.
Source: Copenhagen Economics based on GlobalData and WIPO patent database, see link.

Figure A.5. Medicines included by year of approval

Number of medicines



Source: Copenhagen Economics based on GlobalData database and WIPO patent database, see link.

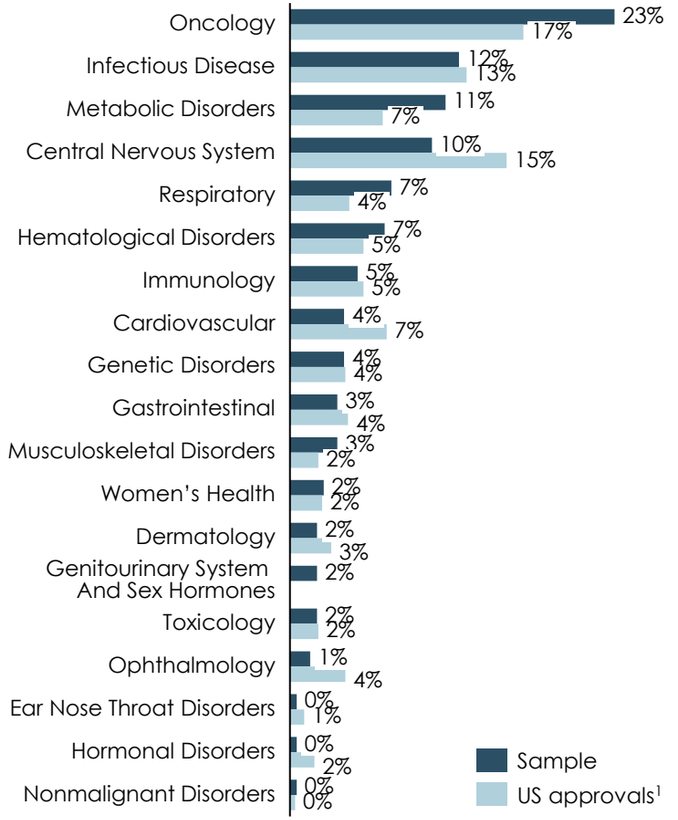
Figure A.6. Medicines by molecule type

medicine type	No. of medicines in sample (%)
Small molecules	80 (58%)
Biologics	59 (42%)

Source: Copenhagen Economics based on GlobalData database and WIPO patent database, see link.

Figure A.7. Medicines by therapeutic area

Share of medicines



Notes: 1) Share of medicines approved in the US after 1 January 2013 by therapeutic area.
Source: Copenhagen Economics based on GlobalData database and WIPO patent database, see link.

Notes: 1) GlobalData is a proprietary database, see link. / 2) This is a commonly used methodology to link patents to the corresponding medicines in markets outside the US. See for instance Copenhagen Economics (2018). / 3) WIPO v1.4.0, see link.

Footprint analysis using input-output modelling (1/2)

In this study, we assess the pharmaceutical industry's contribution to the Brazilian economy in terms of value added and the number of jobs supported throughout the economy. We analyse the contribution through three effects: direct, indirect, and induced contribution.

The **direct contribution** measures the economic activity generated directly in the pharmaceutical industry. The **indirect contribution** measures the contribution arising along the value chain of the pharmaceutical industry. The **induced contribution** captures consumer spending in the Brazilian market funded by wages paid in the pharmaceutical industry and those employed in its value chain. The indirect and induced contributions are calculated using so-called **multipliers**.

To estimate the three contributions, we build an input-output model using an input-output table from the World Input–Output Database (WIOD).[1] An input-output table is built around industries and contains information on inter- and intra-industry purchases. Thus, the table captures the flow of purchases throughout the value chain in an economy – i.e., who buys from whom, and what the wider upstream effects of this are. In this analysis, we follow the standard input–output model assumptions[2] with several additional assumptions listed below.

Current footprint of the pharmaceutical sector in Brazil

We base our estimate of the current footprint of the pharmaceutical industry on the input-output table from WIOD. The pharmaceutical industry defined in WIOD includes innovative medicines, generics/biosimilar medicine, and other types of medicines, e.g. medicines for animals. As we are only interested in the footprint of the innovative and generic industries, we split the total industry into two segments: innovative + generic, and other. This split is based on revenue data of the medicine sales in Brazil in 2019 as reported in ANVISA.[3] The resulting split is 95% for innovative and generic medicines, and 5% for other types of medicine.

The data from WIOD are provided in 2014 USD values, and to transform this into 2021 USD values, we first convert the values into Brazilian reals using the 2014 exchange rate. Second, we correct for Brazilian inflation, and third, we convert back to USD using the 2021 exchange rate.[4] This conversion from 2014 to 2021 values assumes unchanged productivity in the period. Our measure of total GDP in 2021 is 11% lower than the 2021 GDP reported by The World Bank. We accept this difference, as we proxy GDP as gross value added plus taxes based on WIOD tables. This is not exact GDP but a close approximation.

The number of jobs supported by the pharmaceutical industry in Brazil is estimated in the input-output model using 2014 employment data from WIOD. However, we employ direct employment numbers from Interfarma (2022)[5], in which the direct 2021 employment in pharmaceuticals for human use (i.e. the innovative and generic and biosimilar industry) is reported. The indirect and induced supported number of jobs is calculated by applying the indirect and induced multipliers from the input-output model on direct employment.

Realizing Brazil's strategic potential

When calculating the size of Brazil's strategic potential, we apply assumptions and parameters to the input-output model showing the current situation. We use the following parameters and assumptions:

We assume that the direct pharmaceutical industry in Brazil could reach a share of 0.7% of GDP if Brazil were to reach its strategic potential. 0.7% of GDP is the average size of the industry in Germany and the United Kingdom. We estimate that the pharmaceutical industry in Brazil currently accounts for 0.4% of GDP, implying that the direct effect of the pharmaceutical industry in Brazil could increase by 54%. This is an instantaneous effect in which we, crudely, assume that no other sector in the economy will grow alongside. To estimate the indirect and induced multipliers in the strategic potential scenario, we set up input–output models for both Germany and the United Kingdom.[6] We do so to get an estimate of the economic footprint and multipliers of the pharmaceutical industry in markets that have a more developed pharmaceutical industry.

