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COMPETITION AND PRODUCT DIFERENTIATION. BIOSIMILARS' ENTRY VERSUS BIOLOGICAL DRUGS

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The structure of the paper

1. Introduction

2. A first look at the data

3. An economic framework for analysing biosimilars versus biological products

4. Discussion and Conclusion

1. INTRODUCTION

- **Starting point of biologic drugs had remarkable effects on public health but any new step is difficult**
- **Problem: biological drugs are not accessible to all patients need due to high costs and financing difficulties especially since 2008 crisis. This is so even if patients' health and welfare should be the highest priority**
- **The relevance of this analysis stems from growing health spending in these products. Inside OECD pharmaceutical expenditure, % of biological drugs are increasing and expected to be 20% in 2017 (oncology, nephrology, rheumatology, etc. as suggests IMS Institute for Healthcare Informatics)**

1. INTRODUCTION

- **Growth biologics market is influenced by use of monoclonal antibodies (degenerative and tumor diseases)**
- **Biosimilars share and its competence degree is small (not less than 0.5 %) although it is increasing (Farfan *et al.*, 2014)**
- **Pharmaeconomics as drug economic evaluation (most efficient technology) has been growing: how much do you pay for a fixed health gain or return ? (Cutler, 2014)**
- **It is important to disentangle this idea: generate savings and find efficient alternatives in medicines for healthcare systems**

1. INTRODUCTION

- **Basic: clinical guidelines, best practices, protocols by consensus in groups of scientific societies. Nevertheless, it causes problems to doctors if they pretend to order last generation drugs difficult to achieve (Van de Vooren et al., 2015)**
- **Even more diseases (rheumatism, cancer, ...) with these medications could become in more chronic and long-run spending**
- ***To control pharmaceutical expenditure: if you treat older patients it could be possible to decrease the price of a drug to “reasonable” level (which are?) as you can “pay” (in Spanish Regional Health Services if we focus on top 10 drugs in cost terms there were 6 of it up to 48,000 euros in cancer disease) and to be “negotiated” (sharing risk?, maximum expenditure ceiling ... but not for sick patients?). The question is to take into account the drug values***

2. A FIRST LOOK AT THE DATA

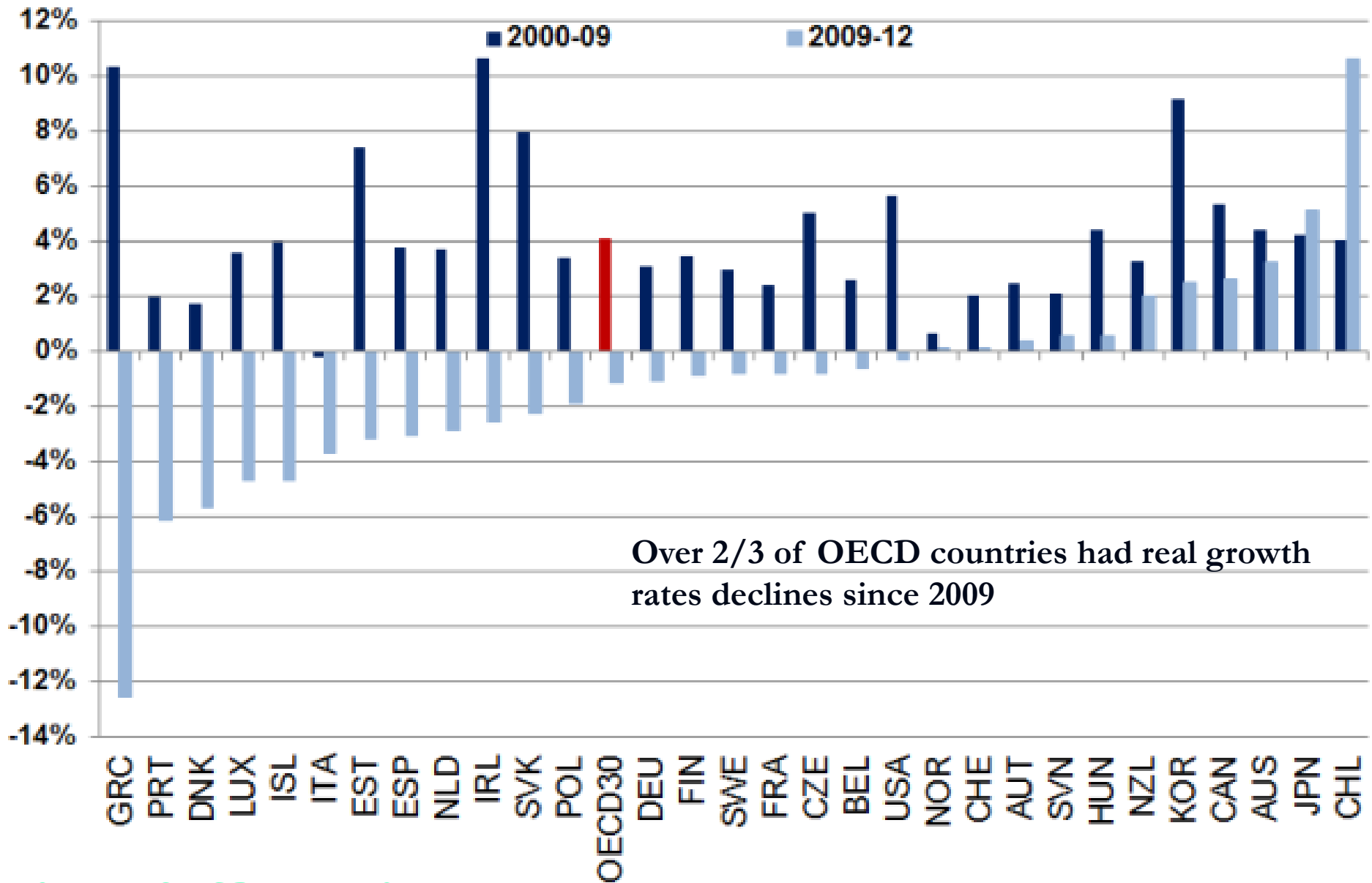
Health care expenditure as % GDP in OECD countries for 2000-2013
(Source: OECD, 2014)



