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Drug Price Regulation: Value Based Alternatives For Personalised Drugs In The Presence Of Asymmetry Of Information

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Abstract

Personalised drugs may improve health outcomes, but they increase heterogeneity in patients responses and, possibly, R&D costs. Competition, regulation and pricing play a strategic role both to determine how the benefits of the drug are split between the industry and consumers and to make profitable to invest in assessing such heterogeneity. Drug price regulation has shifted from cost-based formulas to value based ones, but which value should be considered is still debated. In this paper we evaluate the incentives to disclosing patients heterogeneity arising from the combined effect of different value based prices schemes and competition a two period model. We show that the incentive in determining the extent of patients heterogeneity depends more on competition than on the price reimbursement scheme. Industries in fact use effectiveness differentials as a strategy for market differentiation to avoid direct competition. In general, the incentives to differentiate among patients are higher for the incumbent than the first firm to enter the market. As a result, average prices may be higher than the societal value of the drug.

1 Introduction

In the quest to improve health outcomes, drugs are being increasingly personalised. According to Schork (2015) more than 20% of NME's approved by FDA can be considered personalised medicine and by the end of the current year, in oncology, 75% of new products will be listed for multiple indications (Aitken et al. 2015). The ability to profile patients and to tailor new drugs to their characteristics has some drawbacks: effectiveness is deemed to rapidly decrease as soon as patients characteristics do not match the target patient; salami slicing (Lakdawalla, 2018; Gibson and von Tigerstrom, 2015)) may be used to maximise profits, leading to prices that do not reflect value for money (Bach, 2014;

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Kaltenboeck and Bach, 2018; Howard et al., 2015; Yu et al., 2017b; Salas-Vega et al., 2020)). Heterogeneity in patients responses also opens important questions about the relationship between price schemes and incentives to assess such heterogeneity, which entails higher costs for the industry. Randomised clinical trials need to be larger since patients must be stratified and the clinical trial process may be longer (Pertile et al., 2014); the industry will incur these extra costs only if the increase in expected profit is larger than the additional costs. In this context competition, regulation an pricing play a strategic role, as the literature as long suggested (Bardey et al., 2010; Bouvy and Vogler, 2013; Civan and Maloney, 2009; Danzon et al., 2005a; Danzon and Epstein, 2008; Danzon et al., 2005b; Houy and Jelovac, 2015)). The question of whether the pricing schemes in use are a sufficient incentive to invest in personalised medicine is still high on the political and economic agenda Kaltenboeck and Bach (2018); Yu et al. (2017a); DiMasi et al. (2016).

Since Gravelle (1998), drug price regulation has shifted from cost-based formulas to value based ones. The idea behind value-based prices is to reimburse drugs according their effectiveness (usually measured by the quality adjusted expected life years the drug allows to gain) and to society willingness to pay for such an increase (Claxton et al. (2008, 2011); Danzon et al. (2012); Eichler et al. (2011)). However, which value should be considered (the marginal value, the average value, some other definition) is still debated(Sussex et al., 2013; Hawkins and Scott, 2011; Levaggi, 2014).

Claxton (2007) argues that *marginal* value-based prices (MVBP) allow to reduce the cost of new drugs, but they may also reduce the incentives to innovation. Average value based schemes (AVBP) produce more incentives to innovation, especially when the population is very heterogeneous (Levaggi and Pertile (2020b)), but at the cost of a higher price. Finally, Chandra and Garthwaite (2017); Kaltenboeck and Bach (2018) propose to use indication based prices (IVBP) where the price may be indication-specific, i.e. the price depends on the different effectiveness across treatments.

Levaggi and Pertile (2020a) show that, in a static framework and in the presence of asymmetry of information, the use of these formulas gets to very similar results and that it may not encourage research into patients heterogeneity. However, R&D decisions are taken in a long run perspective and in a competitive setting. In this paper we propose to evaluate the incentives arising from the combined effect of different value based prices schemes and competition a two period model where industries enter the market in subsequent time periods.

We show that the incentive in determining heterogeneity in patients benefits depends more on competition than on the price reimbursement scheme. Industries use effectiveness differential as a strategy for market differentiation and to avoid direct competition. In general, the incentives to differentiate among patients are higher for the incumbent than for the first firm to enter the market. As a result, average prices are higher than the societal value for the drug. The paper is organised as follows in section 2 we present the main model, in Section 3 we present the main results which are discussed in Section 4 , which also concludes the paper.

2 The model

At time $t-1$ company A develops an active principle X to treat a population of patients normalised to 1. The response to treatment is heterogeneous: for a first group $n < \frac{1}{2}$, effectiveness (in terms of QALY gained) is equal to E_H; for the other group $(1-n)$ it is equal to E_L with $E_H > E_L$. The two groups could be distinguished by observable elements, such as the indication for which the drug is used, or some specific characteristic. Assessing the effectiveness differential has a cost F_A; if the company incurs this cost, information on the differential is private to the firm, which may decide to reveal it or not. We assume that no other drug is available to treat these patients. At time 0, B develops another active principle Y which, for the sake of simplicity, has the same characteristics in terms of effectiveness as active principle X and a cost F_B to assess its effectiveness differential. The drug can be commercialised at time 2, in competition with the drug produced by$A$. The price for the new drugs is set by the regulator that may use three alternative schemes:

- **marginal value based** (MVBP) price. The price is set according to the effectiveness of the marginal patient; the price is equal to λE_H if the firm asks listing for the most effective indication (target population n), or it will be equal to λE_L if listing is asked for both types of patients[1]:

$$\begin{aligned} p^M(n) &= \lambda E_H \\ p^M(1) &= \lambda E_L \end{aligned} \tag{1}$$

  where λ is the shadow value of health.

- **average value based** (AVBP) price. The price is set according to the average effectiveness (across groups of patients) of the new drug. If the firm asks for listing for the first n patients, the price will be equal to λE_H. If it asks to list for both types and reveal the effectiveness differential, the average weighted effectiveness is equal to $E_A = nE_H + (1-n)E_L$ and on this average effectiveness the price is set:

$$\begin{aligned} p^A(n) &= \lambda E_H \\ p^A(1) &= \lambda E_A = \lambda \left(nE_H + (1-n)E_L \right) \end{aligned} \tag{2}$$

- **indication value based** (IVBP) prices. The drug will be marketed under two prices λE_H for the first group of patients and λE_L for the second group:

$$\begin{aligned} p^I(n) &= \lambda E_H \\ p^I(1-n) &= \lambda E_L \end{aligned} \tag{3}$$

[1] In theory, another alternative would be possible: to list only for the second group of patients $p^M(1-n) = \lambda E_L$. This alternative is not very appealing: In the short run is always dominated by $p^M(1) = \lambda E_L$; in the long run it is always dominated by other alternatives

If the company decides not to invest F to determine the effectiveness differential, or it decides not to reveal this information, it will list for a drug with a level of effectiveness $E = nE_H + (1-n)E_L$ for a price λE, independently of the value based scheme used.

At time $t-1$ (0) company A (B) needs to decide whether to invest $F_i \qquad i = A, B$ to assess the effectiveness differential; to simplify matters we assume that this does not cause any delay in developing the drug. The industry maximises profits, which in each period are defined as:

$$\Pi_t(p, x) = (p(x) - c)x, \tag{4}$$

where c is the marginal cost to produce the drug and x is the number of patients to whom the drug will be sold. The timing of the game can be described as follows:

1. A (at $t-1$) and B (at 0) decides whether to incur the cost F_i to determine the effectiveness differential, without observing the strategy of their competitor.

2. The regulator sets a pricing rule such that the price equals the monetary value of the benefit of the treatment.

$$p(n) = \lambda f(E) \tag{5}$$

   It is assumed that the regulator can commit to this rule.

3. At time 1, A acts as a monopolist; at time 2 also B enters the market. Knowing the pricing rule defined in Eq. 5, and the expectations about the strategy of its competitor, each firm decides its listing strategy. We assume that whichever strategy firm A chooses for period 1, it is committed to follow the same strategy also in period 2. Market entry is determined by cost effectiveness considerations.When the industry reveals the effectiveness differential for the drug, the latter is E_H for the first n patients and E_L for the $(1-n)$ group. The effectiveness when the industry does not reveal the differential is $E = nE_H + (1-n)E_L$. When two drugs have the same cost effectiveness, the rules for determining which one will be marketed are as follows:

   - the drug with the better ICER ($\frac{\Delta E_i}{\Delta p_i}$; $i = H, L$) with respect to the comparator (no drug) wins the market;
   - if the drugs have the same ICER, the one with the highest effectiveness will be marketed;
   - if they share also the same level of effectiveness the market is shared equally.