The multipliers from the German and British footprint analyses are not used directly in our model of Brazil's strategic potential, as the trade patterns in European countries and Brazil differs significantly; in Germany and the United Kingdom, the pharmaceutical sector on average imports 32% of its inputs, whereas the corresponding share is 13% in Brazil. This difference in import shares implies that the indirect multiplier in Brazil is larger than in Europe, as more inputs are produced nationally instead of imported. Using multipliers from the German and British models would therefore underestimate the impact in Brazil due to the differences in trade patterns.

To correct this difference in import patterns, we perform the input–output analyses for Germany and the United Kingdom changing the industries' import share such that we get a 'synthetic' Germany and a 'synthetic' United Kingdom with import shares of 13% in the pharmaceutical sector like Brazil.[7] That way, we get an estimate of the indirect and induced multipliers in the strategic potential scenario while taking the differences in trade patterns into account.

In theory, when less is imported, more inputs must be produced domestically all else equal. For simplicity, we do not alter output, wages, or employment in any other sector, as sensitivity checks show that the effect is negligible.

Notes: 1) World Input-Output database (WIOD). / 2) Standard assumptions of an input-output model are that it is a static model implying no constraints on capital or labour, and that the model does not clear and there are no price effects. In addition, an input-output model uses sector averages for interregional purchases, number of jobs, etc. Impacts are measured linearly from the current economic situation. / 3) ANVISA (2021). / 4) The 2014 exchange rate follows from WIOD (see note 1). Brazilian inflation is captured in the OECD consumer price indices (CPI), see link. For the 2021 exchange rate, the average exchange rate for Brazilian Reals to US Dollars in 2021 is used, see link. / 5) Interfarma (2022). / 6) The input-output analyses for Germany and the United Kingdom are also based on input-output tables from WIOD. / 7) This is done by scaling the domestic inputs and changing imports correspondingly to ensure unchanged outputs.

Footprint analysis using input–output modelling (2/2)

For GDP, we arrive at an average indirect multiplier of 1.66 and an induced multiplier of 1.80. The estimated multipliers are multiplied by the marginal direct effect, i.e., the 54%, as well as the current industry to estimate the indirect and induced effect in the strategic potential scenario.

Effect on employment in the pharmaceutical industry

As for GDP, we estimate the effect on the number of jobs supported by the pharmaceutical industry using the input–output model. Again, we use the multipliers to estimate the current footprint in the pharmaceutical industry. All figures for the number of jobs supported by the pharmaceutical industry are reported as a sum of the innovative and generic industries, and not split into the two. This is due to a lack of data on the employment split between the two sub-industries.

To estimate the impact on the number of jobs supported in the strategic potential scenario, we start from the increase in GDP of 54% (see previous page). However, we do not assume that an increase in GDP leads to a proportional increase in the number of jobs supported due to economies of scale and increased productivity. Rather, we assume that an increase in GDP of 1% leads to an increase in the number of jobs supported by 0.8%.[1] This assumption is important, as the impact on GDP in the strategic potential scenario is driven by an increase in the size of the innovative industry, which is characterised by relatively more productive and high-paid jobs than the generic and biosimilar industry. The potential indirect and induced effects for employment are again computed by the average German and British effects; with an indirect multiplier of 2.18 and an induced multiplier of 2.55.

Common for both the potential GDP effect and the number of jobs supported is that the strategic potential shows what Brazil might achieve if the ecosystem in the pharmaceutical sector becomes one of the world's leading. A transformation to such an ecosystem will take many years, and the calculation is therefore a best guess as to what Brazil could achieve if the strategic potential is realised.

Notes: 1) Based on PwC (2009).

APPENDIX C
RESULTS

Results
SCM – availability of innovative medicine

Availability of innovative medicines – evidence from Taiwan

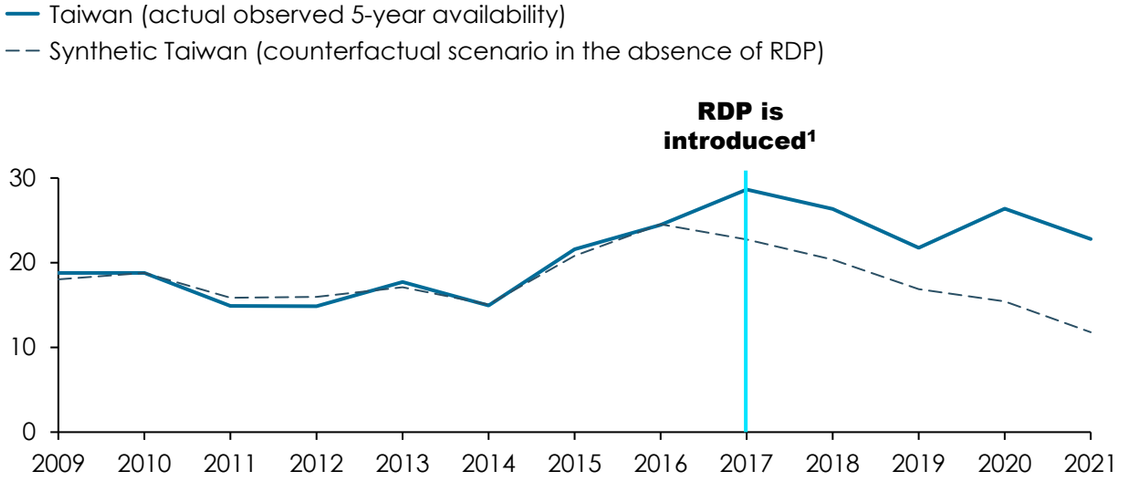
We use information on Taiwan to estimate the effect of RDP on the availability of innovative medicines, as we do not have data on both availability and introduction of RDP from other markets. Evidence from Taiwan shows that RDP increases the average 5-year availability of innovative medicines by 8.2 percentage points per year, see Figure A.8. We estimate the effect using the following model specification:

$$(6)\ \ln(y5\_avail) = \ln(y5\_avail)_{2009} + \ln(y5\_avail)_{2010} + \ln(y5\_avail)_{2011} + \ln(y5\_avail)_{2012} + \ln(y5\_avail)_{2013} + \ln(y5\_avail)_{2014} + \ln(y5\_avail)_{2015} + \ln(y5\_avail)_{2016} + \ln(GDP\_capita),$$

where $y5\_avail$ is the variable for availability of new innovative medicines and GDP_capita is GDP per capita in PPP adjusted 2020 values.

