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Reference Pricing System and Competition: Case Study from Portugal

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Aim To characterize the patterns of competition for a sample of drugs in the Portuguese pharmaceutical market before (January 2002-March 2003) and after (April 2003-June 2003) the introduction of the reference pricing system (RPS).

Methods We performed a descriptive, retrospective, longitudinal analysis, with monthly observations from January 2002 until June 2003 of 15 homogeneous groups. The groups represented the upper limit of public pharmaceutical expenditure in the RPS segment in 2003 (n = 270). Measures of competition were: 1) number of presentations; 2) prescriptions' concentration in the generic and originator (brand) segments, using Herfindahl-Hirschman Index (HHI); and 3) dominant positions of market leader in the homogeneous group. A correlation analysis between the number of presentations, the HHI, and the dominant position of the market leader was performed using Pearson coefficient of correlation.

Results The structure of the market changed with the introduction of RPS. We found an increasing number of generic presentations (from 4 ± 3 to 7 ± 4; mean ± standard deviation) and a decrease in the HHI for the generics market segment (from 0.7 ± 0.2 to 0.6 ± 0.3). There was a negative correlation between those variables that increased after the introduction of RPS (from -0.6 to -0.8). The HHI for brands and the dominant positions remained unchanged.

Conclusion After the implementation of RPS, the increased competition was mainly driven by economic and social agents in the generics market segment but not in the brands market segment.

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Reference Pricing System (RPS) is a drug reimbursement system in which the third payer defines the price that they will support for a group of interchangeable drugs (1). The difference between the public price and the reimbursed price will be borne by the patients. The system was introduced in March 2003. It intends to foster generic competition as a way to promote rational containment of increasing pharmaceutical expenditure. In fact, according to Organisation for Economic Co-operation and Development (OECD) data, pharmaceutical expenditure in Portugal in the year before the reform was 23.3% of total health expenditure. This value is higher than the average value in OECD countries, which was 17.2% in the same period (2).

In Portugal, pharmaceutical prices are regulated but pharmaceutical companies are free to decrease the prices of drugs. Physicians have the exclusive right to issue prescriptions; however pharmaceutical professionals may consider the possibility of substitution at consumer's request only, if this is explicitly allowed by physicians.

RPS is based on homogeneous groups of drugs. The homogeneous group consists of drugs with the same composition of active substances for which there are marketed generics. The formation of homogeneous group was subject to the principle of exchange of drugs with the same therapeutic effect, ie, drugs that have the same dosage of active substances and similar pack size. The threshold for the state support, the reference price, is defined by the public price of the highest priced generic drug in each homogeneous group. The patient must pay the difference between the reference and public prices, when choosing a drug which costs more than the reference price.

According to Aronson et al (3), this system can induce a rapid decrease in the public retail price of brand name drugs, allowing a control of pharmaceutical expenditure in the short run. Also, copayments can affect the demand through substitution or income effects, "because something that was previously available free of charge now involves a cost to the patient, although the reference drug is still free to the patient" (4).

Schneeweiss et al (5) consider that "this is one of the only drug cost containment policies [...] that saved substantial costs without unintended outcomes on patient health status or use of expensive services." These characteristics of RPS are also highlighted by Maclure (6), when saying that "a cap like maximum allowable costs for one drug class in which prices vary widely, can result on little or no adverse health effects." Increasingly, the practice of substitution of branded drugs by the equivalent generic drugs guarantees the necessary conditions to promote efficiency through lower price drugs, by ensuring the same criteria of quality, safety, and final outcome of the pharmaceutical care.

According to Pammolli (7), the efficiency can be ensured by "generic competition, as an instrument for reducing prices and countervailing exclusivity power granted by patents," and "as for industrial policy and competitiveness issues, an increased market competition in the off-patent segment of the market can contribute to foster efficiency and to design adequate incentives to innovate [...] promoting patterns of industrial reorganization and selection and, moreover, allowing higher prices and returns on investment for innovative products that are still on patent." Also, according to Glissandi et al (8) "most of the main recent structural reforms involve off-patent active substances and aim at increasing competition among equivalent products," as in the RPS together with the pharmacist's right to substitution.

This research was developed in order to explain the impact of RPS on the Portuguese pharmaceutical market structure, and to investigate whether the number of presentations changed after the introduction of RPS, and if the change was observed for both generics and brands segments. The aim of the study was to analyze drug pattern utilization, ie, the prescription concentration in generics and brands segments, and the dominant position of market leader. In fact, when new chemically similar presentations enter the market, the Portuguese law requires that they must have a lower price. So, they can be perceived as potential substitutes by social agents and foster competition by decreasing prescription concentration. If the drugs with lower prices prove to be perfect substitutes, their impact will also decrease the dominant position of the market leader.

