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CHEAP OR TIMELY DRUG? PRACTICAL IMPACT OF EXTERNAL REFERENCE PRICING POLICY IN THE EUROPEAN UNION

AUTHORS

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Background

One of the major determinants of medicine prices in the EU markets is the external reference pricing (ERP) system, used to mitigate the public health-care expenditure.

Studies show that aggressive ERP rules and consequently low price levels may indirectly obstruct the availability of medicines in several ways. To protect global revenue, marketing authorisation holders may delay, sequence or withhold launch of a medicine in countries with such conditions. [1]

Objectives

Our work aimed to analyze the consequences of ERP rules for both companies and the national authorities through optimal market access timing. The following analyses were done over a **5-year** time horizon:

- **The impact of various launch sequence strategies on projected earnings**
- **The evolution of the average price for each strategy**
- **Total price erosion per country at the end of the simulation**

Methods

An ERP sequence simulation was developed to determine the country-level price evolution over time. ERP rules and baskets (as of March 2019) for individual countries were implemented. Revenues were estimated on the basis of additional country data (willingness to pay, population size, frequency of price revisions, currency volatility).

Initial conditions

- A fictional medicine was present on the market in **the following countries:**
  - Finland
  - Germany
  - Luxemburg
  - United Kingdom
- An initial price of the medicine was **1,000 USD** in all countries.
- The medicine was launched to **25 EEA countries**.
- The whole launch sequence consisted of **60 rounds**, one round simulating a month, together **5 years**.
- During the first **25 rounds**, the medicine was consequently launched on individual markets.
- **External price referencing** was implemented from the first round until the end of the simulation. Each country could reference according to their ERP rules, referencing to the previous prices of their basket countries.
  - Willingness to pay of a country was considered
  - Currency volatility affected the prices
- Expected revenues were calculated based on the evolution of the medicine's **price**, **country population and disease prevalence** (equal in all countries).
- The initial country order in the launch sequence was chosen based on **four launch sequence strategies** (Table 1).
  - **GDP strategy:** by order of GDP per capita in PPP Int$ (largest to smallest)
  - **POP strategy:** by order of population size (largest to smallest)
  - **CHE strategy:** by order of health expenditure (largest to smallest)
  - **RAN strategy:** random sequence (for comparison)

Genetical Algorithm

A genetical algorithm was developed to search for a launch sequence which would maximize the revenues. The most successful sequence obtained during the search was then evaluated as a separate strategy called "best genetic sequence" **(BGS)**.

A genetic algorithm is a search heuristic that is inspired by the theory of natural evolution. This algorithm reflects the process of natural selection where the fittest individuals (sequences) are selected and then combined to produce new (potentially superior) sequences. [2]

Results

01 Performance of the initially defined strategies

Four initial strategies were tested to obtain prices and projected revenues, calculated based on the evolving prices, determined by the ERP model. **Up to the 25th round**, each strategy launched the medicine with a distinct sequence of countries. See Figure 1.

Subsequently, the products remained on market **in all countries** until the 5th year mark (60th round). It can be seen that they **differed** in their revenue per round mainly **in the launch portion of the simulation**. After that, they had similar revenue per round, since they already had the product in the same set of countries.

02 Search for the best strategy

A new strategy was defined as the best sequence, found by the **genetic algorithm search (Best genetic sequence - BGS)**. The algorithm was designed to maximize the total revenue of a sequence. The resulting sequence **BGS** is shown in Figure 2. Although we see it certainly produced a better result than the **RAN**, **CHE** and **GDP** strategy, it didn't manage to achieve a superior revenue to the **population strategy (POP)**.

A detailed comparison of final revenues is found in the Figure 3. The **POP** strategy exceeded the **BGS** strategy by **1% (365 million $)**. The **GDP** strategy had the lowest total revenue, lagging behind POP strategy by **9% (2,2 billion $)**.

03 Price evolution of the selected strategies

Price evolution for the selected strategies is shown in the Figure 4. The average price of the medicine across countries for tested strategies is much alike during the launch phase of the simulation. The average price varies more between strategies during the second phase, nevertheless not exceeding **1% in the difference** between minimal and maximal average price across strategies. The total drop in the average price for the whole simulation was **-17% for all strategies**.

04 Total price erosion in countries with ERP system

The best performing strategy (POP) in terms of total revenues was used in the analysis of total price erosion across countries using the ERP same environment. Figure 5 shows **the final percent reduction** of the **first established price** in a country. **Poland** (-25%) **and Romania** (-25%) experienced the most aggressive erosion. On the other side, **Ireland** (-7%) **and Denmark** (-8%) experienced the mildest price erosion. The average price erosion was **-14,7%**. We see that with a few exceptions countries which are referenced most frequently generally encounter more extensive price erosions.