The markets included in the donor pool are all markets with data on availability in which a similar change did not happen in the same period. We show the outcomes of the analysis in Figure A.8.

Figure A.8. Availability of innovative medicines in Taiwan
Availability in percent of new innovative medicines



Description	Availability analysis
Average effect of RDP on availability	+8.2 percentage points per year between 2018 and 2021
Placebo effect rank	3 out of 16
Estimated p-value	0.19
Factors controlled for	GDP per capita and log to 5-year availability in pre-treatment years, i.e., 2009-2016
Markets in donor pool	Belarus, Brazil, Egypt, Hong Kong, Indonesia, India, Korea, Lebanon, Mexico, Philippines, Singapore, Serbia, Thailand, Vietnam, and South Africa

Notes: Based on synthetic control method. / 1) Ministry of Health and Welfare, Taiwan (2017, 2018), see link and link. Implemented in 2017.
Source: Copenhagen Economics based on data from IQVIA, World Bank, WHO, WGI, and National Statistics, R.O.C. (Taiwan).

Results
SCM – healthcare expenditures (1/2)

When using the synthetic control method to estimate the effect of RDP on healthcare expenditure, data allow us to run the estimation on five markets: Canada, Chile, Japan, Taiwan, and Croatia.

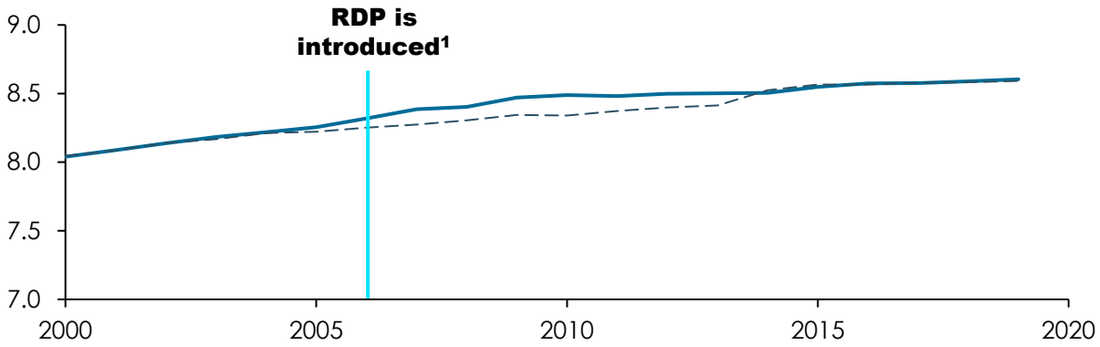
We use the following specification to estimate the effect of RDP on healthcare expenditures:

$$(7)\ \ln(healthcare\ exp) = pre - treatment\ levels\ of \ln(healthcare\_exp) + \ln(GDP\_capita) + share\ of\ population\ aged\ 65 +.$$

We show the outcome of these analyses in Figures A.9-A.13 on this and the next page.

Figure A.9. Healthcare expenditure in Canada

Log healthcare expenditure per capita, PPP-adjusted, constant 2020 values

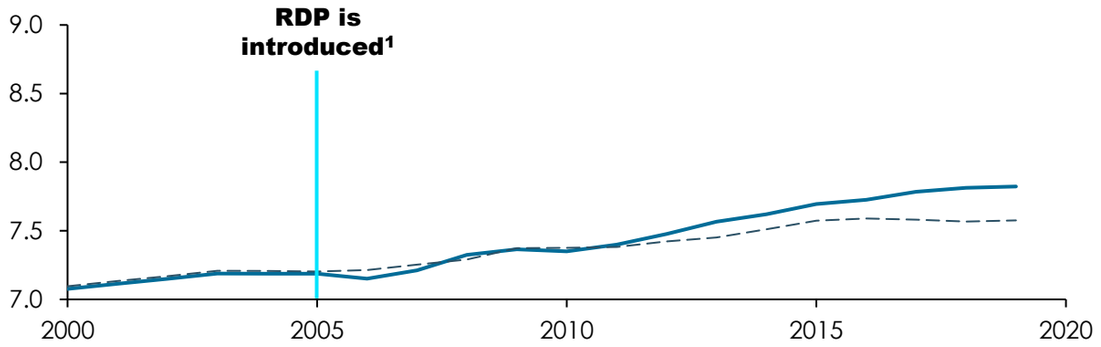


Description	Healthcare expenditure analysis
Average effect of RDP on healthcare expenditure	+12% per year in the years 2007-2013
Placebo effect rank	41 out of 51
Estimated p-value	0.80
Factors controlled for	GDP per capita, share of population aged 65+ and log healthcare expenditure in pre-treatment years, i.e., 2000-2005.
Markets in donor pool	See Table A2

Notes: Based on synthetic control method. / 1) 2006, 8 years.
Source: Copenhagen Economics based on data from IQVIA, World Bank, WHO, and WGI.