METHODS

Data sources

The data were collected monthly between January 2002 and June 2003 for 15 homogeneous groups (n = 270) by the Sub-Regions of Health and presented to National Institute of Pharmacy and Drugs (INFARMED).

Sample

The research was based on consumption data of 10 drugs that are classified according to the Anatomical Therapeutic

Chemical classification system, which is recommended by World Health Organization (9) for international drug utilization studies. They belong to 15 homogeneous groups that represent the upper limit of RPS public pharmaceutical expenditure in 2003. We studied large and medium packages of omeprazole, captopril, lisinopril, and simvastatine (8 groups), two dosages of ranitidine (2 groups), and one package and one dosage of 5 drugs (5 groups).

The sample consisted of the following active substances (Table 1): 1) 2 antiulcer agents – ranitidine (antagonist of H_2 receptors) and omeprazole (proton pump inhibitor); 2) 1 platelet aggregation inhibitor – ticlopidine; 3) 4 antihypertensive agents that inhibit angiotensin converting enzyme – captopril, enalapril, lisinopril, enalapril/hydrochlorothiazide; 4) 1 lipid modifying agent – simvastatin (hydroximetylglutaril coenzyme A reductase inhibitor); 5) 1 antimicrobial agent – ciprofloxacin (fluoroquinolone); and 6) 1 antidepressant agent – fluoxetine (selective serotonine reuptake inhibitor).

Variables

The study was divided in 2 phases: before (January 2002-March 2003) and after the introduction of RPS (April 2003-June 2003). The following variables were considered: 1) the number of competing presentations in the homogeneous group; 2) concentration of prescriptions, calculated using the Herfindahl-Hirschman Index (HHI) for the 15 homogeneous group in relation to the prescription of brand name drugs and in terms of generic drugs; and 3) the dominant positions of the market leader in the homogeneous group.

Methods to measure competition

Generic competition, and subsequent price decreases, could be improved by increasing the number of presentations on the market, especially when this market segment is not well developed. In Portugal, in 2002 the share of generics was only 5.59% of the total value of the pharmaceutical market (10).

Also, the potential increase in copayment may stimulate the segment of price-sensitive consumers, and thus serve as an incentive for generics market access and consumption. Ekelund (11) and Moreno-Torres et al (12) showed, however, that RPS can restrain the entry of new generics presentations. There is no evidence on this effect in the Portuguese market.

The necessary conditions to allow efficient competition have been established in the industry, both from the theoretical and empirical perspective (13). The authors proposed that at least one of the following situations should be in place: 1) there should be at least 5 comparable competitors in the market; 2) none of the competitors should occupy a dominant position, which means that the mar-

TABLE 1. Characteristics of the sample according to Anatomic Therapeutic Chemical Classification, homogenous group, dosage, pack and reference price (RP)

ATC Classification*		Homogenous group	Active substance	Dosage (mg)	Pack units)	RP (€)
A02BA	antagonists of H_2 receptors	124	Ranitidine	150	40-89	0.49
		126	Ranitidine	300	40-89	1.13
A02BC	proton pump inhibitors	120	Omeprazole	20	20-39	1.15
		121	Omeprazole	20	40-89	1.14
B01AC	platelet aggregation inhibitors	136	Ticlopidine	250	40-89	0.45
C09AA	angiotensin converting enzyme inhibitors	31	Captopril	25	40-89	0.23
		32	Captopril	25	>89	0.22
		68	Enalapril	20	40-89	0.81
		95	Lisinopril	20	40-89	0.43
		96	Lisinopril	20	>89	0.39
C09BA	angiotensin converting enzyme inhibitors and diuretics combination	64	Enalapril: Hydrochlorothiazide	20:12.5	40-89	0.41
C10AA	HMGCoA reductase inhibitors	127	Simvastatin	20	20-39	1.01
		128	Simvastatin	20	40-89	0.80
J01MA	fluoroquinolones	52	Ciprofloxacin	500	>13	1.30
N06AB	selective serotonine reuptake inhibitors	76	Fluoxetine	20	40-89	0.59

*Anatomic Therapeutic Chemical Classification (9).

ket leader should not possess a market share above 40% without the existence of any competitive products with the same characteristics; and 3) the admission into the different segments of the market should be free.