Conclusions

Our analysis provides a notion of how the companies consider the launch of an innovative product on the EU market. We defined **four baseline strategies**, which served as a benchmark for maximising revenues. In this aspect, the strategy of launching to countries with the **largest population first (POP strategy)** was the winning one, prevailing over the least successful strategy by **9%**. The search for optimised sequence by the genetic algorithm improved the performance from baseline strategies, but lagged in total revenues behind the winning strategy by **1%**.

We found that different strategies did not have a strong impact on the evolution of the **average price**, it staying roughly within **1%** range across all strategies. The analysis of **price erosion** found substantial differences across countries, with a span from **-7% to -25%** of the initial price.

The apparent consequence of launch sequencing are delays in the availability of innovative medicines, negatively affecting predominantly countries with **smaller markets** and aggressive **ERP rules**. Countries with higher population size, small ERP basket and value-based pricing are reasonably prioritized for market entry. In addition, companies may occasionally avoid disclosing the "real" price of the medicine by settling on confidential agreements with health insurance funds or single national fund (NHS-like). [1]

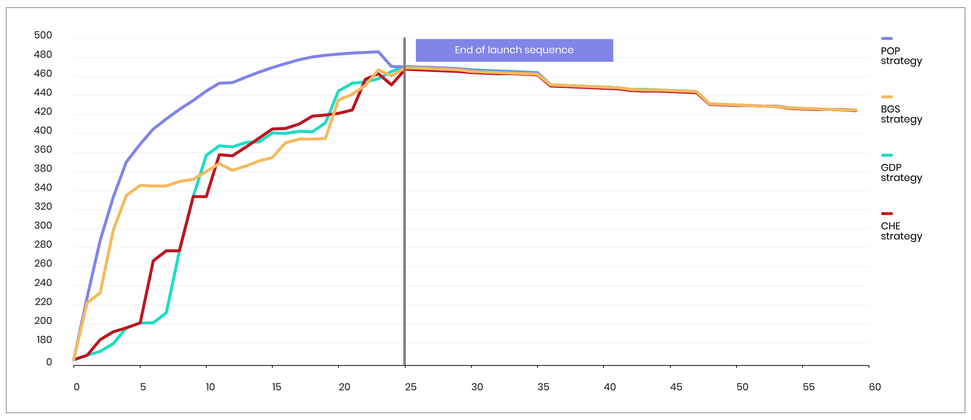
The suggestion for **national policies** on how to keep prices of pharmaceuticals low while ensuring their good availability could be setting **weaker ERP rules** (e.g. average rather than minimum price / fewer basket countries) and take advantage of confidential price discounts, which reduces the risk of further price erosion in other markets and increases the appeal of such markets for companies.

References

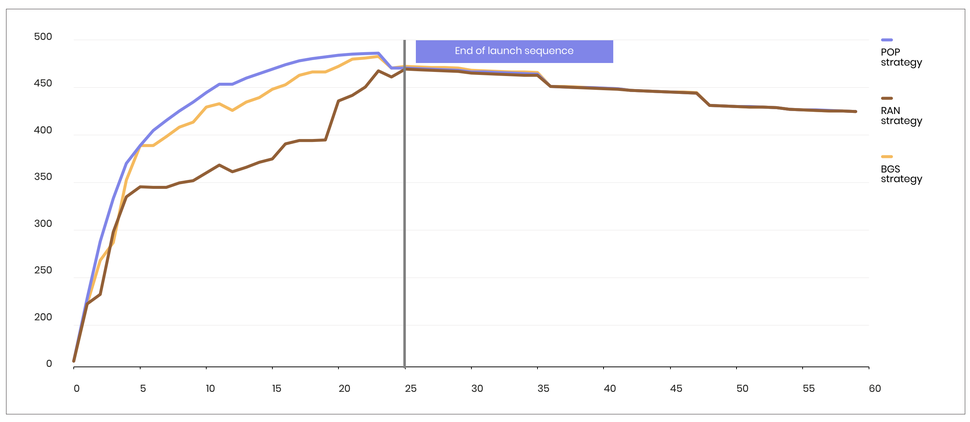
[1] Does external reference pricing deliver what it promises? Evidence on its impact at national level. Panos Kanavos. Published in 2019.

[2] Holland, J. H. Genetic algorithms, Scientific American. Published in 1992.