Figure A.10. Healthcare expenditure in Chile

Log healthcare expenditure per capita, PPP-adjusted, constant 2020 values

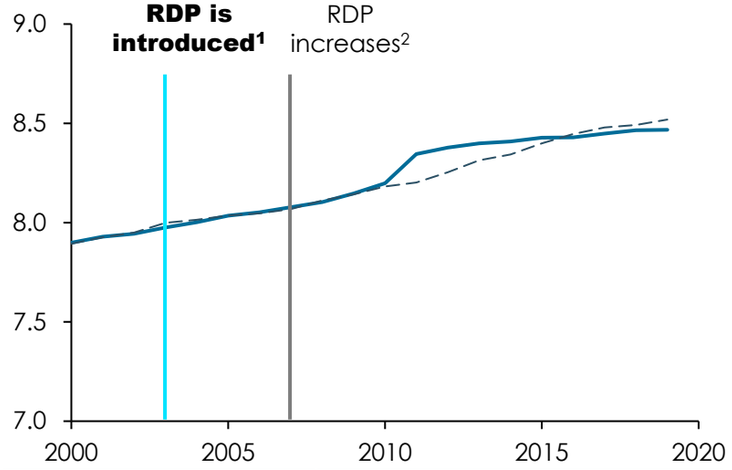


Description	Healthcare expenditure analysis
Average effect of RDP on healthcare expenditure	+15% per year in the years 2011-2019
Placebo effect rank	12 out of 51
Estimated p-value	0.24
Factors controlled for	GDP per capita, share of population aged 65+ and log healthcare expenditure in pre-treatment years, i.e., 2000-2004.
Markets in donor pool	See Table A2

Notes: Based on synthetic control method. / 1) 2005, 5 years.
Source: Copenhagen Economics based on data from IQVIA, World Bank, WHO, and WGI.

Results
SCM – healthcare expenditures (2/2)

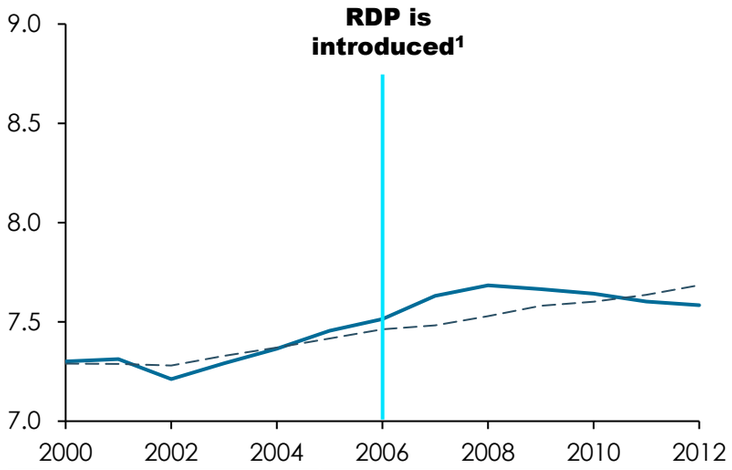
Figure A.11. Healthcare expenditure in Japan
Log healthcare expenditure per capita, PPP-adjusted, constant 2020 values



Description	Healthcare exp. analysis
Average effect of RDP on healthcare expenditure	+8% per year in the years 2010-2015
Placebo effect rank	4 out of 12
Estimated p-value	0.33
Factors controlled for	GDP per capita, share of the population aged 65+ and log healthcare expenditure in pre-treatment years, i.e., 2000-2002
Markets in donor pool	Australia, Belarus, Brazil, Switzerland, Egypt, Indonesia, India, Mexico, Singapore, Thailand, and Vietnam

Notes: Based on synthetic control method. / 1) 2003, 6 years. / 2) 2007, to 8 years.
Source: Copenhagen Economics based on data from IQVIA, World Bank, WHO, and WGI.

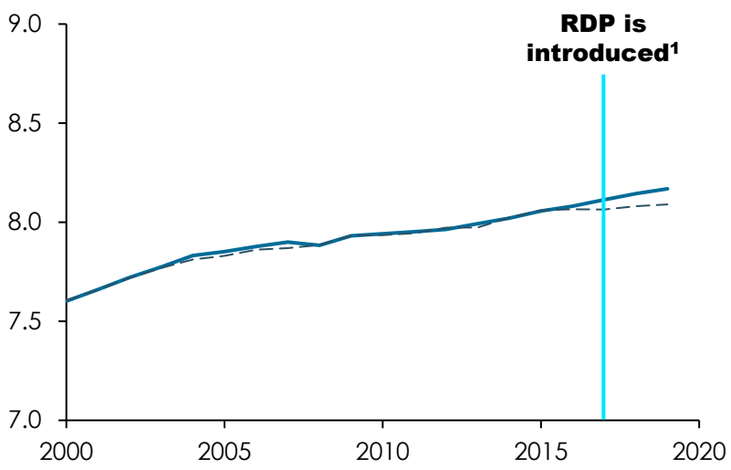
Figure A.12. Healthcare exp. in Croatia
Log healthcare expenditure per capita, PPP-adjusted, constant 2020 values



Description	Healthcare exp. analysis
Average effect of RDP on healthcare expenditure	+11% per year in the years 2007-2010
Placebo effect rank	35 out of 51
Estimated p-value	0.68
Factors controlled for	GDP per capita, share of the population aged 65+ and log healthcare expenditure in pre-treatment years, i.e., 2000-2005
Markets in donor pool	See Table A.2

Notes: Based on synthetic control method. / 1) 2006, 6 years.
Source: Copenhagen Economics based on data from IQVIA, World Bank, WHO, and WGI.

Figure A.13. Healthcare exp. in Taiwan
Log healthcare expenditure per capita, PPP-adjusted, constant 2020 values



Description	Healthcare exp. analysis
Average effect of RDP on healthcare expenditure	+7% per year in the years 2018-2019
Placebo effect rank	3 out of 31²
Estimated p-value	0.10
Factors controlled for	GDP per capita, share of the population aged 65+ and log healthcare expenditure in pre-treatment years, i.e., 2000-2016
Markets in donor pool	See Table A.2

Notes: Based on synthetic control method. / 1) 2017, 5 years. / 2) Fewer markets are included as intervention happened relatively recently.
Source: Copenhagen Economics based on data from IQVIA, World Bank, WHO, and WGI.

Results
SCM – clinical trials (1/2)

When using the synthetic control method to estimate the effect of RDP on clinical trials, data again allow us to run the estimation on five markets: Canada, Chile, Japan, Taiwan, and Croatia.

