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Pharmaceutical Net Price Transparency across European Markets: Insights from a Multi-Agent Simulation Model

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About the Vlerick Healthcare Management Centre

The Vlerick Healthcare Management Centre (HMC), led by professor Walter Van Dyck, is a European, Brussels-based non-profit independent think tank and education provider advancing innovative and actionable management and policy solutions in the healthcare and life sciences fields. The Vlerick HMC is fully owned by Vlerick Business School, a Public Utility Foundation, and funded by grants from public institutions and private organisations.

This Vlerick Policy Paper is the result of a joint research project conducted with professor Massimo Riccaboni of IMT School for Advanced Studies Lucca, Italy

About IMT School for Advanced Studies Lucca



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The IMT School for Advanced Studies Lucca is a Public University School for Higher Education and Research with a special statute that focuses on the analysis of economic, societal, technological and cultural systems.

Within the Institute, professor Massimo Riccaboni leads AXES, The Laboratory for the Analysis of Complex Economic Systems, which is a research unit whose work spans different fields of economics: from economic theory to applied econometrics, from international economics to political economy, from spatial and urban economics to industrial organization and business economics. They all share a common interest in original economic research that provides information critical to policymaking with a problem-solving approach.

In their research they are keen to incorporate skills and tools from different disciplines, including graph theory, the physics of complex systems, data science or political science. In fact, they believe that a modern approach in economics requires considering the solution of economic problems more important than sticking to academic disciplines. Under such a multidisciplinary perspective, they strive to utilize the most recent developments in big data and machine learning, seeking to combine them with more traditional econometric approaches.



This multi-agent simulation model-based research on net price transparency in Europe conducted by Vlerick HMC and IMT Lucca as Principal Investigators and reported on in this Vlerick Policy Paper also informed the study cited by Bentata et al (2020).

Executive Summary

In innovative drug markets the widespread practice across the EU of country-specific confidential agreements reached between national payers and innovative pharmaceutical manufacturers continues to be a highly disputed basis for pharmaceutical health policy making. With pharmaceutical health policy striving for fair and sustainable pricing under increasing budgetary pressures, public stakeholders are more and more willing to be involved in transparent access decision-making related to novel medicines, considered to be a societal good. Full net price transparency is believed by many to promote price competition and to increase equity by making presently unaffordable pharmaceutical products accessible to patients in lower-income markets. To investigate the viability of a net price transparency (NPT) system we develop and analyse a multi-agent model representing the European country-level situation to conduct counterfactual analyses of various NPT systems. In line with previous recent NPT research in other geographical, regulatory and market contexts, we find that a full NPT system encompassing higher- and lower-income EU countries would not be viable. This while, counterintuitively and acting as rational economic agents, middle- and lower-income countries would not be deciding to join and give up their confidential agreement system with the pharmaceutical industry. Also, a full NPT system would be seen to be unjust while violating Ramsey pricing and distributive justice principles. Maximally, a partial price transparency system could be a viable solution if entailing only the group of high-income countries including UK and Germany committing to NPT, leaving all other countries free to opt for confidential discounts. Viability of this solution is contingent upon UK or Germany accepting a higher price than they could get in their present confidential rebate system. Finally, in a dynamic game theoretic analysis, we show that middle- and lower-income countries, might be joining the high-income group later. In any case, a net price transparency system would delay access in middle- to lower-income countries. Hence, we conclude that even a partial transparency system would be a challenging case to reach from a political perspective and it will negatively impact population health improvement by the novel therapy, especially in lower-income countries.

Please cite as;

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This work constitutes the formal modelling component of the encompassing empirical health policy study into the consequences of a net price transparency policy across European markets, to be cited as:

Bentata, P., Czech, M., Greiner, W., Groot, W., Gyger, P., Marques-Gomes, J., Mestre-Ferrandiz, J., Pistollato, M., Riccaboni, M., Ross-Stewart, K., Van Dyck, W., Voncina, L., Wilsdon, T., 2020. The consequences of greater net price transparency for innovative medicines in Europe: Searching for a consensus, Charles River Associates, London.

1. Introduction

Price transparency is currently a heavily debated topic in pharmaceutical markets (Shaw & Mestre-Ferrandiz, 2020) after the resolution of the World Health Assembly in 2019 to “Take appropriate measures to publicly share information on the net prices of health products” (WHO, 2019). In particular, the WHO guideline on country pharmaceutical pricing policies suggests that countries should “Share the net transaction prices of pharmaceutical products with relevant stakeholders, *within and external to the country*” (WHO, 2020, p. 22). Policy interventions by European payers have led to pricing regulations that have taken medicinal markets away from perfect competition.¹ Predominantly monopsonist public payers enter into a bargaining process with innovative pharmaceutical manufacturers, the latter exhibiting monopolist behaviour, at least for their most innovative disease modifying therapies, which are seen to lead to unsustainable prices. However, the evidence that net price transparency (NPT) per se leads to lower prices is extremely limited and the generalizability of results is unclear (WHO, 2020). Two studies of the Single Exit Price programme in South Africa are mentioned in the systemic review of the WHO (2020). A more recent scoping review on this topic (Ahmad et al., 2020) identifies only three studies reporting the outcomes of drug price transparency initiatives (the two studies in South Africa and one more in the Philippines) concluding that “the effect of drug price transparency initiatives on price control is still inconclusive”.

Despite that, price transparency is believed by many to promote price competition and increase equity by making presently unaffordable products accessible to the patients in lower-income countries. Price transparency may sustain competition in fragmented generic drug markets forcing prices to converge to marginal cost (Berdud et al., 2019). Also, transparency can facilitate joint pharmaceutical procurement and the pooling of demand. Finally, in innovative drug markets the widespread practice across the EU of country-specific confidential rebates, as opposed to net price transparency, continues to be a highly disputed basis for pharmaceutical health policy making.² As a result, pharmaceutical health policy is progressively moving from pure value-based pricing to fair and sustainable pricing driving public stakeholders towards willingness to be involved in transparent democratically represented decision-making related to HTA of novel medicines.³

In this paper we contribute to the current debate by investigating the joint effect of NPT and external reference pricing (ERP) schemes in Europe.⁴ Our main focus is on innovative drug pricing since this is by far the most relevant segment of the pharmaceutical markets

¹ In the European Union, the Transparency Directive (EU, 1989) mandates the publication of the list prices of all reimbursable medicines.

² 16th World Congress on Public Health October 2020 – Abstract Round table 6F: What is the evidence for and against price transparency in pharmaceutical pricing and procurement?

³ 16th World Congress on Public Health October 2020 – Abstract Round table 4F: Fair processes and fair pricing: Examining deliberative processes and the role of HTA for UHC.

⁴ On the effect of ERP in Europe see Toumi et al. (2014) and Fontrier et al. (2019).

in terms of sales, innovation, health impact and growth trends.⁵ Therefore, we model the European market as bilateral monopolistic bargaining between manufacturers of in-patent drugs with multiple payers. Our simulation results show that price transparency can have “harmful side effects” (Kyle & Ridley, 2007) providing further evidence about the crucial role of differential pricing in Europe (Towse et al., 2015). When combined with ERP, NPT can increase prices paid in low-income European countries, delay or deter the launch of products in marginal markets. Therefore, low-income countries should be left free to sign confidential agreements to secure lower prices.

The remainder of this work is structured as follows. Section 2 provides some background information on the current debate about the expected impact of NPT among practitioners and in the literature. Section 3 illustrates our methodological approach. Section 4 describes the results of our simulations. Finally, we discuss our findings and their importance, how they contribute to the extant policy debate and possible improvements in Section 5.