Pharmaceutical expenditure (as a percentage of total expenditure on health)

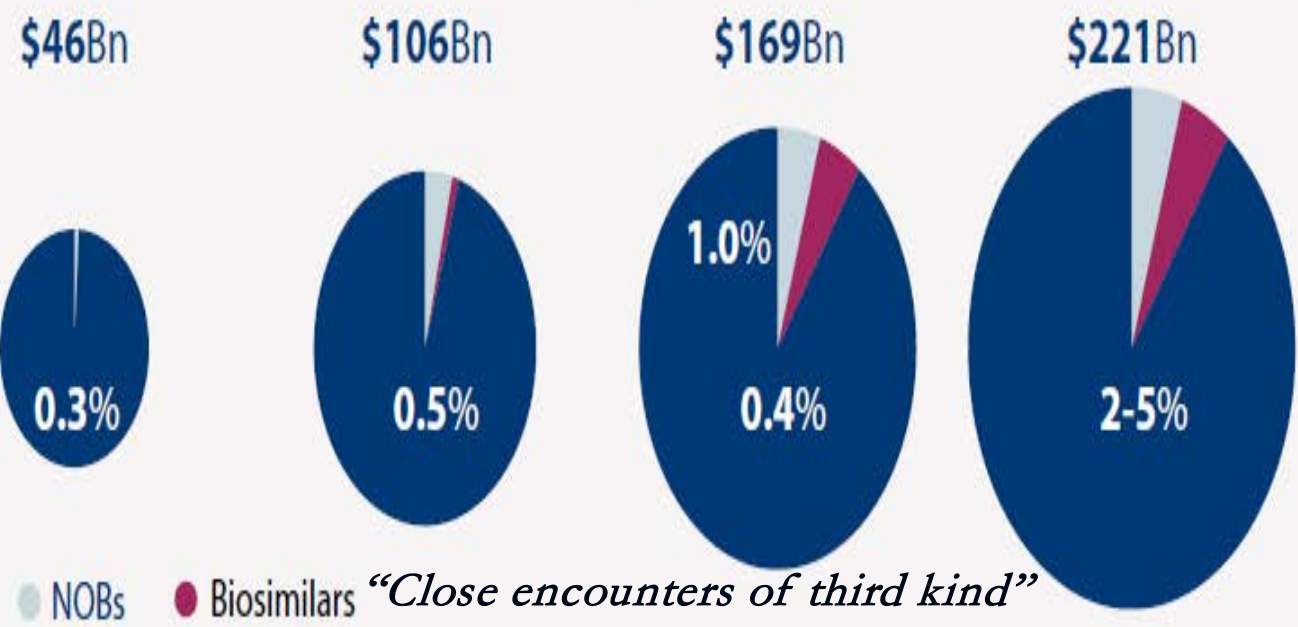
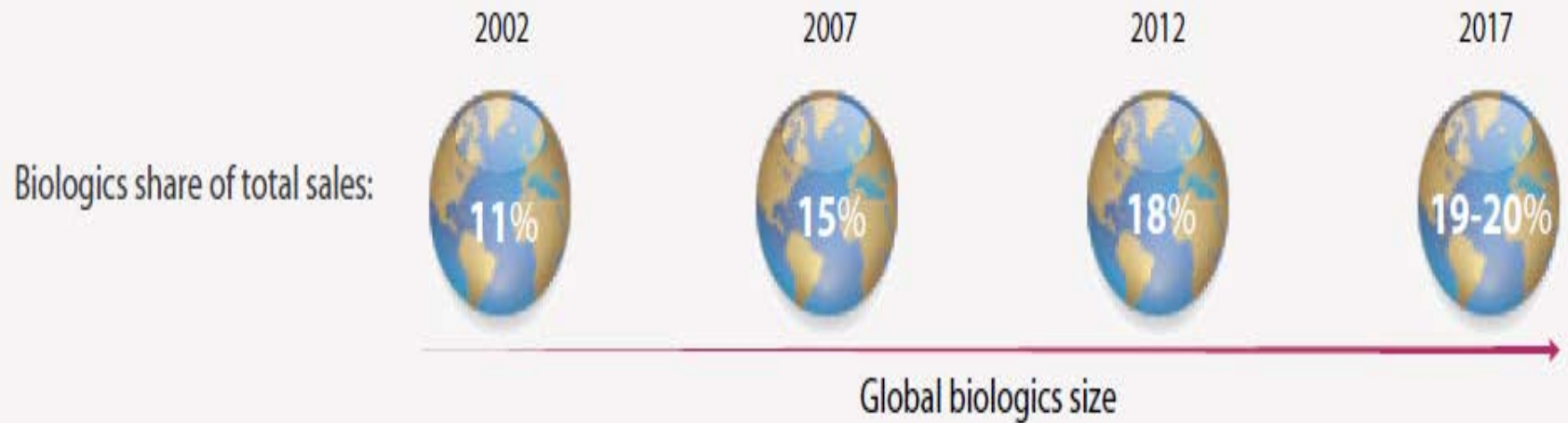
Percentage	2006	2007	2008	2009	2010	2011	2012
Australia	14,3	14,3	14,6	14,7	15,4	14,7	..
Austria	12,9	13,1	13,1	11,9	11,8	11,7	11,5
Belgium	18,9	18,6	18,1	18,1	17,9	17,1	16,6
Canada	17,4	17,2	17,0	17,0	16,6	17,1	..
Chile	13,0	12,3	12,4	11,6	13,2	13,1	13,0
Czech Republic	22,8	21,5	20,4	21,5	19,9	20,0	21,1
Denmark	8,3	8,5	8,0	7,3	7,4	6,8	6,3
Estonia	23,5	21,4	20,7	23,5	21,8	21,5	21,5
Finland	14,7	14,8	14,8	14,2	13,9	13,4	13,3
France	16,7	16,7	16,5	16,2	16,0	15,6	15,2
Germany	14,7	15,0	15,0	14,9	14,7	14,1	13,9
Greece	22,7	24,8	..	27,8	28,3	26,8	24,9
Hungary	31,0	30,6	31,1	32,5	32,9	34,2	31,8
Iceland	14,2	13,5	14,6	15,7	15,8	15,4	14,5