Competition is rather soft: if the active principle has same characteristics, the market is shared equally among the two. In actual fact other scenarios may be possible: a) an extremely competitive one where when in a market there are

two competitors, the profit is driven to zero for both competitors (competition) or a scheme where the incumbent has a first entry move advantage: when the active principles are equal the first to enter (A in our case) gets all the market (predator). We have preferred to use this intermediate case because it presents less incentives to avoid direct competition which instead comes out as the main strategy used by industry A and B to choose whether to differentiate the drug [2]. To determine the extra profit that industry A and B may obtain by investing in finding patients heterogeneity, we will start by considering a model where this information can be acquired by both players at no cost.

3 Results

The profit of both firms depends on the strategy of the opponents. A moves first (since it enters the market in 0) and can observe the relevant information to determine B's reaction conditional on its choice. The game is solved by backward induction in the Appendix; in what follows we present the main results.

The possible strategies for A and B are are:

1. List for the first n patients. The industry reveals that the drug is effective only for the first group of patients; effectiveness equal to E_H.

2. Reveal the effectiveness differential. This allows to regulator to know that for the first group of n patients the drug has a level of effectiveness equal to $E_H$while for the rest of the population $(1-n)$ the effectiveness is lower (E_L)

3. Do not reveal the effectiveness differential. The drug is listed for all the patients; effectiveness equals average effectiveness E.

4. Ask for listing only for the second group of $1-n$ patients; effectiveness equal to E_L.

and the resulting equilibrium depends on the price set by the regulator and the quantity that each industry can sell. In what follows, for each scheme, we present the equilibrium strategy and the market outcome.

3.1 Marginal value based prices

In a static context, where the industry is a monopolist, there is no incentive to reveal the effectiveness differential (Levaggi and Pertile, 2020a).When the market is up to competition in at least one period, the presence of a competitor influences the best strategy (See Table A.4in appendix). The state-contingent best reply by industry B depends on a combination of the effectiveness differential ($\frac{E_H}{E_L}$) and the share of patients for which the drug is most effective (n). In general, B tries to differentiate its strategy from A, i.e. it tries to get its own

[2]The results for the other cases are available on demand.

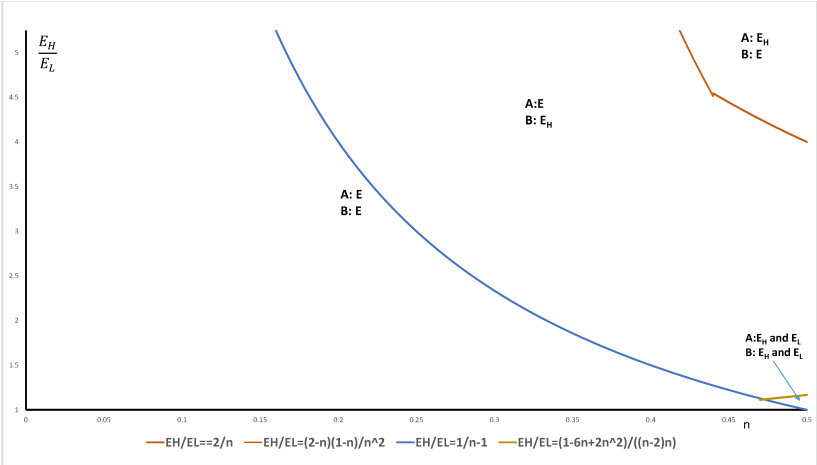

Figure 1: Equilibrium strategies under Marginal Value Based

market niche instead of competing with A. This is an interesting result since the model is set in context setting where competition is less aggressive [3].

For A, the best strategy depends on the effectiveness differential and on n as shown in Figure 1, which is drawn using the results presented in tableA.5 in the Appendix. On the horizontal axis the number of patients with the highest effectiveness (n) is depicted while on the vertical axis the ratio $\frac{E_H}{E_L}$ is used.

In general, A (the first industry to enter the market) has less incentive than B (the second one) to reveal the effectiveness differential. This strategy is not optimal only for two extreme cases: when the ratio $\frac{E_H}{E_L}$ is quite high and n very large or when $\frac{E_H}{E_L}$is rather low and n very large. In the former case the price and the market are relatively advantageous for both industries to share the benefits by selling the drug only for to first group of patients. In the other case, both industries reveal the differential in effectiveness and sell the drug to both patients types for a price equal to λE_L.

3.2 Average value based prices

This scheme implies a pooling among patients: the cost effectiveness ratio for the first group is $\frac{\lambda E}{E_L} < 1$ while for the second group is $\frac{\lambda E}{E_H} > 1$. The average cost effectiveness is λ and this is also the level that is reached if the industry decides to enter the market without revealing the effectiveness differential[4]. This is the reason why, in a short-run context, the industry has no incentive to revealing the effectiveness differential (Levaggi and Pertile, 2020a). When

[3] If two active principles equal in everything enter the same market, they share the profit equally.

[4] In this case the cost effectiveness ratio would in fact be equal to $\frac{\lambda E}{E} = \frac{\lambda(nE_H+(1-n)E_L)}{nE_H+(1-n)E_L} = 1$

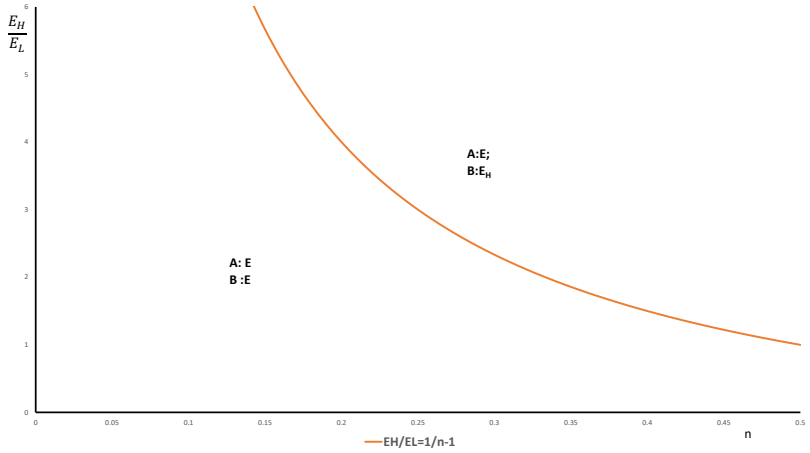

Figure 2: State contingent equilibria under Average Value Based Prices

the market is up for competition, as per MVBP, the state-contingent best reply by industry B is to differentiate its strategy from A (as shown in Table A.9) only if the difference in effectiveness is sufficiently high. In this case, for B it is never optimal to reveal the differential in effectiveness by listing for both groups of patients. This result may seem counter-intuitive, but it depends on the cost effectiveness ratios implied by the pooling described above: the pooling mechanism makes entry rather easy on the market for the first n patients.

Figure 2 summarises the equilibrium conditions presented in Table A.10. On the horizontal axis the size of the more effective patients group (n) is depicted while on the vertical axis the ratio $\frac{E_H}{E_L}$ is used.

For company A (which enters first), there is no incentive to reveal the effectiveness differential: in this way it is able to get the same cost effectiveness ratio across patients groups[5]. For the entrant, the decision depends on the effectiveness differential and on the size of the more effective group. If the ratio $\frac{E_H}{E_L}$ is sufficiently high and n sufficiently large, the best answer by B is to differentiate its product by listing only for the first group of patients. In this way, both drugs have the same cost effectiveness, but the one proposed by B is more effective.

3.3 Indication value based prices

In a short-run context, the information on the effectiveness differential has no economic value (Levaggi and Pertile, 2020a); this is not the case if another active principle may be commercialised in the second period. The best reply by B is presented in Table A.14. Only if $\frac{E_H}{E_L}$ is sufficiently high, B will not reveal its private information; in this way the drug for the second t group $(1-n)$ seems more effective.