2. Net price transparency

In July 2020, we conducted an online survey through SurveyMonkey on NPT among 16 European payers active in 10 European markets (France, Germany, Greece, Italy, Netherlands, Poland, Portugal, Spain, Sweden, UK).⁶

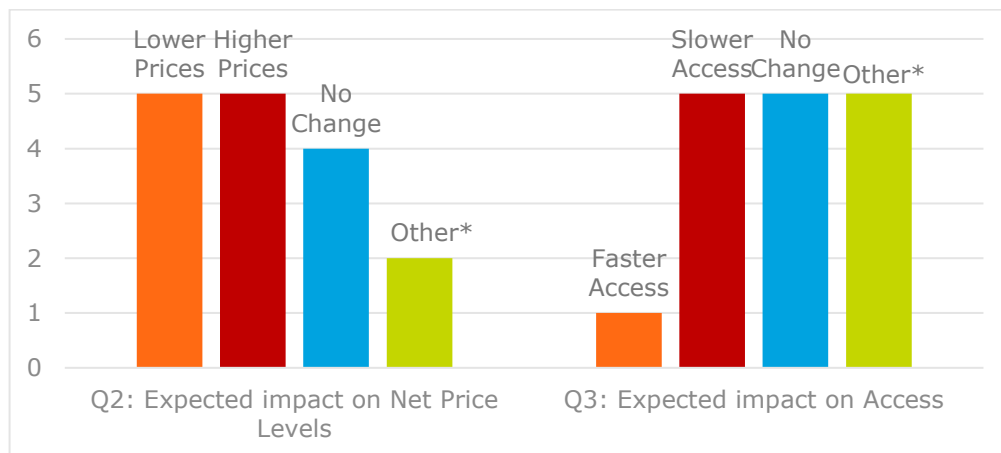


Figure 1: Payer expectations for the impact of greater NPT on net price levels and patient access (n = 16)

*Other: Respondents indicated that they could not predict the outcome or there would be a mix of outcomes (e.g. both higher and lower prices) dependent on current price levels and product characteristics. Source: Bentata et al. (2020)⁷

⁵ In 2018, across the OECD generic markets only make up between 8.9 and 43% of the total pharmaceutical market in terms of estimated value. Similarly, the generic market shares range between 9.1% and 41% in 2019, but only a few countries have reported data (OECD Health Data, last updated on July 1, 2020).

⁶ See Bentata et al. (2020) for a detailed description of the survey’s result.

⁷ Payer Survey. Q2: “What do you expect to happen (i.e. not what you would like to happen) to the prices of innovative medicines in your market, if the level of price transparency is increased in all European markets,

Despite general support to greater NPT by the majority of the payers (10 out of 16 payers), only some of them believe greater NPT would result in lower net prices and many recognise the potentially negative impacts that greater NPT could have on patient access (see Figure 1). Moreover, we found that the majority of payers prefer to observe the net price information of within a restricted group of EU markets similar to their own (Figure 2).

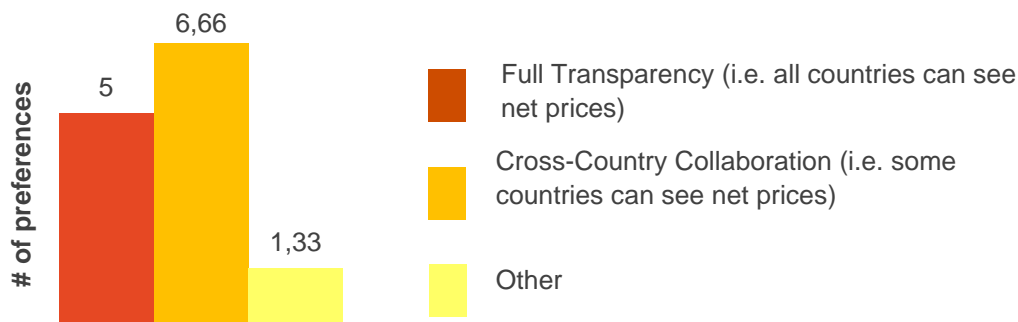


Figure 2: Payer level of interest in the net price information from all European countries or a group of countries*

* The question "Please indicate which of the following methods for increasing price transparency would be most attractive to you?" has been repeated for 3 hypothetical products. Other: respondents indicated a preference for ex-post price transparency.

Source: Bentata et al. (2020)

More interestingly, when we analyze the interest of payers in the net prices of other European markets we notice that, somehow surprisingly, payers in higher-income countries are not interested to know the net prices in lower-income countries, with the only exception of German payers who are interested in the net prices in all other European markets (see Table 1).

To make sense of this preliminary evidence on the interest of European payers to limit NPT to similar countries and their concern for the potential harmful consequences of NPT in terms of higher prices and delayed access in this study we develop a multi-agent model allowing us to simulate the effect a counterfactual NPT policy would have on the net pharmaceutical prices reached in the various EU markets. We took as a starting position the currently –predominantly politically – contested practice of rebates on list prices reached in country-level agreements following confidential negotiations with pharmaceutical manufacturers⁸. When combined with an international reference pricing policy, NPT would imply that the minimum price reached in the total basket of EU

including yours (so the confidential prices negotiated in your market are known to others) and, at the same time, assuming that pharmaceutical companies would strategically react to the disclosure of confidential agreements?". Q3: What do you expect to happen (i.e. not what you would like to happen) to the time to access innovative medicines in your market, if: the level of price transparency is increased in all European markets, including yours (so the confidential prices negotiated in your market are known to others) and, at the same time, assuming that pharmaceutical companies would strategically react to the disclosure of confidential agreements?".

⁸ See among others Gerkens et al (2017).

countries would be made visible for reference in all other countries that then could command this lowest price for the same product across Europe, with some delay depending on the timing of the ERP and the composition of the reference countries selected by member states (Toumi et al., 2014).

Responders' nationality (#)	Mostly interested in the net prices of country:													
	DK	NL	SE	Fi	GB	DE	BE	AT	FR	PL	PT	IT	ES	GR
Denmark (0)		n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
The Netherlands (2)														
Sweden (1)														
Finland (0)														
United Kingdom (2)														
Germany (2)														
Belgium (0)	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.		n.a.	n.a.	n.a.	n.a.	na	n.a.	n.a.
Austria (0)	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.		n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
France (2)														
Poland (1)														
Portugal (1)														
Italy (2)														
Spain (2)														
Greece (1)														

Table 1: Payers' interest in the net price of other European markets by nationality of the payer*⁹

* Level of interest "extremely high" (top level of the Likert scale) are reported in orange.

Such a policy would imply changes in the Bertrand-Nash equilibrium prices reached as a result of the country-level bargaining process taking place. In such bargaining process countries' policymakers choose to trade-off between firm profits and immediate societal welfare. Countries' bargaining power is given by the confidential rebate they are able to get from the pharmaceutical manufacturer quoting a value-based price (VBP).

The microfoundations of bargaining under transparency have been recently studied in the context of pay negotiations in labour markets (Cullen & Pakzad-Hurson, 2020). In their study, Cullen and Pakzad-Hurson found that the employee was not able to negotiate the pay level up to the now transparent desired higher level, while the firm stated that it could not afford to propose this while the employees' peers would immediately command a commensurate pay rise. In contrast, given non-transparency they came to the conclusion that the employee, sceptical of the firm's proposal, might bargain more aggressively. Hence, they conclude that in the labour market context full transparency led to the counterintuitive effect of the firm –not the employee– getting price-setting or bargaining power.

⁹ Payer Survey. Q10; "Assuming that you have not yet started the price negotiation process for Product [X,Y,Z], please indicate your level of interest, for each of the following European markets, in having increased net price transparency for Product [X,Y,Z]. Note: Net Price Transparency can also refer to the details of the agreements put in place that impact the net price, e.g. price-volume agreements". Three hypothetical product profiles have been considered (X, Y and Z).