Ireland	17,1	16,9	16,8	16,7	17,9	17,5	17,1
Israel (1)	12,8	13,1	12,9	13,5	13,2
Italy	19,6	19,2	18,1	17,5	16,9	16,6	16,0
Japan	19,5	19,9	19,7	20,7	20,3	20,8	..
Korea	23,9	22,7	22,5	22,0	21,5	21,3	19,8
Luxembourg	8,8	9,7	9,3	9,3	9,0	9,0	8,7
Mexico	3,5	5,2	5,5	5,0	5,5	6,6	6,6
Netherlands	10,3	10,5	9,9	9,7	9,4	9,3	..
New Zealand	11,3	10,4	9,7	9,5	9,5	9,4	..
Norway	8,7	8,0	7,5	7,3	7,4	6,9	6,7
Poland	27,2	24,8	23,0	22,9	22,7	22,5	20,9
Portugal	21,2	21,0	20,3	19,4	18,5	17,9	..
Slovak Republic	29,7	27,9	27,6	26,6	27,5	27,4	25,4
Slovenia	19,9	19,2	18,0	18,4	19,1	18,9	19,2
Spain	19,1	18,6	18,3	18,2	18,3	17,4	..
Sweden	13,4	13,1	12,9	12,7	12,5	12,0	11,6
Switzerland	10,4	10,3	10,1	10,1	9,7	9,4	9,2
United Kingdom	12,3	12,0	11,5	7
United States	12,6	12,6	12,3	12,4	12,0	11,9	11,5