Another approach to measure competition is presented by Besanko et al (14) who consider that the intensity of competition depends on the market structure as measured by the HHI. This index equals the sum of the squared market shares of all the drugs in the market. When HHI is below 0.2 there is a perfect competition, between 0.2 and 0.6 an oligopoly emerges, and if it is 0.6 or above a monopoly is in place.

The dominant position of market leader is another variable that we used to measure competition; it is calculated as the market share of the most prescribed drug in their group of active substances (13).

Statistical analysis

The adopted quantitative methodology consists of a longitudinal retrospective and descriptive analysis, calculating averages of the variables before and after the introduction of RPS. The structure of competition was analyzed in 2 dimensions: the behavior of economic agents through the number of presentations on the market, and the intervention of social agents, medical and pharmaceutical doctors, through HHI and the dominant position of the market leader.

Pearson correlation coefficient was also calculated before and after the introduction of RPS. This allows the determination of the association between the number of presentations in the market, the HHI, and the dominant position of the market leader.

Data were analyzed using the SPSS, version 14 (SPSS Inc., Chicago, IL, USA). Statistical analysis was performed using Wilcoxon test for comparison of averages. For correlation study, we used t-test to compare the averages in the 2 groups. A *P* value <0.05 was considered statistically significant.

RESULTS

Number of competing presentations

The number of competing presentations increased with the introduction of RPS from an average (±standard deviation) of 10±5 before the introduction of RPS to 13±6 after the introduction of RPS (Table 2). However, the market did not achieve the conditions of perfect competition, ie, there were not more than 5 competing presentations for all homogeneous groups (Table 3). There were 2±0 presentations for homogeneous group lisinopril 20 mg (large pack) and 27±2 presentations for homogeneous group simvastatin 20 mg (medium pack). Indeed, homogeneous group lisinopril 20 mg (large pack) was the only one that retained a monopoly profile. Homogeneous group captopril 25 mg (large pack) and homogeneous group simvastatin 20 mg (large pack) had 5±4 and 5±3 competitors on the market before the introduction of RPS, which increased to 13±1 and 14±2 after the introduction of RPS, respectively. Homogeneous group lisinopril 20 mg (medium pack) had 6±0 competing presentations before the introduction of RPS, which decreased to 5±1 after the introduction of RPS.

Even if these values do not imply the absence of competition, they are borderline values and can be considered together with other factors in the evaluation of the nature of competition in this segment, since any modification of this parameter can yield a new framework of efficiency achievement.

Omeprazole (medium pack) had 19±3 presentations, which was the greatest number of presentations before

TABLE 2. Average values (±standard deviation) of the variables under research, before and after the introduction of the reference pricing system (RPS)

Variables	Before the introduction of RPS	N	After the introduction of RPS	N	*P* (t-test)
Total number of presentations	9.98±5.17	225	13.3±6.43	45	0.000
Number of generic presentations	4.00±3.09	225	6.93±4.33	45	0.000
Number of brand presentations	8.81±3.78	225	9.67±3.89	45	0.170
Herfindahl Hirschman Index (HHI)*	0.32±0.23	212	0.29±0.24	45	0.370
HHI generics	0.68±0.23	194	0.56±0.26	45	0.002
HHI brands	0.39±0.26	211	0.38±0.29	44	0.728
Dominant position market leader†	0.42±0.25	208	0.38±0.22	45	0.376

*According to Besanko et al (14).
†According to Puig Junoy (13).

TABLE 3. Number of presentations in the market, before and after the introduction of the reference pricing system (RPS), regarding each homogeneous group

	Number of presentations				
Homogeneous groups	Before the introduction of RPS	No.	After the introduction of RPS	No.	*P* (Wilcoxon test)
Captopril 25 mg (medium pack)	12 ± 0	15	7 ± 5	3	0.090
Captopril 25 mg (large pack)	5 ± 4	15	13 ± 1	3	0.051
Ciprofloxacin 500 mg (large pack)	15 ± 1	15	17 ± 1	3	0.051
Enalapril:hydrochlorothiazide 20 mg:12.5 mg (medium pack)	8 ± 1	15	8 ± 1	3	–
Enalapril 20 mg (medium pack)	11 ± 1	15	11 ± 2	3	0.138
Fluoxetine 20 mg (medium pack)	12 ± 2	15	15 ± 1	3	0.051
Lisinopril 20 mg (medium pack)	6 ± 0	15	5 ± 1	3	0.051
Lisinopril 20 mg (large pack)	1 ± 1	15	2 ± 0	3	0.042
Omeprazole 20 mg (medium pack)	19 ± 3	15	22 ± 1	3	0.051
Omeprazole 20 mg (large pack)	8 ± 3	15	15 ± 1	3	0.051
Ranitidine 150 mg (large pack)	17 ± 0	15	18 ± 0	3	0.051
Ranitidine 300 mg (large pack)		15	12 ± 1	3	0.042
Simvastatin 20 mg (medium pack)	11 ± 5	15	27 ± 2	3	0.055
Simvastatin 20 mg (large pack)	5 ± 3	15	14 ± 2	3	0.051
Ticlopidine 250 mg (large pack)	11 ± 2	15	14 ± 0	3	0.042

