Free-Riding in Pharmaceutical Price Regulation: Theory and Evidence*

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Abstract

We present a model of the strategic interaction among authorities regulating pharmaceutical prices in different countries and the R&D investment decisions of pharmaceutical firms. Regulators' decisions affect consumer surplus directly, via prices, and indirectly via firms' profits and R&D investment policies, which in turn affect patient health. The positive externality of a price increase in one country provides an incentive for other countries to free-ride, and we show how country-level characteristics affect optimal pricing decisions and equilibria. Our theoretical predictions are tested using price data for a set of 70 cancer drugs in 25 OECD countries. We find evidence of behaviour that is consistent with the free-riding hypothesis and which, in line with the theoretical predictions, differs according to country-level characteristics. Countries with comparatively large market shares tend to react to increases in other countries' prices by lowering their own prices; in countries with comparatively small market shares, regulators' decisions are consistent with the objective of introducing the product at as low a price as possible. We discuss the policy implications of our results for incentivising global pharmaceutical R&D and the recent proposal to move towards a joint pharmaceutical procurement process at the European level.

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1 Introduction

According to the World Health Organisation, one of the biggest challenges facing health care systems is *'the balance between ensuring long-term sustainability... with appropriate access for patients and fair reimbursement for innovation'* (WHO, 2015a, page 133). This statement reflects the conflict between, on the one side, the payers, and on the other side, the biomedical industry. The former group seeks to tighten regulation, so as to curb health care expenditure and ensure that new products that are reimbursed represent 'good value for money'; the latter group warns that stricter regulation risks weakening incentives to invest in R&D. Evidence of a positive relationship between drug prices and R&D intensity is provided, for example, by Giaccotto et al. (2005) and Civan and Maloney (2009). The industry's argument is also supported by referring to additional evidence showing that the number of new drugs approved per $bn spent on R&D is declining (Pammolli et al., 2011; Scannell et al., 2012) and the average R&D cost of new drugs is on an upward trend (DiMasi et al., 2003, 2016). The conflict reflects the well-known trade-off between static and dynamic efficiency (Leibenstein, 1966). According to Berndt (2002, page 45), *'The resolution of this static versus dynamic efficiency conflict is likely the single most important issue facing the pharmaceutical industry.'*

Although the majority of studies of pharmaceutical price regulation focus on the static dimension, interest in the relationship between the static and dynamic dimensions is growing. Some contributions to the literature focus on specific types of regulation, such as cost-effectiveness thresholds (Jena and Philipson, 2008), value-based pricing (Danzon et al., 2015) and risk-sharing agreements (Levaggi et al., 2017). This literature is typified by modelling either a single regulator, or several regulators making decisions independently of each other. However, the biomedical industry tends to operate on a global scale, and so new products are potentially made available everywhere, irrespective of the country in which the product was developed. Hence, a stronger incentive to invest in R&D provided by one country increases the probability that innovation is available in other countries. Such a spillover effect can create the potential for free-riding behaviour, a matter which has not escaped the attention of both academic and policy debates. For example, Filson (2012, page 112) notes that *'small subgroups in the population can benefit by free riding on the U.S. states willing to support market prices, but the United States as a whole benefits from maintaining market pricing everywhere'* and the OECD (2008, page 21) comments *'countries whose policies restrict the prices pharmaceutical firms can charge for their products were, it was suggested, potentially free-riding on the rewards and incentives for innovation provided by others'*. The idea is that regulators may find it convenient to exploit the static efficiency benefits that low prices bring, while at the same time relying on higher prices set in other countries to incentivise R&D investment.

Filson (2012) calibrates a Markov-perfect equilibrium model and concludes that consumers in the United States tend to be better off without pharmaceutical price regulation: the long-term losses in dynamic efficiency that greater price regulation would bring outweigh the short-term gains in static efficiency. In Filson's framework, firms act to maximise profits given a set of exogenous price caps imposed in a group of countries. The welfare analysis is based on a comparison of the equilibria resulting from different combinations of policies across countries. Filson's baseline parameterisation suggests that countries other than the United States, where

prices are typically regulated, free-ride on the willingness of the United States to support market prices. Filson's assumption of exogenous policies, however, does not allow one to answer the question of why some countries are more inclined to free-ride than others.

Our study is further motivated by recent steps that the European Union has taken toward joint procurement for pharmaceuticals. In April 2014, the European Commission approved the Joint Procurement Agreement (JPA), which enables European countries to organise joint procurement procedures for medical countermeasures aimed at combating serious cross-border threats to health. More generally, joint procurement of pharmaceuticals is feasible under European Directive 2014/24/EC. A better understanding of strategic interaction in pharmaceutical drug regulation is essential for predicting the impact of collaborative actions, both within the EU and globally. Internally, collaborative actions would imply mitigating, if not eliminating, strategic interaction between countries. Externally, the strategic position of countries collaborating under a single regulator, with a large market share, might be different from that of several regulators with smaller market shares. As a result, centralisation of procurement in Europe may have a substantial impact on the strategic interaction between the United States and European countries.

This paper is related to at least three separate strands of literature. First, there is a theoretical and empirical literature which studies strategic interaction among policy makers in a number of fields where spillover effects occur. The best known field is probably environmental policies with global impacts, such as those designed to control the emission of pollutants (Murdoch and Sandler, 1997). Another is taxation of capital income in the presence of capital mobility. In this case, a reduction in the tax rate in one country implies a negative externality for other countries, because it shrinks their tax bases (see, for example, the seminal paper by Zodrow and Mieszkowski, 1986). Theory predicts the so-called 'race to the bottom' of capital income tax rates, and an under-provision of public goods. Devereux et al. (2008) provide empirical evidence supporting the theoretical prediction of strategic interaction in this area. Another field is the strategic interaction among different countries in designing tariff policies, owing to the negative externality associated with a tariff set in one country on the exporter's terms of trade (Beshkar et al., 2015). Directly related to pharmaceutical R&D, but not to price regulation, is Kyle et al.'s analysis of free riding in public funding of medical research (Kyle et al., 2017). Using data from the U.S. National Institutes of Health between 2007 and 2014, the authors find that a 10% increase in United States government research funding for infectious and parasitic diseases leads to a 1% reduction in funding by other funders in the following year and a 4% reduction in the aggregate spend of other governments. The authors interpret the results as evidence that other countries free-ride on the United States in terms of research funding.

A second strand of literature concerns the international dimension of intellectual property protection. This is particularly relevant for the pharmaceutical market because of the key role played by innovation and the fact that pharmaceutical companies operate on a global scale. There is also scope for strategic interaction in this area, because stronger protection of intellectual property in one country may provide incentives to invest in R&D in that country, and this investment may benefit other countries. Grossman and Lai (2004) study strategic interaction in the definition of patent policies between a 'Northern' country, with comparatively large R&D productivity, and a 'Southern' country. They show that, in a noncooperative equilibrium, patent protection is stronger where R&D capacity and market size are greater. Another key question in this litera-

ture concerns the welfare implications of parallel trade. The dominant view is that parallel trade weakens incentives to invest in R&D, by reducing profits in countries where patents have yet to expire (Barfield and Groombridge, 1998, 1999; Danzon, 1998; Danzon and Towse, 2003). Grossman and Lai (2008) challenge this view by showing that, under some conditions, parallel trade may lead to greater investment in R&D. The impact of parallel trade on the optimal regulation of pharmaceutical prices is important for this result. Interestingly, the authors also find that optimal pricing polices depend on the relative size of the market and that the relationship between relative market size and optimal price is not strictly monotonic. Key differences between this literature and our analysis are that we focus on pricing policies in situations where intellectual property is protected and that our countries differ along a number of dimensions, but not in R&D productivity. This is because the debate on free-riding in pharmaceutical price setting has mainly concerned countries which are similar in this respect (that is, they are typically 'Northern' countries).

Finally, our work is related to the applied literature studying the determinants of drug prices.[1] Most relevant for us are those studies that adopt a comparative approach. Cabrales and Jiménez-Martín (2013) use data from 25 countries over 6 years to investigate the impact on prices of sales, the number of competitors, molecule age, GDP per capita, the country's level of health expenditure and the level of regulation. Similar determinants are analysed by Kanavos and Vandoros (2011) for 100 drugs across 19 therapeutic categories in 15 OECD countries. In Kyle and Qian (2014), the focus is on the effect on prices of patent status and the burden of disease for 60 countries over 13 years. Several other contributions study the determinants of prices within countries.[2] Variables typically considered in these analyses include the age of the drug, its therapeutic advance and the number of substitutes.

To the best of our knowledge, a formal analysis of strategic interaction in pharmaceutical price regulation and its implications for incentivising R&D investment, taking into account both static and dynamic efficiency considerations, has yet to be proposed in the literature. Nor has an empirical study been conducted to investigate whether or not regulators actually free-ride. This paper aims to fill these two gaps.

The first part of our work develops a theoretical model of strategic interaction among different countries in setting regulated prices for pharmaceuticals. Pricing policies affect consumer surplus directly, and indirectly via firms' profits and R&D investment policies, which in turn affect patients' health. We follow a similar modelling approach to that used in the aforementioned literature on spillover effects. First, we derive best response functions from the theoretical model and study how these functions, and the resulting price equilibria, are affected by country characteristics. We derive a series of theoretical predictions which we then test empirically. To this end, we exploit the Pricing Insights IMS database to construct a data set of 25 OECD countries which includes 70 branded cancer drugs authorised by the European Medicines Agency between 2007 and 2017.

Our theoretical results predict that, if the weight on consumer surplus in the regulator's ob-

[1] OECD (2008, Chapter 2) provides an extensive review.

[2] See, among others, Lu and Comanor (1998) for the United States, Ekelund and Persson (2003) for Sweden and, separately, for the United States, Benda et al. (2004) for Canada, and Puig-Junoy and González López-Valcárcel (2014) for Spain.

jective function is sufficiently large, prices are strategic substitutes and therefore there may exist an incentive to free-ride. We discuss two types of equilibria: those where both countries price above the minimum price the firm is willing to accept in order to serve the national market and those where the constraint is binding for one of the two countries. The impact of country characteristics on equilibrium price is different in the two types of equilibria. In particular, we focus on the role of the size of the national market relative to the global market as a key determinant of both the type of equilibrium and, given the type of equilibrium, the optimal price.