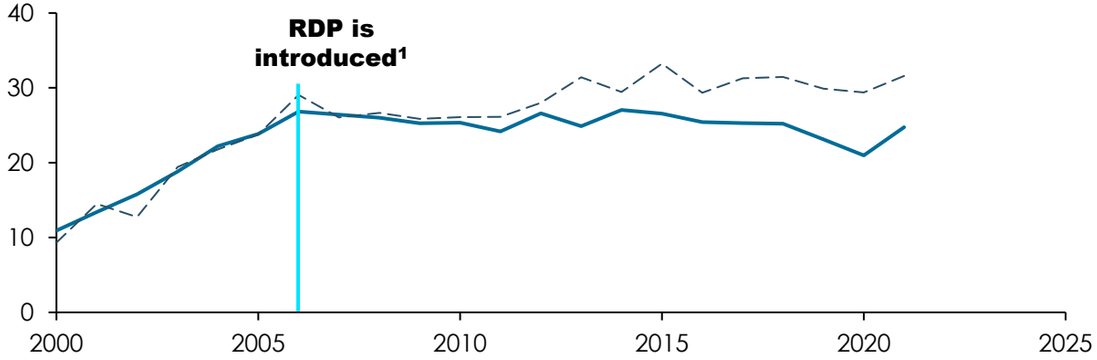
We use the following specification to estimate the effect of RDP on clinical trials:

(8) $\ln(clinical\ trials\ per\ million\ capita) = pre - treatment\ levels\ of \ln(clinical\ trials\ per\ million\ capita) + \ln(GDP\ per\ capita)$.

We show the outcome of these analyses in Figures A.14-A.18 on this and the next page.

Figure A.14. Clinical trials in Canada

Number of clinical trials per million capita

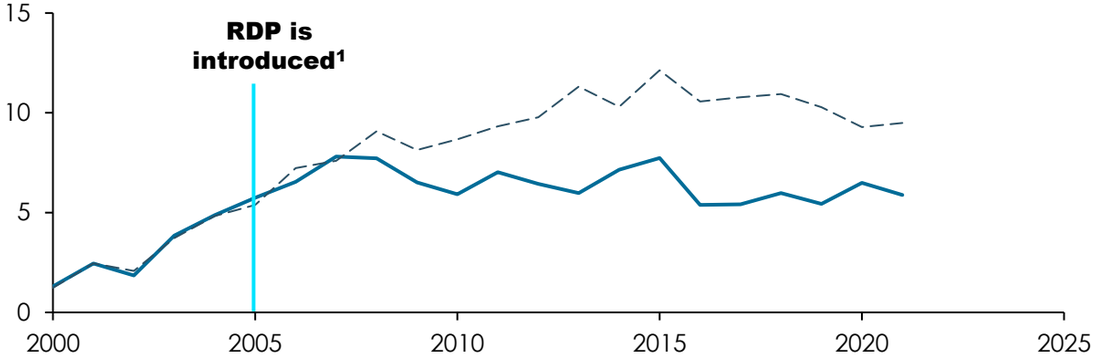


Description	Clinical trials analysis
Average effect of RDP on clinical trials	-5.2 clinical trials per million capita per year in the years 2011-2021.
Placebo effect rank	13 out of 17
Estimated p-value	0.76
Factors controlled for	GDP per capita, and clinical trials per million capita in pre-treatment years, i.e., 2000-2005
Markets in donor pool	See Table A.2

Notes: Based on synthetic control method. / 1) 2006, 8 years.
Source: Copenhagen Economics based on data from IQVIA, World Bank, WHO, and WGI.

Figure A.15. Clinical trials in Chile

Number of clinical trials per million capita

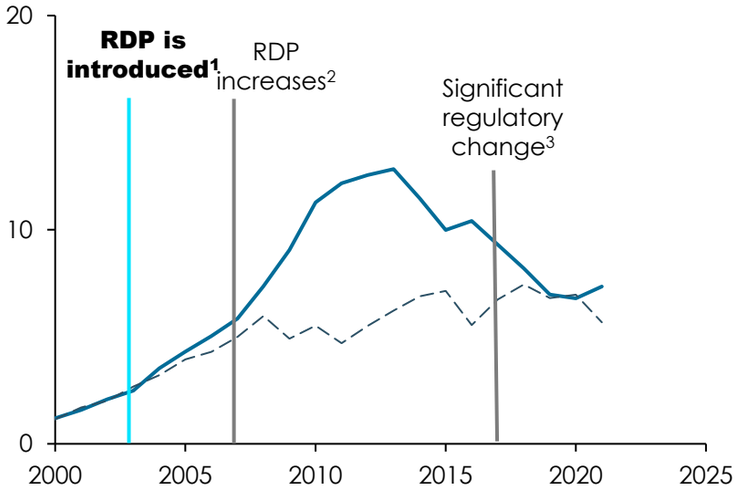


Description	Clinical trials analysis
Average effect of RDP on clinical trials	-3.6 clinical trials per million capita per year in the years 2008-2021.
Placebo effect rank	7 out of 17
Estimated p-value	0.41
Factors controlled for	GDP per capita, and clinical trials per million capita in pre-treatment years, i.e., 2000-2004
Markets in donor pool	See Table A.2

Notes: Based on synthetic control method. / 1) 2005, 5 years.
Source: Copenhagen Economics based on data from IQVIA, World Bank, WHO, and WGI.