[5]the cost effectiveness ratio in this case is equal to λ

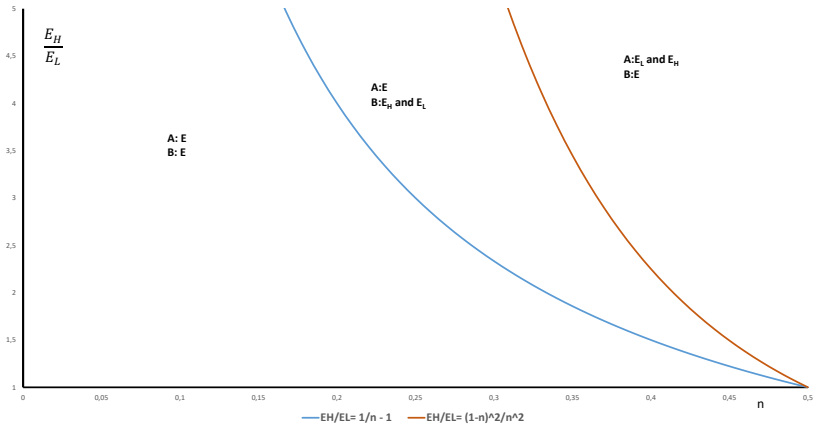

Figure 3: State contingent equilibria under Indication Based Prices

The best strategy for A depends on the effectiveness differential and on n. Figure A.15 summarises the equilibrium conditions presented in Table A.15. On the horizontal axis the size of the more effective patients group (n) is depicted while on the vertical axis the ratio $\frac{E_H}{E_L}$ is used.

As per the other two schemes, industries try to differentiate their listing strategy in order to get a sub-market as monopolist. The difference with the other schemes is that when it is profitable for A (which enters first) to reveal the effectiveness differential, it lists for both groups of patients.

3.4 Comparing the different schemes

The results presented above show that, in a competitive context, the incentives to reveal the heterogeneity in patients responses are higher for the entrant than for the incumbent. Figure 4 summarises the solutions presented in Table 1.

Under AVBP, A has no interest in revealing the effectiveness differential; by not revealing this information the drug for the $(1-n)$ group of patients appears to be more effective and it is easier to protect this market from B in period 2.

On the contrary, if the effectiveness differential is sufficiently large, MVBP and IVBP schemes produce and incentive for industry A to reveal the effectiveness differential with some interesting differences. For the same n, the effectiveness differential should be higher for A to reveal (at least partially) patients heterogeneity under MVBP than under IVBP. It is also interesting to note that when the conditions are satisfied for both models, under MVBP, only the patients with the highest effectiveness will be treated, while under IVBP both market are served. For example, let us consider Cetuximab. Bach (2014) show that the survival rate is about 1.64 when used for a target of patients and only 0.23 when it is used for other indications, which means that $\frac{E_H}{E_L} \simeq 7.13$. Under

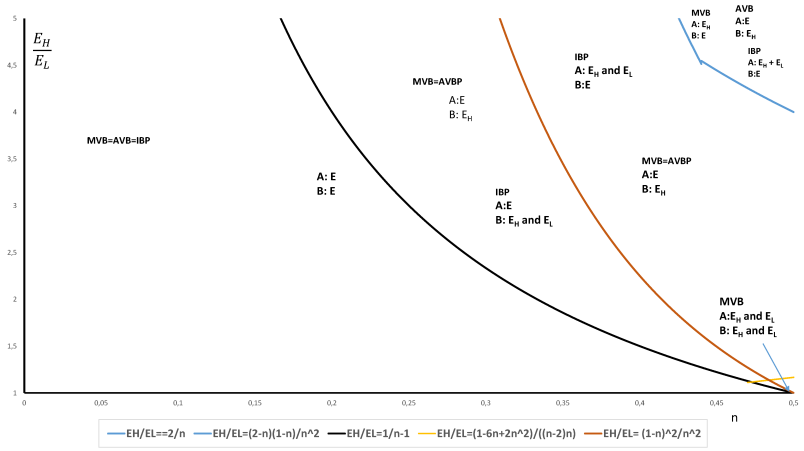

Figure 4: Comparing the different schemes

MVBP, only if $n > 0.375$ A would list for the first group while under IVBP it is necessary a smaller group ($n > 0.27$). Expenditure for the regulator is going to be lower under MVBP only because the second group of patients is untreated. In terms of cost effectiveness, the two models are instead the same. IVBP in this context may perhaps avoid legal battles as the one that followed the off label use of Bevacizumab for age-related macular degeneration (AMD) [6].

The best strategy for B is quite consistent across models: it tries to differentiate its product and avoids when possible to supply a drug equal to the one proposed by firm A. For a drugs as Cetuximab, B will list for the first group for $n > 0.12$; under MVBP and AVBP. If the price is set using IVBP, B's strategy is more complex for $0.12 < n < 0.27$ it lists for both markets and reveal the effectiveness differential; for $n > 0.27$ it does not reveal the effectiveness differential. This result is quite interesting, given that it has been derived in a setting where competition is not so fierce: in fact if two equal products enter the same market, the latter is shared equally. These results seems to be supported by recent anecdotal evidence on cancer drugs such as Pembrolizumab and Nivolumab where the first drug to enter (Nivolumbab) was listed for all the patients while for Pembrolizumab listing was asked only for a specific subgroup of patients with high levels of PD-L1 (see Aitken et al. (2015); Levaggi and Pertile (2020a). Nivolumab could also be more effective for the subgroup of patients with high levels of PD-L1, but the manufacturer may have opted for entering the market at an early stage without investing time and effort in determining the differential. This may have allowed Pembrolizumab to get listed for this group for which they could show their drug to be more efficient.

[6] Bevacizumab has been approved for treating colon cancer, but later physicians have started using it off label to treat age-related macular degeneration (AMD). The price is the same for both treatments, but since the quantity to be used for AMD is much lower, its price for this indication is extremely low (See Lakdawalla (2018) for more details).

In general, all the schemes allow a fair access to drugs by patients; only MVBP, produces a sub-optimal result when the effectiveness differential is rather high: in this case, A has an interest in listing only for the most effective group (n) in the first period. This result is in line with Levaggi and Pertile (2020b): when patients groups are quite heterogeneous, it is more convenient for the industry to list only for the most remunerative patients. Interestingly, all the schemes foresee a price higher than optimal. The maximum value based price for the drug with access to all the patients would imply a total expenditure equal to $\lambda 2\left(nE_H + (1-n)E_L\right) = \lambda 2E$. In actual fact, expenditure C is going to be higher because, in the quest to avoid direct competition, both industries may sell the drug to the target group for which it is less effective at a price higher than what the drug is worth. The ability of MVBP to produce a fairer allocation of the benefits of the drug between the industry and the patients is rather limited in a context of asymmetry of information: in fact only for the combinations of n and $\frac{E_H}{E_L}$ in the right corner of Figure 4 this scheme entails lower expenditure ($\lambda 2E_L$) and access to all the patients. The analysis of expenditure highlights a very important problem that is common across schemes: the asymmetry of information between the regulator and the industry allows the latter to increase its profits.

3.5 The value of information

The case of the industry that does not deliberately reveal the differential information on effectiveness may be questioned on ethical and legal grounds. However, from a policy point of view, this scenario may be interpreted in terms of incentives companies have in promoting research aimed at assessing effectiveness across patients groups.We can then interpret the results presented above in terms of the value that the information on the effectiveness differential has for the firms. When the profit is maximised by the strategy of not revealing such information, the industry has no interest in incurring extra costs to acquire it; in the other case the extra profit that obtained using this information will have to be evaluated against the cost to acquire it (F). To get a better understanding of the value of information in this context, we will now explicitly consider the best strategy of firm A and B in a context where for one or the other it is too costly to assess the effectiveness differential.

The value of information depends on the expectations that each firm has about the costs of the competitors. In what follows we show the value of information for the case where both firms expect the competitor to be able to invest in finding the differential, so that we can use the results presented in table 1 to derive the difference in profit the industry can obtain by revealing the effectiveness differential. This is also the value of information for the industry, i.e. the maximum amount it is willing to spend.