Consistent with the theoretical predictions, the empirical analysis shows that regulators react differently to the pricing policies of other countries according to the relative size of the market. In particular, in countries with comparatively large markets, prices tend to be lower (higher) the higher (lower) is the average price in countries that have previously adopted the new drug, which is in line with the free-riding hypothesis. Instead, for countries with a relatively small market share, prices are unaffected by the pricing decisions made by other countries. The empirical analysis also suggests that, for countries with a relatively large market share, equilibrium prices are increasing in the size of the market share, while the opposite is true for countries with a relatively low market share. Thus our empirical results lend support to the free-riding hypothesis in pharmaceutical pricing and suggest that joint procurement at the European level would substantially change European countries' strategic position relative to the United States.

Section 2 presents our theoretical analysis, using a two-country model of strategic interaction in pharmaceutical pricing and innovation. In section 3, we obtain best response functions, conduct comparative static analyses and derive predictions for optimal investment and pricing policies. These are tested in section 4. Section 5 discusses our results and concludes.

2 The model

We model two countries, A and B, which are assumed to comprise the global market, in which a single profit-maximising firm may sell a new drug. In each country, there is a single authority responsible for regulating the prices of new drugs that are approved for commercialisation ('the regulator'). Patient-level marginal willingness to pay (MWTP) for the drug in country c, $c \in \{A, B\}$, is given by the linear inverse demand function:

$$\text{MWTP}^c(q^c) = \kappa^c \delta(I) - bq^c. \tag{1}$$

The quantity q^c may be interpreted as the average level of consumption of the drug by each of N^c patients eligible to receive it in country c.[3] I is the level of R&D investment, a choice variable for the firm. An increase in I is assumed to improve the effectiveness of a drug, implying a positive impact on MWTP via the function δ, for which it is assumed that $\delta(0) = 0, \delta_I > 0, \delta_{II} < 0$ and

[3] If it is assumed that all patients in country c are identical, the negative slope of the MWTP function results from the standard assumption of decreasing marginal utility of consumption. With heterogeneous patients, a more realistic interpretation is that patients may or may not consume a fixed quantity of the drug, this quantity being determined by clinical guidance relating to what is the best average dosage (ignoring second-order effects). In this case, the slope of the MWTP function is still negative because an increase in q^c means that the drug is extended to sub-groups of patients for whom it is comparatively less effective.

$\lim_{I \to 0} \delta_I = \infty$. For the types of increasing and strictly concave functions typically employed in economics, this also implies $\delta_{III} > 0$. We retain this additional assumption. The parameter κ^c accounts for cross-country differences in willingness to pay due, for example, to differences in preferences or per capita income. b is the slope coefficient, assumed equal in each country for simplicity.

If the drug is introduced to market c, we assume that the quantity consumed equates the reimbursement price chosen by the regulator, p^c, with MWTP^c. This assumption is compatible with a system in which patients are fully insured and the regulator enforces an efficient level of consumption (e.g. by using gate-keeping mechanisms), or systems in which there is no health insurance and drug expenditure is fully out-of-pocket. The individual demand function for country c is then obtained by rearranging Eq. (1):

$$q^c = \frac{\kappa^c \delta(I) - p^c}{b}. \tag{2}$$

2.1 The firm

The firm chooses I so as to maximise profit from sales in the global market:

$$\Pi(I; p^A, p^B, \boldsymbol{\beta}) = N \left[\mathbf{1}_{p^A \geq r^A} n^A (p^A - m) q^A + \mathbf{1}_{p^B \geq r^B} (1 - n^A)(p^B - m) q^B \right] - I, \tag{3}$$

where m is the marginal cost of production, $N = N^A + N^B$ is the size of the global population eligible to receive the treatment, normalised to 1 in what follows, and $n^A = N^A/N$ is the relative size of country A's market. The indicator function $\mathbf{1}$ accounts for the fact that the new drug is marketed in country c if and only if p^c exceeds a reservation price $r^c \geq m$, where r^c is decreasing in the size of the market in country c. This means that r^A (r^B) is decreasing (respectively, increasing) in n^A. The assumption is reasonable if, from the perspective of the firm, the opportunity cost of not selling in a market is greater, the greater is the size of that market.[4] This assumption will be important for the empirical analysis. Finally, $\boldsymbol{\beta} \stackrel{\text{def}}{=} (n^A, m, \kappa^A, \kappa^B, r^A, r^B)$.

2.2 Regulators

Regulators are responsible for setting prices so as to maximise welfare in their respective countries, assumed to be a weighted average of internal consumer surplus and the firm's profit accru-

[4] A simple way to model this is to assume that the firm will only sell in country A (for example) if its profit on sales exceeds an exogenous threshold value, $R > 0$:

$$n^A (r^A - m) q^A (p^A; p^B) \equiv R.$$

From this it follows that $r^A_{n^A} < 0$. Justification for this assumption may be found in the presence of fixed costs of marketing the new drug in the country, or other circumstances that we do not explicitly model. There is evidence that even essential pharmaceuticals may not be available in some markets, and this is most frequent in low and middle income countries (Hogerzeil and Mirza, 2011). This occurs despite the fact that the marginal cost of production is typically almost negligible for most pharmaceutical products (Newhouse, 2004; Barton and Emanuel, 2005).

ing to that country:

$$W^A(p^A; p^B, \boldsymbol{\beta}) = \alpha^A \text{CS}^A + (1-\alpha^A)\lambda\Pi, \tag{4a}$$

$$W^B(p^B; p^A, \boldsymbol{\beta}) = \alpha^B \text{CS}^B + (1-\alpha^B)(1-\lambda)\Pi, \tag{4b}$$

where $\text{CS}^c = N^c \int_{p^c}^{\kappa^c\delta(I)} q^c(p^c)\text{d}p^c = \frac{N^c}{2b}\left[\kappa^c\delta(I) - p^c\right]^2$ is consumer surplus, λ is the fraction of global firm profit accruing to country A and α^c and $(1-\alpha^c)$, $0 \leq \alpha^c \leq 1$, are, respectively, the weights placed on consumer surplus and profits.

Allowing social welfare to depend on the firm's profit is meant to account for the fact that, for regulators of countries with a comparatively large pharmaceutical industry, setting comparatively high prices may be an indirect way of subsidising the domestic industry (Wagner and McCarthy, 2004; Espin et al., 2011).

2.3 Timing

We solve the model assuming that the regulators choose their optimal prices simultaneously and non-cooperatively (following Grossman and Lai 2004) and that the solution leads to a stationary equilibrium in which both countries adopt. In solving for optimal prices, we assume that each regulator knows the firm's optimal policy for the choice of R&D investment level as a function of the prices it faces. This allows us to establish the regulators' best response functions and the Nash equilibrium which, in turn, are used to carry out comparative statics analyses and derive testable hypotheses.

The timing in the model is assumed to be as follows: in the first stage, regulators in both countries simultaneously set prices to which they can commit (Grossman and Lai, 2008).[5] In the second stage, knowing the prices set in the two countries, the firm chooses its optimal level of R&D investment.

3 Optimal investment and pricing policies

We use standard methods to solve the model backwards, starting by establishing the policy which defines the firm's optimal level of R&D investment as a function of the prices chosen by the regulators. In doing this, we introduce the simplifying assumption that both countries adopt the new drug, i.e. $\mathbf{1}_{p^A \geq r^A} = \mathbf{1}_{p^B \geq r^B} = 1$.

3.1 The firm's optimal investment policy

The firm solves:

$$\Pi^*(I; p^A, p^B, \boldsymbol{\beta}) = \max_{I>0} \Pi(I; p^A, p^B, \boldsymbol{\beta}).$$

[5] It may seem unrealistic that regulators set prices before the firm invests in R&D. However, lacking commitment, regulators would be tempted to price at marginal cost of production once R&D costs are sunk. Foreseeing this, firms would decide not to invest in R&D. Hence, commitment in this context can be justified by a reputation argument. See Grossman and Lai (2008) for a discussion on this point.

The first order necessary condition for the optimal investment policy, $I^*(p^A, p^B, \boldsymbol{\beta}) > 0$, is:

$$\delta_I(I^*) = \frac{b}{[n^A(p^A - m)\kappa^A + (1 - n^A)(p^B - m)\kappa^B]}. \tag{5}$$

Given the assumptions $\lim_{I\to 0} \delta_I = \infty$ and $\delta_{II} < 0$, the second order condition is satisfied at a value of $I^* > 0$. Concavity of $\delta(I)$ implies that an increase in either p^c or κ^c both have a positive impact on I^*. Moreover:

$$\frac{\mathrm{d}I^*}{\mathrm{d}n^A} \gtreqless 0 \quad \text{if} \quad (p^A - m)\kappa^A \gtreqless (p^B - m)\kappa^B.$$

The above relationship suggests that the impact of an increase in the market share of the own country on I depends on the relative price, adjusted for the parameter κ^c. However, optimal prices as set by regulators are, in turn, a function of the exogenous parameters n^c and κ^c. These dependencies are investigated in the next subsection.

3.2 Optimal pricing

The two regulators face the same problem: to choose the optimal price in their own country, knowing that the other regulator shall simultaneously do likewise, and knowing that the firm's optimal investment policy is defined by Eq. (5). Here we consider the problem faced by the regulator in country A. A similar approach applies for the regulator in country B.

It is convenient to observe that, for a given price combination (p^A, p^B), the firm's optimal investment policy, as defined by Eq. (5), fixes δ and therefore the position of the MWTP function in both countries. Therefore, for a given value of p^A there is just one value of q^A which is consistent with both the firm's optimal investment decision and the rule equating price and MWTP. We define this as the 'feasible quantity function' $\hat{q}^A$:

$$\hat{q}^A(p^A; p^B, \boldsymbol{\beta}) = \frac{\kappa^A \delta(I^*(p^A; p^B, \boldsymbol{\beta})) - p^A}{b}, \tag{6}$$

which is helpful for the following analysis of the optimal choice of p^A. We introduce the assumption that $\hat{q}^A_{p^A p^A} < 0$ and discuss it in Appendix A.1.