Results
SCM – clinical trials (2/2)

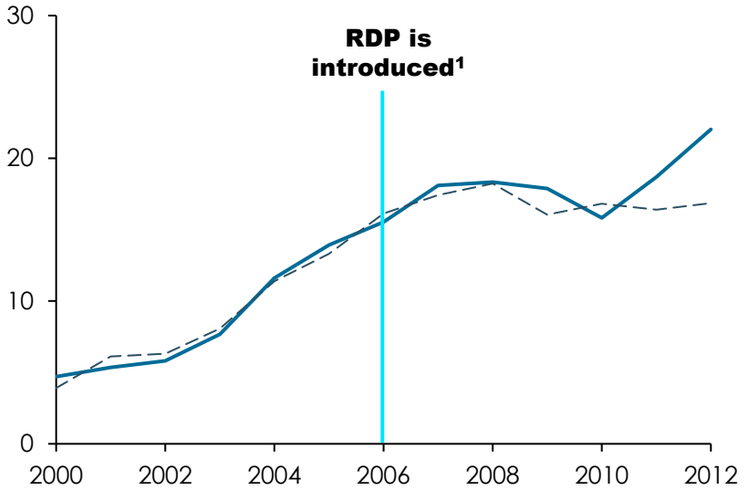
Figure A.16. Clinical trials in Japan
Number of clinical trials per million capita



Description	Clinical trials analysis
Average effect of RDP on clinical trials	3.5 clinical trials per million capita per year in the years 2004-2017.
Placebo effect rank	4 out of 17
Estimated p-value	0.24
Factors controlled for	GDP per capita, and clinical trials per million capita in pre-treatment years, i.e., 2000-2002
Markets in donor pool	See Table A.2

Notes: Based on synthetic control method. / 1) 2003, 6 years. / 2) 2007, to 8 years. / 3) Nakamura and Shibata (2020). Implementation of the Clinical Trials Act. Cases leading to change happened in 2013-2014.
Source: Copenhagen Economics based on data from IQVIA, World Bank, WHO, and WGI.

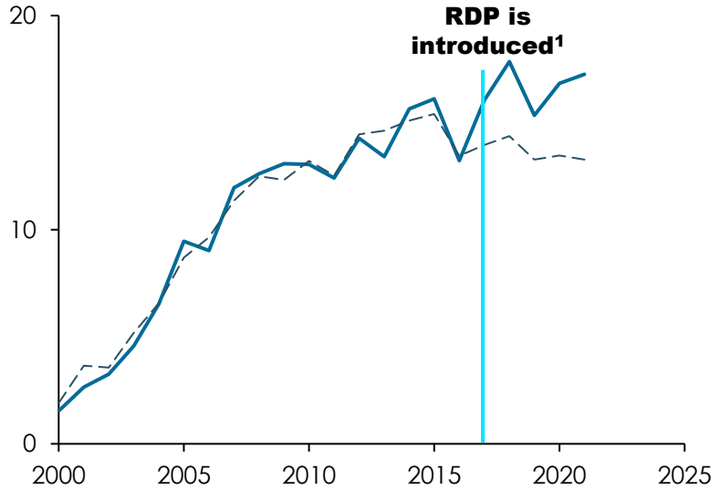
Figure A.17. Clinical trials in Croatia
Number of clinical trials per million capita



Description	Clinical trials analysis
Average effect of RDP on clinical trials	1.5 clinical trials per million capita per year in the years 2007-2012.
Placebo effect rank	8 out of 17
Estimated p-value	0.44
Factors controlled for	GDP per capita, and clinical trials per million capita in pre-treatment years, i.e., 2000-2005
Markets in donor pool	See Table A.2

Notes: Based on synthetic control method./ 1) 2006, 6 years.
Source: Copenhagen Economics based on data from IQVIA, World Bank, WHO, and WGI.

Figure A.18. Clinical trials in Taiwan
Number of clinical trials per million capita



Description	Clinical trials analysis
Average effect of RDP on clinical trials	3.2 clinical trials per million capita per year in the years 2018-2021.
Placebo effect rank	5 out of 15²
Estimated p-value	0.33
Factors controlled for	GDP per capita, and clinical trials per million capita in pre-treatment years, i.e., 2000-2002
Markets in donor pool	See Table A.2

Notes: Based on synthetic control method. / 1) 2017, 5 years. / 2) Fewer markets are included as intervention happens relatively recently.
Source: Copenhagen Economics based on data from IQVIA, World Bank, WHO, and WGI.

Results
DPD with system GMM - availability

Table A.4. The link between RDP and availability

Percentage point (pp) increase in availability of new innovative medicines associated with RDP

Dynamic panel data model with system generalised method of moments (GMM) (1/2)	
Variable	**Availability[1]**
RDP	**0.0918**** (se = 0.0376) [p = 0.018]
$Availability_{t-1}$	0.8075*** (se = 0.1597) [p = 0.000]
$Availability_{t-2}$	-0.1602 (se = 0.1764) [p = 0.368]
Log of GDP per capita[2]	0.1995* (se = 0.0999) [p = 0.051]
Log of GDP per $capita_{t-1}$	-0.2714** (se = 0.1037) [p = 0.012]
Log of healthcare per capita	0.1815 (se = 0.1009) [p = 0.078]
Log of healthcare per $capita_{t-1}$	-0.1138 (se = 0.0797) [p = 0.160]
Share of population aged 65+	0.0139 (se = 0.0618) [p = 0.824]
Share of population aged $65+_{t-1}$	-0.0165 (se = 0.0625) [p = 0.793]
Log of population in million	0.6420 (se = 0.7335) [p = 0.385]
Log of population in $million_{t-1}$	-0.6535 (se = 0.7120) [p = 0.383]
Year 2011	-0.0021 (se = 0.0139) [p = 0.880]
Year 2012	0.0067 (se = 0.0142) [p = 0.642]
Year 2013	0.0205 (se = 0.0146) [p = 0.165]

…

Dynamic panel data model with system generalised method of moments (GMM) (2/2)	
Variable	**Availability[1]**
Year 2014	0.0111 (se = 0.01421) [p = 0.439]
Year 2015	0.0497*** (se = 0.0131) [p = 0.000]
Year 2016	0.0376*** (se = 0.0125) [p = 0.004]
Year 2017	0.0270*** (se = 0.0073) [p = 0.000]
Year 2019	-0.0062 (se = 0.0078) [p = 0.431]
Constant	0.2818 (se = 0.5854) [p = 0.632]
N (markets)[3]	53
T (years)	11 (2009-2019)
AR(1)[4]	-3.1191*** [p = 0.0018]
AR(2)[4]	0.7547 [p = 0.4504]
AR(3)[4]	-0.1598 [p = 0.8731]
Sargan[5]	74.4658*** [p = 0.0004]
Hansen[5]	41.4619 [p = 0.3222]