In the context of hospital purchasing of medical devices another recent empirical study finds that through the same bargaining process mechanism, transparency could have the countervailing effect that suppliers may be “less willing to offer low prices if they know that those prices will then be included in the database and potentially hurt them in subsequent negotiations with other buyers” (Grennan & Swanson, 2020, p. 12), which is also corroborated in other studies they cite (Duggan & Scott Morton, 2006; Grennan, 2013). Their results showed that transparency in the form of access to benchmarking information effectively led to the highest prices falling, most likely among the high-quantity brands, but also to some of the lowest prices to increase, particularly among low-quantity buyers (Grennan & Swanson, 2020).

Finally, in a recent study a structural model of demand and supply for pharmaceuticals in the US and Canada was estimated simulating the impact of a counterfactual international reference pricing rule (Dubois, Gandhi & Vasserman, 2019). This way, Canadian prices obtained through negotiation with the national payer were allowed to act as a price ceiling in the United States. The results of their simulation find a modest decrease in US prices and a substantial increase in Canadian prices, together with modest consumer welfare gains in the US and substantial losses in consumer welfare in Canada. Moreover, they find pharmaceutical profits to increase in net, which counterintuitively shows that net price transparency between the referenced country Canada and the referring country US results in bargaining power to shift from the healthcare system to the firm (Dubois et al., 2019).

The effects demonstrated by their analysis are in addition to the negative impacts that previous work has shown international reference pricing to have on entry in referenced countries (Danzon & Chao, 2000; Danzon, Wang, & Wang, 2005; Maini & Pammolli, 2019). Their findings are in principle also applicable in price-regulated European pharmaceutical markets, absent international reference pricing. Only, given the multi-country context and the present confidential nature of the bargaining process there is a need for further study. Given the confidential nature of key pricing assumptions in these markets, a counterfactual simulation modeling approach is warranted.

3. Methodology

We built a multi-agent simulation model exploring counterfactual net transparency ruling across the EU countries, each acting as monopsonist buyers, called national payers. In our model we consider only the case of manufacturers of in-patent pharmaceutical products acting as monopolists, hence not facing competition when negotiating the price and reimbursement of new drugs. This would typically be the case of a new in-patent drugs but exclude generics, the latter which cannot be studied without considering competitive effects. Limiting our study to the case of drugs with no therapeutic competitors is warranted given the affordability challenges they are seen to present to national health systems, especially orphan drugs (Danzon, 2018; Sarpatwari &

Kesselheim, 2019). Similarly, innovative drugs tend to lead to higher prices since they face little or no in-patent competition after launch.

We model price setting for pharmaceuticals in Europe with a Nash bargaining model in which firms maximize profits, while government regulators maximize consumer welfare, as in Dubois et al. (2019).¹⁰ In a two-stage simulation design, first, countries are allowed to negotiate with manufacturers a national price both exhibiting a bargaining power resulting in a confidential rebate and a Nash equilibrium net price p obtained in each country for the quoted value-based price (VBP). The latter which was obtained by averaging the published list prices for the respective countries over the period 1996 – 2008¹¹, which were normalized taking the average EU price as a basis, and by subtracting from these normalized average country prices a confidential rebate uniformly set for all countries.¹² Normalized country market size¹³ multiplied with a firm margin assumed to be fixed at 25% on p equals producer surplus. Country market size multiplied with the obtained difference between VBP and p equals country surplus. Modeling reality using these simplifying assumptions was necessary given the confidential nature of company marginal costs, margins and rebates obtained. Country surplus is determined by their relative historical price position, thus all exhibiting the same payer purchasing power.

Then, in a second step, we assumed net price transparency, which we modelled so that the country having negotiated the lowest price of the total set of EU countries would now become the referent country to the other countries in their negotiations with pharmaceutical companies. Following negotiation of the quoted VBP, a new Nash equilibrium country price p^* will be the result. Assuming constant firm bargaining power the profit or firm surplus expected for the total market including all individual European countries is modelled to equal the sum of the individual country profits obtained. Population size and country bargaining power assumed to remain constant, individual country payer surplus obtained in the new Nash equilibrium will depend on the extent to which each country's p was higher or lower than the EU average. As a result, countries paying more than average in the previous round, typically high-income countries like Germany, the Netherlands or Denmark will gain from net price transparency seeing their $(VBP - p^*)$ differential raise, amplified by their relative market size. Countries paying less than EU average, typically low-income countries like Greece or Spain, inversely amplified by their market size – i.e. with smaller countries losing more than larger countries – will proportionally lose from net price transparency. Therefore, we compare the result of single country independent Nash bargaining with manufacturers with a counterfactual policy combining external reference pricing with net price transparency. Thus, we assume that the adoption of full NPT in Europe introduces *de facto* a “most favoured nation” regime. The objective of this rule is to reduce prices in the referencing country since it ensures that prices paid in the referencing countries are at least as low as those in the reference country. However, in equilibrium, with full transparency such a rule will also

¹⁰ See also Pedersen and Grepperud (2020).

¹¹ Source: Pharmaceutical Industry Database, maintained at IMT Lucca (Pammolli and Riccaboni, 2007, Pammolli et al., 2011).

¹² As a baseline scenario we consider a 30% discount. Alternatively, we considered 5%, 10% and 20% confidential rebates in our analysis. In reality, net price discounts are unknown but are likely to vary across markets. Therefore, in our analysis we also consider the case of different confidential rebates across countries.

¹³ Normalization was done taking OECD-reported country-level absolute pharmaceutical spending and expressing each country's PPP market size as a percentage of the largest pharmaceutical spending country reported (source: <https://data.oecd.org/healthres/pharmaceutical-spending.htm>).

affect the net price in the referenced country since pharmaceutical companies may negotiate rates in the referenced country taking into account the impact on the price they can set in other European countries.

We measured the country-specific effect of full net price transparency reporting as a normalized p^*/p . Countries winning or losing from transparency would see this indicator to be respectively below or above 1. This would be the result of a shifting country payer surplus normalized to the surplus they reached in the previous round, keeping payer surplus across all markets constant to the sum of individual country payer surpluses obtained in the previous round. Countries with an unfavourable p^*/p ratio would be reluctant to participate in a net price transparency system. This makes such a scheme not sustainable in the European Union since some countries are better off not disclosing their confidential discounts.

Finally, we were on the one hand inspired by payers of countries like the Netherlands or Germany claiming to have already implemented full transparency in a recent survey (Bentata et al., 2020). On the other hand, we found opinions conceptually proposing – but not empirically tested – differential pricing solutions to leave lower-income countries the right to be non-transparent and potentially obtain better confidential deals (Kalo, Annemans, & Garrison, 2013). Also, some EU countries have decided to rally their purchasing power by forming cross-country alliances such as BeNeLuxA (O'Mahony, 2019) or the Valetta declaration. This is why we used our computational model to quantitatively investigate the potential for partial transparency as opposed to full transparency.

4. Results

Using our model we study the effect of implementing a NPT policy replacing the present discriminatory pricing system based on country-level confidential pricing agreements reached between national payers and pharmaceutical firms. The NPT regime makes the ERP system in Europe much more effective by revealing the actual net price being paid in each and every country. Since net prices are immediately accessible to all payers in Europe, they can introduce price ceiling (or most favoured nation) rules to limit reimbursement to the lowest price in Europe. First, we will assume a full transparency policy, defined as NPT, where all European countries would participate. Then, in a counterfactual analysis we will study the sensitivity of countries' decision to enter a full transparency policy to the bargaining power they potentially exhibit in reaching confidential pricing agreements with the pharmaceutical firm.