The regulator in country A solves:

$$W^{A*}(p^A; p^B, \boldsymbol{\beta}) = \max_{p^A \geq r^A} W^A(p^A, I^*(p^A; p^B, \boldsymbol{\beta}); \boldsymbol{\beta}).$$

Solving the maximization of W^A with respect to p^A, noting that the Envelope Theorem may be used to eliminate the derivative of Π with respect to I^* from the maximisation problem:

$$\begin{aligned} W^A_{p^A} = n^A \left[\alpha^A \, b \, \hat{q}^A \frac{\partial \hat{q}^A}{\partial p^A} + (1 - \alpha^A)\lambda \left(\hat{q}^A + \frac{m - p^A}{b} \right) \right] \leq 0, \\ p^A - r^A \geq 0, \quad (p^A - r^A) W^A_{p^A} = 0, \end{aligned} \tag{7}$$

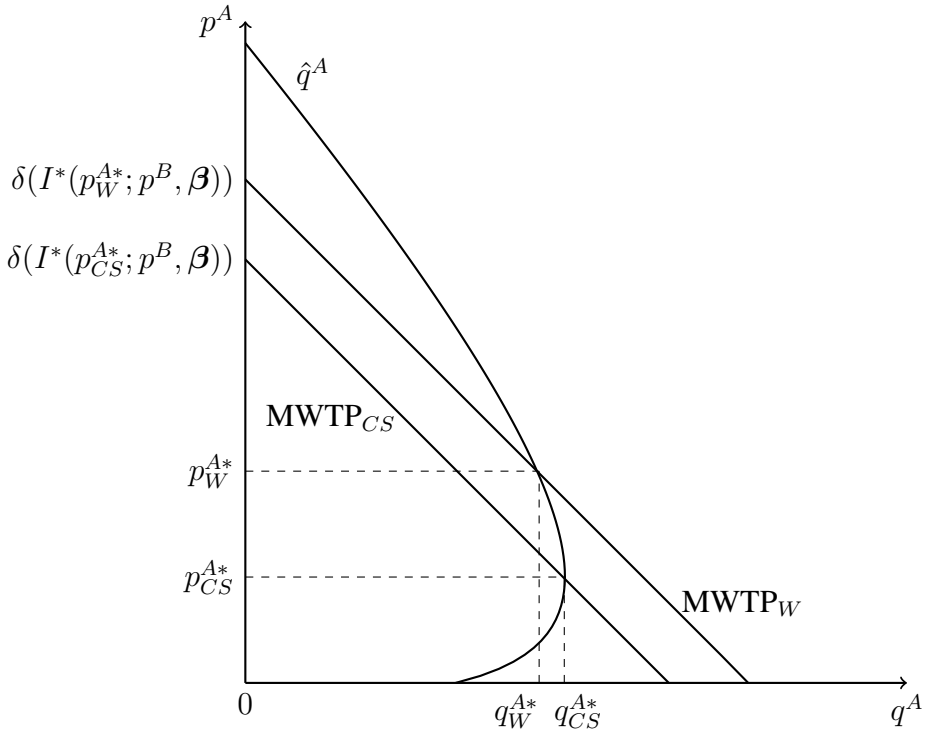


Figure 1: Feasible quantity function $\hat{q}^A$ and two inverse demand functions showing optimal levels q^{A*} resulting from the optimal choice of price p^{A*}. MWTP$_{CS}$ is the inverse demand function which solves the regulator's problem when only consumer surplus matters for welfare (giving $(q_{CS}^{A*}, p_{CS}^{A*})$). MWTP$_W$ is the inverse demand function which solves the regulator's problem when both consumer surplus and profit matter for welfare (giving (q_W^{A*}, p_W^{A*})).

where $\hat{q}^A$ is defined in Eq. (6). If $\alpha^A = 1$ (only consumer surplus matters for welfare), Eq. (7) shows that, when an interior solution exists, welfare maximization is equivalent to maximizing $\hat{q}^A$. If $\alpha^A = 0$ (only profits matter for welfare), when an interior solution exists, marginal revenue equals marginal cost.

Figure 1 provides a graphical illustration. Each value of p^A on the vertical axis is associated with a value of $I^*(p^A; p^B, \boldsymbol{\beta})$ (see Eq. (5)), which defines the position of the MWTP function. The corresponding feasible quantity function $\hat{q}^A(p^A; p^B, \boldsymbol{\beta})$ results from the rule of equalisation between price and MWTP. The figure illustrates $\hat{q}^A$ as a function of p^A which, according to the assumption that was introduced above, is strictly concave. It also shows two possible optima for the regulator in country A and the corresponding MWTP functions: $(q_{CS}^{A*}, p_{CS}^{A*})$ for when only consumer surplus matters for welfare and (q_W^{A*}, p_W^{A*}) for a value of $0 < \alpha < 1$, meaning that both consumer surplus and profits matter.

In the event that the first line of Eq. (7) is negative when $p^A = r^A$, the corner solution $p^A = r^A$ results for $W^A > 0$. This situation can be interpreted as one in which country A exploits its strategic position to set the price to the minimum value such that the firm is willing to serve the national market.

Finally, we note that, at an interior solution, the first line of Eq. (7) may be recast as an adjusted Lerner's Index:

$$\frac{p^{A*}-m}{p^{A*}} = -\frac{1}{\epsilon^A \lambda}\left[\lambda + \frac{\alpha^A}{1-\alpha^A}\left(-1+\kappa^A \frac{\partial \delta}{\partial I^*}\frac{\partial I^*}{\partial p^A}\right)\right]. \tag{8}$$

Compared with Lerner's Index for the standard monopolist's problem, Eq. (8) has an extra term. This accounts for the weighted adjustment to mark-up over marginal cost that is made as a result of the welfare function including consumer surplus rather than solely profit. The term accounts for the marginal impact of p^A on consumer surplus via the direct price effect (-1) and the indirect impact on the MWTP function ($\kappa^A(\partial\delta/\partial I^*)(\partial I^*/\partial p^A)$) via the R&D incentive.

3.3 Best response functions

When $W^A_{p^A} = 0$ at a maximising value of p^A (so that $W^A_{p^A p^A} < 0$), the implicit function theorem may be used to show that, for any parameter θ, $\mathrm{d}p^{A*}/\mathrm{d}\theta = -W^A_{p^A\theta}/W^A_{p^A p^A}$. Hence for the parameters p^B, n^A and κ^A, for an interior solution, the sign of $\mathrm{d}p^{A*}/\mathrm{d}\theta$ is the same as the sign of the following expression:

$$\frac{\partial \hat{q}^A}{\partial \theta}\left[\alpha^A b \frac{\partial \hat{q}^A}{\partial p^A} + (1-\alpha^A)\lambda\right] + \alpha^A b \hat{q}^A \frac{\partial^2 \hat{q}^A}{\partial p^A \partial \theta}, \tag{9}$$

where $\theta = p^B, n^A$, or κ^A.

When $\theta = p^B$, Eq. (9) may be used to establish the slope of the best response function for country A. If $\alpha^A = 1$, so that only consumer surplus matters for welfare, we note that, for an interior solution, it must be the case that $\partial \hat{q}^A/\partial p^A = 0$ (refer to Eq. (7)). In this case, application of the implicit function theorem leads to a closed form solution for the slope of country A's best response function (with a similar argument yielding the best response function for country B when $\alpha^B = 1$):

$$\frac{\mathrm{d}p^{A*}}{\mathrm{d}p^B} = -\frac{\kappa^B(1-n^A)}{\kappa^A n^A}; \quad \frac{\mathrm{d}p^{B*}}{\mathrm{d}p^A} = -\frac{\kappa^A n^A}{\kappa^B(1-n^A)}. \tag{10}$$

So for this special case, the slopes of the best response functions depend only on the product of ratios of the κs and the relative sizes of the market. The functions are downward-sloping and prices are strategic substitutes. If $0 < \alpha^A < 1$ (both consumer surplus and profits matter for welfare), the contribution to welfare of the profit component is positive because $\partial \hat{q}^A/\partial p^B > 0$ (refer again to Eq. (7), for the case of $\alpha^A < 1$). Hence, for α^A sufficiently close to zero, prices are strategic complements.

In principle, therefore, the best response functions may be negatively or positively sloped and possibly non-monotonic. Since the analysis of incentives to free-ride on other countries is the main motivation for our work, in what follows we shall restrict attention to negatively sloped best response functions, which are a necessary condition for free-riding behaviour to exist. In other words, we assume that the weight on consumer surplus is sufficiently large within each country's welfare function to make prices strategic substitutes.

Consider now the impact of changes in some of the main parameters of interest on the position of the best response function, i.e. on the value of $p^{A*}(p^B)$. These results will be useful in section 3.4, where we consider the comparative statics of equilibrium price levels. It is again useful to start by assuming that $\alpha^A = 1$, so that only consumer surplus matters. In this special case, as already noted, $\partial\hat{q}^A/\partial p^A = 0$ at the optimal price, and so the sign of Eq. (9) is the same as the sign of $\partial^2\hat{q}^A/\partial p^A\partial\theta$. For $\theta = n^A$, the following proposition applies.

Proposition 1. *If only consumer surplus matters for country A's welfare and the marginal impact of p^A on the feasible quantity $\hat{q}^A$ is increasing in its market share, then the optimal price $p^{A*}(p^B)$ is increasing in country A's market share.*

Proof. See Appendix A.2.

Corollary 1. *Other things being equal, when only consumer surplus matters for welfare in both countries, the sign of $\partial p^{B*}/\partial n^A$ is the opposite to that of $\partial p^{A*}/\partial n^A$.*

Proof. Holding the total size of the market fixed, an increase in n^A implies a reduction in the size of country B's market. Therefore a similar argument as that used for the proof of Proposition 1 may be used to prove Corollary 1.

Intuitively, the condition of Proposition 1, namely that the marginal impact of p^A on the feasible quantity $\hat{q}^A$ is increasing in n^A, means that the upward shift of the MWTP function implied by an increase in the price p^A is greater the greater the market share, n^A. This may happen because, other things being equal, an increase in price strengthens the incentive to invest in R&D more when it occurs in a country with a comparatively large market share, owing to the larger impact that an increase in price has on profits. Whether the condition is satisfied or not depends on the functional form of $\delta(I)$. In Appendix A.2, we show that the condition under which Proposition 1 holds ($\partial^2\hat{q}^A/\partial p^A\partial n^A > 0$) is satisfied by some common functional forms of $\delta(I)$.

When $\alpha^A < 1$, so that both consumer surplus and profits matter for welfare, we can no longer eliminate the first two terms in Eq. (9) when establishing the sign of $\partial p^{A*}/\partial n^A$. The sign of $\partial\hat{q}^A/\partial n^A$ is ambiguous because it is the same as the sign of $\partial I^*/\partial n^A$, and this may be positive or negative (refer to the end of section 3.1). The sign of $\partial\hat{q}^A/\partial p^A$ is also ambiguous, since it depends on whether p^{A*} lies above or below the consumer surplus maximising price (refer to Figure 1). Overall, it is the case that, as long as the weight on consumer surplus in the regulator's objective function is sufficiently close to 1, an increase in n^A shifts country A's best response function upwards. Using similar arguments to those in Corollary 1, the effect of changing n^A on p^{B*} is the opposite to that of the effect on p^{A*}.