The incentives to invest to verify the effectiveness differential are quite similar across schemes. IVBP produces a stronger incentive than the other schemes to research into patients heterogeneity for A, provided that $\frac{E_H}{E_L} < \frac{(1-n)^2}{n^2}$. In this respect this scheme is more effective than the other two in making industries

	MBPS	AVBP	IVBP
$\frac{E_H}{E_L} > max\left\{ \begin{array}{c} \frac{2}{n} \\ \frac{1-n+(1-n)^2}{n^2} \end{array} \right.$	A: E_H; B: E C $\lambda\left(2nE_H+(1-n)E\right)$ pat $n+1$ Π_A $2\lambda nE_H$ Π_B $\lambda(1-n)E$	A: E; B: E_H C $2\lambda E+\lambda(1-n)E_L$ pat 2 Π_A $\lambda\left(2-n\right)E$ Π_B λnE_H	A: $E_H$and E_L;B: E C $2\lambda E+\lambda nE_H$ pat 2 Π_A $\lambda 2nE_H+(1-n)E_L$ Π_B $\lambda(1-n)E$
$\frac{(1-n)^2}{n^2} < \frac{E_H}{E_L} < max\left\{ \begin{array}{c} \frac{2}{n} \\ \frac{1-n+(1-n)^2}{n^2} \end{array} \right.$	A: E B: E_H C $2\lambda E+\lambda(1-n)E_L$ pat 2 Π_A $\lambda\left(2-n\right)E$ Π_B λnE_H	A: E B: E_H C $2\lambda E+\lambda(1-n)E_L$ pat 2 Π_A $\lambda\left(2-n\right)E$ Π_B λnE_H	A: $E_H$and E_L B: E C $2\lambda E+\lambda nE_H$ pat 2 Π_A $\lambda 2nE_H+(1-n)E_L$ Π_B $(1-n)E$
$\frac{1-n}{n} < \frac{E_H}{E_L} < \frac{(1-n)^2}{n^2}$	A: E; B: E_H C $2\lambda E+\lambda(1-n)E_L$ pat 2 Π_A $\lambda\left(2-n\right)E$ Π_B λnE_H	A: E; B: E_H C $2\lambda E+\lambda(1-n)E_L$ pat 2 Π_A $\lambda\left(2-n\right)E$ Π_B λnE_H	A: E; B: $E_H$and E_L C $2\lambda E+\lambda(1-n)E_L$ pat 2 Π_A $\lambda\left(2-n\right)E$ Π_B λnE_H
$\frac{E_H}{E_L} < \frac{1-n}{n}$	A: E; $B:E$ C $2\lambda E$ N 2 Π_A λE Π_B λE	A: E; $B:E$ C $2\lambda E$ pat 2 Π_A λE Π_B λE	A: E; $B:E$ C $2\lambda E$ pat 2 Π_A λE Π_B λE

Table 1: Market share when the industry can observe the differential

	MBP	AVBP	IVBP
$\frac{E_H}{E_L} > max \begin{cases} \frac{2}{n} \\ \frac{1-n+(1-n)^2}{n^2} \end{cases}$	$\frac{\lambda(nE_H-3(1-n)E_L)}{2}$ 0	0 $\frac{\lambda(nE_H-(1-n)E_L)}{2}$	$\frac{\lambda(nE_H-(1-n)E_L)}{2}$ 0
$\frac{(1-n)^2}{n^2} < \frac{E_H}{E_L} < max \begin{cases} \frac{2}{n} \\ \frac{1-n+(1-n)^2}{n^2} \end{cases}$	0 $\frac{\lambda(nE_H-(1-n)E_L)}{2}$	0 $\frac{\lambda(nE_H-(1-n)E_L)}{2}$	$\frac{\lambda(nE_H-(1-n)E_L)}{2}$ 0
$\frac{1-n}{n} < \frac{E_H}{E_L} < \frac{(1-n)^2}{n^2}$	0 $\frac{\lambda(nE_H-(1-n)E_L)}{2}$	0 $\frac{\lambda(nE_H-(1-n)E_L)}{2}$	0 $\frac{\lambda(nE_H-(1-n)E_L)}{2}$
$\frac{E_H}{E_L} < \frac{1-n}{n}$	no value for A or B		

Table 2: The value of information for A (above) and B (below) when industries expect the competitor to have invested in determining the effectiveness differential

invest in this differential from the start.

B has a higher return from the investment in terms of the number of cases where the latter is profitable, however the return is often lower (profit in Table 2 is highest in the first line). If the cost to determine the effectiveness differential (F) is lower than the expected profit, the industry will invest in determining patients heterogeneity, otherwise this information will be lost. In appendix B we show the incentives to invest when A thinks that B will not invest and vice versa. The qualitative conclusions are however quite similar.

4 Discussion and conclusions

The advances in genomic medicine allow to develop effective treatments, but increase heterogeneity in patients responses, which opens new important questions related to the incentives that the industry may have in researching into such heterogeneity. Indication-based prices have been proposed as a way to provide a pricing scheme more in line with the observed heterogeneity in patients responses, but from our analysis this scheme appears only slightly more effective than others in attaining this objective. In a competitive setting the most important driver for personalising drugs seems to be avoiding competition. This means that a trade off may emerge between innovation and personalisation. In general, the company that enters a market where there are no competitors have less incentives than an industry that wants to enter a market where other drugs already exist; in other words who enters first may be prone to avoid differentiation, unless the effectiveness differential is quite high.

The results presented in this section may explain the observed trend in the development of new drugs, especially as concerns oncological drugs. In general this analysis show that the combined effect of uncertainty, asymmetry of information and the need to reduce competition makes personalised drugs a rather costly option. It may well be for this reason that IVBP usually pay a non linear price for the drug (λ is decreasing in the level of effectiveness), and

this may be reason why some authors think that these schemes are too costly (Bach (2014); Kaltenboeck and Bach (2018); Yu et al. (2017b)). In some countries, forms of IVBP are often introduced through performance based Managed Entry Agreements (MEA) (Carlson et al., 2017; Panos et al., 2010; Towse et al., 2018; Dabbous et al., 2020)). MEA should allow to differentiate the effectiveness differential ex-post, but also in this case to a remarkable cost (Gamba et al. (2020); Ferrario and Kanavos (2015)). In the light of these results, it may however be advisable to research the welfare properties of these schemes and their incentives to research into patients heterogeneity.

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A Best strategies and game solutions when the effectiveness differential can be costlessly observed

A.1 Background

Market entry determined by cost effectiveness considerations; the indicator is ICER (incremental cost effectiveness, i.e. $\frac{\Delta E}{\Delta C}$

When the industry reveals the effectiveness differential for the drug, the latter is E_H for the first n patients and E_L for the $(1-n)$ group. The effectiveness when the industry does not reveal the differential is $E = nE_H + (1-n)E_L$.

When two drugs have the same cost effectiveness, the rules for determining which one will be marketed are as follows:

- the drug with the highest effectiveness will be marketed
- if they share also the same level of effectiveness the market is shared equally.

The market equilibrium is found using a backward induction method.We will first consider the best reply by B given the strategy used by A and we will then determine which is the best strategy for A if the latter wants to maximise the profit. The effectiveness differential is known only by the industry which may decide to use it at its own advantage. The strategies for A and B are symmetric and can be summarised as follows:

1. Ask for listing only for the first n patients;
2. Reveal the effectiveness differential and compete on both markets;
3. Do not declare the effectiveness differential. They list for a drug with a level of effectiveness equal to E;
4. Ask for listing only for the second group of $1-n$ patients. However, this strategy is always dominated by the one of the other three and it will not be considered.

A.2 Marginal value based

The price is determined on the basis of the effectiveness of the marginal patient.

A.2.1 A lists for the first n patients

A gets the first market for a price equal to λE_H.

Best reply by B

Let us consider the alternatives for B

1. list for the first n patients. Profit for B is $\frac{\lambda}{2}nE_H$
2. declare the effectiveness differential. The price will be equal to λE_L.For the first n patients, the drug has the same effectiveness, but a lower price. B gets all the market. For the $(1-n)$ patients it represents the only alternative. The profit for the industry will be equal to λE_L:
3. do not declare the effectiveness differential. The industry asks listing for a drug with a uniform level of effectiveness equal to $E = nE_H + (1-n)E_L$ for a price equal to λE. For the first n patients, both drugs have the same cost effectiveness (λ), but the alternative proposed by A is more effective. A wins this market. B gets the market for the $(1-n)$ patients and gets a profit equal to $\lambda(1-n)E = \lambda\,(1-n)\,(nE_H + (1-n)E_L)$

Let us consider the case $\frac{E_H}{E_L} > \frac{2}{n}$. The first strategy is better than the second one. Let us then compare it with the third one:

$\frac{1}{2}\lambda nE_H - \lambda(1-n)\,(nE_H + (1-n)E_L) = \left(\left(\frac{1}{2}n - (1-n)\,n\right)E_H - (1-n)^2\,E_L\right)\lambda$

For n$<\frac{1}{2}$, $\frac{1}{2}\lambda nE_H - \lambda(1-n)\,(nE_H + (1-n)E_L) < 0$

B does not declare the differential in effectiveness and gets a profit equal to $\lambda(1-n)\,(nE_H + (1-n)E_L)$

If $\frac{E_H}{E_L} < \frac{2}{n}$, the second strategy is better than the first one. Let us compare with the the third one.