Following, we investigate the potential viability of various partial transparency systems, where only a subset of countries would enter the NPT policy, leaving the others to their present confidential agreements.

Finally, in a dynamic game theoretic thought experiment we study the effect of time discrimination in the entry decision of groups of countries to a NPT system, distinguishing

between high-, middle-, and lower-income countries and studying the effect of their non-coordinated but shown to be interrelated entry decisions.

4.1. Overall effect of net price transparency on payer surplus and price

Transforming the present EU discriminatory pricing system to a full price transparency policy will lead higher-income countries to raise their payer surplus, some countries to safeguard their surplus, and lower-income countries to lose surplus. Therefore, lower income countries will experience an increase of pharmaceutical expenditure for innovative drugs versus pure value based pricing. Figure 3 shows that this effect is larger for high-income countries profiting from a large price drop but featuring a smaller market size, like Denmark, then it is for Germany with its large market size. Austria, France, and Belgium stay at par in the payer surplus they exhibit. In contrast, low-income countries from Portugal to Greece will see their payer surplus dropping dramatically while, keeping total industry profits constant, having to absorb the lost producer surplus in the high-income countries. In effect, net price transparency leads to payer surplus redistribution from low-income countries to high-income countries.

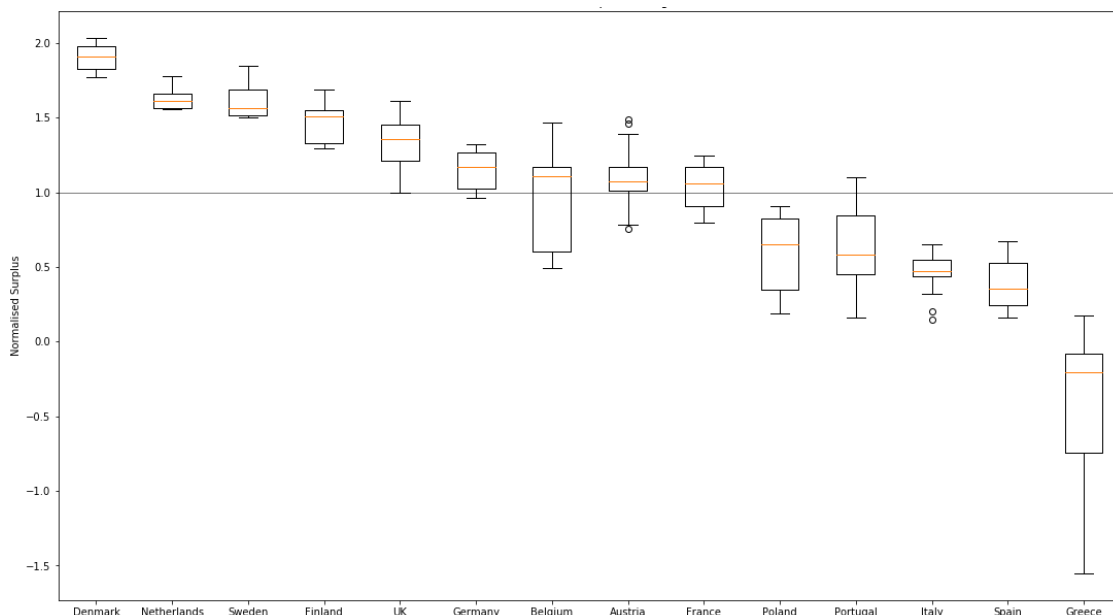


Figure 3: Normalised change in country payer surplus under net price transparency*

* The range of variation of normalised surplus a country depends on historical relative yearly average prices in each country

The redistribution of payer surplus leads to a price distribution across countries in which the lowered payer surplus countries will have to accept a p^* level that is above their presently bargained price p . In contrast, countries benefiting from a higher payer surplus

will see their p^* now being lower than their presently bargained price p . As can be verified in Figure 4, this would lead for countries like Greece and Denmark that they would respectively see their average price level raise by 60% and descend by 40% if they would decide to make their prices transparent to all other members of the NPT system. With a confidential discount of 30% in all countries before NPT, this translates in a raise by 12% of the average list price in Greece and a reduction of about 14.3% of the average list price in Denmark.

These results, obtained from our computational study are in line with and expand upon research cited above in the varying contexts of labour markets, medical devices and the US-Canada counterfactual studies (Cullen & Pakzad-Hurson, 2020; Dubois et al., 2019; Grennan & Swanson, 2020).

Not only would it be economically irrational for countries suffering from a raise in general price levels to join a NPT system. It would also be unjust while being the opposite of the Ramsey pricing principle, a second best price discrimination policy maximizing payer surplus by allowing firms to charge more to countries exhibiting low price elasticity i.e. to the richer countries. Here, violating the Ramsey principle is unjust, insofar as it promotes a single price that no longer distinguishes between the different countries' levels of ability to pay. Finally, the high normalized price differentials will also disproportionately stress the affordability for and accessibility of countries to pharmaceutical products potentially leading to no or later access, which violates the idea of distributive justice (Rawls, 1971).

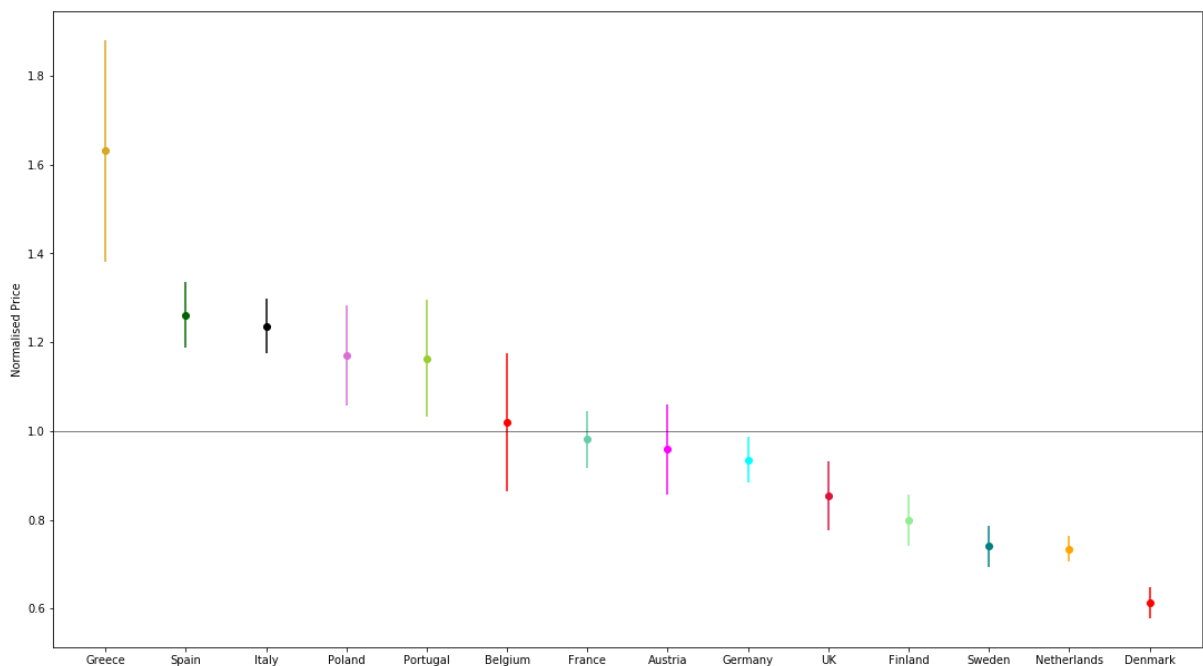


Figure 4: Normalised price change (p^*/p) under full net price transparency

From the previous, it can be concluded that it would be economically irrational for countries to decide to join the NPT system when facing a higher average price than they get now in their confidential agreements reached for innovative pharmaceuticals. But how sensitive would this entry decision be to the bargaining power they potentially exhibit in reaching confidential pricing agreements with the pharmaceutical firm?