Now consider the comparative statics results for κ^A. Letting $\theta = \kappa^A$ in Eq. (9), similar arguments may be used to observe that, when the weight on consumer surplus in the welfare function is sufficiently large, the sign of $\mathrm{d}p^{A*}/\mathrm{d}\kappa^A$ is driven by the sign of the term $\frac{\partial^2\hat{q}^A}{\partial p^A\partial\kappa^A}$. The following proposition summarizes the result for the case where $\alpha^A = 1$.

Proposition 2. *If only consumer surplus matters for country A's welfare, then the optimal price* $p^{A*}(p^B)$ *is increasing in* κ^A.

Proof. See Appendix A.3.

Finally, we briefly comment on the impact of the fraction of the global profit accruing to countries A and B, λ and $1-\lambda$ respectively, on the best response functions. Given that an increase in λ corresponds to an increase in the weight on the profit component of the welfare function for country A, referring to Eq. (7) it follows that an increase in λ (respectively, $1-\lambda$) implies an increase in $p^{A*}(p^B)$ (respectively, $p^{B*}(p^A)$), as long as the profit maximizing price exceeds the consumer surplus maximizing price.

3.4 Equilibria

Section 3.3 showed that, without placing additional restrictions on parameter values, best response functions may slope upwards or downwards, meaning that prices may be strategic substitutes or complements. This has implications for the properties of the Nash equilibria. Given that our objective is to obtain testable hypotheses for settings in which regulators may have an incentive to free-ride on each other, we restrict our attention to unique stable Nash equilibria (refer to section 2.3) in pure strategies which result from negatively sloped best response functions, such that both countries adopt the new drug.

With this focus in mind, two types of Nash equilibria, as illustrated in Figure 2, are relevant. Figure 2(a) shows a standard Nash equilibrium with interior solutions, meaning that the equilibrium values p^{A*} and p^{B*} are strictly greater than their respective reservation prices. Figure 2(b) shows a Nash equilibrium involving a corner solution for country A ($p^{A*} = r^A$), owing to the fact that A's best response function lies below that of B over the whole relevant domain. This type of equilibrium is also relevant in other fields, such as environmental economics, in games where regulators strategically interact in setting their emission levels (see, for example, Finus, 2001).

Consider now the comparative statics for an interior Nash equilibrium when prices are strategic substitutes. For a parameter θ, substitute $p^{A*}(\theta)$ and $p^{B*}(\theta)$ into the first order conditions:

$$W^A_{p^A}(p^{A*}(\theta), p^{B*}(\theta), \theta) \equiv 0, \tag{11a}$$

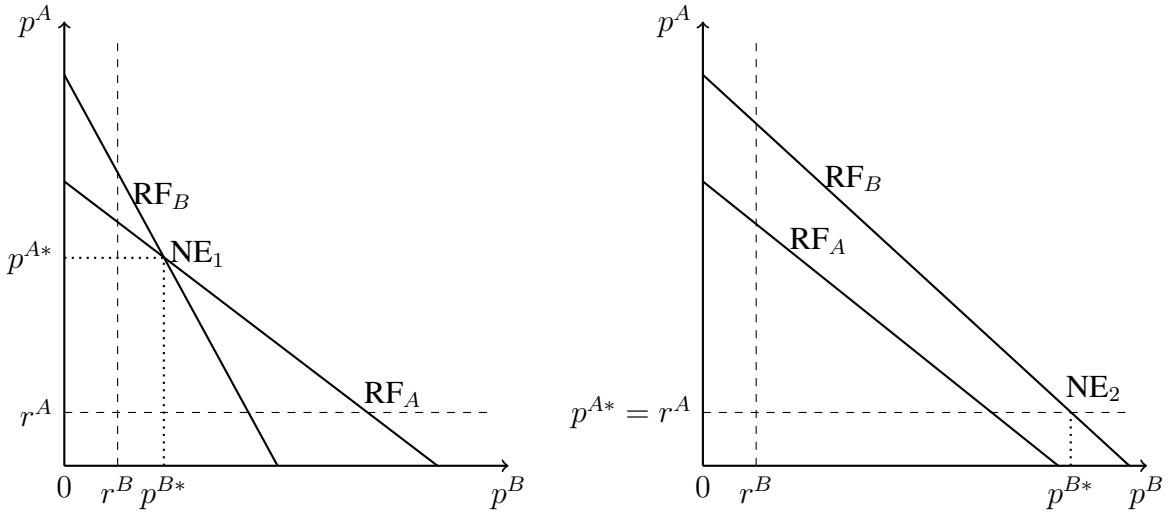
$$W^B_{p^B}(p^{A*}(\theta), p^{B*}(\theta), \theta) \equiv 0. \tag{11b}$$

Differentiating with respect to θ gives:

$$\begin{bmatrix} W^A_{p^Ap^A} & W^A_{p^Ap^B} \\ W^B_{p^Bp^A} & W^B_{p^Bp^B} \end{bmatrix} \begin{bmatrix} p^{A*}_\theta \\ p^{B*}_\theta \end{bmatrix} = \begin{bmatrix} -W^A_{p^A\theta} \\ -W^B_{p^B\theta} \end{bmatrix}. \tag{12}$$

Using these results and Cramer's Rule in Eq. (12), one has:

$$p^{A*}_\theta = \frac{\begin{vmatrix} -W^A_{p^A\theta} & W^A_{p^Ap^B} \\ -W^B_{p^B\theta} & W^B_{p^Bp^B} \end{vmatrix}}{|\mathbf{H}|}. \tag{13}$$



(a) Downward-sloping, intersecting best response functions showing interior solution NE$_1$.

(b) Non-crossing best response functions showing a corner solution for country A.

Figure 2: Reaction functions and Nash equilibria

A similar result applies for the partial derivative of p^{B*} with respect to θ.

Given our focus on stationary equilibria, we may refer to the ideas of Dixit (1986) to conclude that the denominator of Eq. (13), which is the determinant of the Hessian of a dynamical system in (p^A, p^B), will be positive. Hence the sign of p^{A*}_θ is determined by the sign of the numerator of Eq. (13). In principle, this allows us to study the comparative statics for the impact of any parameter in the model on the Nash equilibrium prices at an interior equilibrium.

Here our main focus is on the role of the relative market size of country A, n^A, for the following reasons. First, this parameter has been studied in other papers, albeit with a different focus (e.g. Grossman and Lai 2008). Second, in section 1, we discussed the EU proposal to move toward joint procurement, something which would have a large impact on the relative market size of a European contracting authority, and a smaller impact on other dimensions, such as the average level of GDP per capita in the EU (which is related to the parameter κ in our model).

We summarize the impact of a change in n^A in the following proposition:

Proposition 3. *When prices are strategic substitutes, the conditions of Proposition 1 are sufficient to imply that an increase/decrease in n^A implies an increase/decrease in country A's price in a stable equilibrium involving an interior solution.*

The result may be proved by replacing θ with n^A in Eq. (13). The condition is sufficient because, under the conditions of Proposition 3, the determinant is the sum of two strictly positive terms.

Now that the difference between equilibria involving an interior and a corner solution has been introduced, it is interesting to investigate the role of the model parameters in determining whether the relevant Nash equilibrium is of one type or the other. The comparative statics

analysis of section 3.3 has shown that several parameters affect the position of the best response functions and hence potentially also affect the relevant type of equilibrium. The impact of n^A on the type of equilibrium is described in the following Corollary.

Corollary 2. *If the conditions under which $\partial p^{A*}/\partial n^A > 0$ hold, and the initial equilibrium involves a corner solution for country A ($p^{A*} = r^A$), then an increase in the relative size of country A's market from n^A to $n^A + \epsilon$, keeping the other parameters fixed, may lead to a new equilibrium with interior solution $p^{A*} > r^A$.*

The corollary follows immediately from the analysis of the dependency of the position of the best response functions on n^A. In particular, we showed in Proposition 1 that, under reasonable assumptions, an increase in n^A shifts country A's best response function upwards and B's downwards. Therefore, if initially A's best response function lies below B's, the increase in n^A may imply a shift from an equilibrium where $p^A = r^A$ to one with interior solutions. The negative relationship between r^A and n^A that was assumed in section 2.1 reinforces this tendency. This situation is illustrated with a simulation in Appendix B, where we show how an increase in n^A shifts the equilibrium from a corner solution to an interior one for country A.

3.5 Summary of theoretical predictions

Before moving to a brief summary of the theoretical predictions that will be tested in the next section, a comment on possible issues related to the link between the theoretical and the empirical analysis is in order. While we have studied theoretically the interaction between two heterogeneous countries, the empirical analysis necessarily involves several heterogeneous countries. Studies combining theoretical and empirical analysis in other frameworks where spillover effects exist face the same issue and use diverse approaches. For example, Devereux et al. (2008) study a theoretical model with several identical countries, but allow for heterogeneity in the empirical analysis. Our approach is similar to that of Beshkar et al. (2015), who study a theoretical model with two heterogeneous countries and extend the empirical analysis to several countries.

For the Nash equilibria which form the focus of our work, prices are strategic substitutes, and this represents one form of free-riding behaviour. Further, we have shown that two different classes of Nash equilibria exist: interior solutions and corner solutions (refer to Figure 2). Proposition 3 has shown that, for interior solutions, an increase/decrease in the relative size of the market of one country increases/decreases the Nash equilibrium price in that country.

A corner solution arises when the best response functions do not intersect. In this case, assuming adoption of the new drug by both countries, the country whose best response function lies below that of the other country will price at the reservation price, and the other country prices optimally (Figure 2(b)). In this case, we would expect that:

1. when countries price at the reservation price, their prices are independent of prices set in other countries;

2. price is lower, the larger is the relative size of a country for which the reservation price is a binding constraint, because of the negative relationship between market size and reservation price.

Concerning the impact of different parameter values on the type of equilibrium, Corollary 2 discusses the conditions under which an increase in n^A may imply a shift from a corner to an interior solution. An implication of this corollary is that, given a sample of countries, interior solutions may be more likely for countries with comparatively larger market sizes.

Proposition 2 shows that an increase in κ^c shifts the best response function upwards. Hence, we also expect this variable to have a positive impact on price. Finally, the fraction of global profits accruing to one country is also expected to have a positive impact on its price, as long as the profit maximizing price exceeds the consumer surplus maximizing price.

4 Empirical framework

To test the theoretical predictions and to estimate the impact of different variables on the prices set by regulators when a product is introduced into the market, we estimate the following model:

$$\ln[FRP_{i,c,t}] = \alpha + \gamma \ln[\text{avg}(P_{i,-c,t-1})] + \mu \frac{N_{i,c,t}}{Ntot_{i,t}} + \boldsymbol{\delta}' \mathbf{H}_{c,t} + \zeta_i + \epsilon_{i,c,t}, \tag{14}$$

where i denotes the drug, c denotes the country, t denotes time and $-c$ denotes 'all countries other than c' that have already adopted the drug. $\epsilon_{i,c,t}$ is the idiosyncratic error term, assumed to have the usual properties.