the introduction of RPS, while lisinopril 20 mg (large pack) had 1 ± 1 presentation, which was the lowest number of presentations. After the introduction of RPS, the simvastatin 20 mg (medium pack) had the greatest number of 27 ± 2 presentations, and lisinopril 20 mg (large pack) had the lowest number of 2 ± 0 presentations. The only exceptions were enalapril/hydrochlorothiazide and enalapril 20 mg (medium pack), which showed no significant difference in the average number of presentations before and after the implementation of RPS.

Prescription concentration

After the introduction of RPS, the HHI decreased in all homogeneous groups (Table 4), which means that there was an increase in competition. However, the increase was not significant, probably because the number of observations after the introduction of RPS was too small.

However, we can observe 2 different competition profiles in the sample:

a) in the homogeneous groups where HHI was lower after the introduction of RPS, but remained at the same level of competition, ie an oligopoly according to the categories previously defined by Besanko et al (14) – enalapril/hydrochlorothiazide ($HHI_{pre\ SPR} = 0.49 \pm 0.04$; $HHI_{post\ SPR} = 0.41 \pm 0.00$), fluoxetine ($HHI_{pre\ SPR} = 0.14 \pm 0.01$; $HHI_{post\ SPR} = 0.12 \pm 0.00$), and ticlopidine ($HHI_{pre\ SPR} = 0.19 \pm 0.03$; $HHI_{post\ SPR} = 0.15 \pm 0.00$).

b) in the homogeneous group where HHI decreased to levels that are classified as a new kind of competition profile, ie, from a monopoly to an oligopoly or even the achievement of a competitive structure, which was the case in homogeneous groups of omeprazole 20 mg (large pack), simvastatin 20 mg (medium pack), and simvastatin 20 mg (large pack). In the homogeneous group of omeprazole, the HHI was 0.23 ± 0.08 before the introduction of RPS and dropped to 0.11 ± 0.00 after the introduction of RPS, which means that the oligopoly changed to a perfect competition. In the homogeneous group of simvastatin, 2 types of changes occurred: before the introduction of RPS monopoly changed to an oligopoly for the 20 mg (medium pack) and to a perfect competition for the 20 mg (large pack). The HHI was 0.71 ± 0.17 (medium pack) and 0.60 ± 0.34 (large pack) before the introduction of RPS, and 0.41 ± 0.02 (medium pack) and 0.15 ± 0.03 (large pack) after the introduction of RPS.

Concentration of prescriptions – generics segment

The average HHI for generics decreased after the implementation of RPS, for all but one homogeneous group (Table 5). The values varied from 0.68 ± 0.23 to 0.56 ± 0.26. Before the introduction of RPS, generics segment had a higher concentration of prescriptions, mainly above 0.6, with the exception of 3 homogeneous groups. After the introduction of RPS, HHI decreased to values mainly between 0.2 and 0.6. Competition gains were

achieved, but not a highly competitive environment, when HHI dropped below 0.2. Tthe values obtained were not significant, probably because the number of observations after the introduction of RPS was too small.

In the generic drugs segment, the market before the introduction of RPS was highly concentrated, with HHI between 0.91 ± 0.09 for the homogeneous group of ticlopidine 250 mg (large pack) and 0.37 ± 0.05 for the homogeneous group of fluoxetine 20 mg (medium pack), which means that there was a competitive deficit in this segment. For the homogeneous group of simvastatin 20 mg (medium pack), which achieved the greatest number of presentations on the market after the introduction of RPS, the HHI was 0.85 ± 0.21. After the introduction of RPS, the HHI decreased to 0.33 ± 0.07. In this homogeneous group, the nature of competition turned from a monopoly to oligopoly.