To explore bargaining power sensitivity in the simulation model, we define a negotiation advantage as how much more or less bargaining power a country has compared to the rest. In our model we had three different standard rebates 5%, 10%, and 30%. When we have a standard rebate of 30% and a country has a negotiation advantage of 10%, then that means that this country has a rebate of 40%, while the other countries still have a rebate of 30%.

In Figure 5 below, the y-axis is the normalised price change, the x-axis is the countries' bargaining advantage and then we see how the countries' normalised price develops as they gain a higher negotiation advantage in reaching confidential price agreements.

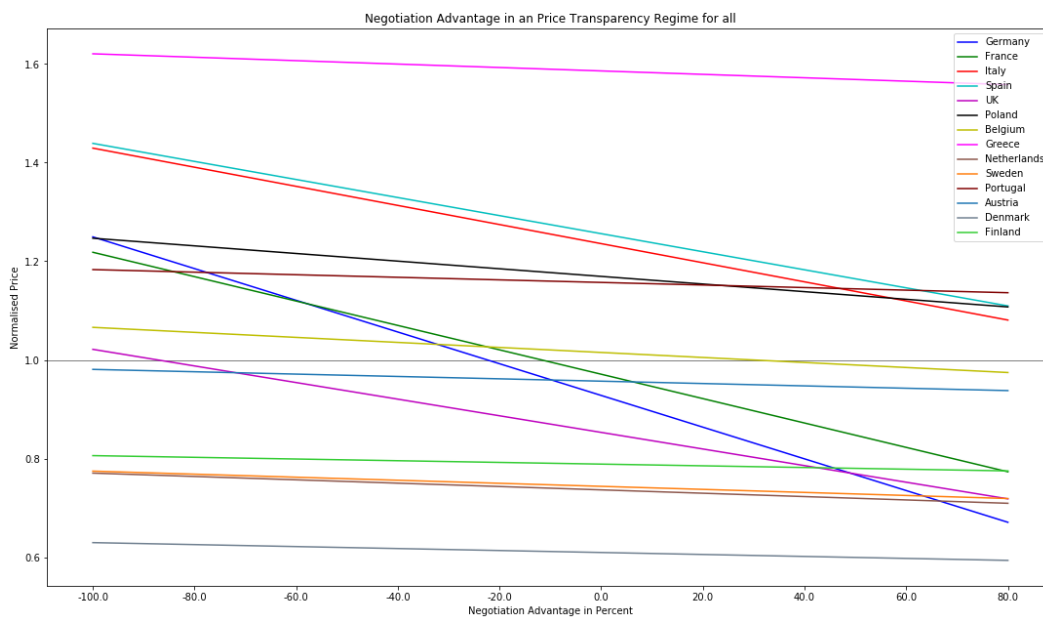


Figure 5: Country indifference to net price transparency as measured by their negotiation advantage*

* The analysis refers to the case of a reference confidential discount rate of 30%. Similar plots for 5% and 10% rebates are available upon request.

From Figure 5 we conclude that Denmark, the Netherlands, Sweden, Finland, and Austria should always be interested in joining a full NPT system. This while they would always get a better price under NPT regardless of the bargaining power advantage they could build in confidential agreements.

Germany and France should be interested in full NPT even if they would suffer from 20% poorer bargaining deals in reaching their present confidential agreements. This is, even if Germany and France could only get current confidential rebates of respectively 10% or 20%, in comparison to all other countries remaining at 30%.

The UK should be interested in NPT while then obtaining better prices than they could reach in confidential agreements. This while, even if they would be paid a bonus of $80-30=50\%$ to provide access in the UK¹⁴, they would get a better price in an NPT system.

In contrast, Belgium would become indifferent to NPT or reaching confidential agreements if they could increase their present bargaining power by 30%. Before that point, they should prefer to stick with confidential agreements.

Finally, Greece, Spain, Italy, Poland, and Portugal would never benefit from NPT while they would never get a better price under NPT regardless of the bargaining power advantage they could build in their confidential agreements.

All in all, since confidential discounts are not known, in our analysis we consider a baseline scenario according to which all countries have the same level of confidential discounts. When we allow countries to be able to negotiate different levels of confidential discounts, we find that only four countries (UK, France, Germany and Belgium) might change their interest in NPT depending on their bargaining power in the current setting. However, since in all the simulated scenarios we considered there will always be a set of lower-income countries suffering from the negative consequences of NPT, we conclude that this regime is not sustainable on a voluntary basis.

4.2. Moving from full to partial transparency

If full transparency is not an answer, would partial transparency be the answer? Inspiration for this is the claim from high-income countries like The Netherlands or Germany to already share their negotiated price, regardless other countries' reactions. Others suggest that awaiting a European regulatory framework to monitor and enforce international reference pricing such as net price transparency one could as a second-best solution leave lower-income countries to confidential pricing agreements (Kalo et al., 2013).

4.2.1. Partial transparency recursive analysis

To conduct a thought experiment on the possibilities regarding partial transparency we build a recursive model depicted in Figure 6 in which we ordered the countries according to their average list price, with the countries with the highest average list price on the left. Figure 6 shows the normalised price change for each country as we add more

¹⁴ This of course is a simulation result emulating a counterfactual thought experiment which would never materialize in reality i.e. it would mean that the UK would be paid 50% of the actual price by the manufacturer to actually carry the product. This simulation result interpretation is that the UK would almost always benefit from joining an NPT system.

countries to the transparency group starting from the high-income countries, being the most interested to join NPT.

We explore partial transparency by recursively adding one country to a multi-country partial transparency scheme. Starting from the left, Denmark, given its current bargaining power reaching confidential agreements would obtain the same price with NPT, hence be indifferent to both systems. Adding the Netherlands would improve Denmark's price position to become even more advantageous. This in contrast to the latter country that would have to wait until Sweden, Finland, and the UK would join the group until its price obtained from an NPT policy would get them to better prices than under confidential agreements. The same holds for Sweden and Finland that both have to wait until the UK turns to NPT. A partial transparency system limited to this group of Nordic country is viable only if the UK would "sponsor" the partial transparency policy by accepting a price disadvantage of about 8%. This is unlikely to happen since UK payers declared to be not interested at all in NPT (see Table 1).