$\lambda(1-n)\,(nE_H + (1-n)E_L) - \lambda E_L, > 0$ if $E_H > E_L\ (\ 1 + \frac{1}{1-n})$

This condition is never verified for $n < \frac{1}{2}$ hence the best strategy for B is to declare the effectiveness differential for a profit equal to λE_L

	$\frac{E_H}{E_L} > \frac{2}{n}$	
A	E_H	$\lambda nE_H + \lambda nE_H$
B	E	$\lambda(1-n)\,(nE_H + (1-n)E_L)$
	$\frac{E_H}{E_L} < \frac{2}{n}$	
A	E_H	λnE_H
B	$E_H$and E_L	λE_L

Table A.1: Outcome when A lists only for the first n patients

A.2.2 A reveals the differential in effectiveness

A sells both markets for a price equal to λE_L.

Best reply by B

In this case the best strategy for B is to do the same, any other strategy would bring to no market share

A	E_H and E_L	$\frac{3}{2}\lambda E_L$
B	E_H and E_L	$\frac{1}{2}\lambda E_L$

Table A.2: Outcome when A reveals the effectiveness differential

A.2.3 A does not reveal the effectiveness differential

A lists for a price equal to $\lambda\left(nE_H + (1-n)E_L\right)$and an effectiveness equal to $E = nE_H + (1-n)E_L$

Best reply by B

1. list for the first n patients. Effectiveness equal to E_H and price equal to λE_H. B gets this market. Profit equal to $\lambda n E_H$;

2. declare the effectiveness differential. B to get the market for the first n patients. For the second group, the cost effectiveness is the same, but the drug offered by A appears to be more effective (E against E_L) . Profit is equal to $\lambda n E_L$;

3. do no declare the effectiveness differential. The market is shared equally. Profit equal to $\frac{\lambda E}{2} = \frac{\lambda(nE_H+(1-n)E_L)}{2}$.

The first alternative is always dominated by the second one. We can then compare alternative 1 with 3

If $\frac{E_H}{E_L} > \frac{(1-n)}{n}$, B lists for the first n patients with a profit equal to $\lambda n E_H$.

If $\frac{E_H}{E_L} < \frac{(1-n)}{n}$, B does not reveal the differential in effectiveness. Profit equal to $\frac{\lambda E}{2} = \frac{\lambda(nE_H+(1-n)E_L)}{2}$

		$\frac{E_H}{E_L} > \frac{(1-n)}{n}$
A	E	$\lambda(nE_H + (1-n)E_L) + \lambda(1-n)(nE_H + (1-n)E_L)$
B	E_H	$\lambda n E_H$
		$\frac{E_H}{E_L} < \frac{(1-n)}{n}$
A	E	$\frac{3}{2}\lambda E$
B	E	$\frac{1}{2}\lambda E$

Table A.3: Outcome when A does not reveal the effectiveness differential

The state-contingent equilibria are summarised in Table A.4

		Best strategy by A		
Best strategy by B		E_H	E_L and E_H	E
	E_H			$\frac{E_H}{E_L} > \frac{1-n}{2}$ $A : \lambda(2-n)E$ $B : \lambda n E_H$
	E_H and E_L	$E_H < \frac{2E_L}{n}$ $A : \lambda n E_H$ $B : \lambda E_L$	$A : \frac{3}{2}\lambda E_L$ $B : \frac{1}{2}\lambda E_L$	
	E	$\frac{E_H}{E_L} > \frac{2}{n}$ $A : 2\lambda n E_H$ $B : \lambda(1-n)E$		$\frac{E_H}{E_L} < \frac{1-n}{2}$ $A : \frac{3}{2}\lambda E$ $B : \frac{1}{2}\lambda E$
	E	$A : 2\lambda n E_H$ $B : \lambda(1-n)E$	$A : 2\lambda E_L$ $B : 0$	$A : \frac{3\lambda E}{2}$ $B : \frac{\lambda E}{2}$

Table A.4: State-contingent equilibria under Marginal Value Based Prices

A.2.4 Best reply by A

At the first stage A decides which is the best strategy to maximise welfare given the best reply by B.

Let us assume that $E_H > 2\frac{E_L}{n}$. This also implies that $\frac{E_H}{E_L} > \frac{(1-n)}{n}$

The play-offs for A given the reaction function of B are:

$\lambda n E_H + \lambda n E_H = 2\lambda n E_H$

$\frac{3}{2}\lambda E_L$

$\lambda(nE_H+(1-n)E_L)+\lambda(1-n)(nE_H+(1-n)E_L)=\lambda(2-n)(nE_H+(1-n)E_L)$

$2\lambda n\frac{E_H}{E_L} > \frac{3}{2}\lambda$, if $\frac{E_H}{E_L} > \frac{3}{4n}$ which is always true in the interval considered. Let us then compare 1) with 3)

If $E_H > \frac{(2-n)(1-n)}{n^2}E_L$, A chooses to list only on the first market with a profit equal to $2\lambda n E_H$

If $\frac{2}{n} < \frac{E_H}{E_L} < \frac{(2-n)(1-n)}{n^2}$ A chooses to list for both market without revealing the differential in effectiveness for a profit equal to $\lambda(2-n)(nE_H+(1-n)E_L)$

Let us now assume that $\frac{(1-n)}{n} < \frac{E_H}{E_L} < \frac{2}{n}$

In this case the pay-offs are

$\lambda n E_H$

$\frac{3}{2}\lambda E_L$
$\lambda\left(2-n\right)\left(nE_H+(1-n)E_L\right)$

Since $n<\frac{1}{2}$, the third dominates the first one. Comparison between alternative 2) and 3)

If $\frac{E_H}{E_L}>\frac{1-6n+2n^2}{2(n-2)n}$, A chooses to list for both market without revealing the differential in effectiveness for a profit equal to $\lambda\left(2-n\right)\left(nE_H+(1-n)E_L\right)$

If $\frac{E_H}{E_L}<\frac{1-6n+2n^2}{2(n-2)n}$ A reveals the effectiveness differential and gets a profit equal to $\frac{3}{2}\lambda E_L$

Let us now consider the case
$\frac{E_H}{E_L}<\frac{(1-n)}{n}$
The pay-offs for A given the reaction function of B are
λnE_H
$\frac{3}{2}\lambda E_L$
$\frac{3}{2}\lambda(nE_H+(1-n)E_L)$

In this case the third alternative dominates the others. A chooses to list for both market without revealing the differential in effectiveness for a profit equal to$\frac{3}{2}\lambda(nE_H+(1-n)E_L)$

The pay-off matrix for the game is presented in Table A.5 sotto c'e' un problema
$\frac{(1-n)}{n}<\frac{E_H}{E_L}<\frac{2}{n}\frac{E_H}{E_L}<\frac{1}{2}\frac{1-6n+2n^2}{(n-2)n}$

		Best strategy by A		
Best strategy by B		E_H	E_L and E_H	E
	E_H			$\frac{(1-n)}{n}<\frac{E_H}{E_L}<\frac{2}{n}$ $\frac{E_H}{E_L}>\frac{1}{2}\frac{1-6n+2n^2}{(n-2)n}$ $A:\quad\lambda\left(2-n\right)E$ $B:\qquad\lambda nE_H$
	E_H and E_L		$\begin{cases}\frac{(1-n)}{n}<\frac{E_H}{E_L}<\frac{2}{n}\\ \frac{E_H}{E_L}<\frac{1}{2}\frac{1-6n+2n^2}{(n-2)n}\end{cases}$ $A\quad:\frac{3}{2}\lambda E_L$ $B\quad:\frac{1}{2}\lambda E_L$	
	E	$max\begin{cases}\frac{2}{n}\\ \frac{1-n+(1-n)^2}{n^2}\end{cases}$ $A:\quad2\lambda nE_H$ $B:\qquad\lambda E$		$\frac{E_H}{E_L}<\frac{(1-n)}{n}$ $A\quad:\frac{3}{2}\lambda E$ $B\quad:\frac{1}{2}\lambda E$

Table A.5: Outcome Marginal Value Based

A.3 Average value based

The price is determined on the basis of the effectiveness of the average patient, i.e. λE_H. if the industry lists only for the first n patients; λE if it lists for all the patients and λE if it does not reveal the effectiveness differential.