For most of the homogeneous groups, the HHI decreased between the two periods with the exception of capto-

TABLE 4. Herfindahl Hirschman Index (HHI) before and after the introduction of the reference pricing system (RPS), by homogeneous group

	Herfindahl Hirschman Index				
Homogeneous groups	Before the introduction of RPS	No.	After the introduction of RPS	No.	*P* (Wilcoxon test)
Captopril 25 mg (medium pack)	0.38 ± 0.06	15	0.65 ± 0.27	3	0.054
Captopril 25 mg (large pack)	0.33 ± 0.13	11	0.22 ± 0.04	3	0.054
Ciprofloxacin 500 mg (large pack)	0.12 ± 0.01	15	0.11 ± 0.00	3	0.054
Enalapril:hydrochlorothiazide 20 mg:12.5 mg (medium pack)	0.49 ± 0.04	15	0.41 ± 0.00	3	0.054
Enalapril 20 mg (medium pack)	0.29 ± 0.06	15	0.23 ± 0.02	3	0.054
Fluoxetine 20 mg (medium pack)	0.14 ± 0.01	15	0.12 ± 0.00	3	0.054
Lisinopril 20 mg (medium pack)	0.35 ± 0.02	15	0.34 ± 0.00	3	0.054
Lisinopril 20 mg (large pack)	0.85 ± 0.16	6	0.93 ± 0.00	3	0.054
Omeprazole 20 mg (medium pack)	0.15 ± 0.02	15	0.17 ± 0.01	3	0.054
Omeprazole 20 mg (large pack)	0.23 ± 0.08	15	0.11 ± 0.00	3	0.051
Ranitidine 150 mg (large pack)	0.12 ± 0.01	15	0.12 ± 0.00	3	0.142
Ranitidine 300 mg (large pack)	0.17 ± 0.01	15	0.17 ± 0.00	3	0.054
Simvastatin 20 mg (medium pack)	0.71 ± 0.17	15	0.41 ± 0.02	3	0.054
Simvastatin 20 mg (large pack)	0.60 ± 0.34	15	0.15 ± 0.03	3	0.054
Ticlopidine 250 mg (large pack)	0.19 ± 0.03	15	0.15 ± 0.00	3	0.054

TABLE 5. Herfindahl Hirschman Index (HHI) for generic drugs before and after the introduction of the reference pricing system (RPS), in each homogeneous group

	Herfindahl Hirschman Index (generics)				
Homogeneous groups	Before the introduction of RPS	No.	After the introduction of RPS	No.	*P* (Wilcoxon test)
Captopril 25 mg (medium pack)	0.69 ± 0.16	15	0.96 ± 0.01	3	0.054
Captopril 25 mg (large pack)	0.69 ± 0.17	11	0.61 ± 0.00	3	0.142
Ciprofloxacin 500 mg (large pack)	0.52 ± 0.02	15	0.36 ± 0.03	3	0.054
Enalapril: Hydrochlorothiazide 20 mg: 12.5 mg (medium pack)	0.75 ± 0.11	15	0.74 ± 0.02	3	0.500
Enalapril 20 mg (medium pack)	0.42 ± 0.08	15	0.52 ± 0.11	3	0.500
Fluoxetine 20 mg (medium pack)	0.37 ± 0.05	15	0.26 ± 0.00	3	0.054
Lisinopril 20 mg (medium pack)	0.97 ± 0.11	15	0.90 ± 0.17	3	0.158
Lisinopril 20 mg (large pack)	1.00 ± 0.00	6	1.00 ± 0.00	3	–
Omeprazole 20 mg (medium pack)	0.50 ± 0.03	15	0.39 ± 0.02	3	0.054
Omeprazole 20 mg (large pack)	0.65 ± 0.33	9	0.22 ± 0.00	3	0.054
Ranitidine 150 mg (large pack)	0.60 ± 0.21	15	0.43 ± 0.00	3	0.054
Ranitidine 300 mg (large pack)	0.81 ± 0.12	15	0.63 ± 0.01	3	0.054
Simvastatin 20 mg (medium pack)	0.85 ± 0.21	12	0.33 ± 0.07	3	0.054
Simvastatin 20 mg (large pack)	0.80 ± 0.27	6	0.34 ± 0.06	3	0.054
Ticlopidine 250 mg (large pack)	0.91 ± 0.09	15	0.70 ± 0.06	3	0.054

pril 25 mg (medium pack) because it was delisted and replaced by a large pack.

Although there was a change from monopoly to oligopoly in most homogeneous groups, due to the introduction of RPS, perfect competition conditions were not achieved in any of the homogeneous groups.

Prescription concentration – brands segment

In the brands segment, the HHI decreased in 6 homogeneous groups and increased in 4 homogeneous groups (Table 6). Again the values were not significant, probably because the number of observations after the introduction of RPS was too small.