Notes: Significant at the 10% (*), 5% (**) and 1% (***) level. Standard errors in parentheses and p-values in brackets. / 1) Percentage of unique new and innovative molecules (new active substances that have been approved by major global regulatory bodies) launched in a market compared to all new and innovative molecules launched globally, within a 5-year lookback period (encompasses medicines launched locally (numerator) and globally (denominator) between the year of record and 5 years prior). / 2) Full names of control variables are log of GDP per capita (purchasing power parity (PPP) adjusted) in constant 2020 values, log of healthcare expenditures per capita (PPP-adjusted) in constant 2020 values, share of population aged 65+, log of population in million, and year dummies. / 3) See Table A.2 in Appendix A for an outline of markets included. The panel is strongly balanced. / 4) AR(#) are Arellano-Bond tests for AR(#) in first differences. / 5) Sargan and Hansen tests are tests of overidentifying restrictions. Difference-in-Hansen. tests hold. Source: Copenhagen Economics based on data from IQVIA, WHO and World Bank.

Results
DPD with system GMM – healthcare expenditures

Table A.5. The link between RDP and healthcare expenditures
Percentage increase in healthcare expenditures associated with RDP

Dynamic panel data model with system generalised method of moments (GMM) (1/2)	
Variable	**Healthcare expenditures[1]**
RDP	**0.1414*** (se = 0.0815) [p = 0.0887]
Healthcare expenditures$_{t-1}$	0.6007** (se = 0.2875) [p = 0.0416]
Healthcare expenditures$_{t-2}$	0.0222 (se = 0.2589) [p = 0.9320]
Log of GDP per capita[2]	0.3275* (se = 0.1702) [p = 0.060]
Share of population aged 65+	0.01670* (se = 0.0095) [p = 0.080]
Log of population in million	0.0162 (se = 0.0154) [p = 0.297]
Year 2002	0.0772** (se = 0.0317) [p = 0.018]
Year 2003	0.0768** (se = 0.0293) [p = 0.011]
Year 2004	0.0343 (se = 0.0218) [p = 0.121]
Year 2005	0.0120 (se = 0.0168) [p = 0.238]
Year 2006	0.0052 (se = 0.0158) [p = 0.745]
Year 2007	0.0032 (se = 0.0122) [p = 0.791]
Year 2008	0.0140 (se = 0.0114) [p = 0.223]
Year 2009	0.0426** (se = 0.0183) [p = 0.024]
Year 2010	0.0106 (se = 0.0192) [p = 0.584]
Year 2011	-0.0032 (se = 0.0154) [p = 0.838]

…

Dynamic panel data model with system generalised method of moments (GMM) (2/2)	
Variable	**Healthcare expenditures[1]**
Year 2012	0.0045 (se = 0.0127) [p = 0.725]
Year 2013	0.0012 (se = 0.0107) [p = 0.914]
Year 2014	0.0115 (se = 0.0076) [p = 0.138]
Year 2015	0.0319*** (se = 0.0078) [p = 0.000]
Year 2016	0.0229*** (se = 0.0076) [p = 0.004]
Year 2018	-0.0056 (se = 0.0072) [p = 0.445]
Year 2019	0.0046 (se = 0.0091) [p = 0.613]
Constant	-0.8707 (se = 0.7877) [p = 0.274]
N (markets)[3]	53
T (years)	20 (2000-2019)
AR(1)[4]	-1.1403 [p = 0.2542]
AR(2)[4]	0.0570 [p = 0.9545]
AR(3)[4]	0.6439 [p = 0.5197]
Sargan[5]	30.3184*** [p = 0.0069]
Hansen[5]	16.9258 [p = 0.2602]

Notes: Significant at the 10% (*), 5% (**) and 1% (***) level. Standard errors in parentheses and p-values in brackets. / 1) Log of healthcare expenditures in PPP-adjusted constant 2020 values. / 2) Full names of control variables are log of GDP per capita (PPP-adjusted) in constant 2020 values, share of population aged 65 +, log of population in million, and year dummies. In addition, first and second lag of log of healthcare expenditures are included. / 3) See Table A.2 in Appendix A for an outline of markets included. The panel is strongly balanced. / 4) AR(#) are Arellano-Bond tests for AR(#) in first differences. / 5) Sargan and Hansen tests are tests of overidentifying restrictions. Difference-in-Hansen tests hold.
Source: Copenhagen Economics based on data from IQVIA, WHO and World Bank.

Results
FE with AR(1) – healthcare expenditures

Table A.6. The link between RDP and healthcare expenditures
Percentage increase in healthcare expenditures associated with RDP

Fixed effects linear models with an autoregressive (AR(1)) disturbance	
Variable	**Healthcare expenditures[1]**
RDP	**0.009987** (se = 0.0117[4]) [p = 0.394[4]]
Log of GDP per capita[2]	-0.0677* (se = 0.0376) [p = 0.072]
Share of population aged 65+	0.0029 (se = 0.0125) [p = 0.817]
Log of population in million	0.3797 (se = 2372) [p = 0.110]
Year 2000	1.3903*** (se = 0.4226) [p = 0.001]
Year 2001	1.2219*** (se = 0.3715) [p = 0.001]
Year 2002	1.0584*** (se = 0.3256) [p = 0.001]
Year 2003	0.9277*** (se = 0.2844) [p = 0.001]
Year 2004	0.7985*** (se = 0.2474) [p = 0.001]
Year 2005	0.6928*** (se = 0.2143) [p = 0.001]
Year 2006	0.5934*** (se = 0.1847) [p = 0.001]
Year 2007	0.5171*** (se = 0.1581) [p = 0.001]
Year 2008	0.4443*** (se = 0.1343) [p = 0.001]
Year 2009	0.3755*** (se = 0.1128) [p = 0.001]
Year 2010	0.2967*** (se = 0.0941) [p = 0.002]