A.3.1 A lists for the first n patients

In this case A lists for the first n patients for a price equal to λE_H

Best answer by B The alternatives:

1. Declare E_H for a price equal to λE_H. Profit equal to $\frac{\lambda}{2} n E_H$
2. Declare E_H and E_L for a price λE. The drug is equally effective for the first n patients, but cheaper. It is the only alternative for the second group. Profit: $\lambda \left(nE_H + (1-n)E_L\right)$.
3. Do not declare the effectiveness differential. They list a drug whose effectiveness is E for all the patients for a price equal to λE. The ICER is the same for the first n patients, but less effective. Only alternative on the second market. Profit equal to $\lambda(1-n)\left(nE_H + (1-n)E_L\right)$

The second alternative is always the best

A	E_H	$\lambda n E_H$
B	E_H and E_L	$\lambda \left(nE_H + (1-n)E_L\right)$

Table A.6: Outcome if A lists only for the first n patients

A.3.2 A reveals the effectiveness differential

A lists for both markets and declares a level of effectiveness equal to E_H for the first n patients and equal to E_L for the last $(1-n)$. The price is set on the basis of the average effectiveness, i.e.$\lambda \left(nE_H + (1-n)E_L\right)$

Best answer by B

1. Declare E_H for a price equal to λE_H In this case it would not get any market share since $\lambda E_H > \lambda \left(nE_H + (1-n)E_L\right)$. Profit equal to 0
2. Declare E_H and E_L for a price λE. The two drugs have the same C/E ratio, the industries share the market equally $\frac{\lambda}{2}\left(nE_H + (1-n)E_L\right)$
3. Do not declare the effectiveness differential. They list a drug whose effectiveness is E for all the group of patients for a price equal to λE. In this case the price is the same, but effectiveness is lower for the first n patients and higher for the last $(1-n)$. Industry B gains this market for a profit equal to $\lambda(1-n)\left(nE_H + (1-n)E_L\right)$

For $n < \frac{1}{2}$, alternative 3) is the winning strategy.

A	E_H and E_L	$\lambda \left(1+n\right)\left(nE_H + (1-n)E_L\right)$
B	E	$\lambda \left(1-n\right)\left(nE_H + (1-n)E_L\right)$

Table A.7: Outcome given that A reveals the differential in effectiveness

A.3.3 A does not reveal the effectiveness differential

A lists a drug whose effectiveness is E for all the patients for a price equal to λE.

Best answer by B

1. Declares E_H for a price equal to λE_H Effectiveness E_H and profit equal to$\lambda n E_H$.
2. DeclaresE_H and E_L for a price λE. It gets the market for the first n patients. Same price, higher effectiveness. For the second group of patients the drug sold by A is better. Profit $\lambda n(nE_H + (1-n)E_L)$.
3. Does not declare the effectiveness differential. They list a drug whose effectiveness is E for all the patients for a price equal to λE. Market shared equally with a profit equal to$\frac{\lambda}{2}\left(nE_H + (1-n)E_L\right)$.

Given that $n < \frac{1}{2}$, alternative 3) is better than alternative 2).

Let us then compare alternative 3) with 1)

$\lambda n E_H - \frac{\lambda}{2}\left(nE_H + (1-n)E_L\right)$

$\frac{E_H}{E_L} > \frac{1-n}{n}$

B declares E_H for a profit equal to $\lambda n E_H$;

$\frac{E_H}{E_L} < \frac{1-n}{n}$

B declares E for a profit equal to $\frac{\lambda}{2}\left(nE_H + (1-n)E_L\right)$

		$\frac{E_H}{E_L} > \frac{1-n}{n}$
A	E	$\lambda(2-n)\left(nE_H + (1-n)E_L\right)$
B	E_H	$\lambda n E_H$

		$\frac{E_H}{E_L} < \frac{1-n}{n}$
A	E	$\frac{3}{2}\lambda\left(nE_H + (1-n)E_L\right)$
B	E	$\frac{1}{2}\lambda\left(nE_H + (1-n)E_L\right)$

Table A.8: Outcome for A and B given that A does not reveal the differential in effectiveness

The state contingent strategies are summarised in Table A.9

		Best strategy by A		
Best strategy by B		E_H	E_H and E_L	E
	E_H			$\frac{E_H}{E_L} > \frac{1-n}{n}$ $A : \lambda(2-n)E$ $B : \lambda n E_H$
	E_H and E_L			
	E	$A : \lambda n E_H$ $B : \lambda(1-n)E$	$A : \lambda(1+n)E$ $B : \lambda(1-n)E$	$\frac{E_H}{E_L} < \frac{1-n}{n}$ $A : \frac{3\lambda E}{2}$ $B : \frac{\lambda E}{2}$
	E	$A : \lambda n E_H$ $B : \lambda(1-n)E$	$A : \lambda(1+n)E$ $B : \lambda(1-n)E$	$A : \frac{3\lambda E}{2}$ $B : \frac{\lambda E}{2}$

Table A.9: State contingent equilibria under Average Value Based Prices

A.3.4 Best reply by A

At the first stage A decides which is the best strategy to maximise welfare given the best reply by B.

Let us assume $\frac{E_H}{E_L} > \frac{1-n}{n}$. The three pay-offs are

$\lambda n E_H$

$\lambda(1+n)\left(nE_H + (1-n)E_L\right)$

$\lambda(2-n)\left(nE_H + (1-n)E_L\right)$

In this case it is always better to list for all the patients without revealing the effectiveness differential.

$A : E\ \lambda(2-n)\left(nE_H + (1-n)E_L\right)$

$B : E_H\ \lambda n E_H$

$\frac{E_H}{E_L} < \frac{1}{n} - 1$

The pay-offs are

$\lambda n E_H$

$\lambda(1+n)\left(nE_H + (1-n)E_L\right)$

$\frac{3}{2}\lambda\left(nE_H + (1-n)E_L\right)$

Given that $n < \frac{1}{2}$, the third alternative is again the most profitable. For A it is better to list for all the patients without revealing the effectiveness differential.

Table A.9 summarises the state contingent equilibria under average value based prices. The pay-off matrix for the game is presented in Table A.10

		Best strategy by A		
Best strategy by B		E_H	E_H and E_L	E
	E_H			$\frac{E_H}{E_L} > \frac{1-n}{n}$ $A: \lambda(2-n)E$ $B: \lambda n E_H$
	E_H and E_L			
	E			$\frac{E_H}{E_L} < \frac{1-n}{n}$ $A: \frac{3}{2}\lambda E$ $B: \frac{1}{2}\lambda E$

Table A.10: Outcome Average value based

A.4 Indication based prices

The price of the drug is set according to the effectiveness of each group of patients. If the industry declares the effectiveness differential the drug will be sold under two different prices. $\lambda E_H$and λE_L. However the industry may also decide to enter only a market or it may also decide not to declare the effectiveness differential. In this case the drug has an effectiveness equal to E for all the patients and the price reimbursed is λE

A.4.1 A lists for the first n patients

A lists for the first n patients for a price equal to λE_H

Best answer by B

1. Declare E_H for a price equal to λE_H. Profit equal to $\frac{\lambda}{2} n E_H$
2. Declare E_H and E_L for a price λE_H and λE_H.Drug is equally effective for the first n patients and only alternative for the second group. Profit: $\frac{\lambda}{2} n E_H + \lambda(1-n)E_L$
3. Do not declare the effectiveness differential. They list a drug whose effectiveness is E for all the patients for a price equal to λE. The price is the same for the first n patients, but less effective. Only alternative on the second market. Profit equal to $\lambda(1-n)\left(nE_H + (1-n)E_L\right)$

The second strategy is always better than the first one.

$E_H < E_L\left(1 + \frac{1}{1-2n}\right)$

B lists for both drugs . Profit $\lambda(1-n)\left(nE_H + (1-n)E_L\right)$

If $E_H > E_L\left(1 + \frac{1}{1-2n}\right)$ B does not declare the effectiveness differential and it asks to be listed for a drug with effectiveness equal to E.