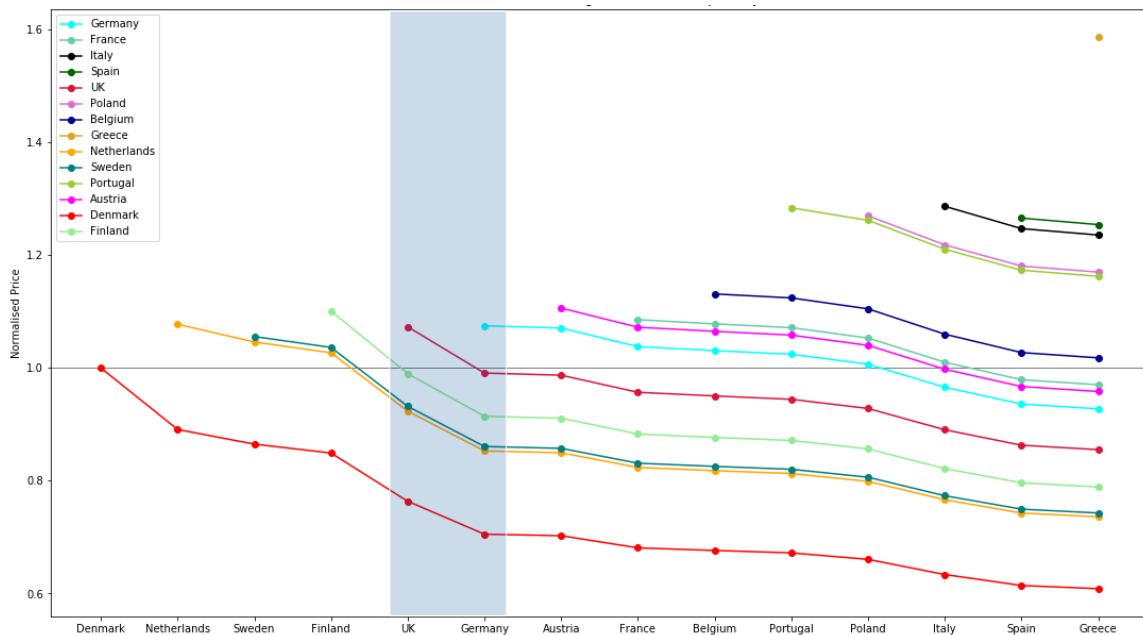


Figure 6: Country indifference to net price transparency following other country joining decisions*

* The shaded area illustrates the potential region of feasibility of a partial NPT regime. The group of high-income countries that might take part in this NPT coalition are Denmark, the Netherlands, Sweden, Finland, UK and possibly Germany.

Then, only when Germany turns into an NPT system, a critical mass of high-income countries would benefit from NPT. However, as can be observed from Figure 6, also in this case the last joined Germany would "sponsor" the partial transparency policy by accepting a price disadvantage of about 8%.

Continuing this counterfactual reasoning, if Germany would not accept this position, it would have to wait until Austria, France, Belgium, Portugal, Poland, and Italy would join

NPT before its prices would outperform the confidential agreement system. Only, for all countries starting from Belgium it would never be beneficial to join given they could never get better prices than they have under their current non-transparent confidential agreement systems.

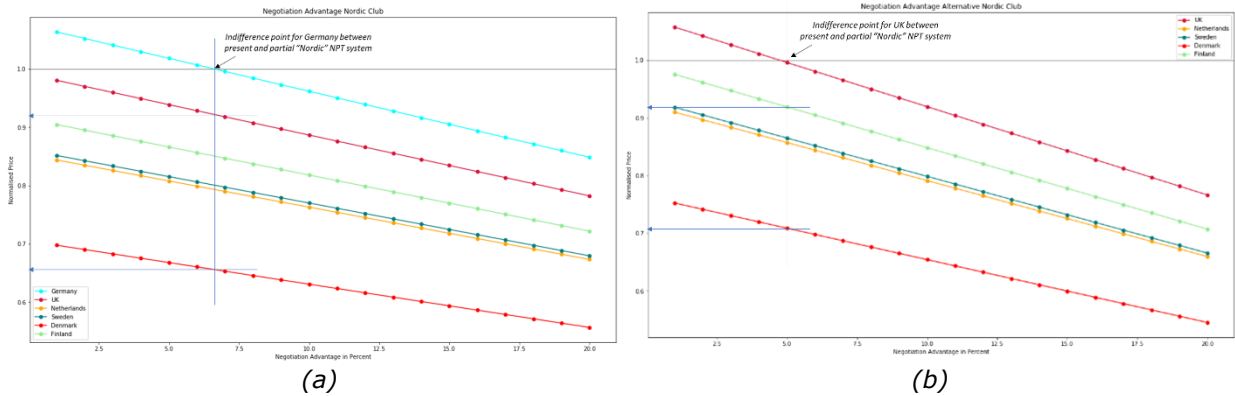


Figure 7: Country indifference to net price transparency following other country joining decisions to a partial "Nordic" transparency system. (a) the indifference condition for Germany taking part in the partial NPT initiative with 5 countries. (b) the indifference condition for UK taking part in a restricted NPT initiative with Denmark, the Netherlands, Sweden and Finland.

Concluding, a partial transparency system could only be viable if the group of high-income countries including UK and possibly Germany would commit to price transparency, leaving all other countries to non-transparency. Now, assume Germany would join this "Nordic" partial NPT system¹⁵, and further assume it would not do this as a sponsoring agent, but only when being indifferent between its present and the partial NPT drug pricing system. Then, from Figure 7a above it can be verified that it will only be indifferent if the total "Nordic" group can create a joint demand-side negotiation advantage of at least 7%. This NPT-based increased payer bargaining power would imply that the participating countries will benefit from a price drop ranging from 7% for the UK to 34% for Denmark.¹⁶ Another possibility, if Germany does not accept to take part in the NPT initiative, is to limit transparency between Denmark, the Netherlands, Sweden, Finland and UK. Figure 7b shows that UK will only be indifferent if the restricted "Nordic" group can create a joint demand-side negotiation advantage of at about 5%. However, the benefits of NPT for the other countries is reduced.

To what extent would such a partial NPT system reserved for the high-income countries be politically reachable or even be viable? To convince candidate member countries to coordinate their pharmaceutical purchasing, NPT among its members is a mere intermediary step. It needs joint assessment of value and procurement to work, providing a convincing negotiation advantage to country-led negotiations.

¹⁵ Consider that new drugs are priced freely for the first 12 months after launch in Germany.

¹⁶ As before, the percentage price reduction is computed as $(p^*-p)/p$ where p is the current confidential net price without price transparency and p^* is the price transparent among the Nordic countries taking part in the partial NPT initiative.

4.2.2. Partial transparency in cross-country collaboration initiatives

Another partial transparency scenario is given by the cross-country collaboration initiatives BeNeLuxA and la Valetta.

Our model shows that the benefit of having such an international collaboration is unevenly distributed across the participating countries (see Figure 8). These countries that had a higher than EU average list price before benefit, while those that had a below EU average list price are worse off.

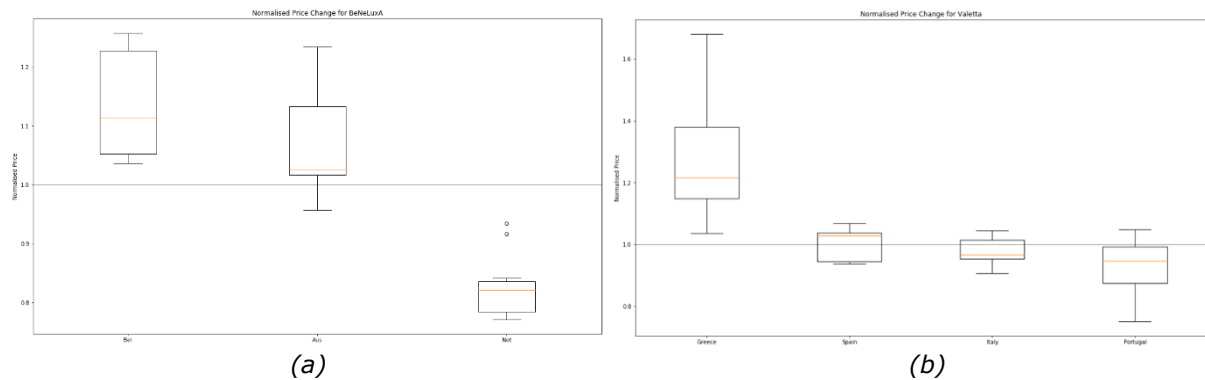


Figure 8: Normalised price change under partial (a) "BeNeLuxA-only" and (b) Valetta-only net price transparency

While we do not have price-volume elasticity information we estimated the extra negotiation power needed in the collaborations to off-set the disadvantage for those countries now facing a higher price than before (see Figure 9). For Valetta we would need an extra negotiation advantage of 10% above the present confidential rebate we assumed to be at 30% for all countries in order for the worst-off country (Greece) to be indifferent between joining the transparency group or not. For BeNeLuxA we would need an extra negotiation advantage of 8.3% of the group for Belgium to become indifferent to their present confidential rebate system versus net price transparency.