…

Panel B. Fixed effects linear models with an autoregressive (AR(1)) disturbance	
Variable	**Healthcare expenditures[1]**
Year 2011	0.2229*** (se = 0.0774) [p = 0.004]
Year 2012	0.1698*** (se = 0.0627) [p = 0.007]
Year 2013	0.1237** (se = 0.0497) [p = 0.013]
Year 2014	0.0851** (se = 0.0381) [p = 0.026]
Year 2015	0.0432** (se = 0.0278) [p = 0.016]
Year 2016	0.0432** (se = 0.01852) [p = 0.020]
Year 2017	0.0152 (se = 0.0101) [p = 0.132]
Constant	7.6565*** (se = 0.0947) [p = 0.000]
N (markets)	53
T (years)	20 (2000-2019)
Autoregressive coef.[3]	0.9011

Notes: Significant at the 10% (*), 5% (**) and 1% (***) level. Standard errors in parentheses and p-values in brackets. / 1) Log of healthcare expenditures in PPP-adjusted constant 2020 values. / 2) Full names of control variables are log of GDP per capita (PPP-adjusted) in constant 2020 values, share of population aged 65 +, log of population in million, and year dummies. / 3) See Appendix B for further description of our interpretation of the autoregressive coefficient. / 4) Note that the autocorrelation implies that the standard errors are biased (but the point estimate is still unbiased), which makes hypothesis testing invalid. We have estimated a simple fixed effects model with clustered standard errors, which allows for valid inference even with autocorrelation This yields a p-value for of 0.426 for the point estimate of the association between RDP and healthcare expenditures, which supports a statistically insignificant long-run effect of RDP on healthcare expenditures.
Source: Copenhagen Economics based on data from IQVIA, WHO and World Bank.

Results
DPD with system GMM – clinical trials

Table A.7. The link between RDP and clinical trials
Increase in clinical trials per million capita associated with RDP

Dynamic panel data model with system generalised method of moments (GMM) (1/2)	
Variable	**Clinical trials[1]**
RDP	**2.8656*** (se = 1.4789) [p = 0.0581]
Clinical trials$_{t-1}$	0.8634*** (se = 0.1276) [p = 0.0000]
Clinical trials$_{t-2}$	0.0971 (se = 0.1327) [p = 0.4677]
Log of GDP per capita[2]	1.6801 (se = 8.1418) [p = 0.837]
Log of GDP per capita$_{t-1}$	-2.2278 (se = 7.4164) [p = 0.765]
Log of healthcare per capita	0.0201 (se = 8.5652) [p = 0.998]
Log of healthcare per capita$_{t-1}$	0.2025 (se = 8.4784) [p = 0.981]
Log of physicians per 1,000	3.2652 (se = 5.6063) [p = 0.563]
Log of physicians per 1,000$_{t-1}$	-3.8770 (se = 5.8148) [p = 0.508]
Year 2002	1.2965 (se = 1.1149) [p = 0.250]
Year 2003	3.7296*** (se = 1.0436) [p = 0.001]
Year 2004	4.2434*** (se = 1.4003) [p = 0.004]
Year 2005	1.4977 (se = 1.1128) [p = 0.184]
Year 2006	3.6369*** (se = 0.9430) [p = 0.000]
Year 2007	0.6884 (se = 0.9767) [p = 0.484]
Year 2008	1.1431 (se = 0.8696) [p = 0.106]
Year 2009	0.5399 (se = 0.9527) [p = 0.573]

…

Dynamic panel data model with system generalised method of moments (GMM) (2/2)	
Variable	**Clinical trials[1]**
Year 2011	1.4154** (se = 0.6678) [p = 0.039]
Year 2012	1.9663** (se = 0.8889) [p = 0.031]
Year 2013	0.4085 (se = 0.7653) [p = 0.596]
Year 2014	0.7991 (se = 0.9134) [p = 0.385]
Year 2015	2.2016*** (se = 0.7816) [p = 0.007]
Year 2016	-1.4069 (se = 1.0219) [p = 0.174]
Year 2017	0.8543 (se = 0.6994) [p = 0.227]
Year 2018	0.6119 (se = 0.8549) [p = 0.477]
Constant	2.3412 (se = 15.7552) [p = 0.882]
N (markets)[3]	54
T (years)	19 (2000-2018)
AR(1)[4]	-2.7415*** [p = 0.0061]
AR(2)[4]	1.6106 [p = 0.1073]
AR(3)[4]	-0.8287 [p = 0.4073]
Sargan[5]	93.8441*** [p = 0.0071]
Hansen[5]	39.1098 [p = 0.9922]

Notes: Significant at the 10% (*), 5% (**) and 1% (***) level. Standard errors in parentheses and p-values in brackets. / 1) Number of clinical trials per million capita. / 2) Full names of control variables are log of GDP per capita (purchasing power parity (PPP) adjusted) in constant 2020 values, log of healthcare expenditures per capita (PPP-adjusted) in constant 2020 values, log of physicians per 1,000 inhabitants, and year dummies. / 3) See Table A.2 in Appendix A for an outline of markets included. The panel is unbalanced. / 4) AR(#) are Arellano-Bond tests for AR(#) in first differences. / 5) Sargan and Hansen tests are tests of overidentifying restrictions. Difference-in-Hansen tests hold.
Source: Copenhagen Economics based on data from IQVIA, WHO and World Bank.

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Regulatory data protection for pharmaceuticals

How adopting regulatory data protection will impact patients, industry, and Brazilian society

Authors

Christian Jervelund, Partner
Emil Löfroth, Managing Economist
Nikolaj Siersbæk, Senior Economist, Ph.D.
Malwina Mejer, Senior Economist, Ph.D.
Elisa Pau, Economist
Lærke Kilsdal, Economist

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About the study

This study was conducted between December 2022 and February 2023. All analyses were carried out by Copenhagen Economics. All conclusions are by Copenhagen Economics.

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