	$\frac{E_H}{E_L} > \left(1 + \frac{1}{1-2n}\right)$	
A	E_H	$2\lambda n E_H$
B	E	$\lambda(1-n)\left(nE_H + (1-n)E_L\right)$
	$\frac{E_H}{E_L} < \frac{1-n}{n}$	
A	E_H	$\frac{3}{2}\lambda n E_H$
B	E_H and E_L	$\frac{\lambda}{2}nE_H + (1-n)E_L$

Table A.11: Outcome for A and B given that A lists only for the first n patients

Outcome for A and B given that A lists only for the first n patients

A.4.2 A reveals the effectiveness differential

A lists for both markets and declares a level of effectiveness equal to E_H for the first n patients and equal to E_L for the last $(1-n)$.

Best answer by B

1. Declare E_H for a price equal to λE_H Effectiveness E_H and profit equal to $\frac{\lambda}{2}nE_H$
2. Declare E_H and E_L for a price λE_H and λE_HThe drug is equally effective Profit: $\frac{\lambda}{2}\left(nE_H + (1-n)E_L\right)$
3. Do not declare the effectiveness differential. They list a drug whose effectiveness is E for all the patients for a price equal to λE. In this case for the (1-n) patients the drug is more effective and B gets the market . Profit $(1-n)\lambda\left(nE_H + (1-n)E_L\right)$.

For $n < \frac{1}{2}$,3) is the best answer.

A	E_H and E_L	$\lambda\left(nE_H + (1-n)E_L\right) + \lambda n E_H$
B	E	$\lambda(1-n)\lambda\left(nE_H + (1-n)E_L\right)$

Table A.12: Outcome for A and B given that A reveals the effectiveness differential

Outcome for A and B given that A reveals the effectiveness differential

A.4.3 A does not reveal the effectiveness differential

A lists a drug whose effectiveness is E for all the patients for a price equal to λE

Best answer by B

1. Declare E_H for a price equal to λE_H Effectiveness E_H and profit equal to$\lambda n E_H$

2. Declare E_H and E_L for a price λE_H and λE_HIt gets the market for the first n patients. Profit $\lambda n E_H$

3. Do not declare the effectiveness differential. They list a drug whose effectiveness is E for all the patients for a price equal to λE. Market shared equally with a profit equal to$\frac{\lambda}{2}\left(nE_H + (1-n)E_L\right)$

1) and 2) are indifferent. The choice between 1-2 and 3):
$\frac{E_H}{E_L} > \left(\frac{1}{n} - 1\right)$,
B declares E_H and E_L. Profit equal to $\lambda n E_H$.
$\frac{E_H}{E_L} < E_L\left(\frac{1}{n} - 1\right)$,
B declares E. Profit equal to :$\frac{\lambda}{2}\left(nE_H + (1-n)E_L\right)$

	$\frac{E_H}{E_L} > \left(\frac{1}{n} - 1\right)$	
A	E	$\lambda(2-n)\left(nE_H + (1-n)E_L\right)$
B	E_H and E_L	$\lambda n E_H$
	$\frac{E_H}{E_L} < \frac{1}{n} - 1$	
A	E	$\frac{3}{2}\lambda\left(nE_H + (1-n)E_L\right)$
B	E	$\frac{1}{2}\lambda\left(nE_H + (1-n)E_L\right)$

Table A.13: Outcome if A reveals the effectiveness differential

Table A.14 summarises the state-contingent equilibria under indication based prices.

		Best strategy by A		
		E_H	E_L and E_H	E
Best strategy by B	E_H			$\frac{E_H}{E_L} > \frac{1-n}{n}$ $A : \lambda(2-n)E$ $B : \lambda n E_H$
	E_L and E_H	$\frac{E_H}{E_L} < 1 + \frac{1}{1-2n}$ $A : \frac{3}{2}\lambda E_H$ $B : \frac{\lambda}{2}E_H + (1-n)\lambda E_L$		$\frac{E_H}{E_L} > \frac{1-n}{n}$ $A : \lambda(2-n)E$ $B : \lambda n E_H$
	E	$\frac{E_H}{E_L} > 1 + \frac{1}{1-2n}$ $A : 2\lambda E_H$ $B : (1-n)\lambda E$	$A : 2\lambda n E_H + \lambda(1-n)E_L$ $B : \lambda(1-n)E$	$\frac{E_H}{E_L} < \frac{1-n}{n}$ $A : \frac{3}{2}\lambda E$ $B : \frac{\lambda}{2}E$
	E	$A : 2\lambda E_H$ $B : (1-n)\lambda E$	$A : 2\lambda n E_H + \lambda(1-n)E_L$ $B : \lambda(1-n)E$	$A : \frac{3}{2}\lambda E$ $B : \frac{\lambda}{2}E$

Table A.14: State contingent equilibria under Indication Based Prices

A.4.4 Best reply by A

At the first stage A decides which is the best strategy to maximise welfare given the best reply by B.

If $\frac{E_H}{E_L} > \frac{1}{n} - 1; \frac{E_H}{E_L} > 1 + \frac{1}{1-2n}$, the alternatives are:

$\lambda\left(nE_H + (1-n)E_L\right) + \lambda n E_H$

$\lambda n E_H + \lambda n E_H$

$\lambda\left(nE_H + (1-n)E_L\right) + \lambda\left(nE_H + (1-n)E_L\right)(1-n) = \lambda(2-n)\left(nE_H + (1-n)E_L\right)$

The first alternative is always dominated by the second one. Let us compare 2) and 3)

$\lambda\left(nE_H + (1-n)E_L\right) + \lambda n E_H - \lambda(2-n)\left(nE_H + (1-n)E_L\right)$

If $\frac{E_H}{E_L} > \frac{(n-1)^2}{n^2}$, the best answer is to declare E_H and E_L. Profit equal to $\lambda\left(nE_H + (1-n)E_L\right) + \lambda n E_H$

If $\frac{E_H}{E_L} < \frac{(n-1)^2}{n^2}$, the best answer is to declare E. Profit equal to $\lambda(2-n)\left(nE_H + (1-n)E_L\right)$

If $\frac{E_H}{E_L} < \frac{1}{n} - 1; \frac{E_H}{E_L} > \left(1 + \frac{1}{1-2n}\right)$ the alternatives are:

$\lambda n E_H + \lambda n E_H$

$\lambda\left(nE_H + (1-n)E_L\right) + \lambda nE_H$
$\lambda\left(nE_H + (1-n)E_L\right) + \frac{\lambda}{2}\left(nE_H + (1-n)E_L\right)$

The first alternative is always dominated by the second one. Let us compare 2) and 3)

$\lambda nE_H - \frac{\lambda}{2}\left(nE_H + (1-n)E_L\right)$

The first alternative is better than the third one only if $\frac{E_H}{E_L} > \left(\frac{1}{n} - 1\right)$ which is not compatible with the $\frac{E_H}{E_L} < \left(\frac{1}{n} - 1\right)$

If $\frac{E_H}{E_L} < \left(\frac{1}{n} - 1\right)$ the best answer is to declare E. Profit equal to $\frac{3}{3}\lambda\left(nE_H + (1-n)E_L\right)$

$\frac{E_H}{E_L} > \frac{1}{n} - 1; \frac{E_H}{E_L} < \left(1 + \frac{1}{1-2n}\right)$

$\lambda nE_H + \frac{\lambda}{2} nE_H$
$\lambda\left(nE_H + (1-n)E_L\right) + \lambda nE_H$
$\lambda\left(nE_H + (1-n)E_L\right) + \frac{\lambda}{2}\left(nE_H + (1-n)E_L\right)$

When $\frac{E_H}{E_L} < \left(1 + \frac{1}{1-2n}\right)$, B changes its best reply to A when the latter chooses to enter only in the first market. As shown above this reduces the profit for A in this case. Since this alternative was always dominated by other alternatives, the results presented above are valid also for the case where $\frac{E_H}{E_L} < \left(1 + \frac{1}{1-2n}\right)$. The pay-off matrix for the game is presented in Table A.15

