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Therapeutic reference pricing and drug innovation incentives☆

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ABSTRACT

Therapeutic reference pricing (TRP) of pharmaceuticals is widely thought to steer drug innovation incentives away from 'me-too' innovations with little therapeutic benefit. However, the present paper shows that, if the feasible scope for innovation is to develop drugs with different degrees of differentiation from existing drugs within the same therapeutic class, TRP reduces innovating firms' incentives for therapeutic differentiation and leads to entry of drugs that are *less* differentiated from the existing drugs in the market. In this case, the pro-competitive effects of TRP are reinforced by changes in innovation incentives. On the other hand, TRP leads to lower health benefits unless incentives for therapeutic differentiation are excessively strong in the first place.

1. Introduction

The pharmaceutical industry is one of the most research intensive, with annual spending on R&D totalling USD 114 billion across 33 OECD countries in 2018 (OECD, 2021a). Pharmaceuticals also constitute one of the largest components of total health expenditures, with a spending share that is increasing in many countries.[1] A long-standing concern for policymakers is that the industry allocates too much of its R&D spending on developing drugs that yield only minor therapeutic gains compared with existing alternatives, so-called 'me-too' drugs (González et al., 2016).

Policymakers can in principle affect the incentives for 'me-too' versus drastic innovation through the design of price regulation and reimbursement schemes. In particular, reimbursement schemes based on *therapeutic reference pricing (TRP)* are widely thought to be a viable instrument to steer R&D investments more towards drastic innovations (Garattini et al., 2007; Pekarsky, 2010; Galizzi et al., 2011). The argument is fairly straightforward and has been formalised by Bardey et al. (2010). TRP has a pro-competitive effect, yielding lower drug prices, for drugs that belong to the same therapeutic cluster. All else equal, this reduces the return to 'me-too' innovations and makes it relatively more profitable to avoid therapeutic competition by developing drugs for which there are no existing therapeutic alternatives.[2,3]

This argument relies, however, on the assumption that drastic innovations constitute a feasible option. In reality, the vast majority (85–90 percent) of new drugs have little or no advantages over existing therapeutic alternatives (Santos et al., 2019). In the present paper I show that, if the relevant choices for an innovator only consist of various degrees of differentiation from an existing drug within a given therapeutic category, then TRP has the *opposite* effect: it shifts innovation incentives in the direction of 'me-too' innovations. This conclusion is based on a simple model where an innovating firm faces the following basic trade-off: by spending more resources on R&D, it can enter the market with a drug that is more therapeutically differentiated from existing drugs, which dampens the intensity of price competition. The marginal gain from such differentiation depends, however, on the price elasticity of demand. TRP makes demand more price elastic, which reduces the incentives for differentiation. In equilibrium, this leads to entry of new drugs that are less differentiated

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[1] In 2019, retail pharmaceuticals accounted for one sixth of total health expenditures in OECD countries, with in-hospital pharmaceuticals contributing another 20 percent on top of that (OECD, 2021b).

[2] However, the empirical evidence on the relationship between TRP and R&D investments is lacking (Wettstein and Boes, 2019).

[3] See also Bardey et al. (2016), who study how drug reimbursement rules affect producers' entry decisions in a horizontal differentiation framework.

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from the existing ones. In this case, the price-reducing effects of TRP are reinforced by its effect on innovation incentives. On the other hand, the effect on total health benefits is negative unless incentives for therapeutic differentiation are socially excessive to begin with.

2. Model

Consider a therapeutic market for on-patent prescription drugs where patients are uniformly distributed on [0, 1] with total mass equal to one, and where each patient needs one unit of drug treatment. There are two available drugs in the market, each located on the same unit line. An incumbent drug, denoted I, is located at 0, while a new entrant, denoted E, is located at $y > 0$. Differences in patient and drug locations reflect heterogeneity in therapeutic responses, in the sense that the therapeutic benefit of a particular drug treatment is higher if the patient is located closer to the drug. The degree of therapeutic differentiation between the two drugs is therefore captured by the Euclidean distance between them, given by y.

A patient's utility of a particular drug treatment is assumed to be given by therapeutic benefits net of patient copayments. In case of a perfect match between a patient and a particular drug, the therapeutic benefit is given by v. Otherwise, this benefit is deflated by therapeutic mismatch costs that are convexly increasing in the Euclidean distance between the drug and the patient. The utility of a patient located at x and prescribed drug i, located at z_i (where $z_I = 0$ and $z_E = y$), is thus given by

$$u_i(x) = v - t(x - z_i)^2 - c_i, \tag{1}$$

where the parameter $t > 0$ measures the relative importance of therapeutic mismatch, and c_i is the patient copayment for drug i.