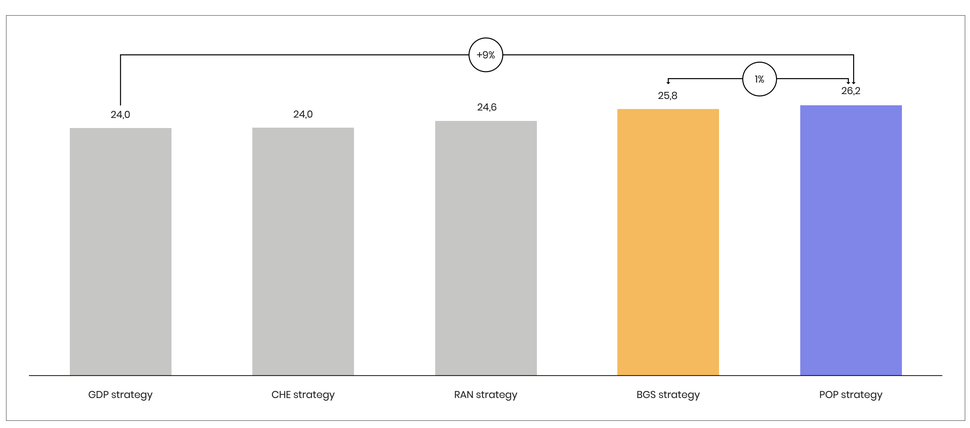
↓ Figure 1 — **Revenue per round for selected strategies (million $)**



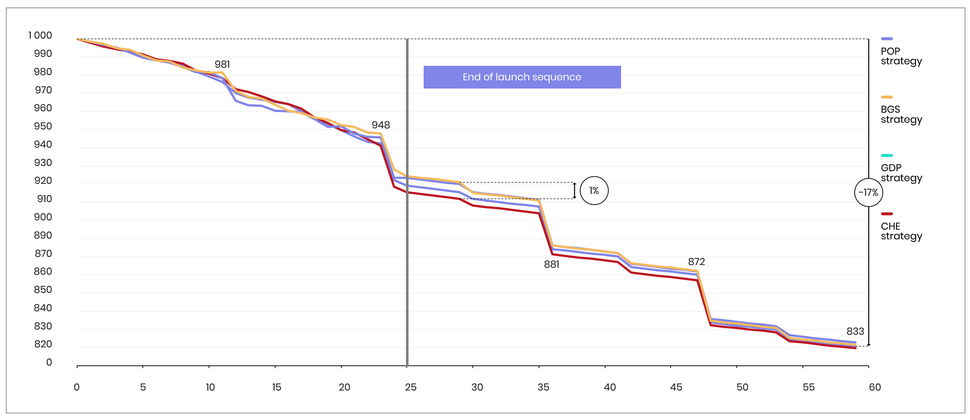
↓ Figure 2 — **Winner (POP) strategy against RAN and BGS strategies**



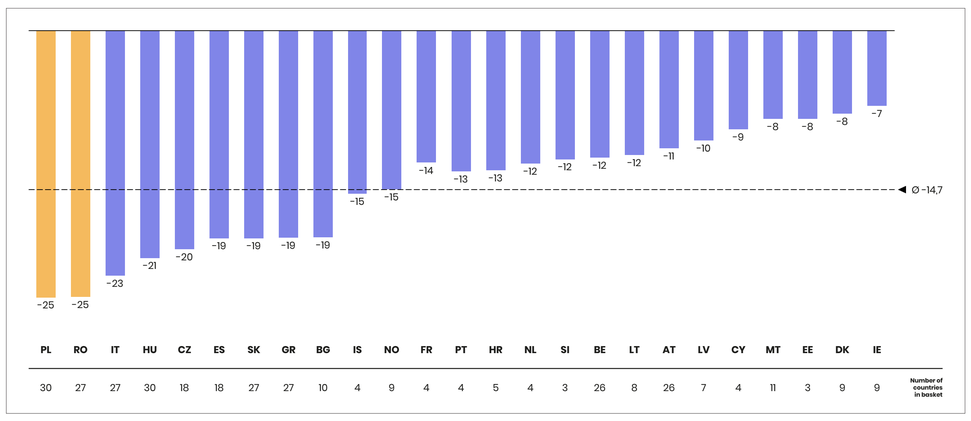
↓ Figure 3 — **Final revenues of strategies (billion $)**



↓ Figure 4 — **Average medicine price per round for selected strategies ($)**



↓ Figure 5 — **Total price erosion for POP strategy (% of initial price)**



↓ Table 1 — **Launch sequence strategies**

	AT	BE	BG	CY	CZ	DK	EE	ES	FR	GR	HR	HU	IE	IS	IT	LT	LV	MT	NL	NO	PL	PT	RO	SI	SK
GDP strategy	3	7	25	14	11	5	16	10	8	19	23	21	2	6	9	17	22	18	4	1	20	15	24	12	13
CHE strategy	3	7	23	16	14	5	19	11	6	15	21	18	4	8	9	20	24	10	2	1	22	13	25	12	17
POP strategy	12	7	13	23	9	14	22	3	1	8	18	11	17	25	2	19	21	24	6	16	4	10	5	20	15
RAN strategy	11	5	21	19	25	14	6	20	3	2	15	10	17	18	1	9	12	7	16	13	4	22	23	24	8
BGS strategy	21	17	20	19	15	9	24	2	4	8	11	13	18	6	1	25	22	12	10	14	5	7	3	23	16