The average HHI in the brands segment remained stable after the introduction of RPS as opposed to the period before the introduction of RPS. Regarding the individual homogeneous groups, there were competition gains after the introduction of RPS, where 5 homogeneous groups had HHI below 0.2, compared with 3 homogeneous groups in the period before the introduction of RPS. Also the HHI values were lower than the values observed for generics segment, both before and after the introduction of RPS.

Before the introduction of RPS, the HHI in the brands segment had the lowest value of 0.14 ± 0.01 for the homogeneous group of ciprofloxacin 500 mg (large pack), and the highest one of 0.61 ± 0.02 for homogeneous group enalapril/hydrochlorothiazide 20 mg:12.5 mg (medium pack). These values were lower than the ones obtained for the generics segment in the same period, which means that the level of competition was higher in the branded drugs segment. A decrease in this variable was observed in the period after the introduction of RPS for 6 homogeneous groups. The lowest one of 0.14 ± 0.00 was observed in the homogeneous group of omeprazole 20 mg (medium pack), and the highest one of 0.35 ± 0.00 in the homogeneous group of lisinopril 20 mg (medium pack). For the remaining homogeneous groups, the HHI increased; namely for captopril 25 mg (medium pack), ciprofloxacin 500 mg (large pack), enalapril/hydrochlorothiazide 20 mg:12.5 mg (medium pack), and ranitidine 150 mg (large pack).

A broad approach to this indicator in the branded drugs segment (Table 6) allows the identification of those homogeneous groups in which the HHI decreased: fluoxetine 20 mg (medium pack), lisinopril 20 mg (medium pack), omeprazole 20 mg (large pack), simvastatin 20 mg (large pack), and ticlopidine 250 mg (large pack). This shows that the introduction of the RPS probably raised the levels of competition. In spite the decrease in HHI, competitiveness was favored in only 4 homogeneous groups: fluoxetine, omeprazole, simvastatin, and ticlopidine. The homogeneous group of captopril 25 mg (medium pack) was the only one in which a high concentration was observed after the introduction of RPS, changing from an oligopoly to monopoly.

TABLE 6. Herfindahl Hirschman Index (HHI) for branded drugs before and after the introduction of the reference pricing system (RPS), in each homogeneous group

	Herfindahl Hirschman Index (brands)				
Homogeneous groups	Before the introduction of RPS	No.	After the introduction of RPS	No.	*P* (Wilcoxon test)
Captopril 25 mg (medium pack)	0.53 ± 0.15	15	0.94 ± 0.08	2	0.090
Captopril 25 mg (large pack)	0.61 ± 0.34	11	0.27 ± 0.12	3	0.054
Ciprofloxacin 500 mg (large pack)	0.14 ± 0.01	15	0.17 ± 0.00	3	0.054
Enalapril:hydrochlorothiazide 20 mg:12.5 mg (medium pack)	0.61 ± 0.02	15	0.63 ± 0.00	3	0.054
Enalapril 20 mg (medium pack)	0.39 ± 0.01	15	0.38 ± 0.01	3	0.054
Fluoxetine 20 mg (medium pack)	0.22 ± 0.02	15	0.19 ± 0.00	3	0.054
Lisinopril 20 mg (medium pack)	0.38 ± 0.01	15	0.35 ± 0.00	3	0.054
Lisinopril 20 mg (large pack)	1.00 ± 0.00	5	1.00 ± 0.00	3	–
Omeprazole 20 mg (medium pack)	0.17 ± 0.01	15	0.14 ± 0.00	3	0.054
Omeprazole 20 mg (large pack)	0.26 ± 0.05	15	0.19 ± 0.00	3	0.054
Ranitidine 150 mg (large pack)	0.14 ± 0.00	15	0.15 ± 0.00	3	0.054
Ranitidine 300 mg (large pack)	0.22 ± 0.01	15	0.22 ± 0.00	3	0.054
Simvastatin 20 mg (medium pack)	0.86 ± 0.06	15	0.80 ± 0.03	3	0.054
Simvastatin 20 mg (large pack)	0.61 ± 0.32	15	0.21 ± 0.01	3	0.054
Ticlopidine 250 mg (large pack)	0.21 ± 0.02	15	0.19 ± 0.00	3	0.054

Dominant position of the market leader

The pattern of dominant positions of market leaders changed after the introduction of RPS (Table 7), but the difference was not significant. For 3 homogeneous groups, the dominant position of the market leader increased, but the highest value observed was 0.35, well below the 0.4 value of a monopolistic market (Table 2).