		Best strategy by A		
Best strategy by B		E_H	E_H and E_L	E
	E_H			
	E_H and E_L			$\frac{1-n}{n} < \frac{E_H}{E_L} < \frac{(1-n)^2}{n^2}$ $A:\ \lambda(2-n)E$ $B:\ \lambda nE_H$
	E		$\frac{E_H}{E_L} > \frac{(1-n)^2}{n^2}$ $A:\ \lambda E + \lambda nE_H$ $B:\ \lambda(1-n)E$	$\frac{E_H}{E_L} < \frac{1-n}{n}$ $A:\ \frac{3}{2}\lambda E$ $B:\ \frac{1}{2}\lambda E$

Table A.15: Outcome for Indication Value Based Prices

B Best strategies and of the game solutions. A thinks that B will not invest in finding the effectiveness differential

B.1 Marginal value based

The last row in table A.4 shows the equilibrium values for a game where B declares effectiveness E. Let us then determine which is the best strategy for A

in this context

By comparing the profit of A it is possible to show that:
$\frac{E_H}{E_L} > \frac{3(1-n)}{n}$
A: E_H
$\frac{1+3n}{3n} < \frac{E_H}{E_L} < 3\frac{1-n}{N}$:
A:E
$\frac{E_H}{E_L} < \frac{1+3n}{3n}$
$A : E_2; B : 0$

B.2 Average value based

The last row in table A.9 shows the equilibrium values for a game where B declares effectiveness E. By comparing the profit of A it is possible to show that:
$\frac{E_H}{E_L} > \frac{3(1-n)}{n}$
A:E_H
$\frac{E_H}{E_L} < \frac{3(1-n)}{n}$
A:E

B.3 Indication value based

The last row in table A.14 shows the equilibrium values for a game where B declares effectiveness E. By comparing the profit of A it is possible to show that:
$\frac{E_H}{E_L} > \frac{1-n}{n}$
A: E_H and E_L
$\frac{E_H}{E_L} < \frac{1-n}{n}$
A: E

The equilibrium strategies are presented in Table A.16

Best strategy by B		Best strategy by A		
		E_H	E	E_L and E_H
		Marginal Value Based		
	E	$\frac{E_H}{E_L} > \frac{3(1-n)}{N}$ $A: \quad 2\lambda n E_H$ $B: \quad \lambda(1-n)E$	$\frac{1+3n}{3n} < \frac{E_H}{E_L} < \frac{3(1-n)}{n}$ $A: \quad \frac{3}{2}\lambda E$ $B: \quad \frac{1}{2}\lambda E$	$\frac{E_H}{E_L} < \frac{1+3n}{3n}$ $2\lambda n E; 0???$
		Average Value Based		
	E	$\frac{E_H}{E_L} > \frac{3(1-n)}{N}$ $A: \quad 2\lambda n E_H$ $B: \quad \lambda(1-n)E$	$\frac{E_H}{E_L} < \frac{3(1-n)}{n}$ $A: \quad \frac{3}{2}\lambda E$ $B: \quad \lambda(1-n)E$	
		Indication Value Based		
	E	$\frac{E_H}{E_L} > \frac{1-n}{n}$ $A: \quad \lambda(E+nE_H)$ $B: \quad \lambda(1-n)E$	$\frac{E_H}{E_L} < \frac{3(1-n)}{n}$ $A: \quad \frac{3}{2}\lambda E$ $B: \quad \lambda(1-n)E$	

Table A.16: Game solution when information for B is too costly

C B thinks that for A information is too costly

In this case, A does not reveal the effectiveness differential and sells the drug on both markets revealing and effective equal to E.

C.1 Marginal value based

The state contingent answers are presented in Table A.4 It is in fact sufficient to take column 3 to find the outcomes

C.2 Average value based

The state contingent answers are presented in Table A.9 It is in fact sufficient to take column 3 to find the outcomes. It is now sufficient to compare the profits for A with the outcomes in Table... to find the value of information in this case. For average value based, since A's best strategy when it knows the information is not to reveal it, the effectiveness differential has not value for A

C.3 Indication value based

The state contingent answers are presented in Table A.14 It is in fact sufficient to take column 3 to find the outcomes

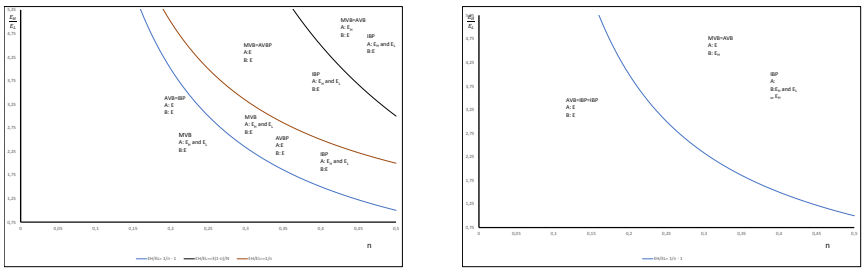

Figure A.5:

Using the results in table in the appendix it is possible to draw a picture similar to Figure 4.

If the value of information is "sufficiently high" for B not to invest in determining the effectiveness differential, A has a greater incentive to reveal it. The results is in line with what observed in the previous section: even in this setting where the effects of competition are not so striking, industries have an interest in not competing with one another. In this case, if A knows that B will not differentiate its drug, is has an incentive in investing to be able to differentiate. Finally, since we have assumed that both industries are equal, we should also determine whether an asymmetric equilibrium (only one firm invests to find the effectiveness differential is feasible. Using figure 5, 5 table x and table y we can determine the value of the information for A and B under this setting. The value of the information for B and A is summarised in Table A.17.

Let us consider the first two columns first. By comparing the results in Table 1 and xx we can see that under MVBP, B has an interest in paying to assess the effectiveness differential only when $\frac{1}{n} < \frac{E_H}{E_L} < \frac{3(1-n)}{n}$ or $\frac{E_H}{E_L} < \frac{1-n}{n}$. In the former case the value of information is equal to $\lambda n E_H - \frac{\lambda E}{2}$ and $\frac{\lambda E}{2}$ respectively. On the other hand when B lists for an undifferentiated drug, the best answer by A is to differentiate only if the effectiveness differential is very high or very low. When A does not differentiate its drug, the information has a value or B only if $\frac{E_H}{E_L} > \frac{1-n}{2}$. The general conclusion that can be drawn from table A.17 is that the value of information is quite different for A and B and it is never symmetric, as one might expect. As shown above for the case where information could be costlessly obtained, the industries best strategy is to differentiate their strategy from the competitor. For B the value of information is similar ($\lambda n E_H - \frac{1}{2}\lambda E$) for all the models, but the range of values is higher for IVBP and lowest for AVBP. In any case, the highest value of such information is...?????

	Costly information for B		Costly information for A	
	A???	B	A	B
MBPS	$\frac{E_H}{E_L} > \frac{3(1-n)}{n}$ $2\lambda n E_H; \frac{3\lambda E}{2}$ $\frac{E_H}{E_L} < \frac{1}{n}$ $2\lambda E_L - \frac{3\lambda E}{2}$	$\frac{1}{n} < \frac{E_H}{E_L} < \frac{3(1-n)}{n}$ $\lambda n E_H - \frac{\lambda E}{2}$ $\frac{E_H}{E_L} < \frac{1-n}{n}$ $\frac{\lambda}{2} E$	$\frac{E_H}{E_L} > max \begin{cases} \frac{2}{n} \\ \frac{1-n+(1-n)^2}{n^2} \end{cases}$ $2\lambda n E_H - \frac{3}{2}\lambda E$	$\frac{E_H}{E_L} > \frac{1-n}{2}$
AVBP	$\frac{E_H}{E_L} > \frac{3(1-n)}{n}$ $2\lambda n E_H - \frac{3}{2}\lambda E$	$\frac{1-n}{n} < \frac{E_H}{E_L} < \frac{3(1-n)}{n}$ $\lambda n E_H \frac{1}{2}\lambda E$		$\frac{E_H}{E_L} > \frac{1-n}{n}$ $\lambda n E_H$
IVBP	$\frac{E_H}{E_L} > \frac{1-n}{n}$ $\lambda (n E_H + E) - \frac{3\lambda E}{2}$	$\frac{(1-n)^2}{n^2} < \frac{E_H}{E_L} < \frac{3(1-n)}{n}$ $\lambda n E_H - \frac{\lambda E}{2}$	$\frac{E_H}{E_L} > \frac{1-n}{n}$ $\lambda (n E_H + E) - \frac{3}{2}\lambda E$	$\frac{E_H}{E_L} > \frac{1-n}{n}$ $\lambda n E_H - \frac{1}{2}\lambda E$

Table A.17: The value of information