The regressand $\ln[FRP_{i,c,t}]$ is the natural logarithm of the first reimbursed price of drug i in country c, which takes place at time t, that is, the price when the product was firstly made available and reimbursed (and is the equivalent of the price chosen by the regulator in the theoretical section). The focus on the introductory price is common to other contributions in the literature on price determinants (Puig-Junoy and González López-Valcárcel, 2014; Ekelund and Persson, 2003; Lu and Comanor, 1998).

$\ln[\text{avg}(P_{i,-c,t-1})]$ is the natural logarithm of the average price set in the other countries where drug i is offered, in the period immediately prior to the period in which drug i was reimbursed in country c. The coefficient γ is therefore the elasticity of the first reimbursed price with respect to the average price in the other countries at the time of reimbursement. Therefore, if prices are strategic substitutes (under the free-riding hypothesis), its sign will be negative. $\ln[\text{avg}(P_{i,-c,t-1})]$ is peculiar to our model of strategic interaction: while previous contributions have considered the impact of regulatory characteristics of the market, such as the use of external reference prices, on optimal pricing (Kanavos and Vandoros, 2011; Kyle and Qian, 2014), to the best of our knowledge, no contribution has investigated the extent to which the launch price of a drug in one country is affected by the prices set in other countries.

We use the average of the lagged price for two reasons. Firstly, drugs are not introduced into markets simultaneously and it seems reasonable to assume that there exists a lag in the response to prices set in other countries. If this is the case, ignoring the lagged effect may miss much of the strategic interaction effect. Secondly, the use of the lagged value prevents the problem of reverse causality in the estimation of Eq. (14).[6]

[6]Similar reasons lead to the same choice of model specification in the paper by Fredriksson and Millimet (2002) on strategic interaction in environmental policy.

The theoretical results highlight that a country's relative market size is a key variable for the determination of its optimal pricing policy. To test this, we include as a regressor $N_{i,c,t}/Ntot_{i,t}$, the ratio of country c's prevalence[7] of diseases treated by product i to the total prevalence, where $Ntot_{i,t}$ is the sum of the annual prevalence of disease over all countries included in the sample. With only a few exceptions (Cabrales and Jiménez-Martín, 2013; Kyle and Qian, 2014), the total market size is not considered among the determinants of pharmaceutical prices in empirical analyses.

$\mathbf{H}_{c,t}$ is a vector of country-varying, time-varying, regressors which includes GDP per capita and the level of pharmaceutical exports as proxies for the variables κ and λ. Finally, ζ_i is a product fixed effect, the inclusion of which is intended to capture the drug's quality and therapeutic advance, both of which are unobserved. A product fixed effect is also essential because our price measure is the price per mg, but the standard course of treatment varies across drugs (Cabrales and Jiménez-Martín, 2013; Kyle and Qian, 2014).

4.1 Data

Our data set comprises the 108 non-generic human drugs in the Anatomic Therapeutic Chemical class L01 (Antineoplastic agents) that were authorized by the European Medicines Agency (EMA) between January 1995, when the EMA was established, and 30th March 2017.[8] We focus on oncology therapies because, together with statins, they represent the two largest therapeutic classes in terms of sales value (OECD, 2008). Further, in recent years, this therapeutic area has been characterised by a number of key innovations, which have had substantial impacts on the survival and quality of life of patients (PhRMA, 2016), as well as on costs. Indeed, much of the growth in prescription drug sales in the coming years is forecast to come from some of the newest cancer immunotherapies (EvaluatePharma, 2017).

Of these 108 products, 38 were excluded from the analysis, leaving 70 for the estimation of Eq. (14). In addition, some single observations on drugs included in the sample were dropped because, at the time of the first reimbursement, the drug was not patent protected or the product was launched in the country prior to the period covered by the data. Furthermore, since Eq. (14) regresses the first reimbursed price on the average price set by other countries, the observation relating to the first country or countries to launch the product is dropped because the average price is missing. Appendix C discusses these matters in more detail and lists the drugs included in the final sample. The sample size is 883 observations.

Quarterly prices for the period 2007–2017 were retrieved from the Pricing Insights IMS database for the 25 countries which, in 2007, were members of the OECD. Table 5 in Appendix C lists the countries and the dates from which price data are available. Although it might be claimed that regulators also take into account prices set in non-OECD countries when setting their prices, WHO (2015b) and Espin et al. (2014) show that they refer to countries which are located in the same region, with comparable income levels and similar socioeconomic conditions. For cross-

[7] Unless stated otherwise, in the remaining part of the paper, the term 'prevalence' is used to indicate the absolute number of individuals suffering from a disease.

[8] Since Regulation (EC) No. 726/2004, all new cancer drugs have to be centrally approved by the EMA.

country comparisons, we express prices in Euro by using period specific exchange rates (as in Kanavos and Vandoros 2011).

We compute the price per mg because the same product may be available with a different pack size and/or different strength in different countries, and we wish to make prices comparable both within, and across, countries. Moreover, when different pack sizes and/or different strengths are available for the same product at the same time within one country, we refer to the lowest price per mg, assuming that this is the relevant price for the payer. In 85.3% of observations we refer to the *price to the hospital* per mg. However, in some countries, mandatory rebates are in force. When this is the case, we consider the *manufacturer less mandatory rebates price* per mg (13.5% of observations). For the remaining observations, where neither is available, we refer to the *price to pharmacies* (0.6%) or to the *retail price* (0.6%).

$N_{i,c,t}$ and $Ntot_{i,t}$ are proxied by the number of potential consumers at the country level and over all countries, respectively. Prevalence data are extracted from the Global Burden of Diseases (GBD) 2015 database (Catalá López and Tabarés Seisdedos, 2016). The GBD cause and sequelae list is organised hierarchically: we consider the prevalence at Level 3, which contains the finest level of detail for causes captured in GBD 2015. In particular, we extract data for the 28 different neoplasm causes available in the data set (see Table 7 of Appendix C). To match each drug i with its market size, we consider the therapeutic indication(s) reported by the EMA. According to these indications, each drug is matched to one or more of the 28 'Level 3' neoplasm causes identified by GBD 2015. When a drug has more than one indication, prevalence is obtained as the sum of prevalences over all diseases with an indication. Since prevalence data are available only at five year intervals, prevalence is considered constant within the intervening four years.

Finally, $\mathbf{H}_{c,t}$ includes the natural logarithm of GDP per capita in current Euro, as a proxy for ability to pay (as in Cabrales and Jiménez-Martín, 2013; Kyle and Qian, 2014). These data are gathered from the World Bank Indicators. $\mathbf{H}_{c,t}$ also includes the natural logarithm of the export of medicinal and pharmaceutical products in current Euro as a proxy for the importance of the pharmaceutical industry in the country. These data are obtained from the United Nations Conference on Trade and Development Statistics. Since both variables are expressed in US $, for consistency with the way that price data are treated, we convert them to Euro, using the quarterly exchange rate as reported in the Pricing Insights IMS database.

4.2 Empirical results

Column (1) of Table 1 shows the results of the estimation of Eq. (14) for the full sample. This regression shows no evidence of a relationship between the first reimbursed price and the lagged average price in countries where the drug is available. The coefficient of the other key variable of our model, the relative prevalence, is also not statistically significant.

However, the results in column (1) are of limited interest as a test of the theory if it is the case that interior solutions are relevant for some countries in the sample and corner solutions are relevant for others. The theory predicts a different impact of the key variables of the model – price in the other countries and relative market size – according to whether the Nash Equilibrium involves an interior or a corner solution. According to Corollary 2, an increase in the relative size of the market, keeping the other parameters fixed, may imply a shift from a corner to an

interior solution. Hence, based on this theoretical result, in columns (2) and (3) we show the results for sub-samples defined according to whether $N_{i,c,t}/Ntot_{i,t}$ is above or below its median value, computed over all countries and all diseases.

Column (2) shows that, as predicted by the theory, for countries with a relatively large market share ($N_{i,c,t}/Ntot_{i,t}$ above the median), i.e. those for which an interior solution is more likely (Corollary 2), the impact of the average price set by other countries on the first reimbursed price is negative and statistically significant. In particular, a 1% increase in the average price set by other countries is associated with a reduction of roughly 0.16% in the first reimbursed price. This is consistent with prices being strategic substitutes and may be interpreted as being evidence of free-riding. Column (2) also shows that the effect of relative market size on the first reimbursed price is, instead, positive and (weakly) statistically significant (Proposition 3): an increase of one percentage point in the country's relative market size is associated with a 0.49% increase in the price.

In contrast, column (3) of Table 1 shows that, for countries with a relatively small market share, there is no impact of the price set in other countries on the first reimbursed price. Moreover, in contrast to the results in column (2), column (3) shows evidence of a negative effect of the relative market size on the first reimbursed price: an increase of one percentage point in the country's relative market size is associated with a -10.00% decrease in the price. Both of these results are consistent with the theoretical predictions for a corner solution. Hence, the results reported in column (3) may be interpreted as illustrating a different form of free-riding: countries with a relatively small market share exploit their strategic position to set the first reimbursed price at the minimum level which ensures access to the new drug for their patients.

Concerning the results for the other covariates reported in Columns (1) to (3) of Table 1, first reimbursed prices are increasing with the marginal willingness to pay as proxied by GDP per capita (Proposition 2) and with the importance of the pharmaceutical sector in the country, as proxied by the export of medicinal and pharmaceutical products. These findings are consistent with the theoretical predictions and, for GDP per capita, are consistent with most of the existing literature (Kyle and Qian, 2014; Cabrales and Jiménez-Martín, 2013).

Table 1 used the median value of $N_{i,c,t}/Ntot_{i,t}$ as the threshold to split the sample. The threshold is unobserved, however, and absent knowledge of its value, we perform sensitivity analysis of the results by setting the threshold at different levels. Table 2 presents results for the samples split according to a range of thresholds defined by the 2nd to the 8th deciles of the relative prevalence of the disease. The subscripts a and b of the estimated coefficients denote, respectively, parameter estimates from the model estimated for the subset of observations lying 'above' and 'below' the threshold.