Patient copayments depend on the reimbursement scheme. Suppose that patients pay a share $\alpha \in (0, 1)$ of the drug price as long as this price does not exceed a threshold level r. Any positive difference between the drug price and this threshold has to be paid in full by the patient. Let p_i be the price of drug i. If $p_E \geq p_I$, which will later be shown to hold in equilibrium, patient copayments are given by

$$c_I = \alpha p_I \quad \text{and} \quad c_E = \alpha r + p_E - r. \tag{2}$$

Suppose also that r is a function of the two drug prices in the market, such that

$$r = \beta p_I + (1 - \beta) p_E, \tag{3}$$

where $\beta \in [0, 1]$.

The above described drug reimbursement scheme corresponds to *therapeutic reference pricing* (TRP) for all $\beta \in (0, 1]$, where r is the reference price and β measures the strictness of the reference pricing scheme. If $\beta = 1$, the reference price is defined as the price of the cheapest drug in the market, which is a fairly common practice in real-world reference pricing schemes. The special case of $\beta = 0$ captures an alternative reimbursement scheme, namely *fixed percentage reimbursement*, where $c_i = \alpha p_i$, $i = I, E$, which will be used as a benchmark for comparison.

I assume that the location of the new drug, and thus the degree of therapeutic differentiation, results from a deterministic R&D process where it is more costly to develop a drug that is more therapeutically differentiated from the existing drug in the market. More specifically, I assume that the cost of drug innovation is given by a function $\phi(y)$, which is increasing and strictly convex for $y \in [\underline{y}, 1]$, where $\underline{y} > 0$. We can think of the lower bound $\underline{y}$ as the threshold for patent infringement, such that locations in the interval $[0, \underline{y})$ are not feasible.

Finally, I assume that each drug is produced by a profit-maximising pharmaceutical firm, and, for simplicity, that variable production costs are zero. Post-innovation profits for drug i are therefore given by

$$\pi_i = p_i q_i, \quad i = I, E. \tag{4}$$

The firms are assumed to play the following two-stage game: (i) the innovator chooses how much to therapeutically differentiate its new drug from the existing one, measured by y, before (ii) the two firms compete in prices.

3. Therapeutic competition

For a given degree of therapeutic differentiation, y, utility-maximising drug prescription choices yield the following demand functions for the two drugs[4]:

$$q_I = \frac{y}{2} + \frac{c_E - c_I}{2ty} \quad \text{and} \quad q_E = \frac{2 - y}{2} + \frac{c_I - c_E}{2ty}, \tag{5}$$

where c_I and c_E are given by (2)–(3), and the equilibrium drug prices in the post-innovation subgame are found to be given by[5]

$$p_I = \frac{(2 + y)\, ty}{3(\alpha + (1 - \alpha)\beta)} \quad \text{and} \quad p_E = \frac{(4 - y)\, ty}{3(\alpha + (1 - \alpha)\beta)}. \tag{6}$$

The corresponding equilibrium drug demand is

$$q_I = \frac{1}{3} + \frac{y}{6} \quad \text{and} \quad q_E = \frac{2}{3} - \frac{y}{6}, \tag{7}$$

and the post-innovation profits are

$$\pi_I = \frac{(2 + y)^2\, ty}{18(\alpha + (1 - \alpha)\beta)} \quad \text{and} \quad \pi_E = \frac{(4 - y)^2\, ty}{18(\alpha + (1 - \alpha)\beta)}. \tag{8}$$

It is easily verified that the new drug has both higher price and higher demand than the incumbent drug, which in turn makes it more profitable. This reflects the therapeutic advantage of the new drug; i.e., drug E yields a higher therapeutic benefit than drug I for a majority of the patients as long as $y < 1$. Furthermore, increased therapeutic differentiation dampens price competition and leads to higher prices and profits for both drugs (i.e., $\partial p_i/\partial y > 0$ and $\partial \pi_i/\partial y > 0$). This is true under fixed percentage reimbursement ($\beta = 0$) and under TRP ($\beta > 0$).

Since prices and profits are monotonic in β, the qualitative effects of TRP on the equilibrium outcome can easily be assessed by considering a marginal increase in β. From (6)–(8), it follows that

$$\frac{\partial p_i}{\partial \beta} < 0, \quad \frac{\partial q_i}{\partial \beta} = 0, \quad \frac{\partial \pi_i}{\partial \beta} < 0, \quad i = I, E. \tag{9}$$

Thus, TRP intensifies drug price competition and leads to lower prices and profits. These are well-known short-run effects, caused by the following mechanism. Reference pricing makes drug demand more price elastic for prices above the reference price, which gives the producer of the high-priced drug an incentive to reduce its price. It also gives the producer of the low-priced drug an incentive to reduce its price, since this will increase the patient copayment for the competing drug through a reduction in the reference price. The resulting effect is a price reduction for both drugs.[6] Notice, however, that the price reduction is larger for the high-priced drug, such that the copayment difference, and thus

[4] The therapeutic benefit parameter v is assumed to be sufficiently large such that the market is always fully covered.

[5] The equilibrium is derived under the assumption that $p_I \leq r \leq p_E$, which holds in equilibrium. It is straightforward to verify that neither firm has any incentive to unilaterally deviate from this equilibrium in a way that implies $p_I > p_E$.