Annual growth of pharmaceutical expenditure in real terms



Source: [OECD Health Statistics 2014](#)

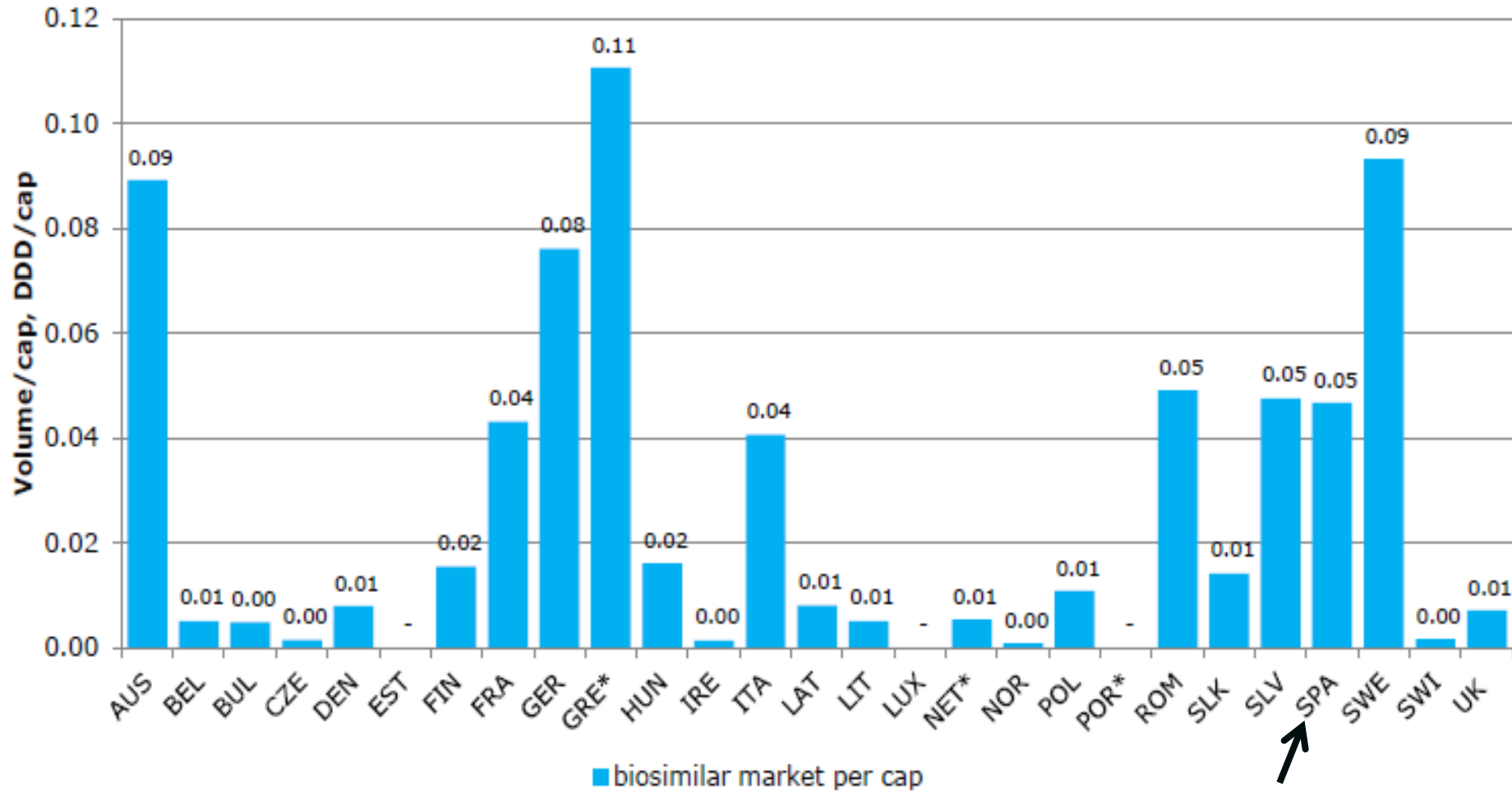
The biologics market



Source: IMS Health Thought Leadership, September 2013

GRE, SWE and AUS have a higher consumption per capita of biosimilar products than GER, UK is notably low along with several small European markets