The results show that setting the threshold at progressively higher deciles increases the absolute value of the estimate of the free-riding effect ($\hat{\gamma}_a$), as well as the statistical significance of the estimate. However, as the threshold increases, more observations fall below the threshold, which appears to dilute the effect of market share below the threshold ($\hat{\mu}_b$) and, ultimately, it is not statistically significant. Overall, however, the results in Table 2 are consistent with the findings reported in columns (2) and (3) of Table 1. The theoretical prediction of a positive impact of market share on prices above the threshold (Proposition 3) is supported by statistical significance for only some values of the threshold. Finally, the last two columns of Table 2 report the results

	(1) Full sample ln[FRP]	(2) Above 50% threshold ln[FRP]	(3) Below 50% threshold ln[FRP]
ln(avg(price others lag))	-0.061	-0.164**	0.065
	(0.055)	(0.078)	(0.084)
N/Ntot	0.162	0.485*	-10.523*
	(0.212)	(0.275)	(5.670)
ln(GDP per capita)	0.150***	0.084*	0.145***
	(0.018)	(0.044)	(0.023)
ln(export)	0.014***	0.020*	0.017***
	(0.005)	(0.012)	(0.006)
Observations	883	441	442
R^2 (within)	0.130	0.086	0.194

Product FE included; Standard errors in parentheses; * $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$.

Table 1: Results using a 50% threshold for relative population size.

of a test of the null hypothesis that the estimated coefficients $\hat{\gamma}$ and $\hat{\mu}$ are the same in the two sub-samples. In the majority of cases, the null hypothesis is rejected at the 5% significance level, which is consistent with the theory as long as interior and corner solutions are more relevant above and below the threshold, respectively. As a robustness check, in Table 8 of Appendix C, we repeat the analysis using standard errors clustered by country. The qualitative nature of the results for the effect of price set by other countries above the threshold, and market share below the threshold, is unchanged. Instead, above the threshold, market share is no longer significant for any decile.

Table 3 shows the results obtained by adding country fixed effects to Eq. (14). These are intended to absorb differences across countries in price control policies, as well as other country-specific heterogeneity such as the characteristics of the country's health care commissioning system, which are unobserved to us. Table 3 shows that, while results for the price set by other countries are qualitatively unchanged, the effect of the relative market size almost disappears. These results are not surprising, since the variability of the relative market size is very limited within countries. Importantly, however, this specification shows that regulators react differently to the pricing policies of other countries according to the relative size of the market. In particular, the evidence concerning the negative slope of the best response function is confirmed for the sub-sample of countries with comparatively large markets. A series of further robustness checks, which report findings in line with the aforementioned results, are presented in Appendix D.

Taken together, the empirical results lend broad support to the predictions of the theoretical model that were summarised in section 3.5. There is reasonably strong evidence that, for countries with relatively large market shares, prices are strategic substitutes and free-riding occurs. Further, for these countries, there is some evidence that equilibrium prices are increasing in the relative size of the market (Proposition 3). Yet for countries with relatively small market shares, the evidence suggests that prices are set as low as possible, consistent with the idea that there

$\frac{N}{Ntot}$ threshold		Country/product above threshold		Country/product below threshold		Wald test	
Decile	$\frac{N}{Ntot}$	$\hat{\gamma}_a$	$\hat{\mu}_a$	$\hat{\gamma}_b$	$\hat{\mu}_b$	$\hat{\gamma}_a = \hat{\gamma}_b$	$\hat{\mu}_a = \hat{\mu}_b$
2^{nd}	0.0057	-0.063	+0.364	+0.028	-38.969***	can't reject	reject***
3^{rd}	0.0067	-0.086	+0.296	+0.081	-40.533***	can't reject	reject***
4^{th}	0.0082	-0.121*	+0.430*	+0.094	-22.093**	reject*	reject***
5^{th}	0.0104	-0.164**	+0.485*	+0.065	-10.523*	reject**	reject**
6^{th}	0.0153	-0.230***	+0.508	+0.112	-7.436**	reject***	reject**
7^{th}	0.0423	-0.284***	+0.301	+0.085	-1.002	reject***	can't reject
8^{th}	0.0676	-0.453***	+0.229	+0.062	+0.021	reject***	can't reject

Product FE included; * $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$. Subscripts a and b on $\hat{\gamma}$ and $\hat{\mu}$ denote results above and below the threshold, respectively. Results for the 5th decile are taken from columns (2) and (3) of Table 1.

Table 2: Results for different thresholds.

$\frac{N}{Ntot}$ threshold		Country/product above threshold		Country/product below threshold		Wald test	
Decile	$\frac{N}{Ntot}$	$\hat{\gamma}_a$	$\hat{\mu}_a$	$\hat{\gamma}_b$	$\hat{\mu}_b$	$\hat{\gamma}_a = \hat{\gamma}_b$	$\hat{\mu}_a = \hat{\mu}_b$
2^{nd}	0.0057	-0.102*	-0.307	+0.016	-16.103	can't reject	can't reject
3^{rd}	0.0067	-0.092	-0.669	-0.006	+1.911	can't reject	can't reject
4^{th}	0.0082	-0.110*	-0.665	+0.008	+7.486	can't reject	can't reject
5^{th}	0.0104	-0.151**	-0.714	+0.008	+13.286*	reject*	reject*
6^{th}	0.0153	-0.162**	-0.673	+0.044	+5.623	reject**	can't reject
7^{th}	0.0423	-0.237***	+0.376	+0.223	-1.315	reject***	can't reject
8^{th}	0.0676	-0.386***	+0.812	+0.014	-1.398	reject***	reject*

Product and country FE included; * $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$. Subscripts a and b on $\hat{\gamma}$ and $\hat{\mu}$ denote results above and below the threshold, respectively.

Table 3: Results for different thresholds with country FE.

exist corner solutions. Further, for these countries, there is evidence of a negative relationship between price and relative market size, which would be consistent with the idea that the reservation price is falling in the relative size of the market.

5 Conclusion

The pharmaceutical industry is responsible for a large proportion of R&D investments, upon which the availability of future innovation depends. The willingness to invest in R&D is strongly related to the profits that companies expect to make, which in turn depend on prices and access to the market of innovations. The fact that prices in most countries are regulated, and regulation is specific to each country, implies a spillover effect: an increase in prices and profits in one country

benefits all countries by inducing larger R&D investments and, as a result, creates more benefits for patients. The outcome of strategic interaction among countries may be an incentive for some countries to free-ride. For example, it has been suggested that countries might free ride on the higher prices allowed in the United States, which stimulate R&D investment, while enjoying the benefits of lower prices in terms of patient access and expenditure burden.

To the best of our knowledge, this is the first paper to model explicitly this strategic interaction, with the aim of providing insights into how the specific characteristics of different countries affect their optimal policies. Using a two-country model, we first study which characteristics of one country affect its optimal pricing policy, given the prices set by the other. We show that, under reasonable conditions, prices are strategic substitutes and an increase in the relative size of the market of one country tends to shift its best response function upwards. The key underlying mechanism for the latter result is that an increase in prices in one country has a sizeable impact on the industry profits and hence on incentives to invest in R&D only if the size of the market is sufficiently large. We also show that there may exist equilibria where, in one country, the price is as low as the reservation price, and the strategic interaction leads the other country to raise its price to provide incentives to invest in R&D. This may also be considered a form of free-riding.

In line with the theoretical predictions, our analysis of the prices set for 70 cancer drugs in 25 OECD countries between 2007 and 2017 shows evidence of behaviour that is consistent with the free-riding hypothesis and which differs according to country-level characteristics. Countries with comparatively large markets tend to react to increases in other countries' prices by lowering their own prices. This seems to confirm a prediction of the theory in that, as long as the weight on consumer surplus in the regulator's objective function is sufficiently large, prices are strategic substitutes. On the other hand, when the relative size of the market is small, regulators' decisions seem to be consistent with the objective of introducing the product at as low a price as possible. In particular, they do not react to pricing policies of other countries and they set prices which are decreasing in the relative size of their own market. It is important to clarify that the approach of our study is positive rather than normative. Hence, the evidence that pricing policies are consistent with the free-riding hypothesis should not be interpreted as evidence that prices are lower than would be desirable from the societal perspective. This is because there exist other relevant mechanisms which may affect the efficiency of drug prices such as, for example, the presence of asymmetric information on R&D costs (Light and Kantarjian, 2013; Prasad and Mailankody, 2017), which are not accounted for in the model.

The model also provides a conceptual framework with which to analyse real world proposals to coordinate pricing policies. On 10 April 2014, the European Commission approved a Joint Procurement Agreement (JPA), which will enable all EU countries collectively to procure pandemic vaccines and other medical countermeasures. This has led to the creation of a European facility for the joint procurement of medical countermeasures in the context of cross-border health threats (i.e. communicable diseases). Interestingly, in 2015, the American Chamber of Commerce to the European Union issued a position paper calling for a *'more strategic use of procurement to stimulate innovation uptake'*. The document claims that *'a more strategic assessment of value for money can be achieved to stimulate investment in innovation and foster effective, resilient and accessible health systems in Europe'*. With reference to our model, the implementation of joint procurement in Europe would make the real world relationship between

the United States and Europe more akin to our two-country model described above. According to our results, if dynamic efficiency concerns are relevant in defining price setting policies, joint procurement would substantially change Europe's strategic position by increasing the relative size of the reference market for the single procurement authority.

Underlying the joint procurement proposal is the idea that it would lead to lower prices for European countries. This is in line with the idea that an increase in the relative market size would reduce the minimum price that the firm is willing to accept, i.e. this is the expected impact for a corner solution. However, our model shows that an increase in the relative size of the market makes a corner solution *less* likely. Therefore, the assessment of the net impact of moving towards join procurement in Europe should also consider the change in the strategic position of Europe with respect to the rest of the world and, in particular, the United States. Our model suggests that it is not obvious that moving to a single European regulator would lead to lower prices. Finally, since EU legislation permits single countries to decide freely whether to join the procurement agreement or not, the model could provide some insights to study which countries are more likely to join the initiative.

Although we believe that the model can make a valuable contribution to the literature by providing a basis for a formal analysis of strategic interaction in the trade-off between static and dynamic efficiency, we also acknowledge a number of limitations that future research should aim to overcome. The most important observation is that there are other mechanisms that may affect the dependency of the optimal policy in one country on the policy adopted in other countries, such as external reference pricing. Ideally, these mechanisms should also be accounted for in the model. Furthermore, the model assumes that the drug is 100% reimbursed by the payer, who is also responsible for the definition of the level of demand. This assumption is more suited to some classes of drug than others. For example, insurance coverage tends to be higher for very costly drugs, which are often drugs targeting very severe health conditions and life threatening diseases. In these cases, payers actually play a key role in the definition of demand, by heavily regulating access to the technology. Lakdawalla and Sood (2009) investigate the role that insurance may play in mitigating the trade-off between static and dynamic efficiency, and an extension in this direction would be important for classes of drugs for which the patient's decision is central in selecting the alternative for treatment. Finally, direct public investment in R&D, as well as other policies that may affect investment decisions (such as tax regimes), could be incorporated into our framework.