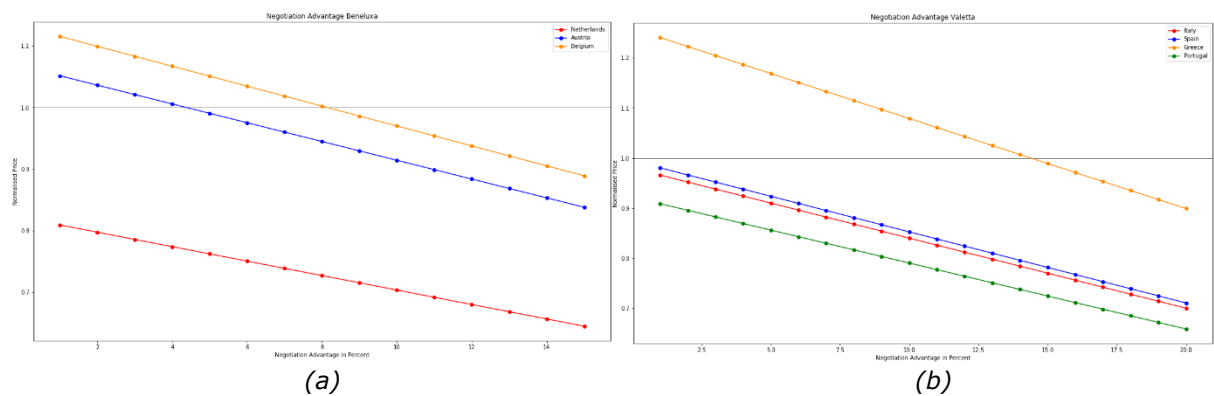


Figure 9: Country indifference to net price transparency following other country joining decisions to a partial (a) "BeneLuxA" or (b) "la Valetta-only" transparency system

In conclusion, joint negotiation initiatives replicate on a smaller scale the same harmful consequences of NPT: some countries will be worse off because of full transparency. However, when joint procurement is implemented it is possible to satisfy a feasibility condition if the increase in the bargaining power of national payers is sufficiently higher than in the current regime.

4.3. Time to market access in a net price transparency regime

In the previous section we have investigated the impact of a NPT regime as the result of a one-shot multi-agent Nash bargaining problem between the manufacturer of an innovative drug and multiple EU payers. Our main conclusion is that NPT is not sustainable if countries are left free to choose if to adhere to the NPT regime or to negotiate confidential discounts, since some countries will always prefer to limit transparency based on their expected resultant price change. Another potential way out to make an NPT regime viable might be to delay product launches in some European market. As mentioned above, lower income countries being reassured to be able to obtain a better national confidential price than a European transparent price when joining an NPT system might decide to wait or to never join a partially transparent system, as reported by some payers of lower-income countries (Bentata et al., 2020).

In this section we consider a more realistic alternative scenario in which countries can decide *when* to authorize access to innovative drugs. Again, we assume that whenever a drug is launched in a given European market the price will be visible to all payers and an external reference pricing mechanism will guarantee price convergence.

To study this phenomenon, in contrast to the static analysis above this would require a dynamic analysis with temporal discrimination. To simplify our treatment, we consider the case with only four players: the manufacturer, a high-income payer, a mid-income payer and a lower-income payer. Doing so, we distinguish between three groups of countries. Given the price benefit they would experience we assumed the above-identified "Nordics" (A) group (Denmark, The Netherlands, Sweden, Finland, UK and Germany) to join the NPT system immediately at product launch. Then we distinguished between a "presently almost indifferent to NPT" (B) group entailing Belgium, Austria and France, and a "presently losing to NPT" (C) group of countries entailing Poland, Portugal, Italy, Spain, and Greece. Clearly this simplified 4 players game can be extended to the case with more payers involved without any loss of generality.

While the NPT system joining decision taken by each group is contingent upon the joining decision of other groups, interactive decision theory is required. This can lead players to play pure or mixed Nash equilibrium strategy games. A player has a strategy set of moves available, given the moves of other players. A pure strategy player makes a move (joining NPT or not) regardless the other player's moves they are facing. A mixed strategy player assigns a probability to each of the set of pure strategies available in the non-coordinated game they are playing.

Striving for computational simplicity, in our dynamic game theoretic analysis we aggregated the NPT system joining decision to three payers, each representative of the groups of countries A, B and C, respectively. We assume that Group A has already joined a partially transparent system and a given innovative drug is launched in the A-group market at time 0. Then we analyse the decision of groups B and C to be taken in a non-coordinated game looking for a Nash equilibrium either in pure or mixed strategies. Groups B and C will decide in which period the drug will be made available to patients in their markets. In any given period t the price will depend on the number of countries in which the drug is available. More precisely, the price at discrete time t is $p_t^*(c)$, where c is the set of countries in which the drug is available at time t (A, B, C, AB, AC or ABC), computed as in the previous section. The payoff of the payers will be the net present value of the surplus. Payers can have different discount rates δ_i with $i = \{A,B,C\}$. The drug monopolistic market duration is set to last τ periods with τ set to be the same in all markets. As an illustrative case, in Table 1 we consider the normal-form game for players B (in row) and C (in column) with $\delta_B = .05$ and $\delta_C = .09$, $\tau = 4$ and moves 0 to 7, i.e. players can decide in which period to enter between 0 and 7.

In our computational thought experiment we assumed each group to be present in the market for 4 periods accumulating the net present value of their payer surplus. Initially, only Group A is assumed to be present in the market at time 0. Table 1 below represents the surplus accumulated by Groups B and C joining Group A at $t = 0$ up to 7. Group impatience to earn payer surplus was represented by a discount factor of .05 and .09 for Group B and C, hence with C assumed to be more impatient.¹⁷ The payoff of players is represented in the standard way as a matrix cell (x,y) where following game theory notation, x is the payer surplus of the Row player (Group B), and y represents the payer surplus for Column player (Group C).

	0	1	2	3	4	5	6	7
0	(3.5, 1.0)	(3.3, 1.2)	(3.1, 1.4)	(2.9, 1.5)	(2.7, 1.7)	(2.7, 1.5)	(2.7, 1.4)	(2.7, 1.3)
1	(3.3, 1.0)	(3.5, 1.1)	(3.3, 1.3)	(3.1, 1.4)	(2.9, 1.6)	(2.7, 1.5)	(2.7, 1.4)	(2.7, 1.3)
2	(3.1, 1.0)	(3.3, 1.1)	(3.6, 1.1)	(3.4, 1.3)	(3.2, 1.5)	(2.9, 1.4)	(2.7, 1.4)	(2.7, 1.3)
3	(2.9, 1.0)	(3.2, 1.1)	(3.4, 1.2)	(3.6, 1.2)	(3.4, 1.4)	(3.2, 1.3)	(2.9, 1.3)	(2.7, 1.3)
4	(2.7, 1.1)	(3.0, 1.1)	(3.2, 1.2)	(3.4, 1.2)	(3.6, 1.3)	(3.4, 1.2)	(3.1, 1.2)	(2.9, 1.2)
5	(2.6, 1.1)	(2.6, 1.2)	(2.8, 1.3)	(3.0, 1.3)	(3.2, 1.4)	(3.4, 1.2)	(3.2, 1.1)	(3.0, 1.1)
6	(2.5, 1.1)	(2.5, 1.2)	(2.5, 1.4)	(2.7, 1.4)	(2.9, 1.5)	(3.1, 1.3)	(3.3, 1.1)	(3.1, 1.0)
7	(2.4, 1.1)	(2.4, 1.2)	(2.4, 1.4)	(2.4, 1.5)	(2.6, 1.6)	(2.8, 1.4)	(2.9, 1.2)	(3.1, 1.0)

Table 2: Normal form game. Payer group total surplus relative to Group C total surplus obtained when joining the NPT system group after 0 to 7 periods; Row player is Group B and Column player is Group C; $\delta_B = .05$, $\delta_C = .09$, $\tau = 4$.