In the other 8 homogeneous groups, where the value decreased; we identified 3 different profiles:

a) the dominant position remained higher than 0.4 in enalapril/hydrochlorothiazide (from 0.68 ± 0.04 to 0.59 ± 0.00), enalapril (from 0.49 ± 0.07 to 0.39 ± 0.02), and lisinopril 20 mg (medium pack) (from 0.50 ± 0.02 to 0.47 ± 0.01);

b) the dominant position decreased from 0.64 ± 0.35 to 0.26 ± 0.07 for simvastatin 20 mg (large pack);

c) the dominant position remained below 0.4 for ranitidine 150 mg and ticlopidine 250 mg.

We can assume that competition gains were obtained only in the case of the homogeneous group of simvastatin 20 mg (large pack).

Correlation analysis

There was a significant negative correlation between the total number of competing presentations and HHI (from -0.65 to -0.56 after the introduction of RPS); we can see the same situation in the case of the total number of compet-

TABLE 7. Dominant position of market leader before and after the introduction of the reference pricing system (RPS) in each homogeneous group

	Dominant position (active substance)				
Homogeneous groups	Before the introduction of RPS	No.	After the introduction of RPS	No.	*P* (Wilcoxon test)
Captopril 25 mg (medium pack)	0.58 ± 0.04	15	0.52 ± 0.08	3	0.142
Captopril 25 mg (large pack)	0.36 ± 0.14	9	0.33 ± 0.15	3	0.500
Ciprofloxacin 500 mg (large pack)	0.17 ± 0.03	15	0.12 ± 0.00	3	0.054
Enalapril:hydrochlorothiazide 20 mg:12.5 mg (medium pack)	0.68 ± 0.04	15	0.59 ± 0.00	3	0.054
Enalapril 20 mg (medium pack)	0.49 ± 0.07	15	0.39 ± 0.02	3	0.054
Fluoxetine 20 mg (medium pack)	0.18 ± 0.03	15	0.23 ± 0.01	3	0.054
Lisinopril 20 mg (medium pack)	0.50 ± 0.02	15	0.47 ± 0.01	3	0.054
Lisinopril 20 mg (large pack)	0.96 ± 0.00	4	0.96 ± 0.00	3	–
Omeprazole 20 mg (medium pack)	0.17 ± 0.04	15	0.35 ± 0.02	3	0.054
Omeprazole 20 mg (large pack)	0.30 ± 0.10	15	0.19 ± 0.04	3	0.054
Ranitidine 150 mg (large pack)	0.21 ± 0.02	15	0.17 ± 0.00	3	0.054
Ranitidine 300 mg (large pack)	0.24 ± 0.04	15	0.28 ± 0.00	3	0.054
Simvastatin 20 mg (medium pack)	0.82 ± 0.11	15	0.61 ± 0.02	3	0.054
Simvastatin 20 mg (large pack)	0.64 ± 0.35	15	0.26 ± 0.07	3	0.054
Ticlopidine 250 mg (large pack)	0.32 ± 0.04	15	0.25 ± 0.00	3	0.054

TABLE 8. Pearson coefficients correlation between the number of presentations. HHI, and the dominant position of market leader, before and after the introduction of the reference pricing system (RPS)*

Variables	Before the introduction of RPS	No.	After the introduction of RPS	No.
Number of total presentations:				
HHI	-0.65†	212	-0.56†	45
DP market leader	-0.39†	208	-0.40†	45
Number of generic presentations:				
HHI generics	-0.56†	225	-0.76†	45
HHI brands	-0.16‡	211	-0.146	44
DP market leader	-0.32†	208	-0.21	45

*Abbreviations: HHI – Herfindahl Hirschman Index; DP – dominant position; RPS – Reference pricing system; N – number of observations.
†$P < 0.01$.
‡$P < 0.05$.

ing presentations and the dominant position of the market leader (from -0.39 to -0.40 after the introduction of RPS) (Table 8). A significant negative association was also obtained for the total number of generic presentations and HHI in the generics segment (from -0.56 to -0.76 after the introduction of RPS).

So, we also conclude that when an increase in the number of competitors in the market is observed, the prescription concentration decreases. However, a different conclusion was obtained regarding the association between the number of generics presentations and HHI in the brands segment and the dominant position of the market leader. None of the variables were significantly correlated with the number of generic presentations after the introduction of RPS.

DISCUSSION

We observed that after the introduction of the RPS, there was a new market structure, compatible with competition gains:

a) The number of competing presentations increased.

b) The prescription concentration decreased.

c) The dominant position of market leader decreased.

In fact, when the number of presentations increases, there is a potential advantage of pricing decrease, which could promote consumption according to the price elasticity of demand. As a result, the segmentation of drugs demand may contribute to the decrease in prescription concentration, possibly targeting the dominant position of market leader and decreasing it.