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A Proofs

A.1 Strict concavity of $\hat{q}^A$

In Section 3 we introduce the assumption that $\hat{q}^A_{p^A p^A} < 0$. Here we investigate the conditions under which it holds and show that these are satisfied for some very standard functional forms for the production function δ. Given the definition of $\hat{q}^A$ in Eq. (6),

$$\frac{\partial^2 \hat{q}^A}{\partial p^A \partial p^A} = \frac{\kappa^A}{b}\left[\frac{\partial^2 \delta}{\partial I^2}\left(\frac{\partial I^*}{\partial p^A}\right)^2 + \frac{\partial \delta}{\partial I}\frac{\partial^2 I^*}{\partial p^A \partial p^A}\right]. \tag{15}$$

The application of the implicit function theorem to Eq. (5) enables us to obtain an expression for $\partial I^*/\partial p^A$, from which the expression for $\partial^2 I^*/\partial p^A \partial p^A$ follows.

After substituting these partial and cross-partial derivatives into Eq. (15) and performing standard algebraic simplifications, Eq. (15) may be written as,

$$\frac{\partial^2 \hat{q}^A}{\partial p^A \partial p^A} = \frac{b n^A (\kappa^A)^2}{\xi^4 (\partial^2\delta/\partial I^2)}\left[3\kappa^A n^A - b\kappa^A n^A \frac{\partial^3\delta/\partial I^3}{\xi(\partial^2\delta/\partial I^2)^2}\right]. \tag{16}$$

where $\xi = n^A(p^A - m)\kappa^A + (1 - n^A)(p^B - m)\kappa^B > 0$. Since the term that multiplies the expression in brackets is negative, the condition that ensures that $\hat{q}^A$ is strictly concave in p^A is:

$$\frac{\partial^3\delta/\partial I^3}{(\partial^2\delta/\partial I^2)^2} < \frac{3\xi}{b}. \tag{17}$$

Although the interpretation of the condition is not immediately intuitive, it is easy to see that it holds, for example for a logarithmic functional form. To see this, start by calculating the ratio between the third derivative and the squared second derivative for the specific functional form of interest. Substitute the value of I^* that solves Eq. (5) into this expression, observing that the first order condition for I^* can be written as $\delta_I(I^*) = \frac{b}{\xi}$. For the case of the logarithmic function, $\frac{\partial^3\delta/\partial I^3}{(\partial^2\delta/\partial I^2)^2} = \frac{2\xi}{b}$, so that the condition is always satisfied.

A.2 Proof of Proposition 1

When $\alpha^A = 1$, $\partial\hat{q}^A/\partial p^A = 0$ at the value of p^A that maximizes W^A. Hence the sign of $\partial p^{A*}/\partial n^A$ is the same as the sign of $\partial^2\hat{q}^A/\partial p^A \partial n^A$ (refer to Eq. (9)). This proves the proposition.

In what follows we explore under which conditions $\partial^2\hat{q}^A/\partial p^A\partial n^A > 0$ is satisfied. From Eq. (6) it may be shown that:

$$\frac{\partial^2 \hat{q}^A}{\partial p^A \partial n^A} = \frac{\kappa^A}{b}\left[\frac{\partial^2 \delta}{\partial I^2}\frac{\partial I^*}{\partial p^A}\frac{\partial I^*}{\partial n^A} + \frac{\partial \delta}{\partial I}\frac{\partial^2 I^*}{\partial n^A \partial p^A}\right]. \tag{18}$$

Using a similar approach to that of section A.1, $\partial I^*/\partial n^A$ and $\partial^2 I^*/\partial n^A\partial p^A$ can be derived from Eq. (5). The substitution of these expressions into Eq. (18) leads, after a series of algebraic steps,

to the following expression:

$$\frac{\partial^2 \hat{q}^A}{\partial p^A \partial n^A} = \frac{(\kappa^A)^2}{\xi^4(\partial^2\delta/\partial I^2)}\Big[2n^A\left[\kappa^A(p^A-m)-\kappa^B(p^B-m)\right]-(p^B-m)\kappa^B + \\ -\frac{bn^A\left[\kappa^A(p^A-m)-\kappa^B(p^B-m)\right]}{\xi}\frac{\partial^3/\partial I^3}{(\partial^2/\partial I^2)^2}\Big],$$

where the definition of ξ is the one introduced in section A.1.

Hence if:

$$\frac{\partial^3/\partial I^3}{(\partial^2/\partial I^2)^2}\left[\kappa^A(p^A-m)-\kappa^B(p^B-m)\right] > \frac{2\xi\left[\kappa^A(p^A-m)-\kappa^B(p^B-m)\right]}{b} - \frac{\xi\kappa^B(p^B-m)}{n^A b},$$

then $\partial^2\hat{q}^A/\partial p^A\partial n^A > 0$ and $p^{A*}(p^B)$ is strictly increasing in n^A.

Following the same steps that were described in section A.1, it can be verified that the condition is satisfied for the increasing and concave functional forms most commonly used in economics.

A.3 Proof of Proposition 2

Using similar reasoning to that used in the proof of Proposition 1, when $\alpha^A = 1$, the sign of $\partial p^{A*}/\partial\kappa^A$ is the same as the sign of

$$\frac{\partial^2\hat{q}^A}{\partial p^A\partial\kappa^A} = \frac{1}{b}\left[\frac{\partial\delta}{\partial I}\frac{\partial I^*}{\partial p^A} + \kappa^A\left(\frac{\partial^2\delta}{\partial I^2}\frac{\partial I^*}{\partial\kappa^A}\frac{\partial I^*}{\partial p^A} + \frac{\partial\delta}{\partial I}\frac{\partial^2 I^*}{\partial\kappa^A\partial p^A}\right)\right] \tag{19}$$

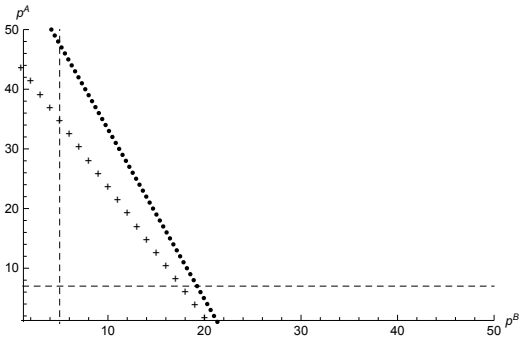
Expressions for the partial and cross-partial derivatives in this equation can be obtained from Eq. (5) and substituted into Eq. (19), which leads to the following expression:

$$\frac{\partial^2\hat{q}^A}{\partial p^A\partial\kappa^A} = \frac{b\kappa^A n^A}{\xi^4(\partial^2\delta/\partial I^2)}\Big[-n^A\kappa^A(p^A-m)-2\xi-\frac{bn^A\kappa^A(p^A-m)\partial^3\delta/\partial I^3}{\xi(\partial^2\delta/\partial I^2)^2}\Big]. \tag{20}$$

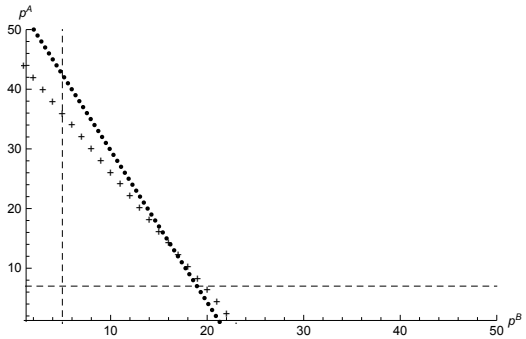
Since the term multiplying the expression in brackets is negative, the assumption $\partial^3\delta/\partial I^3 \geq 0$ is sufficient for $p^{A*}(p^B)$ to be strictly increasing in κ^A.

B Simulations

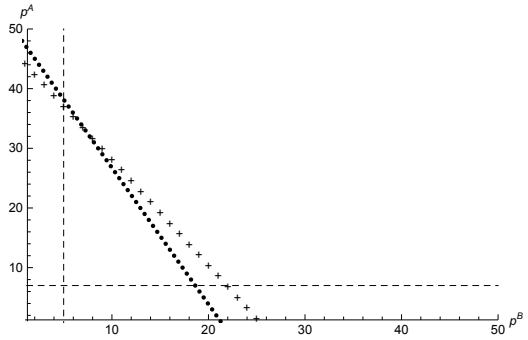
The aim of this section is to use a simulation to illustrate the mechanism described by Corollary 2, which plays an important role for the interpretation of our empirical results. In particular, we will show a situation where, as a result of the increase in n^A, country A moves from a corner to an interior solution. We use a logarithmic function for $\delta(\cdot)$ ($\delta(I) = \ln[I]$) and assume the following functional form for the reservation price: $r^c = 5 + (n^c)^{-\frac{1}{2}}$. The other parameter values are: $\kappa^A = 25$, $\kappa^B = 20$, $N = 100$, $r^A = 7$, $r^B = 5$, $m = 1$, $\alpha^A = 0.6$, $\alpha^B = 0.8$, $\lambda = 0.85$.



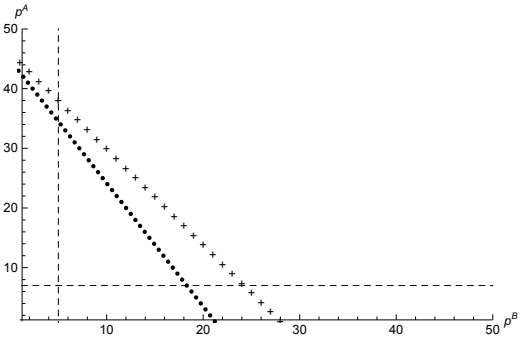
(a) $n^A = 0.22$. Equilibrium prices: $p^A = r^A = 7.13$, $p^B = 19.54$.



(b) $n^A = 0.24$. Equilibrium prices: $p^A = 14.33$, $p^B = 16$.



(c) $n^A = 0.26$. Equilibrium prices: $p^A = 33.58$, $p^B = 7$.



(d) $n^A = 0.28$. Equilibrium prices: $p^A = 37.78$, $p^B = r^B = 6.17$.

Figure 3: Nash equilibria for different values of n^A. '+': $p^{A*}(p^B)$; 'o': $p^{B*}(p^A)$.