¹⁷ In this example we set the values of the discount rates and the duration of the monopolistic regime to describe a simple illustrative version of the game. In Table 2 we consider alternative scenarios for different values of the parameters of the model.

As an example, if Group B decides to join Group A after one year (Row=1) and Group C decides to join the A Group immediately at start (Column=0) their respective payoffs are represented as (3.3, 1.0). In order to improve readability, surplus was normalized to the actual Group C surplus in period 0 set equal to 1.

The game in Table 2 has only one pure strategy Nash equilibrium with simultaneous entry in period 4, that is to say access to market B and C is delayed at period 4 when the surplus of Group B is 3.6 and the surplus of group C is 1.3. In this game, player C has an incentive to postpone entry to ensure a period of time in which groups A and B are no more in the market and player C can obtain a lower price since $p_t^*(C) < p_t^*(B,C) < p_t^*(A,B,C)$. Similarly, player B wants to wait for player C to be present in the market to reduce p^* , since $p_t^*(A,B,C) < p_t^*(A,B)$. Irrespective of Group B's decision, Group C, the group of lower-income countries face the decision to enter early the NPT system but at higher prices, or to wait until the high-income countries have left the market, thus obtaining a lower price. In contrast, the decision of Group B to join Group A, is contingent upon the decision taken by Group C.

The main conclusion from our game theoretical analysis is that a NPT system delays access in lower- and middle- income countries. It is worth noticing that in this case the negative effect of NPT is not limited to low-income countries (Group B) but it implies also delayed access in mid-income countries, since they wait for Group C entrance to benefit from ERP to the lower and transparent prices in market C.

This result holds even when considering alternative parameter settings (see Table 3). In some cases, the game has no pure strategy Nash equilibria but a mixed strategy equilibrium.

	Delta <= 0.04	0.05 <= Delta <= 0.09	Delta >= 0.10
Delta <= 0.04	[(6, 6), (6, 12), (12, 12), (12, 6)]	[(6, 6)]	[(6, 6), (6, 0), (0, 0), (0, 6)]
0.05 <= Delta <= 0.08	[(6, 6), (6, 12), (0, 12), (0, 6)]	[(6, 6)]	[(6, 6), (6, 0), (0, 0), (0, 6)]
Delta >= 0.09	[(0, 6)]	[(0, 6)]	[(0, 6)]

	Delta <= 0.04	0.05 <= Delta <= 0.07	Delta >= 0.08
Delta <= 0.03	[(7, 7), (7, 14), (14, 14), (14, 7)]	[(7, 7)]	[(7, 7), (7, 0), (0, 0), (0, 7)]
0.04 <= Delta <= 0.07	[(7, 7), (7, 14), (0, 14), (0, 7)]	[(7, 7)]	[(7, 7), (7, 0), (0, 0), (0, 7)]
Delta >= 0.08	[(0, 7)]	[(0, 7)]	[(0, 7)]

Table 3: Solution of the market access game with the discount rates δ of Group B (in row) and Group C (in column) ranging from .01 to .10. We consider two alternative scenarios with $\tau = 5$ (top table) and $\tau = 6$ (bottom table). For mixed strategy equilibria we report the support in terms of pure strategies.

By increasing the discount rates the players are more impatient and tend to accelerate access. Table 3 provides alternative scenarios, when we consider a range of discount rates between .01 and .10 and different durations of the monopolistic phase. We find that Group C always delays entry, i.e. regardless of B's pure strategy. Conversely, it

can be verified that Group B, when being more impatient (i.e. B's δ is high) than the situation depicted in Table 2, this mid-income player will be inclined not to postpone access and join the A group from the beginning. Mixed senses of urgency to join the NPT system, then, lead to mixed Nash equilibrium strategies between Groups B and C.

Intuitively, the delay depends inversely on δ . Also, the delay depends positively on τ , i.e. the duration of the monopolistic phase in the high-income market. When the market can ensure high prices for a long enough period in Group A markets, payers in other market will procrastinate entry to avoid the negative NPT consequences in their markets.

In conclusion, we find that NPT implies later access in mid and low-income countries. Our result is robust to different assumptions in terms of discount rates and duration of the monopolistic market regime for innovative drugs.

5. Conclusions

We built a multi-agent simulation model exploring counterfactual net transparency ruling across EU country payers, each acting as monopsonist national buyers. In our model we considered only the case of in-patent innovative pharmaceutical product manufacturers acting as monopolists, hence not facing competition when negotiating the price and reimbursement of new drugs.

We used counterfactual multi-agent computational simulation to model reality using simplifying assumptions, this given the confidential nature of company marginal costs, margins and rebates obtained. All countries in our model exhibiting the same payer purchasing power and country surplus was determined by their relative average historical price position (Pammolli & Riccaboni, 2007). Manufacturer's producer surplus being kept constant, led countries to be engaged in a zero-sum game with all other countries, leading to shifting surpluses following the implementation of a net price transparency policy.

Results from our computational model are fully in line with previous studies indicating an increasing imbalance between rich and poor countries, with the latter paying now more for the value they get. This violates distributive justice (Rawls, 1971) going against the spirit of Ramsey pricing principles in which, to enhance distributive justice a mark-up is implemented to those countries featuring highly inelastic demand.¹⁸

Also, from our game theoretic dynamic analysis we conclude that a net price transparency system implies delays in market access, potentially in middle-income countries but surely in lower-income countries. This while joining the high-income countries from the beginning would mean they would have to accept transparent but significantly higher national prices. Which is the reason why they would robustly delay joining the NPT system.

¹⁸ Ramsey pricing principles are generally accepted and approved as means to facilitate access to lower-income countries and are applied in other parts of the HCS to positive effects (e.g. Vaccine tiered pricing).

Hence, we conclude that even a partial transparency system reserved for high-income countries would be a challenging case to reach from a political perspective. To what extent would it be viable? To convince even high-income candidate member countries to coordinate their pharmaceutical purchasing, NPT among its members is a mere intermediary and yet insufficient step. It needs joint procurement to work, providing a convincing negotiation advantage to country-led negotiations that presently result for these payers in outperforming confidential rebates.

While providing the largest and most acute societal challenge, our study was limited to highly innovative but typically high-priced medicines, which led to monopolistic behaviour, as typically found in orphan disease markets. Future studies should extend our thinking to include also non-differentiating and generic drugs leading to oligopolistic or even pure competitive manufacturer behaviour, as found for example in medical device markets. To have meaningful results for the life sciences purchasing and reimbursement system this would mean extending our computational model to cope with competitive pricing behaviour. Finally, to ensure robust externally valid results from our computational model would require most recent medicine pricing and price-volume elasticity data for all of the European markets studied. Clearly, lack of transparency about historical net prices limits empirical research in this field.

All in all, our theoretical analysis contributes to better understanding why payers in Europe are concerned in terms of the potential negative consequences of NPT in terms of prices and delayed access. More in general we find that a NPT regime is not sustainable on a voluntary basis. Especially not for payers of lower-income countries who should be free to apply confidential discounts.

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