European Biosim. Market, country rank by volume, DDD



Source: IMS MIDAS Q6 2011 Note: * IMS data covers the retail channel only

3. AN ECONOMIC FRAMEWORK FOR ANALYSING BIOSIMILARS VERSUS BIOLOGICAL PRODUCTS

- **Summarizing literature and introduce our approach to model biosimilars market**
- **Grabowski et al. (2007) models biosimilar markets as monopolistic competition but price decrease is not as greater than in the generics.**
- **Chauhan, Towse and Mestre (2008) in a duopoly model with differentiation, show that price depends on elasticity demand. Moreover, as Hidalgo (2014)**
- **Empirical evidence: Price falls lower than we expected (Rovira, Espin, García and Olry, 2011) and no independent data in order to validate results**
- **Our proposed theoretical model is useful to assess the impact**

3. AN ECONOMIC FRAMEWORK FOR ANALYSING BIOSIMILARS VERSUS BIOLOGICAL PRODUCTS: OUR PROPOSED MODEL

Bertrand competition with homogeneous products (branded and generics)

STEP 1: inverse demand function • Branded and generics are considered as the same

$$P = \alpha - \beta(q_i + q_{-i})$$

- So, they are equally affected by prices

STEP 2 Profit maximization program

$$\text{Max } [P - C(q_i)]q_i$$

- Cost functions might be or not the same
- 2 companies compete in prices

STEP 3 Solution

$$P = \text{Marginal Cost}$$

- If MC are equal for both companies
- No profits, market equally shared, and social welfare is maximized

3. AN ECONOMIC FRAMEWORK FOR ANALYSING BIOSIMILARS VERSUS BIOLOGICAL PRODUCTS: OUR PROPOSED MODEL

But, simple Bertrand model does not correspond with competition between biological and biosimilars BECAUSE PRODUCTS ARE NOT PERFECTLY HOMOGENEOUS. As a consequence, we modify inverse demand function for firms 1 and 2, or i and $-i$

STEP 1:

$$P_1 = \alpha - \beta q_1 - \gamma q_2$$

$$P_2 = \alpha - \beta q_2 - \gamma q_1$$

- We allow for differences in prices
- We allow for product differentiation by adding different elasticities effects of prices in demand function

- If $\beta \neq \gamma$, then there is product differentiation
- γ/β provides the **DEGREE OF DIFFERENTIATION**:
 - $\gamma \rightarrow 0$, differentiation is maximized
 - $\gamma \rightarrow \beta$, differentiation is minimized, so $\gamma/\beta = 1$

3. AN ECONOMIC FRAMEWORK FOR ANALYSING BIOSIMILARS VERSUS BIOLOGICAL PRODUCTS: OUR PROPOSED MODEL

STEP 2:

Profit maximization program for firm i and $-i$

$$\text{Max}_{P_i} [P_i - C(q_i)] q_i$$

- Still Bertrand competition and companies choose prices
- We assume constant marginal costs:

We use:

$$C(q_i) = c_i q_i$$

$$q_i = \frac{\alpha}{\beta} - \frac{1}{\beta} P_i - \frac{\gamma}{\beta} q_{-i}$$

So that, the program becomes:

$$\text{Max}_{P_i} [P_i - c_i] \left\{ \frac{\frac{\alpha}{\beta} \left(1 - \frac{\gamma}{\beta}\right)}{\left(1 - \frac{\gamma^2}{\beta^2}\right)} - \frac{1}{\beta \left(1 - \frac{\gamma^2}{\beta^2}\right)} P_i + \frac{\frac{\gamma}{\beta} \cdot \frac{1}{\beta}}{\left(1 - \frac{\gamma^2}{\beta^2}\right)} P_{-i} \right\}$$

3. AN ECONOMIC FRAMEWORK FOR ANALYSING BIOSIMILARS VERSUS BIOLOGICAL PRODUCTS: OUR PROPOSED MODEL

STEP 3:

Following first order conditions, reaction functions are:

$$P_i = \frac{\alpha \left(1 - \frac{\gamma}{\beta}\right) + \frac{\gamma}{\beta} P_{-i} + c_i}{2}$$

And Nash equilibrium, rearranging terms is:

$$P_i^* = \frac{\alpha \left(1 - \frac{\gamma}{\beta}\right) \left(1 + \frac{\gamma}{2\beta}\right) + \frac{\gamma}{2\beta} c_{-i} + c_i}{2 \left(1 + \frac{\gamma}{2\beta}\right) \left(1 - \frac{\gamma}{2\beta}\right)};$$

$$q_i^* = \frac{\alpha \left(1 - \frac{\gamma}{\beta}\right) \frac{\gamma}{2\beta} - \left(1 - \frac{\gamma}{2\beta}\right) c_i + \frac{\gamma}{2\beta} c_{-i}}{2\beta \left(1 + \frac{\gamma}{\beta}\right) \left(1 - \frac{\gamma}{\beta}\right) \left(1 + \frac{\gamma}{2\beta}\right) \left(1 - \frac{\gamma}{2\beta}\right)}$$

3. AN ECONOMIC FRAMEWORK FOR ANALYSING BIOSIMILARS VERSUS BIOLOGICAL PRODUCTS: OUR PROPOSED MODEL

STEP 3:

Finally, we calculate the profit for firm i at equilibrium

$$\Pi_i = \frac{1}{2^2 \beta \left(1 + \frac{\gamma}{\beta}\right) \left(1 - \frac{\gamma}{\beta}\right) \left(1 + \frac{\gamma}{2\beta}\right)^2 \left(1 - \frac{\gamma}{2\beta}\right)^2} \cdot \left[\begin{aligned} & \alpha^2 \left(1 - \frac{\gamma}{\beta}\right)^2 \left(1 + \frac{\gamma}{2\beta}\right)^2 - \\ & - \left(1 - \frac{\gamma}{2\beta}\right) \left[1 - 2 \left(1 + \frac{\gamma}{2\beta}\right) \left(1 - \frac{\gamma}{2\beta}\right) \right] c_i^2 + \\ & + \alpha \left(1 - \frac{\gamma}{\beta}\right) \left(1 + \frac{\gamma}{2\beta}\right) \left[1 - 2 \left(1 + \frac{\gamma}{2\beta}\right) \left(1 - \frac{\gamma}{2\beta}\right) - \left(1 - \frac{\gamma}{2\beta}\right) \right] c_i + \\ & + \left(\frac{\gamma}{2\beta}\right)^2 c_{-i}^2 + \\ & + 2\alpha \frac{\gamma}{2\beta} \left(1 - \frac{\gamma}{\beta}\right) \left(1 + \frac{\gamma}{2\beta}\right) c_i + \\ & + \frac{\gamma}{2\beta} \left[1 - 2 \left(1 + \frac{\gamma}{2\beta}\right) \left(1 - \frac{\gamma}{2\beta}\right) - \left(1 - \frac{\gamma}{2\beta}\right) \right] c_i c_{-i} \end{aligned} \right]$$

3. AN ECONOMIC FRAMEWORK FOR ANALYSING BIOSIMILARS VERSUS BIOLOGICAL PRODUCTS: OUR PROPOSED MODEL

- This is a MODEL OF PRODUCT DIFFERENTIATION. We do not model vertical differentiation (a different approach)
- Solution of the model is clearly depending on the two dimensions in which firms i and j may differ:

- γ/β : how different the products are $\frac{\gamma}{\beta} \in (0,1)$
- The cost:

$$C_i \neq C_{-i}$$

- Without loss of generality, let's assume that $\beta=1$ so that $\gamma/\beta = \gamma$

$$\beta = 1 ; \text{ then } \frac{\gamma}{\beta} = \gamma \quad \text{with } \gamma \in (0,1)$$