We start by assuming $n^A = 0.22$ for the first simulation and then increase the value by 0.02 in three subsequent rounds. Figure 3 illustrates the results. The relevant value of n^A is reported in the figure's legend, together with the Nash equilibrium approximated values of prices.

Since no closed form solution exists for $p^{c*}(p^{-c})$, in Figure 3 best response functions are approximated by a discrete number of numerical solutions. In Figure 3(a), country A's best response function lies below country B', leading to a Nash equilibrium where $p^A = r^A$ and country B responds optimally. Consistent with the results of section 3.3, a first increase in n^A shifts country A's and B's best response functions respectively upwards and downwards. Increasing n^A from 0.22 to 0.24 (Figure 3(b)) implies a move from an equilibrium where country A is at a corner to an interior solution (Corollary 2). A further increase (Figure 3(c)) increases the Nash equilibrium price for country A (Proposition 3), still keeping both prices above the respective reservation levels. Finally, with a further increase in n^A country B's price is at a corner, with country A responding optimally.

C Data

Table 4 lists the 70 antineoplastic drugs included in our sample. 38 products were excluded for the following reasons. 6 do not treat cancer, while 3 treat some types of cancer for which prevalence data are not available from our source. 2 are hybrid drugs which lack the degree of innovation that is central in our analysis (a hybrid drug is similar to an authorised drug containing the same active substance, except that there exist certain differences e.g. with reference to strength, indication or pharmaceutical form). 12 drugs were not on patent in any country in the sample during the period considered for the analysis. In these cases, the price may be affected by generic competition, which is not accounted for in our theoretical model. 2 products are included in the original EMA list but not in our price data set because of their very recent market launch. 9 drugs have complete missing data on the dependent variable, because they were introduced in all countries before the period covered by our data. 4 drugs are lost because they were introduced only in one country, or in several countries but in the same period, so that it was not possible to calculate $\ln[\text{avg}(P_{i,-c,t-1})]$.

Table 5 lists the 25 OECD countries in the sample and the first month for which price data are available.

For each country, column 2 of Table 6 shows the number of on-patent products launched and reimbursed during the period covered by our sample, listed according to country. For the case of the United States, in the IMS data set reimbursement status is '*not coded*', so we consider the product as reimbursed, making the assumption that at least one insurer reimburses it. Comparison of columns 2 and 3 of Table 6 shows the effect on the number of products of excluding observations (some of which are excluded because they refer to the first country or countries which introduced the drug). Concerning Portugal and Luxembourg, the small number of products reflects the paucity of data in the IMS database for these two countries.

Table 7 lists the 28 different neoplasm causes available in the GBD 2015 data set for which we have prevalence data available for estimation of Eq. (14).

Abraxane	Darzalex	Iressa	Opdivo	Unituxin
Adcetris	Empliciti	Jakavi	Perjeta	Vargatef
Afinitor	Erbitux	Javlor	Pixuvri	Vectibix
Arzerra	Erivedge	Jevtana	Portrazza	Venclyxto
Atriance	Evoltra	Kadcyla	Sprycel	Vidaza
Avastin	Farydak	Keytruda	Stivarga	Votrient
Blincyto	Gazyvaro	Kisplyx	Tafinlar	Xalkori
Bosulif	Giotrif	Kyprolis	Tagrisso	Xaluprine
Cabometyx	Halaven	Lenvima	Targretin	Yervoy
Caprelsa	Ibrance	Lonsurf	Tasigna	Yondelis
Cometriq	Iclusig	Lynparza	Teysuno	Zaltrap
Cotellic	Imbruvica	Mekinist	Torisel	Zelboraf
Cyramza	Imlygic	Ninlaro	Trisenox	Zydelig
Dacogen	Inlyta	Onivyde	Tyverb	Zykadia

Table 4: List of the 70 antineoplastic drugs included in the sample.

			2007		2010	2011	
Country	March	June	September	December	September	March	June
Austria	X						
Belgium	X						
Czech Republic							X
Denmark			X				
Finland	X						
France	X						
Germany	X						
Greece		X					
Hungary		X					
Ireland			X				
Italy	X						
Japan						X	
Korea						X	
Luxembourg					X		
Netherlands		X					
Norway	X						
Poland		X					
Portugal		X					
Slovak Republic					X		
Spain	X						
Sweden	X						
Switzerland		X					
Turkey					X		
United Kingdom	X						
United States				X			

Table 5: First month for which price data are available for the 25 OECD countries in the sample.

Country	Launched and reimbursed: in the period	in the sample
Austria	64	61
Belgium	45	41
Czech Republic	28	28
Denmark	60	54
Finland	45	42
France	49	48
Germany	63	57
Greece	42	42
Hungary	27	27
Ireland	51	43
Italy	46	46
Japan	33	31
Korea	23	23
Luxembourg	1	1
Netherlands	32	30
Norway	58	54
Poland	20	20
Portugal	1	1
Slovak Republic	20	20
Spain	48	45
Sweden	50	48
Switzerland	44	43
Turkey	17	17
United Kingdom	62	58
United States	49	4

Table 6: Number of products launched and reimbursed in each country.

Bladder cancer	Leukemia	Ovarian cancer
Brain and nervous system cancer	Lip and oral cavity cancer	Pancreatic cancer
Breast cancer	Liver cancer	Prostate cancer
Cervical cancer	Malignant skin melanoma	Stomach cancer
Colon and rectum cancer	Mesothelioma	Testicular cancer
Esophageal cancer	Multiple myeloma	Thyroid cancer
Gallbladder and biliary tract cancer	Nasopharynx cancer	Tracheal, bronchus and lung cancer
Hodgkin lymphoma	Non-Hodgkin lymphoma	Uterine cancer
Kidney cancer	Non-melanoma skin cancer	
Larynx cancer	Other pharynx cancer	

Table 7: List of neoplasm causes, as identified by the GBD 2015.

D Robustness checks

As a robustness check, in Table 8 we present the same results as in Table 2 but with standard errors clustered by country. The qualitative nature of the results is unchanged, with the only difference that the price set by other countries is no longer significant at the fifth decile for observations above the threshold, and market share is no longer significant at the fifth and the sixth decile for observations below the threshold. Moreover, market share for bigger countries is no longer significant, independently of the threshold.

$\frac{N}{Ntot}$ threshold		Country/product above threshold		Country/product below threshold	
Decile	$\frac{N}{Ntot}$	$\hat{\gamma}_a$	$\hat{\mu}_a$	$\hat{\gamma}_b$	$\hat{\mu}_b$
2^{nd}	0.0057	-0.063	+0.364	+0.028	-38.969**
3^{rd}	0.0067	-0.086	+0.296	+0.081	-40.533**
4^{th}	0.0082	-0.121	+0.430	+0.094	-22.093*
5^{th}	0.0104	-0.164	+0.485	+0.065	-10.523
6^{th}	0.0153	-0.230**	+0.508	+0.112	-7.436
7^{th}	0.0423	-0.284**	+0.301	+0.085	-1.002
8^{th}	0.0676	-0.453***	+0.229	+0.062	+0.021

Product FE included; clustered (country) standard errors;
* $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$. Subscripts a and b of the estimated coefficients denote results respectively above and below the threshold.

Table 8: Results for different thresholds, clustered standard errors.

We also estimate the following model:

$$\ln[FRP_{i,c,t}] = \alpha + \gamma \ln[\text{avg}(P_{i,-c,t-1})] + \eta \ln[N_{i,c,t}] + \theta \ln[Ntot_{i,c,t}] + \boldsymbol{\delta}' \mathbf{H}_{c,t} + \zeta_i + \epsilon_{i,c,t}. \tag{21}$$

Here, we replace the relative size of the market ($\frac{N}{Ntot}$) with the national size (N) and the total size ($Ntot$) of the market. Once more, the model is estimated firstly on the full sample and then separately for observations lying above and below the median value of $\frac{N}{Ntot}$. Results, presented in Table 9, show a negative effect of the average price set by other countries for the full sample: this result is driven by observations above the median value of $\frac{N}{Ntot}$. Only for observations below the median, it is the market size which is statistically significant, and with a negative impact: a 1% increase in national prevalence is associated with a 0.1% decrease in prices. In all model specifications, total market size has a negative and significant coefficient. Interestingly, for observations below the 50% threshold, the effect of total prevalence is higher than the effect of national prevalence.

Table 10 shows the results for different thresholds defined on $\frac{N}{Ntot}$: the difference in behaviour above and below the threshold is confirmed. Moreover, confirming results presented in Table 9, $Ntot$ has always a negative and significant effect (with few exception: below the 40% threshold, and above the 70% and 80% thresholds).

	(1) Full sample ln[FRP]	(2) Above 50% threshold ln[FRP]	(3) Below 50%threshold ln[FRP]
ln(avg(price others lag))	-0.104*	-0.221***	0.034
	(0.055)	(0.077)	(0.083)
ln(N)	-0.008	0.013	-0.065**
	(0.008)	(0.015)	(0.030)
ln(Ntot)	-0.678***	-0.886***	-0.455***
	(0.117)	(0.183)	(0.164)
ln(GDP per capita)	0.117***	0.100**	0.119***
	(0.019)	(0.043)	(0.024)
ln(export)	0.015***	0.008	0.017***
	(0.005)	(0.012)	(0.006)
Observations	883	441	442
R^2 (within)	0.165	0.136	0.220

Product FE included; * $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$.

Table 9: Results for a different model specification.

$\frac{N}{Ntot}$ threshold		Country/product above threshold		Country/product below threshold		Wald test	
Decile	$\frac{N}{Ntot}$	$\hat{\gamma}_a$	$\hat{\nu}_a$	$\hat{\gamma}_b$	$\hat{\nu}_b$	$\hat{\gamma}_a = \hat{\gamma}_b$	$\hat{\nu}_a = \hat{\nu}_b$
2^{nd}	0.0057	-0.111*	+0.007	-0.057	-0.087**	can't reject	reject***
3^{rd}	0.0067	-0.134**	+0.003	+0.013	-0.114**	can't reject	reject***
4^{th}	0.0082	-0.179**	+0.009	+0.070	-0.093**	reject**	reject***
5^{th}	0.0104	-0.221***	+0.013	+0.034	-0.065**	reject**	reject***
6^{th}	0.0153	-0.277***	+0.009	+0.070	-0.063**	reject***	reject**
7^{th}	0.0423	-0.301***	-0.014	+0.029	-0.030*	reject**	can't reject
8^{th}	0.0676	-0.454***	-0.022	+0.008	-0.015	reject***	can't reject

Product FE included; * $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$. Subscripts a and b of the estimated coefficients denote results respectively above and below the threshold.

Table 10: Results for a different model specification, different thresholds.