[6] These first-order price effects are also reinforced by second-order effects due to prices being strategic complements.

demand, remains unchanged, which in turn implies that total health benefits are also unaffected. Thus, for a given value of y, the only effect of TRP is to shift profits from pharmaceutical firms to patients and insurers.

4. Drug reimbursement and innovation incentives

How does the reimbursement scheme affect drug innovation incentives? Suppose that the insurer is able to commit to a particular reimbursement policy, such that the innovation decision is made under the expectation that the reimbursement scheme remains constant. Suppose also that the properties of $\phi(y)$ is such that the subgame perfect Nash equilibrium outcome is an interior solution at the innovation stage, i.e., that the optimal location of the new drug is given by $y^* \in \left(\underline{y}, 1\right)$. This optimal location is then implicitly given by

$$\frac{\partial \pi_E}{\partial y} = \phi'\left(y^*\right), \tag{10}$$

and it easily verified that $\partial^2 \pi_E / \partial y^2 < 0$ for $y \in \left(\underline{y}, 1\right)$ and $\beta \in [0, 1]$. The effect of TRP on innovation incentives, i.e., the sign of $\partial y^* / \partial \beta$, is then given by the sign of

$$\left| \frac{\partial^2 \pi_E}{\partial \beta \partial y} \right|_{y=y^*} = -\frac{(1-\alpha)(4-y^*)(4-3y^*)t}{18(\alpha+(1-\alpha)\beta)^2} < 0, \tag{11}$$

which establishes my first main result:

Proposition 1. *Compared with a drug reimbursement scheme based on fixed percentage reimbursement, therapeutic reference pricing shifts drug innovation incentives in the direction of more 'me-too' innovations.*

Since TRP intensifies price competition, one would perhaps expect that innovating firms would have an incentive to counteract this effect by differentiating their new drugs more from the existing ones in order to dampen price competition, but this is not true if it is not possible to escape therapeutic competition altogether. On the contrary, TRP will in this case give innovating firms an incentive to differentiate *less*; i.e., it will shift innovation incentives in the direction of more 'me-too' innovations. The reason is that the marginal profit gain of differentiation is inversely related to the price elasticity of drug demand. A higher degree of differentiation has an anti-competitive effect under both reimbursement schemes, but, because of the higher price elasticity under TRP, there is simply less room for the innovating firm to increase its price in response to more differentiation than what is the case under the benchmark reimbursement scheme. Consequently, the incentives for therapeutic differentiation are weaker.

The result in Proposition 1 has some further implications worth mentioning. First, since $\partial p_i / \partial y > 0$ and $\partial \pi_i / \partial y > 0$, for $i = I, E$, the innovation incentives *reinforce* the pro-competitive effects of TRP, leading to even lower prices and profits than what a static analysis would suggest. However, these innovation incentives also imply a potential welfare trade-off. For a given degree of therapeutic differentiation, the total health benefits in the post-innovation equilibrium are given by

$$\begin{aligned} H(y) &= \int_0^{\frac{1}{3}+\frac{y}{6}} \left(v - tx^2\right) dx + \int_{\frac{1}{3}+\frac{y}{6}}^{y} \left(v - t(y-x)^2\right) dx \\ &\quad + \int_y^1 \left(v - t(1-x)^2\right) dx \\ &= v - \frac{t}{3} + \frac{(8-5y)(4-y)ty}{36}, \end{aligned} \tag{12}$$

implying that

$$\partial H / \partial y > 0 \text{ if } y < \frac{4\left(7-\sqrt{19}\right)}{15} \approx 0.7. \tag{13}$$

Thus, as long as the degree of therapeutic differentiation is not too large, a lower degree of differentiation leads to a loss in total health benefits.

Proposition 2. *Compared with a drug reimbursement scheme based on fixed percentage reimbursement, the price-reducing effects of therapeutic reference pricing are reinforced by changes in innovation incentives. On the other hand, when innovation incentives are taken into account, therapeutic reference pricing leads to lower health benefits unless the incentives for therapeutic differentiation are excessively strong to begin with.*

5. Concluding remarks

Contrary to conventional wisdom, therapeutic reference pricing (TRP) does not necessarily shift drug innovation incentives away from 'me-too' innovations. In situations where the feasible scope for innovation is to develop drugs with different degrees of therapeutic differentiation from existing drugs within the same therapeutic class, TRP reduces innovating firms' incentives for therapeutic differentiation and leads to entry of drugs that are *less* differentiated from the existing drugs in the market. The reason is that the marginal gain of therapeutic differentiation is negatively correlated with the price elasticity of drug demand, which is higher under TRP. This is a mechanism that generalises beyond the present model. My analysis here is based on a model of therapeutic competition in a Hotelling framework, which is common in the literature (e.g., Miraldo, 2009; Brekke et al., 2022), but the main results would be qualitatively similar in an equivalent model based on a vertical differentiation framework.[7]

Data availability

No data was used for the research described in the article.

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[7] Details are available upon request.