- Also, let us assume that costs for firm j are a fraction of costs for firm i . Thus,

$$C_j = s \cdot C_i ; \quad \text{with } s \in (0,1)$$

3. AN ECONOMIC FRAMEWORK FOR ANALYSING BIOSIMILARS VERSUS BIOLOGICAL PRODUCTS: OUR PROPOSED MODEL

With those assumptions, the solution of the model is now:

$$P_i^* = \frac{\alpha(1-\gamma)\left(1+\frac{\gamma}{2}\right) + \left(\frac{\gamma}{2}s+1\right)C_i}{2\left(1-\frac{\gamma^2}{4}\right)}; \quad P_j^* = \frac{\alpha(1-\gamma)\left(1+\frac{\gamma}{2}\right) + \left(\frac{\gamma}{2}+s\right)C_i}{2\left(1-\frac{\gamma^2}{4}\right)}$$

$$q_i^* = \frac{\alpha(1-\gamma)\frac{\gamma}{2} - \left[1-(1+s)\frac{\gamma}{2}\right]C_i}{2(1-\gamma^2)\left(1-\frac{\gamma^2}{4}\right)}; \quad q_j^* = \frac{\alpha(1-\gamma)\frac{\gamma}{2} - \left[\left(1-\frac{\gamma}{2}\right)s - \frac{\gamma}{2}\right]C_i}{2(1-\gamma^2)\left(1-\frac{\gamma^2}{4}\right)};$$

And difference between P_i and P_j becomes:

$$P_i^* - P_j^* = \frac{\left(1-s\left(1-\frac{\gamma}{2}\right) - \frac{\gamma}{2}\right)C_i}{2\left(1-\frac{\gamma^2}{4}\right)}$$

3. AN ECONOMIC FRAMEWORK FOR ANALYSING BIOSIMILARS VERSUS BIOLOGICAL PRODUCTS: OUR PROPOSED MODEL

- P_i increases with its cost (C_i)
- P_i increases with cost of firm j (parameter s) (THE LOWER THE COST OF BIOSIMILARS, THE LOWER THE PRICE FOR BIOLOGICALS)
- It is more complex to see the interesting effect of differentiation:

$$\frac{\delta P_i^*}{\delta \gamma} = \frac{\left(1 + \frac{s\gamma}{2}\right) c_i + \left(1 + \frac{\gamma}{2}\right) \alpha(1-\gamma)}{2\left(1 - \frac{\gamma^2}{4}\right)} \left[\frac{\gamma \left(\left(1 + \frac{s\gamma}{2}\right) c_i + \left(1 + \frac{\gamma}{2}\right) \alpha(1-\gamma) \right)}{4\left(1 - \frac{\gamma^2}{4}\right)^2} + \frac{\frac{s \cdot c_i}{2} + \frac{1}{2} \alpha(1-\gamma)}{2\left(1 - \frac{\gamma^2}{4}\right)} \right] > 0$$

- **So, a lower differentiation increases both Prices!?!?**
- However, as expected and for low large values of s and γ , difference between P_i and P_j decreases.

$$\frac{\delta (P_i^* - P_j^*)}{\delta \gamma} = \frac{\left(1 - \frac{\gamma}{2}\right) (1-s) c_i}{2\left(1 - \frac{\gamma^2}{4}\right)} \left[\frac{\gamma \left(1 - \frac{\gamma}{2}\right) (1-s) c_i}{4\left(1 - \frac{\gamma^2}{4}\right)^2} - \frac{\frac{1}{2} c_i}{2\left(1 - \frac{\gamma^2}{4}\right)} \right] < 0$$

3. AN ECONOMIC FRAMEWORK FOR ANALYSING BIOSIMILARS VERSUS BIOLOGICAL PRODUCTS: OUR PROPOSED MODEL

- A final scenario analyzed corresponds to the realistic case in which biosimilar cost is a function of degree of differentiation.
- Interpretation: the lower the differentiation (the closest to the biological product), the more expensive to produce and market access.

- In the model, is included as follows:

$$s = f(\gamma) = \theta \cdot \gamma; \quad c_j = f(\gamma) \cdot c_i = \theta \cdot \gamma \cdot c_i$$

being $s, \gamma, \theta \in (0, 1)$

- The simplest case would be when $\theta=1$ and as a consequence, $\gamma=s$

3. AN ECONOMIC FRAMEWORK FOR ANALYSING BIOSIMILARS VERSUS BILOGICAL PRODUCTS: OUR PROPOSED MODEL

The new solution of the model is:

$$P_i^* = \frac{\alpha(1-\gamma)\left(1+\frac{\gamma}{2}\right) + \left(\frac{\theta\gamma^2}{2} + 1\right) c_i}{2\left(1-\frac{\gamma^2}{4}\right)}; \quad P_j^* = \frac{\alpha(1-\gamma)\left(1+\frac{\gamma}{2}\right) + \left(\frac{1}{2} + \theta\right) \gamma c_i}{2\left(1-\frac{\gamma^2}{4}\right)}$$

$$q_i^* = \frac{\alpha(1-\gamma)\frac{\gamma}{2} - \left[1 - (1+\theta\gamma)\frac{\gamma}{2}\right] c_i}{2(1-\gamma^2)\left(1-\frac{\gamma^2}{4}\right)}; \quad q_j^* = \frac{\alpha(1-\gamma)\frac{\gamma}{2} - \left[\left(1-\frac{\gamma}{2}\right)\theta\gamma - \frac{\gamma}{2}\right] c_i}{2(1-\gamma^2)\left(1-\frac{\gamma^2}{4}\right)};$$