We found a significant association between the number of presentations and the prescription concentration before and after the introduction of RPS, and also between the number of presentations and the dominant position of market leader. Considering Pearson coefficient, we found that after the introduction of RPS the association with the number of presentations remained negative for both HHI (from -0.65 to -0.56) and dominant position of market leader (from -0.39 to -0.40), but there was a change in the magnitude of association. There was a decrease in HHI, but also an increase in the dominant position of market leader.

So, the number of presentations – that increased after the introduction of RPS – seems to be the driving force of competition on the Portuguese pharmaceutical market. In fact, the results suggest that after the introduction of RPS, the prescribers changed their behavior, namely prescribing other drugs than market leaders in the homogeneous group, which usually are brands.

Regarding the association between the number of generics and the dominant position of market leader, as well as HHI for generics and HHI for brands, we found a new association profile. In fact, the association between the number of generics and the dominant position of market leader, before and after the introduction of RPS, decreased from -0.32 to -0.21. Compared with the results obtained for the association between the number of total presentations and the dominant position of market leader, it seems that generics had a lower impact on the dominant position of market leader than the total number of presentations after the introduction of RPS. These values may suggest demand segmentation. Even in the presence of generics, as alternatives with lower prices, there is still a segment of consumers that prefer brand drugs.

Regarding the association between the number of generics and the HHI for generics, there was an increase from -0.56 to -0.76, however in the brands segment the association remained basically unchanged. Here again we found evidence that the impact of generics after the introduction of RPS was higher in the generics market segment than in the brands segment.

Regarding this topic, Pavcnick's found a negative correlation between HHI and the number of generics on the German market: -0.89 for oral antidiabetics and -0.86 for drugs for peptic ulcer disease (15). These values are higher than those obtained for Portuguese market, which could be compatible with a higher impact of RPS in Germany than in Portugal.

The obtained results revealed that both economic and social agents reacted immediately to the RPS. The former induced the entry of generics at the market and the latter changed their prescription patterns.

However, it is not enough to modify the economic or social agents' behaviors to increase competition in the pharmaceutical market, and promote cost containment as the main goal of RPS. It is also necessary that social agents, both prescribers and consumers, are well informed about the benefits of the system, and switch their preferences to the lowest priced drugs, with the same

active substance. This, in turn, could possibly decrease both the HHI and the dominant positions for generics and brands market segments. Only by optimizing the full demand of drugs, considering the opportunities promoted by the economic agents, it will be possible for RPS to foster efficiency through increased competition.

Nonetheless, the present research revealed a competition deficit induced by social agents in the brands segment. Regardless of the fact that HHI values decreased after the introduction of RPS, meaning that drugs from a wide range of presentations were prescribed, they were not low enough to overcome the dominant positions already established before the introduction of the RPS. The association between HHI for brands and the number of generic presentations – according to Pearson coefficient – was negative but weak, and remained basically unchanged after the introduction of RPS. This fact shows that gains in efficiency are only partially obtained in brands segment, even after the entry of new generic presentations to the market.

Considering all the homogeneous groups in the sample, we saw no common pattern. However there are two homogeneous groups that deserve special attention. In the homogeneous group of simvastatin, the major gains regarding competition were achieved. Simvastatin had second pharmaceutical expenditure in the RPS in Portugal after omeprazole. In this case we observed the greatest number of presentations in the sample after the introduction of RPS and the largest decrease in prescription concentration: in one of the homogeneous groups from monopoly to oligopoly and in the other from oligopoly to competition. The largest HHI decrease was observed in the generics segment.

We can summarize that competition gains were achieved in the generics market segment but not in the brands segment.

The RPS reimbursement system intends to promote the consumption of drugs that have the lowest copayment for consumers. This occurs when the drug with the lowest price is preferred in the RPS environment of chemically similar drugs. So, RPS is perceived as an opportunity for economic agents, with new market segments emerging for price-sensitive consumers.

The limited number of observations after the introduction of RPS is a limitation of this study, which we can be overcome with a larger sample. Also, as we deal with time series data, another kind of specific analysis should be performed.

Our data allow the conclusion that not all players act according to the goals of the system. An improvement in the incentives system is needed, tailored to improve the behavior of those agents that could contribute to overcome this constraint.

As mentioned by Segura (1), RPS has a really great potential to control pharmaceutical expenditure but only if it is well integrated in a pharmaceutical policy fostering an active contribution of all the agents in the pharmaceutical chain.

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