And difference between P_i and P_j becomes:

$$P_i^* - P_j^* = \frac{\left(\frac{\theta}{2}\gamma^2 - \left(\frac{1}{2} + \theta\right)\gamma + 1\right) c_i}{2\left(1-\frac{\gamma^2}{4}\right)} > 0 \text{ for } \theta \leq 1 \text{ and } \gamma \leq 1$$

3. AN ECONOMIC FRAMEWORK FOR ANALYSING BIOSIMILARS VERSUS BIOLOGICAL PRODUCTS: OUR PROPOSED MODEL

- P_i increases with its cost (C_i)
- P_i increases with the cost of firm j (parameter θ) (THE LOWER THE COST OF BIOSIMILARS, THE LOWER THE PRICE FOR BIOLOGICALS)
- In order to look at differentiation effect, we derivate and obtain:

$$\frac{\delta P_i^*}{\delta \gamma} = \frac{\left(1 + \frac{\gamma^2 \theta}{2}\right) c_i + \left(1 + \frac{\gamma}{2}\right) \alpha(1-\gamma)}{2\left(1 - \frac{\gamma^2}{4}\right)} \left[\frac{\gamma \left(\left(1 + \frac{\gamma^2 \theta}{2}\right) c_i + \left(1 + \frac{\gamma}{2}\right) \alpha(1-\gamma) \right)}{4\left(1 - \frac{\gamma^2}{4}\right)^2} + \frac{\frac{\theta \cdot \gamma \cdot c_i}{2} + \frac{1}{2} \alpha(1-\gamma)}{2\left(1 - \frac{\gamma^2}{4}\right)} \right] > 0$$

- **Again, and opposite to expected, lower differentiation increases both Prices!?!?**

- However, as expected and for low large values of s and γ , difference between P_i and P_j decreases.

$$\frac{\delta(P_i^* - P_j^*)}{\delta \gamma} = \frac{\left(-\frac{1}{2} - \theta + \theta \gamma\right) c_i}{2\left(1 - \frac{\gamma^2}{4}\right)} + \left[\frac{\gamma \left(1 - \frac{\gamma}{2}\right) (1-s) c_i}{4\left(1 - \frac{\gamma^2}{4}\right)^2} - \frac{\frac{1}{2} c_i}{2\left(1 - \frac{\gamma^2}{4}\right)} \right] < 0$$

4. DISCUSSION AND CONCLUSIONS

- Biologics add value to health systems and health marginal efficiency gains but their cost is expensive
- Expiration of patents on these products has created a possibility for biosimilars market that some people would see as "new generics market" but they are small (0.5% of total) and heterogeneous depending on country
- Can we encourage biosimilars market to reduce pharmaceutical expenditure? Problems:
 - Generics are exact copies. Biosimilars are similar but not identical (no interchangeability property is fulfilled)
 - Biosimilar production costs are greater than generic ones due to lower number of companies expected
 - EMA or FDA approval even if there will be fast, it remains more expensive (safety and efficacy) than in the case of generics
 - Using International Non property Name (INN) is more complicated than with generics and is still fighting "legal actions"

4. DISCUSSION AND CONCLUSIONS

■ Factors to consider in future models:

Dynamic modelling&sensitivity analysis: Grabowski et al. model and our proposed theoretical framework are “comparative static” models. They do not take into account interaction between competitors. We will consider product attributes as dependent in part upon firm strategy

- Evolution and learning regulation
- Acceptability of biosimilars by clinicians
- Track pricing and reimbursement policies
- INCENTIVES both demand and supply side: Who buys? At what price? (hospital, doctor, patient, central purchasing?) What influences the decision of a clinical (their relationship with the industry and clinical trials? or the compliance ... and the idea of keeping fixed chronic patients treatments)? Marketing need to make the products will be acknowledged